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 Bₛ 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 ¹⁴ Dynamic Nuclear Polarization followed by cross polarization to carbon (DNP-CP) using a modified low cost benchtop console (Keao) equipped with an external amplifier (Tomco) and a SPINlab-like dissolution DNP polarizer i.e. using the same fluid path and allowing for hyperpolarisation of a full human dose. Cross polarisation (CP) using Laboratory Frame De- and Remagnetisation (LAFDR) was found superior to alternative sequences at the limited Bₛ 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 10,000 ¹¹ by 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 ¹⁴, which has a faster build-up, followed by polarization transfer to e.g. ¹³C.¹ However, strong Bₛ 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 issue¹ and recently polarization build-up on protons with $\tau_{\text{up}}=690$ s and 70 % polarization has been presented².

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 Bₛ=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 is achieved in only 20 min (fig. C).
3. Using ¹⁴C-TEMPOL as the substrate for non-persistent radicals gives a too narrow EPR-line for efficient ¹³C DNP resulting in poor DNP-CP performance (fig. D).
4. Introduction of hyperfine coupling to the unpaired electron by ¹⁴C labelling in position 2 increases the EPR linewidth by 40 Hz, but a combination of ¹⁴C and therefore still inefficient DNP-CP (fig. E).
5. Deuterating the methyl group of PA increases the ¹⁴C DNP build-up rate by 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 Bₛ=5 kHz, direct ¹³C DNP still outperforms the DNP-CP. However, the goal is to implement local tuning of the probe to achieve sufficient Bₛ fields to increase the transfer efficiency. We expect that sufficiently strong Bₛ fields are achievable for this setup to outperform direct ¹³C DNP both with respect to build-up rates and polarisation levels.

References