Measurement of the Iron Oxide and Gadolinium Based Contrast Agent Relaxation Properties in the Presence of the Saline and Glucose Molecules during Low-Field MRI

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Abstract. *The contrast agents are usually used in clinical practice for the enhanced contrast imaging of the human tissue. They are iron oxides or gadolinium based nanoparticles in a carrier fluid. In a previous study we have found, that the elevated levels of the human metabolites can change the relaxation properties of the magnetite nanoparticles during 4.7 T MRI. Therefore the aim of this paper is to find out if the different concentration levels of the saline and glucose molecules, which are typical for the several pathological processes, can change the relaxation properties of these contrast agents during low-field MRI (0.178). We have found that physiological concentration of the saline and glucose molecules have little, but not negligible influence to the signal intensity for different concentration of the contrast agent (maximum ≈ 30% in comparison with water). The different concentration of the saline and glucose molecules alters the signal intensity for the selected pulse sequence and contrast agent concentration in a similar way, with maximum intensity change up to 17%. Such changes are hardly visible to the naked eye in low-field MRI, however they can have influence to the post-processed data analysis, e.g. in relaxation time comparison. Definitely, these findings should be verified in standard high-field MRI tomographs 1.5 and 3 T, before final conclusions.*

Keywords: MRI, Contrast Agents, Contrast Changes, NaCl and Glucose Molecules

1. Introduction

Currently, the Magnetic Resonance Imaging (MRI) is a technique routinely used in clinical practice. MRI provides an anatomical picture of tissue based on different intrinsic contrast. Contrast in MRI arises from the difference in signal intensity, which can be modified by intrinsic parameters (spin density ρ, relaxation times T_1 and T_2) and by the pulse sequence parameters (repetition time TR, echo time TE). Modification of TR and TE results in T_1, T_2 or proton density weighted imaging. For contrast enhancement in clinical practice the paramagnetic contrast agents (CA) are often used. The signal enhancement is caused by coupling of proton magnetic moments with larger magnetic moments of paramagnetic nanoparticles [1]. The contrast agents can be either iron oxides or gadolinium based nanoparticles. In this study we focused on MRI contrast properties of both types of contrast agents in the presence of the saline and glucose molecules. NaCl and glucose are the essential molecules of the human body. The modified concentration levels of these molecules are usually accompanied with different pathological processes. The aim of the study, due to our previous results [2], is to find out, if the altered concentration of the saline and glucose molecules can have influence to the MRI contrast in the presence of clinical contrast agents (iron oxides and gadolinium based).

2. Subject and Methods

The MRI experiments were performed at the Institute of Measurement Science SAS Bratislava, using the ESAOTE E-Scan XQ 0.178 T system. For image data processing and anlysis we used the following software tools: Marevisi, developed by NRC - Institute for Biodiagnostic, Winniped, Canada and Matlab - Mathworks Inc., Natic, USA. Firstly, we have investigated eight different concentrations of contrast agent in various pools - distilled water, NaCl, glucose and NaCl + glucose together. Molecules were in physiological concentration: NaCl - 9 g/l and glucose - 1 g/l. Secondly, the one concentration of contrast agent was choosen (similar to in-vivo application, Resovist - iron oxide nanoparticles concentration was 103.3 μg/ml and MultiHance - gadolinium concentration was 1.3 mg/ml) and investigated with different concentrations of saline and glucose molecules: NaCl - 0, 4.5, 9 and 13.5 g/l, glucose - 0, 0.5, 1 amd 1.5 g/l. As an iron oxide contrast agent model was choosen the Resovist (Bayer Schering Pharma AG), which consists of carboxydextran coated iron oxide nanoparticles and as a gadolinium one the MultiHance (ALTANA Pharma AG), which consists of gadobenate dimeglumine molecules. Images were acquired using both spin echo (SE) and gradient echo (GE) sequences in T_1 and T_2 weighted modes. For each contrast agent the most appropriate pule sequence and parameters for contrast imaging were selected.

3. Results

We have tried to identify the signal changes induced by the contrast agent relaxation time modification in system with saline and glucose molecules. Several types of the pulse sequences have been investigated to find out the most appropriate parameters. Both for the iron oxide and gadolinium based contrast agents, the least suitable pulse sequence for the enhanced contrast imaging were GE sequences. Finally, we selected T_2 weighted Turbo Spin Echo sequence (TR = 3000 ms and TE = 120 ms) for the Resovist contrast imaging and T_1 weighted Spin Echo sequence (TR = 600 ms and TE = 26 ms) for the MultiHance contrast imaging. In Fig. 1a and Fig. 2a are shown the contrast changes for different Resovist and MultiHance concentrations in distilled water with physiological concentration of saline and glucose. As is shown in Fig. 1b and 2b, the saline and glucose molecules in physiological concentration have little, but not negligible effect to the decay (for the Resovist) or the increase (for the MultiHance) of the signal intensity. The maximum change for the iron oxide sample is ≈ 30%, while for the gadolinium sample it is only ≈ 15% in comparison with water.

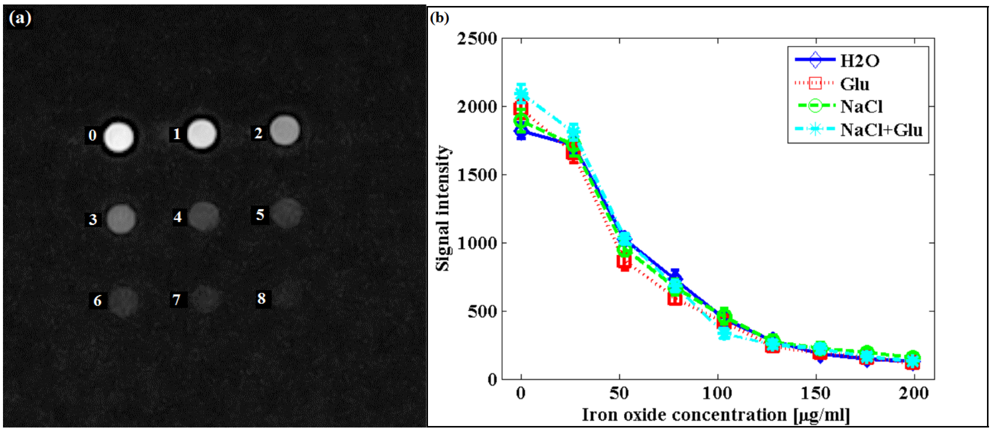

Fig. 1. (a) Different concentration of the Resovist in distilled water and physiological concentration of saline and glucose molecules ([0] - 0 μg/ml, [1] - 26.6 μg/ml, [2] - 52.7 μg/ml, [3] - 78.2 μg/ml, [4] - 103.3 μg/ml, [5] - 127.9 μg/ml, [6] - 152.1 μg/ml, [7] - 175.8 μg/ml, [8] - 199 μg/ml).
(b) Plot of the signal intensity in dependence on the iron oxide concentration in various pools. Used pulse sequence: Turbo Spin Echo T_2, TR = 3000 ms, TE = 120 ms.

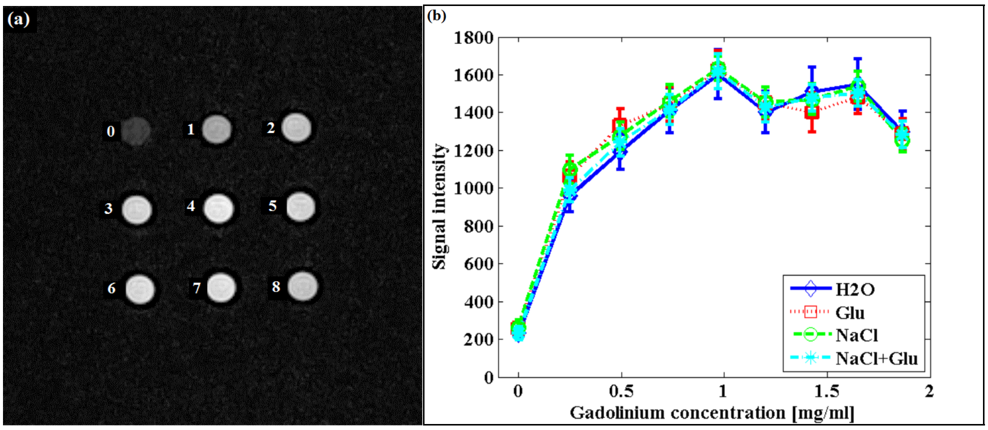

Fig. 2. (a) Different concentration of the MultiHance in distilled water and physiological concentration of saline and glucose molecules ([0] - 0 μg/ml, [1] - 0.249 mg/ml, [2] - 0.494 mg/ml, [3] - 0.734 mg/ml, [4] - 0.969 mg/ml, [5] - 1.2 mg/ml, [6] - 1.426 mg/ml, [7] - 1.648 mg/ml, [8] - 1.866 mg/ml).
(b) Plot of the signal intensity in dependence on the gadolinium concentration in various pools. Used pulse sequence: Spin Echo T_1, TR = 600, TE = 26.

Similar signal intensity changes we have found for the samples with different concentration of the saline and glucose molecules. For the selected pulse sequence and contrast agent concentration it is change up to 17% for the Resovist and 16% for the MultiHance. The data for the iron oxide concentration 103.3 μg/ml and the gadolinium concentration 1.3 mg/ml for the selected pulse sequence are shown in Fig. 3. In the Table 1 is shown increase or decrease of the signal intensity for the saline and glucose samples in comparison with contrast agent in distilled water. The increase of the signal intensity we observed only in Resovist samples with the highest concentration of the NaCl molecules and the lowest concentration of the glucose molecules. In all other samples we observed the decrease of the signal intensity in comparison with distilled water. The range of the changes for both CA is hardly visible to the naked eye, during the low-field MRI, in comparison to the intensity changes influenced by the different CA concentration (≈ 110% for the Resovist and ≈ 280% for the MultiHance, Fig. 1a, 2a).

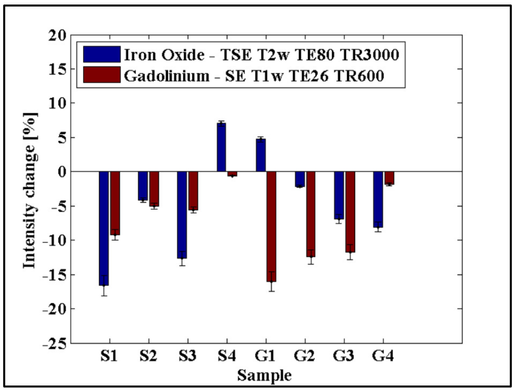

Fig. 3. Contrast agents relative signal intensity (compared to distilled water) for the selected pulse sequences in dependence on the different concentration of the NaCl and glucose molecules. Samples: S1 - 4.5 g/l NaCl, S2 - 9 g/l NaCl, S3 - 13.5 g/l NaCl, S4 - 18 g/l NaCl, G1 - 0.5 g/l glucose, G2 - 1 g/l glucose, G3 - 1.5 g/l glucose, G4 - 2 g/l glucose.

Table 1. Signal intensity increase (↑) or decrease (↓) in % for the saline and glucose samples in comparison with contrast agent (Resovist and MultiHance) in distilled water. Samples: S1 - 4.5 g/l NaCl, S2 - 9 g/l NaCl, S3 - 13.5 g/l NaCl, S4 - 18 g/l NaCl, G1 - 0.5 g/l glucose, G2 - 1 g/l glucose, G3 - 1.5 g/l glucose, G4 - 2 g/l glucose.

CA / SAMPLE	S1	S2	S3	S4	G1	G2	G3	G4
Resovist	↓(16.6)	↓(4.1)	↓(12.7)	↑(7.0)	↑(4.7)	↓(2.1)	↓(6.9)	↓(8.1)
MultiHance	↓(9.2)	↓(5.0)	↓(5.6)	↓(0.6)	↓(16.1)	↓(12.4)	↓(11.8)	↓(1.8)

4. Discussion

Several types of the pulse sequences have been investigate to find out the most appropriate parameters for the Resovist and MultiHance enhanced contrast imaging. The least suitable pulse sequences both for iron oxide and gadolinium particles imaging were GE sequences. Probably it is caused by tiny magnetic field inhomogeneities from the paramagnetic nanoparticles in Resovist and MultiHance, to which the GE sequences are very sensitive. As the most appropriate sequence for the Resovist imaging we found out the T_2 weighted Turbo Spin Echo sequence with TR = 3000 ms and TE = 120 ms. For the MultiHance imaging it is the Spin Echo sequence with TR = 600 ms and TE =120 ms. Physiological concentration of the saline and glucose molecules had little but not negligible influence to the signal intensity in dependence on the contrast agent concentration (Fig. 1b, 2b). Similar situation we have found for the samples with different concentration of the saline and glucose molecules. For the selected pulse sequence and contrast agent concentration the change is up to 17% for the Resovist and 16% for the MultiHance. Although, the changes are not very dramatic and are hardly visible to the naked eye during the low-field MRI, they can have influence to the specific data analysis (e.g. relaxation time calculation) and alter the conclusions for the processes associated with the altered levels of the saline and glucose molecules. These findings are in agreement with our previous results with magnetite nanoparticles and human body metabolites during 4.7 T MRI, although in that case the changes were significantly higher [2]. Therefore, before the final conclusions, it is necessary to verify these results in standard high-field MRI tomographs 1.5 and 3 T.

5. Conclusions

We have found out that various concentrations of the saline and glucose molecules have the influence (in the specific pulse sequences) to the signal intensity during low-field MRI with iron oxide and gadolinium contrast agents. The changes are up to 17% and although they are hardly visible to the naked eye, they can have influence to the post-processed data analysis of the processes associated with the altered levels of the NaCl and glucose molecules. Also we have not found out very significant influence (30%) of the saline and glucose molecules in physiological concentration to the signal intensity of the samples with the different concentration of the both investigated contrast agents. However, these findings should be verified in standard clinical MRI tomographs (1.5 and 3 T) before final clinical conclusions.

Acknowledgements

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