



The Femtosecond Blade:

Applications in Corneal Surgery

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Surgeons use a number of devices to create incisions in tissue. These include steel and gem blades, radio frequency, high-pressure waterjet, and electrocautery technologies. Interestingly, while lasers have an established place in the operating room, as cutting tools they play a minor role. Until recently, a major limiting factor was the lack of three-dimensional precision found with each of three types of laser-tissue interaction: photocoagulation, photoablation, and photodisruption.

Photocoagulation employs continuous wave laser light applied to absorbing targets, inducing both primary and secondary thermal effects in surrounding tissues.¹ While they are effective for certain applications such as retinal photocoagulation procedures, these lasers cannot deliver precise tissue cutting. In photoablation, highly absorbed light (ultraviolet, infrared) is used to vaporize tissue. Photoablative and photothermal ablative lasers are used ex-

tensively in corneal refractive surgery and skin resurfacing because the depth of laser penetration can be exquisitely controlled.² However, fine incisions are not easy to achieve due to the relatively large effective spot diameters associated with ablations produced using pulsed lasers.

In contrast to these two mechanisms, photodisruption does not require a specific absorber target, or chromophore. This characteristic makes photodisruption potentially useful for cutting tissues at arbitrary locations in space, as long as the tissue path to the target location is reasonably transparent to the photodisrupting beam. Until recently, surgical use of photodisruptive lasers was limited to those operating in the nanosecond time scale regime, where collateral tissue effects significantly limited potential applications. The recent development of femtosecond laser surgical systems now makes much higher levels of surgical precision possible. The tremendous growth in LASIK refractive surgery has provided the impetus for development of a new type of laser cutting tool: the photodisrupting femtosecond laser "blade."

The ideal scalpel: femtosecond laser photodisruption

The ideal surgical scalpel would offer flexible, programmable incision geometries, micrometer feature sizes (or "kerfs") with minimal collateral tissue damage, and efficient and consistent cut quality. These requirements are successfully addressed by a combination of the precise and determin-

istic nature of femtosecond photodisruption, the selection of a laser wavelength transparent to the target, and a sophisticated, computer-controlled laser scanning and delivery system.

Photodisruption begins with laser-induced optical breakdown (LIOB), when a strongly focused, short-duration laser pulse generates a high-intensity electric field, leading to the formation of a mixture of free electrons and ions that constitutes the plasma state. The optically generated hot plasma expands with supersonic velocity, displacing surrounding tissue. As the plasma expansion slows, the supersonic displacement front propagates through surrounding tissue as a shock wave. The shock wave loses energy and velocity as it propagates, relaxing to an ordinary acoustic wave that dissipates harmlessly. Adiabatic expansion of the plasma occurs on a time scale which is short in comparison to the local thermal diffusion time constant, effectively confining thermal damage.

Ions recombine into various molecular species and the cooling plasma eventually forms a cavitation gas bubble centered on the laser focal volume. This cavitation bubble principally consists of CO_2 , N_2 , and H_2O gases, which diffuse through the tissue after the photodisruption event.

While these features describe photodisruption generally, the specific nature of the process depends on the pulse duration, energy, and focusing geometry of a particular system. Shorter and lower energy pulses and tighter focusing are associated

with faster, smaller, and more deterministic photodisruption features.

Although it has been performed since the early 1980s, ophthalmic photodisruption until fairly recently had been limited to a few intraocular procedures due to the relatively large energies needed to initiate LIOB with nanosecond lasers.³ To use a photodisrupting laser as a scalpel, individual pulses must be placed contiguously to create incisional planes of flat or curved geometry. The large feature sizes and significant collateral tissue effects associated with nanosecond lasers produce a "postage stamp" effect, in which the bits of uncut tissue between adjacent photodisruptions are large enough to produce rough or ragged cuts.⁴ Reducing either the focal spot size or the pulse duration of the laser decreases the threshold energy for LIOB. While small spot size is a requirement, beam delivery systems capable of scanning over large areas or volumes become impractical for f -numbers faster than $f/1$. On the other hand, the laser pulse duration can be decreased by six orders of magnitude from the nanosecond to the femtosecond regime.

The LIOB threshold fluence decreases as the pulse duration falls from nanoseconds to ~ 20 femtoseconds, exhibiting a weak dependence below a few hundred femtoseconds. Consequently, the use of extremely short pulses does not greatly reduce the photodisruption energy. However, the large optical bandwidth and high intensities of pulses shorter than a few hundred femtoseconds make pulse gener-

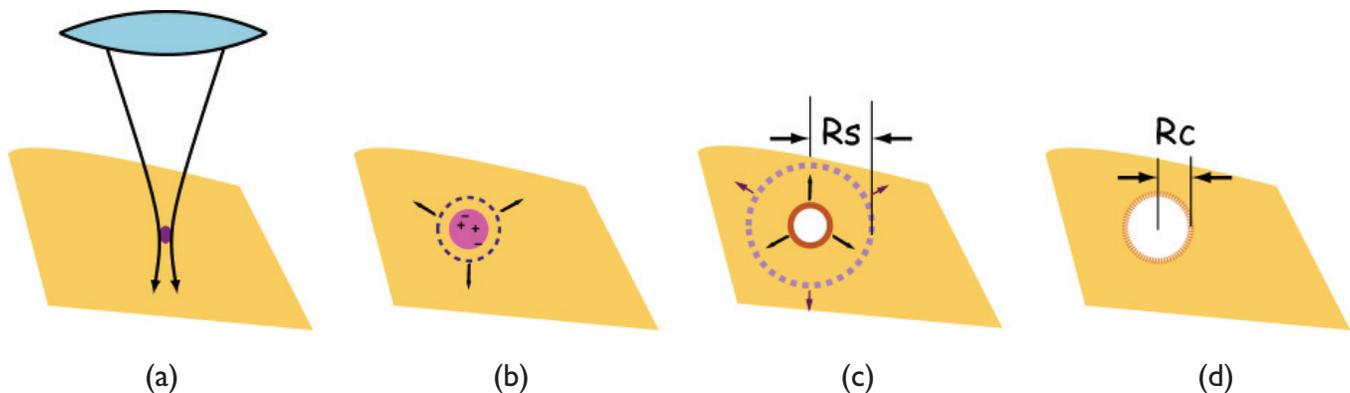


Figure 1. Illustration of photodisruption processes. (a) Focused laser pulse propagates in tissue with intensity designed to initiate optical breakdown only at beam focus. (b) Optical breakdown produces a high-density plasma which expands outward at supersonic speeds with a shock wave front at the leading expansion edge. (c) Rapidly cooling plasma condenses, producing an expanding cavitation gas bubble. (d) Cavitation bubble reaches a maximum size, then collapses, rebounds. Finally, a small static bubble persists for a short time. R_s is the radial distance at which the shock wave propagation velocity has slowed to ordinary acoustic wave speeds, while R_c is the maximum cavitation bubble radius.

ation and amplification difficult at energies useful for surgery, and extremely short pulses experience temporal broadening and other undesirable nonlinear phenomena (self-phase modulation, self-focusing, etc.). Practical pulse durations for surgical photodisruptive lasers therefore fall in the several hundred femtosecond range.⁵⁻⁷

Table 1 summarizes LIOB threshold fluence and the scale of secondary photodisruptive phenomena for several pulse durations. While these phenomena depend in detail on pulse energy, tissue elasticity, laser wavelength and focal geometry, general statements can be made about the dependence secondary photodisruptive effects have on pulse duration, primarily because LIOB threshold fluence falls with pulse width.⁵ A lesser factor is the observed drop in the laser energy absorbed and converted by plasma into secondary photodisruptive phenomena for pulses shorter than a few picoseconds.¹³ The result is that the photodisruptive shock wave size (the radial propagation distance to decay to an acoustic wave) and the cavitation size (maximum bubble radius) for pulses in the hundred femtosecond range are much smaller than those generated by picosecond and nanosecond pulses.

The small amount of energy deposited and the rapid (faster than 1 μs) adiabatic expansion of the plasma prevent significant heat transfer to surrounding tissue. Narrow collateral tissue damage zones have been demonstrated in *ex vivo* tissue experiments with femtosecond photodisruption.^{10,12}

Another important feature of femtosecond photodisruption is the deter-

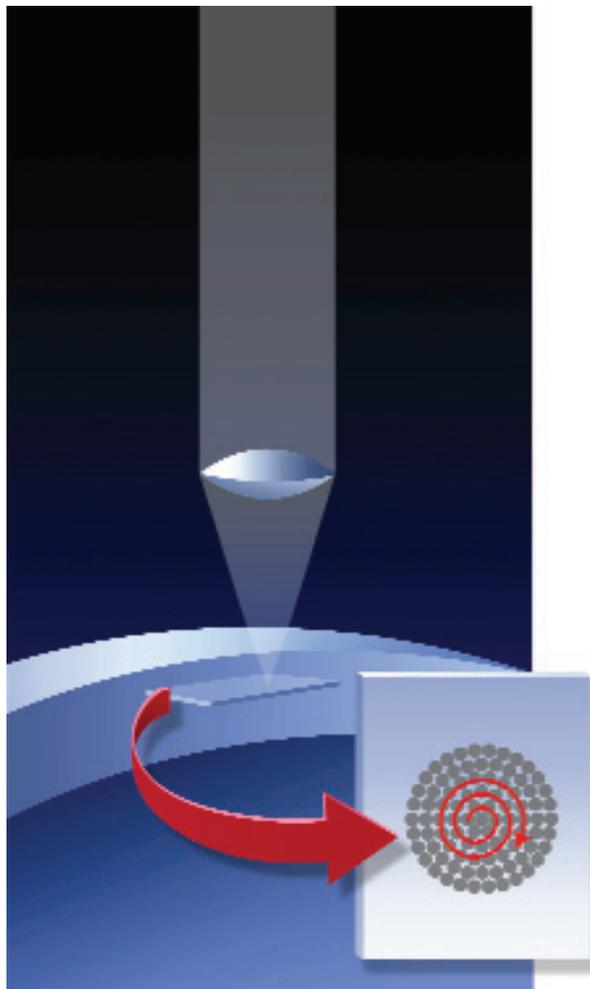


Figure 2. Schematic representation of incision created by a scanned photodisrupting laser pulse train. Though any pattern can be realized, high-speed scanning of a moderately strongly focused beam is best achieved with a scanning geometry that is cylindrically symmetric. The spot-to-spot spacing and individual photodisruption feature size determine the smoothness and quality of the incisional plane.

Table 1. Fluence threshold, shock wave radial extent and cavitation bubble radial extent in cadaver, bovine, and porcine corneas as a function of laser pulse duration.^{8,9,11}

Pulse width	Threshold fluence (J/cm ²)	R _s , radial extent of shock wave (μm)	R _c , radial extent of cavitation (μm)
150 fs	1.5	20	3-15
500 fs	1.6	20	3-15
60 ps	14	200	30-120
10 ns	185	700	300-1200

ministic nature of the optical breakdown process.

In general, optical breakdown proceeds by avalanche ionization, a highly nonlinear process in which the strong electrical field of the laser accelerates charge carriers that ionize other atoms, producing an “avalanche” of ionization. For picosecond or longer pulses, avalanche ionization is initiated by carriers present in the material or introduced into it, with optical breakdown then proceeding in a probabilistic fashion.

Femtosecond pulses are associated with electric fields strong enough to produce seed carriers through multiphoton and tunnel ionization. These seed carriers initiate the avalanche ionization process. The resulting optical breakdown process is very deterministic and repeatable, with obvious benefits to the incisional quality achievable.

Corneal tissue is transparent in the visible and near-infrared, allowing optical breakdown to occur at any depth or location without affecting tissue outside the photodisruption zone. The only limitation to creating arbitrary incision planes is that they must be written from the deepest

planes to the shallowest, because the static gas bubbles that briefly persist in tissue shadow the laser if the focus is moved to a plane below the previously produced bubbles.

Using a femtosecond laser with pulse repetition rates in the kHz range and a computer-controlled scanning optical delivery system, localized micro-photodisruptions can be placed in a contiguous fashion to produce incisions of any shape to produce high-precision tissue separations.

First applications in the cornea

The cornea presents an attractive initial target for femtosecond laser surgical applications because it is easily accessible and lacks blood vessels. Since photodisruptive lasers do not coagulate blood vessels, the lack of vascular structures in the normal cornea obviates the need for additional techniques to control bleeding. Cornea is only 500-600 μm thick centrally, permitting delivery of femtosecond pulses with negligible nonlinear effects. Four surgical procedures have been cleared for use in the United States by the Food and Drug Administration:

- creation of corneal flaps for LASIK;
- anterior lamellar corneal transplantation;
- keratomileusis;
- creation of channels for corneal implants.

The first of these procedures represents a good example of the utility of the femtosecond blade. To understand the advantages of femtosecond flap cutting, it is important to understand the limitations of the LASIK procedure. Introduced in the early 1990s, laser-assisted *in situ* keratomileusis (LASIK) has become the dominant surgical technique to correct simple refractive errors such as myopia, hyperopia, and astigmatism. Traditional LASIK uses a mechanical blade (called a microkeratome) to create a corneal flap, exposing internal corneal layers (stroma) for subsequent excimer laser ablation.

Although microkeratomers are now widely used, outcome variability and patient anxiety remain concerns. In fact, flap creation with microkeratomers is responsible for the majority of intraoperative and postoperative LASIK complications, occurring in as many as 5% of cases.¹⁴ Intraoperative complications most commonly involve abrasions of the epithelium (the sensitive outer layer of protective cells), but also include "buttonholed" flaps and incomplete cuts. Postoperative complications include flap slippage or dislocation, in-growth or down-growth of the epithelium into the stroma, and severe inflammation (diffuse lamellar keratitis). These

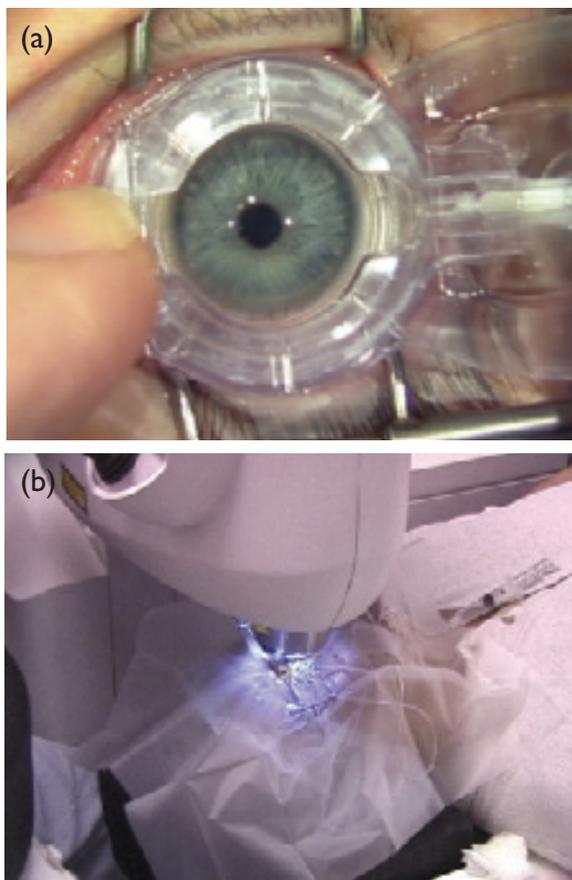


Figure 3. (a) Suction ring fixes eye for (b) positioning of optical contact flat at tip of laser.

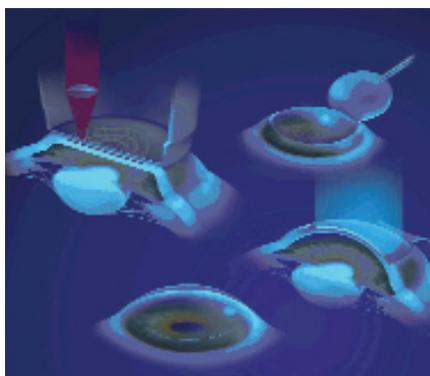


Figure 4. LASIK with fs-laser-cut flap. After appulating cornea with flat contact glass, the focal plane of the femtosecond laser is scanned in a spiral pattern below the tissue surface at a distance selected by the surgeon (typ. 160 μm). To create a side cut, the laser is scanned along a circle at the spiral plane circumference while the focusing lens is raised until the arc cut reaches the corneal top surface. A hinge is created by shuttering the laser beam during a segment of the circular scan. The surgeon lifts the flap and an excimer laser ablates the exposed corneal stroma to produce a refractive change.

events can significantly delay recovery of visual acuity and may even lead to permanent loss of visual acuity.

Even in normal operation, the accuracy and precision of the microkeratome contrasts significantly with that of the subsequent excimer laser ablation of the stroma. Microkeratome flap depth can vary significantly both between and within cuts, depending on patient factors (corneal curvature, orbit size), as well as variations in individual instruments, blades, and operator skill. Surgeon control of microkeratomers is limited, with little flexibility to accommodate individual surgical requirements imposed by corneal thickness, pupil location, or refractive state.

A key factor in improving the precision of LASIK flap creation with the femtosecond laser is good control of the focal plane with respect to the corneal surface. To accomplish this, a suction ring and an optical contact flat located at the tip of the laser delivery system fixate and appanate, or temporarily flatten, the front surface of the eye. The optical contact flat is securely attached to the suction ring by an internal cylindrical clamp, mechanically coupling the eye to the beam delivery system (Fig. 3).

A flap is created by scanning a spiral pattern of laser pulses at the appropriate depth to create a resection plane parallel to the appanated corneal surface (Fig. 4). An arc is then scanned with progressive movement closer to the surface to create a hinged side cut. Following creation of the flap, the suction ring is released and the appanating contact lens removed. The flap is then elevated and the excimer laser treatment performed. A representative procedure sequence is illustrated in Fig. 5.

Other FDA-cleared procedures listed above are performed in a similar manner to the flap-cutting procedure.

FEMTOSECOND LASERS IN THE OPERATING ROOM

Corneal flaps for LASIK

The first large clinical series using the femtosecond laser for LASIK flaps suggests that the laser technique may offer both safety and performance advantages over current mechanical methods.¹⁶ No opera-

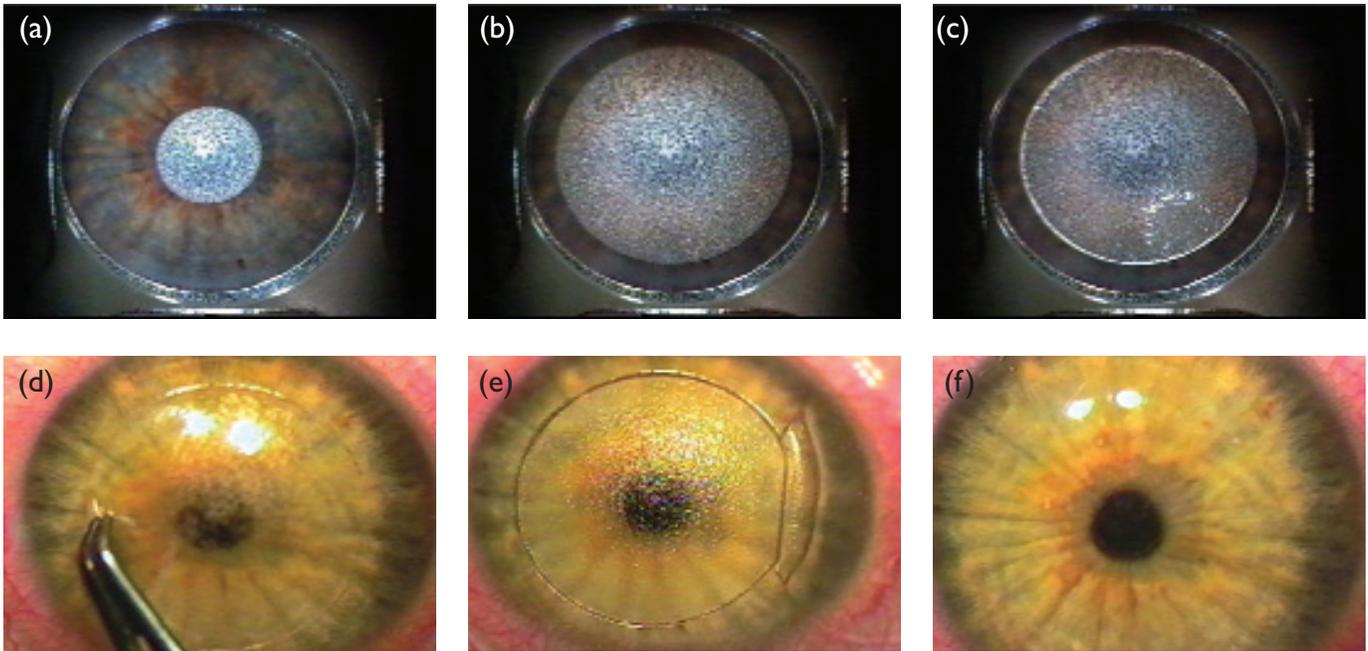


Figure 5. Intraoperative and postoperative photographs of femtosecond laser flap creation: (a) surgical view of planar resection after corneal applanation, demonstrating beginning of layer of microcavitations 160 μm below the corneal surface; (b) continued scanning produces a plane at the desired flap diameter; (c) successive arc cuts are stacked as the scanning objective lens is moved away from the cornea to create the hinged side-cut flap architecture; (d) and (e) elevated corneal flap demonstrating well-defined side cuts and excellent tissue bed quality; (f) typical postoperative appearance at 1 week.

tive or post-operative complications were noted in over 200 procedures, with the only undesired events being interrupted procedures due to loss of applanation. The nature of femtosecond laser resection allows these cases to be completed on the same surgical day with the same outcomes obtained in uninterrupted cases. The absence of a delay following such an event is an advantage over traditional keratomes, in which after an aborted resection a three-month wait is generally recommended before a second attempt. Importantly, excimer laser nomograms developed for traditional LASIK with the microkeratome appear to apply equally well to the new all-laser procedure, suggesting that the femtosecond laser does not remove significant amounts of tissue in a single layer. This finding is consistent with *ex vivo* and animal model studies in which micrographs and histologic evidence indicate only small zones of tissue are removed.

In contrast to a traditional mechanical microkeratome, femtosecond surgical technology allows the surgeon precise control over flap parameters that may affect clinical outcomes. These include flap thickness, diameter, hinge position and

angle, and side (entry) cut angle. Future investigations will need to evaluate the clinical significance of the increased flexibility in flap architecture afforded by this new technology.

Anterior lamellar corneal transplantation (lamellar keratoplasty)

In contrast to flap creation in LASIK, the goal of lamellar keratoplasty is therapeutic: the replacement of diseased or damaged superficial corneal tissue with normal tissue from a cadaver donor eye. Clinical indications for this procedure include corneal scarring, corneal ectasia, peripheral or central corneal thinning or perforation. While lamellar keratoplasty has been performed for decades using simple manual instruments and microkeratomes, most corneal surgeons continue to find these procedures difficult to perform with precision and reproducibility. Full thickness corneal transplants (penetrating keratoplasty) are therefore used in most clinical situations, despite the association of this technique with more significant complications and longer delays in the restoration of functional vision. A reproducible femtosecond laser lamellar keratoplasty procedure has the potential to dramati-

cally alter the surgical approach to anterior corneal dysfunction.

To perform lamellar keratoplasty, a complete circular side cut is used to create a free corneal cap in both the recipient and donor eyes (instead of the partial side cut that creates a hinged corneal flap for LASIK). Once it is placed on the recipient bed, the donor cap is held in place by the hydrostatic pressure provided by the pumping action of the endothelial cell layer at the posterior surface of the cornea. Sutures are often used to secure positioning until healing occurs (Fig. 6). The precision provided by the femtosecond laser allows the recipient and donor corneas to be cut with high accuracy, guaranteeing proper fit of the donor corneal graft in the recipient bed. An exciting new possibility offered by femtosecond lasers is the use of novel sealing or locking geometries to improve stability and healing at the donor-recipient tissue interfaces.

Early clinical experience with femtosecond laser anterior lamellar keratoplasty has indicated that the surgical technique is much easier to perform with the femtosecond blade than with traditional keratoplasty blade instrumentation. No intraoperative complications were noted

in any of the 15 cases performed, while best corrected visual acuity developed much faster than in traditional procedures. As with traditional lamellar transplants, preservation of the recipient deep corneal stroma and endothelium can reduce the risk of graft rejection, seen more commonly in full thickness corneal transplants. Since the internal cavity of the eye is not accessed, serious complications such as intraocular infection and bleeding are also minimized.

Perfecting the femtosecond blade

As a remotely controlled, programmable, noninvasive scalpel, the femtosecond laser blade can be used to create precise, arbitrarily shaped incisions. Two applications have been described here, but many additional uses in the cornea and in other target structures are possible.

In the cornea, these include removal of tissue for refractive corrections, creation of channels for corneal implants, and other novel transplant techniques. Removal of tissue for refractive procedures using only femtosecond lasers could be realized through the excision of laser-cut lenticular volumes, or through direct volumetric destruction of tissue (intrastromal procedures). These applications are under investigation by our team.^{10,15}

Other obvious targets include the rest of the transparent ocular tissues: lens, capsule, and vitreous. Conditions that could benefit from the unique features of the femtosecond laser scalpel include the treatment of secondary cataracts, the modification of intraocular implants, and the cutting of vitreal strands or vitreomacular tractions.

A new type of application is under exploration through the extension of femtosecond laser cutting technology into non-transparent tissues. Subsurface machining of incisions, channel and other flow features in sclera may lead to novel glaucoma treatments. Biology points towards this technology because confined and subsurface surgical features may avoid the wound healing response that plagues other filtering surgery procedures for the treatment of glaucoma. The optical problem is overcoming strong scattering in non-transparent tissue, and the most

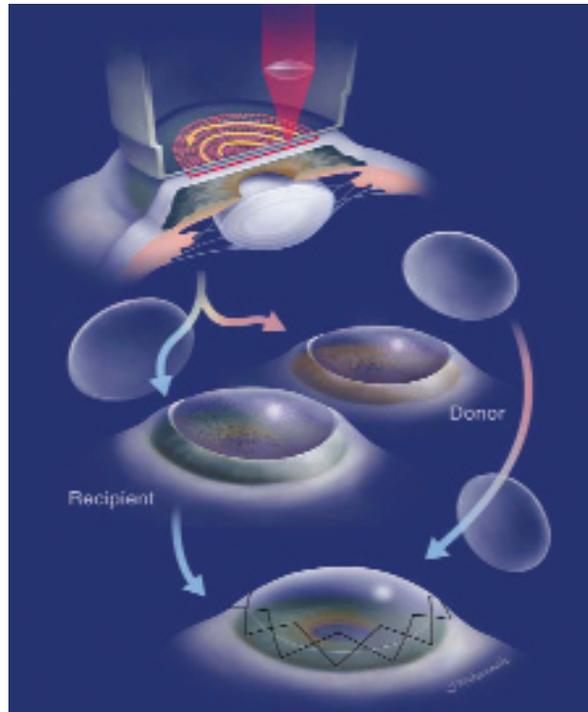


Figure 6. Schematic of anterior corneal transplant procedure: The diseased anterior corneal tissue is removed from the host cornea using the flap-cutting scan pattern without creating a hinge. An anterior section of donor cornea tissue is similarly harvested, fitted, and sutured to the bed of the host cornea. The donor tissue is cut to a slightly larger thickness than the host to account for tissue swelling that resolves after the donor tissue is acted on by physiologic pump mechanisms of the host.

promising approach is to use a laser wavelength long enough to substantially reduce the scattering but short enough to avoid strong infrared absorption by water.¹⁷ Available windows exist in spectral bands centered on 1300 and 1700 nm. Still to be developed are femtosecond sources in these bands that are robust, compact, inexpensive and capable of delivering LIOB suprathreshold fluences at depths of interest.

The general technology trend will be toward the development of high energy femtosecond laser sources and optical scanners which approach the 100 kHz repetition rate range, and large-field scanning objectives which can maintain spot sizes reasonably close to diffraction-limited performance over large fields and modest depth of focus. This will be particularly important for volumetric applications such as intrastromal refractive procedures.

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