Single radiofrequency source for MR and hyperthermia studies

Rama Jayasundar

Department of NMR, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110 029, India

Hyperthermia is an experimental/adjuvant therapeutic modality for cancer. Combining hyperthermia with the non-invasive metabolic studies using magnetic resonance (MR) is an interesting area of research and can provide useful information. In this paper, feasibility of using the same radio frequency source for carrying out combined hyperthermia and MR studies is demonstrated. A conventional RF hyperthermic applicator has been evaluated for use as an MR transmit/receive coil.

COMBINING hyperthermia, a therapeutic modality in the treatment of cancer[1], with non-invasive metabolic studies using magnetic resonance (MR) is an interesting area of research[2–4]. The combination offers the possibility of non-invasive monitoring of the metabolic effects of hyperthermia, simultaneous with its delivery. Since the processes underlying thermal cell kill are still poorly understood, this could provide vital information about the physiological processes in the field of hyperthermic oncology.

In the experimental models for hyperthermia, choice of the heating method is generally based on the accessibility of the tumour and the heating techniques available. Since the aim of this work was to induce hyperthermia and also carry out simultaneous MR studies, it was thought appropriate to use the same radio frequency (RF) source for delivering hyperthermia and for exciting the nuclei for MR studies. This study demonstrates the feasibility of such an idea.

A detailed discussion on electromagnetic (EM) wave propagation, interaction of EM waves with materials and the electrical properties of tissue cells in the context of hyperthermia is provided elsewhere[2]. The term 'RF hyperthermia' covers a wide variety of techniques in which the elevation of temperature is achieved using EM power in the frequency range 1–100 MHz (ref. 5). The wavelengths associated with RF are considerably longer than the dimensions of parts of the human body. For example, at 13.56 MHz, a commonly used frequency for RF hyperthermia, the wavelength in free space is 22 m. With a dielectric constant in tissue as high as 100, this would still correspond to a wavelength in tissue in excess of 2 m. Hence, RF can be used for heating deep-seated tumours.

Also, due to the long wavelengths associated with RF, its electric (E) and magnetic (B) fields close to the applicator can be considered to be stationary. If the quasi-static B field is the major contributor to the heating process, then heating may be considered in terms of the induced electric field and the associated induced currents. If, however, the E field is dominant, then the heating process is discussed in terms of displacement or capacitive currents. However, conduction current is the major source of heating at such frequencies. The techniques used for RF heating are referred to as capacitive and inductive heating, the main difference between these being in their differential absorption of power by different tissues.

Figure 1 shows the idealized models for capacitive and inductive heating applicators. In capacitive RF heating, a pair of electrodes is placed on either side of the sample, with the generator, electrodes and the sample forming a closed circuit (Figure 1 *a*). The region between the capacitor plates consists of five layers of non-magnetic lossy dielectrics. Layers 1, 2 and 3 represent skin, fatty tissue and muscle, respectively. According to EM theory, the fields between the capacitor plates must satisfy Maxwell's equations[6]. This requires that the total current (conduction plus displacement) be continuous at layer boundaries.

If, for simplicity, the electric field is assumed to be perpendicular to the capacitor plates, then

$$E_m(\sigma_m + j\omega\varepsilon_m) = E_n(\sigma_n + j\omega\varepsilon_n), \quad (1)$$

where m and n refer to the mth and nth layers, E is the peak electric field strength in V/m, σ is the conductivity in W/m, ε_m and ε_n are permitivity of the material, and $\omega = 2\pi\upsilon$, where υ is the frequency of oscillation of the field. The heat generated in the mth layer, in W/m^3, is given by,

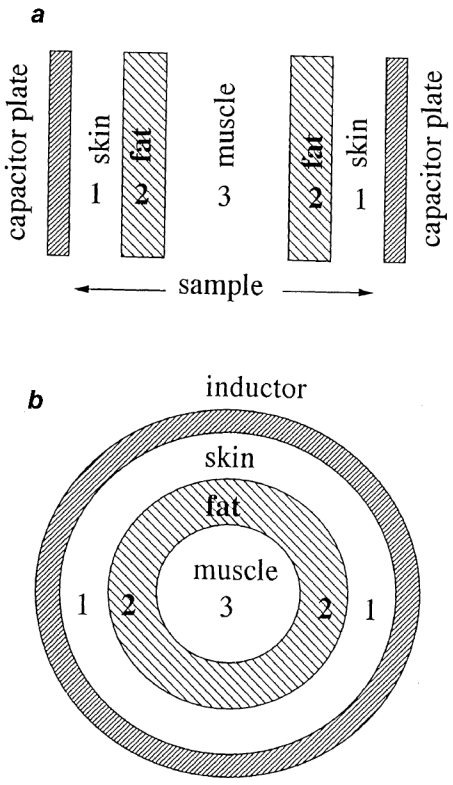

Figure 1. Models of (*a*) capacitor and (*b*) inductor-type hyperthermic applicators.

e-mail: ramajayasundar@hotmail.com

$$H_m = \frac{1}{2}\sigma_m |E_m|^2 . \quad (2)$$

Thus,

$$\frac{H_m}{H_n} = \frac{\sigma_m}{\sigma_n}\left|\frac{E_m}{E_n}\right|^2 = \frac{\sigma_m}{\sigma_n}\left|\frac{\sigma_n + j\omega\varepsilon_n}{\sigma_m + j\omega\varepsilon_m}\right|^2 . \quad (3)$$

Substituting the representative values for the parameters, the heat generated in any two layers can be determined. For example, at 27.12 MHz, the heat generated per unit volume in the subcutaneous fat layer would be 1.5–5.6 times higher than that generated in the skin and muscle layers[7]. Also, if one considers the tissues through which current travels as being resistors in series, fat has significantly higher resistivity than most of the other tissues (roughly 2000 Ω-cm for fat, 600 Ω-cm for skin and 400 Ω-cm for viscera)[7,8]. So, when a given current is passed through the layers, greater resistive heating of fat (compared to muscle) occurs, leading to excessive surface heating.

Figure 1 *b* shows an inductive-type applicator. It encircles the three concentric layers of non-magnetic lossy dielectric, representing skin, subcutaneous fat and muscle, respectively. The RF current is terminated in the applicator which emits a rapidly-varying magnetic field. Since biological materials are essentially non-magnetic, the time-varying magnetic field passes through the tissues unperturbed, inducing eddy currents in the conductive tissues.

Maxwell's equations, which must be satisfied in the region encompassed by the inductor, require that the flux lines of the E field be concentric circles if the magnetic field is axially directed inside the coil. Hence, the E field at the boundary between layers is tangential to the layers and has the same value on each side of the boundary. Therefore, $E_m = E_n$ with E_m and E_n representing the E field at the mth and nth layer. The heat generated at these two layers, in W/m^3, is in the ratio

$$\frac{H_m}{H_n} = \frac{\sigma_m}{\sigma_n}\left|\frac{E_m}{E_n}\right|^2 = \frac{\sigma_m}{\sigma_n}. \quad (4)$$

Now, the heat generated in the subcutaneous fat layer is only 20–70% of the heat generated in the skin or muscle layers[7]. Thus, if the electric field is oriented parallel to the layer interfaces, excessive unwanted heating of the fat layer can be significantly reduced. Thus, inductive heating has the advantage that conductive tissues such as muscle and blood are primarily heated compared to the fat layer. A number of reports exist in the literature on the use of inductive heating in cancer treatment[8,9]. An inductive hyperthermic applicator has been evaluated for its role both as a hyperthermic applicator (in an MR environment) and an MR transmit/receive coil.

The coil type and circuitry and matching network used in this study are shown in Figure 2. In hyperthermia, this type of coil is known as 'magnetrode' and is placed around the sample to be heated[8]. This coil has been used here as an MR volume resonator. It was fabricated from a copper sheet wound over a perspex former in such a way that the ends overlap in a non-conducting manner (Figure 2 *a*). The area of overlap and the gap between the layers provided the capacitance. Polytetrafluoroethylene (PTFE) sheets were used as dielectric between the overlapping ends. The coil had a diameter and height of 3.8 cm.

The coil circuit (Figure 2 *b*) employs inductive coupling. 'Power matching' between the RF transmitter and coil was achieved by controlling the magnetic flux linkage between the coupling loop that terminated the transmission line and the coil. The frequencies used for RF heating were 34, 84 and 130 MHz. The first two frequencies correspond to the phosphorus and proton resonance frequencies, respectively, at the magnetic field strength (2 T) used in this study. The power used was 50 watts (90% duty cycle).

Agar phantoms consisting of 0.8% agar (DIFCO Lab, UK) with different concentrations of NaCl (0, 100, 150 and 200 mM) were used. Temperature was monitored using a home-built constantan–manganin thermocouple connected to a digital thermometer (Model Bat 8, Bailey Instruments, UK). The thermocouple and the entire set-up for the temperature measurements were modified to enable them to work in an MR set-up without causing interference[3].

All the ^{1}H MR data were acquired on a Oxford Research System Biospec II spectrometer equipped with a 31-cm horizontal bore 2.0 T superconducting magnet (Oxford Instrument Ltd, UK). The experiments included heating agar phantoms (at 84 MHz) with the coil shown in Figure 2 *a* and subsequent T_1 measurements with the same coil. The duration of the heating pulse required for attain-

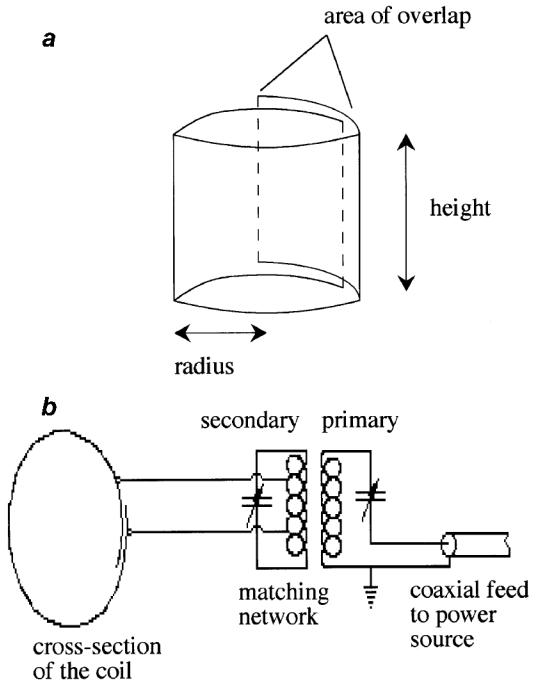

Figure 2. Diagrammatic representation of (*a*) coil and (*b*) matching network.

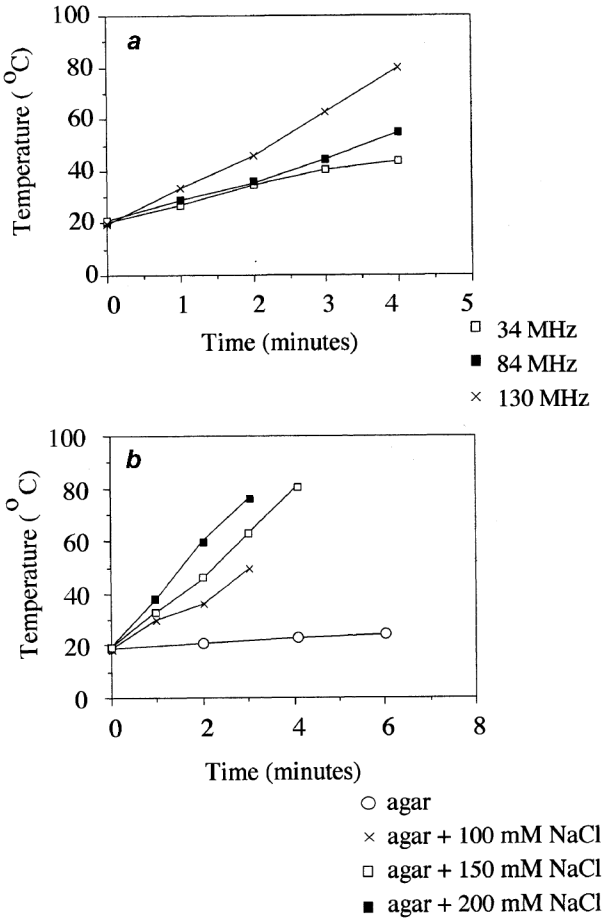

Figure 3. *a*, Increase in temperature at the three frequencies, 34, 84 and 130 MHz; the agar phantom contained 150 mM of NaCl; *b*, Dependence of the rate of increase in temperature with ionic strength in agar phantoms. Frequency used was 84 MHz.

ing a particular temperature was determined and calibrated outside the magnet. The method of progressive saturation recovery was used for T_1 measurements[10]. The sequence is $(90° - AQ - TD)_n$, where 90° denotes the calibrated 90° pulse, AQ the signal acquisition and TD the time delay between pulses and n the number of times the entire sequence is repeated. T_1 measurements were carried out at different temperatures, ranging from 6 to 55°C and also at different ionic strengths. For the lowest temperature, the sample was kept in a refrigerator prior to the experiment.

Figure 3 *a* shows the results of heating agar at different frequencies. It can be seen that the rate of increase in temperature increases with frequency. Figure 3 *b* illustrates the dependence of the rate of increase in temperature on ionic strength. It shows that the rate of increase in temperature increases with ionic strength. The temperature dependence of T_1 in agar phantoms of varying ionic strengths (0 to 200 mM NaCl) is illustrated in Figure 4. It can be seen that the increase in T_1 with temperature for

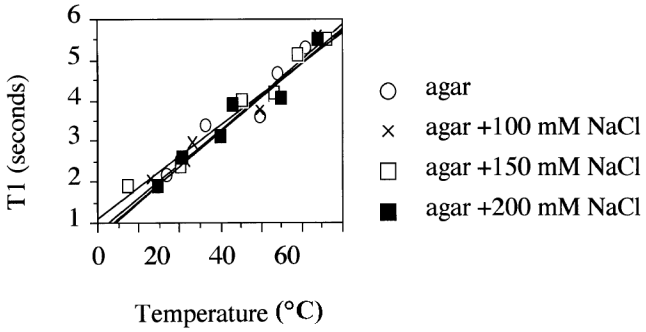

Figure 4. Temperature dependence of T_1 in agar phantoms of differing ionic strengths. RF heating was at 84 MHz.

each sample is similar and that ionic strength has little influence on the T_1s, particularly in the temperature range of interest for hyperthermia (37–45°C).

The increase in the rate of increase of temperature with frequency (Figure 3 *a*) is a consequence of the variation of the absorbed power density as the square of the applied field, whereas the dependence of the rate of increase in temperature with ionic strength is due to the relationship between power absorbed and conductivity of the material (eq. (2)). These experiments illustrate not only the feasibility of using the same RF source for carrying out both hyperthermia and MR studies, but also using a conventional hyperthermic applicator for inducing hyperthermia within the magnet as well as for MR measurements.

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