Ultrashort T2* Relaxometry in Iron Labeled Tumors

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Introduction

Superparamagnetic iron oxide (SPIO) nanoparticles are widely used to influence the T1, T2 and T2* relaxation times of labeled cells and tissues. The T2* relaxation time is the most sensitive parameter to detect SPIO-labeled cells and T2* relaxometry is expected to play a major role in quantification and monitoring of labeled stem cells in cellular therapies. T2* relaxometry is usually performed by multiple gradient echo imaging. However, in tissues containing highly concentrated iron labeled cells, T2* can be below 2 milliseconds and therefore the signal decay is too rapid for regular gradient echo times. Taking advantage of the relative long T2 decay of cell bounded SPIO [1], we have developed a new method to measure fast decaying T2* relaxation using a series of spin echo images. In this study, we investigated the in vivo quantification of short T2* in rats with iron labeled tumors.

Methods

Sequence Development: Measurement of ultrashort T2* was achieved by acquiring a series of spin echo images as shown in Figure 1. The first echo was obtained as a regular spin echo image. The next images were acquired by shifting the readout towards the T2* decay by steps below 1 ms. This allows sampling of the T2* decay curve from the spin-echo signal. *In vivo Experiment:* C8161 melanoma cells were labeled with Feridex-protamine sulfate (FEPro) complexes using procedures previously described [2]. 2×10^6 FEPro labeled or unlabeled (control) melanoma cells were implanted subcutaneously bilaterally into the flanks of 5 nude rats. MRI was performed approximately two weeks after the inoculation of tumor cells on a 3T Intera whole-body scanner (Philips Medical System, Best, The Netherlands) using a dedicated 7 cm rat solenoid rf-coil (Philips Research Laboratories, Hamburg, Germany). Regular T2* map was acquired with multiple gradient echo sequence (MGES) [TR/TE = 1540/16 ms, 13 echoes, 256×256 matrix, 17 slices, Slice-thickness = 1.0 mm, FOV = 80 mm, NEX = 4]. To measure the short T2*, five sets of spin echo images were obtained with the readout echo shifted 0 ms, 0.4 ms, 0.8 ms, 1.2 ms and 2.3 ms respectively, with the following parameters: TR/TE = 1000/6.4, 144 × 144 matrix, 17 slices, Slice-thickness=1.5 mm, FOV = 80 mm, NEX = 4. *Data analysis:* Data analysis was performed using an in-house IDL software tool. T2* maps were derived using mono-exponential fitting. Both datasets (i.e. regular T2* map and the short T2* map) were combined and displayed as T2* map.

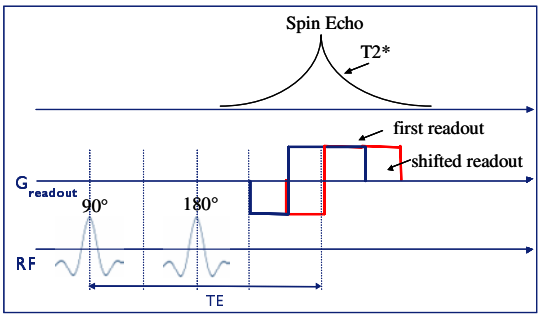

Figure 1. Sequence diagram of ultrashort T2* measurement.

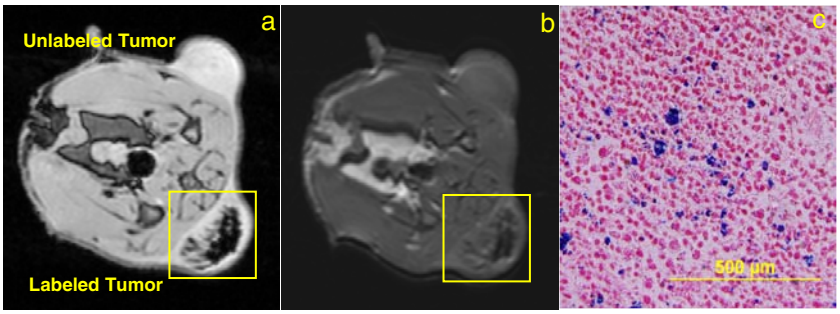

Figure 2. a. Axial gradient echo image of a tumor rat. b. Axial spin echo image with an echo shift of 0.8 ms. c. Plussian blue stained tumor slice with highly concentrated iron labeled cells.

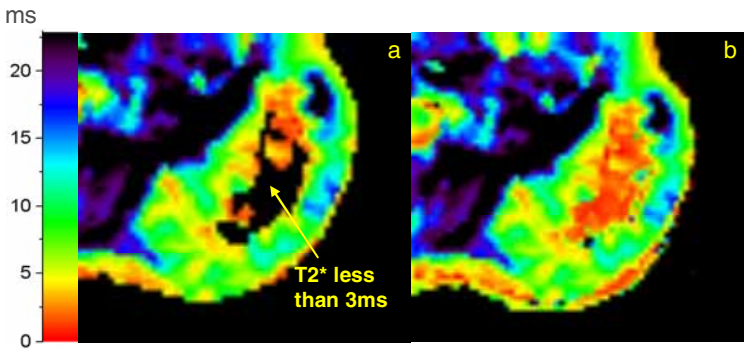

Figure 3. a. Regular T2* map masked by a signal threshold to remove noise. The signal void in the center of the tumor corresponds to T2* less than 3ms where iron labeled cells were highly concentrated. b. Ultrashort T2* map overlaid on regular T2* map illustrates the nice distribution of the iron labeled cells.

Results

Ultrashot T2* relaxometry maps and MGES conventional T2* maps were obtained in 4 rats. Figure 2a shows an axial gradient echo image of flank tumors in a rat. The signal void in the labeled tumor was induced by highly concentrated iron labeled cells as illustrated in Figure 2c. However, the spin echo image of the same tumor (Figure 2b) suffers less signal decay given the relatively long T2 relaxation time of cell bounded SPIO. The T2* map measured using MGES (Figure 3a) illustrates areas of high T2* values on the tumor boarder indicative of serial dilution of the FEPro labeling as the tumor grows. The MGES T2* map failed to detect any signal due to the fast T2* decay induced by heavily concentrated labeled cells in the center of the tumor. As a comparison, the ultrashort T2* maps (Figure 3b) demonstrate T2* values in the center of the tumor of approximately $\leq$1 ms, which corresponds to areas of highly concentrated iron labeled cells in Figure 2a.

Conclusion

A new approach was proposed for measurement of ultrashort T2* relaxation times in cells and tissues. In vivo MR experiments demonstrate that this method can measure ultrashort T2* values down to 1 ms or less in highly concentrated iron labeled cells. Combined with the conventional T2* map, the new technique is expected to improve the in vivo quantification and monitoring of tissues containing heavily iron labeled cells.

Reference

1. Weissleder et al. JMRI 1997;7:258-263.
2. Arbab et al. Blood 2004;104(4):1217-1223.