Laser Welding with an Albumin Stent: Experimental Ureteral End to End Anastomosis

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ABSTRACT

Porcine ureters were anastomosed using an albumin stent and diode laser in vitro. The albumin stent provided precise apposition for an end to end anastomosis and enhanced welding strength. The anastomosis seam was lasered with an 810 nm diode laser using continuous wave and pulse light through a hand-held 600 µm noncontact optical fiber. Tensile strength, burst pressures, operative times, total energy and thermal damaged were measured in this study.

The results demonstrated that using an albumin stent to laser weld ureteral anastomoses produces strong weld strengths. The liquid albumin solder also provided satisfactory welding strength. There were no significant differences of tissue thermal damage between the albumin stent alone, liquid solder alone and both combination groups. Thermal damage to tissue depended on laser setting and energy. This study determined the appropriate laser setting parameters to perform in vivo ureteral end to end anastomosis.

Keywords: ureter, laser welding, Albumin, Laser soldering

1. INTRODUCTION

In comparison with conventional surgical techniques, laser-assisted tissue welding could minimize urolithiasis, foreign body reaction and tissue damage in urology. Laser welding as a primary closure technique has been used for the urethra,[2,4,7] ureter,[3] and vas deferens [6] and bladder [9] reconstruction. Protein solder in those applications plays a very important role in enhancing welding strength [1,8]. However, some problems still limit the application of this technique in the clinical setting. It is difficult to get precise apposition of tubular organs, and thermal injury is a major consideration for fine tissue repair, particularly in muscular and asymmetrical tubular organ anastomoses such as ureter or vascular.[6] These problems would cause unreliable welding, delaying wound healing processes, increase fibrosis formation and lead to stricture at anastomosis site.

In this study, an albumin stent was used to laser weld ureteral end to end anastomoses in a sutureless procedure. The stent supported the ureteral stump intraluminally to provide the precise end to end apposition and acted as a scaffold to provide an adequate drain tunnel for local tissue healing without producing ischemia. A 810 nm diode laser was set on continuous wave and pulse mode to assess laser energy, burst pressure, tensile strength, operative time and tissue thermal damage.

2. MATERIALS AND METHODS

2.1. Preparation of PSH Stent and Solder

25% Human serum albumin (Michigan Dept. of Public Health, MI) was filtered through an ultrafilter membrane (YM 30, Amino) using the ultrafiltration system (Model 8400, Amicom, MA) to concentrate it to 52~55% (w/v). 10mM indocyanine green (ICG) (Sigma, I2633, MO) solution was filtered for sterilization (Gameo 25ES, Fisher) and added to the 50% albumin at 1:100 (v/v) and mixed well for 3 min. The albumin and ICG mixture were exposed at room temperature until the solvent evaporated and became moldable. The moldable albumin was shaped into a hollow stent with an outer diameter of 3.5 mm, an inner diameter of 2.0 mm and 1.5 cm in length. The stent was stored at 4 °C in the dark until used (**Fig 1**). The procedure was performed with sterile techniques.

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The liquid solder was made of 52~55 % (w/v) albumin with ICG. The final ICG concentration was about 0.1 mM. The solder was stored in a 1ml syringe at 4 ^{0}C in the dark until used

2.2. Laser System

Laser treatments were performed with a diode laser module (Diomed Limited, Cambridge, UK) coupled to a quartz silica non-contact fiber optic (600 μm diameter). The laser system consists of a phased array of gallium-aluminum-arsenide semiconductor diodes, and the major wavelength output of the diode laser is 810 nm. An aiming beam allowed the operator to visualize the spot size of the laser during activation. The spot diameter was 1-2 mm at a distance of 2 mm. The laser was setting at three modes: 1.0 W continuous wave; 2.0 W at 0.1 sec. pulse width, 0.2 sec interval (3.3 Hz); and 1.0 W at 0.1 sec pulse width, 0.1 sec interval (5Hz). Operative time was recorded with a built-in laser meter monitor. Before and after welding, output energy of the optical fiber was measured using an energy meter (Vector H310, Scientech, CA).

2.3. In Vitro Experiments

Fresh ureter segments were harvested from domestic swine with minimal trauma and immediately placed in sterile 0.9% saline solution at 4 ^{0}C.

The study was divided into three groups. In group 1, thirty two ureters were completely transected and were anastomosed end to end using an albumin stent alone with laser settings a 1.0 W continuous wave, 1.0 W 5Hz pulse, and 2.0 W 3.3 Hz pulse, respectively. In group 2, thirty-two ureters were anastomosed using an albumin stent combined with liquid solder at the three laser setting modes. Thirty-one ureters in group 3 were anastomosed using liquid solder only at the same laser settings.

In all the groups, the samples were divided into 3 portions; one was tested for burst pressure, one for tensile strength and the other for histological evaluation.

2.4. Measurements of Burst Pressure and Tensile Strength

A perfusion system was set up for burst pressure testing. 0.9% NaCl with 1% Methylene Blue solution was infused a flow rate of 2ml/min through the welded ureter to dissolve the albumin stent in 20-30 min. After the stent was dissolved, the pressure transducer was switched on and recorded the peak pressure. When the ureter didn't break during the burst pressure testing, the samples were sent for histological examination.

The welded ureters were soaked in 37 ^{0}C saline solution overnight after welding and then tested for tensile strength. The breaking force was recorded using a tensile tester (Vitrodyna V1000, Liveco, VT). The standard load cell was 5000 g.

2.5. Histological Studies

The tissue samples were immediately fixed in 10% formalin solution. The specimens were dehydrated and embedded with paraffin wax and then sliced longitudinally for H & E and Trichrome staining. The slides were observed with a Leica microscope (Leica DMRB, Germany) under normal light and polarization reflected light. The area of thermal damage was distinguished by a color change and loss of birefringence under the light microscopy.[11] The thermally damaged area was measured under 50 X magnification.

2.6. Statistical Analysis:

Statistical comparisons of all groups were examined using Student T-test. All data are expressed as average ± standard deviation. P values <0.05 were considered statistically significant.

3. RESULTS

A summary of all data of tensile strengths, burst pressures, operative times and actual energy is listed in **Table. 1**.

There were significant differences in the tensile strengths and burst pressures of the combination of albumin stent and solder when compared to the stent alone or solder alone ($p<0.05$). The 1.0 W 5 Hz laser setting produced the lowest the tensile strengths and burst pressures of all groups. No significant difference in operative time was seen among the three groups. However, the differences in operative time were significant. However, a significantly higher laser energy was recorded for the laser setting of 1.0 W continuous wave, and consequently, the thermal injured area significantly increased on this mode.

Table 1. The summary of tensile strength, burst pressure, operative time and actual energy at welding techniques *

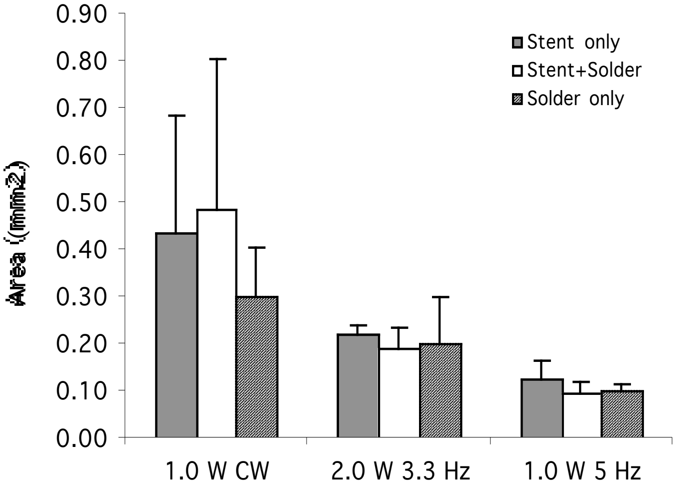
	Tension (Gram). (N)	Burst Pressure (mmHg).(N)	Operative time (Sec.)	Actual E (W)
Group 1: Stent Only				
1.0 W CW	69 ± 30(5)	136 ± 45(6)	95 ± 11	51 ± 7
2.0 W 3.3Hz	62 ± 17(4)	133 ± 58(6)	132 ± 25	23 ± 7
1.0 W 5 Hz	32 ± 13(5)	73 ± 30 (6)	142 ± 19	20 ± 3
Group 2: Stent +Solder				
1.0 W CW	97 ± 30(4)	183 ± 25(6)	130 ± 10	70 ± 7
2.0 W 3.3Hz	82 ± 24(5)	185 ± 27(6)	156 ± 21	23 ± 6
1.0 W 5 Hz	48 ±16 (5)	61 ± 46 (6)	162 ± 32	23 ± 6
Group 3: Solder Only				
1.0 W CW	73 ± 20(5)	93 ± 35 (6)	125 ± 13	68 ± 8
2.0 W 3.3Hz	45 ± 17(4)	77 ± 35 (6)	148 ± 11	23 ± 3
1.0 W 5 Hz	29 ± 14(4)	59 ± 40 (6)	169 ± 21	24 ± 5.

*Average ± SD

Higher burst pressures were observed in group 2 using the albumin stent and solder together. The burst pressure was over 200 mmHg in both the stent and solder combination group (7/12) and in the stent alone group (2/12). The bursting pressure could not be recorded due to the limitation of the pressure transducer. However, in group 3, using solder alone, the average burst pressure were 93, 66 and 54 mmHg on 1.0 CW, 2.0 W 3.3 Hz and 1.0 W 5 Hz mode, respectively.

Tissue thermal damage was noticed in all samples. Thermally coagulated ureteral tissue was indicated by loss of birefringence in the extracellular matrix under a polarized light microscope and the sharp color change corresponded to the coagulated area in a H & E stain with a normal light microscope. The damaged cells became swollen and lost their fine structure (**Fig. 3**). There were no significant differences in damaged area between using the albumin stent and liquid solder. A significant difference in area of tissue damage was observed among the various laser setting groups. The laser setting of 1.0 W CW produced more tissue thermal injury at the anastomosis site. (**Fig. 2**)

Fig. 2. Thermal damaged and Laser setting (Mean ± SD)



4. DISCUSSION

Successful ureteroureterostomy depends on precise surgical technique. A watertight, tension-free, mucosa to mucosa anastomosis is required to minimize postoperative fibrosis and stricture formation for this technique. The laser tissue welding technique has interested urologists due to its many advantages, such as no foreign body reaction, no lithogenesis, providing a watertight seal immediately, and causing less tissue trauma when compared to conventional techniques. The laser soldering technique shows the promise in terms of welding strength and reliability. Albumin is being widely used as a safe soldering agent for laser welding due to its complete immunological biocompatibility [1,8].

We used a dissoluble albumin stent to support ureteral stump intraluminally for precise end to end apposition. A conventional stent used during ureteral surgery serves to align the area of anastomosis, provide a mold around which ureteral healing can occur, prevent extravasation by diverting the urine past the anastomosis, and alleviate obstruction from postoperative edema. However, conventional stent may also cause decreased peristalsis and low pressure reflux. Previous research indicated that irreversible and deleterious renal and ureteral changes could take place with prolonged ureteral stenting.[12.] The albumin stent provided the largest diameter scaffold to fit comfortably in local within the ureteral lumen for healing and adequate diversion without producing ischemia. The albumin is temporary since it dissolves in 30 minutes in the ureter. At same time, it acts as solder to join ureteral stumps with laser welding.

The ureter is a hollow muscular organ, which is very sensitive to extra-circumstantial irritation. When using liquid solder to weld a tubular organ, such as a ureter, a rigid and fix coagulated ring might limit its muscular diastole, and thereby produce a stricture. Furthermore, the lack of a scaffold makes it more difficult to get precise apposition for different diameter vessels in a spatulated end to end fashion. The albumin stent was designed to intraluminally support the vessel edge to get a precise mucosa to mucosa apposition. The stent is comprised of human albumin and ICG so that it acts not only as an intraluminal stent, but also as a laser solder component. The laser energy passes through the tissue and is directly absorbed at the tissue and the stent interface. The laser irradiated part of the albumin stent is denatured by the laser energy and forms a solid non soluble ring to approximate the vessel edges. The undenatured component is dissolved by urine in 10-20 min. The denatured albumin is biocompatible and degradable during the wound healing procedure [1]. In our previous studies, we have demonstrated that the denatured albumin was degraded by 4 weeks[10]. However, the post surgery ureter stricture was noticed in the previous study due to the thermal damaged caused by laser irradiation. We designed this study to seek better laser parameters for clinical applications. Our results showed that the albumin stent could be used to reinforce the strength of laser welding and provided satisfactory water tight sealing at ureteral anastomosis. Recently, several investigators have used highly concentrated solder to enhance the welding strength. Those studies showed laser weld strengths depend on solder concentration [5]. Our data agrees with those previous results. In our study, combination with albumin stent and liquid solder provided the strongest weld strength.

The ideal laser welding process is to create maximum tensile strength and to minimize tissue thermal injury. Unfortunately, laser soldering still is an experiential operative process. Surgeons estimate the laser effects based on visual feedback during laser welding. Significant variation was present in the different groups due to the lack of a standard end point in the laser welding process. Various laser and energy settings were screened for controlling tissue thermal injury and increasing weld strength. In this study, the laser setting was on continuous wave and pulse mode. On CW mode, higher energy exposure to the tissue increased thermal injury. However, on pulse mode, an appropriate low energy exposure could make a same weld of tensile strength as high energy, but significantly decreased thermal injury in the ureter model. Our results showed that 2.0 W 3.3 Hz setting was the best candidate for further study.

In conclusion, the strength of ureter laser soldering can be successfully enhanced using an albumin stent and a diode pulse laser. The application of the albumin stent provided a convenient, fast, and reliable method for ureterouretreostomy using laser tissue welding. The best welding result in this study was achieved by using an albumin stent with liquid solder and a 2.0 W 3.3 Hz pulse. In the near future, this technique could be applied to ureteral anastomosis, vascular anastomosis as well as other tubular organ anastomoses.

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