ELSEVIER

Information Sciences 123 (2000) 271–280

INFORMATION SCIENCES
AN INTERNATIONAL JOURNAL

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Real-time ultrasound-guided fuzzy control of tissue coagulation progress during laser heating

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Received 26 November 1998; received in revised form 28 May 1999; accepted 23 October 1999

Abstract

Laser coagulation is a minimally invasive therapy that utilizes laser energy to thermally kill benign and malignant lesions such as cancers, at the temperature range of 55–85°C. It is of clinical importance to control the laser deposition into the tissue in such a way that the lesion will be destroyed while the surrounding healthy tissue will remain intact. However, a primary technical difficulty in achieving this goal lies in the fact that the relationship between the delivered laser energy and the tissue damage is nonlinear and time-varying, which cannot be accurately predicted or rigorously modeled due to the significant difference in various physical properties of even similar tissues. In this paper, we present a novel real-time ultrasound-guided fuzzy laser control system for coagulation. Current status of tissue coagulation depth, noninvasively measured by an innovative ultrasound system that we recently developed, was fed into a fuzzy proportional-derivative (PD) controller, which periodically adjusted output power of a 1064 nm Nd:YAG laser. The ultrasound-guided system was tested in 21 in vitro experiments in which fresh sheep liver samples were irradiated by the laser with a coagulation setpoint ranging from 4 to 14 mm with a 2 mm increment. We provide analytical

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PII: S0020-0255(99)00134-6

analysis and design of the fuzzy controller, which turns out to be an inherently nonlinear PD controller with self-tuning variable gains. We also present the hardware and software implementation of the entire measurement and control system. Our control system is unique, and it is the first laser control system that is guided by noninvasive ultrasonic measurement in real-time.

Keywords: Fuzzy control; PID control; Laser control; Thermal therapy; Coagulation; Ultrasound; In vitro

1. Introduction

Therapeutic application of heat, generated by laser, radio-frequency irradiation, microwaves and high-intensity focused ultrasound, has been widely accepted for treatment of tumors and lesions. Different thermal therapies use different temperature ranges [10]: (1) tissue hyperthermia that takes place at 43–50°C and causes cell death, (2) tissue coagulation that starts at about 55°C and leads to protein denaturation, and (3) tissue vaporization, charring, and ablation at 100°C or above. Clinical studies show that thermal therapies hold great promise to offer safer, less expensive and less invasive treatment than traditional surgery. To effectively treat tumors at a critical position (e.g., brain) without damage to the surrounding tissue, it is vital to know, quantitatively and in real-time, the geometry of the treated tissue. However, accurate mathematical prediction of thermal damage or tissue thermal response is extremely difficult due to the complicity of thermal energy transportation in tissue, tissue heterogeneity, blood perfusion, and heating power and duration. Thermal therapies are currently performed with the unaided eye. Damage information deep within the tissue is unavailable. Two common obstacles to widespread applications of thermal therapies have been: (1) the lack of a noninvasive detection method for real-time measurement of the treated tissue volume, and (2) the lack of an automatic feedback control technique that could produce a precisely desired treated treatment.

To address the first obstacle, noninvasive methods have been proposed, including computed tomographic (CT) imaging, magnetic resonance (MR) imaging, and ultrasound imaging. The CT results are discouraging. MR imaging systems could produce good contrast images of thermal lesions, but they are too expensive and bulky. The results of B-scan ultrasound monitoring are observational, qualitative and inconsistent.

Much effort has also been made to overcome the second obstacle. An adaptive controller was developed to regulate a Nd:YAG laser and an infrared radiometry detector was employed to provide feedback information [7]. A PID plus band-bang feedback control system was developed for focused ultrasound

hyperthermia using thermocouples for temperature measurement [5]. Relying on thermocouples, we recently developed a fuzzy PD laser temperature control system for hyperthermia, coagulation and welding [3]. Temperature control for tissue fusion was also studied [1]. A nonlinear multivariable control method was proposed for interstitial laser hyperthermia, with temperature being measured by thermocouples [11]. Other advances in the feedback control of laser interstitial hyperthermia include those presented in [2,6,12]. A fiber-optical radiometer was used in feedback temperature control of tissue irradiated by a CO_2 laser [4]. A multi-point feedback temperature control system was proposed for hyperthermia under ultrasound phased-array heating, in which a modified PI controller were used in the simulation study [9]. One common problem of most of these control systems is the use of *invasive* manners to obtain the feedback signals. For the other systems, using fiber-optical radiometers, though noninvasive, can only measure temperature on the tissue surface, offering little information on temperature or damage status in the deep tissue layers.

In this paper, we present the design, analysis and implementation of a real-time fuzzy laser coagulation control system. Compared with the existing control systems, our system is based on the ultrasound detection system that we have developed, which is capable of noninvasively and automatically determining the propagation of laser-induced coagulation front deep in the tissue (e.g., 12 mm) in real-time [8]. This real-time, automated ultrasound system, being the only in existence, represents the state-of-the-art progress in overcoming the first obstacle mentioned above.

2. Materials and methods

2.1. Experiment setup

Fig. 1 shows the experiment setup for ultrasound-guide fuzzy control of laser-induced tissue coagulation. A fresh whole sheep liver, harvested immediately after animal sacrifice, was immersed in a $50 \times 25 \times 30$ cm^3 glass tank filled with 23°C tap water, and placed on an 8-mm-thick Plexiglas plate over a 3-cm-diameter circular hole in the center. To prevent the tissue from floating, it was fixed on the plate with a rubber band on each of its four sides. The tissue was irradiated by a 1064 nm Nd:YAG laser (TRIMEDYNE OPTILASE™ 1000 Modified 90W) whose energy was delivered via a 600 μm-diameter optical fiber. A Panametrics 13 mm-diameter 10 MHz broadband single-element spherical focused ultrasound transducer was used to detect progressive coagulation front in the tissue being heated. The transducer and the Plexiglas plate were arranged in such a way that the transducer beam axis vertically passed the center of the circular hole of the plate and the beam passed completely without being obscured by the plate. The optical fiber and the transducer were arranged

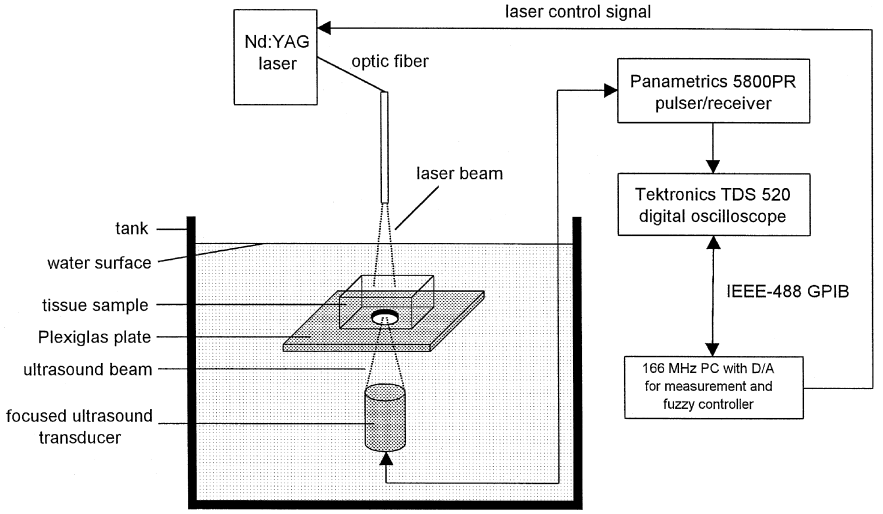

Fig. 1. Experiment set-up for ultrasound-guide fuzzy control of laser tissue coagulation.

to be coaxial. The transducer was connected to a Panametrics 5800PR pulser/receiver, where the ultrasound signals were amplified and filtered, and the processed signals were digitized at 250 MHz by a Tektronics TDS 520 digital oscilloscope. The digitized signals were then sent to a Pentium 166 MHz PC through an IEEE-488 GPIB board. The signal acquisition, occurred every 11–14 s, was controlled by a LabView^{TM} program that we developed. The exact sampling period at a particular time is a variable but only varies slightly, depending on the quality of the ultrasound signals. Prior to the control experiments, this ultrasound measurement system had already been tested in 35 experiments in which we irradiated fresh canine liver samples at various laser intensity and exposure time. The root mean square difference between ultrasonically and visually determined coagulation depths was 0.77 mm, and the mean absolute error was 0.6 mm. The reader is referred to [8] for more details. We developed a C program that used the digitized ultrasound signals to compute in real-time the latest coagulation front in the tissue. The computed result was sent to a fuzzy PD controller, also implemented in C, that outputted its control action to a National Instruments 12-bit D/A converter and adjusted the laser control signal. The full range of the converter is 0–5 V. The C programs were called by a main LabView program with a graphical user interface that we developed for the measurement and control. As the fuzzy controller took little computing time, the sampling period of the entire control system was 11–14 s, the smallest achievable by our equipment.

The laser control signal regulates driving current of the laser, resulting in adjustment of laser output power. Laser thermal effect on tissue is determined

by laser intensity, I in W/mm^2, as it involves with laser spot size on tissue surface πr^2, where r is the spot radius, as well as with the delivered laser power, P in W, which is the product of laser output power on console multiplied by the efficiency of the optical fiber

$$I = \frac{P}{\pi r^2}. \tag{1}$$

In our experiments, $r = 5$ mm. We found the relationship between laser output power and laser control signal, S in V, was nonlinear and had a threshold of about 2.46 V, below which laser output power was zero. We conducted experiments (up to 4.0 V corresponding to about 50 W laser power, high enough for our experiments) and processed the resulting data using the least-squares fitting, obtaining the following relationship:

$$S = -0.0002P^2 + 0.0392P + 2.4615, \qquad S \in [2.4615, 4]. \tag{2}$$

Combining (1) and (2), we obtain

$$S = -1.23245I^2 + 3.0772I + 2.4615. \tag{3}$$

The heart of the laser control system is a fuzzy PD controller. It calculates new laser intensity at every sampling time (denoted as $I(n)$). We then convert $I(n)$ to $S(n)$ using formula (3) and send it to the D/A converter as the output of the fuzzy controller. At time 0, $S(0) = 2.4615$ V, which correspond to $I(0) = 0$.

During the experiments, the control system was turned off when the coagulation depth setpoint had been reached. We could see a circular tissue surface area bleached by the laser heating. The liver was then moved so that laser could irradiate a new tissue area. After several experiments, we cut the tissue into two parts along a vertical plane passing the center of every bleached surface area. This was a plane in which the ultrasound beam was lying during laser heating. We could see an area of pallor caused by laser heating, surrounded by non-irradiated dark red tissue. We regarded the boundary of this pale area as the coagulation front and measured the vertical distance from the center of the bleached circular tissue surface area to the front of the coagulated region. This distance was regarded as the coagulation depth in the tissue. We also took pictures of these areas for records.

2.2. The fuzzy PD controller

Our fuzzy controller is of Mamdani type and uses the following input variables:

$$e(n) = D - d(n), \quad r(n) = e(n) - e(n-1),$$

where D is a coagulation depth setpoint, and $d(n)$ coagulation depth at sampling time n. These two input variables are fuzzified by two input fuzzy sets shown in Fig. 2, namely "Small" and "Large." Four fuzzy control rules are used:

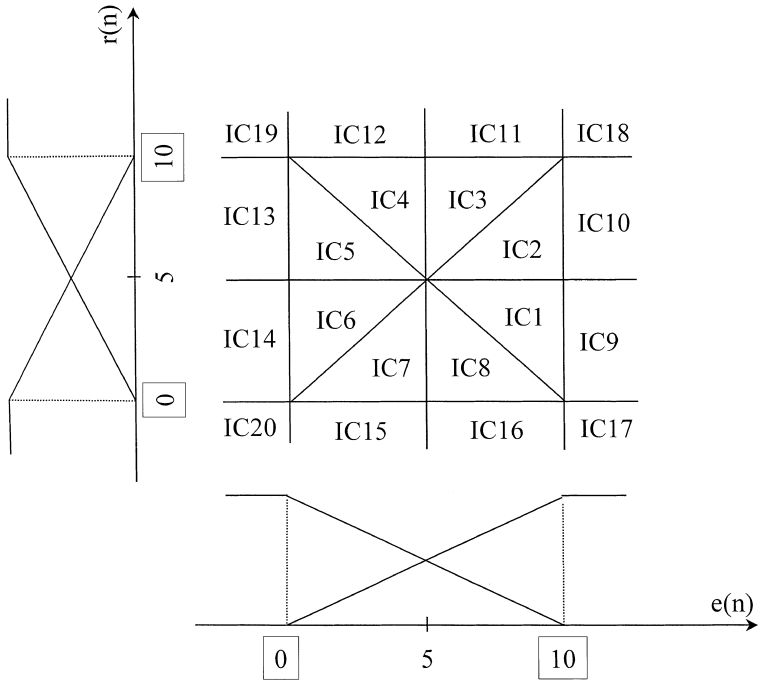

Fig. 2. Division of the input space into 20 regions for analytical structure derivation of the fuzzy controller. Input fuzzy sets for the input variables are also shown.

1st rule: IF $e(n)$ is Large AND $r(n)$ is Large THEN $I(n)$ is Large,
2nd rule: IF $e(n)$ is Large AND $r(n)$ is Small THEN $I(n)$ is Medium,
3rd rule: IF $e(n)$ is Small AND $r(n)$ is Large THEN $I(n)$ is Medium,
4th rule: IF $e(n)$ is Small AND $r(n)$ is Small THEN $I(n)$ is Small,

where "Large", "Medium" and "Small" for laser intensity $I(n)$ are three singleton output fuzzy sets at 2, 1 and 0, respectively. We denote them as $I_L = 2$, $I_M = 1$ and $I_S = 0$, respectively. We use Zadeh fuzzy logic AND operator for the ANDs in the rules and employ the popular centroid defuzzifier for the defuzzification:

$$I(n) = \frac{I_L \cdot \mu_1 + I_M(\mu_2 + \mu_3) + I_S \cdot \mu_4}{\mu_1 + \mu_2 + \mu_3 + \mu_4}. \tag{4}$$

Here, μ_i is the ANDed membership from the ith fuzzy rule.

This fuzzy controller is similar to that studied in [13] and hence its analytical structure can be derived using the technique developed in that paper. Basically, we first divide the input space into 20 regions shown in Fig. 2, each of which is an Input Combination, or IC, of $e(n)$ and $r(n)$. In each IC, we analytically

Table 1
Analytical structure of the PD fuzzy controller

IC number	$I(n)$
IC1 & IC2	$(e(n)+3r(n))/(20+4r(n))$
IC3 & IC4	$(20-e(n)+r(n))/(60-4e(n))$
IC5 & IC6	$(20+e(n)-r(n))/(60-4r(n))$
IC7 & IC8	$(r(n)+3e(n))/(20+4e(n))$
IC9 & IC10	$(10+r(n))/20$
IC11 & IC12	$(10+e(n))/20$
IC13 & IC14	$r(n)/20$
IC15 & IC16	$e(n)/20$
IC17 & IC19	$1/2$
IC18	1
IC20	0

derive the structure for Eq. (4) and the results are given in Table 1. One can see that the fuzzy PD controller is actually a nonlinear PD controller with self-tuning variable gains due to the denominators changing with $e(n)$ and $r(n)$ in IC1–IC8. Also, note that in IC3–IC6, there are offsets in the numerators. This kind of controllers can outperform the linear PID controller [13].

3. Results

The system was tested in 21 in vitro experiments in which fresh sheep liver samples were irradiated by the laser with the coagulation setpoint ranging from 4 to 14 mm with a 2 mm increment. Fig. 3 illustrates in detail one of the experimental results and Fig. 4 shows results of all the experiments. The control system performed quite well except for the setpoint of 4 mm. In three of the four experiments, there was no visible, to the naked eye, coagulative damage, although we believed that coagulation had taken place. Had a sensitive histology examination been carried out, the coagulation depth could have been measured. However, we have failed to find a suitable histology method after more than 40 histology examinations in our previous studies with the help of our expert histologist. We also should single out experiment # 19. The coagulation damage is much less than the setpoint (about 4 mm apart) most likely because 10 mm was the maximal coagulation depth achievable no matter how long the tissue would be irradiated. This experimental result is considered "outlier."

Excluding this outlier and all the 4 mm experiments, we tabulate the results in Table 2 to provide some statistical information regarding the accuracy of the control experiments. According to the table, the maximum coagulation depth in each of the five groups is always on or below the corresponding setpoint. This is partially due to the error of the ultrasound detector (As stated above,

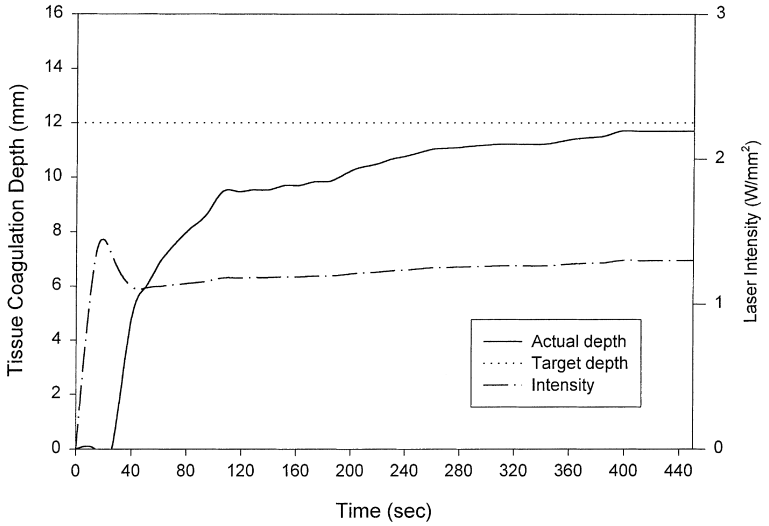

Fig. 3. One experimental result: progress of ultrasonically measured coagulation depth and the corresponding laser intensity.

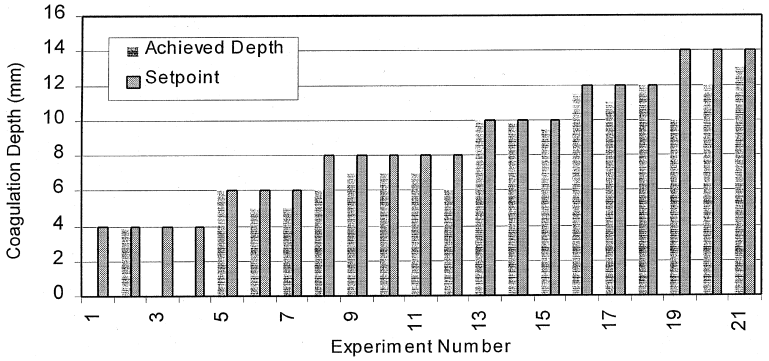

Fig. 4. All the experimental results as compared with the corresponding setpoints.

Table 2
Statistical information regarding the accuracy of the control experiments

Coagulation depth setpoint (mm)	Controlled coagulation depth (mm)		
	Mean	Minimum	Maximum
6	5.33	5	6
8	6.67	6	7
10	9.77	9.5	10
12	11.5	11	11.5
14	12.5	12	13

the mean absolute error between ultrasonically and visually determined coagulation depths was 0.77 mm).

4. Conclusions

We have presented a novel real-time ultrasound-guided fuzzy control system for regulating laser coagulation damage in tissue. We have conducted analytical analysis and design as well as implementation of the fuzzy controller, which turns out to be an inherently nonlinear PD controller with self-tuning variable gains. The system was tested in 21 in vitro experiments in which fresh sheep liver samples were irradiated by the laser with a coagulation setpoint ranging from 4 to 14 mm with a 2 mm increment. The results are satisfactory. This control system is unique, and it is the first laser control system that uses noninvasive ultrasonic measurement for obtaining the feedback signal in real-time.

Acknowledgements

This research was supported in part by an Advanced Technology Program Grant from Texas Higher Education Coordinating Board and a Biomedical Engineering Research Grant from the Whitaker Foundation awarded to Hao Ying. The authors are grateful to Brent Bell for his help in setting up the laser.

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