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Submillimeter magnetic particle imaging with low symmetrical field gradient

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Abstract

Magnetic particle imaging (MPI) requires high field gradient to acquire sharp point spread function used to refine spatial resolution for submillimeter imaging of cells and small animal models. Since the steep field gradient potentially causes difficulty in the sample handling and the signal processing, minimizing the field gradient is more practical even though it degrades the spatial resolution. By modulating relaxation responses of magnetic nanotracers at two distinctive frequencies: 2 kHz and 1MHz, we reconstructed images of Resovist® sample placed in a 1.4×1.4 mm2 field of view. This modulated MPI implements 2 sets of permanent magnets of which the same polarity faces one another to create a 2 Tm-1 symmetrical field gradient on the xy plane and 3 Tm-1 on the z axis. Although the spatial resolution appears poor to differentiate two-neighboring circular phantoms of dense liquid samples, we could visualize a 1-mm ring-shaped solid sample with 0.1 mm thickness.

I Introduction

The development of magnetic particle imaging (MPI) can be potentially advanced to the field of bioanalytical cellular imaging to study such nanoscale drug uptake and cytotoxicity. However, to compete with the existing fluorescence microscopy, MPI must acquire micrometer resolution, where the spatial decoding originally relies on the nonlinear magnetization response of magnetic nanoparticles.[1] In addition to optimizing the excitation frequency and amplitude,[2] increasing field gradient associated with the point-spread function (PSF) can be a promising strategy integrated with careful sample handling and ultrasensitive magnetic sensing systems.[3] The utilization of large magnetic nanotracers can also be potential to improve signal-to-noise ratio (SNR), while the accompanying relaxation effects can be reduced by using a pulsed excitation.[4] Our recent work alternatively proposes a method which modulates the harmonic-rich low-frequency magnetization with the high frequency moment relaxation.[5] To achieve micrometer resolution, this protocol is effective under a high field gradient, as well as the distinctive primary and secondary excitation frequencies. Here, we introduce low field gradient to improve the practicality of the modulated MPI system.

II Material and methods

The modulated MPI scanner uses two sets of permanent magnets to produce 2 Tm^{-1} symmetrical field gradient on the xy axes, while the z axis experiences 3 Tm^{-1} (Fig. 1); the usual gradient for MPI may be less than 2 Tm^{-1}. The resulting field-free point (FFP) is then manipulated by two perpendicular oscillatory fields, $\mathbf{H}_x$ and $\mathbf{H}_y$, with identical frequencies at $f_x = 2000\,\mathrm{Hz}$ and $f_y = 2010\,\mathrm{Hz}$, thus moving in a dense Lissajous trajectory. An additional high-frequency z axis ($\mathbf{H}_z$) field is applied at frequency $f_z = 1\,\mathrm{MHz}$ to induce the Neel relaxation of magnetic tracers. Eq. (1) describes that the relaxation modulation spatially encodes the FFP movement as a distorted

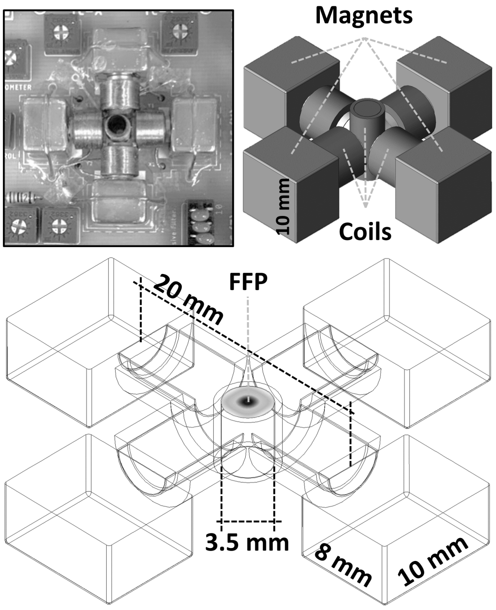

Figure 1: System configuration of submillimeter MPI scanner with 4 NdFeB magnets creating a symmetrical xy field gradient.

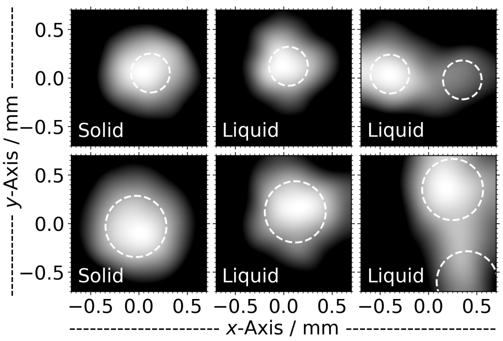

Figure 2: 2D image of the solid and liquid samples within capillary glass tubes with inner diameter of 0.4 and 0.6 mm.

z axis magnetization $\mathbf{M}_z^*$.[5] We used a 12.5 MS/s sampling rate to capture the $\mathbf{M}_z^*$ signal. The z axis magnetization ($\mathbf{M}_z$) itself depends on the equilibrium susceptibility (χ_z) of the tracers and their relaxation time distribution ($\rho_t au$) for a given $\mathbf{H}_z$ and $G_z z$ fields; G_z is the field gradient on the z axis. The low-frequency magnetizations on the xy axes, $\mathbf{M}_x$ and $\mathbf{M}_y$, must also satisfy Eq. (2), while Brownian particle dynamics may contribute to the relaxation time τ for the liquid sample, thus increasing the amplitude sensitivity of the modulated signal, a_x and a_y.

$$\mathbf{M}_z^* = \mathbf{M}_z(1 + a_x\mathbf{M}_x + a_y\mathbf{M}_y) \tag{1}$$

$$\mathbf{M}_z(z,t) = \chi_z\left[G_z z + \int\left(\mathbf{H}_z - \frac{\partial \mathbf{H}_z}{\partial t}\right)\frac{\rho_\tau d\tau}{1+(2\pi f_z \tau)^2}\right] \tag{2}$$

To evaluate the MPI scanner, we used 28 mg-Fe mL^{-1} Resovist® (Fujifilm, Japan) contained within the capillary glass tubes with the inner diameter of 0.4, 0.6, and 1 mm. While pulsating $\mathbf{H}_x \perp \mathbf{H}_y \perp \mathbf{H}_z$ fields at a 10 s interval with a 0.5 % duty cycle, $\mathbf{M}_z^*$ of the tracers is measured as an electromotive force V_S by using a gradiometric receive coil with K geometric sensitivity; μ_0 is the magnetic permeability of free space.[6] This signal further passes through a 1-MHz bandpass filter to extract the amplitude modulation at a narrow bandwidth $f_z \pm f_{x,y}^n$, relative to the noise fluctuation, prior to data averaging. The spatial decoding of the signal coordinate within the sample into 2D image is based on the temporally equidistant mapping of the signal on the predefined Lissajous trajectory of the FFP, further followed by re-gridding and spatial filtering.

$$V_S(t) = -\mu_0 K \int\int\int \frac{\partial \mathbf{M}_z^*(x,y,z,t)}{\partial t})dx\,dy\,dz. \tag{3}$$

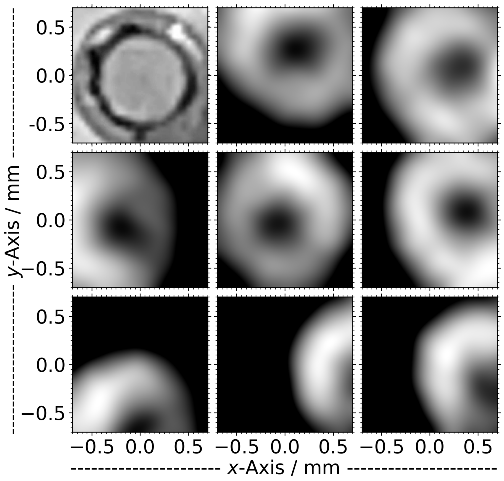

Figure 3: 2D images of 1-mm ring-shaped solid sample (top-left reference image) in different positions and z-axis orientations.

III Results and discussion

Fig. 2 describes that the achieved spatial resolution is poor to clearly distinguish two neighboring circular phantoms of liquid samples. Since we used more than 10 times lower field gradient than our previous work [5], we cannot expect high resolution. In this case, the small a_x and a_y parameters determining the ratio of the amplitude difference relative to the maximum amplitude may be responsible for the blurry image. Nevertheless, Fig. 2 indicates that the existence of Brownian relaxation may distort the PSF. Here, for more linear magnetization response (solid samples), the circular image is geometrically preserved even though it is more broadening.

From Fig. 2, it appears that solid sample is favorable to evaluate the actual spatial resolution. We then used a 1-mm ring shaped solid sample with 0.1 mm thickness. Shown in Fig. 3, the fine mechanical movement

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of the sample can be clearly captured by the modulated MPI scanner. Furthermore, a slight change in the z axis orientation of the sample makes the image more three-dimensionally. Based on the inner diameter of the reconstructed images, the actual spatial resolution should reach approximately 0.5 mm. In the future, to improve this value while keeping the field gradient as low as possible, we plan to optimize the FFP trajectory density; 2 Tm^{-1} is within the gradient range of the commercial MPI scanners.

IV Conclusions

The modulated MPI is a prospective imaging strategy to enable submillimeter resolution due to the fine temporal sampling of the magnetic signals and high SNR. However, this method relies on the amplitude sensitivity of the modulated magnetization response to decode the spatial coordinate of the signal within the sample, which further depends on the field gradient. Under 2 Tm^{-1} symmetrical xy field gradient, we were unable to clearly differentiate two adjacent 0.4-mm circular phantoms of liquid samples. Instead, we can visualize the vicinity of a 1-mm ring-shaped solid sample, suggesting that the actual spatial resolution is approximately 0.5 mm.

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Author's Statement

Conflict of interest: Authors state no conflict of interest. Informed consent: Informed consent has been obtained from all individuals included in this study.

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