Low RF-field strength cross polarization combined with photo-induced non-persistent radicals for clinically applicable dDNP

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Low RF-field strength cross polarization combined with photo-induced non-persistent radicals for clinically applicable dDNP

Work in progress

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Cross Polarisation for SPINlab-like polarisers using non-persistent radicals is demonstrated. The efficiency of the transfer from protons to carbon is modest at the currently achievable low B fields of 4-5 kHz still yielding ¹³C polarisation levels up to 15%. Based on the presented results, we foresee polarisation levels superior to direct ¹³C DNP in our next generation of double-tuned probes incorporating local tune and match.

Abstract
We demonstrate the possibility of ¹H Dynamic Nuclear Polarization followed by cross polarization to carbon (DNP-CP) using a modified low cost benchtop console (Kea2) equipped with an external amplifier (Tomco) and a SPINlab-like dissolution DNP polarizer i.e. using the same fluid path and allowing for hyperpolarization of a full human dose. Cross polarization (CP) using Laboratory Frame De- and Remagnetisation (LAFDR) was found superior to alternative sequences at the limited B fields employed. Faster build-up rates compared to ¹³C DNP are demonstrated using TEMPOL (4-Hydroxy-2,2,6,6-tetramethylpiperidine 1-oxyl) and DNP-CP ¹³C polarisations up to 15 % are achieved using non-persistent UV-induced radicals.

Introduction
Dissolution Dynamic Nuclear Polarization (dDNP) is used to enhance the MR signals in imaging by factors of 10,000² paving the road for metabolic MR studies. However, the polarization build-up on ¹³C typically takes tens of minutes to hours, significantly lowering the versatility and throughput. Recently, studies have shown the possibility of speeding up the process by polarizing ¹H, which has a faster build-up, followed by polarization transfer to e.g. ¹³C.³ However, strong B fields and small sample volumes are used, which makes the technique incompatible with clinical dDNP-MRI. Moreover, for clinical use, and in general to eliminate the relaxation effect, the radical essential for DNP needs to be removed during dissolution. Use of pyruvic acid (PA) non-persistent photo-induced radicals for dDNP has been demonstrated to solve this issue⁴ and recently polarization build-up on protons with ¹³Cpol = 690 s and 70 % polarization has been presented⁵.

Methods
Overview

CP by Laboratory Frame De- and Remagnetisation (LAFDR)

Experimental results

**DNP-CP using TEMPOL as radical**

**DNP-CP using UV-induced radicals**

Results
The efficiency of DNP-CP depends on the build-up rate and final polarisation achieved on protons as well as the transfer efficiency of the CP sequence.

1. For B=0.5 kHz LAFDR (fig. B) was found to outperform other CP sequences (data not shown).
2. On the TEMPOL containing sample, DNP-CP using optimised LAFDR outperforms ¹³C DNP for build-up times < 1 hour, and 20% ¹³C polarisation was achieved in only 20 min (fig. C).
3. Using ¹³C-CP/JPA as the substrate for non-persistent radicals gives a too narrow EPR-line for efficient ¹H DNP resulting in poor DNP-CP performance (fig. D).
4. Introduction of hyperfine coupling to the unpaired electron by ¹³C labelling in position 2 increases the EPR linewidth yielding ¹H build-up, but a polarisation of only 18 %, and therefore still inefficient DNP-CP (fig. E).
5. Deuterating the methyl group of PA increases the ¹H DNP polarization to 62 % and maintains the efficiency of CP. This yields a final ¹³C polarisation of 15% after CP (fig. F).

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Conclusion and Outlook
We have demonstrated DNP-CP on a clinical-compatible SPINlab-like polariser using a low-cost benchtop console equipped with an external amplifier. Moreover, the technique has been combined with non-persistent UV-induced radicals. At the current state, with B=0.5 kHz, direct ¹³C DNP still outperforms the DNP-CP. However, the goal is to implement local tuning of the probe to achieve sufficient B fields to increase the transfer efficiency. We expect that sufficiently strong B fields are achievable for this setup to outperform direct ¹³C DNP both with respect to build up rates and polarisation levels.

References