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A Method for Deriving the Coagulation Boundary of Liver Tissue Using a Relational Model of Viscoelasticity and Temperature in Radio Frequency Ablation

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***Abstract*—Recently radiofrequency (RF) ablation has become increasingly important in treating liver cancers. RF ablation is ordinarily conducted using elastographic imaging to monitor the ablation procedure and the temperature of the electrode needle is displayed on the RF generator. However, the coagulation boundary of liver tissue in RF ablation is unclear and unconfident. This can lead to both excessive and insufficient RF ablation thereby diminishing the advantages of the procedure. In the present study, we developed a method for determining the coagulation boundary of liver tissue in RF ablation. To investigate this boundary we used the mechanical characteristics of biochemical components as an indicator of coagulation to produce a relational model for viscoelasticity and temperature. This paper presents the data acquisition procedures for the viscoelasticity characteristics and the analytical method used for the coagulation model. We employed a rheometer to measure the viscoelastic characteristics of liver tissue. To determine the model functional relationship between viscoelasticity and temperature, we used a least-square method and the minimum root mean square error was calculated to optimize the model functional relations. The functional relation between temperature and viscoelasticity was linear and non-linear in different temperature regions. The boundary between linear and non-linear functional relation was 58.0°C.**

I. Introduction

A. Radiofrequency ablation

Radiofrequency (RF) ablation uses electrical conduction through the tissues to create a complete electrical circuit through the body. RF current is able to pass through tissue because of the abundance of ionic fluid, however tissue is not a perfect conductor and RF current causes resistive heating (the Joule effect) [1]. RF ablation has therefore become a popular treatment modality in the liver, particularly for tumors less than 3.0 cm in diameter. In RF ablation of the liver, the tissue is heated and coagulation necrosis occurs. Direct RF ablation takes place within a few millimeters of the electrode, however, a larger ablation zone is created by thermal conduction heating peripheral areas around the electrode. This percutaneous procedure offers proven effectiveness and has the additional advantage of being minimally invasive.

B. Challenges with RF ablation

RF ablation is a minimally invasive procedure, however, elastographic imaging which depends on tissue viscoelasticity is currently unable to visualize the coagulation area formed in RF ablation. Frequently, coagulation caused by RF ablation results in the tissue becoming denatured by the heating, which leads to variation in the viscoelasticity of the tissue as a whole. Vicoelasticity affects the contrast in elastographic imaging of the ablation periphery, and this can result in underestimation of the observed ablation area [2]. Figure 1 shows coagulation formation in a porcine liver specimen that underwent RF ablation. It is evident in Fig.1 that the boundary of the coagulation area is unclear, because of temperature variations in the area peripheral to the electrode [3], [4]. Using a finite element method, we were able to evaluate temperature distribution produced by RF ablation through the cooling effect of blood vessels [5], [6], [7], [8]. However, this simulation method did not allow the extent of coagulation to be determined in liver tissue. It is essential, though, that the coagulation boundary with respect to the pathological target be clearly determined.

In fact, M. Z. Kiss et al. investigated that viscoelasticity of liver tissue dependences on temperature reveals a local maximum around 70–75°C corresponding to the temperature [9], [10], [11]. However, this study did not determinate functional relation between viscoelasticity and temperature. Therefore, it is possible to measure variations of viscoelasticity with temperature rising.

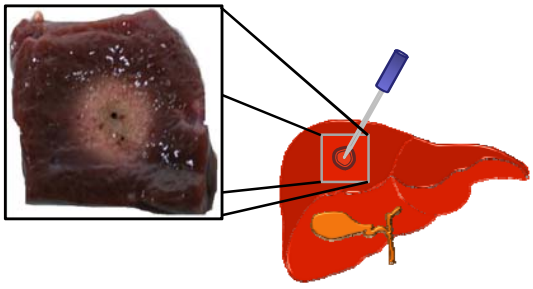

Figure 1. Coagulation formation in RF ablation

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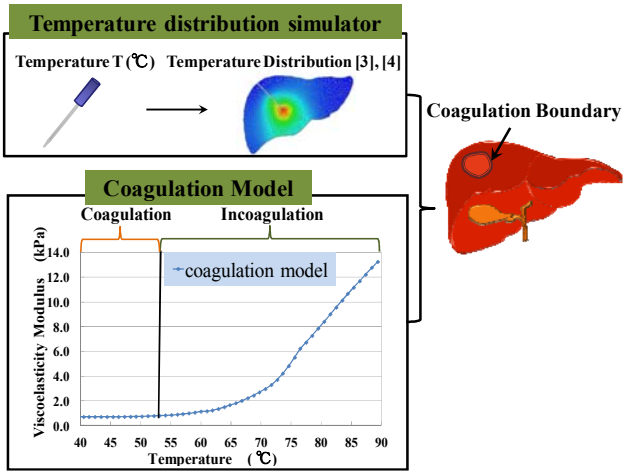

Figure 2. Image system

C. Coagulation model of liver tissue

The purpose of the present study was to develop a new method to determinate the coagulation boundary of liver tissue following RF ablation. To this end we used viscoelasticity as an indicator of coagulation, and from this we derived a coagulation model. From our coagulation modeling of liver tissue in RF ablation, we were able to establish the coagulation boundary through variations of viscoelasticity produced by the increased temperature.

To determine the coagulation boundary in this manner, two procedures are essential, (1) defining the functional relationship between viscoelasticity and temperature, followed by creation of the coagulation model, (2) establishing the boundary, through the changes in viscoelasticity. We compared the coagulation boundary determined using the coagulation model of liver tissue RF ablation with that produced using a temperature distribution simulation (Figure 2).

This paper is organized as follows: Section II presents details of the in vitro experiments that were performed to obtain data relating to viscoelasticity and temperature variation in the porcine liver. Section III describes the analytical method using the least-square method and error of mean square to determine the functional relation between viscoelasticity and temperature, this relationship was used to set up the coagulation model of liver tissue.

II. IN VITRO EXPERIMENT

We determined viscoelastic characteristics produced by the increased temperature in *in vitro* experiments to help us derive the coagulation model.

A. Method

We used a rheometer (AR-G2, TA Instruments) to measure the torque loaded on the specimens and the torsional angle of the specimens (Figure 3). The shear modulus of the specimen was then calculated from these results. To minimize damage to the specimens, the maximum normal stress of the geometer was maximized

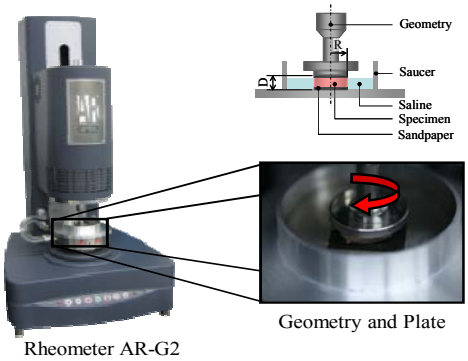

Figure 3. Rheometer and geometry

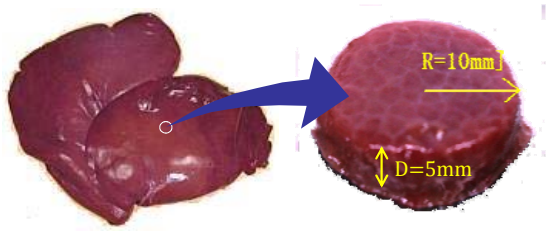

Figure 4. Specimen of porcine liver

1.0 N. In order to determine speed of heating increase we did preliminary experiment. The rate of heating was set up as 0.5°C /min, 1.5°C /min, 1.8°C /min, 2.0°C /min, 2.5°C /min and 3.0°C /min. Porcine liver was put in a plate and was heated up by the temperature controlled hot saline water which was in the plate. The viscoelasticity of specimens increased closely in the same trend. And we took cross-sectional picture of each specimen, and there was no difference according visual judgment. It is suggested that the rate of heating do not affect viscoelasticity increase. Therefore we set up the rate of temperature increase as 1.5°C /min. And temperature range was 20°C~90°C. The sampling rate was 4samples/min.

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.

Figure 4 shows how each specimen which was cut into a cylindrical shape—20 mm in diameter and up to 5 mm in length. For each test, the test specimen was immersed in saline

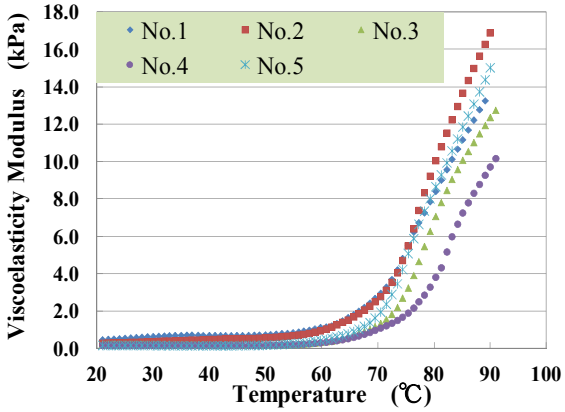

Figure 5. Results of the *in vitro* experiment

solution and sandpaper was attached to the surface of the plate supporting the specimen to prevent slippage.

B. Result

In all, 20 specimens from five porcine livers were used in the experiments. The results of each individual test are shown in Figure 5. From the results in Figure 5, the curve of the viscoelasticity modulus and temperature could be approximated using linear function and non-linear functions across different temperature ranges. Figure 6 shows specimen condition, which was heated ending at different temperature. Variations in the viscoelastic characteristic can be considered as being due to changes in the liver tissue produced by ablation. However, the boundary between linear and non-linear function was unclear on the graph.

To derive a relational model for viscoelasticity and temperature we calculated the average results from the five porcine livers, we used these approximate the experimental results in term of linear and non-linear function. We present details of our analytical method in Section III. Figure 6 shows the state of the specimen before and after ablation.

III. Analysis

To determine the precise coagulation boundary of the liver tissue following RF ablation, 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. A linear and non-linear least-square method was 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

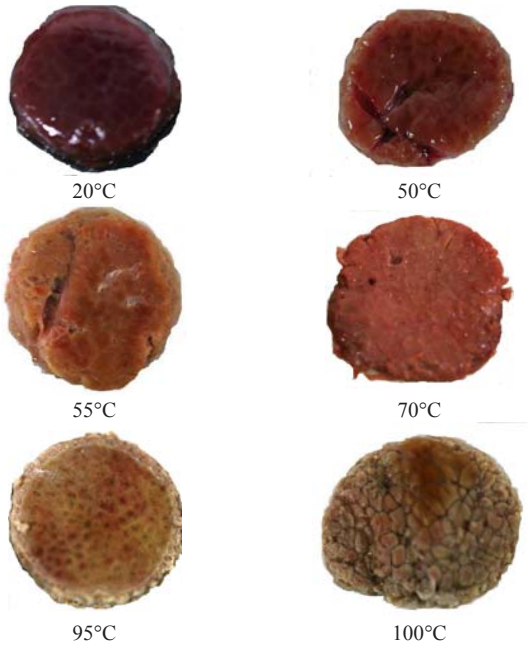

Figure 6. Photo of specimens at different end temperature

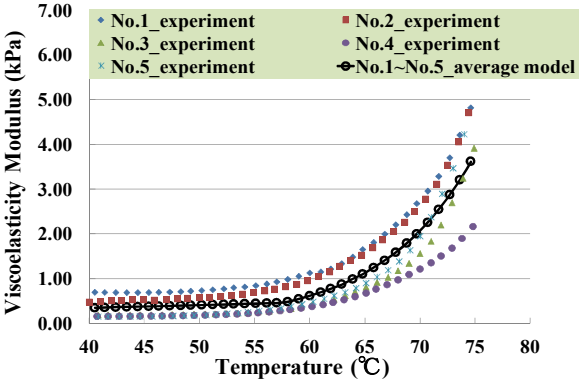

Figure 7. Funtional relationship of individual models

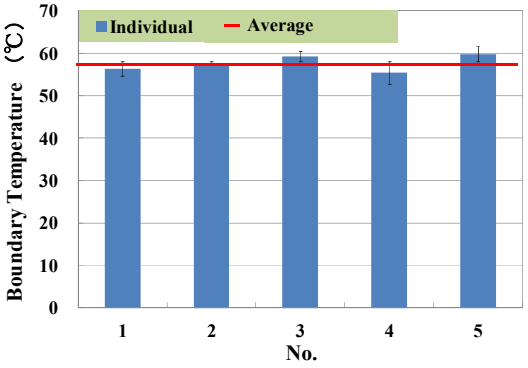

Figure 8. Comparison between average and individual models

TABLE I.
RELATIONAL MODEL FOR VISCOELASTICITY *G*[Pa] AND TEMPERATURE *T*°C

	Temperature range (°C)	
Function of relational model	40.5~57.0	58.0~75.0
	Linear function	Exponential function
	$G = 6.76\,T + 72.7$	$G = 0.426\exp(0.121T)$

functions were 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 58.0°C. The function of the relational model appears in Table I.

To investigate individual variability via our relational model, we calculated a relational model for each of the five livers, and we compared the average model with the five individual models (Figure 8).

IV. Discussion

A. Average relational model and individual relational model

It is evident in Figure 7 that though the viscoelasticity values with the same temperature in the average relational model differed from the values for each individual model, the relationship between variation in viscoelasticity and temperature increase was extremely close.

A comparison of the boundary between the linear and exponential functions is shown in Figure 8. According to Figure 8, the boundary temperature differs between the average relational model and the individual models. The boundary between linear and exponential functions in the average relational model was 58.0°C .

Irreverible denaturation of protein occurs at around 60°C [14]. This is extremely close to the boundary temperature of our average relational model. Thus, the average relational model is suitable for deriving a relationship between viscoelasticity and temperature.

B. Non-linear relational model

The non-linear relational model can be approximated using a quadric or exponential function. Though a quadratic function is advantageous in analysis an exponential function could be used to ascertain the minimum root mean square error between the relational model and our experimental results. That is to say, the exponential function is adequate for deriving the relational model for viscoelasticity and temperature.

C. Variance in viscoelasticity with increasing temperature

According to the experimental results presented in Fig. 5, viscoelasticity increased dramatically in the temperature range of 50°C~65°C [14], [15], [16], [17]. We considered this to have been caused by heat denaturation of protein, which is the main constituent of the liver. Hear denaturation of the liver signifies irreversible damage to the high-molecular-weight proteins and coagulation of the whole tissue. Viscoelasticity varied dramatically as a result of denaturation, variation in viscoelasticity can thus be used to determine the degree of coagulation in liver tissue.

V. CONCLUSION & FUTUREWORK

The objective of this study was to derive a relational model for viscoelasticity and temperature. We measured viscoelasticity with increasing temperature in *in vitro* experiments, and we calculated the approximate functions based on our experimental results. Those results showed that a relational model of viscoelasticity and temperature can be calculated through linear and non-linear functions. 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 work, we intend to analyze our relational model for viscoelasticity and temperature using our temperature distribution simulator, so as to display the viscoelasticity distribution. We intend to compare this viscoelasticity distribution with the tissue coagulation distribution produced by RF ablation to evaluate our analytical method.

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