A Novel Needle-Type SV-GMR Sensor for Biomedical Applications

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***Abstract*—Cancer is the most deadly disease in the world today. There is a variety of different treatment methods for cancer, including radiotherapy and chemotherapy with anticancer drugs that have been in use over a long period of time. Hyperthermia is one of the cancer treatment methods that utilizes the property that cancer cells are more sensitive to temperature than normal cells. The control of temperature is an important task in achieving success using this treatment method. This paper reports the development of a novel needle-type nanosensor based on the spin-valve giant magnetoresistive (SV-GMR) technique to measure the magnetic flux density inside the body via pricking the needle. The sensor has been fabricated. The modeling and experimental results of flux density measurement have been reported. From the information of flux density, the temperature rise can be estimated to permit the delivery of controlled heating to precisely defined locations in *controlled hyperthermia* cancer treatment. The actual experiment with human is under investigation.**

***Index Terms*—Cancer, hyperthermia treatment, magnetic fluid, nanosensor, semi-invasive, spin-valve giant magnetoresistive (SV-GMR) sensor.**

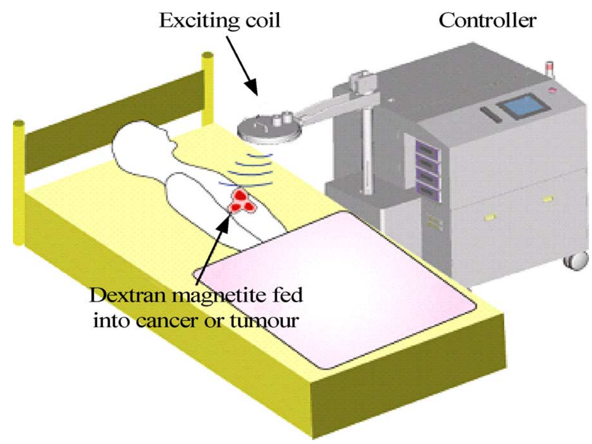

Fig. 1. Schematic representation of controlled hyperthermia-based cancer treatment.

I. Introduction

THE most deadly disease in the world today is cancer. There is a variety of different treatment methods for cancer, including radiotherapy and chemotherapy with anticancer drugs that have been in use over a long period of time. Hyperthermia is one of the cancer treatment methods that utilizes the property that cancer cells are more sensitive to temperature than normal cells. This method can be used for treating cancers of the prostate, liver, bladder, breast, and others. The advantages of this method compared with conventional cancer treatment methods are that they have no side effects and no pain to the patient, they are minimally invasive, and the time for treatment is significantly less compared with other conventional methods such as chemotherapy, radiotherapy, etc. The control of temperature is an important task in achieving success using this treatment method. This paper has reported the development of a novel needle-type nanosensors based on the spin-valve giant magnetoresistive (SV-GMR) technique to measure the magnetic flux density inside the body via a semi-invasive approach. Subsequently, the temperature inside the body can be calculated in an indirect way in order to permit the delivery of controlled heating to precisely defined locations. In the hyperthermia treatment method, magnetic nanoparticles are injected into the affected area. A potential benefit of using magnetic nanoparticles is the use of localized magnetic-field gradients to attract the particles to a chosen site, to hold them there until the therapy is complete, and then to remove them [1]–[4]. The particles absorb heat and, hence, they raise the temperature in a localized area while being excited by a high-frequency electromagnetic field. There are a number of issues that need to be investigated for successful treatment of cancer using hyperthermia. First, it is very important to understand the mechanism by which the temperature of the cancer cells is increased. The careful control of temperature is essential for not damaging healthy cells. Only an accurate measurement and control of temperature leads to a successful treatment by this method. A lot of research has been carried out to obtain a prescribed temperature in a noninvasive way with little success [5]–[9]. Therefore, there is a need to develop a new method of temperature measurement for this type of cancer treatment. The hyperthermia-based cancer treatments are nonsurgical and have several benefits, including fast treatment, reduced complications compared with drug-based therapy, reduced risk of infection compared with surgery, and a short recovery time for the patient.

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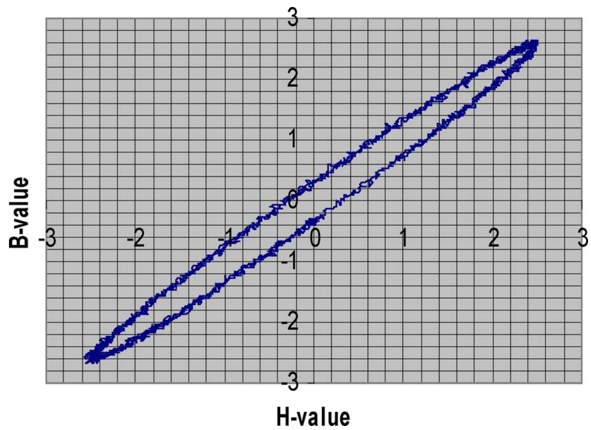


Fig. 2. Measured B-H characteristic of the magnetic fluid used for hyperthermia based cancer treatment.

Recently, a hyperthermia cancer treatment based on induction heating by directly injecting magnetic fluid with magnetic nanoparticles to the tumor has been proposed [10]. To destroy the tumor, a time-varying magnetic field is applied to the nanoparticles for heating up the tumor. The applied heat depends on magnetic flux density, exciting frequency, and amount of nanoparticles. To confirm that the tumor can be destroyed when heating, it is required to measure the temperature of the magnetic liquid inside the body. The control of temperature is an important task in achieving success using this treatment method. However, it is difficult to fabricate temperature sensor of very small size with sufficient accuracy to measure the temperature. So an indirect approach is taken to measure the temperature. This approach is based on the measurement of magnetic flux density of the magnetic liquid. In order to calculate temperature in an indirect way, knowledge about the density of nanoparticles is important to know before and during the treatment. This paper has reported the development of a novel needle-type nanosensor based on the SV-GMR technique to measure the magnetic flux density inside the body via pricking the needle. The sensor has been fabricated. The modeling and experimental results of flux density measurement have been reported here. From the information of flux density, the temperature rise can be estimated to permit the delivery of controlled heating to precisely defined locations in *controlled hyperthermia* cancer treatment. The actual experiment with human is under investigation.

The paper is divided into six sections. After the introduction that covers the first section, hyperthermia treatment based on induction heating is discussed in Section II. The analytical model to estimate the relationship between the volume density of magnetic fluid and the relative magnetic permeability is derived in Section III. The finite-element analysis of the Helmholtz-coil-based complete system is presented in Section IV. The experimental results are reported in Section V. Finally, the conclusion is summarized in Section VI.

II. Hyperthermia Treatment Based on Induction Heating

Hyperthermia treatment is one of the cancer treatment methods used in recent times. Several types of cancer cells are more sensitive to temperatures in excess of 42.5 °C than their normal tissues [11]. As shown in Fig. 1, dextran magnetite (DM), a colloidal suspension of subdomain magnetite particles (magnetic fluid), is fed into the tumor. An ac magnetic field, with frequency of several hundred kilohertz, is applied to the magnetic fluid via external exciting coil. Because of the applied alternating magnetic field, the magnetic fluid consumes power due to its hysteresis property. The losses in the magnetic fluid generate heat that increases the temperature of the tumor tissues. If the temperature can be controlled just above the threshold of 42.5 °C for a prescribed time, the tumor is destroyed.

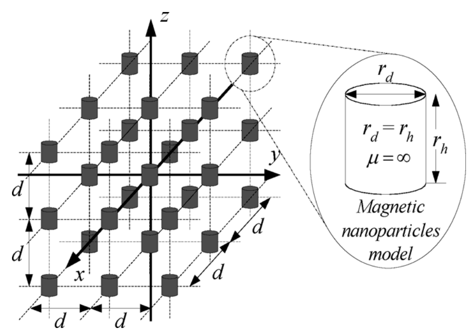
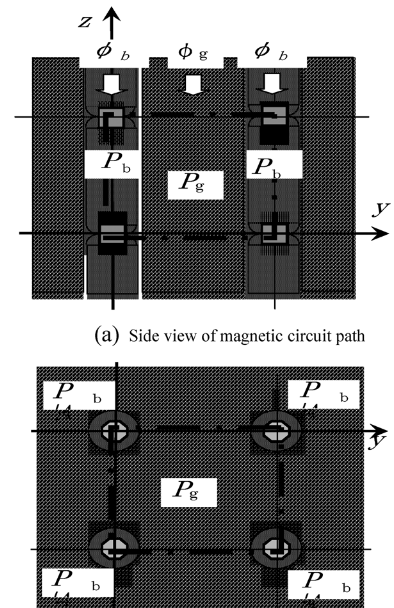


Fig. 3. Model of magnetic nanoparticles uniformly distributed inside the magnetic liquid.



(a) Side view of magnetic circuit path

(b) Top view

Fig. 4. Equivalent magnetic circuit path of magnetic liquid under z-direction external field.

The heat capacity Q (W/cc) generated by magnetite can be calculated as follows:

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

where

f exciting frequency (kHz);
D_w weight density of magnetic fluid (mgFe/cc);

B amplitude of applied magnetic flux density (T); and
k_m a constant of value 3.14×10^{-3} (W/Hz/(mgFe/cc)/ T^2cc) [11].

W represents power in watts, cc represents volume in cubic centimeter, and mg represents weight in milligram.

The coefficient k_m is obtained from the experiment. For the above value of k_m, Resovist, a substance (compound) having a magnetic volume density of 28 mgFe/cc, was chosen and an exciting magnetic field at a frequency of 158 kHz was applied. The measured hysteresis loop (B-H characteristic) of the sample is shown in Fig. 2. If all parameters of (1) are known, the amount of heat used for cancer treatment can be easily calculated. The applied magnetic field can be estimated from basic electromagnetic calculation, assuming that the relative permeability of the human body is approximately one. When DM is injected into the body to treat cancer, the volume density of the magnetic fluid decreases as it is inserted inside cancer tissues. Therefore, the measurement or accurate estimation of the volume density of the magnetic fluid inside cancer tissues is very important for controlling the amount of heat during the treatment. Since the sensor measures the magnetic flux density in the region with magnetic fluid, the relationship between the magnetic permeability and the weight density or the volume density of the magnetic fluid is very useful for calculating the heat. In the following section an analytical model on the correspondence between the magnetic permeability of the magnetic fluid and the volume density is presented.

III. Analytical Model to the Estimate Volume Density of the Magnetic Fluid

The relative magnetic permeability of the magnetic fluid is estimated by the measuring magnetic flux density inside the tissue that was injected with magnetic fluid [12]. The magnetic fluid is basically a mixture of ferrite (iron) particles mixed in water. The iron particles are usually known as magnetic bead. The volume density of the magnetic fluid D_v is calculated based on the relationship between the weight density of the magnetic fluid and the relative permeability.

A. Relationship Between the Relative Permeability and the Volume Density of the Magnetic Fluid

The different variables used in the relationship are defined as follows:

volume density of magnetic fluid
: D_v (measured as a percentage)
weight density of magnetic fluid
: D_w (measured as weight per volume)
specific gravity of magnetic fluid
: γ_m(W-35 sample : $\gamma_m = 1.365$ from data sheet)
specific gravity of magnetic bead
: γ_{f} (magnetic bead for W-35 sample
: $\gamma_{\mathrm{f}} = 4.58$ from estimated value)
weight rate of magnetic bead $\left(\frac{\mathrm{g}}{\mathrm{cc}}\right)$
: w_{f} $\quad w_{\mathrm{f}} = \gamma_m * D_w$. (2)

TABLE I
Relative Permeability of the Magnetic Fluid

Magnetic fluid	Volume density D_v [%]	Relative permeability Cal.	Exp.
Sample 1	0.034	1.14	1.20
Sample 2	0.012	1.048	1.07

The weight density D_v is expressed by the volume density D_w and the specific gravity (ferrite) γ_{f} from

$$D_w = \frac{\text{(weight of beads in 1 cc volume)}}{\text{(weight of combined beads and water of 1 cc volume)}} = \frac{(\gamma_{\mathrm{f}} * D_v)}{((1-D_v)+\gamma_{\mathrm{f}} * D_v)}. \quad (3)$$

This is simplified as

$$D_w = \frac{1}{1+(1/D_v - 1)/\gamma_f} \approx \frac{1}{1+1/D_v\gamma_f} \approx D_v\gamma_f \quad (4)$$

resulting

$$D_v = \frac{1}{1+(1/D_w - 1)\gamma_f} \approx \frac{1}{1+\gamma_f/D_w} \approx D_w/\gamma_f \quad \text{(if } D_v \text{ and } D_w \text{ are small)}. \quad (5)$$

It is assumed that the magnetic nanoparticles are uniformly distributed in the fluid and its occupying shape is cylindrical, where the nanoparticles height r_h is equal to their diameter r_p, as shown in Fig. 3. Let us also assume that the relative permeability is infinite for the nanoparticles and one for the liquid. Based on these assumptions, the permeance of the magnetic liquid has been estimated based on the equivalent magnetic circuit path approach. The existence of magnetic particles with infinite permeability changes the magnetic circuit for the external magnetic field as shown in Fig. 4. Two equivalent magnetic circuit paths are considered, one including and the other not including magnetic particles. The permeance of two magnetic paths are expressed as follows.

The permeance of the magnetic path through magnetic bead is given by

$$P_b = \frac{\mu_o(\pi r_p^2)}{d - r_p} \quad (6)$$

and that through the air is given by

$$P_g = \frac{\mu_o(d^2 - \pi r_p^2)}{d}. \quad (7)$$

Based on (6) and (7), the permeance of the unity volume can be derived as

$$P\left(=\frac{\mu S}{\ell}\right) = \frac{\mu_0\mu^*\, 1^2}{1} = \mu_0\mu^* = (P_b + P_g)\left(\frac{\frac{1}{d^2}}{\frac{1}{d}}\right) = \frac{P_b+P_g}{d}. \quad (8)$$

Equation (8) can be expanded as follows:

$$\mu_0\mu^* = \frac{1}{d}\left(\frac{\mu_0\pi r_p^2}{d - r_p} + \frac{\mu_0(d^2 - \pi r_p^2)}{d}\right).$$

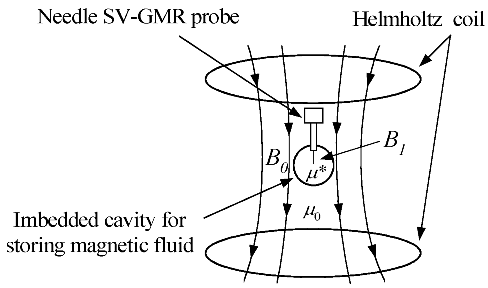
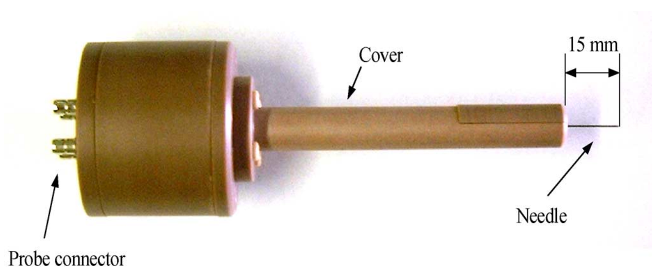
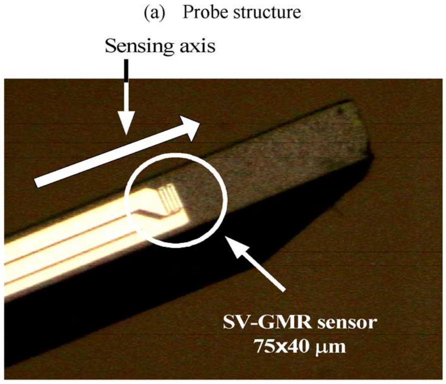


Fig. 5. Model of the magnetic flux inside the embedded cavity.



(a) Probe structure



(b) The needle tip

Fig. 6. Proposed SV-GMR sensor for biomedical application.

After simplification, we get

$$\mu^* = 1 + \frac{\pi r_p^3}{d^2(d - r_p)}$$

$$\text{or} \quad \mu^* = 1 + \frac{4\pi \left(\frac{r_p}{2}\right)^2 r_p}{d^2(d - r_p)}.$$

Therefore, the relative permeability μ^* of the magnetic fluid can be estimated as

$$\mu^* = 1 + 4D_v \quad \text{where} \quad D_v = \frac{\pi \left(\frac{r_p}{2}\right)^2 r_p}{d^2(d - r_p)}. \tag{9}$$

The equation has been verified by experimental results. The vessel with solenoidal shape was filled up with magnetic liquid, and the relative permeability of the magnetic fluid for various compositions was measured by experiment. Table I shows the comparison between the calculated and the experimental permeability which are obviously very close.

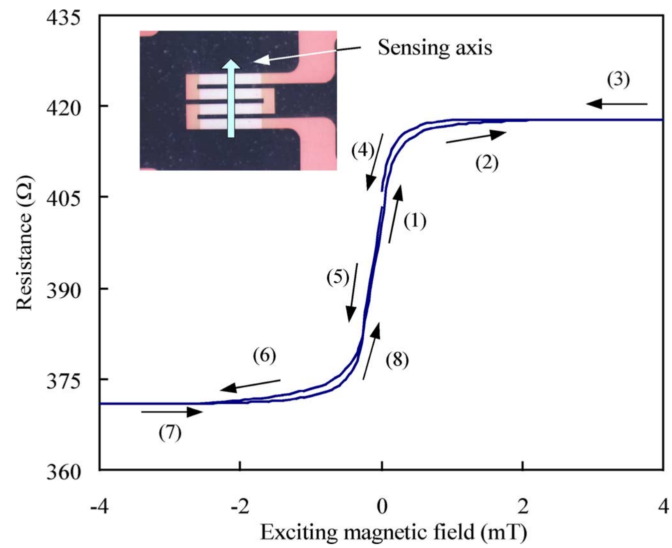


Fig. 7. The dc characteristics of the GMR sensor.

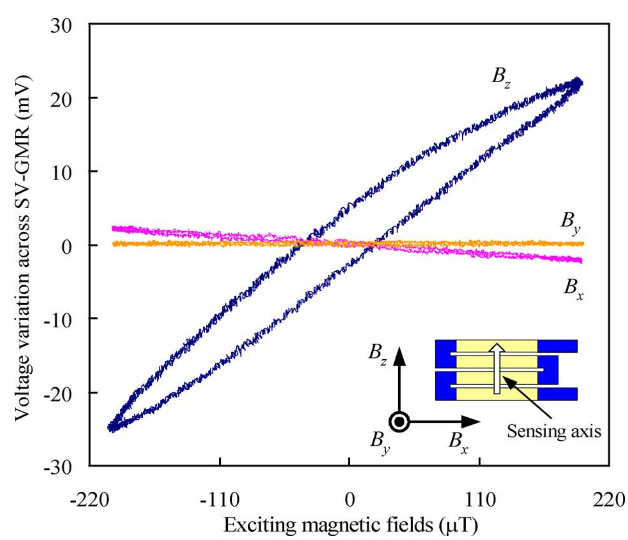


Fig. 8. The ac characteristics of the GMR sensor.

B. Magnetic Flux Density Inside the Magnetic Fluid Under Uniform Magnetic Field

A uniform magnetic flux B_0 is generated by a Helmholtz coil and applied to the magnetic fluid stored in a specified embedded cavity as shown in Fig. 5. The magnetic flux at the center of the embedded cavity B_1 can be expressed as

$$B_1 = \frac{\mu^* B_0}{\{1 + N(\mu^* - 1)\}} \tag{10}$$

where μ^* is the relative permeability which is slightly greater than one and N is the demagnetizing factor of the cavity [13]. From (9) and (10), the relationship between the magnetic flux densities, B_1, B_0, and the volume density D_v may approximately be written as

$$\frac{(B_1 - B_0)}{B_0} \cong 4(1 + N) D_v. \tag{11}$$

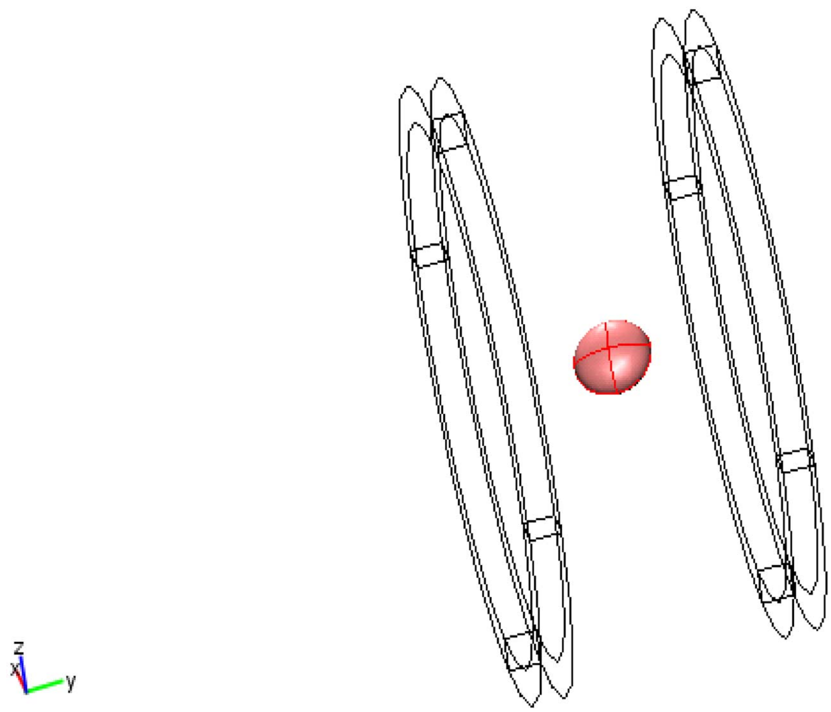


Fig. 9. 3-D finite-element method model for field calculation with elliptical shape of magnetic fluid.

From (11), the volume density of the magnetic fluid can be estimated if the difference between the magnetic flux density inside the embedded cavity and the applied magnetic flux density can be measured. The change of the magnetic flux density is directly proportional to the volume density of the magnetic fluid. However, the shape of embedded cavity influences the difference of magnetic flux density.

C. Proposed SV-GMR Sensor Used for Magnetic Flux Measurement

The needle type SV-GMR sensor, shown in Fig. 6, was fabricated by TDK, Japan, with our designed specification. The fabricated sensor has been applied to measure magnetic flux inside a simulated situation of the human body. The SV-GMR element, with sensing area of 75 μm$\times$ 40 μm, was inserted inside the tip of the needle. The sensing direction is parallel to the needle. A constant current of 0.5 mA is applied to the SV-GMR sensor. Fig. 7 shows the dc characteristics of the sensor. It presents a nominal resistance of 400 Ω and a change of resistance of 10% with a change of flux density of $\pm$2 mT. Fig. 8 shows the ac characteristics of the sensor. From Fig. 8, it is seen that the sensitivity of the SV-GMR sensor is approximately 10 $\mu\mathrm{V}/\mu\mathrm{T}$.

IV. Modeling of Electromagnetic Field Distribution

The flux density distribution inside Helmholtz coils in the presence of magnetic particle with permeabilities very close to air has been carried out using three-dimensional finite-element analysis. The finite-element software FEMLAB has been used for that purpose. The response of the GMR sensor as a function of flux density has been analyzed [14]–[17]. Fig. 9 shows the model of Helmholtz coil having a block of different magnetic permeability with an elliptical shape at the center. The orientation of the shape as well as its size has been changed to see the effect on the magnetic flux density. The field distribution is also analyzed by varying the permeability of the central block. Fig. 10 shows a typical solved model. Fig. 11 shows some results obtained from the finite element analysis. Fig. 11(a) shows the variation of flux density as a function of magnetic permeability for different orientations of the ellipsoid. It is seen that the magnitude of the flux density at the center point does not depend much on the orientation. Fig. 11(b) shows the variation of the flux density at two different locations: one at a reference point that is not affected by the magnetic fluid and another one at the center of the ellipsoid structure. The difference of these two measurements is used for the calculation of the relative magnetic permeability. Fig. 11(c) and (d) shows the effect of changes of permeability on flux density, and vice versa. It is seen that, for a change of 20% of the relative permeability, there is a change of around 13%–14% of the magnetic flux density.

V. Experimental Results

Fig. 12 shows the experimental setup. The square-type Helmholtz coil pair has been used for the generation of an uniform flux density. The flux density has been measured with a Gauss probe as well as with the GMR sensor. A lock-in amplifier is used to measure the voltage across the SV-GMR sensor. The magnetic fluid is kept in a spherical storage tank, with a diameter of 10 mm.

The GMR sensor is used to measure the flux density inside a square Helmholtz coils system to observe its characteristics and ascertain its dependency as a function of exciting current, operating frequency, etc. Also the GMR sensor is used to observe its response to magnetic liquid. Fig. 13 shows the relationship between the exciting current and the measured flux density by the Gauss probe. Fig. 14 shows the relationship between the actual flux density and the GMR output. It is seen that the relationship

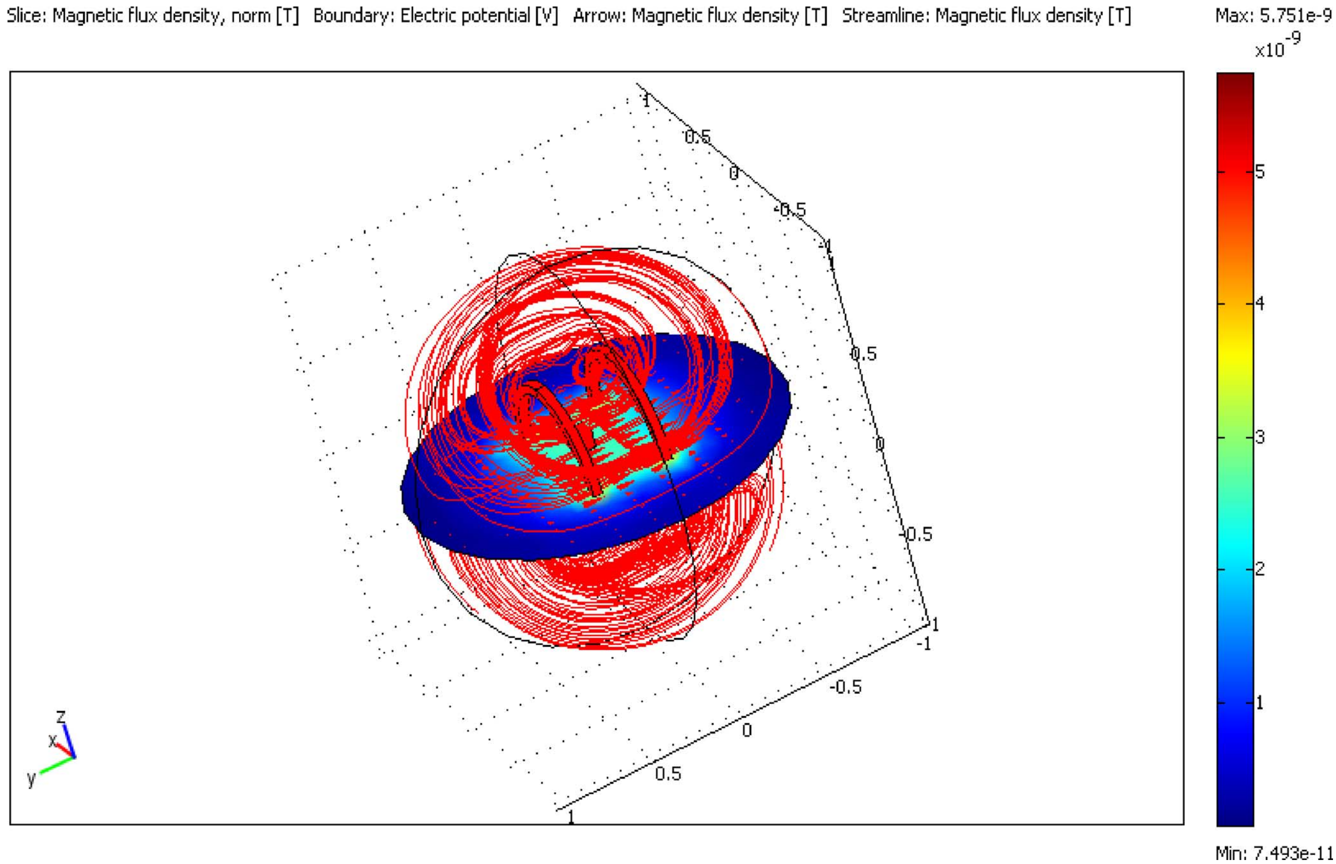


Fig. 10. Solved model of field distribution.

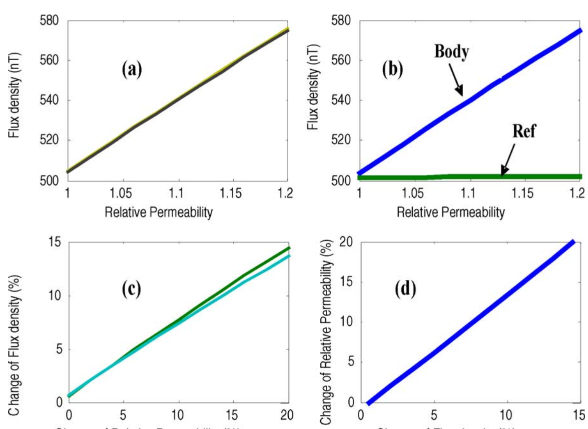


Fig. 11. Results from finite-element analysis for different orientation of ellipsoids.

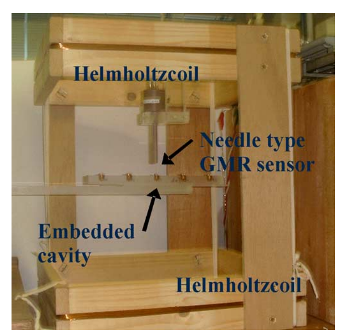


Fig. 12. Experimental setup for measurement.

is linear. So from observing the GMR output the exciting current can be set to produce known amount of flux density. Usually, 100 μT (1000 mGauss) is set during the experiment. Fig. 15 shows the effect of frequency on the output of the GMR sensor. It is seen that the output of the GMR sensor decreases with the increase in exciting frequency for the same value of the exciting current. So during this experiment, a relatively lower frequency of excitation is used.

Fig. 16 shows the variation of the sensor output as a function of the volume density of the magnetic liquid while the needle of the sensor is inserted inside the liquid. This figure denotes the relationship between the volume density of the magnetic fluid and the change of the magnetic flux density. When the cavity is long, the relationship shows the upper limit of the shaded area. For the spherical shape, the lower limit has been obtained. On the other hand, the experimental results show the solid line. It therefore can be concluded that the density of the magnetic fluid inside the body may be estimated with a good accuracy.

VI. Conclusion

A novel sensor based on the spin-valve giant magnetoresistive technique has been developed for a biomedical application. The sensor is planned to be used to measure the volume density of magnetic fluid inside human body. For the hyperthermia cancer treatment based on induction heating, it is important to

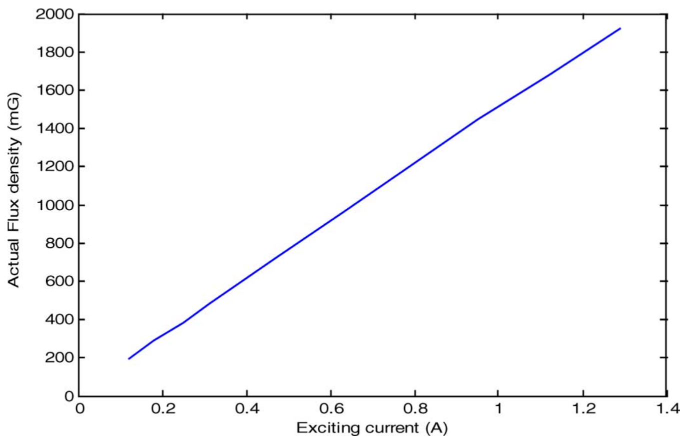


Fig. 13. Actual flux density as a function of exciting current.

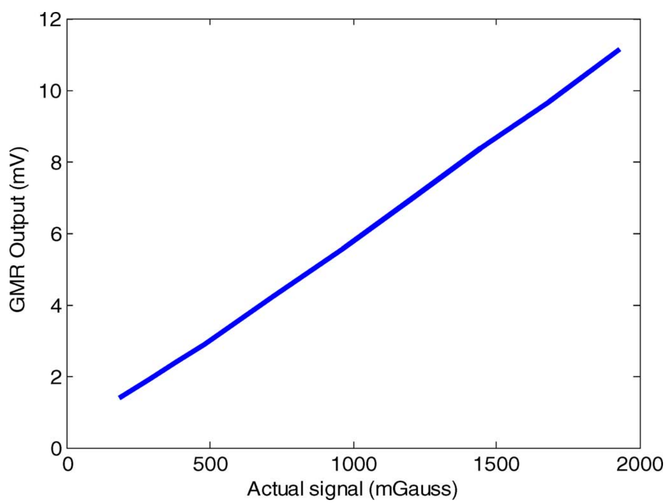


Fig. 14. Actual flux density versus GMR sensor output.

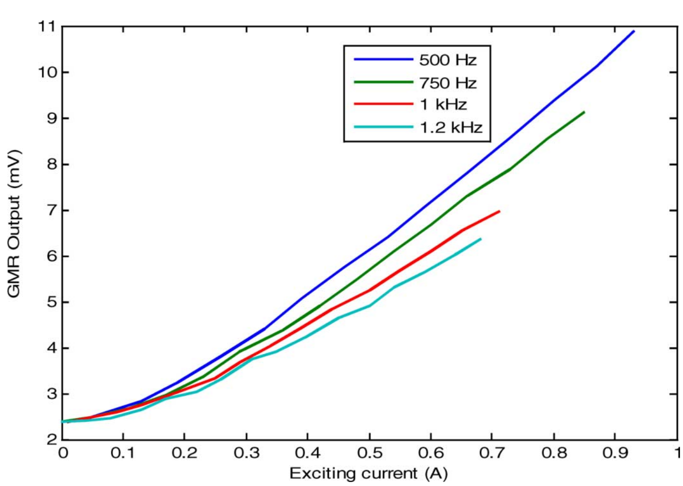


Fig. 15. Exciting current versus GMR signal output for different operating frequency.

estimate the volume density of magnetite inside the body. The relationship between the difference of magnetic flux density and magnetic fluid volume density contained in an embedded cavity has been derived. The use of needle-type SV-GMR sensor enables us to measure the magnetic flux density inside the cavity

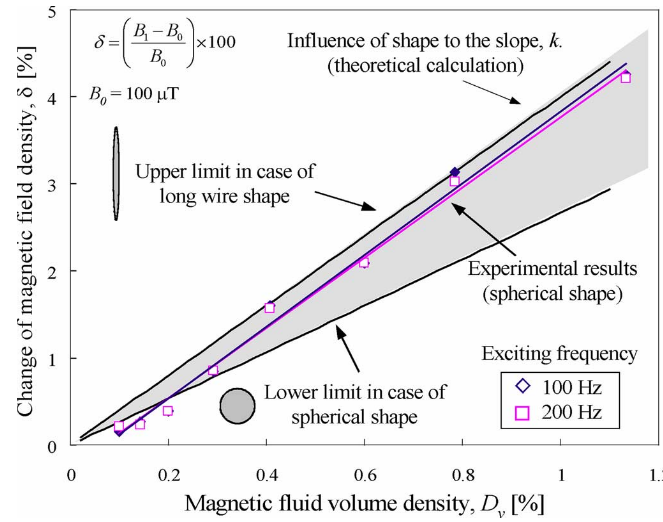


Fig. 16. Experimental results showing the relationship between the volume density of the magnetic fluid and the change of the magnetic flux density.

with minimal disruption. It can therefore be concluded that the volume density of magnetite injected into the body may be estimated by the proposed technique and consequently the sensor will be useful for cancer treatment.

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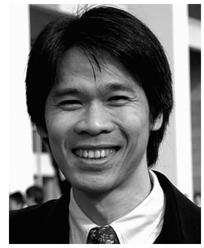

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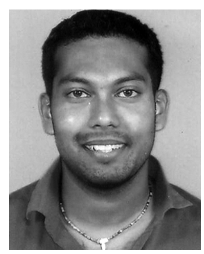

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