Exploration of in vivo Effect Assessment Factor Monitoring by Near-infrared Spectroscopy during LITT

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Abstract: By studying the variation trends of the absorption coefficient ($\mu_a$) and the reduced scattering coefficient ($\mu'_s$), which were monitored in vivo by functional near infrared spectroscopy (fNIRS) system in real time during laser induced interstitial thermotherapy (LITT), the optimized near infrared effect assessment factor would be explored. In vivo measurements of the absorption coefficient ($\mu_a$) and the reduced scattering coefficient ($\mu'_s$) were performed with a functional near infrared spectroscopy system during LITT. Fresh porcine liver tissue samples in vitro and the subcutaneous implanted rat liver cancers were examined in different laser doses and define heating times. The absorption coefficient obtained by the fNIRS increased in the pork liver experiments, but decreased in the rat liver cancer experiments. The reduced scattering coefficient increased in the pork liver experiments and the rat liver cancer experiments, it increased quickly at beginning, and gradually reached the stable state. Therefore, the reduced scattering coefficient is more suitable for reflecting the progress of damage during different biological tissues’ LITT than the absorption coefficient. This conclusion will effectively guide the study of suitable therapy effect assessment system during LITT in real time.

1. Introduction
LITT is a minimally invasive technique involving the placement of laser fiber into the tumors, followed by thermal ablation of targeted lesions by the application of laser energy. Since its first description by Bown [1] in 1983, LITT has developed into a promising local procedure for the treatment of liver tumors. During the past two decades, basic theoretical research and clinical application of LITT have been developed quickly [2]. But the therapy effect assessment in real time during LITT is still a technical problem. The current conventional practice [2-4] is local temperature measurement by using thermocouple, thermal resistor or fiber optic thermometer, another way is to get dynamic temperature by reconstruction method through MRI (magnetic resonance imaging).

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CT (computer tomography), US (ultrasound) and other imaging equipment. But these methods are difficult to popularize, due to the usual tissue infection, or technical difficulties and expensive equipments [5]. Previous experiments [6-13] have proved that the optical properties of biological tissue are affected significantly under the influence of thermal coagulation. And tissue damage degree is reflected through the changes of the optical parameters. The aim of the present study was to analyse the variety trends of the absorption coefficient and the reduced scattering coefficient on fresh porcine liver in vitro and the subcutaneous implanted rat liver cancers during LITT. Discover of these changes will play an important role in on line monitoring during LITT by using the near infrared optical methods.

2. Experimental procedures

2.1. Experimental Set-up

The experiment system was consisted of LITT thermotherapy system and fNIRS monitoring system (Figure 1). LITT thermotherapy system includes: laser (808nm, NL-FC-2.0-763 Laser Light.); optical fiber (built-in three 200µm fibers, one is for laser input, the others are for near infrared light input and output); thermoscope (WSY-4T, diameter 300µm). fNIRS monitoring system includes: USB2000 spectrometer (Ocean Optics) and halogen light source (Mikropack, HL-2000) and monitoring software. fNIRS monitoring software was developed by department of biomedical engineering of Nanjing University of Aeronautics and Astronautics based on Labview7.1 platform, which could real-time record tissue optical properties, blood oxygen parameters and flow parameters in front of the probe [14-15].

![Figure 1. Illustrative diagram of experiment system.](image)

2.2. Preparation and measurements

2.2.1 Pork liver experiments in vitro

Fresh porcine liver tissue in vitro was used for the experiment. The liver tissue would be cut into five tissue specimens (3*3*2.5cm) under room temperature (25°). After put the sample on the experiment platform horizontally, insert the optical fiber and temperature needle vertically into liver tissue about 1cm, adjust their position and fix them. Turn on the laser power switch, preheat for 15 minutes and
then begin the experiment. The optical parameters (the absorption coefficient and the reduced scattering coefficient) were recorded in real time.

2.2.2. Rat liver cancer experiments in vivo

Twelve subcutaneous implanted H22 rat cancer models were used for the experiments. Establishing the subcutaneous implanted cancer model: Cultivate the tumor cell H22 of mouse in vitro, and make out solo cell suspension with phosphate buffered solution after centrifugalization, which is about 107/ml. Then take the injection (about 0.2ml) into the mice at the right axillary fossa. After three weeks, LITT will be performed when the subcutaneous tumors have grown to a diameter about 1.5cm. Fix the rat on the experiment platform after it was dopey, and expose the subcutaneous tumor. Then insert the optical fiber and temperature needle vertically into the tumor, adjust the their position and fix them.

3. Results

3.1. Pork liver experiments in vitro

Groupings of pork liver were shown in table 1, which was the combination of four laser doses (0.76W, 0.95W, 1.23W, 1.42W) and three heating times (450s, 600s, 750s). Each group would be tested five times and test data of each group was given as mean value of the 5 measurement values. In order to ensure an accurate value, the position of optical fiber and temperature noodle should be changed for the next thermotherapy on one specimen after one test was end. The continuous changes in the absorption coefficient and the reduced scattering coefficient of porcine liver in vitro were obtained during LITT (Figure 2).

3.2. Rat liver cancer experiments in vivo

Groupings of rat model were shown in table 2. Each rat would be tested four times in different positions, test data of each tumor was given as mean value of the 4 measurement values. The continuous changes in the absorption coefficient and the reduced scattering coefficient of rat liver cancer in vivo were obtained during LITT (Figure 3).

| Table 1: Grouping for pork liver LITT experiment. (Power: output power from fiber cable) |
|--------------------------------------------------|
| Laser power(W) | 0.76 | 0.95 | 1.23 | 1.42 |
| Heating time(s) | 450s 600s 750s | 450s 600s 750s | 450s 600s 750s | 450s 600s 750s |

| Table 2: Rat grouping in LITT experiment. |
|------------------------------------------|
| Laser power(W) | 1.23(2) | 1.42(2) | 1.88(4) | 2.1(4) |
| Heating time(s) | 600(1) 800(1) | 600(1) 800(1) | 600(2) 800(2) | 600(2) 800(2) |
4. Discussion

LITT is a promising therapeutic option for treating liver tumors. But the suitable on line monitoring procedure is still a key technique problem. Thus, it is necessary to have precise knowledge about optical property changes during LITT, which delivers information about degree of damage in tissue during therapy [16]. The thermal coagulation process of biological tissue is mainly due to protein thermal denaturation, which causes the changes of optical properties of biological tissue [17]. Existing studies [8-13] have shown that the scattering coefficient changes greatly with the cumulative damage, usually 2-4 times than before coagulation, however, in contrast to the scattering coefficient, the absorption changes slightly. And differences of biological organization components led to different changes of their optical properties before and after coagulation progress. The goal of this study was to focus on that these two parameters, which are more suitable used for reflecting the progress of damage during different tissues’ LITT.

The increased changes in the absorption coefficient of porcine liver in vitro were shown in Figure 2a.
The initial value of porcine liver absorption coefficient was about 0.01 cm\(^{-1}\). Then \(\mu_a\) continuously rose with increasing coagulation temperature. \(\mu_a\) increased fast at the beginning, and then rose slowly. \(\mu_a\) rose faster when the laser power was greater. The increased changes in the absorption coefficient of rat cancer in vivo were shown in Figure 2b. In contrast to the porcine liver experiment, the continuous changes in the absorption coefficient of rat cancer decreased during LITT. The initial values of rat tumors were different, due to the different component of tumor samples.

Figure 3a shows the increased changes in the reduced scattering coefficient of porcine liver in vitro. The initial value of \(\mu_s\) was 6 cm\(^{-1}\). Then \(\mu_s\) continuously rose with increasing coagulation temperature. \(\mu_s\) increased fast at the beginning, and then rose slowly, finally it approached a stable state. \(\mu_s\) increased by 195\% over the entire progress and by 165 \% in the first 200s (1.42W). The upward tendency of \(\mu_s\) at different laser powers was similitude, but the rising velocities were different. \(\mu_s\) rose faster when the laser power was greater. The minimal final value of \(\mu_s\) was achieved at 0.95W about 12.6 cm\(^{-1}\), and the maximal final value was achieved at 1.42W about 18.5 cm\(^{-1}\).

Resemblance to the porcine liver in vitro, the reduced scattering coefficient of rat liver cancers in vivo increased during LITT (Figure 3b). The initial value of \(\mu_s\) was 7 cm\(^{-1}\), and \(\mu_s\) continuously rose with increasing coagulation temperatures. It increased fast at the beginning, and then rose slowly, finally it approached a stable state. \(\mu_s\) increased by 73.6\% over the entire progress and by 68.8\% in the first 200s. The upward tendency of \(\mu_s\) at different laser powers was similitude, but \(\mu_s\) rose faster when the laser power was greater. The minimal final value of \(\mu_s\) was achieved at 1.23W about 8.9 cm\(^{-1}\), and the maximal final value of \(\mu_s\) was achieved at 1.42W about 11.7 cm\(^{-1}\).

5. Conclusion
The continuous changes of optical property (the absorption coefficient and the reduced scattering coefficient) on fresh porcine liver in vitro and the subcutaneous implanted rat liver cancers in vivo which got through the fNIRS system during the LITT have been analyzed in this paper. The absorption coefficient increased in the pork liver experiments, but decreased in the rat liver cancer experiments. The reduced scattering coefficient all increased in the pork liver experiments and the rat liver cancer experiments. It increased quickly at the beginning, and gradually approached a stable state. In summary, the reduced scattering coefficient is more suitable for reflecting the progress of damage during different biological tissues’ LITT than the absorption coefficient. This conclusion will effectively guide the study of suitable therapy effect assessment system during LITT in real time.

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References
[1] Bown S G 1983 World J.Surg. 7 700
[2] Hans J S, Frank E, Volkhard U F and Frank U 2002 Med.Laser Appl. 17 147
[3] Thomas J V, Thomas L and Katrin E 2007 Eur Radiol 17 2020
[4] Jiang S C, Zhang X X 2005 Lasers Med Sci. 20 122
[5] Liu J, Deng Z S 2008 Physics of Tumor Hyperthermia (Beijing:Science Press)
[6] Ritz J P, Roggan A and Iabert C 2001 *Lasers Surg Med* **29** 205
[7] Germer C T, Roggan A and Ritz JP 1998 *Lasers Surg Med* **23** 194
[8] Zhu D, Luo Q M, Ceng J, Yu J S and Zeng S Q 2003 *Optics & Optoelectronic Technology* **1** 51
[9] Zhu D, Luo Q M and Zhu G M 2002 *Lasers Surg. Med.* **31** 313
[10] Zhu D, Luo Q M and Zeng S Q 2002 *Chinese J. Lasers* **29** 667
[11] Wei H J, Xing D and He B H 2007 Spectroscopy and Spectral Analysis **27** 868
[12] Wei H J, Xing D and Wu G Y 2006 *Chinese J. Lasers* **33** 852
[13] Ao H L, Xing D and Wei H J 2008 *Chinese J. Lasers* **35** 792
[14] Li R, Qian Z Y and Dai L J 2007 *Computer Measurement & Control* **15** 154
[15] Qian Z Y, Gu Y Q and Liu H L 2005 *Chinese J. Med. Phy.* **22** 463
[16] Ritz J P, Roggan A and Germer C 2001 *Lasers Surg Med* **28** 307
[17] Wei H J, Xing D and Xie S S 2006 *Spectroscopy and Spectral Analysis* **26** 1757