Program Digest, 2019 IEEE International Ultrasonics Symposium (IUS)
Glasgow, Scotland, October 6-9, 2019

Improved Backward Mode Pulsed Magnetomotive Ultrasound via Pre-magnetization of Superparamagnetic Iron Oxide Nanoparticles

Hong-Wei Wang[1], Chih-Chia Huang[2], and Meng-Lin Li[1,3*]
[1]Department of Electrical Engineering, National Tsing Hua University, Hsinchu, Taiwan
[2]Department of Photonics, National Cheng Kuang University, Tainan, Taiwan
3Institute of Photonics Technologies, National Tsing Hua University, Hsinchu, Taiwan
mlli@ee.nthu.edu.tw

Abstract—**Magnetomotive ultrasound (MMUS), capable of imaging *in vivo* magnetic nanoparticle distribution, has shown its potential in extravascular ultrasound molecular imaging, magnetic nano-drug delivery monitoring, and sentinel lymph node identification. To date, most of the research teams in the world mainly implemented forward mode MMUS where the imaging object has to lie in between an ultrasound probe and an electromagnet, which is not clinically translatable. However, in our previously proposed backward mode MMUS, the MMUS displacement map was relatively noisy because of the backward-mode setup. Learning from the principle of magnetic particle imaging, we propose a new strategy to improve the backward-mode MMUS via pre-magnetization of superparamagnetic iron oxide nanoparticles (SPIONs). The new MMUS probe consists of an electromagnet for magnetic excitation and a static magnet for pre-magnetization of SPIONs. The pre-magnetization is to magnetize the SPIONs with a preset magnetic field in advance so that according to the nonlinear characteristics of the SPION magnetization curve, SPIONs can have higher magnetic susceptibility of SPIONs during magnetic excitation; thus increasing the magnetomotive force applied to SPIONs. Therefore, the displacement resulting from the magnetomotion of the SPIONs can be increased, which in turn improves the MMUS detectability of the SPIONs in backward mode. Overall, it has been demonstrated that the effectiveness of the proposed strategy in the improvement of the backward mode MMUS.**

Keywords: magnetomotive ultrasound, magnetic nanoparticles, magnetic particle imaging, pre-magnetization.

I. Introduction

There are several teams in the world currently developing magnetomotive ultrasound (MMUS). The first generation of MMUS was in forward-mode where the object was placed between an ultrasound probe and an electromagnet. The electromagnet cannot move freely with the ultrasound probe. Obviously, this limits the mobility of the ultrasound probe. In addition, in the design of the electromagnet, the excitation signal is a continuous sinusoid signal. Maintaining continuous magnetic field makes electromagnet overheated, and therefore requires an extra bulk cooling system, greatly increasing the footprint of the structure of the MMUS probe. It is not suitable for clinical applications. Our previously proposed backward-mode magnetomotive ultrasound uses cyclic pulsed magnetic field, so we do not need to maintain magnetic field for long time and do not require bulk cooling system, facilitating clinical translation

However, in our previous backward mode MMUS design, the signal-to-noise ratio of the MMUS is low. In order to improve signal-to-noise ratio, we learn from the concept of magnetic particle imaging and the characteristics of superparamagnetic nanoparticles, and propose a new strategy to improve the backward-mode MMUS via pre-magnetization of superparamagnetic nanoparticles.

II. Materials and Methods

A. Magnetomotive force

Previously, we only used the magnetic field generated by the electromagnet to excite the superparamagnetic iron oxide nanoparticles (SPIONs), creating magnetomotive force and thus magnetomotion of the SPIONs. As for how to increase the magnetomotive force and magnetomotion, this is the problem we want to explore.

In the following formula (Eq. (1)), F_{m-z} is the z direction component of the magnetomotive force $F_{m.}$ The F_{m-z} in our design is aligned with the axial direction of the transducer.

$$F_{m-z} = V_{np} f_m X_{np} \cdot \frac{(B_Z \cdot \nabla) B_Z}{\mu_0} \quad (1)$$

We can simply separate the formula into two parts. The first three terms are decided by the properties of the magnetic nanoparticles. In the magnetization curve, S-type characteristics of superparamagnetic nanoparticles can be potentially used to enhance magneto-motive force [1]. The last term represents magnetic field changes and is decided by the magnetic flux density. Both of them influence the magnetomotion of the particles.

B. Pre-magnetization

Learning from the principle of magnetic particle imaging [2], here we propose a new strategy to improve the backward-mode MMUS via pre-magnetization of SPIONs. The new MMUS probe consists of an electromagnet for magnetic excitation and a static magnet for pre-magnetization of SPIONs.

Pre-magnetization is to magnetize the SPIONs with a pre-applied magnetic field in advance before the excitation magnetic field from the electromagnet is applied, providing higher magnetic susceptibility of SPIONs according to the nonlinear characteristics of the SPION magnetization curve and thus increasing the magnetomotive force applied to the SPIONs. Therefore, the displacement resulting from the magnetomotion of the SPIONs can be increased, which in turn improves the MMUS detectability of the SPIONs in backward mode.

As mentioned above, according to the nonlinear characteristics of the SPION magnetization curve, if we pre-magnetize the SPIONs, the SPIONs can have a high magnetic susceptibility. From Eq. (1), magnetomotive force thus increases. SPIONs working regime with and without pre-magnetization is shown in Fig. 1. With this idea, a new backward mode MMUS probe is designed, as illustrated in Fig. 2. In Fig. 2, the static magnet is used for premagnetization of SPIONs.

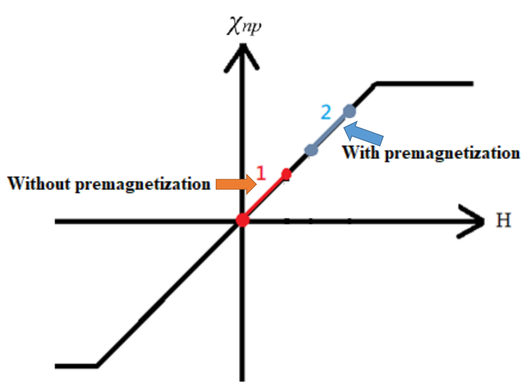

Fig. 1 SPIONs working regime with and without pre-magnetization

C. Displacement Tracking

For the purpose of real-time imaging and low computation load, the phase difference estimator which concept results from the Doppler principle was chosen to be the magneto-motion tracking algorithm. The phase difference obtained by the lag-one autocorrelation along the slow-time beamformed baseband data is used for displacement estimation. Assume f_c is the frequency of the transducer, and τ is the time-delay between the consecutive beamformed data. The tracked displacement in the slow time at each image pixel is given by

$$Displacement = \frac{v_{sound} \cdot \tau}{2} = \frac{v_{sound}}{2}\frac{\Delta\theta}{2\pi f_c}, \qquad (2)$$

where v_{sound} is the speed of sound in the tissue. The denominator, 2, denotes the two-way propagation of the ultrasound signal.

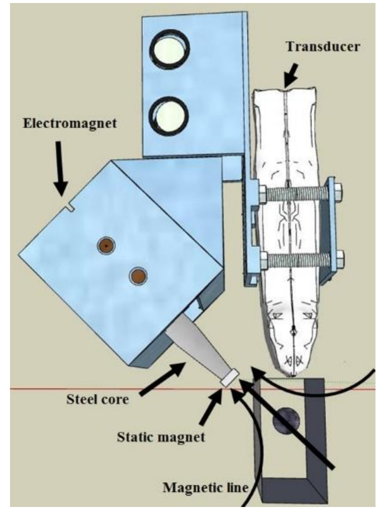

Fig. 2 Setup of the backward-mode MMUS with permanent magnet for premagnetization of SPIONs.

III. Experimental Results

To demonstrate the capability of the backward mode pulsed MMUS imaging with premagnetization idea, a set of tissue-mimicking phantom experiments was performed by embedding 50 mg/ml SPIONs (from Advanced Nano-Optics Lab, National Cheng Kung University) as contrast agents in gelatin phantoms. Because the concentration of the gelatin phantom material represented the tissue stiffness, the 3 g/L gelatin phantom could provide desired mechanical properties of soft tissues according to a formula in [3]. In addition, 0.5 % cellulose particles serving as ultrasound scatterers were added to the phantoms.

The magnetic pulse sequence was designed to be 100 Hz and 5 cycles, and each pulse duration was 10 ms. The ultrafast plane wave imaging was performed by a clinical ultrasound engine (Prodigy, S-Sharp, Taiwan).

The B-mode image of the SPIOs-embedded phantom is shown in Fig. 3(a). It is obvious that the SPIOs region is hard to be visualized from the phantom. Fig. 3(b) shows the displacement map at a specific time without premagnetization permanent magnet.

When the permanent magnet is placed at the front end of the electromagnet, larger SPIONs displacement can be obtained. Fig. 3(c) and Fig. 3(d) shows the displacement map at a specific time with different permanent magnets.

We choose Fig. 3(b) and Fig. 3(d) to represent our previous backward-mode MMUS and current backward-mode MMUS with pre-magnetization of SPIONs, respectively. The displacement profiles in Fig. 4 shows that the displacement increases up to two folds for the case with pre-magnetization of SPIONs. We repeatedly collect maximum displacements five times for the SPIONs in the same location and calculate the mean and standard deviation. The average maximum displacement of the previously proposed backward-mode

MMUS is 2.10 um, and the deviation is 0.07. On the other hand, the average maximum displacement of the backward-mode MMUS with pre-magnetization of SPIONs is 10.67 um, and the deviation is 0.12. The results tell that the MMUS SNR is improved by our new strategy.

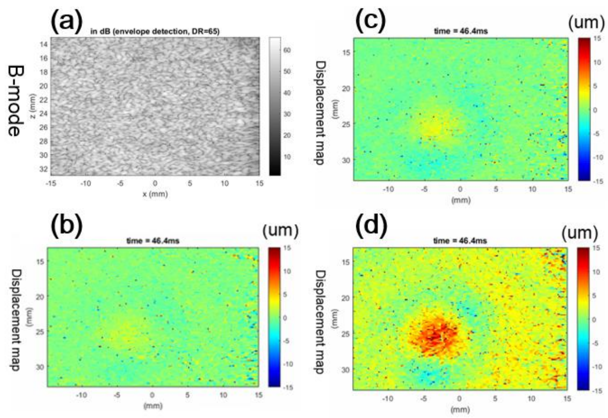

Fig. 3. (a) B-mode image for the phantom with embedded 50mg/ml SPIOs. (b) Displacement map without permanent magnet. (c) and (d) Displacement map with permanent magnet.

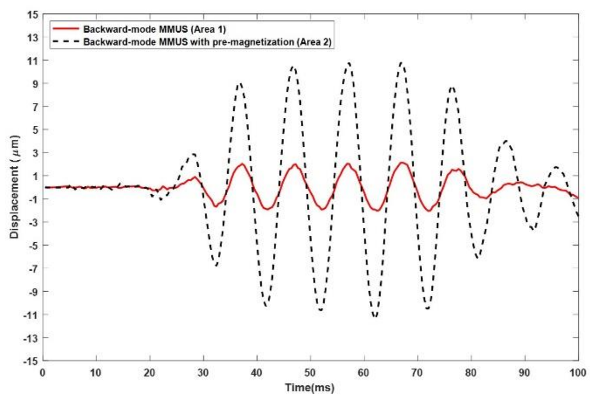

Fig. 4 Displacement profiles with and without pre-magnetization.

IV. Conclusions

Overall, it is demonstrated the effectiveness of the proposed strategy in the improvement of the backward mode MMUS. The results also implicitly indicate a new lightweight design of the MMUS probe consisting a static magnet and a relatively low strength electromagnet, which is more suitable for clinical applications.

Acknowledgments

This work is supported by the Ministry of Science and Technology, Taiwan（MOST 106-2221-E-007-033-MY3.

References

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