A NEW LASER FOR COLLAGEN WOUNDING IN CORNEAL AND STRABISMUS SURGERY: A PRELIMINARY REPORT*

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INTRODUCTION

THE PRESENT PRACTICE OF CORNEAL AND REFRACTIVE SURGERY ENTAILS THE MAKING OF SURGICAL WOUNDS FROM THE EXTERIOR TO A PREDETERMINED LEVEL OF THE STROMA OR THROUGH AND THROUGH THE CORNEAL THICKNESS. THE ABILITY TO CONTROL THE DEPTH OF SUPERFICIAL WOUNDING IN REFRACTIVE SURGERY AND THE ACCURACY OF WOUNDING IN BOTH CORNEAL AND REFRACTIVE SURGERY IS DIFFICULT, VITIATING OFTEN THE INTENDED OPTICAL AS WELL AS ANATOMICAL EFFECTS. WE WOULD LIKE TO REPORT OUR PRELIMINARY RESULTS USING AN EXPERIMENTAL DYE MODIFIED EXCIMER LASER TO CREATE FOUCUSED INTRASTROMAL CORNEAL WOUNDS, WITHOUT MANIFEST DAMAGE TO THE ANTERIOR LAYERS (EPITHELIUM, BOWMAN'S MEMBRANE, AND SUPERFICIAL STROMA), AS WELL AS SPARING DEEPER STROMA AND ADJACENT DESCemet's MEMBRANE AND CORNEAL ENDOTHELUM. THE MINIMAL TISSUE ALTERATIONS APPEAR TO BE EFFECTED THROUGH A NONTHERMAL DISRUPTION (ABLATION) OF CORNEAL COLLAGEN. THIS ABILITY TO CREATE CONTROLLED MIDSTROMAL WOUNDS REPRESENTS A REVOLUTIONARY NEW DIMENSION IN CORNEAL SURGERY WITH POTENTIAL NEW APPLICATIONS, IN PARTICULAR IN CORNEAL REFRACTIVE SURGERY.

WE WILL SHOW ALSO THAT THE SAME LASER WAVELENGTH CREATES PARTIAL ABLATION OF SUPERFICIAL EXTRAOCULAR MUSCLE TENDON PROMISING A NEW METHODOLOGY FOR THE WEAKENING OF EXTRAOCULAR MUSCLES. IF THIS CAN BE ACCOMPLISHED IN VIVO THROUGH TRANSPARENT CONJUNCTIVA IT WILL ADD SUBSTANTIALLY TO

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the safety as well as to the efficacy of strabismus surgery. It is possible that using a wavelength to induce tissue shrinkage, shortening (strengthening) of an extraocular muscle might also be induced.

**INSTRUMENTATION**

The ALS (Automated Laser Systems, Inc) computer aided microsurgery unit (CALM™) (Fig 1) is conceived primarily as a surgical laser incorporating, for intermittent or consecutive use, several wavelengths. The wavelengths used will be chosen not only from clinically proven wavelengths, eg, argon, krypton, carbon dioxide, YAG, and Excimer but also from several new wavelengths calculated theoretically to be more effective for some of the surgical uses planned. It is the first of these new wavelengths, at 595 nm, that has undergone preclinical testing, that is the principal subject of this preliminary report.

Concurrent with laser wavelength investigations is the ongoing design, development, and testing of the several optical mechanical subsystems which will be necessary to deliver laser energy precisely to the targeted area.

**FIGURE 1**
Prototype ALS laser subsystem and X-Y-Z axis controller.
Surgical Laser

1. For maximum comfort and stability the patient lies in a horizontal, supine position on an operating table supported by a base containing the laser optical system (Fig 2). For maximum safety and serviceability it is planned to house the laser driving the system in a vented space outside the operating suite. The transportable table top is fixed in use to an X-Y axis to allow the surgeon to position the patient. Trendelenberg positions are provided for anesthetic emergencies.

2. A rigid, damped, beam support is mounted to the head of the table which in turn supports the computerized, optical video monitored laser delivery objective. Precise positioning is accomplished by an X-Y-Z controller driven by high precision stepper motors. For initial positioning the controller is operated remotely by the surgeon. For surgery it is operated by servos directed by a microcomputer.

3. Approximate localization of the target area is accomplished using a modified optical surgical microscope (6 to 40 ×), and then by a high resolution color video system (to 125 ×). Both view coaxial to the laser objective. Unlike other laser systems incorporating Helium-neon aiming lasers the ALS laser system uses the actual unamplified laser light to locate precisely where the amplified laser energy will be targeted. The electronic viewing system not only significantly improves the range of

![Operating table supported on base containing laser optical systems. Damped rigid beam support over patient's head with laser objective and subsystems.](image)
magnification and precision but also permits digitization of the image for precise computer controlled performance of the surgical procedure.

Topographic and in-depth digitized measurement of reflective surfaces permit verification of quantitative preoperative data (keratometer, pachymeter, extraocular muscle parameters) and precise intraoperative monitoring of surgical parameters for programming and executing operative sequences. Continuous feedback from the optical monitoring system minimizes the possibility of misdirection of laser energy. In the long run, however, it is the speed of delivery of total laser energy required to complete the procedure in minimum elapsed time that assures greatest accuracy. The unique optical design of the ALS laser system provides high speed laser ablation thus preventing misdirection of energy even as a result of involuntary patient movement such as the pulse.

The pulse duration of the ALS laser is approximately 10 psec \((10^{-11} \text{ seconds})\). This is about one thousand times \((1000 \times)\) shorter than the pulse of a Q-switched Nd:YAG laser. The minimal surrounding thermal damage zone permits us to use a wavelength of 595 nm, not possible with YAG laser energies where the damage zone may be as much as 200 \(\mu\). The energy of each pulse being less than 1 mJ, when focused in a spot size of 2 \(\mu\), creates a power density exceeding \(10^{15} \text{ W/cm}^2\), assuring consistent, reproducible plasma formation. In addition the cone angle has been enlarged to 30 to 40 degrees (compared with the 16 degrees of most YAG laser systems). This significantly increases accuracy and decreases the thermal and pressure damage in the critical anterior posterior axis. The resulting narrow incision width (10 to 40 \(\mu\) inclusive of damage zone) resulting from the small spot size makes possible incisions of the minimum width required for incisional procedures, in particular in optical tissue. A linear accelerator (patent applied for) incorporated in the ALS optical system makes two to three times more efficient use of driving laser power than existing lasers.

For the purpose of the preliminary study of new wavelengths ALS has constructed a unique laser subsystem driven by a xenon chloride excited, dimer laser incorporating the optical systems and accelerator of the proposed clinical instrument. In this prototype system the wavelengths undergoing testing are individually generated by a single set of dye cells. To facilitate alignment laser energy is delivered independently of illumination and optical viewing systems using only unamplified laser light to image the target on the high resolution television screen. The vidicon is mounted coaxial to and at the focal plane of the laser objective. Laser energy is targeted manually with a precision X-Y-Z controller which moves the vidicon laser objective pod in relation to the fixed target tissue mounted at 105 mm from the focal plane of the objective lens.
TISSUE MATERIALS AND METHODS

The tissues selected for this study were postmortem eye bank eyes in which cornea and extraocular muscle tendon sheath were treated. The area to be targeted was identified with a 10-0 monofilament nylon suture passed through midstroma of the cornea (Fig 3) and with a 6-0 black silk passed through the superficial layers of muscle tendon sheath (Fig 4). In the cornea the suture was placed in a four part mattress fashion so that when tied some tension was exerted on the suture loops. The laser was focused at the suture level and fired to mark the suture to establish accuracy of alignment and focus. Subsequent laser bursts were directed at

FIGURE 3
Midstromal 10-0 nylon monofilament suture prior to laser treatment which interrupted suture.
FIGURE 4
Six-0 silk suture in extraocular muscle tendon. Laser treatment did not interrupt suture but created superficial tissue alterations.
90 degrees to the etched area in a linear fashion. Finally the suture was cut with laser. All laser bursts were kept within the stroma of the cornea or superficial to the suture in the case of muscle tendon sheath. Overlying conjunctiva had to be removed in order to target muscle tendon sheath because of loss of normal transparency postmortem. Treated tissues were removed in block, fixated in glutaraldehyde 2% and formaldehyde 2% and embedded for electron microscopy or for light microscopy. Postfixation tissue processing for electron microscopy utilized osmium in 0.15 M sodium cacodylate buffer. Electron microscopy staining of ultrathin corneal specimens was with lead citrate and uranyl acetate. For light microscopy hematoxylin and eosin stains were employed. The marking sutures enabled the pathologist accurately to identify the treated areas and to “back into” the treated area with serial sections. Suture tracts also provided control lesions adjacent to laser generated dehiscences.

Maximum calculated laser power densities were directed at targeted tissues. Tests were performed at 20 Hertz and the X-Y axis velocities were kept constant in order to create a linear lesion at the selected depth. At intervals the Z axis was used to vary the depth of the bursts, eg, in cutting the suture of 22 μ using bursts of 2 μ. In all specimens a wavelength of 595 nm with a pulse duration of 10 psec was delivered at a cone angle of 30 to 40 degrees. This was focused into a spot size of 2 μ creating a power density of 10^{15} W/cm^2.

LIGHT AND ELECTRON MICROSCOPIC FINDINGS

Two eye bank corneal specimens, in each of which a 10-0 monofilament nylon suture had been placed in the midstroma and had received laser treatment causing interruption of the suture, were studied by light and electron microscopy. The light microscopic findings disclosed the suture tract, and finally, in serial sections, the suture disappeared from the area of laser interruption creating a suture-free cavity in the midstroma (Fig. 5). The anterior edge of this treated zone appeared roughened and irregular, while the posterior margin bordering the deep stroma had a compacted and slightly posteriorly bowed character. The epithelium throughout the entire specimen was completely denuded, probably an artifact from the late postmortem acquisition of the tissue. Nonetheless, Bowman’s membrane immediately in front of the treated area, the superficial stroma, the stroma deep to the treated area, Descemet’s membrane, and the corneal endothelium all appeared to be unaffected at the light microscopic level by the laser therapy. One-micron sections of the plastic embedded material showed a regular lamellar architecture on either side of the intrastromal suture away from the area of laser treatment. In the region of the
TOP: A segment of 10-0 nylon suture is present in suture tract in an untreated portion of cornea. BOTTOM: Arrow indicates laser treated area. The laser interrupted suture which retracted from stromal cavity. Corneal epithelium is totally missing as a postmortem artifact. Bowman’s membrane, superficial stroma, deep stroma, Descemet’s membrane, and corneal endothelium are apparently unaffected by focused laser treatment (top and bottom, hematoxylin and eosin, × 80).
laser treatment, however, irregular densities of the stroma were observed. Electron microscopic studies performed on suture material in the midstroma away from the laser treated area revealed the tract of the suture between lamellae (Fig 6, top). In the region of the laser treatment the normal collagenous architecture of the lamellae was disrupted (Fig 6, bottom). The collagen strands appeared to be broken, and moderate amounts of electron-dense debris were present in the field of the laser therapy (Fig 7, top). Larger electron-dense fragments appeared to be remnants of the suture material (Fig 7, bottom). The damage to the collagen appeared to extend no more than three lamellae away from the tract of the suture (namely, 20 \times 40 \mu m).

The extraocular muscle tendon studied by light microscopy disclosed the absence of the conjunctiva, which had been peeled away due to its postmortem opalescence to allow direct treatment of the tendon surface. In areas of the tendon at some distance from that of laser treatment, a clear-cut epitendinous connective tissue sheath, probably corresponding to Tenon's capsule, was applied intimately to the regular tendinous collagen (Fig 8, top). In the area that had been treated with the laser, as revealed by the presence of an intratendinous cavity where a 6-0 silk suture had been present for marking purposes, but removed for histopathologic sectioning, considerable thinning of the epitendinous connective tissue sheath was in evidence (Fig 8, bottom).

**DISCUSSION**

In corneal surgery each incision has an optical as well as an anatomical effect. Recently these optical effects have been recognized as clinically significant and attempts made to quantify and control them. Born out of these considerations a new specialty, refractive keratoplasty, has engendered great interest along with some skepticism. Attempts to accurately modify corneal curvatures by relaxing incisions and thickness volume modification have met with some clinical success but the accuracy of correction obtained remains too erratic to justify their routine clinical use, especially in otherwise normal eyes.

Corneal incisions for cataract and keratoplasty too often induce excessive astigmatism necessitating secondary surgical correction. Though corrective techniques are not ideal, surgical intervention in such cases is justified since sight compromising optical errors need to be functionally corrected.

Since conventional corneal surgical incision or refractive modification requires always that Bowman's membrane be compromised continuous
TOP: Transmission electron micrograph revealing a portion of suture (S) in an untreated area. Regular architecture of corneal collagenous lamellae (L) is preserved next to suture tract. BOTTOM: Laser-injured region of corneal stroma is indicated by arrows and measures 20 × 40 μm. Suture has retracted due to photo-disruption in this region of suture tract (ST). Collagen comprising involved lamellae is disrupted, contrasting with regular lamellae (L) outside treatment zone (top, × 14,280; bottom, × 4280).
TOP: Alterations in corneal stroma in laser treated zone. Collagen fibers (C) are interrupted and disorganized. Electron-dense debris (ED), granular material (G), and collagen thin fibrils (F) are present in this area. BOTTOM: Large electron-dense structures (arrows) may represent displaced fragments of nylon suture into stromal region. In addition to electron-dense (ED) and granular (G) alterations of stroma, irregularity of preserved collagen (C) is also shown. One of the collagen fiber bundles displays unfurling fibrils at one end (crossed arrow), and blending of collagen fibers into fibrils (F) at other end (top and bottom, × 27,500).
FIGURE 8

TOP: Untreated area of an extraocular muscle tendon (T) adjacent to sclera (S). Conjunctiva has been peeled away, and an epitendinous lamina of connective tissue, probably corresponding to Tenon's capsule, is present toward the right (arrow). BOTTOM: An area of laser-treated tendon (T) shows dissolution of epitendinous connective tissue, with only fine wisps of collagen remaining (arrow). S, sclera (hematoxylin and eosin, top and bottom, × 220).
and variable refractive changes are induced. Corneal curvatures should be more readily quantifiable and better maintained or modified by surgical intervention if Bowman's membrane could be preserved intact during corneal incision or ablation of deeper stromal structures.

Light and electron microscopic studies of treated cornea and muscle tendon sheath demonstrate that the ALS laser at 595 nm ablated corneal stroma and superficial extraocular muscle tendon sheath in accordance with theoretic calculations. The small spot size and high power density created a minimal blast effect (damage zone) while creating well defined lesions. In corneal sections there was no evidence of laser damage to Bowman's or Descemet's membranes or their respective epithelial and endothelial layers. In muscle tendon sheath only the most superficial layers were disrupted, deeper layers being protected by energy absorption of the opaque tissue. Since power densities and spot sizes can be increased exponentially it can be anticipated that selectively deeper lesions can be achieved proportional to increased power densities and spot sizes selected. It remains to be seen if this can be accomplished without damage to overlying conjunctiva in vivo.

In refractive surgery it would be possible, using intrastromal ablation, to create new corneal curvatures while preserving the anterior optical surface intact, significantly improving quantitation and stability of results. For example, graded removal of corneal tissue in plane from the corneal periphery would increase central corneal curvature to correct hyperopia. Conversely, removing graded layers centrally would correct myopia, as removal in sector would correct astigmatism.

Current muscle tendon sheath surgery, even less accurate in its performance than corneal surgery, lends itself with considerable promise to laser intervention. Here trans-conjunctival, essentially noninvasive, treatable, easily repeatable muscle weakening, or strengthening procedures are feasible. By varying wavelengths, spot size and power density more or less tissue can be ablated either to allow lengthening (by non-thermal ablation) or strengthening (by graded thermal ablation) at a depth determined by the power employed.

Our laser engineers and physicists believe that in addition to tissue ablation there will be wavelengths specific to individual tissue which will, in effect, "laser weld" tissue surfaces more effectively than sutures to give immediate reconstitution of tissue integrity, and in the case of the cornea, optical integrity as well.

**SUMMARY**

It has been shown that using a small spot size 2 to 5 \( \mu \), a dye modified
Excimer laser emitting at 595 nm can produce laser ablation of tissue in corneal stroma without compromising anterior and posterior limiting membranes. The surface of extraocular muscle tendon sheath has been similarly laser modified. An instrument, under prototype construction, designed for clinical application of this laser energy is described as well as clinical implications of such surgical interventions in corneal and extraocular muscle surgery.

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DISCUSSION

Dr Edward Okun. I suppose the reason I was asked to discuss this paper was that this society is sick of hearing about the virtues of the xenon arc, and want me to know that there are other forms of light energy also worth considering. From a historical viewpoint, photocoagulation as we know it began with the xenon arc and then was refined with the argon, krypton, and dye lasers. All operating within the visible spectrum, their use has been extended from retinal and retinal vascular conditions to the anterior segment. With the advent of the CO₂ laser operating in the infrared range photovaporization was achieved, allowing external as well as internal bloodless incisions, still thermal in nature. Next came the YAG laser creating optical breakdown and photodisruption of tissue by forming plasma and associated shock waves. The most recent type of laser application, that of photodecomposition is produced by the Excimer laser. This far ultraviolet laser produces radiation that creates a specific photochemical reaction resulting in tissue ablation without thermal change to the remaining adjacent structures.

Today's interesting paper concerns a dye modified Excimer laser with a unique delivery system capable of focusing its ablative energy into a 2 to 3 μ spot. The present laser experiment operates at 595 nm which does cause some thermal reaction, but the spot is so finely focused and the pulse duration so short, that the
thermal response is said to be negligible. Previous reports on the use of an Excimer laser for the purpose of producing corneal incisions have operated at the wavelength of 193 nm. At that wavelength, organic molecular bonds are broken directly without tissue heating. Forthcoming animal studies will answer the question of whether or not thermal damage can be detected in corneal incisions produced with this new laser. The authors refer to this new laser as a dye modified Excimer laser. I might ask them if this laser is not a dye laser that is powered by an Excimer-like laser, since it does operate within the visible spectrum.

One intended use of this advanced delivery system is to focus the lesions between Descemet's and Bowman's membranes, thus maintaining the basic integrity of the cornea's two limiting membranes. The present study indicates that this may well be possible. It now remains for future studies to determine the effects of this type of ablation on wound healing and refractive changes.

In theory, there are many exciting possibilities brought up by this preliminary report. We will be waiting with great anticipation to see how many of these are realized.

**Dr Steve Kramer.** I just want to add a question following up Doctor Okun's remarks. In terms of the intrastromal lesion between the anterior and posterior lamellae of the cornea, do the authors know how much depth would have to be ablated by that approach to have a refractive effect. My sense is that if the anterior stromal lamellae and the posterior stromal lamellae are intact at all, say 10% of the total thickness of the cornea, there is likely to be almost no refractive effect. I wonder if they have any preliminary observations.

**Dr A. Edward Maumenee.** It is somewhat unusual and out of order but I just returned from the Ergophthalmological Society in Munich, Germany. Doctor Tengroth from Sweden and Doctor John Marshall from the Institute of Ophthalmology in London are working on the computerized Excimer laser and are doing spectacular work. Partially to answer the last question, they said that if you mark a 3 mm in size area over the pupil then with the Excimer laser they can remove 25 μ of tissue and create somewhere between 8 and 12 diopters of hyperopia. They also have been able to completely correct astigmatism and modify myopia. They also stated that strangely enough, and maybe Doctor Jakobiec can answer this, when the epithelium goes back the tissue underlying the epithelium takes on somewhat the characteristics of Bowman's membrane. And yet we have always been told Bowman's membrane does not regenerate. This is going to be one of the future really great instruments in anterior segment surgery, I congratulate the authors on their presentation.

**Dr Suzanne Veronneau-Troutman.** I would like to thank Doctor Okun for his kind discussion. Regarding Doctor Edward Maumenee's remark, I repeat that the laser we are presenting is an experimental dye modified Excimer laser. It differs from other Excimer lasers by its wavelength, pulse duration, cone angle, and delivery system. To my knowledge none of the Excimer lasers currently ad-
Troutman advocated for corneal surgery have succeeded to create a stromal ablation without damage to adjacent structures. The written paper will answer technical questions in more detail. I would like to ask Doctor Jakobiec, a co-author of this paper, to close this discussion.

DR FREDERICK A. JAKOBIEC. Regarding the questions about Doctor Véronneau-Troutman's presentation, I think they are extremely relevant. This research must be regarded as quite preliminary, because the tissues examined were few in number and only of postmortem quality. The focusing of the laser energy on several collagenous lamellae is exquisitely precise and represents a technical tour de force. However, the translation of these findings into clinical situations must be done with extreme caution. Whether a small lesion such as was described today will cause any alteration of the corneal shape is, I think, untested and awaits further animal studies. With respect to what Doctor Edward Maumenee mentioned, I am aware of the Excimer laser that is being investigated by Doctor John Marshall of London and Doctor Stephen Trokel of New York. The type of wounding created by this instrument includes ablating Bowman's membrane and the superficial stroma. It does, however, create a very remarkable wound, as exemplified by the type of healing that Doctor Maumenee alludes to. I have not seen any reports of the results that Doctor Maumenee describes, but what might happen is a healing phenomenon entailing different types of collagen production along with other types of matrix material. Doctor Barbara Streeten told me at this meeting that ten types of collagen are now known to exist, which is a doubling of what I once thought. It is, therefore, possible that in some wounding situations, the epithelium will slide over a certain type of collagenous or matrix substrate produced during healing that resembles Bowman's membrane.