

Intraluminal Albumin Stent Assisted Laser Welding for Ureteral Anastomosis

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Background and Objectives: The success of laser tissue welding or soldering depends on optimal laser settings, solder material, and tissue type and geometry. To develop a practical laser welding technique for ureteral repair, an intraluminal albumin stent was designed to enhance the welding effects on ureteral end to end anastomosis.

Study Design/Materials and Methods: In vitro porcine ureters were anastomosed using an albumin stent alone, the albumin stent plus a solder, and the solder alone. All welding was performed with an 810-nm diode laser with either a continuous wave (1 W, CW) or two pulse modes (2 W, 3.3 Hz; 1 W, 5 Hz). Laser parameters, tensile strength (TS) and burst pressure (BP) of the ureteral anastomosis, and tissue thermal injury were measured.

Results: In the 2-W pulse mode, BP in the albumin stent plus solder group (mean 185 mmHg) and the stent only group (mean 133 mmHg) were significantly higher than the solder only group (mean 77 mmHg, $P < 0.05$). Laser ureteral anastomosis with the stent plus solder group at 1-W CW and 2-W pulse laser modes yielded the highest TS (mean 97, 82 g) and BP (mean 183, 185 mmHg). Among the three modes, the 1 W pulse delivered the lowest energy and yielded the lowest TS and BP in ureteral anastomosis. There was no significant difference in the thermal damage to the tissue among the modes and groups.

Conclusions: Using the albumin stent increased the reliability of ureter end-to-end laser anastomosis. Further studies will be warranted in vivo and other tubular organs as well. *Lasers Surg. Med.* 31:225–229, 2002.

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INTRODUCTION

Laser welding or soldering as a primary closure technique has been studied in various surgical fields. Compared to conventional surgical techniques, laser-assisted tissue welding has remarkable advantages in urology, including providing an immediate watertight approximation, reducing urolithiasis, and minimizing tissue injury and foreign body reaction [1,2]. This technique has been investigated in clinical and laboratory studies for urethra [3–5], ureter [6], vas deferens [7], and bladder [8] repair, using various lasers in combination with protein solders. Protein solders play an important role in welding procedures, enhancing welding strength, and decreasing

tissue thermal damage [1]. However, some of the disadvantages of laser welding have restricted its clinical application. These include low welding strength, poor reproducibility, and extensive tissue thermal damage [8–11]. Another difficulty of the laser welding process is maintaining precise circumferential apposition of the tubular anastomosis during the laser tissue welding [7]. Challenges might also include preventing secondary stricture and obstruction from scar formation in the tubular organ. Practical laser welding must be optimized for the specific physiological and geometric characteristics of tissues and organs.

A solder using human albumin mixed with Indocyanine Green (ICG) was described by Bass [9]. The peak spectral absorbance of the solder, dictated by ICG, is about 800 nm, a wavelength that closely matches to the output of the 810-nm diode laser. In our laboratory, an intraluminal albumin stent was developed to enhance the weld strength of ureteral laser anastomoses. We believed the albumin stent would provide an intraluminal temporary scaffold that might prevent post-op ureteral stricture. In this study, the albumin stent and a solder of albumin with ICG were used alone or combined to weld porcine ureters in vitro in an end-to-end spatulated fashion using an 810-nm diode laser on CW and pulse modes. The laser parameters, burst pressure, tensile strength, and tissue thermal damage were analyzed for future in vivo use.

MATERIALS AND METHODS

Preparation of Albumin Stent

The method involved the combination of native serum albumin with a chromophore. Commercial human serum albumin (25%) (Michigan Department of Public Health, MI) was filtered through an ultrafiltration membrane (YM 30, Amino Co.), and concentrated to 50% (w/v) using

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an ultrafiltration system (Model 8400, Amicom, MA) under 35–45 psi pressure at room temperature. The 50% albumin was mixed extensively with sterilized 10 mM indocyanine green solution (ICG, Sigma, I2633, MO) at 1:100 ratio (v:v) such that the final ICG concentration is 0.1 mM in the mixture. The albumin and ICG mixture was evaporated in a sealed chamber at room temperature until it became moldable. Then, the albumin was molded to produce a hollow cylinder like stent with a 3.5-mm outer diameter, 2.0-mm inner diameter, and 1.5 cm in length (Fig. 1). The stent was packaged in an air-tight opaque container and stored at 4°C. These storage conditions prevented photobleaching and maintained the humidity level, preventing the albumin stent from drying out and becoming brittle. The preparation was performed sterilely.

Preparation of Liquid Albumin Solder

The liquid solder was made with the same process as the albumin stent, but the procedure was stopped before evaporation. The final product of the solder is 50% albumin with 0.1 mM ICG mixture. The solder was then stored in the dark at 4°C in a 1 cc syringe until use.

Laser System

Laser treatments were performed with a diode laser module (Diomed25, Diomed Limited, Cambridge, UK) coupled to a quartz silica non-contact optic fiber (600 μ m diameter). The laser system consisted of a phased array of gallium-aluminum-arsenide semiconductor diodes and the major wavelength output of the diode laser is 810 nm. The distance from optic fiber to target tissue was approximately 2–3 mm. The laser was setup on each of following three modes: 1.0 W continuous wave; 2.0 W at 0.1 seconds pulse width, 0.2 seconds interval (3.3 Hz); and 1.0 W at 0.1 seconds pulse width, 0.1 seconds interval (5 Hz). Laser treatment time (LT) was recorded with a built-in laser meter monitor. Before and after welding, actual energy output (AE) was measured using an energy meter (Vector H310, Scientech, CA).

Laser Welding Techniques

Porcine ureters were harvested atraumatically from sacrificed animals, who receive neither particular medications nor surgical procedures affecting their genitourinary

tracts. The ureters were immediately placed in sterile 0.9% saline solution and transported to the laboratory at 4°C. A fresh ureter was anchored to a perfusion system with a 1-0 silk tie to prevent sliding and leakage. The ureter was transected completely in the middle in a spatulated fashion and repaired immediately with one of our different repair techniques (Figs. 2 and 3).

The study was divided into three groups. In group 1: thirty-two ureters were anastomosed in an end-to-end fashion using an intraluminal albumin stent alone with laser settings of 1 W continuous wave, 1 W 5 Hz pulse, or 2 W 3.3 Hz pulse. Both ends of the ureter were sheathed onto an albumin stent. Two 5-0 PDS sutures were applied to help to re-approximate and position the ureteral stumps. After completion of the anastomosis the sutures were removed. In group 2: thirty-two ureters were anastomosed using a albumin stent combined with liquid solder at the three laser setting modes. The surgical steps were similar to the group 1 with the addition of a layer of liquid solder coated at the junction of anastomosis on the adventitia of the ureter after the stent was positioned. The ureteral stumps were sandwiched between the liquid solder and the stent. The thirty-one ureters in group 3 were anastomosed using liquid solder only at the same laser settings as above. There was no albumin stent used in this group.

In all the groups, the samples were divided into 3 arms: one for burst pressure, one for tensile strength, and the rest for thermal injury evaluation.

Measurements of Burst Pressure and Tensile Strength

A circulating perfusion system with a pressure transducer was set up for burst pressure testing. Saline solution containing Methylene Blue (1%) was infused with a flow rate of 2 ml/min through the welded ureter to dissolve the albumin stent in 20–30 minutes. After the stent was dissolved, the distal end of ureter was closed, the pressure increased, and the maximum burst pressure recorded. The pressure transducer recorded pressures up to 200 mmHg. If the pressure was beyond 200 mmHg during the testing

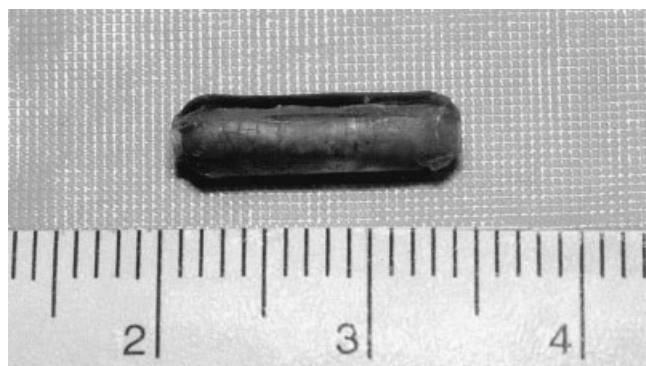


Fig. 1. Intraluminal albumin stent.

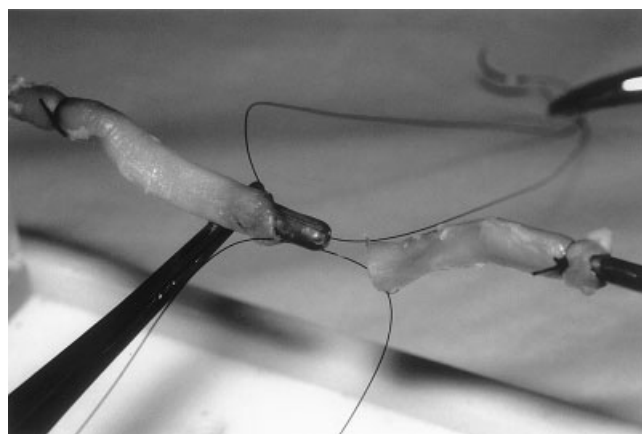


Fig. 2. An albumin stent was inserted into right end of the ureter.

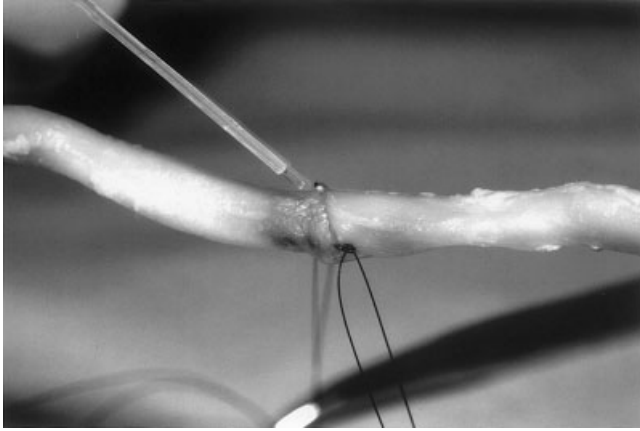


Fig. 3. Ureter ends were approximated with the support of an albumin stent and laser welded.

and the ureteral weld did not fail, the burst pressure would be recorded as 200 mmHg. All samples were sent for histological examination for thermal injury evaluation after burst pressure testing.

The welded ureters were soaked in 37°C saline solution overnight to dissolve undenatured albumin after welding. A tensile tester (Vitrodyne V1000, Liveco, VT) recorded breaking strength of welded ureters. The standard load cell was 5,000 g.

Measurement of Tissue Thermal Injury

The tissue samples were immediately fixed in 10% formalin solution. Specimen were then dehydrated, embedded in paraffin wax, and sliced longitudinally for Hematoxylin-Eosin (H&E) and Trichrome staining. The slides were observed with a Leica microscope (Leica DMRB, Germany) under normal and polarization reflected light. The area of tissue thermal damage was distinguished by a color change and loss of birefringence under the light microscopy [10]. The thermal damaged area was measured under the microscope at 50× magnification.

Statistical Analysis

Statistical comparisons of all groups were examined using Factorial ANOVA. All data are expressed as mean $\pm$ SD. Fisher and Student-Newman-Keuls tests were used to evaluate statistical differences among different groups and among laser settings. P values < 0.05 were considered statistically significant.

RESULTS

The mean laser time (LT) to complete ureteral anastomosis was from 120 to 169 seconds with no significant difference between all groups and laser modes. In the 1 W CW mode, the actual energy (AE) delivered was higher than the pulse modes. However, the AE delivered was similar in all groups having the same laser power setting (Table 1).

Within each group higher tensile strengths (TS) and burst pressures (BP) were generated at the 1-W CW and 2-W pulse modes in the ureteral anastomosis. The laser welding yielded the lowest TS and BP with the 1-W pulse mode. In group 2, stent plus solder, laser assisted ureter anastomosis yielded higher TS and BP compared to the other two groups for each of the laser settings. In this group the TS in CW and 2-W pulse modes were significantly higher than that in the 1-W pulse mode (mean 97, 82 vs. 48 g, $P = 0.013$ and 0.029 , respectively). This value was also higher than that in the group of stent only (mean 69, 62 g, $P = 0.047$ and 0.064) and the solder only (mean 73, 45 g, $P = 0.067$ and 0.069). Furthermore, the BP in the stent plus solder group was significantly higher than that of the solder only in CW mode (mean 183 vs. 93 mmHg, $P = 0.008$) and in 2-W pulse mode (mean 185 vs. 77 mmHg, $P = 0.006$). The highest BP was recorded as 200 mmHg due to the limitation of our equipment. In the stent plus solder group 7 of the anastomosed ureters did not break at pressures of 200 mmHg (7/12, 58%), while in the stent group 2 did not break (2/12, 17%). Using solder alone, the average BPs were 93, 66, and 54 mmHg with the 1 W CW, 2- and 1-W pulse modes, respectively. None of them reached 200 mmHg in burst pressure in this group.

TABLE 1. Summary of Laser Time (LT), Actual Energy (AE), Tensile Strength (TS), Burst Pressure (BP), and Area of Tissue Thermal Injury (T) of Laser Assisted Ureteral Anastomosis (Mean $\pm$ SD)

Group	Sample	LT (seconds)	AE (Joule)	TS (gram, N)	BP (mmHg, N)	T (mm sq.)
Stent only						
1.0 W CW	11	120 $\pm$ 41	51 $\pm$ 27	69 $\pm$ 30 (5)	136 $\pm$ 45 (6)	0.42 $\pm$ 0.27
2.0 W 3.3 Hz	10	132 $\pm$ 25	23 $\pm$ 17	62 $\pm$ 27 (4)	133 $\pm$ 58 (6)	0.37 $\pm$ 0.16
1.0 W 5 Hz	11	142 $\pm$ 39	20 $\pm$ 13	52 $\pm$ 13 (5)	73 $\pm$ 30 (6)	0.31 $\pm$ 0.18
Stent + solder						
1.0 W CW	10	130 $\pm$ 27	70 $\pm$ 37	97 $\pm$ 37 (4)	183 $\pm$ 25 (6)	0.46 $\pm$ 0.28
2.0 W 3.3 Hz	11	156 $\pm$ 31	23 $\pm$ 16	82 $\pm$ 44 (5)	185 $\pm$ 27 (6)	0.29 $\pm$ 0.18
1.0 W 5 Hz	11	162 $\pm$ 36	23 $\pm$ 18	48 $\pm$ 26 (5)	61 $\pm$ 46 (6)	0.36 $\pm$ 0.21
Solder only						
1.0 W CW	11	125 $\pm$ 33	68 $\pm$ 28	73 $\pm$ 29 (5)	93 $\pm$ 35 (6)	0.39 $\pm$ 0.22
2.0 W 3.3 Hz	10	148 $\pm$ 45	23 $\pm$ 13	45 $\pm$ 27 (4)	77 $\pm$ 35 (6)	0.32 $\pm$ 0.16
1.0 W 5 Hz	10	169 $\pm$ 52	24 $\pm$ 15	39 $\pm$ 24 (4)	59 $\pm$ 40 (6)	0.27 $\pm$ 0.17

Unless indicated, otherwise the sample size of each column equals to Sample. } : Significantly different from the comparison.

Tissue thermal damage (T) was noticed in all samples. Thermal damage of ureter tissue was indicated by the loss of birefringence in the extracellular matrix under a polarized light microscope. Sharp color changes corresponded to the thermally damaged area in an H&E and Trichrome stain with a normal light microscope. The damaged cells became swollen and lost their fine structures under microscopic observation. However, the area of T was similar among all groups and laser settings ($P > 0.05$).

DISCUSSION

The ideal laser assisted tissue welding technique is one that creates the optimum welding strength with the least tissue thermal injury. Unfortunately, laboratory results are variable, because of the lack of a gold standard in the assessment of the laser effects during the welding process. Investigators have studied the optimization of solders, lasers, and energy settings for controlling thermal injury and enhancing welding effects [4,8,11]. Previous researches indicated that the strength of laser soldering could be effected by solder concentration. The results showed that laser welds created using high concentration protein solders were significantly stronger than those with low concentration solders [5,11] were. A solid albumin strip was employed to reinforce welding strength in nerve trunks anastomosis [12]. Poppas and his colleagues [13] reported their experimental data, using a 40% human albumin solder to anastomose ureters in vitro with a KTP-532 laser. A successful ureteral anastomosis was achieved without tracking tissue thermal damage. Kirsch [14] also reported ureter extravesical reimplantation using fibrinogen glue plus ICG as solder with 808-nm CW laser in a canine model. Their results indicated that the wound healing process in the laser closure was similar to sutures.

In ureteral surgery ureter stenting is a common procedure to prevent extravasation and ureteral stricture. An inner ureteric bio-absorbable stent was described to reduce the risks of renal infection and damage by urine reflux [15]. Intraluminal dissolvable or absorbable stents were also investigated in vascular [16] and gastrointestinal [17] anastomosis with glues and CO₂ lasers [18] that resulted in simplifying the laser welding procedures without sutures.

In this study, an albumin stent was introduced to assist laser welding for ureteral repair. The albumin stent had a hollow body to allow sufficient urine flow and to scaffold ureteral tissue during wound healing, preventing stricture formation. The stent also acted as solder to assist ureter laser anastomosis. Laser tissue welding or soldering is a thermal process that depends on the heating of the albumin, the unraveling of some of the extracellular matrix proteins, followed by the cooling and adherence of the albumin with adjacent tissue proteins [1,2,9]. The albumin stent prior to laser irradiation was highly water soluble. Irradiation denatured part of the stent and bonded it to the ureteral tissue, forming a rigid ring-like scaffold in the ureteral lumen allowing urine passage (Fig. 4).

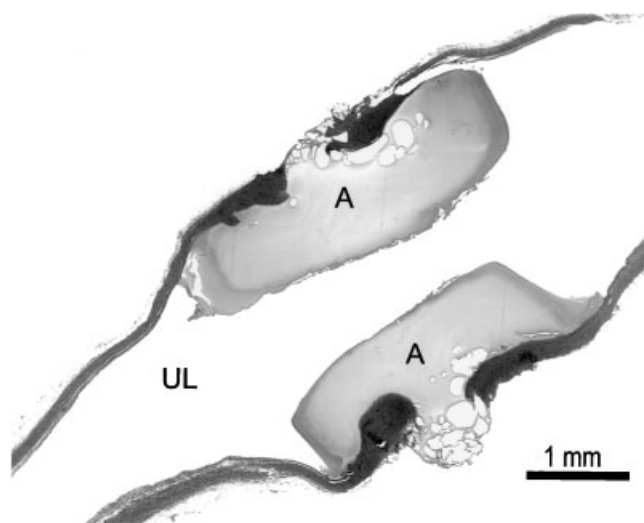


Fig. 4. Longitudinal section of a laser anastomosed ureter using an albumin stent. After irradiation by the laser, the stent remnant (A) is supporting the lumen of the ureter at the anastomosis. The ureteral lumen (UL) is patent. (Hematoxylin & Eosin (H&E) staining, 2.5 $\times$).

This study suggested that using the albumin stent could reinforce the strength of laser welding and provide a watertight seal to improve welding outcomes in the ureteral sutureless anastomoses. Our results demonstrated that TS and BP were significantly higher in the groups using the stent with the 1-W CW and 2-W pulse laser modes. The experimental results found the strongest weld strength in the stent plus solder group. The results also showed that the TS and BP dropped dramatically in the 1.0-W pulse mode. In this study, we tried to minimize laser thermal injury via reducing actual energy to treated tissue. However, the results indicated that there was no significant difference in area of thermal injury between all groups.

In this study, we noted the limitation that the results of the in vitro study might not truly reflect in vivo situation. However, the current study helped us establish the practical laser parameters for further in vivo studies. An in vivo study is underway to answer the feasibility of using the albumin stent in ureteral laser anastomosis.

In conclusion, a successful ureter anastomosis can be achieved, using the albumin stent with an 810-nm diode laser. The intraluminal albumin stent provided an efficient and reliable method for ureteral laser anastomosis. An optimal welding outcome in this study was achieved using an albumin stent plus liquid solder with our laser settings, which are currently being used in an in vivo study. We also expect that the albumin stent could be utilized for laser repair in other tubular organs.

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REFERENCES

1. Kirsch AJ. Laser tissue soldering: State of the art. *Contemp Urol* 1997;41–60.
2. Scherr DS, Poppas DP. Laser tissue welding. *Urol Clin Nor Am* 1998;25(1):123–135.
3. Kirsch AJ, Miller MI, Hensle TW, Chang DT, Shabsigh R, Olsson GA, Connor JP. Laser tissue soldering in urinary tract reconstruction: First human experience. *Urology* 1995;46:261–266.
4. Wright EJ, Uzzo RG, Poppas DP. Urethral reconstruction using high concentration human albumin solder. *J Urol* 1993;150:648–650.
5. Poppas DP, Mininberg DT, Hyacinthe L, Spencer JR, Schlossberg SM. Patch graft urethroplasty using dye enhanced laser tissue welding with a human protein solder: A pre-clinic canine model. *J Urol* 1993;150:648–658.
6. Wolf JS, Soble JJ, Nakada SY, Rarala HJ, Humphery PA, Clayman RV, Poppas DP. Comparison of fibrin glue, laser weld, and mechanical suturing device for the laparoscopic closure of ureterotomy in a porcine model. *J Urol* 1997;157:1487–1492.
7. Kirsch EB, Seidmon EJ, Samaga AM, Jr., Phillips SJ, Tong CK, Shea FJ. Carbon dioxide milliwatt laser in the vasovasostomy of vas deferens in dogs: Part I. *Lasers Surg Med* 1990;10:328–333.
8. Lobik L, Ravid A, Nissenkorn I. Bladder welding in rats using controlled temperature CO₂ laser system. *J Urol* 1999;161(5):1662–1665.
9. Bass LS, Libutti SK, Eaton AM. New solders for laser welding and sealing. *Lasers Surg Med* 1993;(Suppl 5): pp 6, 305.
10. Thomsen S, Pearce J, Cheong W. Changes in birefringence as marker of thermal damage in tissue. *IEEE Trans Biomed Eng* 1989;36(12):1174–1179.
11. Lauto A. Repair strength dependence on solder protein concentration: A study in laser tissue welding. *Lasers Surg Med* 1998;22:120–125.
12. Lauto A, Trickett R, Malik R, Dawes J, Owen E. Laser activated solid protein bands for peripheral nerve repair. *Laser Surg Med* 1996;21:134–141.
13. Poppas D, Sutaria P, Sosa RE, Mininberg D, Schlossberg S. Chromophore enhanced laser welding of canine ureters in vitro using a human protein solder: A preliminary step for laparoscopic tissue welding. *J Urol* 1993;150:1052–1055.
14. Kirsch AJ, Dean GE, OZ MC, Libutti SK, Treat MR, Nowygrod R, Hensle TW. Preliminary results of laser tissue welding in extravesical reimplantation of the ureter. *J Urol* 1994;151:514–517.
15. Lumiaho J, Heino A, Tunninen V, Ala-Opas M, Talja M, Valimaa T, Tormala P. New bioabsorbable polylactide ureteral stent in the treatment of ureteral lesions: An experimental study. *J Endourol* 1999;13(2):107–112.
16. He FC, Wei LP, Lanzetta M, Owen ER. Assessment of tissue blood flow following small artery welding with an intraluminal dissolvable stent. *Microsurg* 1999;19:148–152.
17. Sauer JS, Hinshaw JR, McGuire KP. The first sutureless, laser-welded, end-to-end bowel anastomosis. *Laser Surg Med* 1989;9:70–73.
18. Detweiler MR, Kobos JW, Fenton J. Gastrointestinal sutureless anastomosis in pigs using absorbable intraluminal stents, stent placement devices, and fibrin glue—A summary. *Langenbecks Arch Surg* 1999;384:445–452.