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Visualization of Magnetic Nanoparticles by Ultrasound Strain Imaging

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Summary:
In magnetic drug targeting, superparamagnetic nanoparticles are used as drug carriers. The local accumulation of these particles at the site of the tumor leads to a temporary change in the effective elastic tissue properties in this area. Therefore, mapping this change should allow visualization of the particle distribution. Ultrasound strain imaging is a method to map the local variation of elasticity. This method was tested using a polyvinyl alcohol ultrasound phantom with a magnetic nanoparticle inclusion. It was demonstrated, that this inclusion can be mapped in the proposed way.

Keywords: Ultrasound imaging, ultrasound elastography, magnetic nanoparticles, magnetic drug targeting

Introduction

The goal of modern chemotherapeutic treatment of cancer is dosing the drug in such a way that the tumor is treated efficiently, while the patient tolerates the dose and faces a minimum of side effects. However, these methods can cause damage to normal tissues or fail in eradicating the cancer completely. Magnetic drug targeting (MDT) using magnetic nanoparticles (MNP) as drug carriers has experimentally proven effective in the treatment of tumors for the direct and selective delivery of chemotherapeutic drugs to the tumor region [1]. Yet, real-time imaging of MNP distribution during the magnetically enhanced tumor treatment is still not fully realized. Ultrasound imaging would be a suitable tool for imaging MNP, but the particles' backscatter is too small for direct imaging. However, the accumulation of MNPs in the tumor area should lead to a temporal change in the mechanical properties of the particle-laden tissue. Mapping this change might allow for the detection of the MNPs. Therefore, ultrasound strain elastography was used in this work to map the MNP distribution. In addition, this method would allow performing MDT and MNP-imaging at the same time.

Ultrasound Strain Elastography

Ultrasound strain elastography based imaging allows for the qualitative assessment of tissue elasticity [2]. It provides a noninvasive method through mechanical stress to detect differences in tissue elasticity based on the changes in tissue displacement. Strain images are generated by using the ultrasound transducer to apply minimal pressure to the tissue. The subsequent tissue displacement is tracked between pairs of RF echo frames and the strain is calculated from the axial gradient of the displacement (see Figure 1).

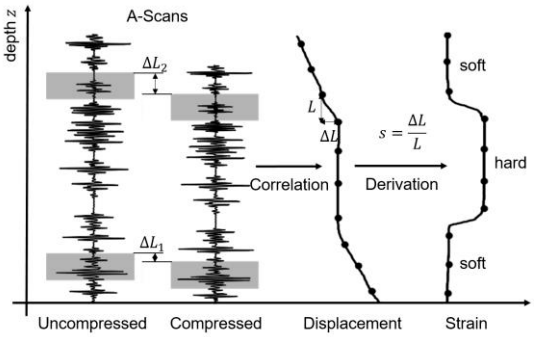

Fig. 1. Determination of local strain obtained from the uncompressed and compressed A-scan/RF-Data.

In the axial derivation

$$s = \frac{\Delta L}{L}, \qquad (1)$$

ΔL is the displacement between pre- and post-compression RF echo frames and L is the size of one frame. The frame size is adjusted according to the mechanical displacement of the transducer. It is four times larger than the induced displacement, to ensure that the displaced echo is

still within the frame. Now, the cross-correlation function of the two RF echo frames is computed:

$$\hat{R}_{xy}(m) = \begin{cases} \sum_{n=0}^{N-m-1} x_{n+m} y_n^*, & m \geq 0, \\ \hat{R}_{xy}(m), & m < 0. \end{cases} \quad (2)$$

N is the frame size and m the delay between the two RF-signals x_n, y_n. The displacement is then calculated from the delay m of the maximum correlation value:

$$\Delta L = \max_m \{\hat{R}_{xy}(m)\} \cdot z_S. \quad (3)$$

z_S is the sampling interval.

Experimental Setup

To investigate the imaging potential of the MNP with ultrasound strain elastography, ultrasound phantoms were created according to [3]. The material used here was polyvinyl alcohol (PVA). The PVA was filled in a mold with a centrally positioned cylindrical recess with a diameter of 20 mm. This opening was filled with PVA containing magnetic nanoparticles (SEON-Dex30) with an iron content of 15.84 mg/ml and a hydrodynamic diameter of 30.23 nm. Hardening of the PVA tissue phantoms was achieved by two overnight freeze-thaw cycles at -20° C.

Ultrasonic measurements were performed using the ultrasound research platform *Verasonics Vantage 64LE* and a linear array transducer (L11-5v, 128 elements, 7.6 MHz center frequency). The transducer was fixed in a mechanical shift device for precise compression. The ultrasound phantom was placed below the transducer. Ultrasound gel ensured acoustic coupling of the transducer and the phantom. Two sets of ultrasound data were measured. One before and one after compression was applied with the transducer. These sets of data were then processed offline. No magnetic field was applied during the measurements.

Results

Four different compression levels (0.1 mm, 0.5 mm, 1 mm and 2 mm) were tested to evaluate the robustness and effectiveness of the elastography method in terms of MNP imaging (Fig. 2). As shown, the correlation-based elastography method was highly dependent on the induced compression. With lower compression (0.1 mm and 0.5 mm), the MNP-inclusion was clearly distinguishable from the surrounding phantom area, with the 0.5 mm compression giving the best results. The area of the stiffest region (yellow) matched the inclusion (dashed circle). Particle-laden tissue is stiffer due to the iron content of the MNPs. At higher degrees of compression, the method failed to find the correct displacement and corresponding strain. This is a typical problem of the correlation method [2].

Conclusion

In this work, imaging of a magnetic nanoparticle inclusion within a PVA ultrasound phantom was presented. Based on a temporal ultrasound strain elastography algorithm the MNP inclusion was mapped. Ultrasound A-Scans were compared frame-wise before and after compression. The displacement between two frames was then computed and used as a measure of strain. This method can help to map the magnetic nanoparticle distribution in context of magnetic drug targeting. Future goals are to enhance the resolution and sensitivity using more sophisticated displacement estimation methods. Additionally, this method will also be tested during magnetic field exposition and under flow conditions.

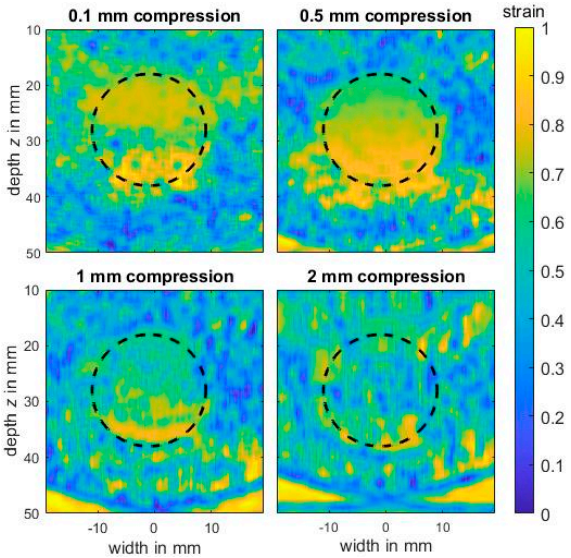

Fig. 2. Computed ultrasound strain images of PVA-phantoms with magnetic nanoparticle inclusion (black dashed circle) at different degrees of compression.

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