Estimation of Specific Power Loss of Heating Mediator (La-Sr-Mn-Cu perovskite) for Magnetic Hyperthermia under 1 MHz Magnetic Field at Different Temperatures

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To estimate specific power losses (SPL) of bulky magnetic hyperthermia heating mediators, a hysteresis loop measurement system in alternating magnetic field at a constant temperature was fabricated. Magnetic properties of a rectangular sample of La-Sr-Mn-Cu perovskite (LSMC) in a temperature range of 20~46°C were estimated from induced electromotive force which arose in a single turn pickup coil located at the center of exiting coil (1 MHz, 3 kA/m^rms). Complex permeability \(\mu\) and \(\mu'\), coercive force \(H_c\), and SPL of the LSMC decreased with increasing the temperature. Phase delay \(\delta\) of magnetic flux density of the LSMC from the applied magnetic field were almost the same among measured temperature range.

Key words: magnetic hyperthermia, hysteresis loop, specific power loss, complex permeability, bulky heating mediator

1. Introduction

Hyperthermia is used in the treatment of cancer because cancer cells are more sensitive to temperatures in the rage of 42.5~45°C than normal tissue. In recent years, magnetic hyperthermia (MHT) is attracting attention since it is minimally invasive and heats tumor locally. In this process, heating mediators, which generate heat by alternating magnetic field (AMF) applied from outside the body, are injected or implanted into a tumor to kill only cancer.¹

Heating mediators studied for MHT are magnetic nanoparticles²⁻¹⁰, electrical conductors¹¹ and bulk magnetic material¹²⁻¹³. For magnetic nanoparticles, there are many reports since they have the potential to be used not only as heating mediators of magnetic hyperthermia but also drug carrier of drug delivery systems and contrast agents of magnetic resonance imaging²⁻¹⁰. In order to achieve clinical application of heating mediator, accurate temperature control is required to minimize damage of normal tissue surrounding the cancer. However, the heating ability of magnetic nanoparticles under AMF is strongly dependent on their concentration²⁻³. It is quite difficult to control their concentration in the human body. When heating mediators of bulky type are used for MHT, their amount in the human body can be controlled feasibly. La-Sr-Mn-Cu perovskites (LSMC) have been reported as one of promising candidates of bulky type heating mediators. LSMC show ferromagnetism and have Curie temperature \(T_C\) close to the body temperature and the \(T_C\) can be controlled by controlling Cu contents. Magnetization of LSMC steeply changes near \(T_C\). Ferromagnetic materials generate heat in AMF and they stop generating heat when their temperature exceeds \(T_C\). Thus, the temperature of LSMC keeps constant in AMF. This property is suitable for MHT heating mediators because the tumor can be maintained a constant temperature without monitoring.

However, it is difficult to measure temperature distribution in the tumor including heating mediators under MHT treatment. If we know specific power loss (SPL) of the heating mediators, we can estimate temperature distribution around them by numerical simulations. The SPLs of magnetic fluids are often estimated by measuring the change in temperature of them under AMF². For bulky heating mediators, it is difficult to estimate SPL accurately by this method since temperature change depends strongly on the distance between thermometer and the heating mediators. Hysteresis loop area measurement is another method for SPL estimation. The SPL of LSMC was evaluated by DC magnetization measurement¹³. However, the hysteresis loop area measurement in AMF is needed for accurate SPL estimation. In fact, there are some reports on SPL estimation of magnetic fluid under AMF fourteen to sixteen. It is difficult to estimate SPL of LSMC because the magnetization of LSMC changes steeply near \(T_C\) and SPL of LSMC changes with temperature. Thus, it is required to control temperature of LSMC. As far as the authors' knowledge, there are no reports on estimation of SPL of LSMC bulky materials by hysteresis loop area measurement in AMF at the controlled temperatures. Thus, in this study, we constructed a system of hysteresis loop measurement in AMF at different temperatures and estimated the SPL of LSMC bulky material.

2. Experimental

The schematic view of measurement system of hysteresis loops of bulky materials in AMF at a constant

126
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The number of turns $N$, the radius $R$, and the length $L$ of an exciting coil are 21, 37 mm, and 118 mm, respectively. A single turn pickup coil with 6.5 mm in radius is wound around in an acryl pipe and the pipe is set along with the center axis of the exiting coil. A rectangular LSMC sample is placed at the center of the pick-up coil. 1 MHz of alternating magnetic field with effective amplitude of 3000 A/m-rms was applied to the sample. Temperature of the sample is controlled by flowing water (20 ~ 46°C).

In order to obtain an LSMC sample with homogenous composition, a polymerized complex method was adopted. $La_2O_3$ (99.99 %, Wako Pure Chemical Industries, Ltd.), $SrCO_3$ (99.99 %, Wako Pure Chemical Industries, Ltd.), $MnO_2$ (99.99 %, Wako Pure Chemical Industries, Ltd.), $CuO$ (99.9 %, Rare Metallic, Ltd.) were dissolved in 300 ml of an aqueous solution containing 200 g of citric acid and 10 ml of 15.6 N of nitric acid. The mixture was stirred at 60°C for 2 h. 100 ml of ethylene glycol was then added and the solution was stirred at 80°C. The obtained polymeric gel was heated at 450°C in a mantle heater. The obtained powder was calcined at 1050°C for 6 h in air. The obtained powder was cooled and pressed into a pellet of which the diameter is 10 mm and the thickness is 0.6 mm and sintered at 1250°C for 15 h in air. The crystal structure of the final sample was examined by powder X-ray diffraction (XRD; Rigaku, RINT2100-Ultima, Cu- $K_α$). The composition of the sample was determined by induced coupled plasma spectroscopy (ICP; Shimazdu, ICPS-7500). The temperature dependence of magnetization was measured using a vibration sample magnetometer (VSM; Toei, VSM-3S-15) at DC field of 40 kA/m. The applied magnetic field $H$ was calculated according to the following equation.

$$H = \frac{NI}{\sqrt{4R^2 + L^2}}$$

$N$ is the number of turns of the exiting coil. $R$ and $L$ denote the radius and length of the coil, respectively. $I$ means applied exiting coil current. The magnetic flux density of the sample $B = \mu_0 \mu H$ was calculated according to the following equation.

Figure 2 shows powder XRD pattern of the obtained sample. This pattern shows a single phase of rhombohedral perovskite was prepared. Figure 3 shows the temperature dependence of magnetization of this sample in DC magnetic field. The magnetization decreased rapidly near 30°C. Curie temperature of this LSMC is estimated to be 35-37°C. However, some magnetization was measured even at 46°C.

3. Results and discussion

Figure 2 shows powder XRD pattern of the obtained sample. This pattern indicates that a single phase of rhombohedral perovskite was obtained. The results of the ICP measurement indicated the composition of the LSMC sample was $La_{0.682}Sr_{0.337}Mn_{0.921}Cu_{0.059}O_3$. The rectangular shaped sample had a density of 6.27 g/cm³. Figure 3 shows the temperature dependence of magnetization of this sample in DC magnetic field. The magnetization decreased rapidly near 30°C. Curie temperature of this LSMC is estimated to be 35-37°C. However, some magnetization was measured even at 46°C.

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Φ is the interlinkage magnetic flux across the pickup coil, \( \mu_{0} \) is the permeability in vacuum, \( \mu \) is the relative permeability of the sample and \( S_{0} \) and \( S \) are the cross-sectional area of the pickup coil and the sample, respectively. \( V \) is the induced electromotive force of pickup coil in which the LSMC sample was set. \( \Phi \) was calculated by integration of induced electromotive force which arose in the pickup coil (eqn. (2)). \( \mu \) was calculated according to the eqn. (4).

\[
\Phi = \mu_{0} \mu H S + \mu_{r} H (S_{0} - S)
\]

\[
= BS + \frac{BS_{0}}{\mu} - \frac{BS}{\mu} = -\int V \, dt \tag{2}
\]

\[
B = \frac{\Phi}{S + \frac{S_{0} - S}{\mu}} \tag{3}
\]

\( \Phi \) is the interlinkage magnetic flux across the pickup coil, \( \mu_{0} \) is the permeability in vacuum, \( \mu \) is the relative permeability of the sample and \( S_{0} \) and \( S \) are the cross-sectional area of the pickup coil and the sample, respectively. \( V \) is the induced electromotive force of pickup coil in which the LSMC sample was set. \( \Phi \) was calculated by integration of induced electromotive force which arose in the pickup coil (eqn. (2)). \( \mu \) was calculated according to the eqn. (4).

\[
\mu = \frac{V - V_{0}}{\mu_{0} H S \omega} + 1 \tag{4}
\]

\[\delta = \Phi = \mu \cos \delta \]

\[\mu' = \mu \cos \delta \]

\[\mu'' = \mu \sin \delta \tag{5}\]

Phase delay \( \delta \) at different temperatures are shown in Table 1. When the temperature of the LSMC sample changed, \( \delta \) did not change. This means that rate of magnetic domain wall motion hardly changes under AMF of a constant frequency because LSMC is the first-order phase transition material.

Figure 5 shows the plot of \( \mu \) (circle) and \( \mu'' \) (square) of \( \text{La}_{0.682} \text{Sr}_{0.337} \text{Mn}_{0.921} \text{Cu}_{0.059} \text{O}_{3} \) under 1MHz of AFM with 3 kA/m-rms amplitude versus temperature.

**Table 1** Phase delay \( \delta \), coercive force \( H_{c} \) and SPL \( P \) of LSMC at various temperature.

| Temperature (°C) | \( \delta \) (degree) | \( H_{c} \) (A/m) | \( P \) (W/g) |
|-----------------|---------------------|------------------|--------------|
| 20              | 4.25                | 380              | 9.3          |
| 36              | 4.35                | 352              | 7.9          |
| 46              | 4.25                | 325              | 4.5          |

\( V_{0} \) is the induced electromotive force of pickup coil without the LSMC sample. \( \omega \) is the angular frequency. The induced electromotive force lags about a quarter period behind the applied exiting coil current, indicating the measurement system is operating correctly. Figure 4 shows the time change of the applied current \( I \) (gray line) and the magnetic flux density \( B \) (black line) of LSMC which is calculated from eqn. (3) at various temperatures. The \( B \) of the LSMC sample decreases with increasing the temperature. It was also observed that \( B \) is delayed with respect to \( I \) and \( B \) decline as the temperature increase. When \( \delta \) is defined as phase delay of the magnetic flux density of the LSMC from the applied magnetic field, the real \( (\mu') \) and imaginary \( (\mu'') \) parts of complex permeability were calculated according to the following equations.

\[
\mu = \mu_{0} \mu H S + \mu_{r} H (S_{0} - S)
\]

\[
= BS + \frac{BS_{0}}{\mu} - \frac{BS}{\mu} = -\int V \, dt
\]

\[
B = \frac{\Phi}{S + \frac{S_{0} - S}{\mu}}
\]

\[
\mu = \frac{V - V_{0}}{\mu_{0} H S \omega} + 1
\]

\[\delta = \Phi = \mu \cos \delta \]

\[\mu' = \mu \cos \delta \]

\[\mu'' = \mu \sin \delta \]

V is the induced electromotive force of pickup coil without the LSMC sample. \( \omega \) is the angular frequency. The induced electromotive force lags about a quarter period behind the applied exiting coil current, indicating the measurement system is operating correctly. Figure 4 shows the time change of the applied current \( I \) (gray line) and the magnetic flux density \( B \) (black line) of LSMC which is calculated from eqn. (3) at various temperatures. The \( B \) of the LSMC sample decreases with increasing the temperature. It was also observed that \( B \) is delayed with respect to \( I \) and \( B \) decline as the temperature increase. When \( \delta \) is defined as phase delay of the magnetic flux density of the LSMC from the applied magnetic field, the real \( (\mu') \) and imaginary \( (\mu'') \) parts of complex permeability were calculated according to the following equations.

\[\delta = \Phi = \mu \cos \delta \]

\[\mu' = \mu \cos \delta \]

\[\mu'' = \mu \sin \delta \]

Phase delay \( \delta \) at different temperatures are shown in Table 1. When the temperature of the LSMC sample changed, \( \delta \) did not change. This means that rate of magnetic domain wall motion hardly changes under AMF of a constant frequency because LSMC is the first-order phase transition material.

Figure 5 shows the plot of \( \mu \) and \( \mu'' \) of LSMC under
1MHz of AFM with 3 kA/m–rms amplitude versus temperature. \( \mu' \) and \( \mu'' \) decrease as the temperature increases. The demagnetizing factor of the revolving ellipsoid, which imitated our sample, is 0.04. Thus, this complex permeability is the specific value of this sample.

The hysteresis loops of LSMC under 1 MHz of AFM at different temperatures are given in Fig. 6. As shown in this figure, the hysteresis loop area shrinks with increase in the temperature. The hysteresis loop measured in AMF well corresponded to that in DC field at 20°C. This fact indicates that \( \delta \) observed in this study did not originate from high frequency field. The coercive force \( H_c \) of LSMC evaluated from these hysteresis loops are listed in Table 1. \( H_c \) slightly declines as the temperature increases. The SPL was calculated according to the following equation.

\[
P = \frac{f}{\rho} \int B dH
\]

\( \rho \) is the density of the LSMC sample and \( f \) is a frequency of AMF. The SPLs, \( P \), of the LSMC at the different temperatures are also shown in Table 1. Both of \( B \) and \( H_c \) of the LSMC sample decrease at the higher temperatures as above mentioned. Consequently, SPLs also waned as the temperature increases.

In this work, we were not able to measure at higher temperature than 46°C because we used an acrylic pipe as water path. If a measuring system which enables us to measure at higher temperature is constructed, we will be able to estimate the SPL of various magnetic materials in a wide range temperature.

4. Conclusions

In order to estimate the specific power loss of bulky materials, the hysteresis loop measurement system in alternating magnetic field (AMF) at a constant temperature was constructed. The temperature of the sample was kept constant by flowing water of which temperature was controlled by a constant temperature water bath. We measured the induced electromotive force of a pickup coil, in which La–Sr–Mn–Cu perovskite (LSMC) was set, under 1 MHz of AMF (3 kA/m–rms). The magnetic flux density and the coercive force of LSMC declined as the temperature increased. The phase delay of the magnetic flux density of from the applied magnetic field hardly changed at all measured temperature. The SPL of LSMC was calculated from the hysteresis loop area. The SPL waned as the temperature increased. Utility of this system enable us the estimation of SLP under AMF of various magnetic materials including the magnetic materials with SPL sensitive to temperature such like LSMC.

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