

Communication

In vitro measurements of temperature-dependent specific heat of liver tissue

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Abstract

We measured the specific heat of liver tissue in vitro by uniformly heating liver samples between two electrodes. We insulated the samples by expanded polystyrene, and corrected for heat loss and water loss. The specific heat of the liver is temperature-dependent, and increases by 17% at 83.5 °C ($p < 0.05$), compared to temperatures below 65 °C. The average specific heat was 3411 J kg⁻¹ K⁻¹ at 25 °C, and 4187 J kg⁻¹ K⁻¹ at 83.5 °C. Water loss from the samples was significant above 70 °C, with ~20% of reduction in sample mass at 90 °C.
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1. Introduction

Knowledge of thermal tissue properties is required to determine tissue heating during thermal therapies, e.g., for models of hyperthermia treatments [1,2] and ablative treatments [3,4]. Additionally, temperature dependence of thermal properties has to be identified, especially for high temperature treatments like radiofrequency ablation (RFA). RFA is a treatment option currently in clinical use mainly for primary and metastatic liver cancer, and increasingly for other cancer types. An electrode is inserted into the tumor during open surgery, laparoscopy, or through a small incision in the skin. The tumor is heated to lethal temperatures above 50 °C by radiofrequency energy, with maximum temperatures in the tissue of approximately 100 °C. Knowledge of thermal conductivity and specific heat of liver tissue at high temperatures is required to determine tissue heating during this treatment.

Data regarding the specific heat of different tissue types are available [5,6] though there are no studies that evaluate the specific heat at temperatures above 50 °C. A previous study reports an increase of heat flow during differential scanning calorimetry (DSC) of liver tissue (which is directly correlated to specific heat) of approximately five times at 80.0 °C compared to values below 70.0 °C due to water vaporization from the sample [7]. This increase would have a significant impact on tissue heating during high temperature thermal therapy. DSC requires small samples (millimeter thickness), since uniform sample temperature must be guaranteed. In small samples, water bound in the tissue may evaporate markedly below the boiling temperature of water, depending on how tight the sealing of the sample is [8]. Thus, DSC may produce different values of specific heat at high temperatures than would be determined inside larger samples. Consequently, the specific heat determined by DSC might be markedly different from the specific heat value that is applicable to high temperature thermal therapy inside a large organ.

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In this study we determined *in vitro* the specific heat of liver tissue in large samples in the temperature range of 25.0–83.5 °C, thus recreating the conditions present in solid organs during ablative therapy.

2. Materials and methods

We performed a total of six experiments in six different samples. We used fresh bovine liver obtained from a local butcher, which we placed in physiological saline solution (0.9% NaCl) at 25.0 °C immediately after removal from the animal. The samples were cut as blocks (5.0 cm × 5.0 cm × 4.0 cm) from the liver, avoiding large vessel structures. These samples were placed between two plate electrodes (5.0 × 5.0 cm) made of sheet metal (Zn-plated Fe). A thin layer of conductive gel was applied to the electrodes to minimize electrical contact resistance that may result from uneven contact. The sample was thermally insulated by 1 cm thick expanded polystyrene ($k=0.03 \text{ W m}^{-1} \text{ K}^{-1}$) on each side in order to reduce heat loss. We placed a mass of 200.0 g on top of this setup to ensure electric contact between sample and electrodes. Six thermally insulated thermocouples (accuracy 0.2 °C) were placed in the center plane between the electrodes inside the sample (see Fig. 1). The temperature was recorded at five samples/s during the experiment. A commercial generator (PDX-500, Advanced Energy) was used to apply radiofrequency energy (375 kHz) with constant power to the sample. We applied 60 W (accuracy 2 W) of power in each trial, which resulted in a heating rate of approximately 10 °C/min. Under ideal conditions, this setup produces uniform heating of the sample, *i.e.*, the thermal conduction term is negligible (see Eq. (1)). However, from preliminary experiments, we found that at high temperatures (above 50 °C)

the heat conduction term was not negligible in our setup. We observed a significant decline in temperature after power was turned off. We corrected for this error using the method described elsewhere [9] and briefly described here for convenience. The heat transfer equation when a sample with heat capacity c is heated by applying power with a mass-specific energy rate p (W kg^{-1}) is:

$$c \frac{\partial T}{\partial t} = \frac{\nabla \cdot k \nabla T}{\rho} + p \quad (1)$$

The temperature rise during power application is almost linear, followed by a slow exponential decay after power is shut off at t_{off} . Since the temperature distribution is the same right before and right after the power is turned off, the heat conduction term (see Eq. (1)) also has to be identical. The heat transfer equation right before t_{off} (*i.e.*, t_{off}^-) is:

$$c \frac{\partial T}{\partial t} \Big|_{t_{\text{off}}^-} = \frac{\nabla \cdot k \nabla T}{\rho} + p \quad (2)$$

Right after t_{off} , no power is applied and Eq. (2) becomes:

$$c \frac{\partial T}{\partial t} \Big|_{t_{\text{off}}^+} = \frac{\nabla \cdot k \nabla T}{\rho} \quad (3)$$

In Eqs. (2) and (3), the time derivatives of temperature $\partial T/\partial t$ right before and after t_{off} are easily obtained from the experiments. If the temperature decline after power shut down is significant, we use Eqs. (2) and (3) to correct for thermal conduction-related temperature changes; from these equations we can calculate the specific heat according to:

$$c = \frac{P}{m \left(\frac{\partial T}{\partial t} \Big|_{t_{\text{off}}^-} - \frac{\partial T}{\partial t} \Big|_{t_{\text{off}}^+} \right)} \quad (4)$$

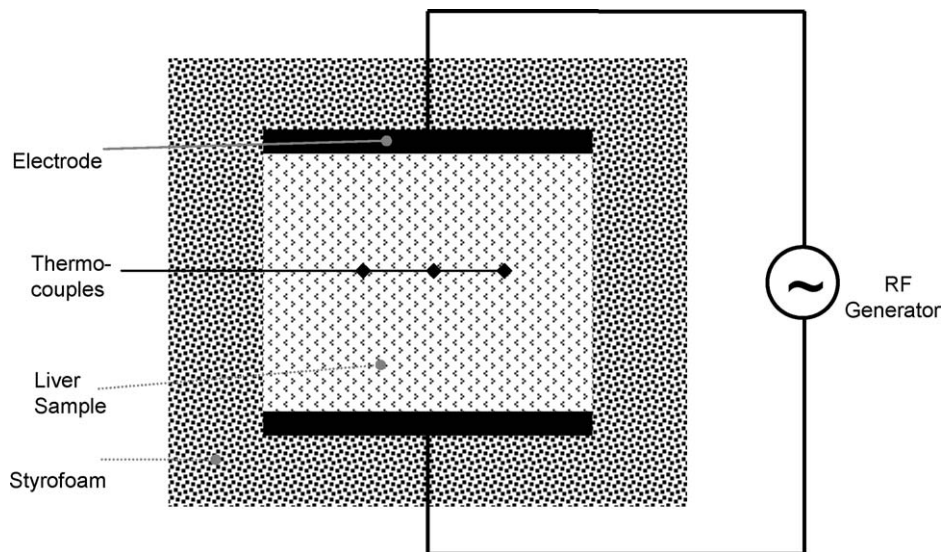


Fig. 1. Experimental apparatus (not to scale): the sample is placed between two plate electrodes. The sample is uniformly heated by an RF generator, and thermally insulated by 1.0 cm thick expanded polystyrene.

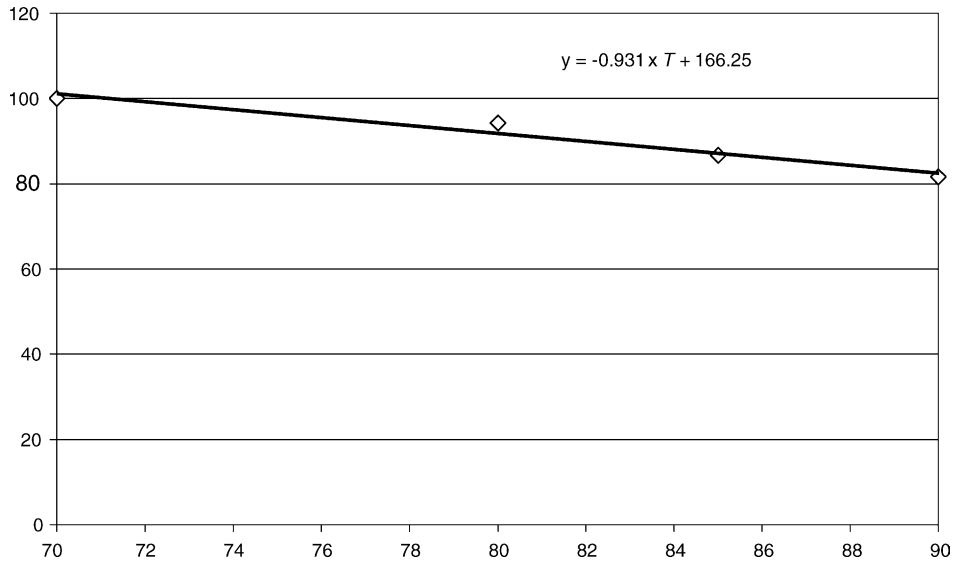


Fig. 2. Mass change of samples during the experiments.

Starting at room temperature (25.0 °C), we heated the samples to 50.0, 60.0, 75.0, and 83.5 °C, with an intermittent 1.5 min cool-down cycle after each of the temperatures was reached so that we could calculate the correction term. To apply the correction for other temperatures within the measurement temperature range, we interpolated the correction term between the distinct temperatures where it was measured as described previously [9]. Before and after each experiment we measured the mass of the sample with a scale (Ohaus CS-200, 0.1 g accuracy). Fig. 1 shows the experimental apparatus.

In preliminary experiments we determined temperature dependence of mass loss by heating samples to 70.0, 80.0,

85.0, and 90.0 °C and measuring mass before, and after heating.

2.1. Statistical analysis

In order to investigate whether the specific heat varies with temperature, we performed a statistical analysis of the collected data in the range of 25.0–83.5 °C. We divided the data into temperature ranges of 25–35, 35–45, 45–55, 55–65, 65–75, and 75–83.5 °C. We performed a paired *t*-test to identify significant differences between different intervals. A *p*-value below 0.05 was considered significant.

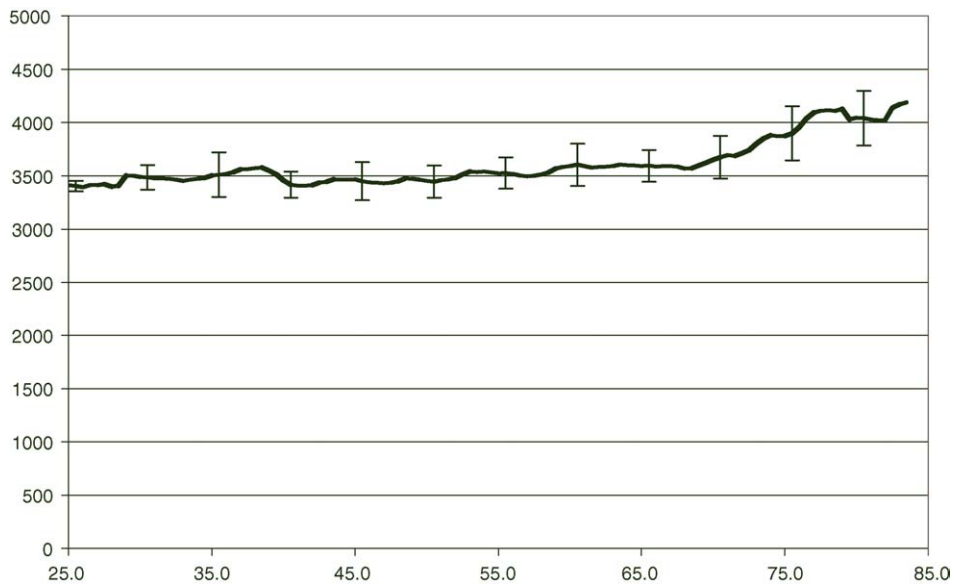


Fig. 3. Specific heat vs. temperature.

3. Results

Fig. 2 shows the mass change obtained from preliminary experiments. Note that there is no appreciable water loss below 70.0 °C, but significant loss above that temperature. Thus, to accurately measure the specific heat the change in sample mass during the experiment must be known.

We determined the specific heat using Eq. (4). Fig. 3 shows the average and standard deviation of the measurements.

The statistical analysis shows that there is no significant change in specific heat at temperatures below 65 °C, but specific heat shows a significant increase by 17% between 65 and 83.5 °C ($p < 0.05$).

4. Conclusion

We measured specific heat of liver tissue in the range of 25.0–83.5 °C. We have found no published data for specific heat above 50 °C, but our data at lower temperatures ($c = 3411 \text{ J kg}^{-1} \text{ K}^{-1}$ at 25 °C) are comparable to previous measurements in beef liver ($c = 3370 \text{ J kg}^{-1} \text{ K}^{-1}$). While there is no significant change below 65.0 °C, specific heat increased by about 17% in the range of 65–83.5 °C ($p < 0.01$). We did not observe the five times increase of specific heat between 70 and 80 °C observed in a previous study [7], where heat flow was measured by DSC, and water loss during heating was assessed. This large reported increase in specific heat resulted from the high amount of water loss at these temperatures due to the small size of the sample. Additionally, different seal conditions produce different results when DSC is used, and especially at higher temperatures errors can be introduced [8]. It may therefore be difficult during DSC to choose the seal condition that corresponds to an in vivo set-

ting where tissue is heated inside a solid organ. In this study we used large tissue samples, which better correlate to tissue heating inside a large organ (i.e., during ablative treatment). This work also revealed that almost 20% of water (mass) is lost when tissue is heated to 90 °C, which must be accounted for in order to accurately measure the specific heat of liver tissue.

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