Temperature distribution measurements in two-dimensional NMR imaging

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This paper represents a preliminary study of the effects of regional temperature distribution in two-dimensional nuclear magnetic resonance (NMR) $T1$ imaging. It is found, as expected, that variations in local temperature appear as variations in the corresponding $T1$ image. The potential use of NMR $T1$ imaging in temperature measurements is evaluated in the case of water and blood samples. Using containers where the temperature could be either known or directly controlled with reasonable accuracy, images are obtained with samples having at least two regions at different temperatures. As expected, $T1$ is found to vary linearly with $1/T$ over the range of 0 °C to about 40 °C for blood. The potential use of $T1$ imaging in hyperthermia applications is also discussed.

INTRODUCTION

The recent development of nuclear magnetic resonance (NMR) imaging has opened a new dimension in noninvasive imaging of the human body. Although various techniques are used in NMR imaging, each technique depends upon the detection and quantification of a signal which is a function of the magnetization relaxation parameters $T1$ (the longitudinal or spin–lattice relaxation time) and T2 (the transverse or spin–spin relaxation time). It is known that the relaxation mechanisms depend on temperature.[1–5] This is especially true in the case of $T1$ for which the primary relaxation mechanism is interaction with the thermal motions of the surrounding molecules. It is therefore of interest to assess the effects of regional temperature variations on the imaged parameters. Thus, techniques which generate cross-sectional images of the $T1$ parameter may also be able to encode temperature distribution information. It is of interest to note that the application of $T1$ imaging to hyperthermia measurements may likely require resolutions of 0.1 °C over about 1 cm^2 with a temporal resolution of about 1 s.[6,7]

This paper presents the preliminary results of the use of a small animal NMR scanner in measuring $T1$ distributions as a function of temperature. The first section briefly outlines the justification for the $T1$ temperature dependence and measurement. The second section describes the materials and methods used in this set of experiments. The results obtained are then presented and analyzed.

BASIC THEORY

One simple model of the $T1$ temperature dependence allows $T1$ (above some minimum temperature) to be approximated as[2]

$$T1 \approx T1^{\infty} e^{-E_{\alpha}/kT}, \tag{1}$$

where E_{α} represents the activation energy of the relaxation process. Thus over small regions of temperature, $T1$ should be linear in $1/T$. It is assumed that the great majority of the signal from biological tissues is from the protons of free water and that the exchange of protons between the important phases is rapid.[2] The tissue of interest is then characterized by a single relaxation time $T1$ which depends upon the various fast exchange components by the relation[1]:

$$(T1)^{-1} = \sum_i f_i (T1_i)^{-1}. \tag{2}$$

Potential variations from such a simple model have been discussed.[4]

A second derivation of the temperature-$T1$ relationship can be obtained from the molecular motion spectrum. It is possible to express $T1$ in terms of the mean correlation time of the motions of the local magnetic moments τ, the gyromagnetic ratio γ, and the time average of the square of the local field (the field due to the magnetic moments of the local molecules) $\overline{H}^2$ (Ref. 5):

$$T1 = \frac{3}{\gamma^2 \overline{H}^2} \frac{1 + \omega_L^2 \tau^2}{2\tau}. \tag{3}$$

Here, ω_L is the Larmor frequency which is a function of the total magnetic field (local plus external).

$$\omega_L = \gamma H_0. \tag{4}$$

The logarithm of the ratio on the right of the equation is plotted as a function of τ in Fig. 1. It is interesting to note that, for fast molecular motions (i.e., short τ), $T1$ depends only on τ and not on the Larmor frequency. This appears to be true for liquids of very low viscosity such as water within the liquid temperature range.

MATERIALS AND METHODS

The NMR scans in this study were performed on a small animal imaging magnet developed in the Radiology Department of the University of California at San Francisco. In the scanner, the intensity of the detected signal is given by[8]

$$I = f(v)\rho(H)e^{-\alpha/T2}(1 - e^{-b/T1}), \tag{5}$$

where $f(v)$ is related to the speed of molecular motion in and out of the imaging region, $\rho(H)$ is the hydrogen density, and

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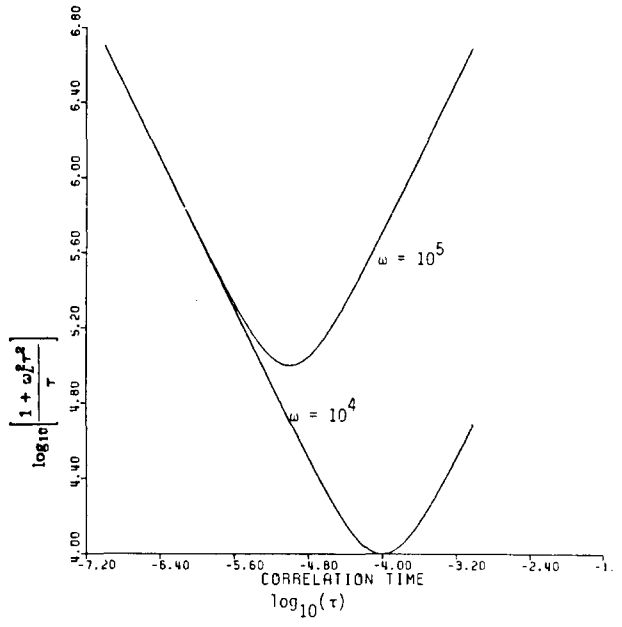


FIG. 1. Plot of $\log_{10}[(1+\omega_L^2\tau^2)/\tau]$ vs $\log_{10}\tau$ in the region around $\omega_L\tau = 1$ for $\omega_L = 10^4$ (lower curve) and $\omega_L = 10^5$ (upper curve). For short values of τ (which seems to be the case for biological tissue at room temperature), it is seen that $T1$ is independent of ω_L, depending primarily on τ which is a decreasing function of temperature (i.e., $\tau \propto 1/T$).

a and b are the $T2$ and $T1$ spin-echo parameters, respectively. By varying b (the time between repeated 90° sampling pulses of the rf field) while holding the other parameters constant, it is found that two intensity measurements suffice to allow determination of $T1$.

$T1$ distribution measurements were performed using samples of water (doped with copper sulfate) and blood at different hematocrits. For the water measurements, three Plexiglas cylinders, each of 2.54 cm outer diameter, and 1.9 cm inner diameter were filled with water which had been doped with copper sulfate in order to obtain a $T1$ in the range of 0.5 to 1 s. One of the tubes was heated to about 90 °C initially and then placed above the other two cylinders (which were at about 30 °C) within the bore of the imaging magnet. Scans were performed as that hot cylinder cooled. Because of the changing $T1$ value during the course of the scan, a small systematic error (<0.05 s) is expected. The temperature could not be measured directly during each scan. The sample was removed before the last scan in order to measure the current temperature. The experiment was also repeated external to the magnet to determine the temperature within the tubes as a function of time.

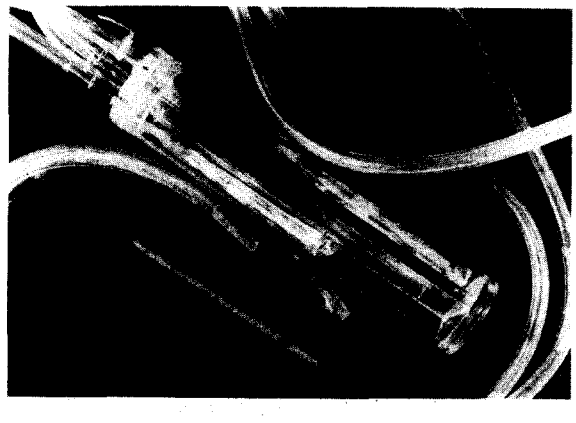
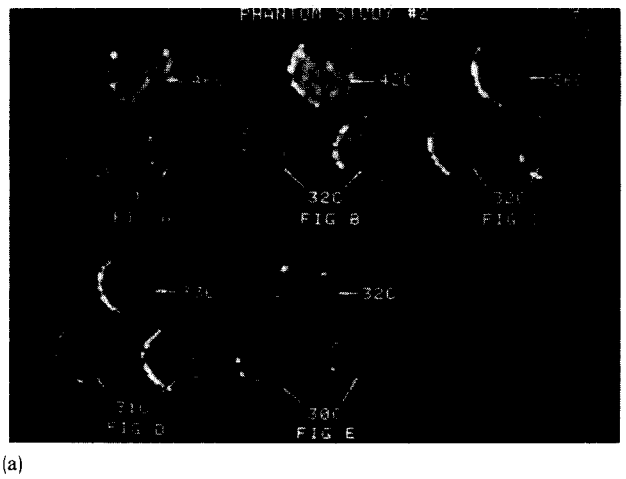


FIG. 2. Two-compartment chamber used to control temperature for blood $T1$ measurements. Water of a controlled temperature is allowed to flow through each chamber allowing samples within the chamber to equilibrate to the temperature of the water.

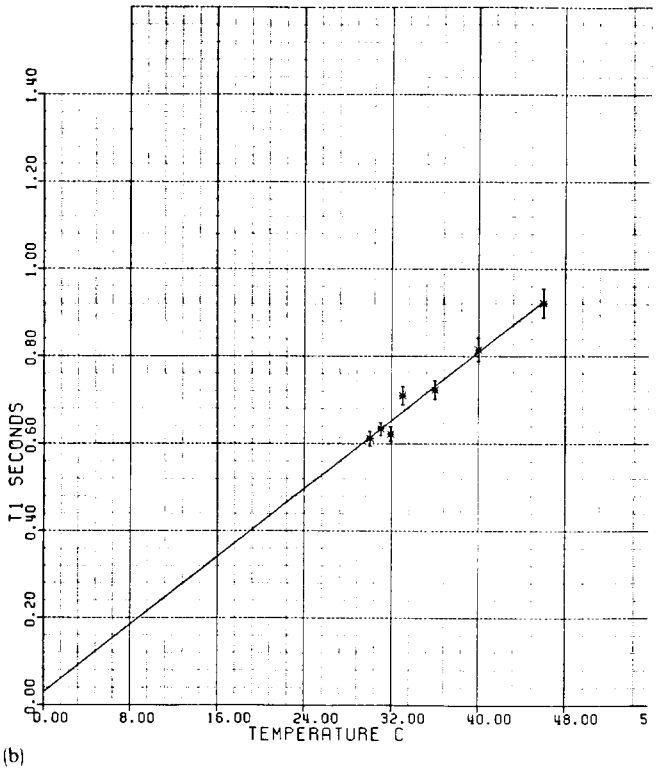
For the blood scans, in attempting to avoid the effects of transient temperature changes and in order to more accurately control the temperature of the samples, a two-compartment chamber was constructed where water from two separate temperature baths could be allowed to flow through each compartment. The samples were then sealed in small plastic bags to form cylindrical chambers with diameters of about 1.5 to 2.5 cm. The temperature of each bath was assumed to equilibrate with the temperature of each sample. It was found that the chamber was not able to maintain large temperature gradients (30 to 5°) and thus a small amount of error exists when large temperature differences were present. This appeared to be true for several initial blood scans. The two-compartment chamber is shown in Fig. 2. In each of the blood scans, one sample was initially cooled to about 1 to 2 °C. For the first set of blood scans, one sample was cooled to about 3° while the other was held at about 19° for the duration of six 1-min scans. For the second set of scans, both samples were cooled to about 1° and then one was slowly warmed while taking several 1-min scans. The temperature was then raised for subsequent scans, allowing $T1$ measurements at various temperatures. For the third set of blood scans (Fig. 4), both chambers were cooled to about 1° and then both were warmed, being maintained at the same temperature during the scans. This final set of data allowed a more accurate estimate of the internal temperature of the sample.

RESULTS

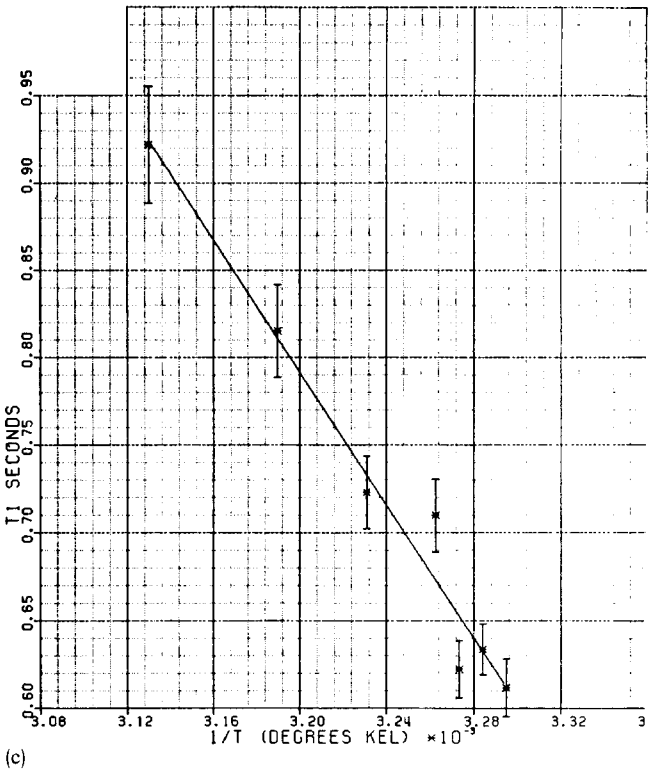
$T1$ images illustrating the effects of temperature variations are given in Figs. 3 and 4 for each of the four experiments. It is found that solving Eq. (5) for $T1$ results in an expression which is ill conditioned (i.e., very sensitive to noise in the intensity measurements) and not unbiased. This observation is evident in the $T1$ images which are computed from small regions in the two-dimensional image and are thus inherently noisy. For this reason, it is advantageous to compute the average $T1$ within a range from the average intensity measurements within the region rather than computing $T1$ on a pixel by pixel basis and then averaging. The results of the $T1$ measurements as a function of temperature are also shown in Figs. 3 and 4. In Fig. 3, the measurements for doped water are plotted. Figure 4 represents one set of measurements for blood. In each case, the $T1$ values are computed from the average intensity values over a region of about 1 cm^2. For Fig. 3, the error limits are computed from the standard errors of the intensities within the averaging areas. For the blood scans, four to six readings (except as noted) were taken within the temperature interval and the



(a)



(b)



(c)

FIG. 3.(a) Images of water cylinders with upper cylinder in each set of images at the higher temperature. The temperature in degrees for the brighter (hotter) tube are (from left to right) 46, 42, 36, 33, 32. (Note that the hotter tube has the semicircular air bubble.) (b) Plot of measured $T1$ vs $1/T$. Six separate measurements have been averaged together.

error bars represent the spread of the values averaged in each region. $T2$ measurements were made concurrently with the $T1$ measurements but no consistent variation with temperature was observed. Although a $T2$ temperature dependence similar to Eq. (3) has been predicted,[5] it is likely that nonthermal relaxation mechanisms succeed in masking the temperature dependence.

DISCUSSION

Several important conclusions can be drawn from this preliminary study. First, it is indeed evident that the $T1$ parameter computed from intensity measurements in the small animal NMR imaging system is capable of reflecting regional temperature changes. A sensitivity of about 2° was obtained from about 5 min of scan data (averaging the data from one 5-min scan or four to six 1-min scans).

Second, these time and precision constraints are remote from the subcentigrade temperature resolution, subminute time resolution required for hyperthermia applications. It is evident that further averaging will increase the temperature sensitivity at the cost of increased scan time. This conflict may be reduced when only the temperature within a small region is desired, allowing the application of single sensitive point techniques. In this case, the total signal originates from a small region and will therefore be small in proportion to the region size. Because the small region is directly sampled, the need for mathematical image reconstruction is removed and repetitive measurements of $T1$ in the region can be rapidly obtained. The fact that at least two intensity measurements separated in time by at least $T1$ are required in order to compute $T1$ places a fundamental limitation on the measurement speed.

A much more serious limitation to the use of NMR for hyperthermia is suggested by the work of Lewa and Majewska[2] where an irreversible decrease in $T1$ was observed

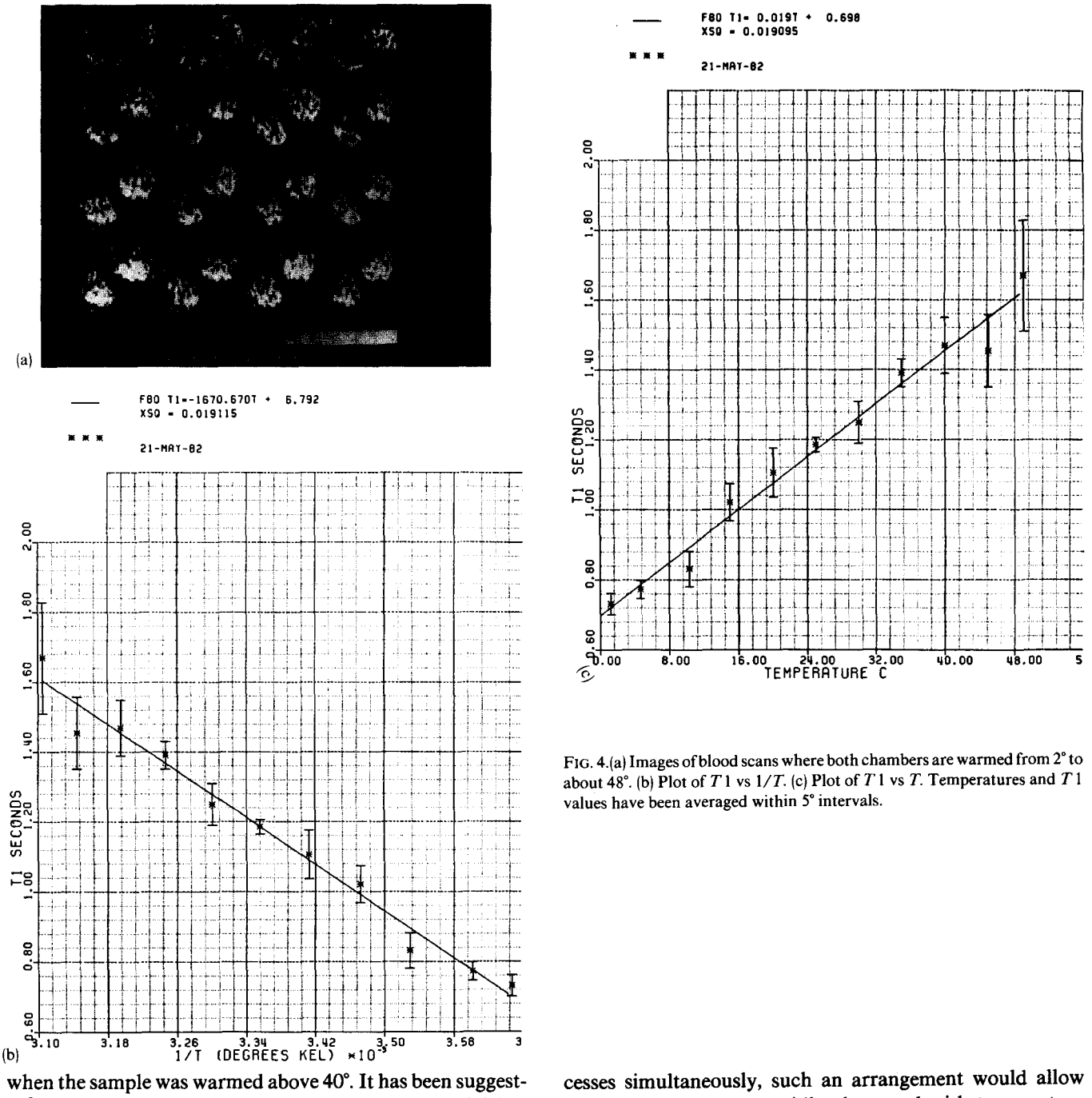


FIG. 4.(a) Images of blood scans where both chambers are warmed from 2° to about 48°. (b) Plot of $T1$ vs $1/T$. (c) Plot of $T1$ vs T. Temperatures and $T1$ values have been averaged within 5° intervals.

when the sample was warmed above 40°. It has been suggested[9] that this is likely due to a lipid phase transition which has been observed in ultrasound imaging. Certainly, the cause of this decrease must be determined and the existence of such a decrease *in vivo* must be ruled out before NMR can be used in hyperthermia applications. Superficially, there would appear to be many technical difficulties involved in heating while using NMR to measure temperature. It has been the author's experience that the field gradients required for NMR imaging can be easily distorted (such as by insertion of poorly shielded "nonmagnetic" metal leads into the uniform field region.) It is likely, however, that heating could still be accomplished by judicious placement (external to the uniform field region) of rf heating coils which operated at nonresonant frequencies. In one potential heating modality, ferromagnetic seeds are implanted in the tumor and can be used effectively to produce localized heating.[10] Even in the event that it were not possible to operate heating and imaging processes simultaneously, such an arrangement would allow heating periods to be rapidly alternated with temperature measuring periods. There are many technical problems, such as blood flow, which have not been addressed here and which may be such as to preclude the implementation of accurate NMR temperature monitoring *in vivo*. Further analysis of these effects need to be performed.

As a final observation, these results do show that care must be taken when interpreting or comparing $T1$ images taken at different temperatures. For example, there will be definite differences between *in vivo* and *in vitro* sample measurements.

ACKNOWLEDGMENTS

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