Continuous hyperpolarization of water via Overhauser DNP for MRI applications

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Introduction

Despite its wide applicability in natural science, NMR and MR imaging still suffer from the inherently low sensitivity. Many efforts have been devoted to overcome this obstacle; one possibility is the use of hyperpolarized contrast agents which exhibit very enhanced NMR signals. One hyperpolarization method for molecules is dynamic nuclear polarization (DNP). Dynamic Nuclear Polarization is a hyperpolarization method, which polarizes nuclear spins in a magnetic field by irradiating unpaired electrons with microwaves. One major issue of this approach is the limited lifetime of the hyperpolarized state thereby restricting the in vivo application and detection of the hyperpolarized molecules to roughly 3 times T_1. This problem is even more pronounced if the hyperpolarization process could not take place in the vicinity of the used MR tomograph due to safety restrictions or space limitation like it is often the case in clinical MR facilities. Therefore, we propose the development of a mobile Overhauser DNP polarizer, based on an inexpensive Halbach magnet.[1,2] The use of a mobile permanent magnet design enables us to minimize the transport time from the hyperpolarization site to the MR tomograph resulting in an efficient use of the non-equilibrium magnetization regardless which scanner of the clinic has to be used.

Material and Methods

The employed Halbach magnet consists of two nested rings of permanent magnets in Halbach arrangement which can be rotated with respect to each other. The Halbach magnet shows an almost vanishing magnetic flux at its outer side and especially is not disturbing the MRI scanner or any other instruments. It can be placed directly next to a 4.7 T superconducting magnet, thus limiting the transport time of the hyperpolarized sample. For the DNP experiments the field strength of the magnet system was adjusted to 0.35 T, corresponding to electron and ^{1}H Larmor frequencies of 9.7 GHz and 14.8 MHz, respectively. For EPR irradiation and NMR detection a Bruker (Karlsruhe, Germany) probehead originally designed for Electron Nuclear Double Resonance (ENDOR) was used. In DNP, the use of mostly toxic radicals becomes crucial with regard to medical applications. Moreover, for *ex-situ* DNP experiments the sample must be transported from the polarization magnet to the MRI scanner and polarization losses due to T_1 relaxation occur. In our experiments it turned out that for TEMPOL (4-Hydroxy-2,2,6,6-tetramethyl-piperidine-1-oxyl) radical containing solutions the fast T_1 relaxation, inherent to the presence of free radicals, makes it hardly possible to detect any enhanced signal *ex-situ*. We implemented a flow system into the mobile DNP polarizer, which overcomes the obstacles of free radicals. The 4-Amino-TEMPO (4-Amino-2,2,6,6-tetramethylpiperidine-1-oxyl) radicals are immobilized in a Sepharose gel matrix and the hyperpolarized radical free fluid is pumped subsequently directly in the MRI scanner.[3-5]

Results and Discussion

Even at flow conditions the NMR signal is enhanced in the Halbach magnet as well as in the MRI scanner (4.7 T) in 1.4 m distance. In figure 1 images at flow conditions are shown acquired for thermally and hyperpolarized water, respectively. The images demonstrate that MRI enhancement via Overhauser DNP can be achieved. Additionally, due to dipolar coupling, the hyperpolarized NMR signal is inverted (not shown here) which provides even for small enhancements an excellent MRI contrast. This makes hyperpolarized water a potential authentic contrast agent for applications like lung perfusion or angiography.

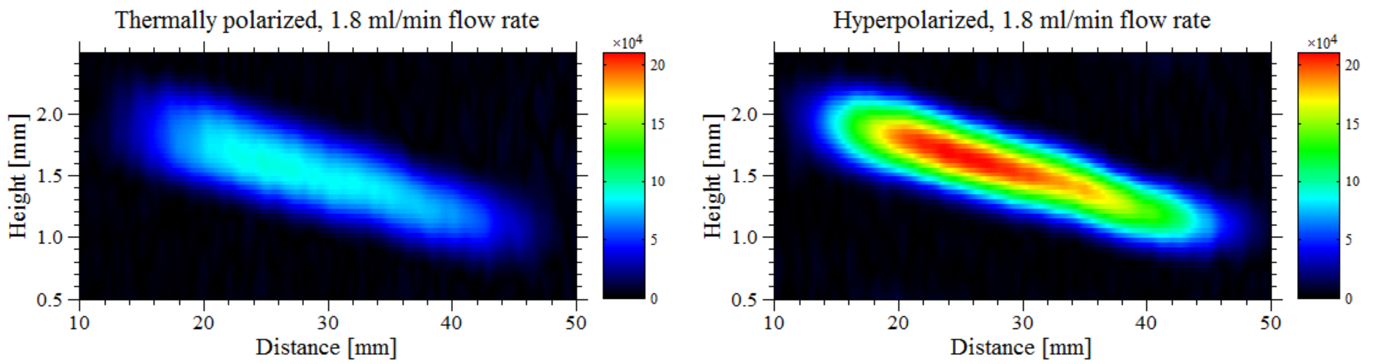

Fig.1: Comparison of thermally polarized and hyperpolarized water in a 700 μm tube. Images are zero filled to four times the number of acquired points.

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