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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].

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 T1 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).
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 T1 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 structure has a promising T1 contrast enhancement though.

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