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P-26

Novel magnetic Prussian Blue nanoparticles for *in vivo* T1 MR-imaging

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1. Introduction

Superparamagnetic contrast agents (CA), used in MR-imaging result hypointense changes on T2-weighted images. Materials with such properties are superparamagnetic iron oxide nanoparticles (SPIONs), which have a relatively high iron content. These particles were investigated in the middle of the 2010s, their contrast enhancement is hard to detect for the human eye, thus it is a hypointense change on images. The other type of nanoparticles, whose properties result hyperintense changes on T1-weighted images, are Gd(III) and Mn(II) containing particles, with different compositions. Due to their toxic effects, there is an urgent need for a new type of CA, which can overcome the drawbacks of both materials, as a multifunctional CA [1].

Prussian Blue (PB) was previously reported as a T2 CA, however it also had some T1 contrast enhancement, related to its small size. Both T1 and T2 contrast enhancement would be possible, using a relatively small Prussian Blue nanoparticles (PBNP) was our main goal; to modify the nanoparticle, thus it could also have T1 contrast enhancing properties [2].

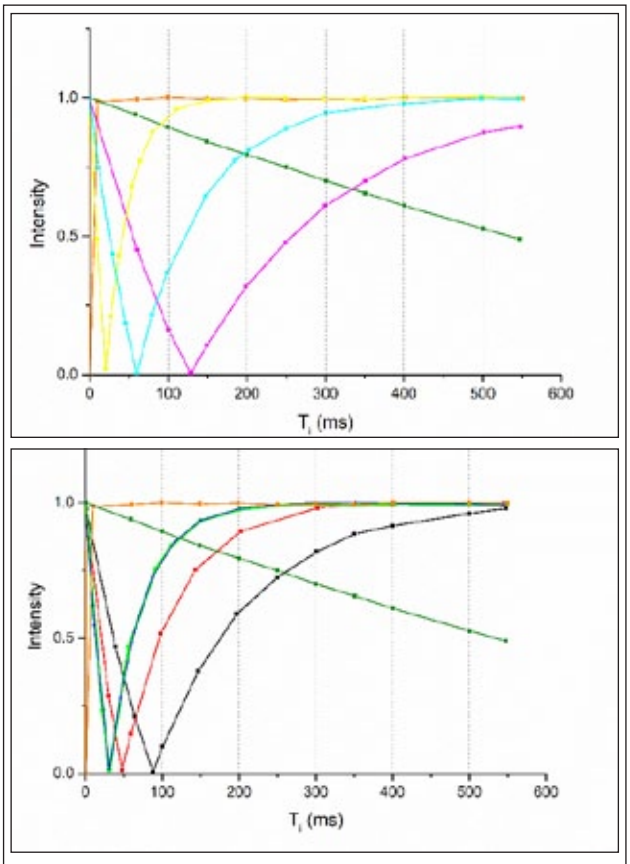

Figure 1 *The relaxivity of the different PB-species, compared to each other CAs.*

2. Materials and methods

To modify the contrast enhancing capabilities of Prussian Blue nanoparticles, we prepared biocompatible (citrate-coated) and non-coated (HCl) PBNP. Hypothetically, Fe(III), which are not occupied by citrate in PB-HCl molecules, would connect to the free carboxyl groups of citrate in PB-AC. The suspensions of these nanoparticles were mixed, in different volume ratios.

The so prepared nanosystems stability was measured via Dynamic light scattering (DLS), for 6 weeks. In vitro MRI contrast enhancing properties were measure with a nanoScan PET/MRI (Mediso Ltd.; Hungary) in a permanent magnetic field of 1 T in a 450 mT/m gradient system. The T1 relaxation values of the samples were measured against different T_i inversion times. After that, in vivo measurements were executed in 3 nu/nu female mice, to investigate the T1 and T2 contrast enhancing properties of the samples. The samples were compared to authorized T1 CA (Gadovist)

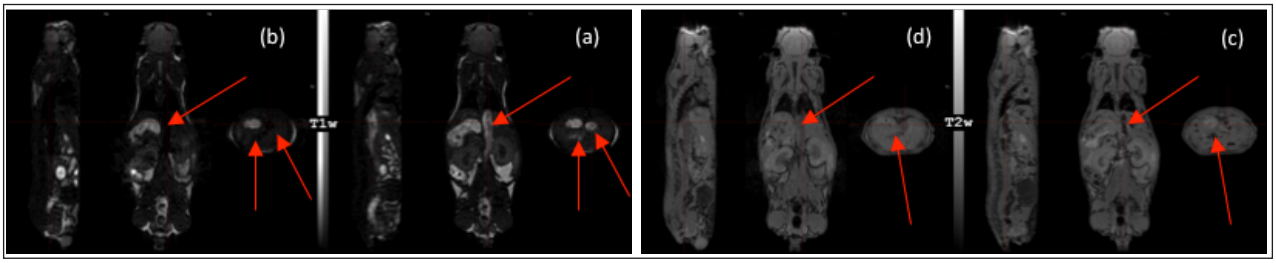

Figure 2 *The PBNP_AC-HCl 1:2 pre (a, c) and post (b, d) injection, on T1 and T2-weighted images. Images (a) and (b) show hyperintense changes in the abdominal aorta and gastrointestinal tract; images (c) and (d) support the information of T1w images; the vascular system appears hypointense.*

and saline solution, which has ultralong relaxivity, and acts as a T2 CA. The results were acquired using two sequences, for T1-weighted images (T1 GRE 3D) TR/TE/FA 11.2/2.1/65, for T2-weighted images (T2 GRE SP 3D) TR/TE 75/4 was used.

3. Results

The average size of the modified PBNPs was 177.11 ± 8.85, according to the 6-week stability test. The different volume ratios had no significant effect on the stability but on the size of the NPs. The bigger the ratio of PB-HCl, the bigger the size. The relaxivity of the different compositions differed. Smaller volumes of PB-HCl either resulted longer T_i inversion times so T1 relaxation, while the 1:2 and 1:3 ratios were hard to distinguish. On the other hand, 1:2 and 1:3 ratios had different particles sizes and, related to that, different stability. PB_AC-HCl 1:2 was injected into the tail vein of the mice.

Post injection, the particles (as T2 CAs) appeared in form of darkening, in the gastro-intestinal tract (GIT) and liver. T1-weighted images revealed the true potential of PBNPs and show their appearance both in these anatomical structures; hyperintense changes on the images are seen in the abdominal aorta.

4. Conclusions

Basically, iron-containing superparamagnetic contrast agents show hypointense changes on T2-weighted MRI images. Our new method to synthesize PBNPs with increased iron content would help the nanosystem to become a multimodal platform for teragnostic use. As a conclusion, the synthesized compound is a promising candidate as new generational, non-toxic and multimodal contrast agent. The PBNP-based iron containing crystal strucure has a promising T1 contrast enhancement though.

5. Acknowledgements

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