CONTROLLED TEMPERATURE PHOTOTHERMAL TISSUE WELDING

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ABSTRACT

Photothermal tissue welding has been investigated as an alternative surgical tool to improve bonding of a variety of severed tissues. Yet, after almost two decades of research, inconsistencies in interpretation of experimental reports and, consequently, mechanism of this photothermal process as well as control of dosimetry remain an enigma. Widespread clinical use may greatly depend on full automation of light dosimetry to perform durable and reproducible welds with minimal thermal damage to surrounding and/or underlying tissues. Recognizing photothermal damage as a rate process, radiometrically measured tissue surface temperature has been studied as an indirect marker of tissue status during laser irradiation. Dosimetry control systems and surgical devices were developed to perform controlled temperature tissue welding using surface temperature feedback from the site of laser impact. Nevertheless, end points that mark the completion of a durable and stable weld have not been precisely identified, and subsequently, not incorporated into dosimetry control algorithms. This manuscript reviews thermal dosimetry control systems of the 1990s in an attempt to systematically indicate the difficulties encountered so far and to elaborate on major issues for photothermal tissue welding to become a clinical reality in the new millennium. © *1999 Society of Photo-Optical Instrumentation Engineers.*[S1083-3668(99)00203-8]

Keywords anastomosis; dosimetry; feedback control; IR radiometry; photocoagulation; temperature control; tissue fusion; tissue welding.

1 INTRODUCTION

Since the early 1980s photothermal tissue welding (PTW) has been investigated as an alternative surgical tool to improve the bonding/anastomosis of a variety of severed tissues. PTW was shown to (1) shorten operative times, (2) reduce bleeding, (3) provide immediate fluid-tight sealing, (4) reduce foreign body response associated with healing around sutures, (5) preserve mechanical integrity of the ''weld site'' in the long run, (6) provide technical ease (however, the surgical technique is not reproducible/obvious to trained surgeons), and (7) achieve successful bonding rates comparable to conventional suture techniques (yet, observations reveal low bond strength in the most critical 36–72 h postoperatively).[1–12]

Currently, practical endoscopic devices are being developed to photothermally bond small and delicate tissues as an alternative to time consuming endoscopic suture techniques. Clinical trials with such devices are believed to lead to a medical breakthrough in minimal invasive surgery. For widespread clinical use of PTW, *reproducibility* of experimental results and *control of dosimetry* are the two major issues that have been addressed frequently by many researchers. In late 1980s, temperature feedback control (TFC) of photocoagulation processes was introduced as a dosimetry control modality. The intent of this manuscript is to overview and discuss surface temperature feedback controlled PTW (STFC-PTW) in 1990s.

2 MOTIVATION FOR THERMAL FEEDBACK CONTROL

During PTW, surgeons typically look for subtle visual clues on tissue surface, such as whitening, desiccation, and shrinkage, as an end point for completion of a photothermal weld. Thus, success rates very much depend on surgical experience, subjective visual feedback, and motor reflexes on the part of the surgeon.

Ideally, automated dosimetry should be based upon indicators and extent of thermal damage to tissue during laser irradiation to (1) respond to thermal changes in tissue at rates much faster than a surgeon's reaction time, and (2) attain the optimum end point for completion of surgery. Yet, as the temperature and extent of coagulation along the severed edges and inside the tissue being irradiated are practically impossible to monitor, models were developed to determine dosimetry parameters prior to treatment using simulations. Such models use optical and thermal properties (OP and TP) of

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tissues to predict their photothermal response.[9,13,14]

In general, light penetrates less as tissue coagulates and dehydrates, leading to dramatic temperature increases.[9,15–27] In other words, both OP and TP are functions of temperature and hydration levels inside the tissue and do not remain constant during laser irradiation. Therefore, computationally intensive real-time *in vivo* measurement or estimation of OP and TP is required for simulation and open and/or closed loop control of photothermal coagulation.[9,13,14] Mathematical simulations of real-time applications can give a good approximation to temperature evolution and necrosis depth in laser irradiated homogeneous tissue.[9,14] However, for any given tissue, the OPs depend on the irradiation wavelength and the two OPs, namely the absorption and the scattering coefficients, are not sensitive to temperature fluctuations in the same way. The scattering coefficient increases drastically when tissue confirmation changes as a result of laser irradiation leading to beam broadening which in return leads to reduced necrosis depth.[9,14]

As initially observed by Mordon and associates, (1) the thermal reaction and absorbed laser energy are strongly dependent on both exposure time and temperature evolution during laser exposure,[28–30] and (2) although thermal damage to tissue can be quantified postoperatively by histology, control of the extent of necrosis is difficult as the full extent of thermal damage needs 48–72 h to develop completely in living tissues.[9,21]

To study thermal properties of bovine joint capsule, which primarily consists of collagen, whose denaturation is believed to play an important role in PTW, Anderson and associates heated specimens in saline baths at constant temperatures for varying times. At 60 and 62 °C, they (1) found out that shrinkage directly correlates with exposure time, and (2) showed that thermal shrinkage of collageneous tissue correlates with denaturation of collagen fibers, and depends on both time and temperature.[31] Earlier, they had demonstrated that disks of tendon, also composed entirely of type I collagen, heated in saline bath under pressure *in vitro* can form very strong and optimal bonds at a narrow temperature window about 62 °C.[32,33]

From these investigations researchers concluded that temperature and exposure time are the two parameters to monitor and to control thermal damage to tissue during PTW. Consequently, attempts were made to use open loop control by adjusting length and sequence of laser pulses in real time during photothermal coagulation. Control parameters were derived from temperature data acquired during laser irradiation of sample tissue specimens.[9,13] Additionally, saline drop[34] or cryogen spray[35] cooling was used to protect superficial tissues from excessive thermal buildup and to induce spatially selective photocoagulation.

For closed-loop TFC of laser irradiation, thermocouples and thermistors were used to measure the temperature of laser irradiated tissues.[36,37] However, these devices are difficult to use and position (embed) in nonaqueous media, and like all contact methods, they may alter the temperature of the irradiated site by absorbing some of the laser light and/or generated heat. Furthermore, the response times of these devices are longer than desired, typically on the order of a few 100 ms or more, close to an experienced surgeon's reaction time.[38] Thus, more recently, the diagnostic capability of infrared (IR) radiation was utilized to remotely monitor surface temperature (ST) of irradiated sample sites in real time. IR thermometry is based on the fact that all bodies at finite temperatures emit IR radiation into free space. This emissive power is given by

$$E(T)=\epsilon\sigma T^4,$$

where ϵ is the emissivity of the body surface, σ is the Stefan–Boltzmann constant (5.67×10^{-12} $\mathrm{W\,m^{-2}\,K^{-4}}$), and T is the absolute temperature of the body. Assuming broadband tissue emissivity remains constant during laser irradiation, STs ($\sim$20 μm thickness) can be monitored using noncontact IR thermometry. In reviews of medical thermography and tissue OPs, $0.97\leqslant\epsilon\leqslant1$ for skin;[39,40] for other tissues, ϵ is slightly lower.[41,42] In general, $\epsilon\sim0.97$;[43] also, in the 2–5 μm IR band, emissivity of skin is independent of wavelength and observed pigmentation in the visible spectrum.[42] However, emissivity decreases when tissues are dehydrated,[40] a possible consequence of temperature increase, a fact usually not taken into account during photothermal laser-tissue interactions. Nevertheless, Love showed that a ±0.01 variation in ϵ will result in only a ±0.01 °C variation in observed temperatures at room temperature,[42] and Çilesiz indicated that a 0.07 uncertainty (0.99–0.92) in emissivity of bodies heated up to 100 °C will result in a maximum error of 4 °C in temperature readings taken at room temperature (Ref. 44, pp. 202–208).

For thermal dosimetry control, tissue ST over time is monitored as an indirect marker of tissue status and denaturation is recognized as a rate process governed by local temperature-time response expressed by the Arrhenius integral as

$$\Omega[T(t)]=A\int e^{[E_\Omega/(RT(t))]}\,dt,$$

where accumulated thermal damage is defined by the dimensionless parameter Ω. A ($\mathrm{s^{-1}}$) is the reaction rate constant for the specific type of tissue, E_Ω ($\mathrm{J\,mol^{-1}}$) the energy required to activate the tissue, R ($8.31\,\mathrm{J\,mol^{-1}\,K^{-1}}$) the universal gas constant, and $T(t)$ (K) the temperature of the tissue in a certain position at time t.[45,46] From Arrhenius integral, laser induced thermal damage increases at a constant rate when tissue temperature is held constant, yet, for linearly increasing temperatures, the rate of increase in damage, i.e., $d\Omega/dt$, is exponential, sug-

gesting an accelerated rate of thermal damage to tissue that is almost instantaneous. Therefore, regulation of ST at a quasi-constant level is hypothesized to result in a slower, but steady, progression of thermal damage to tissue, eliminating exponential increases in the rate of denaturation associated with uncontrolled thermal buildup.[11,13,29,47] Experiments carried out *in vitro* by Welch and associates on arterial and intestinal tissue to test this hypothesis showed that there is a temperature window for optimally strong thermal welds.[47,48] In addition, finite element analysis of STFC-PTW has shown that (1) damage penetration is less affected by laser irradiance, and (2) predictions from constant ST irradiation are less sensitive to actual OPs and their changes during photocoagulation.[49]

3 DOSIMETRY CONTROL SYSTEMS

3.1 BRIEF DESCRIPTION

Research on STFC-PTW has been carried out by several groups affiliated with (1) Tel Aviv University (TAU), (2) the University of Texas (UT), (3) New York Hospital (NYH) and Eastern Virginia Graduate School of Medicine (EVGSM), (4) ABIOMED R & D (ARD) and Harvard Medical School (HMS), and most recently, (5) Lawrence Livermore National Laboratory (LLNL) and the University of California (UC).

The TAU group developed an all fiberoptic radiometric system for TFC of CO_2 laser assisted PTW. A simplified diagram of their experimental setup is shown in Figure 1(a). A silverhalide fiber was used for laser delivery onto the tissue surface. IR radiation emitted by the irradiated tissue was collected by another silverhalide fiber, optically focused onto a photonic thermal detector, and electronically processed by system hardware and software. A special filter was used to filter out IR laser radiation backscattered from tissue surface. Both delivery and collection fibers were held together using a holder to face the same spot and positioned 1 mm above tissue surface to achieve maximal radiometric signal. The radiometric signal was processed by software to provide a feedback signal for on/off control of the laser and a duty cycle adjustment of laser irradiation to achieve a stable tissue ST. Once the desired control temperature was reached, the maximal observed deviation from the control value was $\pm 2.5\,^{\circ}C$.[50,51]

The UT group has been working on thermal feedback control during PTW since late 1980s. A simplified diagram of their prototype experimental system is shown in Figure 1(b) with the detector looking down on the specimen to be welded and laser energy delivered through an optical fiber. During PTW the stationary temperature detector was focused on the site of laser impact and temperature signals were collected from a field of view (FOV) of 0.7 mm at the center of a 2–3 mm diameter laser spot. The temperature signal was processed by control system hardware to provide a feedback signal for on/off control of a laser shutter placed on the laser beam path to adjust the duty cycle of laser irradiation and thus to achieve quasi-constant tissue ST.[47]

The UT prototype system was later modified to eliminate the need to focus temperature sensor and laser delivery separately before each experiment. By insertion of a dichroic beamsplitter on the thermal path laser delivery was incorporated into the sensor housing as seen in Figure 1(c).[48] This confocal design was further improved for *in vivo* experiments and for use at near IR ($\lambda < 1100$ nm) and Ho: yttrium–aluminum–garnet (YAG) laser wavelengths.[11,12]

The feedback control system used by researchers in NYH-EVGSM is shown in Figure 1(d). Their temperature sensor consisted of an industrial IR viewer that was interfaced to a personal computer (PC). The temperature signal was processed by the PC to provide a feedback signal to adjust the output power and duty cycle of an all lines argon ion laser. The laser probe was mounted in a micromanipulator approximately 5 cm above tissue surface. The laser probe and IR viewer were separately controlled by two operators.[52]

ARD developed a microprocessor based control system for temperature data acquisition and real-time laser power control. Fiberoptic laser delivery and an IR radiometer were incorporated into a handheld surgical hand piece. A simplified diagram of their system is shown in Figure 1(e). During PTW their system was capable of controlling tissue ST within ± 2–$4\,^{\circ}C$ of a preset control value in *in situ* PTW.[53,54]

ARD also developed a two-color IR thermometer that made measurements over two separate regions of the IR emission spectrum to determine tissue ST independent of tissue emissivity, which may change as a result of coagulation and dehydration during PTW. However, due to the extremely sensitive nature of the IR detectors needed, a handheld device incorporating two-color thermometers has not yet been feasible for *in situ* PTW.[53,55]

The newest group working on STFC-PTW, the LLNL-UC group, recently developed a two-color IR thermometer using a hollow glass optical fiber to collect IR radiation and a silica optical fiber for laser delivery. A reflective chopper was used to modulate and split the collected IR radiation into two paths to be sensed by two different IR detectors alternately. A hand piece containing the sensing and delivery fibers at a small angle and a guiding wire for depth gauging were used by the operator to perform PTW. A simplified diagram of the system is shown in Figure 1(f). The temperature signal was processed by the control system to provide a feedback signal for on/off control of a laser shutter

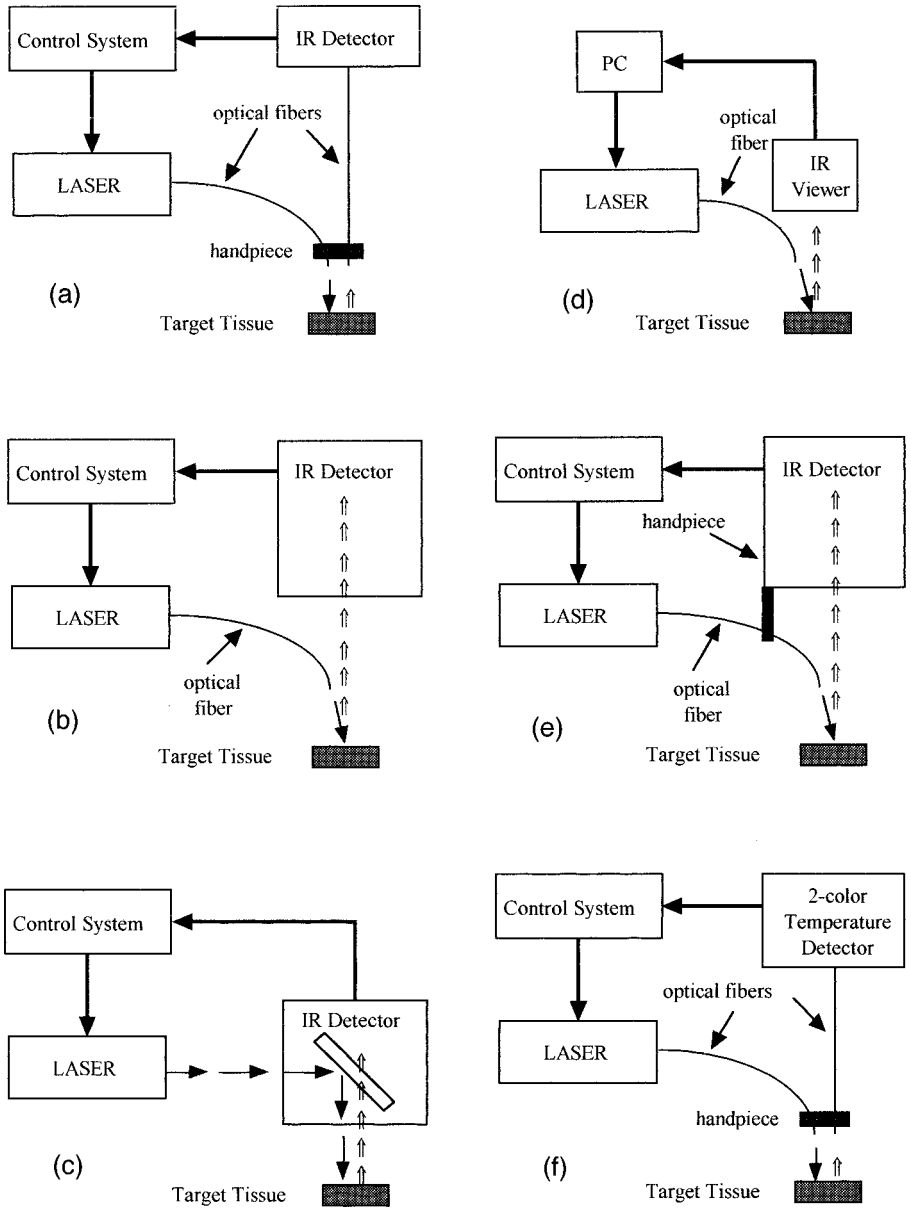

Fig. 1 Simplified diagrams of various dosimetry control systems: (a) TAU system; (b) prototype UT system; (c) final UT system; (d) NYH-EVGSM system; (e) ARD system; and (f) LLNL-UC system.

placed on the laser beam path to achieve quasi-constant tissue ST during PTW.[56] Their system is also capable of controlling tissue ST within ±1.5 °C of a preset control value using proportional integral derivative (PID) control to modulate a diode laser current.[57]

3.2 COMPREHENSIVE CRITIQUE

The specifications of the real-time control systems briefly described in the previous section are compared and contrasted in Table 1. The temperature range of most of the IR thermometers lies within the 30–120 °C band and the accuracy of temperature readings are equal to or better than 2 °C. In cases where the laser wavelength lies within the sensitivity range of the IR detector in use, special filters are used to block backscattered laser light.[12,50]

Except for the LLNL-UC system, all systems use temperature feedback from a single-color (single detector) IR thermometer to control tissue ST. By employing a two-color radiometer,[58] ST can be measured *independent* of (1) changes in ''tissue surface to detector'' distance, and (2) fluctuations in tissue surface emissivity as a result of heating and subsequent dehydration of tissue during laser irradiation.

FOVs of IR thermometers used for STFC-PTW varies between 0.4 and 1.5 mm. Except for TAU and NYH-EVGSM systems, FOV of temperature sensors is significantly smaller than the spot size of the laser

Table 1 Comparison of dosimetry control systems.

System	Laser spot size [mm]	Detector range [μm]	FOV [mm]	Response time [ms]	Accuracy [°C]	Laser irradiation control logic
TAU[i]	=FOV	2–20	=Spot Size	>100	0.2	On–off control of laser powder
UT-1[b]	2–3	2–5	0.7	15	1	On–off control with external laser beam shutter
UT-2[c]	2	2–5	0.6	45	1	On–off control with external laser beam shutter
UT-3[a]	1.5–2	2–5	0.75	50	1	On–off control with external laser beam shutter
NYH-EVGSM[d]	1	8–14	1.5	100	2	Laser shutter control and output power adjustment
ARD[e,f]	0.7–1	8–13	0.4	~30	1	Laser output power adjustment; laser diode current adjustment
LLNL-UC[g,h]	3	2–6/2–12	1	~30	1	On–off control with external laser beam shutter; more recently, laser output power adjustment

[a]Reference 11.
[b]Reference 47.
[c]Reference 48.
[d]Reference 52.
[e]Reference 53.
[f]Reference 54.
[g]Reference 56.
[h]Reference 57.
[i]Reference 59.

beam on tissue surface. In UT, ARD, and LLNL-UC systems, the ''spot size to FOV'' ratio is 2 or larger. In the TAU system this ratio is approximately 1. In other words, assuming the laser beam is of Gaussian shape, the TAU system monitors the ''overall'' temperature across the entire laser beam on tissue surface, whereas in UT, ARD, and LLNL-UC systems the temperature in the central part of the laser beam is monitored. Therefore, temperatures measured with the TAU system may appear lower than those measured by the UT, ARD, and LLNL-UC systems under the same irradiation conditions as a result of the laser power density gradient across the FOV. Hereby one should also recall that calibration of IR radiometers is generally carried out using blackbodies of known temperatures with a uniform temperature field. Finally, the spot size to FOV ratio of the NYH-EVGSM system is 0.66, i.e., by averaging IR emission from a spot larger than the laser beam diameter on tissue surface, the temperatures measured with this system are grossly underestimated with respect to the temperatures induced by laser irradiation.

Generally, the response time (RT) of an IR radiometer is closely related to the modulation frequency of IR radiation determined by a chopper usually placed before a detector. This chopper modulated signal as detected by an IR sensor is very small when compared to major noise sources (such as, 50 or 60 Hz interference). To recover the original temperature signal from the hardware and/or software processed sensor signal with a high signal-to-noise ratio, phase sensitive demodulation techniques, i.e., lock-in amplifiers, are utilized. RTs of IR thermometers are therefore dependent on time constants of lock-in amplifiers. Inherent delays of mechanical shutters and other devices used in dosimetry control systems are additional factors prolonging RTs of TFC systems.

The RTs of TFC systems used for PTW vary between 15 and 100 ms. Currently, the fastest systems are the ARD and LLNL-UC systems with RTs about 30 ms. These groups both adopted diode laser current modulation for STFC-PTW.[53,57] Until diode lasers became available on the market, the general trend in laser irradiation control to achieve quasi-constant or stable tissue STs has been on–off control of laser output power (thus pulse width and duty cycle modulation of laser output) by hardware and/or software control of either an internal or an external laser shutter. To the author's experience, laser current control for bulky lasers, such as an

argon ion laser, has not always been feasible due to comparatively long time delays required for laser current adjustment.

In the most up-to-date versions of TAU, UT, ARD, and LLNL-UC systems, temperature sensing, and laser delivery are incorporated into the same ''temperature sensor/laser delivery'' housing.[11,53,56,59] While the UT group developed a co-aligned/confocal device for *in vivo* laboratory experiments, TAU, ARD, and LLNL-UC groups developed hand pieces for experimental work in a hospital environment and for clinical trials. TAU and LLNL-UC devices rely on all fiberoptic sensing and delivery;[56,59] in contrast, the ARD surgical hand piece delivers laser light with an optical fiber, but sensing is optical;[53] and the UT device is all optical[11] (also see Figure 1). No additional information has been available about the system developed by NYH-EVGSM, which as presented in literature is currently not practical for laboratory experiments.[52]

An all-optical confocal device, such as that developed by the UT group, is useful for experimental work in a laboratory setting, yet it may not be practical for clinical trials. On the other hand, a small surgical hand piece incorporating delivery and sensing optics (fiberoptic and/or else) is very practical from the point of view of the operating surgeon, but its design may prove to be a challenge due to temperature dependent behavior of optical components. It is known that during irradiation tips of delivery fibers get hot. Heated delivery fibers placed very close to or within the FOV of sensing optics may influence signals collected by those IR sensing optics. Additionally, the hand piece may get warmer by heat transfer from the surgeon's hand during a procedure. To overcome this problem, ARD developed compensation techniques to accommodate a range of fluctuating hand piece temperatures.[53] Thus, for TFC to become a reality in clinical trials in the near future, two important issues previously not considered by many researchers should be investigated: (1) reliability of IR temperature readings taken with heated optical elements in a nonstable (fluctuating) temperature field, and (2) effective compensation for their behavior.

For minimal invasive laser surgery with TFC, collecting and sensing fibers may be guided endoscopically to the point of surgery inside the patient's body. Nevertheless, additional issues, such as absorption of IR signals in a fluid environment or keeping the ends of fibers clean and clear at all times should be considered. Furthermore, the use of depth gauges in endoscopic surgery may be difficult if not impractical. Consequently, distance insensitive temperature monitoring using (1) two-color radiometry and (2) a system like the one developed by LLNL-UC group may have to be adopted.

4 REVIEW OF STFC-PTW

A short summary of STFC-PTW by various groups is given in Table 2. STFC-PTW was applied for repair of arteriotomies, venotomies, enterotomies, urethral defects, corneal wounds, urinary bladder, and skin incisions.

The TAU group in association with various medical professionals carried out urinary bladder incision repair *in vivo* using CO_2 laser assisted STFC-PTW and found 55 °C to be the optimal feedback control temperature (FCT) for this tissue. They observed that weld strength decreased sharply when FCT varied by a few degrees about 55 °C.[50,60,61] In the light of the discussion in previous sections, the 55 °C FCT might in reality have been higher, had simultaneous temperature measurements been carried out with a system having a smaller FOV. On the other hand, the NYH-EVGSM group working on urethral repairs using protein solders in argon laser-assisted STFC-PTW found 80 °C to be the optimal FCT.[52] Histologically they observed a significant degree of collagen denaturation and urothelial damage at this FCT which implies that the measured 80 °C surface temperature may have been largely underestimated as the FOV of their system is significantly larger than those of other systems. In addition, there is a very limited number of reported studies from different groups working on STFC-PTW on urologic tissue repair with or without protein solders. Therefore, a meaningful comparative analysis is not yet possible, nevertheless, future studies by different groups on identical tissues may be directed towards investigating a possible correlation between *optimal* FCTs and laser wavelengths, i.e., *interdependence* of laser wavelengths and FCTs.

Arteriotomy and venotomy repairs were carried out using argon ion and near and mid IR lasers. Successful *in vitro* and *in vivo* repairs were reported at various control temperatures ranging from 50 to 120 °C. Successful and durable welds *in vivo* were studied at slightly lower temperatures ranging from 50 to 90 °C and the ARD-HMS group reported that temperature range for suitable welds was very narrow, although durable welds could be created in a broad range of FCTs. They reported that optimal TFC for rat arteriotomy repair *in vivo* using protein solders was 80 °C.[53] Surprisingly, using biological solders arteriotomy repairs were reportedly successful at 65 °C, a temperature generally lower than the denaturation temperature of protein solders used for enhancement of laser assisted welds.[62] According to the LLNL-UC group's preliminary report, patent vessel welds using an argon ion laser were created at 50 °C, the lowest FCT reported in literature for arteriotomy and venotomy repair *in vivo*.[56] However, the LLNL-UC group did not perform any welds at higher temperatures; thus no comparative data on the influence of FCT on weld strength are available from their preliminary report.

Table 2 Comparison of results reported in literature.

Group	Laser wavelength [nm]	Tissue type	Studied FCTs [°C]	Optimal FCTs [°C]	Remarks
TAU	10 600	Urinary bladder (puncture or large opening) repair in rats *in vivo*[e,k]	35,45,50, 60,65,75	55	Strength of welds decreases sharply with increasing or decreasing FCT about 55 °C
	10 600	Corneal wound closure in bovine eyes *et vivo* and in rabbit eyes *in vivo*[l]	55	NA	Control specimens and laser welded wounds heal in similar fashion, yet laser welded wounds are significantly stronger mechanically
	10 600	Cystostomy repair, in rats *in vivo*[j]	55	NA	Significant temperature gradient between tissue surface and inner layers in bladded wall, yet better mechanical strength with laser welding than with sutures
UT-1	488–514	Longitudinal human saphenous venotomy repair *in vitro*[c]	70,80,90, 100,110, 120	100–120	Significant temperature gradients develop along the depth of repair during laser irradiation
UT-2	488–514	Transverse canine enterotomy repair *in vitro*[d]	80,90,95, 100	90–95	Welding is not successful at FCTs less than 80 °C
UT-3	488–514 2090	Complete enterotomy repair in rats *in vivo*[a,b]	90	NA	Although sloughing of tissue bordering repair (sutured, laser welded with and without TFC) results in weak bond strength 36–72 h postoperatively, TFC reduces thermal damage to tissue and improves stability of laser welds
NYH-EVGSM	488–514	Longitudinal urethral defect repair in rats *in vivo* using protein solder[f]	50,60,70, 80,90	80	Effective acute welds can be obtained at FCTs lower than those that produce the strongest welds
ARD-HMS	1950	Acute transverse arteriotomy repair in rats *in vivo*[g]	70–90	80	Temperature range for suitable welds is very narrow
	1320	Full thickness porcine skin incision repair *in vivo* using solder[h]	65,75, 85,95	~80	Laser penetration depth matching tissue thickness results in uniform full thickness heat deposition in tissue
	808 and 1950	Femoral arteriotomy repair in rats *in vivo* using solder[m]	65	NA	Sloughing to tissue bordering repair results in low tensile strengths short term postoperatively TFC (1) reduces collateral spread and depth of thermal damage, and (2) makes tissue welding less dependent on variations in surgeon technique
LLNL-UC	488–514	Longitudinal canine femoral venotomy and arteriotomy repair *in vivo*[i]	50	NA	Increase in collagen crosslink concentration and increased patency rates observed after PTW with TFC

[a]Reference 11.
[b]Reference 12.
[c]Reference 43.
[d]Reference 48.
[e]Reference 50.
[f]Reference 52.
[g]Reference 53
[h]Reference 54.
[i]Reference 56.
[j]Reference 61.
[k]Reference 65
[l]Reference 66.
[m]Reference 67.

Nevertheless, in open loop procedures using saline drip cooling, tissue ST never exceeded 60 °C. The latter is possible, because the ST measured may be that of the thin saline film over the tissue surface. Considering that the ARD-HMS group (with and without using biological solders) could not successfully weld vessels using the 1.95 μm or the 808 nm diode laser at temperatures less than 65 °C, the durability of welds created at a low FCT like 50 °C is controversial and this discrepancy as well as the possible correlation between *optimal* FCTs and laser wavelengths as mentioned above should be further investigated.

The ARD-HMS group emphasized that the degree of acute and chronic tissue damage was highly dependent on FCT during laser irradiation.[54] They observed histologically that the depth of photocoagulation was strongly dependent on FCT supporting the finite element analysis results of Glenn, Rastegar, and Jacques.[49] Sloughing of tissue bordering repair was associated with low tensile strength in the early phase of healing. A similar observation was also made by the UT group in rat enterotomy repair using argon and Ho:YAG laser irradiation at 90 °C FCT,[11,12] optimal welding temperature for this tissue found in an *in vitro* study.[48] ARD-HMS and UT groups observed none or very few latent failures in STFC-PTW and all groups concluded that STFC-PTW (1) provided a degree of control to the PTW procedure, and (2) stabilized the laser assisted repairs to resist spontaneous failures postoperatively. Based on calculated and experimentally validated temperature profiles, the ARD-HMS group postulated that ST should be a proper marker of PTW, *if* the absorption depth of tissue at the laser wavelength used approximately matched tissue thickness.[53] Finally, the UT group and Mordon and associates emphasized the need to identify nonthermal end points such as optical reflectance feedback[63,64] coupled to thermal feedback which may directly lead to a clinically successful reproducible weld, because nonreliable visual cues are still being used as ill-defined end points to complete STFC-PTW procedures.[12,13,29]

5 Concluding Remarks

In the literature on PTW, inconsistencies were frequently mentioned. Yet, to the author's knowledge, no published report or review compared results using the same tissues and lasers under identical experimental conditions, but with different dosimetry control systems. To this date, STFC-PTW experiments reported in literature were carried out under *diverse* experimental and tissue conditions. To ascertain a credible and promising future for STFC-PTW in clinical practice, the performance of different dosimetry control systems should be tested and compared under *standard conditions* using a number of *specified tissue types*. For dosimetry control systems with fairly similar specifications as given in Table I, the diversity in a limited number of experimental observations may only be explained after vigorous analysis of such experimental data.

Identification of *precise nonthermal end points* that mark the completion of a stable and durable weld and the integration of such end points into a dosimetry control system should keep the researchers working on PTW and STFC-PTW busy in the immediate future, because *full automation of dosimetry*, including automated completion of a weld, may be essential for PTW to become a clinical reality in the new millennium.

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