Magnetic Resonance Imaging of PEG Magnetite Nanoparticles with and without BSA Protein

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Abstract. *Aim of the study was to detect whether there is a observation change in MRI contras of magnetite nanoparticles stabilized with PEG, after BSA protein binding on the surface of particles. The reason is applicability of this feature in clinical practice, for molecular imaging of specific substances. Contrast agent can bind to this specific substance (e.g. marker of disease) and the change of MRI contrast will indicate the presence of marker.*

Keywords: MRI, Magnetic Nanoparticles, BSA Protein, Contrast Change

1. Introduction

Magnetic nanoparticles in combination with some proteins, like bovine serum albumin (BSA) or human serum albumin (HAS), have wide range of applications such as drug delivery systems, or as contrast agents for MRI [1-3]. Proteins play role also as biomarkers of various diseases (e.g. inflammation, cancer), and their changes in concentration levels are associated with various pathological processes. Magnetic nanoparticles, as a consequence of proton spins coupling with larger magnetic moments of nanoparticles, reduce the transversal relaxation (T2 relaxation time), increasing thus a relaxivity of water. This can be done also by some proteins. Therefore the goal of this study was determine the degree of influence of BSA protein to the T2 relaxation time, after binding to the magnetic nanoparticles. Such interaction could have an influence on the contrast properties of MRI contrast agents, disturbing such desired MRI information.

2. Subject and Methods

Magnetite nanoparticles with BSA protein and without BSA protein were diluted on 20 samples, so that the each of the samples had half concentration of previous one. The samples were measured at clinical MRI scanner ESAOTE 0.178 T, with Spin Echo T2 weight pulse

Table 1. The table of samples with concentrations.

No.	Concentration [mg/ml]	No.	Concentration [mg/ml]	No.	Concentration [mg/ml]	No.	Concentration [mg/ml]
0	reference	6	0.11875	12	9.277e-3	18	7.248e-5
1	3.8	7	0.029687	13	4.6387e-4	19	3.62e-6
2	1.9	8	0.0148	14	1.16e-4	20	1.81e-6
3	0.95	9	7.42e-3	15	5.798e-5	-	-
4	0.475	10	3.71e-3	16	2.899e-5	-	-
5	0.2375	11	1.855e-3	17	1.45e-5	-	-

sequence, with parameters TR = 1500 ms, TE = 50 ms, 2 acquisitions, 5 mm slice thickness, 0 mm gap, 5 slices, FOV = 256x256. The samples were made at first from magnetic liquid MKPEG-20.000-6C without BSA protein and with concentration of magnetite c_{mag} = 7.6 mg/ml and next from magnetic liquid MKPEG-20.000-BSA-6Cc with binding of protein BSA and concentration of magnetite c_{mag} = 3.8 mg/ml.

3. Results

The Fig.1 and Fig.2 shows relative change of signal/contrast intensity (due to reference) with increase of concentration of magnetic nanoparticles in the samples. Both liquids (with/without BSA protein) were diluted so that the same number of sample has the same concentration for comparison. Progress of curves of both liquids was very similar but not equal. The chart shows, that the biggest change of contrast was achieved with samples 7 to 11 for both liquids. Concentration of magnetit nanoparticles were between 3.71 to 59.375 µg/ml. Recommended concentration of clinical contrast agent - Resovist (on basis of iron oxide) in the bloodstream is approximately 97 µg/ml.

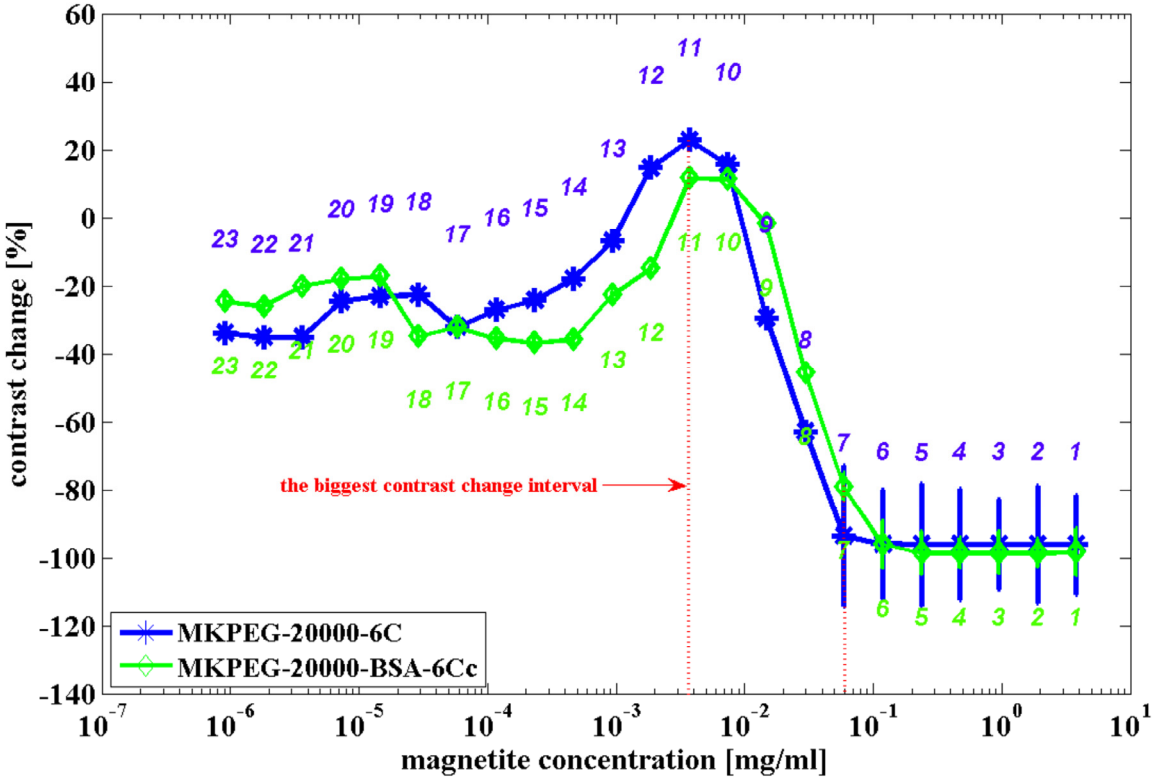

Fig. 1. Relative changes of signal intensity between each samples for both liquid (with/without protein).

The higher concentrations of the magnetite nanoparticles caused large artefacts and measurement error. In fact they have been virtually indistinguishable. The samples 11 to 14 was distinguishable at the border of visibility with the naked eye for our system (approximately 15 % of contrast change), but showed increase of signal intensity with increase of concentration, which not agree with theory, because the iron oxide particles should shorten T_2 relaxation time. The samples 14 to 23 were also hardly distinguishable for us. Therefore, for practical use, in terms of the changes in contrast, as the most appropriate appears the interval with concentration from 3.71 to 59.375 mg/ml for both fluids.

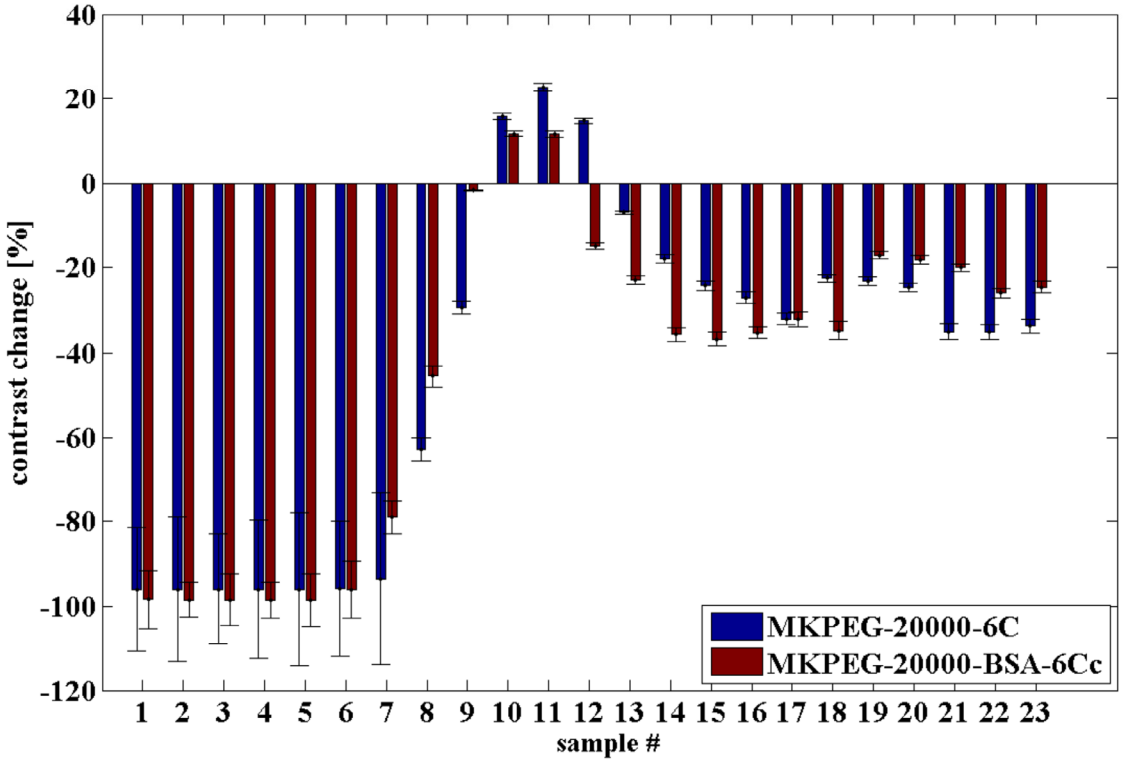

Fig. 2. The image show changes of contrast between each liquid and its concentration.

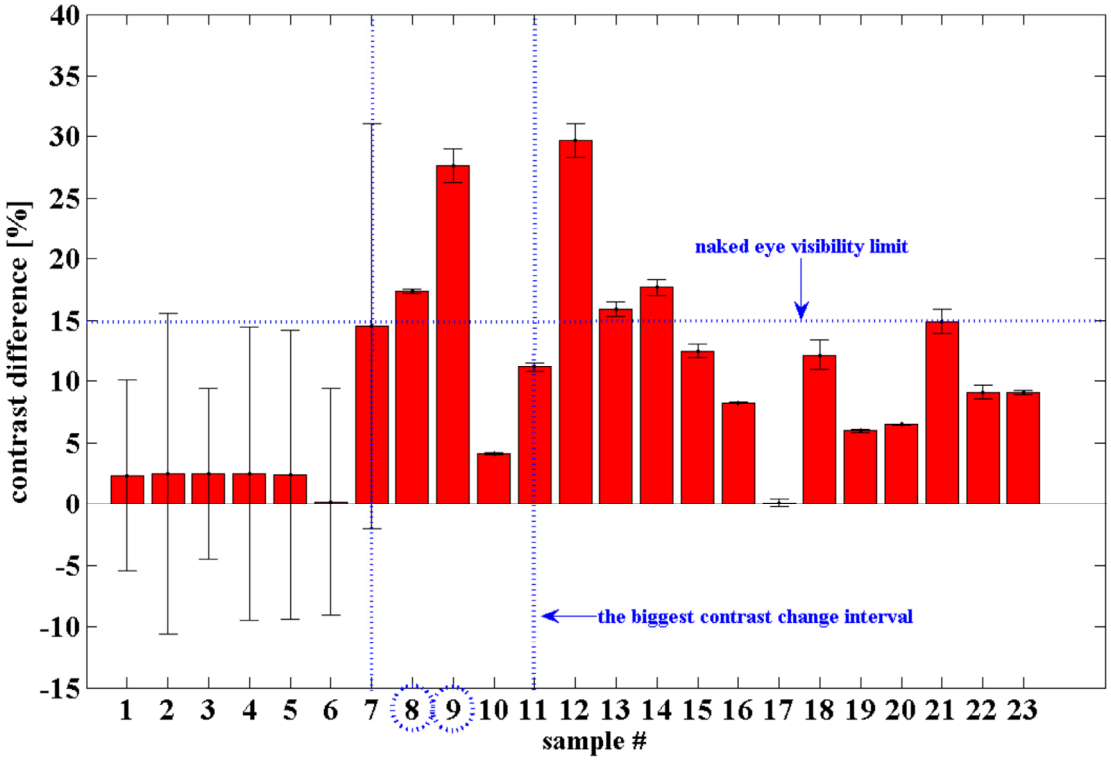

Fig. 3. The figure shows the difference in contrast between individual samples with and without binding of BSA protein.

The Fig. 3 shows, that the highest changes in the contrast between individual liquids is dissymmetrical for samples 7 to 9, 11 to 16, and 19 and 21. Above the border of visibility with naked eye are only 5 samples: 8, 9 12, 13 and 14. The sample number 12 achieved maximum change of contrast (almost 30 %). But this sample is out of interval in the fig.1 (samples number. 7 to 11). Therefore, for practical use of magnetite nanoparticles stabilized with PEG 20000 in clinical practice we recommend to use the concentration interval from 14.8 to 29.7 μg/ml.

4. Discussion and Conclusions

We have shown, that for the magnetite nanoparticles stabilized with PEG 20000 in specific concentration interval exist significant difference in contrast (visible with naked eye) after binding of protein BSA to the surface of particles. This effect can be use in clinical practice for molecular magnetic resonance imaging of specific proteins, as biomarkers of pathological processes.

Acknowledgements

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