International Journal on Magnetic Particle Imaging
Vol 6, No 2, Suppl 1, Article ID 2009014, 3 Pages

Infinite Science Publishing

*Proceedings Article*

# Preliminary experiments for detection of reflected signals from magnetic nanoparticles by ultrasound

H. Huang[1,*] · Y. Ishihara[1]

[1]School of Science and Technology, Meiji University, Tokyo, Japan
[*]Corresponding author, email: instrumentation.huang@gmail.com



**Abstract**

The conventional magnetic particle imaging (MPI) requires large coils and high power inputs that generate a steep magnetic field gradient to reduce image artifacts, without which the blurring of reconstructed images occur. Therefore, a new imaging system based on vibrating magnetic nanoparticles (MNPs) that does not use an alternating magnetic field was proposed to solve this problem. It was observed that the reflection signals from the MNPs could be detected using focused ultrasound. Preliminary experiments were performed to clarify the reflection signal corresponding to the MNPs concentration with an image using a diagnostic ultrasound imaging system. As a result, the MNPs reflection signal's ultrasound image was not acquired at an MNP concentration of 0.6 mol/L(Fe) or less. Therefore, a detailed examination of the concentration and particle size was required to detect the signal from MNPs.

## I Introduction

In a conventional magnetic particle imaging (MPI) method, a signal is detected from magnetic nanoparticles (MNPs) placed in a magnetic field free point (FFP) [1]. However, an interference signal is also generated when the MNP exists outside the FFP, where the MNPs' magnetization is incompletely saturated. Therefore, a below standard magnetic field gradient will result in image artifacts that are not sharp enough, and in blurring of the reconstructed image. In contrast, large coils and high power inputs are required to simultaneously apply the alternating and steep gradient magnetic fields to achieve adequate image quality. A new imaging method based on vibrating MNPs that does without the use of an alternating magnetic field was proposed to solve the problem [2]. With the proposed method, the transducer generated ultrasonic waves are used to vibrate the MNP in the magnetic field gradient, thus varying the magnetic field experienced by the MNP. Similar to the conventional method, the large magnetization signal is detected from the MNP in the FFP (Fig. 1 (a)), and only a small signal is detected from the MNP existing in the strong magnetic field (Fig. 1 (b)). Therefore, the MNP distribution can either be estimated by generating and scanning the local FFP, or by changing the position of the ultrasound focus. For this method, an MNP generated magnetization signal is detected without applying an alternating magnetic field (causes a huge hardware system as well as side effects on the living body due to electrical stimulation and heating). In addition, this method has an advantage that the MNP distribution can be reconstructed with high sensitivity by extracting the first harmonic component. Thus far, the possibility of vibrating magnetic nanoparticles with focused ultrasound has been confirmed based on the experiments using a laser Doppler vibrometer [2]. Therefore, if the ultrasonic wave reflected from the MNP can be acquired instead of the laser Doppler vibrometer, not

 

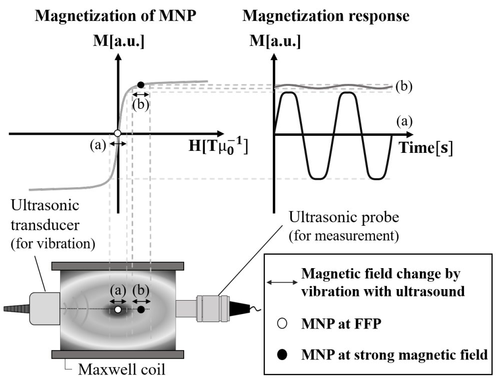


**Figure 1:** Principle of signal generation by MNP vibration.

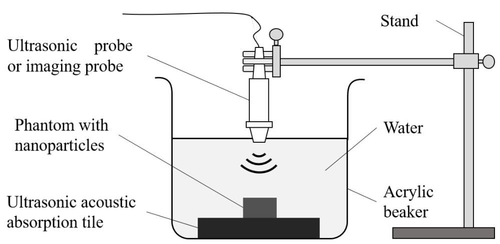


**Figure 2:** Each experimental setup.

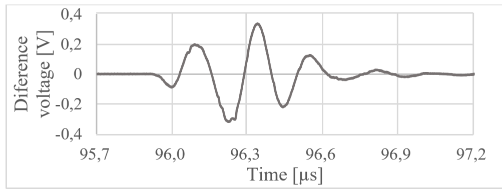


**Figure 3:** Reflection wave from MNPs (by DPR300).

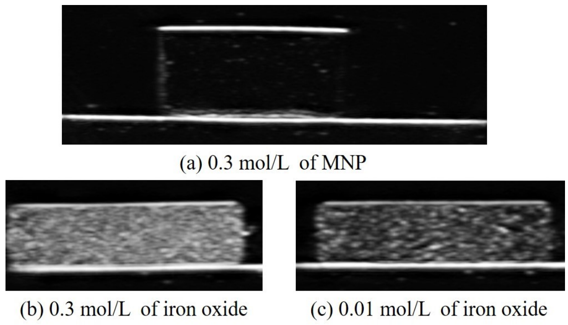


**Figure 4:** Ultrasound images (by JX3).

only will the change in the magnetic field experienced by the MNP can be estimated, but also the possibilities of using reflected waves for imaging will expand. It is for these reasons that we have been developing a system for measuring the MNP reflection using an ultrasonic diagnostic device [3].

In this study, an ultrasound measuring detection system is constructed for the detection of the MNP reflected ultrasound to estimate the displacement of the ultrasound vibrated MNPs. As described above, as the MNPs were vibrated with ultrasonic waves, it is expected that the displacement of MNPs vibrated with ultrasonic waves can be detected. To confirm the feasibility of this method, we evaluate the conditions such as the MNP's concentration that can detect the reflection signal from the MNP with ultrasound images, by performing a basic experiment using an agar phantom mixed with MNPs.

## II Material and methods

A system for detecting ultrasonic reflection signal was constructed, as shown in Fig. 2, for confirming the amplitude of the MNP vibrated by the ultrasonic waves. Two devices were used in this instance. One was an ultrasonic probe (DPR300, Imaginant Inc., NY) of frequency 5.0 [MHz]. The other was a diagnostic ultrasound imaging system (JX3, Medicare Inc., Yokohama) of frequency 8.0-9.6 [MHz]. Using this system, we conducted an experiment to examine how large signals are reflected from the ultrasonic waves irradiated to the MNP.

First, we prepared two types of phantoms. One was the 4 % agar phantom not containing the MNPs, and the other was the 4 % agar phantom uniformly mixed with the MNPs. The ferucarbotran (a drug substance of Resovist, Meito Sangyo Co., Ltd, Nagoya) was used as the MNP, and the concentrations of MNP contained with phantoms were adjusted to 0.3 mol/L(Fe). These phantoms were used to observe the reflection signal. In an experiment using the diagnostic ultrasound imaging system, the acrylic beaker was filled with water and the ultrasonic acoustic absorption tile (EUA101A, Eastek Inc., Tokyo) was placed at the bottom of the beaker. The above-described phantom (placed on the tile) formed into a cylindrical shape of radius 10 mm and a height of 10 mm. In an experiment making use of the ultrasonic probe, the phantom was placed directly at the bottom of the acrylic beaker, and reflected ultrasonic waves were observed.

In the experiment making use of the ultrasonic probe, the reflection intensity at the MNP was calculated by taking the difference between the echo waveforms from the two individual phantom surfaces (with and without MNPs) observed with the oscilloscope. In the experiment making use of the diagnostic ultrasound imaging system, we took each phantom image with different MNPs concentration. Our original program was used in the analysis of the images taken by the diagnostic ultrasound imaging system. The reflection intensity at the MNP from the differences of the histogram between images corresponding to each MNP's concentration phantom was then calculated.

 

## III Results and discussion

Fig. 3 shows the difference signal from two phantom types, and the reflected signal from the MNPs can be detected using the ultrasonic probe. Fig. 4(a) shows the phantom images at MNPs (concentrations of 0.3 mol/L(Fe)) taken with the diagnostic ultrasound imaging system, with no image being obtained to identify the presence of the MNP. Fig. 4(b) and (c) show the ultrasound images of a phantom in which iron oxide (concentrations of 0.3 and 0.01 mol/L(Fe), respectively) was mixed with agar instead of MNPs. The ultrasound images corresponding to the concentration of the iron oxide were acquired as demonstrated in the figures. It was considered that such a difference between MNP and iron oxide was caused by the iron oxide particle size being larger than 1000 nm as well as the ease of the aggregation of the iron oxide in the agar phantom.

With regards to the particle size of magnetic nanoparticles being smaller than that of the ultrasonic wavelength in the living body, it is necessary to evaluate the concentration and aggregate size that are within the detectable range by the ultrasonic diagnostic imaging system. In experiments using the ultrasonic probe, reflected MNP waves were detected as a differential signal from two phantom types. The examination of the differences between the two types of phantom surfaces was necessary, as shown in Fig. (a).

## IV Conclusions

The ultrasound images corresponding to the MNPs concentration were not acquired in under the experimental setup and conditions. Therefore, to demonstrate that MNPs signals are detectable with ultrasound images, experiments carried out with different MNPs concentrations, aggregate size as well as particle sizes are necessary. In addition, it may be necessary to develop a new image processing method for calculating the ultrasonic reflection intensity from the MNPs with high accuracy. After these considerations, a new MPI system to detect signals from vibrating the MNPs using ultrasound wave will be constructed.

## References

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10.18416/ijmpi.2020.2009014