35th Annual International Conference of the IEEE EMBS
Osaka, Japan, 3 - 7 July, 2013

Derivation of the Relationship between the Rate of Temperature Rise and Viscoelasticity for Constructing a Coagulation Model for Liver Radio Frequency Ablation

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***Abstract*— Radio frequency ablation (RFA) is usually conducted using ultrasound (US) imaging to monitor the insertion procedure and the coagulation extent of liver tissue which is contiguous to the RFA electrode. However, when RFA surgery is started, the US image becomes unclear because of water vapor. This disadvantage of RFA can lead to excessive and insufficient RFA thereby diminishing the advantages of the procedure. In the present study, we proposed a simulation system which shows the progress status of coagulation for liver RFA. To derive the coagulation characteristics in liver RFA, we used the viscoelasticity of liver tissue as the coagulation indicator to investigate coagulation development for liver RFA. This paper shows the acquisition procedures for analyzing the relationship between the rate of temperature and viscoelasticity. We measured the complex modulus of porcine liver tissue under different rate of temperature in RFA by controlling the output power. We showed that the viscoelasticity of liver tissue depended on temperature previous temperature increase above 60°C. This result indicates that in RFA, controlling the output power is important to completely coagulate the tumor.**

I. Introduction

A. Radio frequency ablation

Radio frequency ablation (RFA) uses electrical conduction through the tissues to create a complete electrical circuit through the body. Radio frequency current is able to pass through tissue because of the abundance of ionic fluid, however tissue is not a perfect conductor and radio frequency current causes resistive heating (known as the Joule effect) [1]. In RFA these reactions can be performed by the RFA electrode with a 1.5 mm diameter. Therefore RFA has become a popular minimally invasive treatment for liver cancer. In RFA tissue is heated and gradually coagulates over time. To reduce the risk of recurrence of cancer, it is necessary to completely coagulate the tumor.

Manuscript received April 15th, 2012. This work was supported in part by the Global COE Program "Global Robot Academia" from the Ministry of Education, Culture, Sports, Science and Technology (MEXT) of Japan, the High-Tech Research Center Project from MEXT, a Grant-in-Aid for Scientific Research from MEXT (no. 22360108 & no. 22103512), a Waseda University Grant for Special Research Projects (no.2010B-177), and the Cooperative Research Project of the Institute of Development, Agin and Cancer, Tohoku University.

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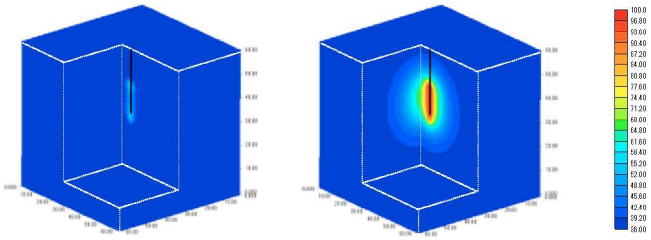
B. Problems of liver RFA

Although RFA is one of minimally invasive treatment, the accuracy of treatment greatly depends on the clarity of the ultrasound (US) image. During RFA, the surgeon watches the US image and controls the output power on a radio frequency generator. According to the US image during RFA, it is difficult to discriminate the coagulation area. Using a finite element method, we were able to estimate the temperature distribution produced by RF ablation through the cooling effect of blood vessels [1]-[5] (Fig.1). However, this simulation method did not allow for the extent of coagulation to be determined in liver tissue. In fact, Kiss et al. showed that viscoelasticity of liver tissue, which is dependent on temperature shows a local maximum approximately 70–75°C corresponding to the temperature, [6], [7], [8], [9], [10], [11].

In our previous study, we found that the rate of the temperature rise in tissue around the electrode needle was different (Fig. 1) [5]. In liver RFA, coagulation is distributed around the electrode needle, and the rate of temperature rise of the point that is close to the electrode needle is larger than that of the point that is far from the electrode needle (Fig. 2).



(a) 15 sec (b) 720 sec

Figure.1 Simulated temperature distribution

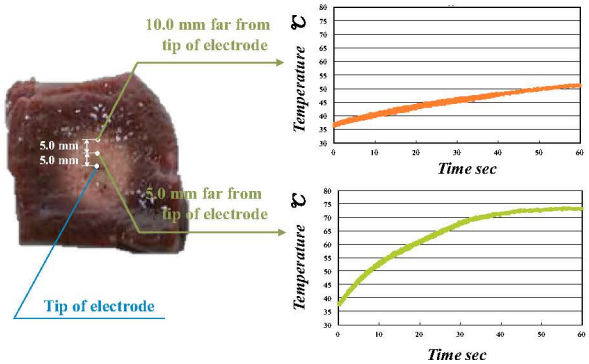


Figure.2 Temperature differences of tissue around electrode

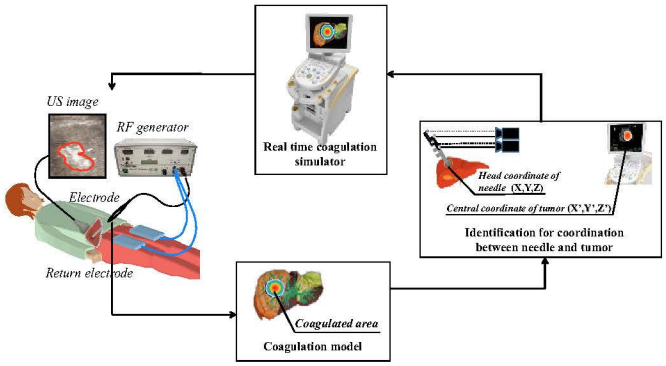


Figure.3 System imaging

A. Purpose

In our study we aimed to develop a system for RFA of the liver to show information on the coagulated area. To estimate coagulation in a quantitative manner, we used the complex modulus of tissue as an indicator of coagulation [12]. The complex modulus was used to estimate the coagulation.

We focused attention on the changes in viscoelasticity in different rates of temperature increases. In this study, we investigated the relationship between the rate of temperature rise and viscoelasticity of liver tissue *in vitro*.

This article is organized as follows. Section II presents details of the *in vitro* experiments that were performed to obtain data relating to the rate of temperature rise in RFA and the complex modulus. Section III describes the experimental results and discusses the relationship between the rate of temperature rise and the boundary of the complex modulus.

II. Method

In this study, we first ablated porcine liver at various increases in temperature. We then measured the viscoelasticity of the ablated liver by using a rheometer. We used porcine liver in this study, which is physically similar to human liver. The specimens were not frozen at any time during the study.

The size of the specimen was at least 20 mm in diameter to measure the viscoelasticity of liver. When we ablated the liver, we used the experimental devices shown in Fig. 4 to obtain an evenly ablated specimen, with a size of 25 mm × 25mm × 18mm before measuring the viscoelasticity. The container for RFA consists of two aluminum electrode plates which ablates the tissue. When we ablated the liver by the device, we had to determine appropriate the RFA output voltage on a generator to control the rate of the temperature rise. Therefore, we first obtained the relationship between the rate of temperature rise and output voltage which is unique to the ablation device. We formed experiments 10 times under each RFA output power (20, 25, 30, and 40[V]), and calculated the average rate of temperature rise.

The relationship between the rate of temperature rise and output voltage is shown in Figure. 5. As shown in Eq. (1), the gradient of Figure.5 indicates the rate of temperature rise.

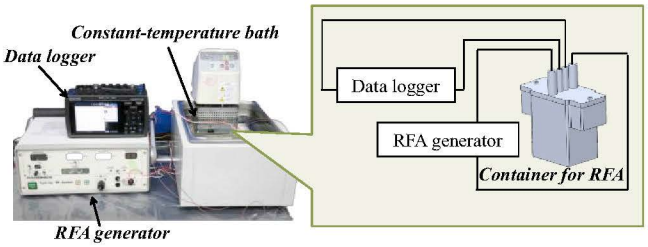


Figure.4 Experimental devices for investigating the relationship between output power and the rate of temperature rise

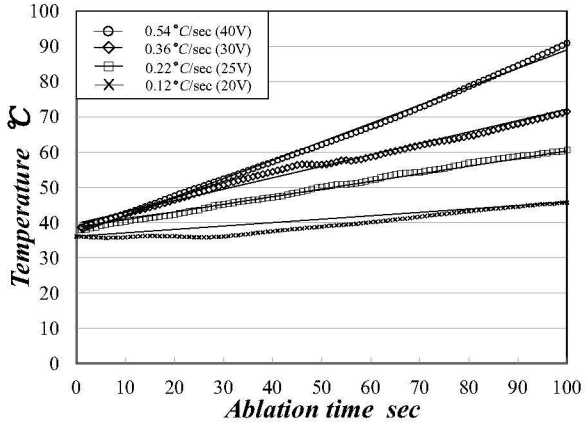


Figure.5 Temperature of the tissue under 20, 25 30, and 40 RFA output voltage

$$v = \frac{dT}{dt} \tag{1}$$

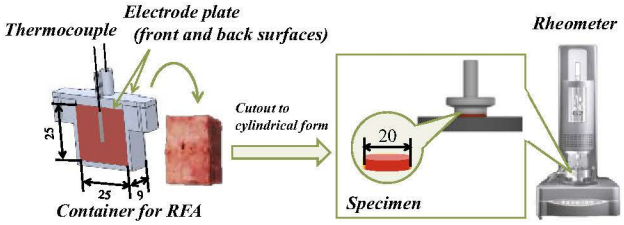


Figure.6 Experimental conditions for measuring viscoelasticit

Fig.5 shows that the rate of increase in temperature depends on output power. Based on this relationship, we controlled the output voltage to perform temperature rise of 0.12, 0.22, 0.36, and 0.54 °C/sec.

We then measured the viscoelasticity of the specimen using a rheometer (AR-G2, TA Instruments). We powered up the RFA when the temperature of the tissue was 36°C, and ablated the tissue until the temperature of tissue became 45°C, 50°C, 55°C, 60°C, 65°C, 70°C, 75°C, 80°C, 85°C, and 90°C. We measured the viscoelasticity of the liver at each of these temperatures mentioned above at each rate of temperature rise by supplying the appropriate voltage based on the experimental results shown in Figure. 6. To minimize damage to the specimens, the maximum normal stress of the geometer was maximized to 0.2 N. A total of 40 specimens from two porcine livers were used in the experiments.

III. RESULTS

The average results of two individuals test are shown in Fig. 6. The viscoelasticity slightly increased with temperature rising in the lower temperature ranges less than 60°C (Fig. 6). There were no differences with different rates of temperature rise. However, in the higher temperature ranges, such as those greater than 70°C, the viscoelasticity increased differently depending on the rate of temperature. Therefore, viscoelasticity depends on the rate of the temperature rise in a high temperature range. Variations in viscoelastic characteristics are due to changes in liver tissue produced by ablation.

To derive a relational model for viscoelasticity and temperature we calculated the average results from five porcine livers. We used these to estimate the experimental results in terms of linear and non-linear functions. We present details of our analytical method in Section IV.

IV. ANALYSIS

To determine the precise increasing tendency of viscoelasticity at different rates of temperature rise in RFA, we attempted to produce a relational model for viscoelasticity and temperature using approximated functions. From our experimental results, a curve of the viscoelasticity modulus and temperature was used as the basis for a relational model of viscoelasticity and temperature approximated by linear and non-linear functions.

Linear and non-linear least-square methods were used to calculate the approximate functions for the relational model. We assessed the non-linear results using an exponential function. An exponential least-square method was used to calculate the approximate functions for the relational model. However, the boundary between linear and non-linear functions was not evident on the graph. To optimize the relational model, we calculated the minimum root mean square error between the relational model and our experimental results. The root mean square error was minimal, and the boundary between the linear and non-linear relational experimental results occurred at 60°C (Fig. 8).

V. DISCUSSION

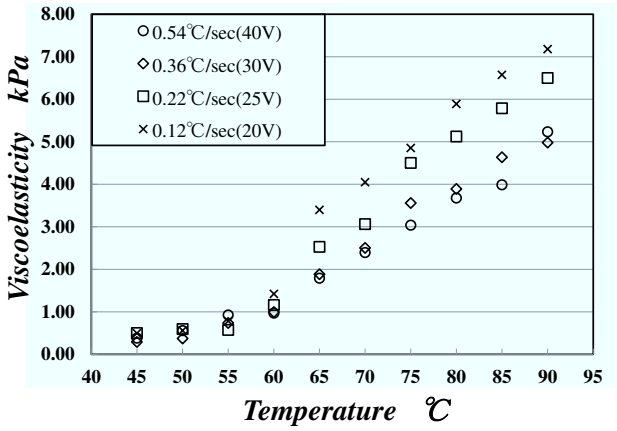


Figure.7 Results between temperature and viscoelasticity

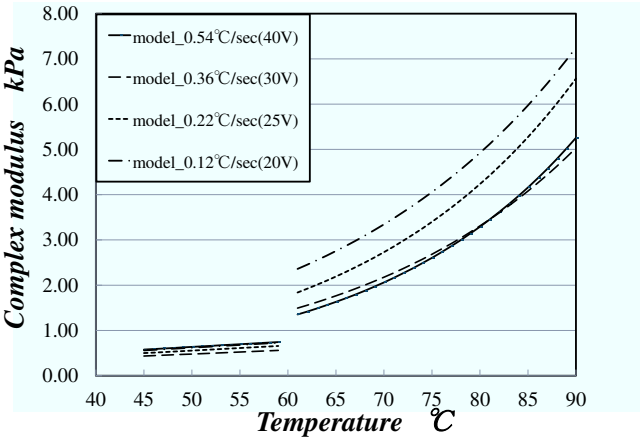


Figure.8 Results of viscoelasticity and temperature with different rates of temperature rise

We found the following two main results (Fig. 7).

(1) The boundary temperature between the linear approximated function within the low temperature range and the nonlinear approximated function within the high temperature range was same for rates of temperature rise. Additionally, the boundary temperature for 4 four different rates of temperature rise was commonly 60 °C

(2) Although viscoelasticity values with the same temperature were similar below 60°C, the viscoelasticity was different with the same temperature above 60°C.

With regard to the first finding, it is well known that irreversible denaturation of protein occurs at approximately 60°C [13], [14], [15], [16]. This is extremely close to the boundary temperature in our study. Therefore, the viscoelasticity of liver tissue could be useful as an indicator for deriving the status of coagulation in RFA.

With regard to the second finding, this suggests that the viscoelasticity of liver tissue only depends on temperatures below 60°C, and above 60°C, viscoelasticity depends on temperature as well as the rate of temperature rise. This indicates that the status of coagulation is affected by the history of temperature rise above 60 °C. This may be because the thermal energy which accumulates to be used for coagulation is different according to the history of temperature rise. Therefore, to estimate the state of coagulation at any area of a tumor during RFA, it is necessary to identify the rate of temperature rise at particular area in real time. In this regard, we consider that it is possible to estimate the states of coagulation at any location of tissue by calculating the rate of temperature rise at these points using the temperature distribution simulator that we developed and by referring to the relationship shown in Fig. 6. Moreover, by using the relationship that we modeled, an operator can determine the ideal status of coagulation distribution to coagulate the tumor completely by controlling the output voltage to perform the appropriate rate of temperature rise.

VI. CONCLUSION & FUTUREWORK

The objective of this study was to investigate the relationship between the rate of temperature rise and coagulation. We

ablated porcine liver tissue under different rate of temperature by controlling the output power, and then measured viscoelasticity of tissue as the indicator of coagulation in *in vitro* experiments. Our results showed that the viscoelasticity depends on the rate of temperature rise above 60°C. We calculated the function of the relational model based on the average experimental results and optimized the relational model in line with those results. In future studies, we intend to analyze the mechanism of coagulation in RFA by using viscoelasticity when the output power changes continuously based on the temperature distribution simulator, to display the distribution of viscoelasticity. We intend to compare this viscoelasticity this distribution of viscoelasticity with the distribution of tissue coagulation produced by RFA to evaluate our analytical method.

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