High-resolution 2D MRI of ^{1}H and ^{13}C hyperpolarized contrast agents at 0.0475 T

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Target audience This work should benefit molecular biologists, chemists, radiologists, physicians, and imaging scientists interested in molecular imaging, cellular metabolism, or studies of hydrogen catalysis.

Purpose Nuclear spin polarization *P* is a key factor contributing to overall MRI sensitivity, and typically amounts to only order 10^{-6}-10^{-5}. But a variety of mechanisms can temporarily increase *P* by orders of magnitude beyond that achievable through static magnetic fields. The resulting increased NMR signal enables a variety of applications, including biomedical use of hyperpolarized (HP) MRI contrast agents to assay cellular metabolism, typically ^{13}C-labeled metabolites reporting on abnormal metabolism such as ^{13}C-succinate. Of the established chemical hyperpolarization techniques Parahydrogen Induced Polarization (PHIP) using Para-Hydrogen and Synthesis Allow Dramatically Enhanced Nuclear Alignment (PASADENA) and more recently Signal Amplification by Reversible Exchange (SABRE) use parahydrogen[1] as a source of hyperpolarization. Previous work[2] showed that imaging at low magnetic field strengths can be more sensitive than that at high field through the introduction of resonance frequency optimized rf coils. Here, the feasibility of low field imaging of ^{1}H and ^{13}C hyperpolarized contrast agents with high spatial resolution using the previously reported imaging system is demonstrated.

Methods A 5.75 mT electromagnet-based polarizer with a valve manifold and PHIP probe similar to that reported earlier[3] was used to produce SABRE-polarized pyridine and PHIP-polarized ^{13}C-succinate for imaging studies. For the SABRE studies 3 mL methanol-d_4 solutions of 7 mM N-heterocyclic carbene complex-based Ir catalyst and 100 mM pyridine were prepared. Following the polarization procedure, the pyridine was transferred through Earth field to the imaging system where gradient echo (GRE) images were acquired. The 5.75 mT polarizer was also used to produce HP ^{13}C-succinate, which was transferred after Quality Assurance (QA) through a polarization-conserving magnetized flexible transfer path to the imaging system. ^{13}C imaging was performed on 1.5 mL of 30 mM ^{13}C-succinate suitable for *in vivo* preclinical use.

Results A ^{1}H image of HP pyridine in 10 mm NMR tube was collected with an in-plane resolution of 94 µm using ^{1}H P = 0.5%. At this micron-scale resolution the maximum SNR was 24. ^{13}C imaging was performed on 1.5 mL of HP ^{13}C-succinate in a 15 mL Falcon tube achieving maximum SNR of 54. Magnetic susceptibility-induced field gradients due to foamed agent were negligible. ^{13}C-succinate QA prior to imaging indicated ^{13}C P = 25±1% *in situ* of the PHIP polarizer and P = 13%±1% after the 22 second long transfer to the low-field MRI system.

Discussion High-resolution images with large fields of view were obtained at a relatively low magnetic field despite limiting factors related to the high *Q* of the RF coils on the maximum imaging spectral width (SW). Hyperpolarized proton images had significantly higher resolution due to inherently higher sensitivity of proton spins, which extends to hyperpolarized MRI including indirect proton detection of hyperpolarized compounds.[4] TR was limited by the hardware, and sub-second imaging speeds can be achieved.

Conclusion High-resolution proton and ^{13}C 2D imaging is demonstrated at low magnetic field strengths. Application of a magnetized transfer system successfully prevented depolarization of the hyperpolarized agent. Achieved SNR is suitable for *in vivo* imaging studies.

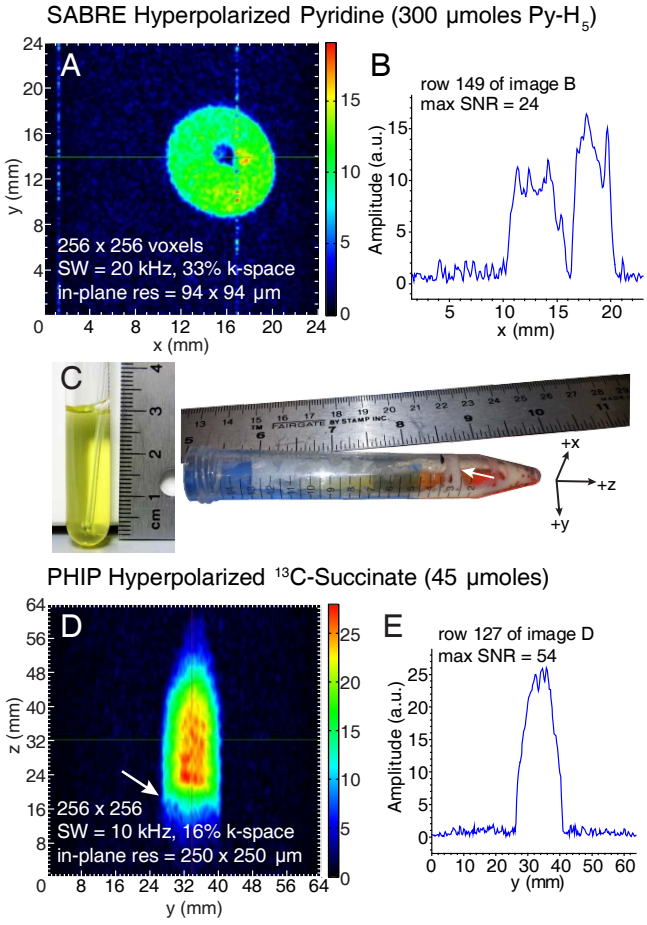

Figure 1. MRI at 0.0475 T with frequency optimized RF probes. (A-B) ^{1}H 2D GRE imaging of pyridine at 94 x 94 µm in-plane resolution imaging (TE = 13 ms, TR = 60 ms, t(Acq) = 12.8 ms) and selected slice across 2D image to demonstrate SNR. Pyridine was hyperpolarized by SABRE at 5.75 mT to polarization P ~ 0.5% at 100 mM in 3 mL. (C) The SABRE and PHIP HP agent phantoms. (D-E) ^{13}C-succinate 250 x 250 µm in-plane resolution GRE imaging (TE = 26 ms, TR = 110 ms, t(Acq) = 25.6 ms) and spatial NMR signal from selected row. Arrows in images mark the location of foamed tracer. ^{13}C polarization for imaging in (D) was P ~ 13%.

References

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