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Determination of the specific heat capacity of healthy and tumorous human tissue ☆

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Abstract

Specific heat capacities c_p of different healthy and tumorous tissues (liver, lung, prostate) were measured using a differential scanning calorimeter (DSC). The obtained values range from 3.6 to 3.9 kJ kg^{-1} K^{-1}. The influence of thermal coagulation of 100°C and of cooling with liquid nitrogen on the tissue and its specific heat capacity was investigated using animal tissues. Owing to desiccation during freezing, the specific heat of the tissue decreased by about 2%.

Keywords: DSC; Specific heat capacity; Tumour

1. Introduction

In the last few years, efforts in investigating local thermal and coalgulative effects in tumour therapy have increased. Hyperthermia (heating tissue in the range between 41.5°C and 50°C) is founded on the fact that tumour cells often have a smaller tolerance limit against heat than corresponding healthy tissue. Membrane damage, disturbances in the synthesis of proteins, DNA and RNA, or changes in

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energy metabolism lead to cell death after some weeks. By heating over 60°C the cells are immediately destroyed due to coagulation effects.

Tissue can be heated by microwaves or ultrasound. As further possibilities for interestitial thermotherapy (ITT) and interstitial hyperthermia (IHT), laser-induced thermotherapy (LITT) and laser-induced hyperthermia (LIHT) are of increasing importance [1,2]. At the moment the most promising applications of thermotherapy are in treating cancer of the liver, lung, pancreas and breast [3–5]. In particular, efforts in the treatment of benign prostatic hyperplasia (BPH) have increased [6,7].

The basis of LITT and LIHT lies in the heating of tissue owing to scattering and absorption of photons and to heat storage and conduction processes. Thus, successful laser tumour therapy requires knowledge of the optical properties of tissues as well as of such thermal properties as specific heat capacity and thermal conductivity. Whereas the optical properties of tissues have been determined with high accuracy by means of Ulbricht spheres [8], the thermal properties of human tissues are rarely available in the literature.

Values for these properties given in the literature have the drawbacks that either they are mainly determined in animal tissues, or the status of the tissue is not reported [9,10], or the specific heat capacities and heat conductivities are only calculated from the known water content of the tissue [11].

In this paper we present calorimetrically determined heat capacities of different healthy and tumorous tissues (liver, lung, prostate). The influence of coagulation was investigated in porcine and bovine liver tissue and the effect of liquid nitrogen freezing (desiccation of tissue) was examined for porcine liver. The latter question was important because the human tissue used in these investigations was stored in nitrogen between surgery and calorimetric experiments.

2. Experimental

2.1. Setup and methodological aspects

The specific heat capacity c_p was determined with a differential scanning calorimeter (DSC 910, Du Pont Instruments (STA/Alzenau)). DSC is increasingly used in calorimetric investigations as the results are obtained in a simple manner and in a relatively short time [12]. In addition, only small specimens (a few mg) are needed to determine the heat capacity. This is especially important of human tissue samples, because the possibly different heat capacities over the whole specimen should be known for tumour treatment. With the experimental setup this can be achieved by averaging the values of different parts of the tissues.

As the heat capacity of tissue is of medical interest in a small temperature range only, it was not necessary to determine the calibration factor E of the DSC in dependence on temperature [13]. Indium, aluminium and sapphire were used as calibration substances. The possible influence of various heating rates β of 5, 10, 20 K min^{-1} on the calibration factor was investigated using the specific melting enthalpy of indium $\Delta H = 28.58$ kJ kg^{-1} as a calibration standard in the chosen

temperature interval [14]. No dependence of the heating rate on the calibration factor was found. To calibrate the calorimeter in the applied temperature range (23–43°C), further heat capacity calibrations were performed from 20°C to 60°C with a heating rate of 5 K min^{-1}. They were based on the well-known specific heat capacities of indium $c_{p_{In}}(40°C) = 0.23538$ kJ kg^{-1} K^{-1}; aluminium $c_{p_{Al}}(40°C) = 0.910391$ kJ kg^{-1} K^{-1}; and sapphire $c_{p_{sapphire}}(40°C) = 0.81118$ kJ kg^{-1} K^{-1} [14], because solid materials with a heat capacity comparable to tissue are not available. No dependence of the calibration factor on the mass of the specimen was found.

Specific heat capacities of the various tissues were determined in a temperature range between $\vartheta_i = 23°C$ and $\vartheta_f = 43°C$ with a heating rate of 3 K min^{-1} and an isothermal period of 3 min after each run. The specimens had masses between 10.6 and 20.6 mg. The tissues were investigated in hermetically sealed sample holders made of aluminium. The thermograms were registered by an $x-y$ recorder (Servogor XY 743, BBC Goerz/Nürnberg). Simultaneously, the differential voltage output was indicated by a digital voltmeter (177 Microvolt DMM, Keithley/München).

Each tissue sample was investigated repeatedly (usually 8 times). The heat flow rate with empty sample holders was determined before each measuring series, so that a large number of reference measurements ($N = 54$) was obtained.

Within each series the sample was weighed repeatedly. The mass remained constant, so that one can assume that no water loss from the tissue appeared during the experiment, as expected for hermetically sealed sample holders.

To examine the influence of tissue freezing with liquid nitrogen and thus of tissue desiccation, the heat capacities of fresh and N_2-frozen porcine liver tissue were determined. In addition, the effect of coagulation was investigated on porcine and bovine liver tissues. To that end, the tissues sealed in the sample holders were heated for a short time to about 100°C.

2.2. Sample material

Specific heat capacities were determined for three different types of human tissue: liver, lung and prostate. In each case there was one larger specimen of tissue available. Liver and lung comprised healthy and tumorous tissue, whereas no healthy tissue for the hyperplastic prostate was available. Liver and lung specimens were frozen in liquid nitrogen after operation and were then kept in a freezer. They were gradually thawed at room temperature before measurement. The prostate specimen was kept cool, but was not frozen for the time between operation and measurement.

Three samples were taken at three different places of the liver tumour. Each sample was measured eight times. Five samples were chosen from the healthy part of the liver and measured eight times each (one sample, only five times). Care was taken that the samples were cut off at different places of the organ, except at the surface, to prevent effects due to loss of water in the tissue.

Two samples were excised from the healthy lung and also measured eight times. Seven samples were taken from tumorous lung tissue and measured eight times each (except for one sample, measured four times).

Four samples were taken from the hyperplastic prostate tissue and measured eight times each.

3. Results

The specific heat capacity c_p was calculated using Eq. (1)

$$c_p = \frac{E\Delta U}{m\beta} \tag{1}$$

with the calibration factor $E = 279.8$ mW V^{-1}, the differential voltage ΔU, the heating rate $\beta = 3$ K min^{-1} and the sample mass m. ΔU was taken from the thermogram (Fig. 1) at a temperature of 37°C corresponding to the human body temperature under healthy conditions. The thermogram given in Fig. 1 for tumorous lung tissue is typical. The broken line indicates the reference curve, the continuous line the measured curve.

Results presented in Table 1 are mean values calculated from the total number N of determinations; the standard deviations are given.

To investigate the influence of nitrogen freezing and of heat coagulation, the heat capacities of fresh porcine and bovine liver tissues were determined for uncoagulated and coagulated samples. Furthermore, uncoagulated and coagulated N_2-frozen porcine liver tissues were monitored. The corresponding results (means and standard deviations) are given in Table 2. No values for N_2-frozen bovine liver are

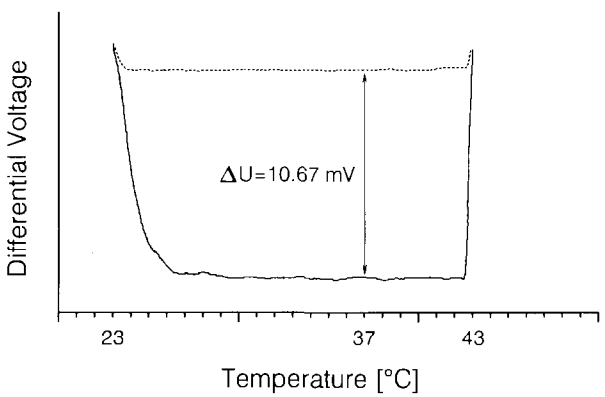

Fig. 1. Thermogram of tissue from a tumorous lung.

Table 1
Heat capacities of tumorous and healthy human tissues in kJ kg^{-1} K^{-1} ± standard deviation (N = number of determinations)

Tissue	Tumorous	N	Healthy	N
Liver	3.758 ± 0.066	24	3.617 ± 0.078	37
Lung	3.795 ± 0.100	52	3.886 ± 0.061	16
Prostate	3.779 ± 0.081	29		

Table 2
Results of t-Test and Mann–Whitney test

Tested tissues	*t* Test		Mann–Whitney test	
	t value	Significance *p*	*z* value	Significance *p*
Liver, healthy/liver, tumorous	7.60	0.000	−5.610	0.000
Lung, healthy/lung, tumorous	−4.76	0.000	−3.557	0.000
Liver, healthy/lung, healthy	12.91	0.000	−5.735	0.000
Liver, tumorous/lung, tumorous	−1.90	0.062	−1.877	0.065
Liver, tumorous/prostate	−1.01	0.316	−1.179	0.238
Lung, tumorous/prostate	0.81	0.423	−0.793	0.428

presented here because the experiments are very time-consuming and only trends are of interest.

4. Discussion

It can be seen from the values in Table 1 that the uncertainty in the results can reach 2.6%. This is due, on the one hand, to variability in the physical properties within the organ. Owing to the size of the samples, the specific heat capacity is determined for only just a relatively small piece of tissue in each measuring run. On the other hand, the uncertainty is caused by the inaccuracy of the calorimeter which can be estimated to be 2.4% from the standard deviation of the corresponding values of the reference material.

Comparing the values in Table 1, one should remember that the value of prostate corresponds to that of a fresh tissue (due to the handling between operation and calorimetric determinations). For N_2-cooled prostate tissue, one may assume a heat capacity c_p of 3.715 kJ kg^{-1} K^{-1}, as it follows from Table 3 that the heat capacity diminishes by about 2% after N_2 freezing due to desiccation of the tissue. Furthermore, it can be seen that the heat capacity of coagulated tissue is somewhat smaller than that of the uncoagulated (Table 3). But the uncertainty of the values in Table 3 is also larger than that in Table 1. This is due to the fact that different samples of porcine and bovine liver were investigated. So the results described above should be regarded as only a trend.

Table 3
Heat capacities of animal tissues in different states (see text) in kJ kg^{-1} K^{-1} ± standard deviation (N = number of determinations)

Tissue	Fresh	*N*	Fresh, coagulated	*N*	N_2	*N*	N_2, coagulated	*N*
Porcine	3.73 ± 0.15	19	3.72 ± 0.18	16	3.66 ± 0.10	13	3.48 ± 0.10	4
Bovine	3.69 ± 0.07	10	3.65 ± 0.09					

To check the significance of differences between the tissues in different states (tumorous or healthy) or of different origin, the mean values of the individual series were investigated by the t-test (all measurements were normally distributed) and the Mann–Whitney test. Within the 5% level, significant differences occurred between the values of healthy and tumorous liver as well as between healthy and tumorous lung values, the difference between tumorous liver and tumorous lung samples is significant at the 6% level. All other differences were not significant. The results are given in Table 2.

However, due to the mentioned uncertainty, these differences again should only be regarded as a trend. The same holds for the results achieved by investigating the effects of coagulation and N_2 cooling.

For thermotherapy of human tumours, the heat capacities given in Table 4 should be used as realistic values for fresh coagulated and uncoagulated tissues. The given values take into account that the heat capacity diminishes due to N_2 cooling during storage of tissue and that the experimental figures are thus lower than those of fresh tissue. It becomes clear from Table 4 that there are — if at all — only small differences between the various tumorous tissues and between healthy and tumorous specimens.

No data about the heat capacity of human tissues in different states are found in the literature, so that it is hard to do a comparison with our values. Often, the specific heat capacity is calculated from Eq. (2) [15] if the water content of the tissue W (in mass%) is known

$$c_p = 4.19(0.37 + 0.63W) \tag{2}$$

in kJ kg^{-1} K^{-1}. In a few cases, values for animal tissue are presented [9,16].

Table 4
Heat capacities of fresh human tissues in kJ kg^{-1} K^{-1} estimated from the experimental values of Table 1 and Table 3

Tissue	Tumorous	Healthy
Liver	3.8	3.6
Lung	3.8	3.9
Prostate	3.8	

Table 5
Heat capacities of tissue found in the literature

Tissue	c_p in kJ kg^{-1} K^{-1}	Refs.
Liver	3.69; 3.628	[9,16]
Lung	3.52; 2.786	[9,16]
Prostrate	3.715	Calculated using Eq. (2)
Muscle	3.8; 3.14 . . . 3.8; 3.543	[9,11,16]

The values shown in Table 5 are taken from the literature. The prostate value was calculated with Eq. (2) from the measured water content $W(\text{prostate}) = 82\%$.

The measured specific heat capacities are in good agreement with the values given in the literature if one takes into account the fact that the specific heats vary slightly for biological samples and that values for human tissues are rare.

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