ESTIMATION OF LOW-CONCENTRATION MAGNETIC FLUID DENSITY WITH GMR SENSOR

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ABSTRACT. This paper describes a new application of a spin-valve type giant magnetoresistance sensor in the biomedical field. The hyperthermia treatment, based on the hysteresis loss of magnetite under external ac fields, requires determination of the content density of magnetite injected inside the body to control the heat capacity. We propose a low-invasive methodology to estimate the density of magnetite by measuring magnetic fields inside the cavity. For this purpose, we investigated the relationship between the density of magnetite and the magnetic fields, and developed a needle-type magnetic probe with a giant magnetoresistance sensor for low-invasive measurement. The experimental results demonstrate the possibility of estimating the low-concentration density of magnetite injected into the body.

Keywords: Giant Magnetoresistance, Hyperthermia, Magnetic Fluid, Density, Estimation and Low-Invasion
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INTRODUCTION

Magnetic nano-particles are attractive materials in biomedical applications [1], [2]. They can be applied to tagging or addressing a biological entity because its sizes are smaller than the biological entity such as cell, virus etc. This means that they can get close to a biological entity of interest. Nano-particles are attracted to a chosen cell, held there until the therapy is complete and then removed. The nano-particles are used for drug delivery system. It is based on the idea that small magnetic particles can be engineered to carry therapeutic chemicals or radiation for tumor control.

Recently, the hyperthermia cancer treatment based on induction heating by directly injecting magnetic fluid with magnetite as magnetic nano-particles to tumor has been proposed [3]. To destroy tumor, ac magnetic fields are applied to magnetite for heating up the tumor. Induced heat capacity depends on magnetic field density, exciting frequency, and content density of magnetite [4]. To confirm that tumor is destroyed with sufficient heat, the amount of magnetite has to be quantified before treatment.

For this purpose, we developed the evaluation method of content density of magnetite based on magnetic measurement. The merits are that the detected particle is only magnetic material and the measuring method is non-destructive and low-invasive. To confirm the measurement, we discussed two points, the relationship between the density of magnetite and magnetic field inside cavity, and a new style probe to measure magnetic fields low-invasively.

BACKGROUND AND METHODOLOGY

Hyperthermia Treatment Based on Induction Heating

Hyperthermia treatment is one of cancer therapy methods. Several types of cancer cells are more sensitive to temperatures in excess of 42.5°C than their normal tissues. As shown in Fig. 1, Dextran magnetite (DM), a colloidal suspension of sub-domain magnetite particles (magnetic fluid), is injected into tumor. AC magnetic fields with frequency of several hundred kHz are applied to magnetic fluid. Because of hysteresis loss, partial eddy-current loss, is induced, tumor tissues are heated directly immediately. If the temperature can be controlled above the threshold of 42.5°C for certain interval, the tumor does apoptosis and is destroyed.

Heat capacity, Q (W/mℓ), generated by magnetite can be calculated as follows:

$$Q = k_m f D_w B^2 \tag{1}$$

where f ; exciting frequency (Hz),
D_w ; magnetic density per weight (mgFe/mℓ),
B ; amplitude of applied magnetic field (T),
k_m ; 3.14×10^{-3} (W/Hz/(mgFe/mℓ)/T^2/mℓ) [5].

The equation denotes that the heat source originates in hysteresis loss because the heat capacity is proportional to exciting frequency.

The coefficient k_m was obtained by experiment. The dextran magnetite, Resovist®, produced by Meito Sangyo Co. and Nihon Schering K.K. was used in the experiment [6]. The liquid fluid has the weight density of 28 mgFe/mℓ. The exciting magnetic fields were applied at frequency of several hundred kHz. According to Eq. (1), sufficient heat used for cancer treatment can be estimated if all parameters are known. Applied magnetic field can be estimated by basic calculation because the relative permeability of the human body is approximately one. For magnetic fluid, whenever magnetite is injected to cancer, magnetic density decreases because it is diffused inside cancer tissue. Therefore, the confirmation of content density inside cancer tissue is needed for controlling sufficient heat for treatment.

Measurement Methodology of Density of Magnetic Fluid

We proposed the evaluation procedure of density of magnetite based on magnetic measurement inside the cavity with magnetite. We considered that there is a relationship between the density of magnetite and the permeability of the cavity as a bulk. The permeability can be estimated by the difference between magnetic fields outside and inside

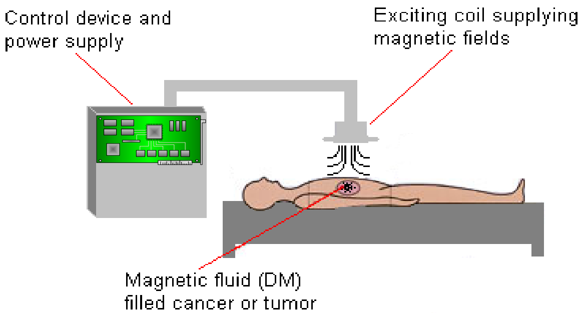


FIGURE 1. Hyperthermia treatment based on induction heating.

the cavity. The process of the calculation relates both the shape of cavity with magnetite and the demagnetizing factor [7]. Then, it is important to discuss the relationship between the density of magnetite and magnetic fields and how to measure magnetic fields inside the cavity.

ESTIMATION OF CONTENT DENSITY OF MAGNTIC FLUID

Relationship between Relative Permeability and Magnetic Fluid Density

The relative permeability of magnetic fluid was estimated by measuring magnetic flux density inside tissue with injected magnetic fluid and the content volume density, D_v, is calculated based on the relationship between volume density and relative permeability. The volume density, D_v , can be expressed in the function of weight density, D_w, as follows,

$$D_v = 1/\{1+(1/D_w - 1)\gamma_f\} \approx D_w/\gamma_f \quad (D_w \langle\langle 1) , \tag{2}$$

where γ_f is specific gravity.

It is assumed that the magnetic nano-particles uniformly distribute in the fluid and its shape is cylindrical with equal height and diameter and also the relative permeability of the nano-particles is infinite and that of liquid is one. Accordingly we estimate the permeance of an equivalent magnetic path through magnetic bead and through air. Based on these assumptions we consider the equivalent permeance of a unit volume. Then an equation is obtained for the relative permeability derived from the equivalent permeance of a unit volume as in reference [8]. Hence, the relative permeability, μ*, of magnetic fluid as a bulk is estimated as follows:

$$\mu^* = 1 + 4D_v \approx 1 + 4D_w/\gamma_f \quad (D_w \langle\langle 1). \tag{3}$$

The equation indicates that the shape and size of magnetic particle do not affect the relative permeability. When the same equivalent path is assumed, the equivalent relative permeability has the same expression even if the particle is spherical. The expression holds on the condition that the cavity includes a little amount of magnetic particle.

We check the equation by experiments. The vessel with toroidal shape is filled up with a magnetic liquid and then the relative permeability was measured by B-H curve tracer. The relationship between relative permeability, obtained from calculation and experiment, and the volume density of magnetic fluid is shown in Fig. 4, the relative permeability is directly proportional to magnetic fluid volume density as a linear function. We presumed that the

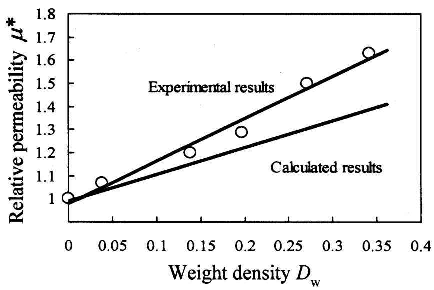
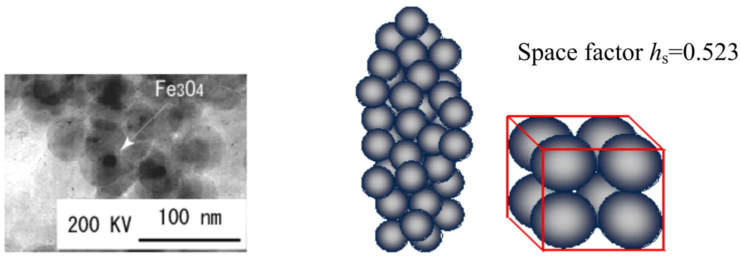


FIGURE 4. Relative permeability vs. weight density of magnetic fluid.



(a) Electron microscopy of magnetic fluid (b) Cluster model of magnetite

FIGURE 5. Microscopic model of magnetite.

un-uniform distribution of magnetic particles causes the difference between the calculated and experimental results.

We assume that magnetic particles are distributed uniformly. But actually the electron micrograph in Fig. 5(a) shows that the particle of magnetite has the cluster structure. Then we thought that the cluster of magnetite distributes uniformly as in Fig. 5(b). When the space factor of spherical magnetite h_s is considered, the effective specific gravity is expressed as,

$$\gamma_f{}' = h_s \gamma_f , \tag{4}$$

where h_s is 0.523. Then Eq. (3) is transformed into the following equation,

$$\mu^* = 1 + 4D_w / h_s \gamma_f \qquad (D_w \langle\langle 1). \tag{5}$$

Fig. 6 shows the calculated and experimental results for the space factor of 0.523 and the results are in better agreement compared with Fig. 4.

Magnetic Flux Density inside Magnetic Fluid under Uniform Magnetic Fields

As shown in Fig. 7, an uniform external magnetic flux, B_0, is generated by Helmholtz coil and applied to magnetic fluid in the specific embedded cavity. The magnetic flux density at the center of the embedded cavity, B_1, can be expressed as,

$$B_1 = \mu^* B_0 / \{1 + N(\mu^* - 1)\} \tag{6}$$

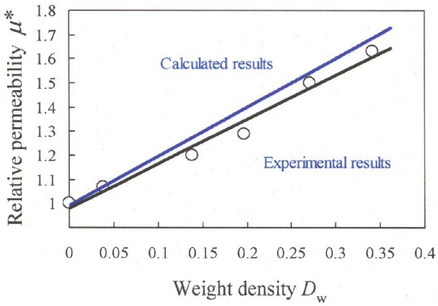


FIGURE 6. Relative permeability vs. weight density of the magnetic fluid (h_s=0.523).

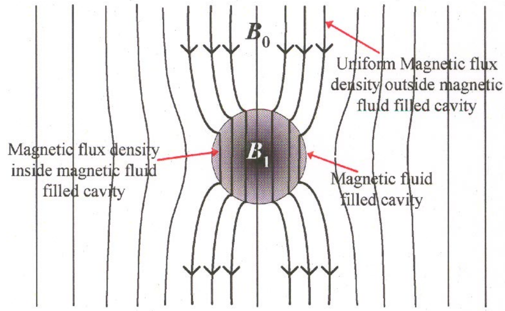


FIGURE 7. Model for estimating the volume density of magnetite. The magnetic flux density inside the imbedded cavity is measured by magnetic sensor.

where N is the demagnetizing factor of cavity [9]. The relative permeability μ^* is slightly greater than one, then we derive the following equation.

$$B_1 \cong B_0\{1+(1-N)(\mu^*-1)\} \tag{7}$$

Replace Eq. (5) into Eq. (6), the change ratio, δ between the magnetic flux densities, B_1 and B_0, can be rewritten as,

$$\delta = (B_1 - B_0)/B_0 \times 100 = 4(1-N)D_w/(h_s \gamma_f) \times 100 \quad [\%] \tag{8}$$

From Eq. (8), the volume density of magnetic fluid can be estimated if the difference of magnetic flux inside the embedded cavity and applied magnetic flux can be measured. The change of magnetic field densities is directly proportional to the volume density of magnetic fluid. However, the shape of imbedded cavity influences the difference of magnetic flux density.

Proposed Giant Magnetoresistance Sensor Used for Magnetic Flux Measurement

The needle-type magnetic sensor, shown in Fig. 8(a), was fabricated in order to be easily applied to measure magnetic flux density inside the human body. The sensor is a spin-valve-type giant magnetoresistance (SV-GMR) device [10]. The SV-GMR element, with sensing area of 75 μm × 40 μm, was fabricated on the tip of the needle. The sensing direction is parallel to the needle. The needle type probe has a bridge structure of GMRs as

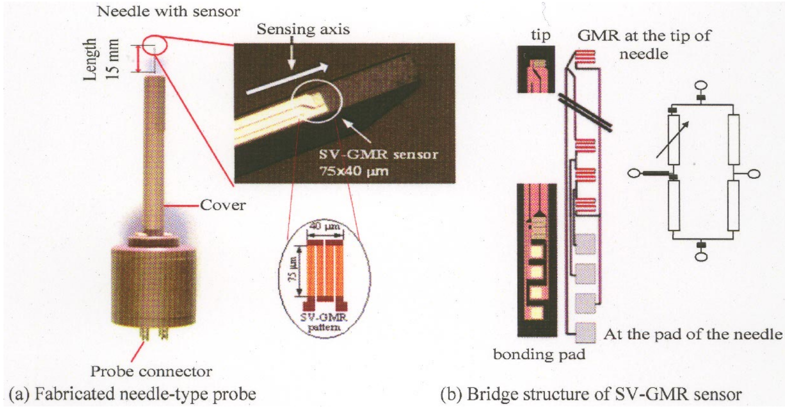


FIGURE 8. Needle type SV-GMR sensor.

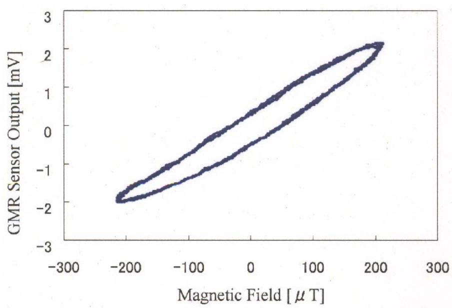


FIGURE 9. Small-signal characteristics of the SV-GMR sensor at 1 kHz. in the sensitive direction.

shown in Fig. 8(b). The current of 5 mA is applied to the SV-GMR sensor. From ac small-signal characteristics, the sensitivity of the SV-GMR sensor is approximately 10 V/T as shown in Fig. 9.

MAGNETIC FLUID DENSITY ESTIMATION WITH MAGNETIC MEASUREMENT

Figure 10 shows the photo of experimental setup. Magnetic fluid is filled into a cylindrical storage tank with diameter of 16 mm and height of 18 mm. An external magnetic flux density with the frequencies of 100 and 200 Hz is generated by Helmholtz tri-coil. The external field of 100 μT with the uniformity of magnetic field ε = 0.03 % is applied to magnetic fluid. Lock-in amplifier is used to measure voltage across the SV-GMR sensor.

The experimental result of the estimation is shown in Fig. 11. The figure denotes the relationship between the volume density of magnetic fluid and the change ratio of magnetic field densities. When the cavity is long (N = 0), the relationship shows the upper limit. The demagnetizing factor N for elliptic body depends on the shape ratio of cavity, m, as shown in Fig. 10. The spherical shape with m = 1 is N = 1/3, and the shape with m = 0.5 is N = 0.413. For two shapes, two solid lines are drawn in Fig. 11. The cylindrical cavity has the ratio length/diameter m = 1.12 in the experiment.

The origin of dextran magnetite for medical application has the weight density D_w = 2.8 %. The weight density D_w of testing magnetic liquids are adjusted from 0.24 to 1.13 % by thinning dextran magnetite. The lowest density is 1/10 less than the original of dextran

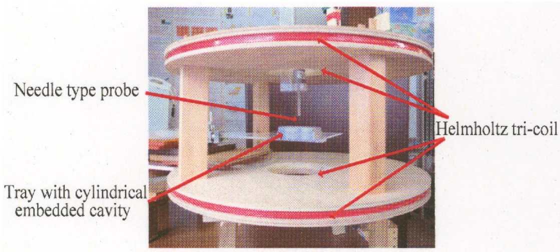


FIGURE 10. Experimental setup for measurement.

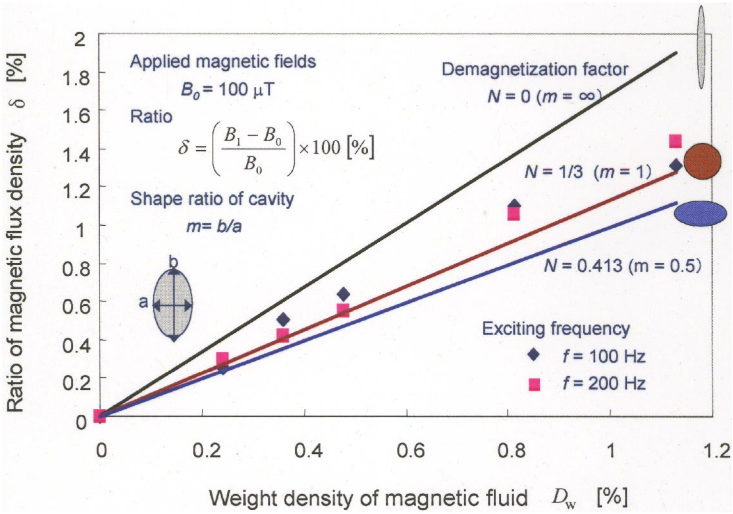


FIGURE 11. Comparisons between the experimental and theoretical result.

magnetite. We have the good agreement between the experimental and theoretical results for low-concentration magnetic fluid.

CONCLUSIONS

To develop the hyperthermia cancer treatment based on induction heating, it is important to estimate the content density of magnetite injected inside the body. We investigated the relationship between the difference of magnetic fields from external field and magnetic fluid volume density containing in an embedded cavity. The use of needle-type SV-GMR sensor enables us to directly measure the magnetic flux density inside the cavity whilst being minimally invasive. We can conclude that the content density of magnetite injected into the body can be estimated by the proposed technique.

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REFERENCES

1. Q. A. Pankhurt, J. Connolly, S. K. Jones, and J. Dobson, *J. Phys. D: Appl. Phys.*, **36**, R167 (2003).
2. C. C. Berry and A. S. G. Curtis, *J. Phys. D: Appl. Phys*., **36**, R198 (2003).
3. K. Tazawa, I. Nagono et al, *Jpn. J. Hyperthermia Oncology Phys. D: Appl. Phys*., **19**, 79 (2003).
4. I. Nagano, H. Nagae, S. Shiozaki, I. Kawajiri, S. Yagitani, K. Katayama, and K. Tazawa: *2nd Kanazawa workshop*, **16**, p. 11 (2006).
5. Y. Tamazaki, I. Nagono, S. Yagitani, T. Maeda, K. Tazawa: *Proc. 2nd Jpn. Aus. NZ. Semi*., p. 241 (2003).
6. K. Tazawa, et al, *Jpn. J. Hyperthermia Oncol*., **86** (1995).
7. T. Ishiguro, S.Tsuboshima, S. Miyakawa : Chokou Maguneto no Sekeito to Oyou (in Japanese), Ch. 1 (Ohmu Sha, Tokyo, 1957).
8. S. Yamada, K. Chomsuwan, S.C. Mukhopadhyay, M. Iwahara, M. Kakikawa and I. Nagano, *J. Magn. Soc. Jpn*., **31**, 44-47 (2007).
9. R. N. Bozorth, *Ferromagnetism*, D. Van Nostrand Co. Inc. New York, 1951, p.846.
10. Y.Fukuda, C.Komkrit, S.Yamada, M.Iwahara, H. Wakiwaka, S. Shoji, *J. Magn. Soc. Jpn*., **28**, 405 (2004).