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In vitro conjunctival incision repair by temperature-controlled laser soldering

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Abstract. The common method of closing conjunctival incisions is by suturing, which is associated with several disadvantages. It requires skill to apply and does not always provide a watertight closure, which is required in some operations (e.g., glaucoma filtration). The purpose of the present study was to evaluate laser soldering as an alternative method for closing conjunctival incisions. Conjunctival incisions of 20 *ex vivo* porcine eyes were laser soldered using a temperature-controlled fiberoptic laser system and an albumin mixed with indocyanine green as a solder. The control group consisted of five repaired incisions by a 10-0 nylon running suture. The leak pressure of the repaired incisions was measured. The mean leak pressure in the laser-soldered group was 132 mm Hg compared to 4 mm Hg in the sutured group. There was no statistically significant difference in both the incision's length and distance from the limbus between the groups, before and after the procedure, indicating that there was no severe thermal damage. These preliminary results clearly demonstrate that laser soldering may be a useful method for achieving an immediate watertight conjunctival wound closure. This procedure is faster and easier to apply than suturing. [DOI: 10.1117/1.3262610]

Keywords: laser tissue soldering; laser tissue interaction; conjunctival; indocyanine green; albumin; porcine eye.

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1 Introduction

The current method of closing conjunctival wounds is by means of suturing. The use of suture materials is associated with several disadvantages, including prolonged operating time, postoperative discomfort, and potential for suture-related complications, such as buttonholes, suture abscesses, granuloma formation, tissue necrosis, and giant papillary conjunctivitis.[1,2] Some operations, mainly glaucoma filtration operations, require watertight conjunctival closure in the immediate postoperative period. Sutures do not always produce a watertight conjunctival closure, and it requires skill to apply them.

The use of fibrin glue was suggested as a possible alternative to the current conjunctiva suturing method for conjunctival autograft in pterygium operation,[3–6] trabeculectomy,[7,8] and a leakage of the filtering bleb.[9–14] Although fibrin glue was shown to be a safe and effective method with shorter operating times and less postoperative discomfort, reopening of the wound accompanied by conjunctival retraction was reported.[6,7] The high cost of the glue is another drawback of this technique. None of those reports studied the strength of the bond nor did they assess the immediate watertightness of the bond.

The use of lasers for tissue welding or soldering is another alternative for incision repair. Jain and Gorisch[15] were first to report that local heating might speed closure and healing, in a process akin to the "welding" of solids. In principle, the general idea is simple. Heating of apposed tissue margins cause fusion. The function of the laser is to produce heat. Laser radiation is absorbed into the material and converted to heat. In order to selectively heat the bonded area, chromophores (radiation absorbing material) were added to the repair site.[16]

Krueger and Almquist[17] and Poppas et al.[18] suggested adding a solder made of blood products over the approximated incision (e.g., albumin or fibrin). Both the solder, which acts as a biological glue, and the underlying tissue are heated by the laser. This method, called laser tissue soldering (LTS), produces a stronger (immediate and long-term) bond with a lower collateral thermal damage. The technique continued to evolve by using a laser whose radiation passes through the tissue. Chromophores, such as indocyanine green (ICG), were added to the solder to absorb the laser beam. In that way, the laser heats the solder and the solder heats the tissue by heat conduction.[19]

Laser tissue bonding (LTB), i.e., the use of laser to repair tissue incisions by either welding or soldering, offers many advantages over the present tissue-bonding methods. The potential advantages include: (*i*) Easier to master and perform, (*ii*) no foreign matter (e.g., staples, thread) is introduced dur-

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ing laser welding and only biocompatible materials are used in laser soldering, (*iii*) the LTB procedure may produce an immediate liquid-tight seal, (*iv*) the above advantages result in a faster healing time and less scarring, and (*v*) easy to use in laparoscopic and endoscopic surgery for soft tissues repair.

Using a laser heating to repair tissue incisions was studied on animal models and on numerous types of tissue, such as the urinary tract,[18,20] blood vessels,[21] skin,[22,23] and dura.[24] A variety of different techniques and lasers have been used in these studies. Several LTB experiments were conducted on ocular tissues, such as cornea and sclera, and demonstrated tissue bonding with acceptable thermal damage.[25–29]

LTS has not yet been tried for the reattachment of the conjunctiva. In the past, we have used temperature-controlled LTS for the closure of cuts in the cornea.[25,26] The purpose of this work is to evaluate LTS as an alternative for closing conjunctival incisions.

2 Material and Methods

2.1 *Temperature-Controlled Laser Soldering System*

In principle, a laser heats a spot on the tissue. Thermal radiation emitted from the surface is proportional to its temperature. Therefore, the spot's temperature is measurable by an infrared (IR) detector. A temperature control module reads the detector's signal determines the surface temperature and in response varies the laser output power in order to maintain a constant set temperature, T_s.

In this research, the laser bonding system was based on a GaAs laser, emitting a wavelength of 828 nm (Sharplan 6040, Lumenis, Yokneam, Israel). The laser was operated in the continuous wave mode with an output power ranging from zero to ~1 W. A solid albumin strip was placed beneath the incision. The albumin and the tissue are nearly transparent at the laser's wavelength; therefore, ICG was mixed with the albumin to increase the solder absorption at the laser's wavelength. The laser emission was delivered to the conjunctiva, using a standard silica fiber. Radiation absorbed by the ICG was converted to heat. In that way, the tissue was heated by heat conduction in vicinity to the solder.

The heated spot emitted infrared radiation whose intensity I depends on the temperature T, according to $I=\varepsilon\sigma T^4$, where ε is the emissivity and σ is Stefan–Boltzmann constant. The emissivity of water is $\varepsilon \approx 1$, and that of soft tissues is practically equal to 1 due to their large water content. The thermal IR radiation, which is emitted from the bonding site, was partially collected by a silver-halide (AgClBr) fiber and delivered to an infrared detector (i.e., radiometer). The silver-halide fiber was developed in our laboratory and has high transmission in the middle infrared range (3–20 μm).[30] The voltage signal generated by the radiometer was read by a personal computer. A custom-designed LabView® virtual instrument (National Instruments, Austin, Texas) calculated the surface temperature from the radiometer signal and controlled the laser output power in order to maintain a constant temperature.

The temperature control system adjusted the laser power in response to the surface temperature in order to maintain an average spot temperature of $T_s = 60\ ^\circ\mathrm{C}$ at the soldering spot. A holder containing both the laser delivery fiber and the radiometer fiber was designed so that the two distal ends of the fibers were positioned 7 mm above the tissue, producing a 2.5-mm-diam heated spot with a maximal power density of 20 W/cm^2. The system is schematically depicted in Fig. 1.

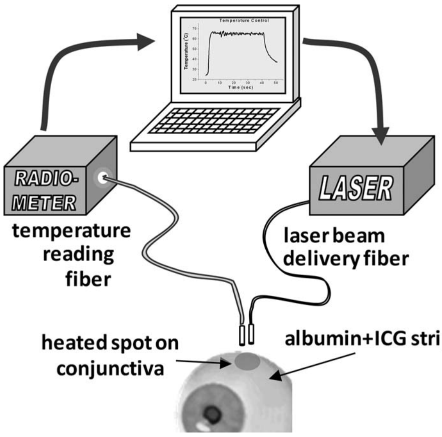

Fig. 1 Schematic drawing of the temperature-controlled fiberoptic laser system. The laser radiation, delivered by optical fiber, heats the albumin and the tissue. Noncontact surface temperature measurement by the radiometer. A computer controls the laser output power according to the radiometers temperature reading.

2.2 *Preliminary Experiments: Defining the Optimal Parameters for Soldering Incisions in the Conjunctiva*

This study was preceded by preliminary (unpublished) experiments on 55 porcine eyes, designed to estimate the optimal laser bonding parameters. We evaluated the laser welding, laser soldering, different set temperatures, solder characteristics, and bonding configurations. First, we evaluated laser welding, with or without chromophore staining, while heated to different set temperatures. Satisfactory bonding was not achieved in our trials using laser welding. Next, laser soldering was evaluated. The globe curvature posed difficulties when laser soldering with liquid albumin. Though the solder was quite viscous, it could not be spread uniformly along the incision, resulting in uneven bond strength. Soldering with a flexible strip of solid albumin solved this problem. The best qualitative results were obtained when the strip was inserted under the incision. The minimal strip thickness, in order to avoid conjunctival to scleral tissue adhesion, was 0.55 mm. Drying of the incision bed prior to the strip insertion was essential in order to prevent the solder strip from dissolving.

2.3 *Solder Preparation*

Flexible solid albumin sheets were prepared by dehydration of an aqueous solution of 27% bovine albumin (ICN Biomedicals Inc., Irvine, California) and 0.7 mg/g of ICG (Sigma-Aldrich Co., St. Louis, Missouri). As mentioned, the ICG had to be added to the albumin solder in order to absorb the GaAs laser radiation. The minimal ICG concentration required to achieve fast temperature rise time (<1 s) was found to be 0.7 mg/gr. Strips of length 12 mm, width 5 mm, and thickness 0.55 mm, were excised from the sheets and used in the *in vitro* experiments. The dimensions of the strips were chosen in order to fully cover the 8-mm incision while keeping safe margins.

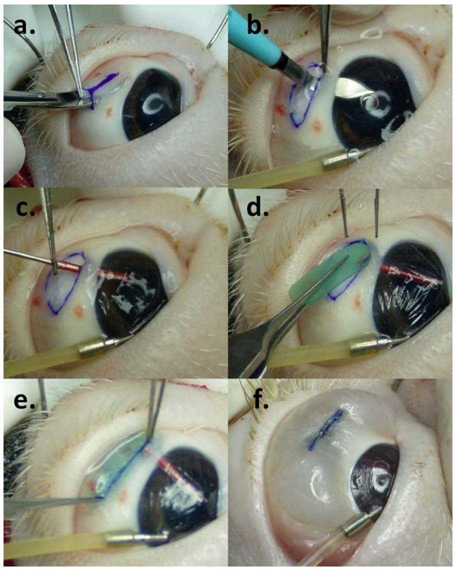

Fig. 2 Conjunctiva laser soldering: (a) Conjunctiva and Tenon's capsule dissection under the incision, (b) penetration of the anterior chamber through a scleral tunnel, (c) insertion of a plastic cannula into the anterior chamber, (d) placement of an albumin/ICG strip under the incision, (e) approximation of the incision's lips, and (f) watertight soldered incision with a high and diffuse conjunctival bleb following leak pressure measurement.

2.4 *Surgical Procedures*

Eyes of six-month-old pigs were obtained from the Institute for Animal Research of Kibbutz Lahav in Israel. In order to preserve the conjunctiva intact, most of the orbital tissue, including the eyelids, was exenterated. The eyes were preserved in a cool chamber (4 °C) up to two days after harvesting. Each globe was mounted on a plastic base; the eyelids were secured to it in four quadrants with pins. Twenty eyes were used for the soldered group, and five eyes for the sutured group (which served as a control group).

The surgical procedure in the laser soldered group was performed by the same surgeon as follows:

1. An incision line of length 8 mm was drawn on the conjunctiva, 5–6 mm posterior to the limbus.
2. The conjunctiva and Tenon's capsule were cut and dissected under the incision [Fig. 2(a)].
3. An anterior chamber maintainer (ACM) connected to an infusion system with water bottle was introduced through a paracentesis at eight o'clock (~240 deg).
4. A scleral tunnel, 3.5 mm wide, parallel to the iris plain was done through the conjunctival incision, using a keratome, starting 2 mm from the limbus [Fig. 2(b)].
5. A plastic cannula 1-cm long (cut from 20-gauge Venflon) was inserted through the scleral tunnel into the anterior chamber, [Fig. 2(c)]. The ACM was opened in order to demonstrate a free passage of liquids through the cannula.
6. The ACM was closed, and the incision area was dried by absorbent material and airflow.
7. A flexible albumin/ICG strip was placed under the conjunctival incision [Fig. 2(d)].
8. The wound edges were approximated using two forceps [Fig. 2(e)] and continuous laser soldering was carried out twice along the length of the incision. Each pass lasted ~1.5 min. No visible endpoint indication was observed.

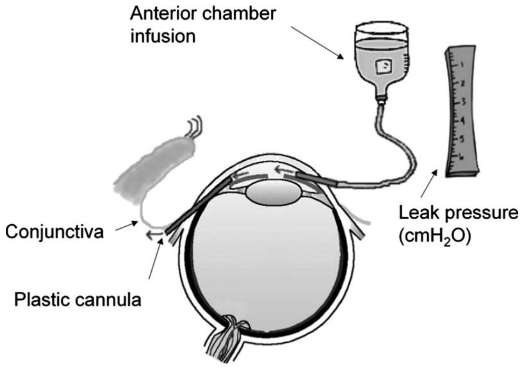

Fig. 3 Leak pressure measurement setup. The height of the anterior chamber maintainer determined the intraocular pressure. The cannula equalized the pressure of the subconjunctival space with that of the anterior chamber.

The surgical procedure in the sutured (control) group was performed as follows: Steps 1–5 were the same as in the laser soldered group, and in step 6, the conjunctival wound was sutured using a 10-0 nylon running suture.

2.5 *Leak-Pressure Measurements*

The leak pressure was defined as the pressure at which any leakage from the eye was noted, either from the bonded incision or elsewhere (e.g., diffused oozing from the conjunctiva or leakage from retrobulbar soft tissue). After reattaching the incision, the infusion was opened and the bottle was maintained at eye level. At this level of 0 mm Hg intraocular pressure (IOP), the elevation of the conjunctiva and formation of filtration bleb was noted. The intraocular pressure was gradually increased by slowly elevating the infusion bottle. The subconjunctival and the anterior chamber pressures were equalized by the cannula (one of its ends was inside the anterior chamber and the other in the subconjunctival space underneath the incision, as explained in step 5 of the surgical procedure). The intraocular pressure was determined by the bottle height. The leakage pressure (in centimeters of H_2O) was recorded by measuring the bottle height when a leakage was first noted. The measurement principle of the leak pressure is illustrated in Fig. 3.

2.6 *Evaluation of the Surface Distortion*

The distortion of the globe surface is a measure by which the damage to the eye's globe, following the reattachment, is assessed. It may also serve as a rough estimate to the thermal damage that follows the soldering procedure. The surface distortion was estimated by comparing the incision length and the distance from the limbus, before and immediately after the tissue bonding.

2.7 *Statistical Analysis*

Student's t-test was carried out for the comparison of the incision length, the incision to limbus distance, and the leak pressure between the soldered and the sutured groups. The differences of leak pressure between eyes of different ages (day 0, day 1, and day 2 postharvesting), within the laser-

Table 1 Leak pressure measurements (mm Hg).

			Leakage pressure (mm Hg)			
		n[a]	Mean	SD[b]	Min.	Max.
Soldered group	Leak from the incision	7	115	39	71	164
	Leak from elsewhere	13	141	49	81	235
	Total	20	132[c]	46	71	235
Sutured group		5	4[c]	8	0	18

[a] *n*, number of eyes;

[b] SD, standard deviation.

[c] Statistical significant difference between the groups ($p < 0.001$)

soldered group, were tested by means of the one-way ANOVA. All the p values were two tailed. The data were processed by the SPSS software.

3 Results

The mean time from harvesting to procedure within the soldered group was 0.75 days (same day $n=7$, 1 day $n=4$, two days $n=9$). All the sutured eyes were one day old (i.e., one day after harvesting) with no statistically significant difference between the groups. The leak pressure measurements are summarized in Table 1 and illustrated in Fig. 4. The mean leak pressure in the soldered group was 132 mm Hg, compared to 4 mm Hg in the sutured group. It is statistically significantly higher in the soldered group than in the sutured group ($p < 0.001$). In seven out of the 20 soldered eyes, the leakage first appeared from the incision. In the other 13 eyes, the leakage first appeared elsewhere: in eight eyes, a diffused oozing was observed from the conjunctival tissue, in four eyes, leakage appeared from the soft tissues posterior to the globe, and in one eye the infusion cannula was ejected and the leakage appeared from the paracentesis. In all the sutured eyes, the leakage first appeared from the incision. The mean leak pressure in the soldered group, in which the leakage was first noted from the incision, was 115 mm Hg, and where the leakage was noted elsewhere, it was 141 mm Hg. In four out of the five sutured eyes, the leakage appeared immediately after opening the infusion (i.e., at a pressure 0 mm Hg).

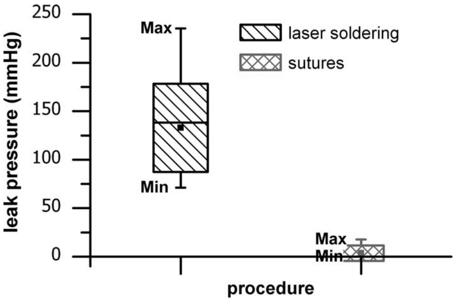

Fig. 4 Leak pressure measurements of the laser-soldered and sutured groups. The mean leak values are represented by the small solid squares, while the standard deviation from the mean value is represented by the large shaded boxes. The horizontal line in each large box is the median.

The tissue distortion measurements are summarized in Table 2. The incision length before reattachment was 8 mm in all eyes. After soldering, it was reduced by 1.2 mm (from 8 to 6.8 mm) as compared to 1 mm (from 8 to 7 mm) after suturing, with no statistical significant difference between the two groups. The mean incision distance from the limbus before reattachment was 6 mm in both groups. After soldering, it was reduced by 1.1 mm (from 6 to 4.9 mm) as compared to 0.6 mm (from 6 to 5.4 mm) after suturing, with no statistical significant difference between the groups.

4 Discussion

In this study a successful laser soldering of conjunctival incisions was achieved in porcine eyes by a temperature-controlled GaAs laser system. We demonstrated an immediate watertight incision bonding using flexible albumin/ICG strips, which served as the biological solder. The mean leak pressure was significantly higher than the one observed in sutured incisions. Furthermore, it was much higher than the IOP of extreme pathological conditions (e.g., acute glaucoma). Immediately after the laser-soldering procedure, a central core of denaturated solid strip was formed while the rest of the strip dissolved to a subconjunctival liquid. At the end of the procedure, the conjunctival surface remained free of any foreign substance [Fig. 2(f)]; hence, the postoperative foreign body sensation and the discomfort might be diminished.

In the LTS procedure the incision edges were held by forceps during the laser application. Immediately after the laser heating, the incision was repaired. If the edges were not brought together by the forceps, they were wide open (due to the globe curvature and the elastic nature of the conjunctiva). Therefore, it is obvious that the pressure the repaired incision resisted was due to the laser heating and not merely due to the placement of the albumin strip underneath the incision.

Heating the conjunctiva resulted in some tissue contracture. Although the incision contracture was larger in the soldered group compared to the sutured group (1.2 versus 1 mm), it was neither statistically nor clinically significant. Incising the conjunctiva by itself causes retraction, which reduces the incision to limbus distance. In the soldered group, this reduction was more pronounced than in the sutured group (1.1 versus 0.6 mm) with neither statistically nor clinically significant. Nevertheless, this study should be followed by an *in vivo* research in order to determine the long-term effects of

Table 2 Tissue distortion measurements.

	Incision length (mm)				Distance from the limbus (mm)			
	Before		After		Before		After	
	Mean	SD[a]	Mean	SD[a]	Mean	SD[a]	Mean	SD[a]
Soldered group	8.0	0.0	6.8	0.7	6	0.1	4.9	0.5
Sutured group	8.0	0.0	7.0	0.4	6	0.0	5.4	0.2

[a]SD, standard deviation

the soldering procedure on the eye's curvature and on the recovery from the thermal damage.

Ocular tissue fusion by laser photocoagulation is a common practice for treating retinal breaks.[31] Photocoagulation induces structural tissue damage stimulating a late healing process, and the formation of a scar which adheres to the tissues.[32] In this type of treatment, the thermal effect induces an irreversible damage to the healthy tissue. On the other hand, tissue bonding by laser soldering is not accompanied by such severe tissue damage. The laser bonding mechanism, although not fully understood, is hypothesised to be related to the denaturation and cross-linkage of collagen and other structural proteins.[33–35] Thus, laser soldering induces reconstruction—a hypothesis supported by a normal histological appearance immediately after bonding.[28]

Prior research has shown that LTB using temperatures as high as 95 °C, results in an adequate bonding strength and a satisfactory wound healing in the postoperative period.[36,37] Therefore, we concluded that histology is redundant in an *in vitro* study, such as the one presented here. Clearly, histology is necessary in future projects that will involve *in vivo* experiments.

In seven out of the 20 laser-soldered eyes and, in all five sutured eyes, the leakage first appeared from the bonded incision. In 13 out the 20 laser soldered eyes, the leakage was first noted elsewhere, and it was recorded as the leakage pressure. With the first appearance of any leakage, the closed system was interrupted and, therefore, the position of the infusion bottle height did not reflect anymore the IOP. Thus, if the leakage first appeared elsewhere, the real incision leak pressure could not be measured and it was actually higher than the recorded one. In other words, the real incision bond strength was higher than the value 132 mm Hg presented in our study.

This study clearly demonstrated an immediate watertight conjunctival closure by laser soldering. The mean leakage pressure in the laser-soldered group was much higher than both the physiological IOP range (10–22 mm Hg) and that of extreme pathologic conditions, such as acute glaucoma attack.

Immediately following a traditional trabeculectomy, the sutured conjunctival incision apparently holds higher pressure than the mean 4 mm Hg observed in our sutured group. Following conventional trabeculectomy, where the conjunctival incision is sutured, the repaired incision resists the intraocular pressure and not the subconjunctival pressure. The subconjunctival and the subocular pressures are not equal due to the pressure decrease over the scleral flap. When elevating the subocular pressure, the subconjunctival pressure is lower than the intraocular pressure. In this work, the bond strength was assessed by the subconjunctival pressure and not by the subocular pressure. Measuring the actual subconjunctival pressure demonstrated a very low leakage pressure in the sutured group. This low pressure might be partially attributed to the suturing by a single layer of the conjunctiva and the Tenon's capsule. Nevertheless, we assume that even a two-layer suturing cannot achieve the same watertight adhesion observed in the laser-soldered eyes.

The clinical importance of an immediate watertight wound closure in ophthalmic surgery, mainly glaucoma filtration surgery, cannot be overemphasized. Immediate watertight conjunctival sealing has numerous significant advantages. A sealed wound reduces the risk for infections, such as endophthalmitis, ocular hypotony, and shallowing of the anterior chamber with its complications (peripheral anterior synechiae, cataract, corneal edema, etc.). Leakage followed by hypotony may cause significant, sometimes irreversible, damage to the eye, such as choroidal effusion and hemorrhage or hyotonic maculopathy. Prolonged leakage from the filtration bleb is a known complication of trabeculectomy and ranges in different reports up to 20%.[38] It may be followed by delayed healing and sometimes requires resuturing. On the contrary, in the presence of an immediate watertight bonding of the incision, an early filtration bleb can be achieved, as was noted in all our soldered eyes [Fig. 2(f)]. We hypothesize that it might reduce the risk of conjunctiva to sclera adhesions and therefore reduce the risk of bleb failure.

The average time of bonding in the laser-soldering group was 5 min. We assume that the soldering time can be greatly shortened by overcoming a technical obstacle of the current method, namely, the approximation of the incision edges. Handling the conjunctiva by two forceps was quite cumbersome and time consuming. This difficulty can be easily overcome by designing a dedicated conjunctival holding and approximating device. Another limitation of this technique is the requirement of a dry environment during strip insertion and soldering. This can be solved by filling the anterior chamber with a viscoelastic substance, when dealing with opened-eye operations, such as trabeculectomy.

5 Conclusion

This work demonstrated an immediate watertight conjunctival closure by laser soldering—a vital requirement following some common eye operations, such as glaucoma filtration. An immediate watertight conjunctival closure is not always achieved by suturing the incision. This laser bonding method, although requiring some technical modifications, could significantly improve the conjunctival reattachment. Conjunctiva LTS has the potential of shortening the operating time, achieving an immediate watertight bond, while reducing the post-operative complications and discomfort. *In vivo* studies are required now to evaluate the safety of this method, as well as to determine its long-term outcome.

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