

PULSED MAGNETO-MOTIVE ULTRASOUND IMAGING

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Motivation/Background In diagnostic ultrasound imaging, microbubbles are used as ultrasound contrast agents to enhance image quality. Furthermore, microbubbles are studied for targeted imaging of inflammation, angiogenesis, and also as adjunct microdevices for cancer treatment, enhanced targeted drug delivery and gene therapy. However, the relatively large size of microbubbles limits the application of ultrasound in molecular and cellular imaging. Recently, we developed a diagnostic ultrasound imaging technique – magneto-motive ultrasound (MM-US) – and demonstrated the ability of MM-US imaging to detect magnetic nanoparticles in iron-laden tissue samples and macrophage cells loaded with nanoparticles. The internal tissue motion was induced by the externally applied harmonic magnetic field. In the current study, we investigate the utility of pulsed magneto-motive ultrasound to noninvasively detect nanocomposites in tissue-mimicking phantoms and phantoms containing living cells. Compared to MM-US imaging using continuous wave excitation, pulsed MM-US imaging has several advantages including less-severe thermal management constrains and increased magnetic flux density thus allowing the imaging of deeper tissue structures.

Statement of the contribution/Methods Initial experiments were performed using a tissue mimicking phantom. In addition, to demonstrate the capability of pulsed MM-US system to image cellular structures, we performed experiments using J774A.1 macrophage cells characterized by non-specific uptake of nanoparticles. Pulsed MM-US system consisted of a solenoid with an iron core and a magnetic field generator capable of producing 20 ms pulses. We used custom-built monocrystalline iron oxide nanoparticles (20 nm mean diameter, 79 emu/g magnetization) stabilized by a dextran coating. The magnetic force acting on nanoparticles was induced by electric pulses applied to a solenoid. The magnetic field strength measured near the tip of the iron core was 3.2 Tesla. To image motion resulting from the application of the pulsed magnetic field, ultrasound images of the tissue were recorded using a linear transducer array operating at 5 MHz. The induced tissue motion was detected using various quantitative and qualitative techniques including Doppler ultrasound, color/power Doppler, and a block-matching speckle tracking method.

Results/discussion Internal displacement in tissue phantoms in response to an externally applied pulsed magnetic field consists of two dominant types of motion: transient motion pronounced at the beginning of the magnetic pulse, and gradually diminishing residual motion of the tissue due to elastic response of the tissue sample. Similar results were observed in both tissue-mimicking phantoms and samples containing passively targeted macrophage cells. Figure 1 demonstrates movement in a phantom exposed to a pulsed magnetic field. Internal movement of the sample with a relatively low concentration of magnetic nanoparticles was detectable using the array-based ultrasound imaging system. Movement was not observed in both the control phantom and normal cells. Since nanoparticles can be conjugated to antibodies or other adhesion ligands, this study suggests that bioconjugated nanoparticles can be used as imaging contrast agents for tissue specific and sensitive site-targeting. In conclusion, the results of this study demonstrate the potential of MM-US for molecular imaging.

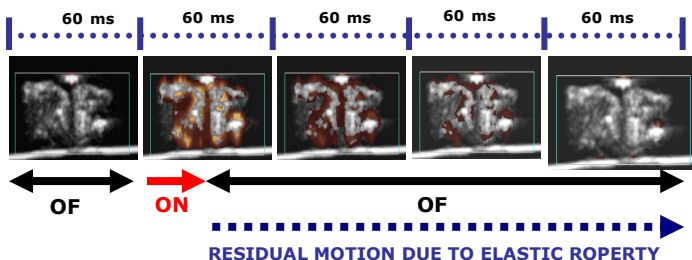


Fig. 1 Power Doppler images of a phantom exposed to pulsed magnetic field (pulse duration = 20 ms, peak magnetic strength in the surface of iron core = 3.2 Tesla)