

Sutureless Liver Repair and Hemorrhage Control Using Laser-Mediated Fusion of Human Albumin as a Solder

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Background: Major liver trauma has a high mortality because of immediate exsanguination and a delayed morbidity from septicemia, peritonitis, biliary fistulae, and delayed secondary hemorrhage. We evaluated laser soldering using liquid albumin for welding liver injuries.

Methods: Fourteen lacerations (6 × 2 cm) and 13 nonanatomic resection injuries (raw surface, 8 × 2 cm) were repaired. An 805-nm laser was used to weld 53% liquid albumin-indocyanine green

solder to the liver surface, reinforcing it by welding a free autologous omental scaffold. The animals were heparinized and hepatic inflow occlusion was used for vascular control. For both laceration and resection injuries, 16 soldering repairs were evaluated acutely at 3 hours. Eleven animals were evaluated chronically, two at 2 weeks and nine at 4 weeks.

Results: All 27 laser mediated-liver repairs had minimal blood loss compared with the suture controls. No dehiscence,

hemorrhage, or bile leakage was seen in any of the laser repairs after 3 hours. All 11 chronic repairs healed without complication.

Conclusion: This modality effectively seals the liver surface, joins lacerations with minimal thermal injury, and works independently of the patient's coagulation status.

Key Words: Albumin solder, Indocyanine green, Liver trauma, Tissue welding.

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The management of liver trauma continues to evolve. The liver is the most commonly injured organ after abdominal trauma.^{1–3} It is the second most commonly injured organ in blunt injuries and the third most commonly injured organ in penetrating injuries.^{1–3} Exsanguinating hemorrhage remains a significant cause of immediate mortality.^{4–6} Clagett and Olsen⁷ in their report on nonmechanical hemorrhage in severe liver injury stated that coagulopathy occurred in 51.5% of patients in their series. Bender et al.⁸ correlated injury grade by the American Association for the Surgery of Trauma scale (Table 1) with mortality. A grade III injury or 3-cm parenchymal depth laceration had 19% mortality and a grade IV injury or a parenchymal disruption involving 25% to 50% of a hepatic lobe had 28% mortality, the mortality rising to 68% and 100% for injury grades V and VI, respectively. Few intra-abdominal injuries are as technically demanding as a major liver laceration, and erudite judgment and innovative surgical techniques are required to prevent intraoperative exsanguination accelerated in some cases by hypothermia, hemodilution, and coagulopathy.

Solid visceral organs such as the liver, spleen, and kidney have a soft parenchyma richly interspersed with vasculature and thinly protected by a delicate fibrous capsule with limited internal fibrous support. This makes them prone to

fracture and laceration with blunt abdominal trauma. Our current standard surgical armamentarium for extensive liver injuries is limited direct suture ligation of parenchymal blood vessels and biliary channels, and parenchymal edge compression with through-and-through mattress sutures tied over free omental pledgets, omental wrapping, packing with reexploration,^{1,3,5,8} mesh hepatorrhaphy,⁶ fibrin sealant,⁹ and ultrasonic aspiration with argon beam coagulation.¹⁰

The use of laser energy to join tissue by heating a protein solder, typically albumin, is referred to as “tissue welding.”¹¹ Poppas et al. first demonstrated laser soldering using liquid albumin solder to anastomose rat urethras in 1988.¹² Oz et al. recognized that adding a light-absorbing chromophore to the albumin would both decrease collateral tissue damage and reduce the amount of laser light required for soldering.¹³ Furthermore, by using indocyanine green (ICG) as the exogenous chromophore, Oz et al. were able to use diode laser operating at 800 nm. These lasers have the advantage of being relatively inexpensive, and their near-infrared light is poorly absorbed by tissue. More recently, Poppas et al. have used highly concentrated albumin solders to improve laser repair strengths,¹⁴ and others have used solid albumin strips.¹⁵ Finally, our group and others have used pulsed lasers to further reduce collateral thermal damage during laser repairs.¹⁶ To date, laser soldering applications have not shown a clear benefit over conventional suture repair, and have not gained clinical acceptance.

In this study, we evaluated laser soldering and modified it for use in the repair of tissues that suture poorly such as solid visceral organs including the liver, spleen, and kidney. We report on a series of acute laser-mediated repairs as well as results of chronic 4-week animal experiments that show

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Table 1 Classification of Liver Trauma (Modified after Moore et al.¹⁷)

Grade	Description of Injury
I	Capsular tear or avulsion Superficial parenchymal injury (<1 cm)
II	Superficial parenchymal injury (1–3 cm deep) Subcapsular hematoma <10 cm Peripheral penetrating wound
III	Deep parenchymal injury (>3 cm) Subcapsular hematoma >10 cm Central penetrating wound Intrahepatic hematoma <3 cm Hilar injury (portal vein branch, hepatic artery branch, hilar ducts)
IV	Massive injury to one lobe Devascularization of more than one segment Intrahepatic hematoma >3 cm Injury to portal vein, hepatic artery, or major branch
V	Extensive liver injury to both lobes Bleeding from hepatic veins or vena cava Retrohepatic vena cava injury

that laser soldering is a promising technique for repairing the liver.

MATERIALS AND METHODS

Two types of liver injury (laceration and segmentectomy) were repaired using conventional suture techniques and by laser soldering. The laceration model was intended to approximate a penetrating knife injury or an isolated liver fracture accompanying blunt trauma, with viable parenchyma on both sides (i.e., grade III on the organ injury scale¹⁷) (Table 1). The raw surface injury or nonanatomic segmentectomy was intended to simulate surgical resection of 40% to 50% of a liver lobe that had been pulverized and shattered by blunt trauma (i.e., a grade IV injury¹⁷) (Table 1). Sixteen acute laser repairs (eight laceration injuries and eight segmentectomies) were evaluated at 3 hours, as were the conventional suture repairs. These repairs were evaluated in terms of intraoperative blood loss, level of hemostasis, and histologic changes at the repair site. Eleven animals (six with laceration injury and five with segmentectomy) were evaluated in a chronic survival study.

Surgical Procedure

All experiments were performed in accordance with the 1996 National Research Council *Guide for the Care and Use of Laboratory Animals* and applicable federal regulations. After proper identification of the animal, anesthesia was induced with tiletamine/zolazepam (Telazol) 8 mg/kg intramuscularly. Isoflurane was given by mask and the animal was intubated. The animal was preloaded before surgery with 4 mL/kg of lactated Ringer's solution, 40 mg of intravenous furosemide (Lasix), and 50 mEq of NaHCO₂ to prevent hypotension, renal failure, and acidosis that is anticipated during and after the clamping of the porta hepatis. Twenty

minutes before the skin incision, a single dose of cefotetan (Cefotan) 500 mg intravenously was given. After initial heparinization with 5,000 units of intravenous heparin, the right femoral artery was cannulated and the arterial blood pressure was monitored. The activated clotting time was monitored preoperatively, after heparinization, and at hourly intervals. The activated clotting time was kept above 200 by adjusting the heparin dosage. This was intended to simulate coagulation failure. The 16 domestic swine used in the acute (3-hour) experiments weighed 31 to 36 kg, and the 11 animals used in the chronic survival study weighed 18 to 23 kg.

The abdomen was opened using a right subcostal incision. A 10 × 10-cm piece of the greater omentum was harvested and kept aside in normal saline solution. The hepatic inflow was encircled with a 4-mm polytetrafluoroethylene (Teflon) tape and occluded using the Pringle maneuver to reduce bleeding in the operative field. All injuries were measured with a ruler. The laceration injury (6 cm long × 2 cm deep) was made using a scalpel incision in the medial segment of the right lobe of the liver. Resecting 40% to 50% of the inferior medial segment of the left lobe created a raw liver surface injury, leaving a surface 8 cm long and 2 cm wide.

The liver was repaired using either laser soldering or conventional suture technique. The hepatic inflow clamp time was not allowed to exceed 10 minutes at a time, with reperfusion instituted for 5 minutes. The total cross-clamp time was between 5 and 22 minutes. This level of induced ischemia was reversible, and no liver dysfunction was manifested postoperatively. In the acute study, the animals remained under anesthesia for 3 hours and were inspected for dehiscence, bleeding, or biliary leakage at the repair sites. In the 2- and 4-week-survival animals, the abdomen was closed in layers without drains. These animals were weaned from anesthesia and extubated. The pigs resumed oral feeding ad libitum 1 hour after recovery from anesthesia. Liver function was monitored preoperatively and 3 days after surgery. No antibiotics were given postoperatively.

Albumin Solder

All laser repairs used viscous solder that contained 50% to 53% (w/v) human serum albumin. The solder was obtained by concentrating 25% human serum albumin using drying and pressure filtration techniques. The concentrated human serum albumin was sterilized using gamma radiation (25 kGy). ICG, a chromophore, was added to the albumin, as 800-nm laser light is selectively absorbed by this chromophore. ICG powder was dissolved in distilled water and sterilized by double filtration through a 0.22- μ m filter. The sterile albumin and ICG were mixed using all aseptic precautions under a laminar flow hood. The solder was repackaged in sterile 5-mL syringes and sealed in presterilized peel packs. About 4 to 5 mL of viscous albumin-ICG solder was used for each experiment. The ICG concentration was 0.09 to 0.11 mmol/L or the solder had an absorption coefficient of 50

cm^{-1} at 805 nm. On the basis of this absorption coefficient, the light is expected to penetrate approximately 200 μm . Spectrophotometric analysis of all solders was accomplished using a Hewlett-Packard model 8452-A diode array spectrophotometer (Hewlett-Packard Co., Palo Alto, CA). This analysis was performed to determine the peak absorption wavelength for each chromophore-enhanced solder and to verify that no shift in peak absorbency occurred when the chromophore was added to the 53% albumin solder.

Laser Delivery System

For the acute experiments, we used an 805-nm pulsed diode laser (Diomed 25) purchased from Diomed Ltd. (London, England). For the chronic study, we used a custom-built system (Coherent FAP) made by Coherent Inc. (Sunnyvale, CA). The diode laser delivered 100-ms light pulses separated by 100 ms into an optical fiber for a total power delivery of 3.6 to 6 W. A collimating microlens (NSG America, Inc., Somerset, NJ) was mounted on the end of the fiber. The microlens face was maintained at a distance of 1 to 3 cm from the surface of the liver and had a spot size of approximately 2 to 4 mm. Before each experiment, the fiber output was calibrated with a power meter. Laser light was delivered to each spot until the green albumin solder visibly blanched.

Laceration Repair

The laceration injury consisted of a single incision (6 cm long and 2 cm deep) made in the medial segment of the right lobe of the liver. One liver laceration in a single animal was repaired using conventional suture techniques. Laser soldering repaired 14 liver lacerations: eight were evaluated acutely after 3 hours, one at 2 weeks, and five at 4 weeks.

For the suture repair, all the individual vessels and bile ducts severed by the laceration that were more than 3 mm in diameter were ligated using 3-0 Vicryl figure-of-8 sutures. Chromic catgut 1-0 on a taper needle was used to place large figure-of-8 sutures to approximate the edges and achieve hemostasis. These sutures were placed about 8 to 10 mm away from the lacerated edge. After placing several sutures, the hepatic inflow clamp was released and the time for the Pringle maneuver was 11 minutes. Additional sutures were placed to achieve hemostasis as needed. Small residual capillary oozing was controlled with electrocautery. After hemostasis, the liver was lightly packed with gauze pieces.

After 3 hours of liver reperfusion, the gauze pieces were removed and the volume of blood loss was measured by subtracting the dry gauze weight from the soaked gauze weight.

For the laser repair, all liver venous sinuses larger than 5 mm were soldered individually by spreading albumin solder over the exposed sinuses and irradiating with the laser. Once these sinuses were closed, the entire incision was filled with albumin solder and the edges were coated manually with finger pressure. As this was done, most of the albumin solder was pushed out of the incision. The surface incision was then

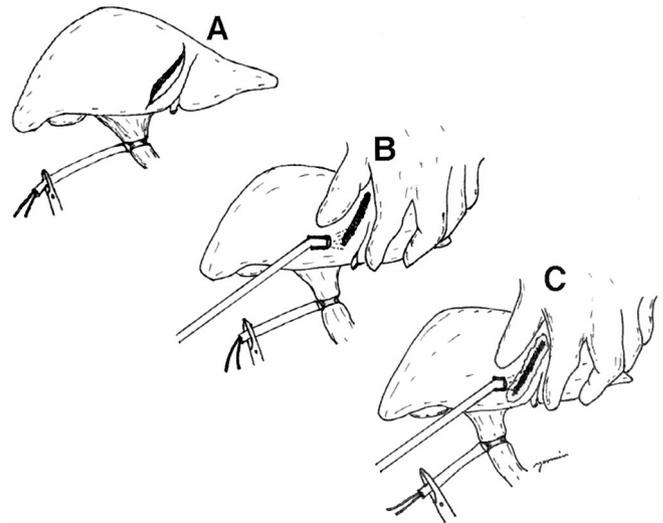


Fig. 1. Laser repair of the laceration injury begins with the Pringle maneuver (A), fusing the top edges of the laceration together (B), and followed by fusing autologous free omentum to scaffold the repair (C).

coated with a thin layer of solder and irradiated to fuse the two edges together (Fig. 1B). The albumin solder changed visibly during irradiation from a viscous dark green liquid to a light green crust. The laser irradiation was not continuous, but typically consisted of several 5- to 20-second periods of laser irradiation. A piece of free autologous omentum was fused over the laser-soldered repair to scaffold and reinforce the laceration extending 5 mm on each side and often done without a cross-clamp, as the first layer was generally completely hemostatic (Fig. 1C).

Resection Surface Repair

A portion of the medial segment of the left lobe of the liver was resected to create a raw surface 6 to 10 cm long and 2.0 to 2.5 cm wide. In one acute animal, this raw surface was repaired using conventional suture techniques. Laser soldering repaired 13 resected surfaces: eight were evaluated at 3 hours, one at 2 weeks, and four at 4 weeks.

In the resection surface repaired by suturing, the severed individual vessels and bile ducts were ligated. Chromic catgut 1-0 on a BP taper needle was used to place large horizontal mattress sutures on the resected edge of the liver 8 to 10 mm away from the edge to achieve hemostasis. Additional sutures were needed after release of the Pringle maneuver and additional point hemostasis was achieved with electrocautery. The clamp time was 9 minutes. The liver was lightly packed with gauze pieces. After 3 hours of liver reperfusion, the blood-saturated gauze pieces were removed and the total blood loss measured.

For the laser-repaired resection surfaces, all the venous sinuses larger than 5 mm were soldered individually first. Next, a thin layer of albumin solder was spread over the

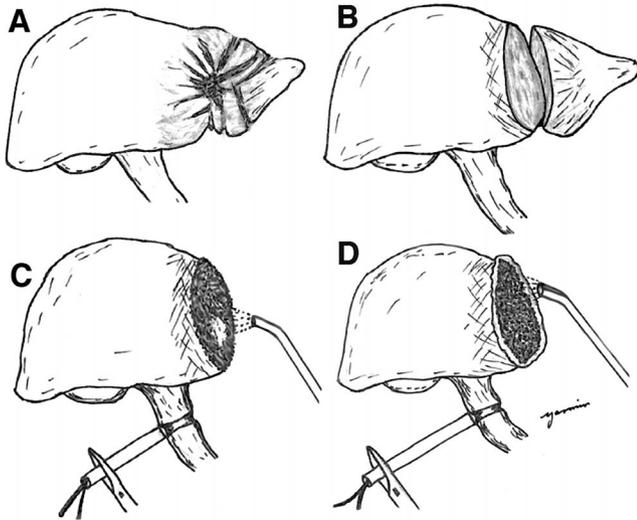


Fig. 2. Laser repair of the blunt trauma injury begins with the Pringle maneuver, resecting the damaged parenchyma, sealing the raw surface, and finally fusing autologous free omentum to scaffold the repair.

entire resected surface and irradiated until a color change was seen. Every repaired raw surface was recoated with albumin solder and covered with autologous omentum that was soldered to the surface (Figs. 2 and 3).

RESULTS

All 16 acute laser-soldering experiments yielded uniformly positive results, with no evidence of dehiscence and with minimal blood loss after 3 hours of heparinization and with normothermic, normotensive liver perfusion (Figs. 3 and 4). The size of the acute laceration was 5.9 ± 0.4 cm in length and 2.3 ± 0.5 cm in depth. The time taken to solder this lesion was 12.5 ± 3.8 s/cm², for a total surface area of 13.8 ± 0.7 cm². The blood loss was 5.4 ± 1.3 mL (Table 2). The size of the raw liver surface repaired was a mean of 7.8 ± 1.9

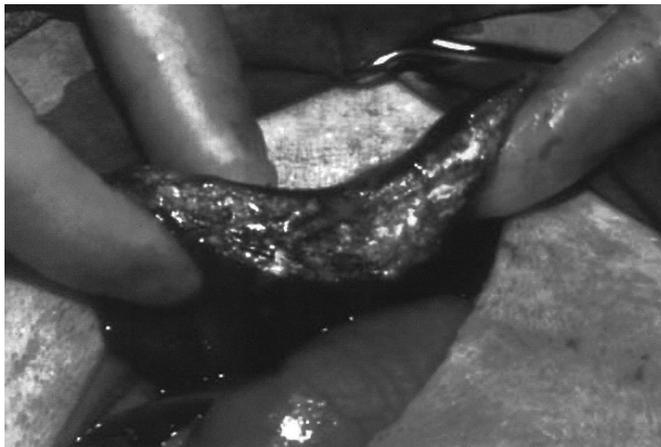


Fig. 3. Laser-repaired resection surface of the left lobe of the liver as seen after release of the hepatic inflow clamp. Hemostasis was achieved before fusing the omentum.

cm in length and 2.3 ± 1.0 cm in width. The time taken to solder this lesion was 9.4 ± 1.7 s/cm², for a total surface area of 37.4 ± 24.4 cm². The blood loss was 5.9 ± 2.0 mL (Table 3).

After 3 hours, all conventional suture repairs were accompanied by grossly visible ischemic changes 1 cm from the edge of the repair that corresponded to the line of compressing mattress sutures. There was a continuous oozing of blood from the sutured raw liver surface, most prominently from the hepatic vein radicals, and the total blood loss was approximately 300 mL as collected by suction and weighing the gauze pieces. The laceration repair was hemostatic after 3 hours, with a total blood loss of about 50 mL.

In the chronic laser fusion survival study, the animals started eating within an hour after the operation. Liver function tests were performed preoperatively and 72 hours postoperatively. The liver function tests performed were total serum bilirubin with direct and indirect fractions, serum glutamic-oxaloacetic transaminase, serum glutamic-pyruvic transaminase, serum alkaline phosphatase, total serum protein, serum albumin, serum globulin, and their ratio. All 72-hour postoperative liver function tests were normal.

The postoperative period was uneventful for all 11 animals. At 2 and 4 weeks, when the animals were killed, both injury models had healed and there was no evidence of biliary leakage, resolving hematoma, or abscess formation. The repaired areas revealed a regenerated remodeled liver.

Histologic examination of the laser-repaired laceration injury showed thermally denatured albumin near the surface of the incision (Fig. 5A and B). A thin shaft of amorphous material defined the rest of the coapted laceration with no evidence of albumin. Complete cell membrane and nuclear disruption was present in the first four to five cell layers ($50 \mu\text{m}$) below the albumin. Since the animals were killed after 3 hours, apoptotic cellular effects of the thermal injury may probably extend 100 to $500 \mu\text{m}$ below this region. Histologic examination showed that the acute laser-repaired liver resec-

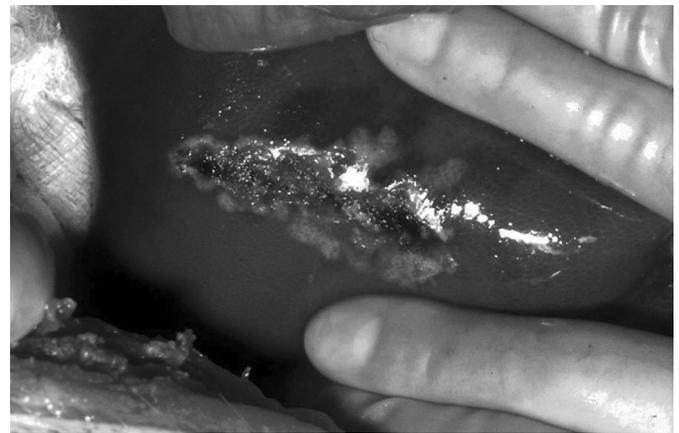


Fig. 4. Laser-repaired liver laceration as seen after release of the hepatic inflow clamp. The laser-soldering zone extends 5 to 8 mm on each side of the incision. Hemostasis was achieved before fusing the omentum for additional support.

tion surfaces were characterized by a layer of denatured albumin solder covered by an outer layer of omentum (Fig. 6A and B). Again, the first four to five cell layers exhibited complete disruption of cell membranes with progressively less cellular damage evident down below the surface.

Two weeks after laceration repair, the denatured albumin was replaced by fibrous tissue, and fibroblasts had infiltrated the soldered site (Fig. 5C and D). Histologic examination performed on the 4-week specimens prepared using a Movat stain showed an inner yellow zone of mature fibrous tissue containing collagen, with an outer blue zone denoting preponderance of proteoglycans and early granulation tissue. The omental scaffold had transformed into an outer capsule containing elastic fibers (Fig. 5E and F).

Two weeks after raw liver bed repair, some denatured albumin remained at the surface and the soldered liver surface had healed, covered by a layer of fibrous tissue (Fig. 6C and D). The 4-week specimens had some residual denatured albumin solder that was being removed by phagocytes. A layer of mature fibrous tissue covered the liver surface and an outer capsule of dark elastic fibers walled off the entire region.

DISCUSSION

Surgery of solid visceral organs such as liver, spleen, and kidney has always proved to be challenging, as these organs bleed profusely if traumatized, and hold sutures rather poorly. This is because they have a soft, richly vascular parenchyma with limited internal fibrous support that is thinly protected by a delicate fibrous capsule. Cogbill et al.,¹⁸ in a multicenter experience with 1,335 severe liver injuries, cited 25%, 46%, and 80% mortality rates with classes III, IV, and V of hepatic trauma, respectively.

Certain groups of moribund patients would benefit from limited nonanatomic segmental resections because the raw surfaces of the liver could be easily repaired with laser-mediated fusion of human albumin used as a solder. Two groups of patients come to mind that might be benefited. One group consists of primary hepatocellular carcinoma in cir-

rhotic patients with limited hepatic reserve and underlying liver dysfunction,^{19–23} and patients in the second group have secondary neoplastic lesions in the liver that can be multiple and recurrent.^{24–28} In instances where large raw surfaces are encountered such as bifurcated liver transplantation and living-related liver transplantation, the raw surfaces of the liver could be easily repaired with laser-mediated fusion of human albumin used as a solder.

The use of lasers to control hemorrhage in the liver has had limited success in the past. Attempts at hemostasis using the CO₂ laser have failed to show significant benefit when compared with the diathermy.²⁹ Other work³⁰ showed that the CO₂ laser is ineffective at sealing vessels larger than 1 mm and that argon and neodymium:yttrium-aluminum-garnet lasers are ineffective at stopping flow in vessels larger than 4.5 mm. These lasers achieve hemostasis by extensive (5–10 mm) thermal coagulation of parenchyma. We believe that incorporating albumin solder into our laser repairs is the primary reason for our success in controlling hemorrhage; the denatured albumin may plug all the severed biliary and venous radicals, and native tissue coagulation is not necessary. This is particularly important because necrotic tissue impairs wound healing, whereas bile leakage induces a fibrinous exudate, leading to the formation of biliary fistulae. This may contribute to postoperative complications of secondary hemorrhage, peritonitis, and abscess formation.

In liver surgery, rapid hemostasis in the presence of coagulation failure may be necessary. In the presence of heparinization, laser-mediated repairs of the segmental resections were completely hemostatic at a rate of 9.4 ± 1.7 s/cm² of laser irradiation of raw liver surface. The lacerations were repaired at a rate of 12.5 ± 3.8 s/cm² of laser irradiation. Reinforcement by a free omental scaffold gave the repairs a measured continuity and prevented accidental delamination of the soldered albumin from the liver. The omental scaffold also increases the welded surface area holding the lacerated edges together, much like an integumentary bandage across the cut edges. This modality effectively seals the liver surface

Table 2 Acute Liver Resected Laceration Repair

Study	Length (cm)	Depth (cm)	SA (cm ²)	Blood Loss (mL)	Time (seconds)	Time/SA (s/cm ²)
1	5.0	3.0	12.0	5	170.0	14.2
2	6.0	2.0	14.0	6	140.0	10.0
3	6.0	3.0	14.0	5	218.0	15.6
4	6.0	2.0	14.0	8	146.0	10.4
5	6.0	2.0	14.0	4	107.0	7.6
6	6.0	2.0	14.0	6	131.0	9.4
7	6.0	2.0	14.0	5	269.0	19.2
8	6.0	2.0	14.0	4	189.0	13.5
Total (n)	8	8	8	8	8	8
Mean	5.9	2.3	13.8	5.4	171.3	12.5
SD	0.4	0.5	0.7	1.3	52.7	3.8
SE	0.1	0.2	0.3	0.5	18.6	1.4

SA, surface area.

Table 3 Acute Liver Resected Surface Repair

Study	Length (cm)	Width (cm)	SA (cm ²)	Blood Loss (mL)	Time (seconds)	Time/SA (s/cm ²)
1	6.5	1.5	19.5	8	146	7.5
2	6.0	2.0	24.0	5	203	8.5
3	7.0	2.0	28.0	3	195	7.0
4	6.5	1.5	19.5	5	236	12.1
5	6.0	1.5	18.0	4	188	10.4
6	10.0	4.0	80.0	6	865	10.8
7	10.0	3.5	70.0	8	667	9.5
8	10.0	2.0	40.0	8	370	9.3
Total (n)	8	8	8	8	8	8
Mean	7.8	2.3	37.4	5.9	358.8	9.4
SD	1.9	1.0	24.4	2.0	265.1	1.7
SE	0.7	0.3	8.6	0.7	93.7	0.6

SA, surface area.

and joins lacerations with minimal thermal injury and works independently of the patient's coagulation status.

One drawback to laser soldering is that a dry operating field is mandatory, and therefore the Pringle maneuver is necessary to perform the procedure. Therefore, for grade IV

and V liver trauma repair, total hepatic isolation may be necessary. That the human liver can safely tolerate ischemia times beyond 20 minutes is irrefutable.³¹⁻³⁵ The maximal

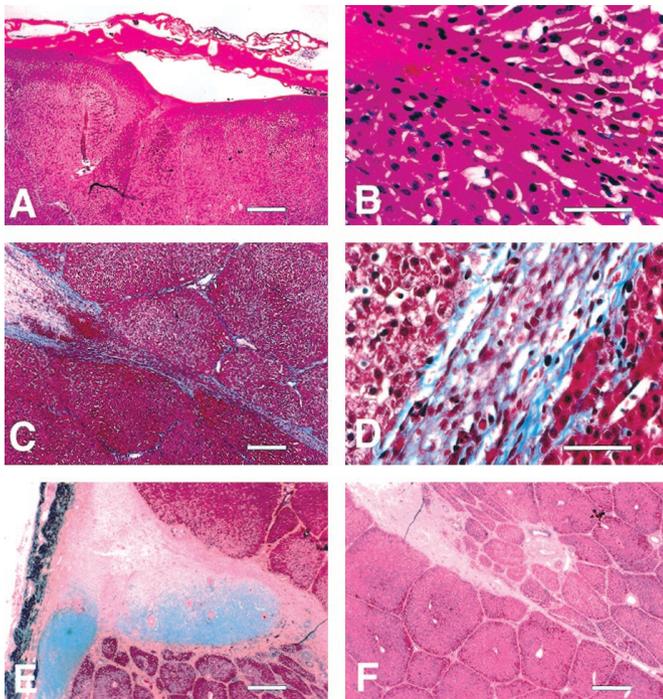


Fig. 5. The laser-repaired laceration injury at 3 hours (A and B, hematoxylin and eosin stain). A, The denatured albumin solder plug fusing the two edges of the laceration. B, The base of the albumin plug and a few red blood cells between the closely approximated cut surfaces of the liver. At 2 weeks, the denatured albumin is replaced by fibrous tissue (C), and which extends into the incision binding it (D). By 4 weeks, complete replacement (E and F) of the albumin by fibrous tissue with early capillary formation has occurred. The incised liver surface is encapsulated with a layer containing elastic fibers. (All bars are 500 μ m long except for those in B and D, which are 50 μ m.)

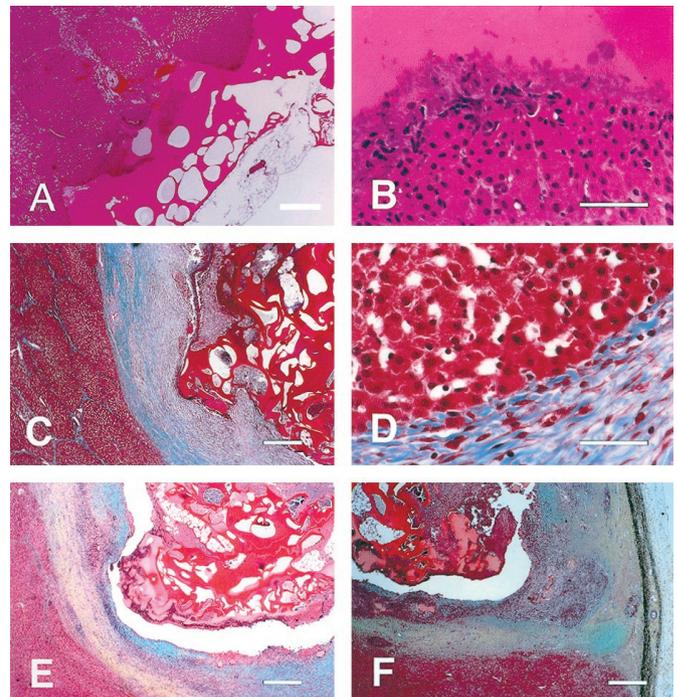


Fig. 6. The laser-repaired resection surface liver injury at 3 hours (A and B, hematoxylin and eosin stain). A, A layer of denatured albumin solder soldering the liver to the omentum. Vapor bubbles formed during laser irradiation probably cause the spaces in the solder. B, A superficial zone of irreversible thermal damage extending four to five cell layers deep at the surface of the liver. C and D, At 2 weeks, the repaired surface of the liver is completely covered with early fibrous tissue and some residual denatured albumin is present on the outer surface. E and F, At 4 weeks, mature fibrous tissue, early capillary formation, and a foreign body reaction to the residual denatured albumin are apparent. F The liver surface encapsulated with a layer containing elastic fibers. (All bars are 500 μ m long except for those in B and D, which are 50 μ m.)

limit of safe portal triad occlusion is yet to be determined. Data provided by Delva et al.³³ and Bismuth et al.,³⁴ stemming from their work with elective hepatic surgery, documented warm ischemic times of up to 90 minutes, with mean cross-clamp times of 32.3 minutes and 46.5 minutes, respectively. Prolonged warm ischemic times did not adversely affect postoperative stay, incidence of hepatic failure, or mortality. Whether an injured liver that has sustained further damage through periods of hypotension can undergo prolonged portal triad occlusion under normothermic conditions is unknown. Pachter et al.,³⁶ in a series of 81 of 113 surviving patients (72%) with complex hepatic injuries (grades III–V) requiring portal triad occlusion, with a range of ischemic time varying from 10 to 75 minutes, used either a single bolus of large dose steroid (30–40 mg/kg methylprednisolone [Solu-Medrol]) and regional hypothermia where the liver was cooled to 27° to 32°C topically by pouring 1 liter of iced lactated Ringer's solution directly on the liver surface, monitoring the temperature with an intrahepatic probe. The mean ischemia time for the group was 32 minutes. In this study,³⁶ there were no instances of hepatic necrosis or permanent hepatic dysfunction. However, the 10 minutes required to complete a laser repair is well within the ischemic time tolerated by injured liver, and blood loss once vascular control is achieved is negligible. The time required for laser soldering could certainly be shortened by using larger laser spot sizes in a continuous mode rather than a pulsed mode with correspondingly higher laser pulse energies. It was also noticed that eye-hand coordination was operator dependant and welding speed improved over time. Another decided advantage of laser soldering is that the 800-nm laser energy is selectively absorbed by ICG dye, and accidental misdirection of the laser beam at the energy levels we use has no effect on the surrounding viscera.

I would like to address the reasons for the changes made to the laser delivery systems between the acute and chronic experiments. The Diomed laser system used for the acute experiments had a doughnut-shaped beam profile with a central laser energy-free zone. The beam was also divergent and therefore it was difficult to get uniform albumin coagulation at varying distances. The Diomed laser system's aiming beam was red, which made it difficult to see the zone being lased on the "red" liver, and adequate soldering is a visually qualified process determined by a change in the color and texture of the albumin solder from a dark green liquid to a white solid crust. The Coherent FAP system was custom made to address the inadequacies of the Diomed system. The laser beam had a uniform profile, was collimated, and the aiming beam was eliminated. Thus, the coagulation was uniform and allowed a variable working distance.

While trying to extrapolate this laser welding technique for human use, we found that human omentum was thick and fatty and could not be used as a scaffold. For human use, a new biomaterial was created. This biomaterial is a solid sheet of pure denatured human albumin 200 to 250 μm thick

(patent pending). On gross examination, it is a transparent, pliable material that contours easily, is insoluble in water, and welds easily. It is made using 25% human serum albumin dehydrated to a concentration of 50% to 57% (w/v) as detailed above. About 1 mL is interspersed between two plastic sheets and rolled through a metal roller set at a predetermined distance (100–300 μm). This is immediately immersed in a water bath at 90° to 100°C for 1 minute. The denatured sheet is vacuum packaged first and then gamma sterilized after double packaging.

The thermal damage sustained by the liver is significantly less for laser-soldered repairs (50–500 μm) than any other modality currently in use. During laser soldering, thermal damage is confined primarily to the albumin on the surface, and heating of the surface of the liver is indirect by thermal diffusion. This depth of damage is about an order of magnitude smaller than that of other techniques that rely on thermal coagulation of parenchyma to achieve hemostasis (e.g., electrocoagulation, argon ion beam coagulation,¹⁰ and focused ultrasound³⁷). A significant layer of ischemic parenchyma that may eventually become necrotic with attendant complications accompanies even suture repair.

Fibrin glue, a combination of fibrinogen, thrombin, and calcium chloride, has been found to be very effective in controlling oozing from raw liver surfaces. Disadvantages of fibrin glue include hypotension if the agent enters the bloodstream, which has led to the death of two patients.³⁸ Acute animal studies⁹ using the recently Food and Drug Administration approved dry fibrin sealant dressings in hypothermic coagulopathic pigs showed posttreatment blood loss ranging from 353 to 1,268 mL within 1 hour and a mortality of 17% at 1 hour. A possible delayed drawback of this treatment is that the dressing pad containing the fibrin sealant is made of Vicryl and could induce a foreign body reaction.

Perihepatic packing is used as a last resort in hypothermic coagulopathic liver trauma patients after repeated attempts at direct surgical control have failed. Subhepatic packing has a significant risk of infrahepatic caval and renal vein compression causing decreased venous return to the heart³⁹ and abdominal compartment syndrome.⁴⁰ It may further compromise ventilation and bowel viability, and cause possible pressure necrosis of the liver.⁵ Removal of the packs may be complicated by rebleeding⁴¹ (Table 4).^{4,5,42–47} In spite of broad-spectrum antibiotics, sepsis has been reported to occur in 10% to 30% of patients.^{5,18,44,45,48}

Argon-enhanced coagulation is a method for operative coagulation of tissues that uses a jet of argon gas encompassing an electrofulguration arc. The argon beam essentially scorches the liver parenchyma, causing coagulative necrosis, and all visible vessels have to be individually underrun with suture. This modality produces venous gas emboli when used on the liver,⁴⁹ with reported fatalities when used laparoscopically.⁵⁰ In a compromised unstable trauma patient, this can possibly precipitate pulmonary dysfunction and adult respiratory distress syndrome. In animal studies,⁵¹ mi-

Table 4 Data from Liver Packing Studies for Hemorrhage

Author and Year	No. of Patients	No. of Patients Packed	Packing Mortality (%)	No. and Type of Complications
Feliciano et al., 1981 ⁴²	465	10	1 (10)	Abscess, 4; hematoma, 1; renal leak, 1; respiratory failure, 4; renal failure, 2
Svoboda et al., 1982 ⁴³	109	12	2 (17)	Rebleeding on removal of packs, 4
Carmona et al., 1984 ⁴⁴	443	17	2 (12)	Subphrenic abscess, 5
Feliciano et al., 1986 ⁴⁵	1,348	66	38 (58)	ARDS, 5; intra-abdominal fluid collection, hematoma, or abscess, 10; biliary fistula, 2; partial small bowel obstruction, 1; renal leak, 1; renal failure, 1; phlebitis, 1; bronchobiliary fistula, 1
Ivatury et al., 1986 ⁴⁶	345	14	8 (57)	Intra-abdominal sepsis, 5; biliary fistula, 2
Baracco-Gandolfo et al., 1986 ⁴⁷	79	36	6 (17)	ARDS, 2; intra-abdominal abscess, 4; pneumonia, 15
Cue et al., 1990 ⁵	Not stated	35	17 (50)	Intra-abdominal abscess, 7; wound infection, 4; pneumonia, 3
Beal, 1990 ⁴	683	35	5 (14)	Intra-abdominal abscess, 7
Pachter et al., 1992 ³⁶	411	6	2 (33)	Intra-abdominal abscess, 1; bile fistula, 1

ARDS, adult respiratory distress syndrome.

oscopic examination of the injury sites revealed zones of carbonized tissue debris, coagulation necrosis, interstitial hemorrhage, and edematous normal tissue. A thin layer of coagulation necrosis remained at 3 weeks. The coagulation injury required to achieve hemostasis was 5 mm in the liver. The energy required to obtain hemostasis in the liver has been shown to cause significant injury when used on small bowel.⁵² At its lowest energy output (40 W) and a tissue interaction time of 1 second, the argon beam coagulator occasionally produced delayed bowel perforation. In a clinical study of 150 hepatic resections by Rees et al.¹⁰ using intermittent portal inflow occlusion, ultrasonic aspiration, and argon beam coagulation, there was a mean blood loss of 814 mL and a 10% rate of significant complications.

If laser soldering can indeed reduce the morbidity and mortality associated with bleeding, biliary leakage, and sepsis after liver surgery, then it may be possible to resect directly invading tumors and primary hepatomas buried deep within the parenchyma, because the raw liver surfaces could be soldered with the laser. All major hepatic resection for trauma or malignancy may no longer need to be performed along anatomic planes; laser soldering could make it possible to resect damaged or diseased liver along nonanatomic planes, thereby simplifying surgery and preserving hepatic parenchyma. An additional advantage is that with laser soldering we can fuse fractured viable liver edges together, a feat not achieved by any other treatment modality. Finally, laser soldering may be translated to the repair of other solid visceral organs such as the spleen and kidney.

CONCLUSION

Laser-mediated fusion of human albumin used as solder opens up unexplored possibilities for the surgeon to take up new challenges. It could potentially be used for nonanatomic liver resections, thereby conserving hepatic parenchyma, both in severe trauma as well as in elective hepatic resections. It is

safe, quick, reliable, and straightforward; has a short learning curve; and works even in the presence of coagulation failure with minimal collateral damage.

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