Quantitative Tracking of Magnetically Labeled Breast Cancer Cells in Rat Brain with A Fast T2 Mapping Technique

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INTRODUCTION

The T2* relaxation time is the most sensitive parameter to detect SPIO labeled cells [1]. Since intracellular SPIOs have much longer T2 compared to free SPIOs, measuring both T2 and T2* relaxation times will reduce the interference from free SPIOs and lead to more accurate quantification of SPIO labeled cells. Previously, we have monitored the development of metastatic brain tumors by MDA-MB-231BR-Luc human breast cancer cells in the nude rats by T2* relaxometry [2]. The T2* histogram of the rat brain demonstrated a significant shift in T2* values to lower than baseline after intracardiac (IC) injection of SPIO labeled breast cancer cells. In the following weeks, a continuous increase in T2* values toward the baseline was observed. Therefore, the purpose of this study was to investigate the feasibility of applying T2 mapping to confirm that the effect measured with T2* was from SPIO labeled cells and not an artifact induced by free SPIOs.

Regular T2 mapping using turbo spin echo approach is based on the acquisition of a number of echoes with a given echo spacing. This multi-echo scan has to be repeated with different phase-encoding steps, until the entire k-space has been covered, resulting in long acquisition time. A fast T2 mapping was proposed using undersampling and k-t reconstruction [3]. Validation of the reconstruction with human brain images demonstrates that T2 relaxation times can be accurately estimated with a reduction in the number of phase–encoding steps. In this paper, T2 maps of the rat brain with IC injection of SPIO labeled breast cancer cells were acquired with the fast T2 mapping technique and the results were compared with the regular T2 mapping to investigate this new technique for in vivo applications.

METHODS

Fast T2 Mapping: The proposed k-space sampling pattern is illustrated in Figure 1. For an undersampling factor of U, only one k-space line is acquired every U phase-encoding steps. The position of the measured readout in k-space is shifted from one echo to the next. For calibration, a number of consecutive k-space training lines are acquired without reduction, preferably in the center of k-space. The proposed method first estimates the missing k-space data. Each missing sample is reconstructed on the basis of a linear combination of its neighbors in the k-t space, as illustrated in Figure 1 for a 3×3×3 neighboring matrix. The T2 map is then calculated from the reconstructed data.

Animal Model: 1×10^6 Feridex-Protamine sulfate (FePro) labeled MDA-MB-231BR-Luc human breast cancer cells were injected into 6-7 weeks old nude rats (n=6). Imaging was performed 1 day before the IC injection as baseline and 1 day after the injection.

MRI: MRI scans were performed on a 3T clinical scanner (Achieva, Philips Medical Systems, The Netherlands) with a 4 cm receive-only RF coil (Philips Research Laboratories, Hamburg, Germany). Regular T2 maps were acquired with a turbo spin echo sequence with TR = 800 ms, FOV = 64 mm × 64 mm, slice thickness = 0.7 mm, 24 echoes 10 ms apart, data matrix = 256 × 256, NEX = 6. T2 maps with undersampling factors of U = 2 and U= 4 were acquired with 32 training lines. T2 of each rat was calculated as the average over a region of interest that covered the brain.

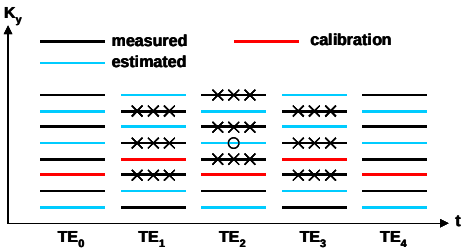

Figure 1. Undersampling pattern used for fast T2 measurement (U = 2). The crosses represent the samples involved in the reconstruction of the missing sample (circle).

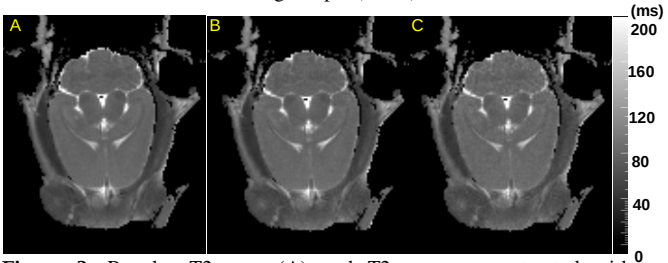

Figure 2. Regular T2 map (A) and T2 maps reconstructed with undersampling factors of U = 2 (B) and U = 4 (C).

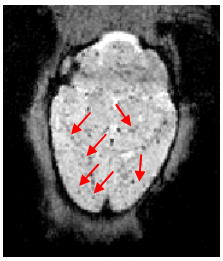

Figure 3. T2*W image of a rat brain after IC injection of SPIO labeled breast cancer cells. Red arrows indicate labeled cells.

RESULTS

Figure 2 illustrates a regular T2 map and T2 maps with undersampling factors of U = 2 and U = 4. The scan time of the T2 maps was reduced from 21 minutes to 12 minutes and 7 minutes, respectively. The T2 maps acquired with undersampling agreed very well with the regular T2 map, with slight noise amplification due to the undersampled acquisition. One day after IC injection, SPIO labeled breast cancer cells were observed in the rat brain as shown in Figure 3. However, the brain T2 was only slightly reduced by 2% compared to the baseline scans as shown in Figure 4A: 81.2 ± 1.56 ms vs. 83.2 ± 0.62 ms for regular T2 map ($p<0.05$), 81.4 ± 1.67 ms vs. 83.3 ± 0.80 ms for T2 map with U = 2 ($p<0.05$), 81.9 ± 1.38 ms vs. 83.3 ± 0.89 ms for T2 map with U = 4 ($p<0.05$). T2 maps with U = 2 and U = 4 both demonstrated very good linear correlations with the regular T2 map (Figure 4B and 4C).

DISCUSSION

Reduction of brain T2 after IC injection of SPIO labeled breast cancer cells was characterized as only 2% with both regular T2 mapping and the fast T2 mapping with undersampling factors of U = 2 and U = 4. Since intracellular SPIOs have much longer T2 compared to free SPIOs, this mild reduction in T2 suggests that the significant alteration in brain T2* we observed previously [2] was mainly induced by SPIOs in labeled cells, not free SPIOs. The fast T2 mapping technique with undersampling factors of U = 2 and U = 4 exhibited similar sensitivities as the regular technique. The results demonstrate that the proposed technique can provide an effective approach for accelerated T2 quantification, especially for experiment with single channel coil when parallel imaging is not applicable.

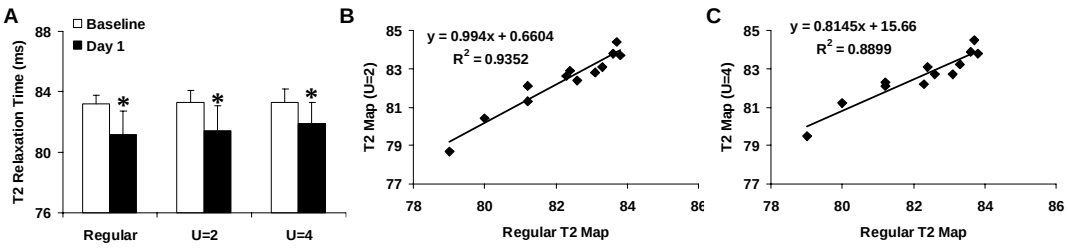

Figure 4. A. T2 of rat brain measured 1 day after IC injection was reduced by 2% compared to the baseline scans (* $p<0.05$ vs. baseline). **B.** T2 maps with U = 2 and regular T2 maps demonstrated an excellent linear correlation with R= 0.97. **C.** T2 maps with U = 4 and regular T2 maps demonstrated a very good linear correlation with R=0.94.

REFERENCE:

1. Bowen C et al. Mag Reson Med 2002;48:52-61; 2.Song HT et al. ISMRM 2007, #879; 3. Senegas J and Dahnke H. ISMRM 2007, #1785.