Selection of ferrite powder for thermal coagulation therapy with alternating magnetic field

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Selection of ferrite powder was carried out to realize a thermal coagulation technique in which tumors are locally heated by an application of alternating magnetic field from external coils. Magnesium ferrite ($MgFe_2O_4$) showed the largest increase in temperature (ΔT) under an alternating magnetic field in all the ferrites examined. For all the samples, ΔT value under alternating magnetic field was increased with an increase in frequency (200–500 kHz). The heating ability for the Mg-ferrite was ca. 1.4 W/g under alternating magnetic field of 4.0 kA/m (200 W, 370 kHz). The heating ability in alternating magnetic field was clearly depended on the magnitude of the hysteresis loss for the ferrite powder.

1. Introduction

Thermal therapies are one of the most important treatments for many kinds of cancer. Investigation of the conventional hyperthermia, in which temperature of tumor and its neighborhood is kept at 43°C, was started in the 1960's [1]. This therapy is based on the fact that only tumors suffer damages in this temperature range [2]. However, this always cannot work well because, for tumors placed deeply in a body, heating often follows burning skin and accurate control of temperature is too difficult.

Recently, instead of the conventional hyperthermia, a percutaneous microwave coagulation therapy (PMCT) [3] and a radio frequency interstitial tissue ablation therapy (RFA) [4] have shown good performances as the thermal coagulation techniques. In these therapies, tumors are inserted percutaneously by antennas like needles, and then microwaves or radio frequency (RF) is radiated. The merit of these therapies is local and selective coagulation of tumors without celiotomy. The same results can be realized by the other thermal coagulation techniques: application of alternating magnetic field from external coils to the tumors filled with ferrite powders. It is not necessary to insert any antenna to patient for each heating method. This leads that the damage of patient becomes much lower. Therefore, it becomes easier to cure patients of multiple liver cancer. The idea of the thermal therapy with ferrite powder was pointed in the 1960's [5]. In recent years, Shinkai *et al.* [6] employed magnetite cationic liposomes' (MCLs) for good affinity to cells and studied heating of a tumor. Complete tumor regression was observed in about 90% of F344 rats by three times of repeated heating. In the hearing, the temperature at the outside skin covering the tumor increased to 44°C. Although it was suspected that they reached higher inside the tumor, they were not measured.

Since our purpose is heating of tumors to sufficient high temperature (60–80°C), we need a method to heat more efficiently. Therefore, we have started the experimental studies: we search the best ferrite powder, the best frequency of an alternating field, the best form of an application coil etc. for the technique. The preliminary results were reported in ref. [7], where we investigate temperature increase for many kinds of ferrite and metal powder on an application of alternating magnetic field with a fixed frequency of 8 MHz. (The frequency of 8 MHz is the same of Thermotoron RF-8 [8].) However, these results are not sufficient because frequency of alternating field is not varied in spite of dependence of magnetic loss on the frequency.

In this paper, we searched the best combination of ferrite powder and frequency of an alternating field in the range of 200–500 kHz and we obtained heating abilities (W/g) for ferrite powders.

2. Experimental setup

Many kinds of ferrite powders (MFe_2O_4, M = Mg, Mn, Fe, Co, Ni, Cu, and Sr) (99.9%: Kojundo Chemical Laboratory Co., Ltd.) were tested as samples for this study. These ferrites were prepared by a solid state reaction method using the mixture of oxides or carbonates. Each sample is equally stored in glass (Pyrex glass) case. An alternating magnetic field was applied to the samples using an external coil. The coil consisted of loops of copper pipe (ϕ6) wound around a PP bobbin (ϕ48 × 40). The copper pipe was cooled by water to keep its temperature and impedance constant. The case with the sample is on a PP (Polypropylene) table at the centre of the coil. Since dielectric loss for PP and Pyrex is very small, we could not detect temperature increase for the empty cases by applying alternating field in our experimental setup. The coil was connected with a power supply (T162-5712B, Thamway Co., Ltd.) through an impedance tuner. Frequency of output current from the power supply was variable from 10 to 500 kHz by 1 kHz and the maximum output power was 500 W. Circuit in the tuner, which consisted of variable capacitor and variable inductor, was controlled to minimize the reflected power. The ranges of the impedance of the capacitor and the inductor were suitable in 100–300 kHz, so that, the reflected power was negligible small under 300 kHz. Since they were somewhat unsuitable over 300 kHz, the reflected power increased with frequency in 300–400 kHz, and it became several percent of the total power and it was supplied as an additional power at higher frequency region (>400 kHz). It must be noted that the strength of the magnetic field weakly depends on the circuit in the tuner because control of the circuit leads to the change of ohmic loss. In the all frequency range (200–500 kHz), the strength of the field was kept constant with use of the calibrated pick-up coil. Before heating, the temperature of the samples was maintained at approximately 25°C (room temperature). For measuring the temperature, we employed an infrared thermometer (505s, Minolta Co., Ltd.) with a resolution of 1°C. The thermometer, which evaluate the temperature from infrared-radiation, was settled 1 m above the sample, so that, it could avoid the influence of the strong field. This distance of 1 m corresponds to a resolution of ϕ10 mm. In the case of the measurement in water, ferrite powder was dispersed by air flowed through Teflon tube (ϕ3 mm) from air tank to avoid local heating (Fig. 1). The hysteresis loss was obtained using B-H analyzer (HP E5060A). For this measurement, the ring type samples were prepared by mixture of ferrite powder and epoxy resin adhesive (4:1 weight ratio).

3. Results and discussion

3.1. Characterization of the ferrite particles

Ferrites for MFe_2O_4, M = Mg, Mn, Fe, Co, Ni, Cu, and Sr were single phase and have the same crystal structure (spinel type) which was confirmed by X-ray diffraction method. In general, these materials show the same magnetic property (ferrimagnetism). The particle sizes for the samples presented in this study are shown in Table I. The size was determined using SEM observation. These samples have enough large particle size which does not influence the magnetic properties [9].

TABLE I The particle size for the ferrite powder

Sample	Particle size (μm)
$MgFe_2O_4$	2–10
$CuFe_2O_4$	8–50
$FeFe_2O_4$	0.1–5
$MnFe_2O_4$	1–5
$NiFe_2O_4$	1–3
$SrFe_2O_4$	1–3
$CoFe_2O_4$	1–3

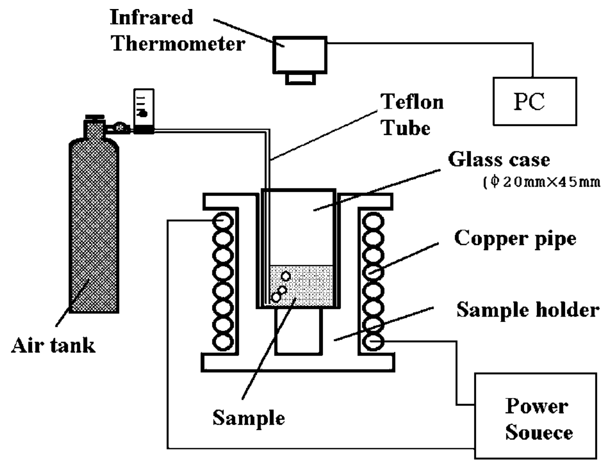

Figure 1 Schematic of the experimental setup for measuring temperature.

3.2. Increase in temperature for various ferrites under alternating magnetic field

Fig. 2 shows the heating properties under alternating magnetic field at 370 kHz for MFe_2O_4, M = Mg, Mn, Fe, Co, Ni, Cu, and Sr (1.0 g, 200 W) powders in air atmosphere. The output power of 200 W corresponds with magnetic field of 4.0 kA/m at the centre of the coil. The temperature was increased by applying of

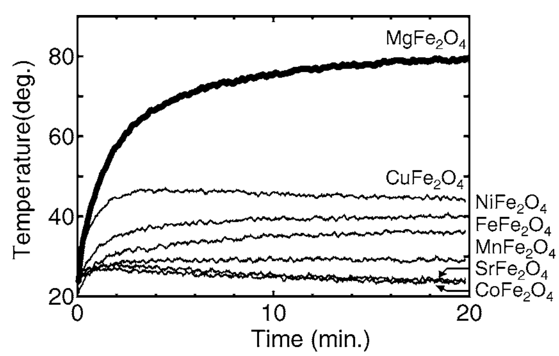

Figure 2 Temperature of ferrite powders (1.0 g) after an application of alternating magnetic field 4.0 kA/m (200 W, 370 kHz). For smoothing, data are plotted after five neighbor points are averaged.

TABLE II Output powers for magnetic field 4.0 kA/m at centre of the coil

Frequency (kHz)	Output power (W)
200	146
250	159
300	197
350	186
370	200
400	201
500	208

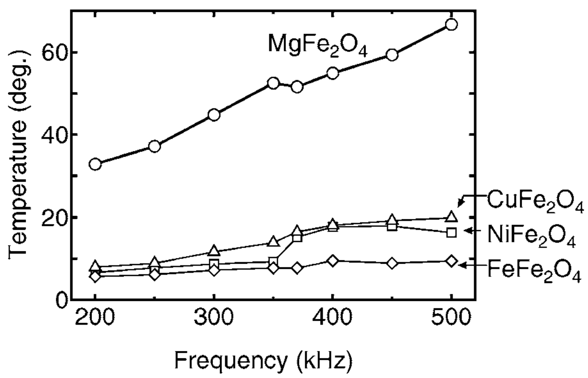

Figure 3 Temperatures of ferrite powders after an application of alternating magnetic field 4.0 kA/m after 20 min as a function of frequency.

alternating magnetic field. The sample temperature reached about the constant value after 20 min. The increase in temperature for $MgFe_2O_4$ sample was considerably higher than those for other ferrites.

The determination of a suitable frequency is very important for the application. At first, we measured heating properties at fixed output power (200 W). In this case, the maximum enhancement of the temperature under alternating magnetic field was obtained at around 360–370 kHz for numbers of ferrites. However, we confirmed that the magnetic field was decreased with an increase in frequency for our apparatus. From this result, we measured heating properties under fixed magnetic field. Table II lists output powers for magnetic field 4.0 kA/m at the centre of the coil. Fig. 3 plots results for the increase in temperature (ΔT) under applying an alternating field (4.0 kA/m) as a function of frequency for four kinds of ferrite MFe_2O_4 (M = Mg, Ni, Cu and Fe) (1.0 g). The application time of the alternating field was 20 min. The increase in temperature for $MgFe_2O_4$ sample was very high for all the frequency examined. The heated temperature was increased with an increase in frequency for all the ferrites.

3.3. Heating ability of ferrite powder

Fig. 4 shows the heating properties under alternating magnetic field (370 kHz) for three typical ferrite samples (1.0 g) in water (10 ml). The output power was fixed to 200 W (4.0 kA/m at the centre of the coil). It was confirmed that the temperature did not increase for water without ferrite powder. The temperature was increased when the ferrite powder added in water. This means that dispersed particles in water also generate a temperature under alternating magnetic field. The temperature increased and achieved to a constant temperature after around 30 min.

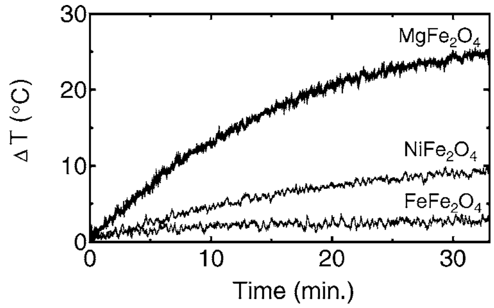

Figure 4 The heating properties under alternating magnetic field 4.0 kA/m (200 W, 370 kHz) for typical ferrite samples (1.0 g) in water (10 ml). For smoothing, data are plotted after five neighbor points are averaged.

The heating ability (W/g) of various ferrite powder was determined using the measurement for the sample in water. We also obtained cooling curves (Temperature vs. Cooling time) after stop of alternating magnetic field for the sample in water (10 ml). Using this curve, we calculated cooling rate ($-\mathrm{d}T/\mathrm{d}t$) and obtained straight relationship between temperature (ΔT) and $-$dT/dt. This relationship can express as a below equation:

$$-\mathrm{d}T/\mathrm{d}t = k_1 \Delta T \tag{1}$$

where k_1 (K/s) is a constant value of cooling rate for the water with ferrite powder. We obtained $k_1 = 1.25 \times 10^{-3}$ for 10 ml. On the other hand, the heating ability k_2 seems to be constant in this temperature region for the ferrites because of its high Curie temperature of ferrites ($>$500 K). From this hypothesis, we can express the heating rate to:

$$\mathrm{d}T/\mathrm{d}t = k_2 \tag{2}$$

where k_2 (K/s) is a constant value of heating rate for the water with ferrite powder. The temperature showed a constant value (T_∞) after around 2000 s, since the heating rate for the ferrite powder reached an agreement with the cooling rate for the samples with water:

$$k_2 = k_1 T_\infty \tag{3}$$

The energy of heating (W/g) for ferrite powder can calculated using:

$$E = k_2 C \tag{4}$$

where C is a heat capacity (J/gK) for the sum of the sample, water and glass vessel (contacted position with water). Table III shows the heating ability of 1.0 g ferrite powder examined. These ferrites have same crystal structure (spinel type) which was confirmed X-ray diffraction method. In general, these materials show same magnetic property (ferrimagnetism). The $MgFe_2O_4$ powder had a maximum value of ca. 1.4 W/g in the ferrites. Other samples showed considerably low heating ability.

TABLE III The heating ability of ferrite powders

Sample	Heating ability (W/g)
$MgFe_2O_4$	1.44
$CuFe_2O_4$	0.31
$FeFe_2O_4$	0.16
$MnFe_2O_4$	0.20
$NiFe_2O_4$	0.41
$SrFe_2O_4$	0.45
$CoFe_2O_4$	0

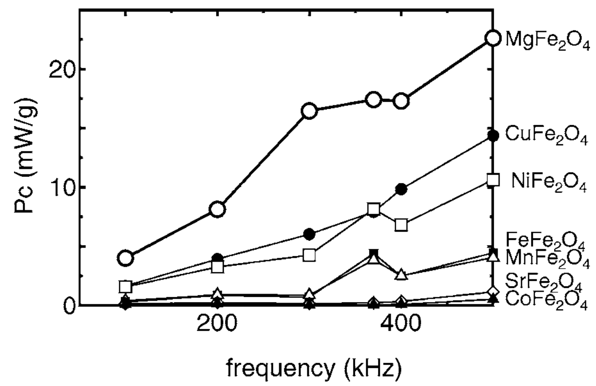

Figure 5 The relationship between the frequency and hysteresis loss for typical ferrite samples. The magnetic field was fixed to 500 A/m.

3.4. Magnetic properties

Magnetic loss usually consists of hysteresis loss, an eddy loss and the other effects. Fig. 5 shows relationship between the frequency and hysteresis loss for typical ferrite samples (magnetic field: 500 A/m). This loss was obtained using hysteresis loops. The hysteresis loss for the $MgFe_2O_4$ showed the highest value in all the ferrites. In addition, it was increased with an increase in frequency for the $MgFe_2O_4$. The heating ability in alternating magnetic field was clearly influenced by the magnitude of the hysteresis loss value for the ferrite. To confirm the relationship between the eddy loss and heating ability, we measured electrical conductivity for the pressed ferrites powders using complex impedance method. However, all the ferrites have poor conductivity and these values no relation with the heating ability. The reason for the high ΔT value in alternating magnetic field for $MgFe_2O_4$ was ascribed to the high hysteresis loss.

4. Conclusion

We searched the best combination of ferrite powder for a thermal coagulation therapy by an application of alternating magnetic field from external coils to the tumors filled with ferrite powders. Experimental results show that application of the field to $MgFe_2O_4$ ferrite powder is the most efficient in our samples. The achieved temperature under fixed alternating magnetic field (4.0 kA/m) was increased with an increase in frequency for $MgFe_2O_4$ ferrite. Mg-ferrite can replace the usual powder "magnetite" although it should be carefully investigated to establish the safety for putting and keeping them in a human body.

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