In situ polarization measurement of hyperpolarized solutions prior to in vivo 9.4T MR experiments

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Introduction

The tremendous gain in signal-to-noise ratio resulting from hyperpolarization techniques and in particular dissolution dynamic nuclear polarization (DNP) opened new perspectives in biomedical MR research [1,2]. The polarization value at the time of the infusion is of high relevance for quantitatively evaluating *in vivo* substrate and metabolites concentrations and for deducing real-time kinetics of *in vivo* biochemical processes. The *in vivo* signal enhancement is however difficult to estimate since the thermal equilibrium signal needed to determine the polarization is too small to be detected once the solution has been infused. Measuring the polarization *ex situ* by inserting part of the hyperpolarized solution in a dedicated NMR setup (sometimes referred to as "polarimeter") is also inaccurate since the hyperpolarized solution is subject, during the transfer between polarizer and imager on one side, and polarizer and polarimeter on the other, to unequal dramatic time variations in magnetic field which strongly affect nuclear spin relaxation. The losses in polarization are therefore different and difficult to quantify. Here we propose an *in situ* method to measure the polarization of the hyperpolarized substrate inside the imager bore at the time of the infusion using the imager console.

Methods

Glassy frozen 4.5 M 1-^{13}C labeled sodium acetate solutions (300 µl 2:1 D_2O/d_6-ethanol with 33 mM TEMPO) were dynamically polarized at 5 T and 1.05±0.05 K using the hardware described in earlier publications [3, 4]. Once polarized, the samples were rapidly dissolved in 5 ml of superheated D_2O using a procedure similar to the one developed by Ardenkjaer-Larsen *et al.*[1]. High-pressure helium gas was applied for 2 s to drive the solution through a 6 m long PTFE tube connecting the polarizer to a custom-designed separator/infusion pump placed inside the 9.4 T imager bore at a distance of 6 cm from the Sprague-Dawley rat leg muscle. A solenoid coil was wound around the pump central compartment and tuned to ^{13}C frequency (see Fig.1). The ^{13}C signal from the collected hyperpolarized 0.2 M 1-^{13}C acetate solution was measured in the pump at the time the infusion into the rat left femoral vein started, i.e., 3 s after dissolution. A volume of 2.2 ml was injected within 9 s. A dual ^{1}H/^{13}C probe with a 10 mm diameter ^{13}C surface coil placed on the rat right leg muscle was used to measure the *in vivo* signals. Both pump and animal ^{13}C coils were connected to the same channel on the MR console (Varian/Inova) trough TTL controlled switches that allowed to swap the excitation/acquisition from one coil to the other in less than 1 s.The signals measured in the pump and the *in vivo* signals were acquired using two different sets of shim parameters.

Results and discussion

The ^{13}C signal from 1-^{13}C acetate was measured at three different stages of a typical *in vivo* hyperpolarized MR experiment (see Fig.2): first, the ^{13}C solid-state polarization build-up was monitored inside the polarizer during the DNP process at 1.05±0.05 K using 5° pulses and compared to the 1K reference thermal equilibrium signal (Fig.2(a)). Following dissolution and transfer into the pump, the ^{13}C signal from the hyperpolarized solution was measured using a 10° flip angle pulse. The liquid-state polarization could be deduced by comparing the signal with a reference signal (Fig.2(b)). Finally, an *in vivo* leg skeletal muscle signal was measured with an adiabatic 30° BIR-4 pulse at the end of the infusion, i.e., 12 s after dissolution (Fig.2 (c)).

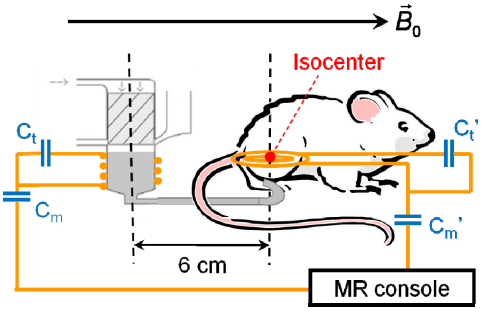

Fig 1: Sketch of the experimental setup inside the magnet bore. The distance between the center of the ^{13}C coil wound around the pump and the animal ^{13}C surface coil was set to 6 cm.

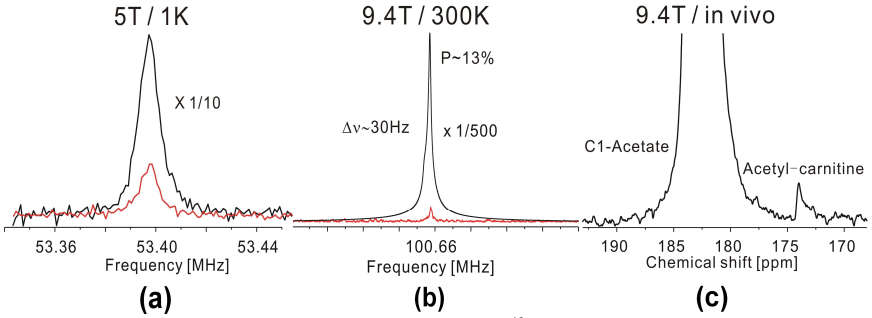

Fig 2: Three consecutive single-shot low-flip angle ^{13}C measurements during a metabolic study: (a) 5 T/1 K solid-state signal in the polarizer (thermal equilibrium shown in red) (b) Liquid-state signal inside the pump when infusion started (thermal equilibrium shown in red) (c) *In vivo* signal in the rat skeletal muscle.

Conclusion

The method presented herein allows for *in situ* evaluation of the liquid-state ^{13}C signal enhancement in the imager bore at the time of the infusion and for an accurate calibration of the polarization prior to each *in vivo* measurement. This add-on is fully compatible with real-time metabolic studies (in the present feasibility study, a spectrum showing the metabolic conversion of acetate to acetyl-carnitine was recorded following acetate infusion (Fig.2 (c)) and it negligibly affects the polarization. It also does not increase the delay between the hyperpolarization procedure and the infusion.

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