

# Liver Repair and Hemorrhage Control Using Laser Soldering of Liquid Albumin in a Porcine Model

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## ABSTRACT

The purpose of this study was to evaluate laser soldering using liquid albumin for welding liver lacerations and sealing raw surfaces created by segmental resection of a lobe. Major liver trauma has a high mortality due to immediate exsanguination and a delayed morbidity and mortality from septicemia, peritonitis, biliary fistulae and delayed secondary hemorrhage.

Eight laceration injuries (6cm long x 2cm deep) and eight non-anatomical resection injuries (raw surface 6cm x 2cm) were repaired. An 805nm laser was used to weld 53% liquid albumin-ICG solder to the liver surface, reinforcing it with a free autologous omental scaffold. The animals were heparinized to simulate coagulation failure and hepatic inflow occlusion was used for vascular control. For both laceration and resection injuries, eight soldering repairs each were evaluated at three hours. A single suture repair of each type was evaluated at three hours.

All 16 laser mediated liver repairs were accompanied by minimal blood loss as compared to the suture controls. No dehiscence, hemorrhage or bile leakage was seen in any of the laser repairs after three hours.

In conclusion laser fusion repair of the liver is a quick and reliable technique to gain hemostasis on the cut surface as well as weld lacerations.

Key Words: Laser, tissue welding, Albumin solder, Indocyanine green, liver trauma.

## 1. INTRODUCTION

The management of liver trauma continues to evolve. The liver is the most commonly injured organ following abdominal trauma. It is the second most commonly injured in blunt injuries and the third most commonly injured in penetrating injuries.<sup>1,2</sup> Exsanguinating hemorrhage remains a significant cause of immediate mortality.<sup>3-5</sup> A 3-cm parenchymal depth laceration has 19% mortality and a parenchymal disruption involving 25-50% of a hepatic lobe has 28% mortality. Few intra-abdominal injuries are as technically demanding as a major liver laceration and it requires erudite judgement and innovative surgical techniques to prevent intraoperative exsanguination accelerated in some cases by hemodilution and coagulopathy.

Solid visceral organs like 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 lacerate with blunt abdominal trauma. Our current standard surgical armamentarium for liver lacerations is limited to mass ligation of the lacerated liver with absorbable sutures, omental wrapping and packing with re-exploration.<sup>1,4,6,7</sup>

Suture repair of the liver may increase parenchymal damage and ischemic tissue loss. Packing may be complicated by persistent hemorrhage and/or abdominal compartment syndrome and requires re-exploration to remove the packing. Biliary fistulae, abscess formation and secondary hemorrhage can also complicate this technique.

The use of laser energy to join tissue by heating a protein solder, typically albumin is referred to as 'tissue welding'.<sup>8</sup> Poppas first demonstrated laser soldering using liquid albumin solder to anastomose rat urethras in 1988.<sup>9</sup> Oz 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.<sup>10</sup> Furthermore, by using Indocyanine green as the exogenous chromophore, Oz was able to use diode laser operating at 800nm. These lasers have the advantage of being relatively inexpensive and their near-infrared light is

poorly absorbed by tissue. More recently, Poppas has used highly concentrated albumin solders to improve laser repair strengths<sup>11</sup> and others have used solid albumin strips.<sup>12</sup> Finally, our group and others have used pulsed lasers to further reduce collateral thermal damage during laser repairs.<sup>13</sup> To date, laser soldering applications have not shown a clear benefit over conventional suture repair, and have not gained clinical acceptance.

In this paper we evaluate laser soldering and have modified it for use in the repair of tissues that suture poorly such as solid visceral organs, like liver, spleen and kidney. We report on a series of acute laser repairs that show that laser soldering is a promising technique for repairing the liver.

## 2. METHODS

Two types of liver injury (laceration and segmentectomy) were repaired using conventional suture techniques and by laser soldering. The laceration model is intended to approximate a penetrating knife injury or an isolate liver fracture accompanying blunt trauma. The non-anatomical segmentectomy simulates surgical resection of the portion of a liver that has been pulverized and shattered by blunt trauma. The laser repairs were evaluated at 3 hours, as were the conventional suture repairs. All repairs were assessed in terms of intra-operative blood loss, level of hemostasis, and ischemic changes at the repair site.

### 2.1 Surgical Procedure:

All experiments were performed in accordance with the 1996 National research Council, "Guide for the Care and Use of Laboratory Animal" and applicable Federal regulations.

After proper identification of the animal, anesthesia was induced with Telazole 8mg/Kg I/M. Isoflurane was given by mask and the animal was intubated. The animal was preloaded prior to surgery with 4cc/kg of ringer's lactate, 40mg of lasix and 50mEq of NaHCO<sub>2</sub> to prevent hypotension, renal failure and acidosis that is anticipated during and after the clamping of the porta-hepatis. After heparinization with 5000 units heparin I/V the right femoral artery is cannulated and the arterial blood pressure monitored. Sixteen domestic swine were used in the acute (3-hour) experiment weighing 31-36 kg.

The abdomen was opened using a right subcostal incision. A 10 x10 cm piece of the greater omentum was harvested and kept aside in normal saline solution. The hepatic inflow was encircled with a 4mm Teflon tape and occluded using Pringle's maneuver to reduce bleeding in the operative field. All injuries were measured with a ruler. The laceration injury (6cm long x 2cm deep) was made using a scalpel incision in the medial segment of the right lobe of the liver. Resecting part of the inferior medial segment of the left lobe, leaving a surface 6cm long by 2cm wide created a raw liver surface injury.

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 re-perfusion instituted for 5 minutes. The total cross clamp was between 5-22 minutes. This level of induced ischemia was reversible and no liver dysfunction was manifested post operatively. In this acute study, the animals remained under anesthesia for three hours and were inspected for dehiscence, bleeding or biliary leakage at the repair sites.

### 2.2. Laser Soldering:

All laser repairs used viscous solder that contained 53-55% (w/vol.) human serum albumin. The solder was obtained by concentrating 25% human serum albumin using drying or pressure filtration techniques. Indocyanine green (ICG) was added to the albumin to absorb the laser light. The three-hour experiments used an ICG concentration of 0.12-0.15mM or an absorption coefficient of 45-60 cm<sup>-1</sup> at 805nm. Based upon this absorption coefficient, the light is expected to penetrate approximately 200µm.

These experiments used an 805nm-pulsed diode laser (Diomed 25, Diomed Ltd., London England) for laser soldering. The laser delivered 100ms light pulses separated by 100ms into an optical fiber. The individual pulse energy was 720 mJ for an average power delivery of 3.6 W. A collimating microlens (Optical Fiber Research) was mounted on the end of the fiber. The microlens face was maintained at a distance of 1-3 cm from the surface of the liver and had a spot size of approximately 2-4mm. 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

### 2.3. Laceration Repair:

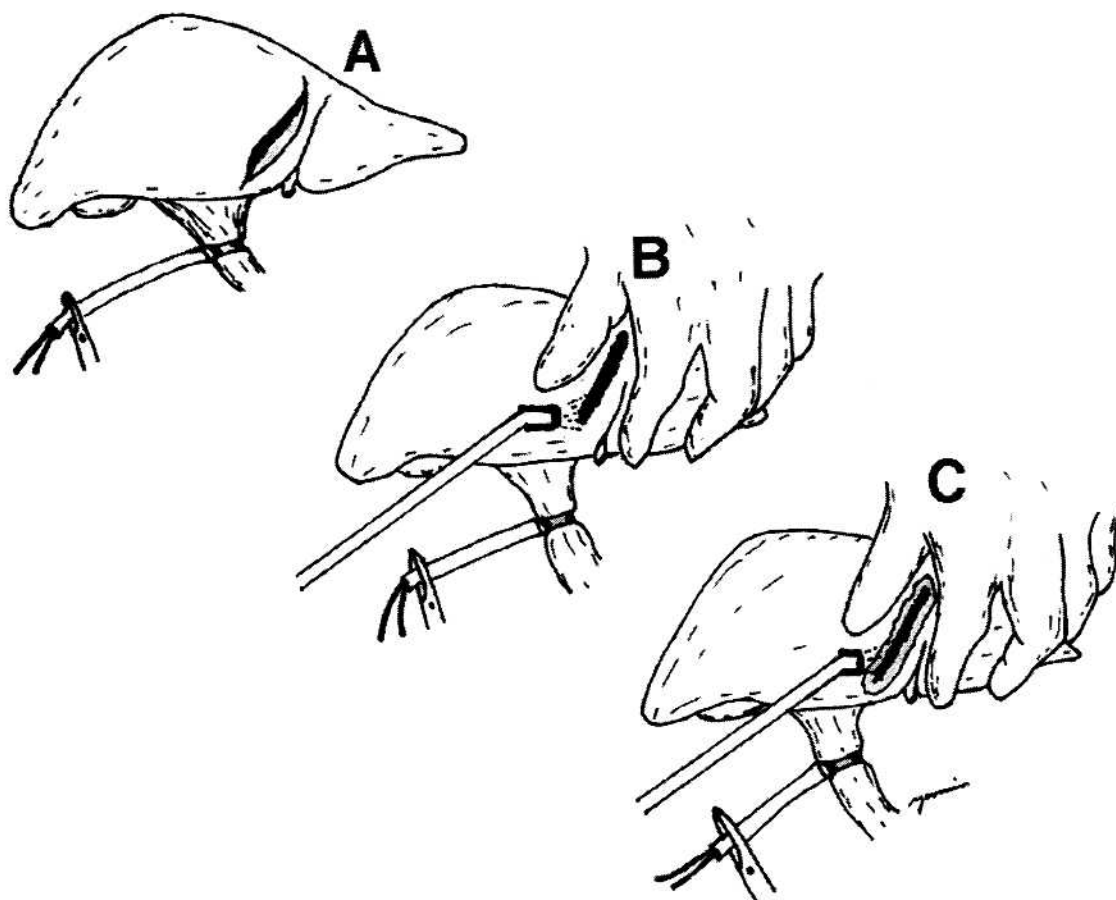
The laceration injury consisted of a single incision (6cm long and 2cm deep) made in the medial segment of the right lobe of the liver. One liver laceration in a single animal was repaired using conventional suture techniques. Laser soldering repaired eight liver lacerations evaluated acutely after 3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

For the suture repair, all the individual vessels and bile ducts severed by the laceration which were more than 3mm in diameter were ligated using 3-0 Vicryl figure-eight sutures. Chromic catgut 1-0, on a BP taper needle was used to place large figure-eight sutures to approximate the edges and achieve hemostasis. These sutures were placed about 8-10mm away from the

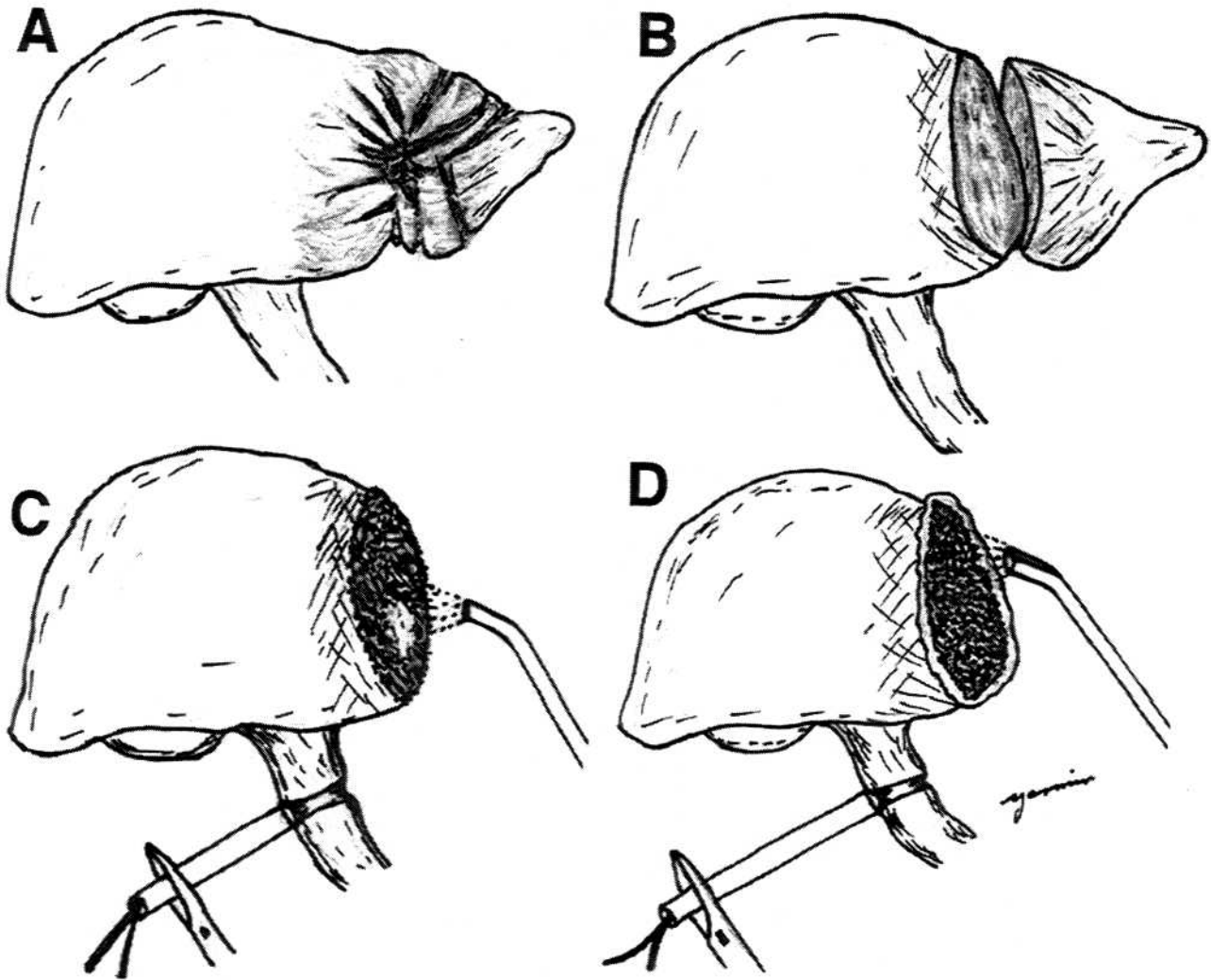
lacerated edge. After placing several sutures, the hepatic inflow clamp was released and the time for the Pringle's maneuver was 11 minutes. Additional sutures were placed to achieve hemostasis as needed. Small residual capillary oozing was controlled with electrocautery. After hemostasis, the liver was lightly packed with gauze pieces.

After three hours of liver reperfusion, the gauze pieces were removed and the volume of blood loss 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 co-apted manually with finger pressure. As this was done, most of the albumin solder was pushed out of the incision. The surface incision was then coated with a thin layer of solder and irradiated to fuse the two edges together (**Figure 1-B**). The albumin solder changed visibly during irradiation from a viscous dark green liquid to a light green crust. A total of approximately  $90 \pm 10$  pulses/cm of laceration or about 1.5-2.0 minutes of laser irradiation was required to repair the entire lesion. The laser irradiation was not continuous, but typically consisted of several 5-20 second periods of laser irradiation. In three of the eight acute laceration injuries, a piece of omentum was fused over the laser-soldered repair to scaffold and reinforce. The free autologous omental scaffold was soldered on the laceration extending 5mm on each side and often done without a cross clamp, as the first layer was generally completely hemostatic (**Figure 1-C**). Fusing the omentum required  $60 \pm 20$  pulses/cm or about one minute of laser irradiation.



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



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

#### 2.4. Resection Surface Repair:

A portion of the medial segment of the left lobe of the liver was resected to create a raw surface 6-8cm long and 2.0-2.5cm wide. In one acute animal, this raw surface was repaired using conventional suture techniques. Laser soldering repaired eight resected surfaces and they were evaluated at 3 hours.

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 8-10mm away from the edge to achieve hemostasis. Additional sutures were needed after release of the Pringle's maneuver and additional point hemostasis was achieved with electrocautery. The clamp time was 9 minutes. The liver was lightly packed with gauze pieces. After three hours of liver reperfusion, the blood saturated gauze pieces were removed and the total blood loss measured.

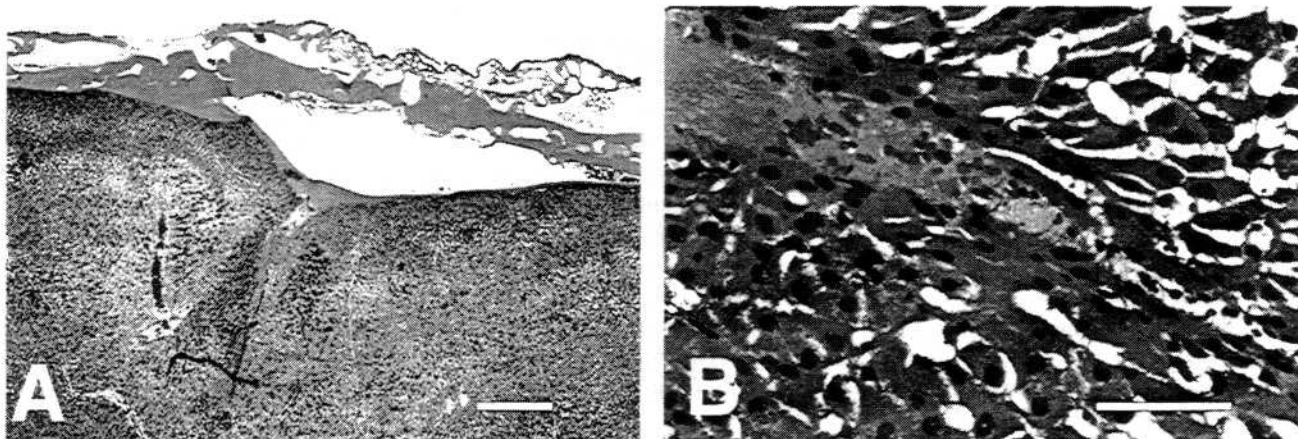
For the laser repaired resection surfaces, all the venous sinuses larger than 5mm were soldered individually first. Next, a thin layer of albumin solder was spread over the entire resected surface and irradiated until a color change was seen. This sealed the surface and required  $12 \pm 5$  seconds of laser irradiation per square centimeter of raw liver surface. Every repaired raw surface was coated with albumin solder and covered with autologous omentum that was soldered to the surface using  $9 \pm 5$  seconds of laser energy per square centimeter of omentum (Figures 2 and 4)



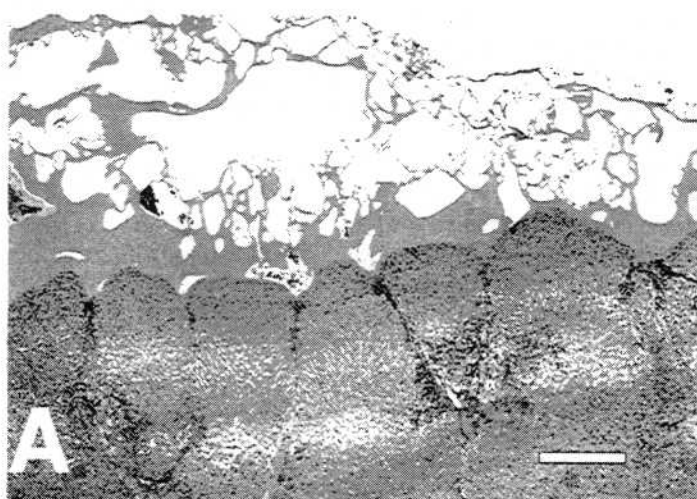
**Figure 3:** Laser repaired liver laceration as seen after release of the hepatic inflow clamp. The laser soldering zone extends 5-8mm on each side of the incision. Hemostasis was achieved before fusing the omentum for additional support.



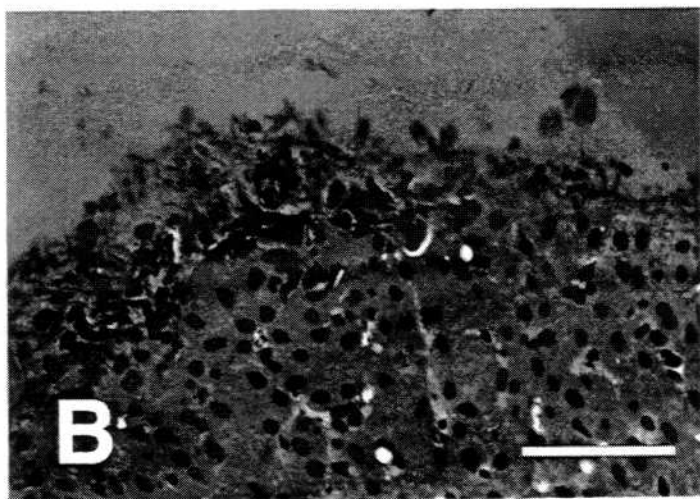
**Figure 4:** Laser repaired resection surface of the left lobe of the liver as seen after release of the hepatic inflow clamp. Hemostasis was achieved before fusing the omentum.



**Figure 5:** The laser repaired laceration injury at three hours. Figure A shows the denatured albumin solder plug fusing the two edges of the laceration. Figure B shows the base of the albumin plug and a few red blood cells between the closely approximated cut surfaces of the liver. (All bars are 500 $\mu$ m long except for those in B and D which are 50 $\mu$ m.)



**Figure 6:** The laser repaired resection surface liver injury at three hours. Figure A shows a layer of denatured albumin solder soldering the liver to the omentum. The spaces in the solder are probably caused by vapor bubbles formed during laser irradiation. Figure B shows a superficial zone of irreversible thermal damage extending 4-5 cell layers deep at the surface of the liver. (All bars are 500 $\mu$ m long except for those in B and D which are 50 $\mu$ m.)



### 3) RESULTS

All 16 acute laser-soldering experiments yielded uniformly positive results, with no evidence of dehiscence and with minimal blood loss (<5ml) after three hours of normothermic, normotensive liver perfusion (**Figures 3 and 4**)

After three hours, all conventional suture repairs were accompanied by grossly visible ischemic changes 1cm 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 three hours with a total blood loss of about 50-ml.

Histological examination of the laser-repaired laceration injury showed thermally denatured albumin near the surface of the incision (**Figure-5**) A thin shaft of amorphous material, defined the rest of the co-opted laceration with no evidence of albumin. Complete cell membrane and nuclear disruption was present in the first 4-5 cell layers (50µm) below the albumin with less severe cellular effects extending 500-1000µm below this.

Histological examination of the acute laser-repaired liver resection surfaces were characterized by a layer of denatured albumin solder covered by an outer layer of omentum (**Figure-6**). Again, the first 4-5 cell layers exhibited complete disruption of cell membranes with progressively less cellular damage evident down to a millimeter below the surface.

### 4. DISCUSSION

Surgery of solid visceral organs like liver, spleen and kidney have 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 which is thinly protected by a delicate fibrous capsule. Elective invasive surgery of the liver, either for removal of primary or secondary neoplastic lesions has a high morbidity associated with secondary hemorrhage and biliary leakage and sepsis especially in this moribund group of patients. Surgery for live related liver transplantation has a potential mortality of 200%.

The use of lasers to control hemorrhage in the liver has had limited success in the past. Attempts at hemostasis using the CO<sub>2</sub> laser have failed to show significant benefit when compared to the diathermy.<sup>14</sup> Other work<sup>15</sup> showed that the CO<sub>2</sub> laser is ineffective at sealing vessels larger than 1 mm and that argon and Nd: YAG lasers are ineffective at stopping flow in vessels larger than 4.5mm. 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 the all severed biliary and venous radicals and native tissue coagulation is not necessary. This is particularly important because necrotic tissue impairs wound healing, while bile leakage induces a fibrinous exudate leading to the formation of biliary fistulae. This may contribute to post-operative complications of secondary hemorrhage, peritonitis and abscess formation.

In liver surgery, rapid hemostasis in presence of coagulation failure may be necessary and all our laser repairs were completely hemostatic at a rate of 12±5 seconds of laser irradiation per square centimeter of raw liver surface. Reinforcement by a free omental scaffold gave the repairs a measured continuity and prevented the accidental de-lamination of the soldered albumin.

One draw back to laser soldering is that a dry operating field is mandatory and therefore Pringle's maneuver is necessary to perform the procedure. However, the ten minutes required to complete a laser repair is well within the ischemic time tolerated by the liver. The time that is required for laser soldering could certainly be shortened by using larger laser spot sizes and in a continuous mode with correspondingly higher laser pulse energies.

The thermal damage sustained by the liver is significantly less for laser solder repairs (typically 0.5-1.0mm) than the 1cm ischemic region seen in the conventional suture repair. During laser soldering, thermal damage is confined primarily to the albumin on the surface, with some heating of the surface of the liver caused by heat conduction. 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,<sup>16</sup> and focused ultrasound<sup>17</sup>). A significant layer of ischemic parenchyma that may eventually become necrotic with attendant complications accompanies even suture repair.

If laser soldering can indeed reduce the morbidity and mortality associated with bleeding, biliary leakage and sepsis following 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. Major hepatic resection for trauma or malignancy may no longer need to be done along anatomical planes; laser soldering could make it possible to resect damaged or diseased liver along non-anatomical planes, thereby simplifying surgery and preserving hepatic parenchyma. Finally, laser soldering may be translated to the repair of other solid visceral organs such as the spleen and kidney.

## 5. CONCLUSION

This laser soldering technique has great promise, and could potentially reduce morbidity and mortality associated with liver trauma and surgery. It is safe, quick, reliable and straightforward even in the presence of heparin and results in minimal parenchymal damage.

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