In vivo and in vitro mapping of the radio frequency magnetic field generated by microsized resonators in a 3T clinical MRI scanner

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Introduction: Magnetic resonance microscopy is being used to image track specific cells that have been labeled with a variety of contrast agents. A common method of labeling makes use of iron-based oxide particles. The large magnetic susceptibility of these agents can lead to "blooming effect" (1) an exaggeration of the region occupied by these particles. In this work we introduce the concept of microresonator devices (MRD) - solid-state devices that generate an electromagnetic field at radiofrequencies either not present in the human body or exactly equal to the frequency of protons. Our long-term goal is to detect a single device, in a single cell, anywhere in a living subject. In this study, we demonstrate such devices can be used for *in vivo* and *in vitro* imaging using a clinical MRI scanner.

Methods: Microelectromechanical systems (MEMS) technology was used to create plated inductors combined with Ta oxide thin film capacitors designed to resonate at 127.7 MHz. To compensate for process variations, an array of devices 15 µm thick and either 300 µm, 500 µm, or 1000 µm in diameter, with parametrically varying capacitor areas, was manufactured and sealed with a water-resistant coating. We determined their RF field using an algorithm (2) that considers two gradient-echo scans at flip angles of 30 degrees and 60 degrees, respectively. All measurements were performed in a GE 3T MRI scanner. To obtain the frequency response of the MRDs, we developed and used an ultra-high-frequency (UHF) scanning microscopy setup (3).

Results: All types of MRDs (300, 500 and 1000 microns) designed and manufactured were detected in an aqueous medium supplemented with 150 mM NaCl. Figure 1A shows a spin echo image (TR=367 ms, TE=14 ms) for an area with 500 microns resonators. A good concordance between MRI and UHF microscopy (Figure 1B) can be seen. The further analysis of UHF images demonstrates that the difference in MRI effects observed between the same types of MRD (500 microns in Figure 1A) is a result of the fact that all of the MRDs are not tuned at 127.7 MHz. Computed and experimentally determined results from the frequency response for an MRD are shown in Figure 1C. The numerical response was computed based on analytical equations. Using these techniques a quality factor of 7.2 (in good agreement with analytical and experimental models, as shown in Figure 1C) was determined for such a device. MRDs were then subcutaneously implanted in the mouse flank and imaged using MRI in a clinical 3T scanner (Figure 2). Direct B1 mapping confirmed the presence of the device and allowed us to evaluate the magnitude of the B1 field generated by MRDs. The maximum value determined from MRD from Figure 2A is 8.62 10^{-7} Tesla.

Discussion: We have demonstrated that microsized resonators can be imaged *in vivo* and *in vitro* using a clinical 3T MRI in about 10 minutes. Future studies are focused on miniaturizing these devices to the cellular scale, generating contrast at RF frequencies not present in the human body, and probing the limits of the MRI sensitivities of these MRDs.

References: **(1)** Oweida el al. *Molecular Imaging* **3** 85(2004); **(2)** E.K. Insko and L. Bolinger, *Journal of magnetic resonance*, series A,**103,** 82(1993); **(3)** R. Ciocan and N. Ida *IEEE Transactions on magnetics*, **40**, 651 (2004).

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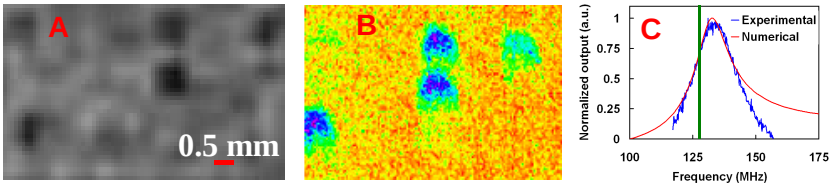

Figure 1 *In vitro* results obtained on MRDs: A) MRI-spin echo; B) scanning UHF microscopy at 127.7 MHz; C) frequency response (experimental and numerical) for an individual MRD used in *in vivo* experiments.

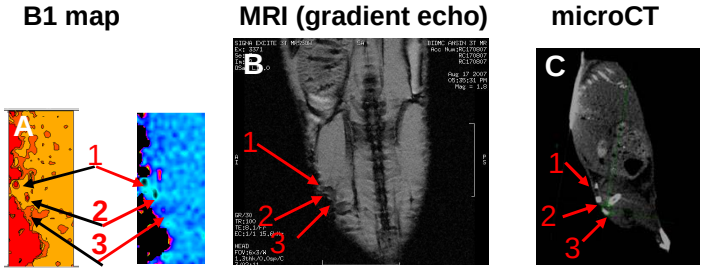

Figure 2 *In vivo* results obtained two active (1, 2) and one non-active (3) MRDs implanted subcutaneously in the mouse flank: A) B1 map (contour and pseudocolor representations); B) MRI image (gradient echo); C) microCT image.