Quantification of different superparamagnetic iron oxide (SPIO) concentrations in diffuse medium using 4.7T Magnetic Resonance Imaging

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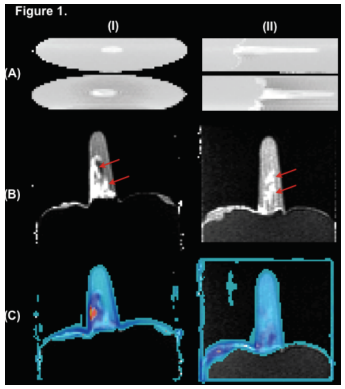
Purpose

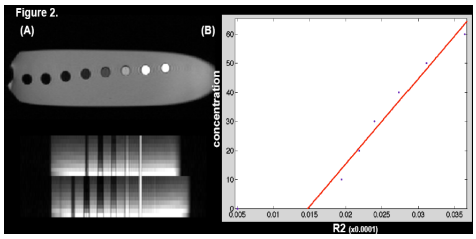
Localization and quantification of the diffuse etiology of infection is a challenging issue to elucidate in vivo in various infectious disease studies. For the proper monitoring of infectious diseases, cellular level changes originating from the immune response to the infection need to be carefully characterized in both temporal and spatial domains. When using magnetic resonance imaging (MRI) techniques for this issue, superparamagnetic iron oxide (SPIO) nanoparticles are by far the most widely used contrast agents for the detection of cellular level changes in-vivo [1]. SPIO nanoparticles in nano-molar to micro-molar concentrations can alter the relaxation rates of many nearby tissue water protons thereby making them conspicuous on post contrast enhanced MRI [2]. However, quantifying in-vivo of SPIO enhanced MRI images in a diffusely variant tissue medium have not been adequately addressed: most studies qualitatively point out the regions with high intensity contrasts and examine signal properties by averaging signals. Here, we designed a multi-compartment agarose gel phantom with 2 different SPIO concentrations to simulate the effects of different diffuse levels on SPIO enhanced MRI. Quantitative post processing techniques were then applied for validations of the effects.

Methods



-***Preparation of agarose phantom***: two different concentration levels (30nM, 60nM) of the SPIO were prepared in 1.5% agarose gel.

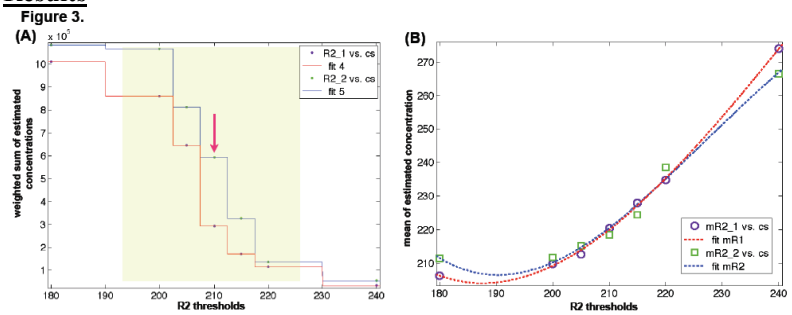
-***MR imaging:*** 3D Imaging was performed at 4.7T Bruker biospin scanner. 3D MSME imaging was performed by using 15 cm-diameter small animal body imaging coil: TR = 6188.175 ms, TE = 12 24 36 48 60 72 84 96 108 120 ms, flip angle = 180, FOV = 7.49x13.59, matrix size = 256x256x350, slice thickness = 2mm, number of averages = 1. R2 map was than calculated for a local iron content estimation (Figure 1A,B-high concentration in upper part and low concentration in lower part). We also calculated gradient magnitude map to check the spatial distributional patterns of R2 map.



-***Estimation of the SPIO-R2 relationship***: To determine the relationship between R2 value and actual nanoparticle concentrations within a voxel, we constructed a phantom containing eppendorf tubes with different SPIO concentrations (figure 2A). The SPIO densities used were 60, 50, 40, 30, 20, and 10 nM. Water-only content was also placed in the phantom. All capillaries were embedded in agarose, and imaging was performed with same parameters describe above. Finally, linear regression function was estimated in R2 vs. SPIO concentration values (figure 2B/estimated function Estimated_Concentration=R2*0.2934- 43.23).

-***Quantification of agarose phantom:*** We applied multiple thresholds ranging from 180 to 240. Based on the linear regression function described above, the R2 value in each voxel was converted to SPIO concentration values. To check distributional signal pattern differences between 2 different concentrations, we calculated maximum value, mean value and total sum of SPIO concentration values above each threshold.

Results



Total sum of estimated SPIO concentrations showed significant differences (>36.43%) in the threshold level 180 to 215. In the range, pattern shifts through x-axis (R2 thresholds) was shown between 2 phantoms. The maximum difference between 2 different concentrations was shown in threshold 210 (>49.32%). Thresholded R2 map by 210 is shown in Figure 1B, and its image gradient map is in 1C). However, the spatial distributional patterns were difficult to detect differences between 2 phantoms by visual inspection. Mean value mapping showed less discrimination power than summation approach as shown in figure 3B. Both phantoms showed same maximum concentration value (300 nM).

Discussions

Most SPIO enhanced in-vivo MRI imaging studies have been focused on both imaging sequence and contrast source selections. Although the importance of those issues still can not be disregarded, post reconstruction and analysis can also be a critical issue for quantification of diffuse changes from SPIO enhanced MRI images. A more precise quantification model, which accounts for possible local imaging biases as well as nanoparticle-cell relationships, should be considered in further studies.

Reference

[1] Iron oxide MR contrast agents for molecular and cellular imaging. *NMR Biomed.* 2004;17:484–99.

[2] Detection and Quantification of Magnetically Labeled Cells by Cellular MRI. Eur J Radiol. 2009 May; 70(2): 258–264.