GMR Sensor Application in Detecting and Estimating Magnetic Fluid Weight Density inside Various Size Tumors

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This paper proposes a novel needle-type giant magnetoresistance (GMR) sensor which has a good potential to be used as a tool, for improving the quality of induction heating type hyperthermia. Relationships are obtained between magnetic fluid parameters such as relative permeability, weight and volume density by analytical analysis. Taking into account the favorable features of the fabricated sensor experimental methods are designed for detecting and estimating the weight density inside various size magnetic fluid filled agar pieces, which simulates actual tumors. Numerical and experimental results are presented showing the relationship between the magnetic fluid weight density and the difference of the magnetic flux density inside and outside tumors.

Key words: GMR sensor, tumor, hyperthermia, permeability, weight density, size dependence

1. Introduction

In induction heating type hyperthermia magnetic fluid is injected into tumors. Magnetic fluid is a colloidal mixture comprising magnetic nanoparticles suspended in water or a hydrocarbon fluid. AC (alternating current) magnetic fields are applied and the magnetic fluid filled tumor is heated by inductive heating. If the temperature can be maintained at the therapeutic threshold of 42 °C for 30 minutes or more the tumor cells can be destroyed¹⁾.

Assuming that tumors are spherical in shape, the cutoff diameters in the tumor, node, metastasis (TNM) staging system for the three different stages depend on the type of tumor. Recent studies have shown that the general cut off point between T1 and T2 tumors is 50 mm²⁾. One of the main problems associated with magnetic fluid injected into tumors is that it spreads inside tissue, reducing its content density. Since specific heat capacity is directly proportional to magnetic fluid weight density, D_w (weight of magnetic nanoparticles /total weight) as well as being clearly correlated with therapeutic outcome³⁾, it is important to estimate D_w inside the body before and after treatment.

The aim of this paper is to introduce a novel needle-type giant magnetoresistance (GMR) sensor which has a good possibility to be used for detection and estimation of D_w inside the body.

2. Needle-Type GMR Sensor

The fabricated needle-type GMR sensor is shown in Fig. 1. The needle is approximately 20 mm in length and is made from a compound of Aluminum Oxide and Titanium Carbide ($\text{Al}_2\text{O}_3/\text{TiC}$). The sensor was made so that it would be minimally invasive when inserted inside the body to estimate D_w . It is also compact in design, inexpensive and can be used easily by a physician in a clinical environment. With signal processing it has the potential to detect and estimate D_w in real-time. The sensor needle can also be inserted at different positions

to estimate D_w in a tumor since it is important to treat tumor regions homogenously.

The key feature of the needle-type sensor is the GMR sensing area of $75\text{ }\mu\text{m} \times 40\text{ }\mu\text{m}$ located at the tip of the needle. The sensor is also designed as a bridge circuit with three other GMR sensing areas, present near the bonding pads (20 mm from the GMR sensing area at the tip). Hence, the magnetic flux density inside (B_i) and outside (B_o) a magnetic fluid filled tumor can be estimated simultaneously. Sensing direction is parallel to the needle (z direction) as shown in Fig. 1(b). The sensitivity of the sensor is $12.5\text{ }\mu\text{V}/\mu\text{T}$ for small signal characterization at 1 kHz.

3. Magnetic Fluid Weight Density Estimation

3.1 Magnetic Fluid Parameters

Two of the most commonly used magnetic fluids in the biomedical field, Dextran Magnetite (DM) and Resovist, are shown in Fig. 2(a). DM and Resovist contain a large number of superparamagnetic iron oxide nanoparticles distributed uniformly, each acting in principle as a hot source⁴⁾, and producing a homogenous temperature. However, it can be seen from the electron microscopy image that the magnetic nanoparticles form clusters. Therefore, the packing factor of spherical magnetite (Fe_3O_4) was taken into account and a spherical cluster model was considered as shown in Fig. 2(b). It is assumed that the magnetic nanoparticle clusters are uniformly distributed in the liquid, cylindrical in shape with equal height and diameter and that the permeability of liquid is 1 and nanoparticles infinity. The permeance of a unit volume is obtained by estimating the permeance of an equivalent magnetic path through magnetic nanoparticles and air⁵⁾. The relative permeability, μ^* , of magnetic fluid (considered as a bulk) is^{3,5)},

$$\mu^* = 1 + C_d D_v \approx 1 + C_d D_w / h_s \gamma_f \quad (D_w \ll 1) \quad (1)$$

where C_d is a coefficient (theoretically 4), D_v is the magnetic fluid volume density, h_s is the packing factor of

Fig. 1 Needle-type GMR sensor.

spherical magnetite (0.523), and γ is the specific gravity of magnetite (4.58).

It can be seen from Eq. (1) that the relative permeability is independent of shape and/or size of magnetic nanoparticles and is proportional to D_w . A vibrating sample magnetometer (VSM) was used to measure the relative permeability for a range of magnetic fluid weight densities, to verify Eq. (1). Figure 3 shows that the experimental results agree with the theoretical estimation.

3.2 Estimation of Magnetic Fluid Weight Density inside Tumors

When a magnetic fluid filled tumor is exposed to a uniform magnetic flux density by a Helmholtz tri-coil as

Fig. 2 Magnetic fluid for biomedical applications.

Fig. 3 Relationship between relative permeability and weight density – Comparison of theoretical and experimental results.

shown in Fig. 4, there will be a difference between B_i and B_o . The magnetic flux density at the center of the cavity⁶⁾ is as follows:

$$B_i = \mu^* B_o / \left\{ 1 + N(\mu^* - 1) \right\} \quad (2)$$

where N is the demagnetizing factor of the cavity.

By substituting Eq. (1) in Eq. (2), the following equation is obtained.

$$\delta = (B_i - B_o) / B_o \approx C_d (1 - N) D_w / (h_s \gamma_f) \quad (D_w \ll 1) \quad (3)$$

From Eq. (3) D_w can be estimated, given that the differential magnetic flux density inside and outside a magnetic fluid filled cavity can be obtained. However, N has an influence which must be taken into consideration. N depends on the aspect ratio s , which refers to the ratio between the long axis and diameter of an ellipsoidal cavity.

The size of the tumor should be considered since out of the 20 mm needle 15 mm is available to be inserted inside the tumor. Since the needle tip should be inserted to the center of the tumor where the flux density is the greatest, the diameter of a given tumor should be less than or equal to 30 mm. This corresponds to T1-T2 tumors. For tumors in the T3 stage for example which are larger than 50 mm a method as shown in Fig. 5 is proposed. Taking advantage of the fact that the distance between the GMR sensing area at the tip and the three

Fig. 4 Differential magnetic flux density inside and outside a tumor.

Fig. 5 Estimation of magnetic fluid weight density inside large cavities.

other sensors near the bonding pads is 20 mm, magnetic flux density is obtained at 20 mm steps. The total change of magnetic flux density is then calculated by the following equation.

$$B_{TotalChange} = \sum_{i=0}^n (B_{i+1} - B_i) \quad (4)$$

4. Results

4.1 Numerical Results

3-D numerical analysis was performed with the aid of FEMLAB. As shown in Fig. 6, a cylindrical cavity of permeability slightly more than 1 was exposed to a uniform magnetic flux density of 100 μ T, supplied by a Helmholtz tri-coil. It can be seen from Fig. 6 that magnetic flux lines converge at the cylindrical cavities which has slightly higher permeability than air. Hence, B_1 is higher than B_0 . From the difference between B_1 and B_0 , D_w can be estimated by Eq. (3).

Figure 7 shows the numerical estimation of the magnetic fluid weight density for the cavity described in Fig. 6 and its comparison to theoretical results. It can be seen that if magnetic flux density can be measured at the center of the cavity, the change in magnetic flux density is approximately equal to the theoretical results. However, since the needle of the GMR sensor is only 20 mm in length, the change in magnetic flux density is obtained by Eq. (4) for large cavities where the needle cannot be inserted into the center of the cavity. The number of steps used in this case was 7. This meant that

Fig. 6 3-D Numerical analysis.

Fig. 7 Comparison of theoretical and numerical results.

the needle was fully inserted in the magnetic fluid filled cavity after 7 steps, but the tip was not at the center of the cavity. Figure 7 shows that this method gives a good approximation to the case where the sensor needle cannot be inserted into the center of the cavity.

4.2 Experimental Results for Small Cavities

Magnetic fluid was injected into cylindrical agar pieces of 18 mm diameter to simulate magnetic fluid filled tumors, as shown in Fig. 8. The cylindrical agar pieces were submerged in potato starch which was the reference medium. A helmholtz tri-coil⁷⁾ was designed and fabricated to produce a uniform magnetic flux density of 100 μ T at 100 Hz. The needle-type GMR sensor was used to measure the change in magnetic flux density inside and outside the magnetic fluid filled cylindrical agar pieces. The GMR sensor output was measured by a digital lock-in amplifier (NF Electronics, LI5640). Figure 9 shows a proportional relationship between the change in magnetic flux density and D_w . The results are also between the theoretical lines for long thin ($s = \infty$, $N = 0$) and short flat ($s = 0.5$, $N = 0.527$) ellipsoidal cavities. D_w concentrations as low as 0.145 % can be estimated by the needle-type GMR sensor. However, since agar cavities without any magnetic fluid showed a change in magnetic flux density of 0.043 %, experimental results for D_w below 0.145 % would have been ambiguous.

Figure 10 shows the change in signal for different sizes of magnetic fluid filled agar pieces. The change in signal corresponds to the difference between the signal obtained for a magnetic fluid filled agar piece and potato starch (reference medium). It can be seen that for a given D_w the change in signal is not very significant for the different sized cavities. The change in signal however increases with D_w , thus verifying Eq. (3).

4.3 Experimental Results for Large Cavities

The method for large cavities explained in section 3.2 was utilized to measure the change in magnetic flux density for magnetic fluid filled cylindrical agar pieces of 63 mm diameter. It can be seen from Fig. 11 that the total change in magnetic flux density increases with D_w and agrees well with theoretical results based on ellipsoidal cavities and numerical results. However,

Fig. 8 Experimental setup.

Fig. 9 Estimation of magnetic fluid weight density in small cavities.

Fig. 10 Detection of magnetic fluid weight density in various size agar pieces.

estimation of low concentration D_w (less than 1 %) proved to be difficult because of noise encountered, while moving the sensor through 20 mm steps. Also, large agar cavities without magnetic fluid gave a change in magnetic flux density of 0.076 %. Hence, the lowest D_w that could be measured for cavities larger than 50 mm was 1.4 %.

5. Conclusion

Cylindrical agar cavities ($s = 1$) of various sizes were employed to simulate tumors at different stages of growth. The experimental results obtained showed a proportional relationship between change in magnetic flux density and D_w for small and large cavities. However, the limit of detection for small cavities were 0.145 % D_w while for large cavities were 1.4 % D_w . This difference was mainly due to the noise encountered while moving the sensor in the latter case. Furthermore, noise sources as well as non-uniform components of the Helmholtz-coil also affected the limit of estimation. Estimation of weight densities less than above stated limits would have resulted in ambiguity.

More experiments are also needed to be performed on very low-concentration magnetic fluid since even after treatment some magnetic nanoparticles tend to stay in the injected region. Given that s and hence N remains the same it was found that the size of the cavity has no effect on the change in magnetic flux density. However, further experiments should also be performed on cavities of different shapes and sizes (different s and N)

Fig. 11 Estimation of magnetic fluid weight density in large cavities.

since tumors come in a variety of shapes.

For all of the above points discussed it is apparent that a more uniform magnetic flux generator, with at least 1/10th more uniformity compared to magnetic fluid weight densities being estimated (0.1 % D_w or less) would be needed along with a shielded environment, for accurate very low concentration magnetic fluid weight density estimation.

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