Original Article - In Vitro Study

Evaluation of Laser Tissue Welding and Laser-Tissue Soldering for Mucosal and Vascular Repair

Yusuf Abbas Mistry, Srivalli S. Natarajan, Suraj A. Ahuja

Department of Oral and Maxillofacial Surgery, MGM Dental College and Hospital, Mumbai, Maharashtra, India

Abstract

Context: Laser tissue bonding (LTB) is believed to have certain advantages over conventional sutures such as fluid-tight closure and minimal scarring and fibrosis. **Aim:** The aim of the present study was to evaluate the bond strength of laser tissue welding and laser tissue soldering in mucosal and vascular repair. **Materials and Methods:** A total of 85 samples of bovine oral mucosa and 85 bovine aortas were bonded using a CO_2 laser and different laser powers. Human serum albumin was used as solder. The breaking load for mucosal samples and the bursting pressure for aorta samples were evaluated. Few specimens were evaluated histologically for thermal damage and other microscopic changes. **Statistical Methods:** Two-way ANOVA was performed as the data were normally distributed and analyzed for significant differences between the groups. This was followed by Simple Main effects (Tuckey's *post hoc* test) to determine the individual variation between groups and also the significant differences within the groups. **Results:** Significantly higher values of breaking load (44.2 ± 3.03 g) and bursting pressure (70.8 ± 12.33 mmHg) were noted when 50% albumin was used. When reinforcing sutures were given the bond strength was further increased (68.0 ± 4.0 g for breaking load) (108.0 ± 12.56 mmHg for bursting pressure). Microscopically, a bridge of solder coagulum formed across the wound. Thermal damage was restricted to the top layers only although it did extend much more laterally adjacent to the wound edges. Few areas of vacuolization and carbonization were seen. **Conclusion:** LTB seems to be a promising new method of wound closure and warrants further evaluation in the form of *in vivo* and clinical studies.

Keywords: CO_2 laser, laser-assisted vascular repair, laser tissue bonding, laser tissue soldering, laser tissue welding

Introduction

In the wound healing process, healing by primary intention is most desirable. This has been traditionally achieved by sutures and staples. However, these methods can cause a foreign body reaction because of the nature of materials used.[1] More importantly, none of these methods produces a watertight seal over the repair.

Methods of wound closure have been continuously evolving and newer and better techniques have been tried. One of these methods is laser tissue bonding (LTB).

Broadly, LTB is divided into three types, namely laser tissue welding, laser tissue soldering (LTS), and dye-enhanced[2] LTS. The mechanism of LTB is not clearly understood; however, it is suggested that it occurs through a local raising of the temperature which leads to the denaturation and coagulation of the proteins.[1,3]

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Laser bonding techniques are believed to have certain advantages over conventional sutures such as increased instant wound strength, fluid-tight closure[4-6] and minimal scarring and fibrosis. On the other hand, thermal damage to tissue is said to be the biggest handicap of this technique.[7] To circumvent this, a biological solder is interposed between the wound edges which selectively absorbs the radiation and prevents thermal damage to the adjacent tissue.[8-11]

The purpose of the study was to evaluate the bonding ability of LTB and compare the bond strengths of successful bonds achieved using different laser parameters and different concentrations of albumin used as solder. Two tissue samples,

Address for correspondence: Dr. Yusuf Abbas Mistry, Department of Oral and Maxillofacial Surgery, MGM Dental College and Hospital, Mumbai - 410 209, Maharashtra, India.
E-mail: yusufmistry@ymail.com

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namely bovine mucosa and bovine aorta were used for mucosal and vascular repairs in an *in vitro* model.

Materials and Methods

Sample size

A sample size of 85 bovine oral mucosa and 85 bovine thoracic aortas were used for bond strength testing. Furthermore, another 40 samples were bonded and sent for histopathological evaluation. Specimens were obtained from local abattoir from animals sacrificed for reasons other than this study and immersed in cold Ringers Lactate solution and stored in the refrigerator at approximately 0°C–4°C for not more than 24 h.

Methodology

A 10,600 nm wavelength CO_2 laser (CO_2 Laser Surgical System Model ML015-CA, Laser Labs, India) with power output range 0.5W–25W was used in free beam continuous mode. Lyophilized Human albumin powder (Sigma-Aldrich, India) was used for the preparation of solder. The following method was used.[12]

a. 1 g of powder dissolved in 2 ml of distilled water to achieve a concentration of 50% albumin
b. 1 g of powder in 4 ml distilled water to achieve a concentration of 25% albumin.

Appropriate laser safety precautions were observed by the operator during the laser welding procedure.

Each of the mucosal and vascular specimens were divided into 4 groups:

1. Laser tissue welding (no albumin)
2. LTS with 25% albumin
3. LTS with 50% albumin
4. Suturing reinforced with LTS with 25% albumin

Each of these groups was subjected to four different laser settings of 0.5W, 0.7W, 1.0W, and 1.5W [Figure 1].

Preparation of mucosa samples

The mucosal specimens were stripped of underlying muscle using a scalpel and cut into 3 cm by 3 cm sections. The samples were allowed to come to room temperature before performing any procedure. All the samples were subjected to the testing on the same day, and no sample was stored for more than 24 h to avoid any tissue degeneration and hence give erroneous results.

A 2 cm incision was given in the center of the specimen leaving approximately 0.5 cm of intact tissue on either side of the incision [Figure 2]. The edges of the incised surface were then approximated as best possible before being exposed to the laser beam.

Preparation of aorta samples

The aorta samples were harvested from the abdominal section of the same bovine models as above. They were stripped of any perivascular tissue and cut into 5 cm long specimens each. They were then mounted on the wooden block and stabilized using rubber bands on both edges. A horizontal incision 2 cm long was made using a scalpel along the length of the specimen near the middle [Figure 3]. The edges of the incised surface were then approximated as best possible using toothed forceps before being exposed to the laser beam.

Bonding procedure

A few droplets of previously prepared albumin solder were placed on the incision using a syringe and needle and spread over the incision edges as described by Chan *et al*.[13] The laser was passed over the apposed edges of the incision, slowly in a horizontal manner till the surface changes in the form of desiccation and color change were seen on the edges [Figure 2]. The edges were then gently tugged with a forceps to see if a bond had formed. If the edges pulled away, then they were reapproximated and the lasing procedure repeated until either a sufficient bond had formed or the edges got charred or burned. If there was no bond by the end of 5 min, the procedure was abandoned, and the specimen was considered as a bond failure.

The solder was re-applied if necessary to cover any remaining defects until no gaps were visible. The visual endpoint was the appearance of whitish discoloration of the bonded surface indicating uniform coagulation of the solder [Figure 3].

In the group where reenforcing sutures were to be used, before applying the solder and lasing it, 4 interrupted sutures using 4-0 silk were placed for mucosa samples, and 3 interrupted sutures with 5-0 prolene were placed for aorta.

Measurement of breaking load

To determine the breaking load a customized tensiometer as described by McNally *et al*.[8] was used. The bonded tissue was suspended by holding it in the upper clamp. Then, the lower clamp was attached along with the preweighed, empty plastic container suspended. Water droplets were added to the plastic container till there was gaping of the bond [Figure 4]. The weight of the plastic container along with thread and clamp (8 g) was added to the weight of water and then recorded as the breaking load.

Measurement of bursting pressure

To determine the bursting pressure a customized device such as one devised by Basu *et al*.[14] was used. Briefly, one end of the vessel was ligated, and the other end was secured to a tubing which was connected to a three-way. The three-way is also connected to a sphygmomanometer and a 50 cc syringe as shown in Figure 5. A reservoir of methylene blue solution was placed in between to prevent the solution from entering the sphygmomanometer. Methylene blue solution was infused slowly through the syringe. The pressure, at which the bonding failed characterized by a blue stream of solution and a sudden drop in pressure, was recorded [Figure 6].

Histological analysis

Following LTB 40 specimens (20 mucosa and 20 aorta) were selected for histological evaluation. Each specimen was subjected to the same methods of laser bonding described above, but instead of mounting them on the apparatus they were fixed in 4% buffered formalin and paraffinized. The blocks were cut into thin sections using a microtome and stained

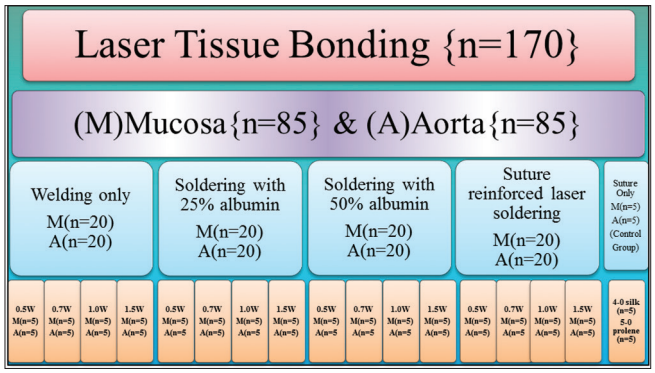

Figure 1: Diagrammatic representation of grouping and subgrouping of the sample

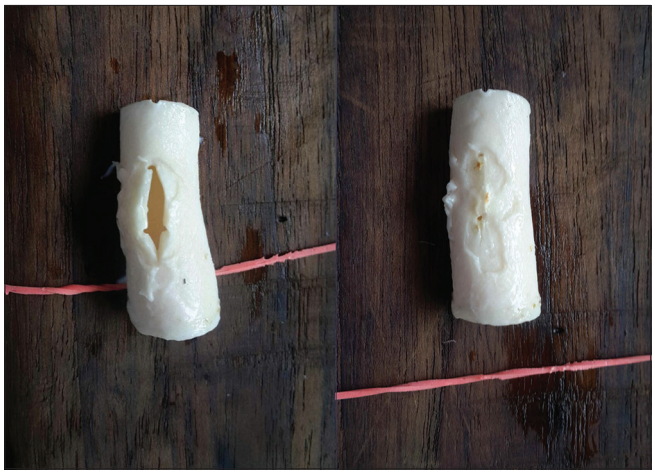

Figure 3: Prepared aorta specimen placed on wooden block (left). End point of a soldered aorta specimen showing a stable bond but also few areas of charring (brown spots) (right)

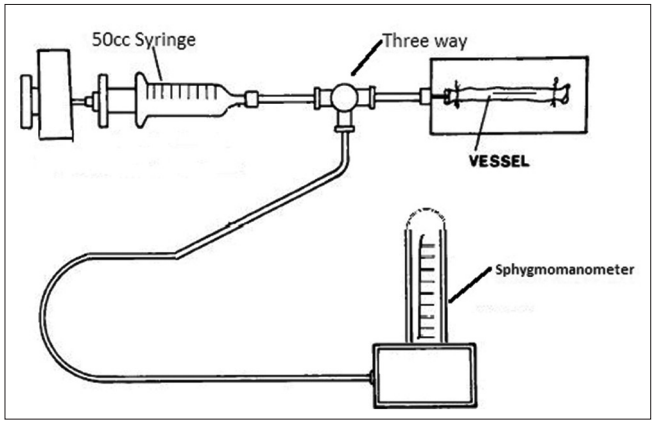

Figure 5: Schematic diagram for measuring bursting pressure

with hematoxylin and eosin using standard protocol. When thus prepared, the slides were mounted on an optical light microscope and evaluated under ×10 and ×45 magnification.

Statistical evaluation

Two-way ANOVA was performed as the data were normally distributed and analyzed for significant differences between the groups. This was followed by simple main effects (Tuckey's *post hoc* test) to determine the individual variation between groups and also the significant differences

Figure 2: Prepared mucosal specimen placed on wooden block (left). End point of lasing in a mucosa specimen as seen by desiccation and surface color change (right)

Figure 4: Measurement of breaking load. It was measured when the bond gave way and a gap was seen

Figure 6: Measurement of bursting pressure. The pressure was recorded when the bond broke characterized by blue stream of solution escaping and sudden drop in pressure

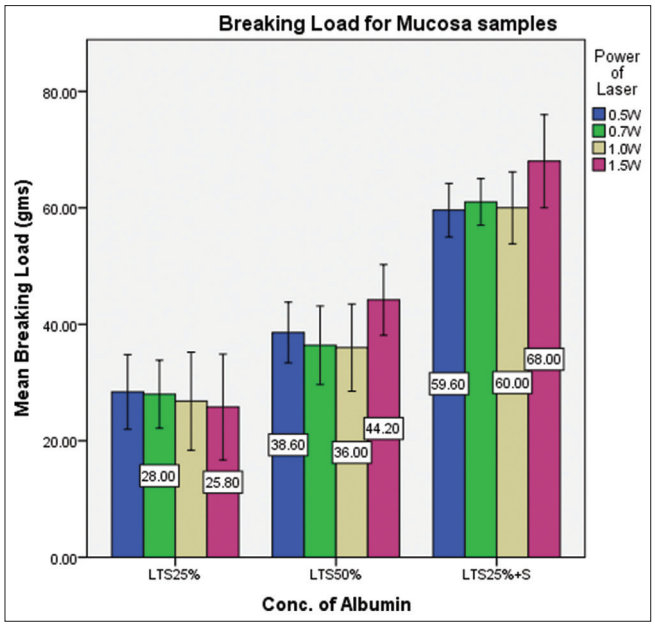

Figure 7: Breaking load values in mucosa samples

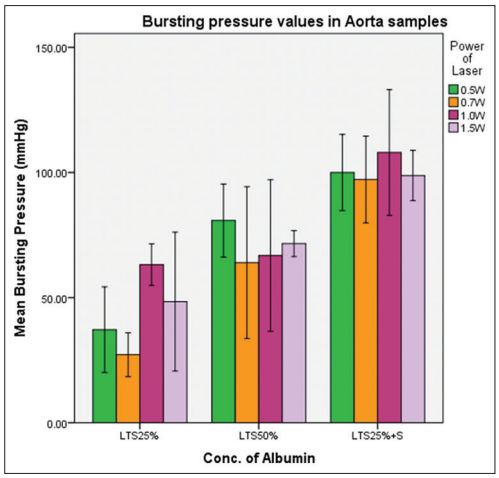

Figure 8: Bursting pressure values in aorta samples

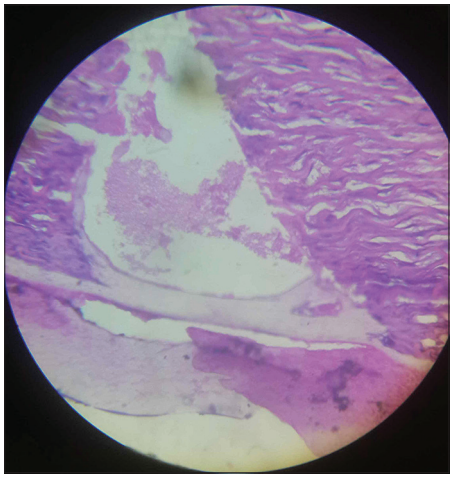

Figure 9: Photomicrograph showing coagulated albumin which forms a solid bridge between the tissue edges which is melted on and between the collagen fibrils. Note the adhesion between the albumin solder and edges of the wound (×45) (laser tissue soldering 50%) (0.5W) (aorta)

within the groups. The level of significance was set at 5%, all $P < 0.05$ were treated as statistically significant.

Observations and Results

Mucosa

In the LTW group for most samples, no proper bond was achieved even after attempting it for 5 min (300 s). The samples formed too weak bonds which either broke spontaneously while handling with forceps or broke immediately when mounted on the apparatus hence unable to give any breaking load reading (means that breaking load was <8 g which was the weight of the container). It was observed that the edges started charring and burning after 5 min and it was apparent that no further bonding would take place. This group was excluded from the statistical analyses.

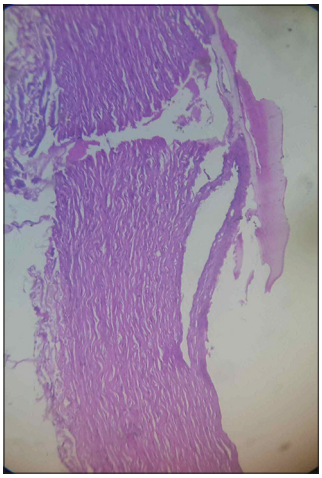

Figure 10: Only surface denaturation of the solder has taken place and solder has not flown to the full depth of wound (×10) (laser tissue soldering 50%) (0.5W) (aorta)

Results for breaking load

A two-way ANOVA was performed on the remaining 3 groups ($n = 60$) that considered the concentration of albumin and the power of laser as independent variables and breaking load (bond strength of repaired tissue sample) as the dependent variable. The test showed that there was a statistically significant effect of the concentration of albumin and the power of laser on the breaking load, ($F [6, 48] = 3.635$ $P = 0.005$).

Simple main effects (*post hoc* Tuckey's) analysis was performed to check for significance within the groups. It showed that there was no significant difference in the breaking load between within the groups for different laser powers in any group ($P = 0.988$, $P = 0.726$, $P = 0.892$, and $P = 0.495$) [Figure 7].

To determine which group was best the same *post hoc* test was used. This further elaborated that the breaking load for LTS 25% + S was significantly more than LTS 50% ($P < 0.001$) which was significantly more than LTS 25% ($P < 0.001$).

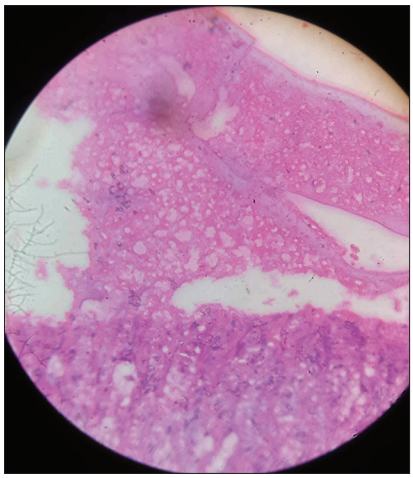

Figure 11: Vacuolization seen suggestive of crossing of threshold temperature >100°C and vaporization of solder (×45) (laser tissue soldering 25%) (1.5W) (mucosa)

Hence, from the above observations, it was concluded that for our study the optimum breaking load was achieved with LTS 25% + Suture group. The highest mean breaking load was achieved with 1.5W power (mean = 68.0 ± 4.0 g)

The optimum breaking load when reinforcing sutures were not used was with LTS 50% group. The highest mean even in this group was at 1.5W (mean = 44.2 ± 3.03 g) even though it was not statistically significant [Figure 7].

Aorta

Even for aorta, none of the samples in the LTW group achieved any kind of bonding even after attempting it for 5 min. All the samples in this group failed to achieve even the loose apposition which was seen in some samples of mucosa. This may be due to the fact that it was very difficult to approximate the cut edges of the incision closely due to the tubular nature of the specimen. Due to our inability to achieve any acceptable bonding in this group, the observations were considered as bond failure.

Results for bursting pressure

A two-way ANOVA was conducted for the other 3 groups (n = 60) using concentration of albumin and the power of laser as independent variables and bursting pressure (in mmHg) as the dependent variable. There was a statistically significant difference in the bursting pressure between the groups, (F [6, 48] =4.653 P = 0.001).

Simple main effects (*post hoc* Tuckey's) analysis showed that the bursting pressure for LTS 25% + S was significantly more than LTS 50% (P < 0.001) which was significantly more than LTS 25% (P < 0.001). This is in perfect agreement with our previous observations in the mucosal study and reiterates the fact that an increase in the concentration of albumin increases the bond strength and thus the bursting pressure and also that shows that when reinforcing sutures are used they act as bolsters and further significantly increase the strength of the bond even at lower concentration of the solder.

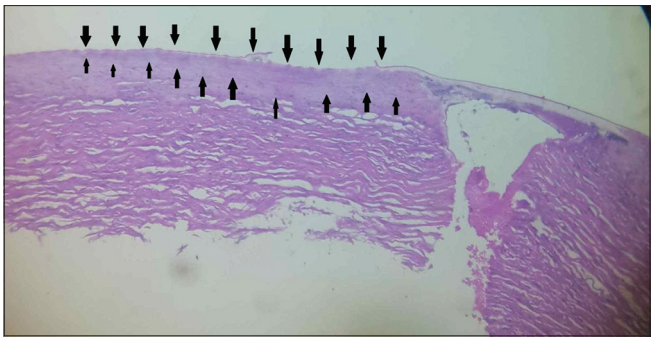

Figure 12: Arrows showing increased intensity of hematoxylin and eosin stain indicating thermal damage. The thermal damage extends more than 2 mm laterally but is confined to the most superficial layer

Simple main effects (*post hoc* Tuckey's) analysis also showed that there was no significant difference in the bursting pressure when comparing the laser powers 0.5W, 1.0W, 0.7, and 1.5W within the group (P = 0.252, P = 1.000, P = 0.495, and P = 0.286, respectively).

Hence, from the above observations, we conclude that the optimum bursting pressure was achieved with LTS 25% + Suture group.

The highest mean was achieved at 1.0W power (mean = 108.0 ± 12.56 mmHg).

When reinforcing sutures were not used, the LTS 50% group showed significantly higher bursting pressure (mean = 70.8 ± 12.33 mmHg) compared to LTS 25% group (mean = 44.0 ± 15.88 mmHg) [Figure 8].

Results for histopathology

Forty specimens were evaluated microscopically in which two samples exhibited severed wall ends, which had probably occurred during histopathological preparation and hence were excluded from evaluation. The remaining 38 samples were evaluated for uniformity of wound coaptation, depth of denaturation of solder, vacuolization, and carbonization and for thermal damage to adjacent areas.

The specimens selected showed adequate geometry at the incision site with the surface layers and subcutaneous tissue aligned properly in 30 cases (79%) and slight-to-moderate discrepancy in the rest (21%) [Figure 9].

All the welds showed an albumin bridge formed between the cut edges and over the outermost layer. None of the samples evaluated showed denaturation of the solder throughout the entire wound [Figure 10]. Vacuolization was seen in 3 of the 10 cases (30%) in which 1.5W power was used. No other sample showed any vacuolization or carbonization. The presence of vacuoles suggests that temperatures crossed vaporization threshold of water (>100°C) [Figure 11].

Thermal damage in the form of protein denaturation extending laterally on varying distances on either side of the incision as evidenced by hyperchromatic hematoxylin and eosin staining pattern was noted [Figure 12]. The depth of

thermal damage was restricted only to the most superficial layer corroborating the fact that the CO_2 laser has a very low penetration depth and there was no damage to the underlying tissues. Thermal damage as determined subjectively by increased intensity of eosinophilia was predominantly confined to the areas adjacent to the incision and in the direct vicinity of the solder.

Discussion

LTB is an experimental technique that is being developed as an alternative to sutures. In comparison to conventional suturing, LTB is less traumatic, nonimmunogenic, provides immediate watertight sealant, and possibly a faster and easier procedure for minimally invasive surgery. Further improvements in the bond strength may be achieved by the use of albumin solder.

During LTB, the radiant energy is converted to heat by the tissue's endogenous chromophores (e.g., water or pigments) or by exogenously applied chromophores in the solder, causing denaturation of proteins and consequent bonding of tissue.

Unfortunately, several drawbacks associated with current LTB techniques have resulted in a delay in the acceptance to use it in the clinical setting. First, the relatively low welding strengths produced with LTB often require additional sutures to reinforce the defect, ultimately defeating the purpose of the modality.[15-17] Second, extensive thermal damage may cause more harm than benefit to the recipient tissue. To overcome these disadvantages, several more refined welding techniques have been developed such as use of liquid and semi-solid solders and temperature feedback control systems.[18-21]

This study explores the optimal parameters of LTB using a CO_2 laser in an *in vitro* model using two tissue specimens, namely bovine oral mucosa and bovine aorta. In this study, we have strived to identify the relation, if any, between the strength of the bond using different powers of the CO_2 laser and different concentrations of albumin solder.

Early studies were carried out by Krueger and Almquist,[22] who used argon laser coagulation of blood to assist in small vessel anastomosis and by Poppas *et al*.,[23] who used egg white albumin and a CO_2 laser in a rat urethroplasty model. Other studies have compared suture closure,[4] fibrin glue repairs,[6] Dermabond (Simhon *et al*. 2004)[3] and different concentrations of albumin solder.[8,9,13,24] These studies demonstrated increased bond strength coupled with decreased thermal injury when albumin solder was used. Coaptation or apposition demands were also greatly reduced.

McNally *et al*.[8] compared different concentration of solder from a range of 20%–60% serum albumin and found that increasing the bovine serum albumin concentration from 25% to 60% greatly increased the tensile strength of the repairs. This is in perfect agreement with our own results where we see a significantly increased strength in tissue bond when 50% albumin was used instead of 25% albumin.

Forer *et al*., (2007)[6] Gil *et al*.[10] and Bleier *et al*.[25] used 0.5W, 1.0W, and 0.7W, respectively, on dura, fascia, and maxillary sinus of rabbits and showed that these setting were feasible for CO_2 laser and resulted in negligible thermal damage.

The concept of using reinforcing sutures and then performing a laser anastomosis or repair was especially helpful in cases where an immediate watertight seal is desirable. The cases where this is applicable is dural repair,[10] gastrointestinal repairs[26] and obviously vascular anastomosis.[14,20] In each case, although the bursting pressures were significantly more in those samples where reinforcing sutures were used some of the advantages of LTB such as lesser time, no foreign object, and technique sensitivity, as pointed out earlier, were sacrificed.

Many other studies have used different models to measure bursting pressures in blood vessels[20] (351 mmHg), ureters[2] (136 mmHg) maxillary sinus mucosa,[25] (34 mmHg), and dura to fascia (Forer *et al*. 2007)[6] (194 mmHg). Most of these studies have used albumin solder and are in good agreement with our own results except those with *in vivo* studies which show more bursting pressure probably due to clotting of blood and healing of tissues in the live model.

The use of solder with more viscosity is something to be desired. Such a solder may help retain the solder between the edges and subsequently the greater thickness of the albumin bridge may increase the bond strength. This was observed by McNally *et al*.[8] and Bleustein *et al*.[9] who used poly-L-lactic-co-glycolic acid and hydroxypropyl methylcellulose respectively, to increase the viscosity and reduce the flow of solder, and achieved greater bond strengths.

The depth of thermal damage was restricted only to the most superficial adventitia corroborating the fact that the CO_2 laser has a very low penetration depth and there was no damage to the media. Thermal damage as determined subjectively by increased intensity of eosinophilia was predominantly confined to the areas adjacent to the incision and in the direct vicinity of the solder. This is in good agreement with the results of Wolf-de Jonge *et al.*(2008).[20]

A newer soldering technique incorporated the added principle of photoenhancement as described by Oz *et al*.[27,28] An absorbing chromophore is added to the solder to focus light absorption in the solder and not in nontarget tissue. This enhanced absorption in the solder allows a lower power density to be used.

Shenfeld *et al*.[29] have tested an optical feedback system in experimental bladder welding. They utilized a CO_2 laser and semiflexible optical fibers for infrared feedback (radiometry), which sensed tissue temperature and controlled laser exposure duration. Stewart *et al*.[30] have done preliminary work in evaluating a 1.9 pm laser coupled to an infrared thermometer system in a closed loop.

When this state of technological advancement is realized, laser welding is likely to replace sutures not only in applications in which a strict advantage is obtained but also

in applications where sutures are adequate, but welding is faster and easier.

Conclusion

LTB techniques for mucosal and vascular repairs, alone or in combination with other surgical technologies, may be a hallmark of surgery in the next century.

This study has shown that although laser tissue welding forms very weak, unacceptable bonding, the addition of a solder considerably increases the bond strength and gives a wider margin for error. However, improvements in the technique are still warranted. We conclude that LTS is a promising new method of wound closure and advances in technique and evolving concepts indicate future clinical applications. This study is a stepping stone to more *in vivo* and clinical trials which will further expand our knowledge in this new field and also define few parameters to optimize its clinical use.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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