Narrow-Band Magnetic Nanoparticle Imaging using Orthogonal Gradient Field

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Magnetic particle imaging (MPI) utilizing nonlinear magnetization of magnetic nanoparticles (MNPs) is a new technique for in vivo diagnosis in medical imaging. We have improved a narrow-band MPI system using an orthogonal gradient field and third-harmonic signal detection. An AC excitation field with $B_{ac} = 1 \text{ mT}$ and $f = 22.75 \text{ kHz}$ was applied, and a third-harmonic signal from MNPs ($f = 68.75 \text{ kHz}$) was detected. The sensitivity of detection was improved by choosing proper diameter of a pickup coil so that we could detect 100 $\mu$g of MNPs located as deep as $z = 50 \text{ mm}$. A spatial resolution of $\sim 4 \text{ mm}$ was achieved by using a gradient field of $1 \text{ T/m}$. We demonstrated the detection of two MNP samples spaced $5 \text{ mm}$ apart and located at $x = 50 \text{ mm}$. The measured contour map of the voltage signal was converted to an MNP distribution using the singular value decomposition (SVD) method. We were able to accurately identify two MNP samples. We also demonstrate the imaging of the letter "K" composed of eleven MNP samples with $7 \text{ mm}$ spacing, which demonstrated the validity of the present method.

Keywords: Magnetic Particle Imaging, third harmonic, orthogonal gradient field, spatial resolution, singular value decomposition.

1. INTRODUCTION

Magnetic particle imaging (MPI) utilizing nonlinear magnetization of magnetic nanoparticles (MNPs) has been widely studied for biomedical applications. In MPI, the position and quantity of the MNPs, which have accumulated in the affected area inside an animal or human body, are detected. MPI presents a new modality for imaging the spatial distribution of MNPs for in vivo diagnostics, such as sentinel lymph node (SLN) detection.

In performing MPI, both an AC excitation field and a DC gradient field are applied to the MNPs. By analyzing the measured contour map of the signal thereby generated from the MNPs, one can reconstruct an image of the spatial distribution of the MNPs. Thus far, several methods have been developed for this purpose, such as harmonic-space MPI, x-space MPI, and narrow-band MPI.

In prior studies, we have constructed a narrow-band MPI system using an orthogonal gradient field and the third-harmonic signal detection, where the DC gradient field is applied perpendicularly to the AC excitation field. We demonstrated the detection of a 100 $\mu$g MNP sample located at a depth of $x = 35 \text{ mm}$ with a spatial resolution of $10 \text{ mm}$. However, it is necessary to improve the detection sensitivity and spatial resolution for practical bio-applications.

In the present study, we report an improvement of MPI using this method. First, we show the measurement system. The detection sensitivity was improved by choosing proper diameter of a pickup coil, while the spatial resolution was improved by using the gradient field of $1 \text{ T/m}$. Next, we quantitatively clarified the so-called system function that relates the measured contour map to the MNP distribution. Finally, we demonstrated the detection of multiple MNP samples located at a depth of $x = 50 \text{ mm}$. The measured contour map was converted to the MNP distribution by using the system function and the singular value decomposition (SVD) method. In this case, we obtained the spatial resolution of about $4 \text{ mm}$.

2. MEASUREMENT SYSTEM

Figure 1(a) shows a conceptual diagram of the MPI system. An AC excitation field $B_{ac}$ with a frequency of $22.75 \text{ kHz}$ was applied in the x-direction by an excitation coil. A gradiometer pickup coil was set in the center of the excitation coil to detect a signal from the MNPs. The gradiometer pickup coil was formed by serially connecting two coils with the baseline of $30 \text{ mm}$. Each coil of the gradiometer was made of $0.2 \text{ mm}$ diameter Cu wire, and the number of turns of each coil was $150$. In order to obtain high cancelling of the excitation field, the $x$ position of the gradiometer was fine tuned. An LC resonant circuit was also used to enhance the third-harmonic signals at $\omega = 68.25 \text{ kHz}$.

The diameter of the pickup coil, $d_p$, was decided based on the points of the signal strength and the cancelling of the excitation field. Fig. 1(c) shows the dependence of the signal flux interlinking the pickup coil on the diameter of the pickup coil. We simulated the case when the MNPs are located $40 \text{ mm}$ below the pickup coil. As shown in Fig. 1(c), the signal flux increased with the diameter $d_b$ and peaked at $d_b = 80 \text{ mm}$. Although the value of $d_b = 80 \text{ mm}$ is preferable to obtain the maximum signal, cancellation of the excitation field becomes more difficult for larger...
values of \( d_c \). Therefore, in the present study, we set the diameter as \( d_c = 20 \) mm. If the cancelling technique is improved, we can choose much larger values of \( d_c \).

Figure 1(b) shows the four-pole gradient coil. Each of the gradient coils has an innermost and outermost side length of 50 mm and 70 mm, respectively. The coils were made of 0.8 mm diameter Cu wire, and the number of turns of each coil was \( N = 200 \). A DC current was supplied to the gradient coils in the direction shown in Fig. 1(b). In this case, the field free point (FFP) was generated at \( x = y = 0 \). Around the FFP, the DC gradient field is perpendicular to the AC excitation field, and was expressed as \( B_{\text{dc}} = (B_x, B_y, B_z) = (G, 0, 0) \), where \( G \) is the field gradient. The value of \( G \) is the same for the \( x \)-axis and the \( y \)-axis direction from the symmetry of the gradient coils. Namely, the field \( B_x \) changes linearly with respect to the position \( y \), while \( B_y \) changes linearly with \( x \). The gradient coil was cooled with water. The maximum allowable current of our gradient coils is 10 A, which gave a field gradient of \( G = 1 \) T/m around the FFP.

For MNP samples, we chose commercial magnetic nanoparticles (Resovist, Fujifilm RI Pharma). Resovist consists of aggregated Fe\(_3\)O\(_4\) nanoparticles, where the size of the elementary Fe\(_3\)O\(_4\) particle is 5–10 nm. The Fe\(_3\)O\(_4\) core was covered with a dextran layer and the mean hydrodynamic diameter of the Resovist is about 60 nm. We filled a cylindrical cell with the Resovist, containing 100 \( \mu \)g of Fe as one sample unit. The cell has a diameter of 1.4 mm and a height of 8 mm, approximately. The sample was located above the gradient coil and was magnetized by the excitation field. When the sample was moved in the \( xy \) plane, the \( z \) component of the third-harmonic signals \( V_3 \) generated from the magnetized samples were detected by the pickup coil. We recorded the signals from a lock-in amplifier and imaged the contour map using a computer.

### 3. SYSTEM FUNCTION FOR MPI

We first clarified the dependence of the third-harmonic signal on the DC field so as to obtain the so-called system function for MPI. The DC field \( B_{\text{dc}} \) was applied perpendicularly to the AC excitation field \( B_{\text{ac}} \). The symbols in Fig. 2 represent the experimental results for different values of \( B_{\text{dc}} \). Here, the vertical axis represents the voltage signal \( V_3 \) normalized by the value at \( B_{\text{dc}} = 0 \). The frequency of the AC excitation field was \( f = 1 \) kHz, and RMS values were \( B_{\text{dc}} = 0.5, 1, 2, 3 \) mT.

As shown, dependence of \( V_3 \) on \( B_{\text{dc}} \) becomes weaker for larger value of \( B_{\text{dc}} \). It is known that the FWHM (full width at half maximum) of the \( V_3 \)-\( B_{\text{dc}} \) relation gives the spatial resolution for MPI. Therefore, the result shown in Fig. 2 indicates that we can obtain better spatial resolution with MPI when we use small values of \( B_{\text{dc}} \).

The \( V_3 \)-\( B_{\text{dc}} \) relation shown in Fig. 2 gives the system function that relates the measured contour map with the MNP distribution. This relation has been analyzed by numerical simulation of the Langevin function [2]. However, numerical simulation is too complex and time-consuming to obtain the system function for MPI.

On the other hand, in the previous study, we showed that the \( V_3 \)-\( B_{\text{dc}} \) relation can be well-approximated by the Gaussian function [11]. In this case, the system function for MPI becomes very simple. Therefore, we use this empirical expression for the \( V_3 \)-\( B_{\text{dc}} \) relation,

\[
g(B_{\text{dc}}) = \frac{V_3(B_{\text{dc}})}{V_3(0)} = \exp\left(- \frac{B_{\text{dc}}^2}{2\sigma^2}\right),
\]

where \( \sigma \) is the dispersion.
The solid lines in Fig. 2 represent the $V_3$-$B_{dc}$ relation calculated with Eq. (1). In the calculation, we choose the value of $\sigma$ for each case of $B_{ac}$ so as to obtain the best fit. As shown, we obtained a good agreement between experiment and calculation. Therefore, we can use Eq. (1) as a system function for MPI.

Figure 3 represents the relationship between $\sigma$ and $B_{ac}$. As shown, the value of $\sigma$ increased almost linearly with $B_{ac}$. The $B_{ac}$-$\sigma$ relationship can be approximated with the following equation.

$$\sigma = 0.66 + 0.51B_{ac}$$ (2)

It can be shown from Eq. (1) that the FWHM in the $V_3$-$B_{dc}$ relation is given by $2.36\sigma$. This means that the spatial resolution for MPI is given by $2.36\sigma G$ when the field gradient $G$ is used. Equation (2) can be used to estimate how the RMS value of the excitation field, $B_{ac}$, affects the spatial resolution.

We note that the value of the excitation field $B_{ac}$ affects both the signal strength and spatial resolution of MPI. As shown in Fig. 2, the spatial resolution can be improved by using a small value of $B_{ac}$. On the other hand, it was shown that the third-harmonic signal from MNPs increases with $B_{ac}^2$, as shown in Fig. 4. These results indicate that we should choose appropriate value of $B_{ac}$ by considering trade-off between the signal strength and the spatial resolution. In the following experiment, therefore, we choose the value of $B_{ac} = 1$ mT in order to satisfy the requirements for signal strength and spatial resolution.

4. MAGNETIC NANOPARTICLE IMAGING

Figure 5(a) shows the contour map of the signal field generated from two MNP sample units. The two MNP sample units were spaced 5 mm apart (center to center) and located at a depth $z = 50$ mm. A gradient field $G = 1$ T/m was applied in order to obtain high spatial resolution for imaging. As shown in Fig. 5(a), we could detect 100 µg

of Resovist located as deep as $z = 50$ mm, although the signal to noise (SN) ratio is not very high.

Next, we convert the contour map to the MNP distribution with the SVD method in order to improve the spatial resolution. In applying SVD, the effect of the gradient field on the signal was modeled as follows.

$$g(x, y) \propto \left( -\frac{G^2 x^2 + G^2 y^2}{2\sigma^2} \right).$$ (3)
Using Eq. (3), we obtained the system function that relates the contour map with the MNP distribution. The details of the SVD method using Eq. (3) can be found in references 11, 12. The reconstructed MNP distribution map is shown in Fig. 5(b). We could clearly identify two MNP sample units spaced 5 mm apart. Therefore, spatial resolution for MPI is better than 5 mm.

Figure 6 shows the waveform of the signal when the MNP sample was moved in the x direction at y = 0. The 3rd harmonic voltage signals $V_3(x)$ and MNP distribution $n(x)$ were shown by the solid and dotted line, respectively. We found that the irregularity of the waveform in $V_3$ disappeared in the MNP distribution. We could get a smooth MNP distribution. A FWHM of about 4 mm was obtained in the MNP distribution case. We note that the spatial resolution expected from Eq. (2) becomes about 3 mm for the case of $B_{ac} = 1$ mT and $G = 1$ T/m. Therefore, the experimental result agrees reasonably with the expected spatial resolution.

Finally, we comment on the application of the present method to the SLN detection in breast cancer operation. In this application, we need to detect MNPs accumulated at SLN that is located at a distance of 30–50 mm below the surface of human body. The obtained results of detection sensitivity and spatial resolution will indicate the feasibility of the system for this application. However, we note that further development of the gradient coil is necessary. Although the gradient coil was placed below the MNP sample in the present experiment, we should develop the gradient coil that is placed on the surface of human body and can generate large gradient field at the SLN position.

5. CONCLUSION

We improved the performance of the narrow-band MPI system using an orthogonal gradient field and third-harmonic signal detection. The present system has detection sensitivity to detect 100 μg of MNPs located as deep as $z = 50$ mm. A spatial resolution of about 4 mm was realized by using a gradient field of 1 T/m. We also quantitatively clarified the so-called system function that relates the measured contour map with the MNP distribution. Using this system function and the SVD method, we demonstrated the detection of two MNP samples spaced 5 mm apart and located at $z = 50$ mm. We could accurately identify two MNP samples. We also demonstrate the imaging of a letter "K" composed of eleven MNP samples spaced 7 mm apart, indicating the validity of the present method.

References


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