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 13C labeled sodium acetate solutions (300 µl 2:1 D2O/d5 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 D2O 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 13C frequency (see Fig.1). The 13C signal from the collected hyperpolarized 0.2 M 1-13C 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 1H/13C probe with a 10 mm diameter 13C surface coil placed on the rat right leg muscle was used to measure the in vivo signals. Both pump and animal 13C 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 13C signal from 1-13C acetate was measured at three different stages of a typical in vivo hyperpolarized MR experiment (see Fig.2): first, the 13C solid-state polarization build-up was monitored inside the imager bore at the time of the infusion using the hardware described in earlier publications [3, 4]. Once polarized, the samples were rapidly dissolved in 5 ml of superheated D2O 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 13C frequency (see Fig.1). The 13C signal from the collected hyperpolarized 0.2 M 1-13C 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 1H/13C probe with a 10 mm diameter 13C surface coil placed on the rat right leg muscle was used to measure the in vivo signals. Both pump and animal 13C 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.

Conclusion
The method presented herein allows for in situ evaluation of the liquid-state 13C 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.

Acknowledgements
This work was supported by the Swiss National Science Foundation (grant 200020_124901), the National Competence Center in Biomedical Imaging (NCCBI), the Centre d’Imagerie BioMédicale (CIBM) of the UNIL, UNIGE, HUG, CHUV, EPFL, and the Leenards and Jeantet Foundations.

References