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## Possible Application of Non-Invasive Thermometry for Hyperthermia Using NMR

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## NMR を用いたハイパーサーミヤ 用非侵襲型温度計の検討

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### Introduction

Hyperthermia has been given increasing attention in the search for an effective therapy for cancer. Non-invasive heating of the deep interior of the target and temperature control through non-invasive measuring of the heated deep-body temperature must be considered for clinical application. For the non-invasive measurement of temperature, the only method so far proposed is application of the temperature-dependence of ultrasound on the propagating velocity<sup>1)</sup>.

In NMR, the position to be measured can be determined by supplying the appropriate intensity of the static magnetic field and the frequency of the oscillatory magnetic field to this position<sup>2)</sup>. It may also be possible to estimate the temperature of a tissue by measuring its relaxation time, since spin-lattice relaxation time  $T_1$  and spin-spin relaxation time  $T_2$  in NMR are variable and temperature dependent<sup>3)</sup>. Another approach is to measure the amplitude of the free induction decay (FID), i.e., the total equilibrium magnetization  $M_0$ ; this is based on the fact that  $M_0$  is inversely proportional to the absolute temperature, shown as<sup>4)</sup>

$$M_0 = N_0 \cdot \frac{\mu^2 H_0}{kT} \cdot \frac{I+1}{3I} \quad (1)$$

Here  $H_0$  is the static magnetic field,  $N_0$  the number of nuclei per unit volume,  $I$  the nuclear spin quantum number,  $\mu$  the nuclear magnetic moment,  $K$  Boltzman's constant and  $T$  the absolute temperature. On the basis of these views it is presumed that NMR will allow measurement of deep-body temperature, non-invasively. We now report our preliminary experiments on using this non-invasive approach.

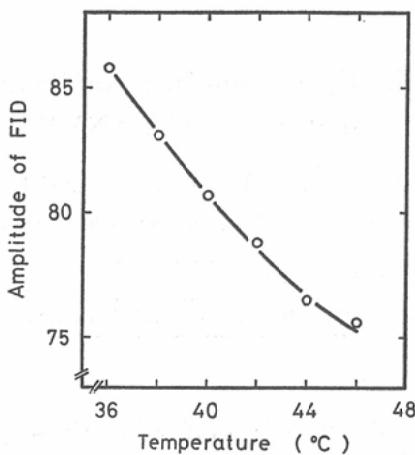


Fig. 1 Temperature-dependence of  $M_0$ . The ordinate represents the amplitude of FID which is proportional to  $M_0$ .

### Methods and Materials

The sample was the 980 mg thigh muscle of a male JCR/ICR mouse. The sample was inserted into a temperature variable probe in which the sample was given a 2.51 kG static magnetic field. Also, the sample was given a 90° pulse of 10.72 MHz oscillatory magnetic field perpendicular to the static magnetic field so that  $M_0$  of the protons in the sample could be measured. Immediately after this application, the free induction decay was observed by measuring the voltage induced in a receiver coil. Amplitude of FID is proportional to  $M_0$ . Eight replicates were taken as measurements at 5-second intervals and the mean values recorded.

### Results and Discussion

Fig. 1 illustrates the temperature-dependence of the amplitude of FID in which it is reduced with rise in temperature.

Since the  $M_0$  value is determined by the number of protons and the temperature, as seen in equation (1), it follows that the deep-interior temperature after hyperthermia can be assessed from the decrease in  $M_0$ , if the temperature before heating is known.

In low temperature physics, the precision of NMR thermometers is estimated to be about 0.1%. The thermometer proposed might be less precise because the volume of object materials is quite small compared with the size of the receiver coil. In addition, precision may be influenced by other factors, such as the local magnetic field generated by the human body, magnetic skin effects and the changes in blood flow with increase in temperature.

The position to be measured can be determined by supplying the appropriate intensity of the static magnetic field and the frequency of the oscillatory magnetic field to this position. The temperature of the determined position can be estimated by measuring the amplitude of FID. Thus we conclude that it is theoretically possible to measure the deep-body temperature non-invasively.

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