MR Technical Developments for Clinical Hyperpolarized ^{13}C-Pyruvate Studies in Prostate Cancer Patients

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Introduction: MR imaging with hyperpolarized [1-^{13}C]-pyruvate has the unprecedented ability to rapidly probe cellular metabolic pathways and is a potentially valuable clinical tool, particularly for cancer imaging [1]. Detection of the conversion of hyperpolarized [1-^{13}C]-pyruvate to hyperpolarized [1-^{13}C]-lactate has enabled the demonstration of elevated lactate in animal models of cancer –including prostate cancer – which correlates with pathologic tumor grade [2]. The goal of this project was to develop and test specialized RF coils and MR methods for a Phase 1 clinical trial of hyperpolarized carbon-13 MR studies in prostate cancer patients.

Hardware Setup: The custom MR coils were designed for a GE 3T MR scanner equipped with a multi-nuclear spectroscopy package, including an 8 kW broadband amplifier. A ^{13}C transmit coil in clamshell geometry was built into a patient table, as shown in Figure 1. Development of the dual-frequency ^{1}H - ^{13}C endo-rectal receiver probe has been described [3]. For calibration and pre-dose testing, a reference sample of 8M ^{13}C-urea was installed inside each endo-rectal probe body. In addition to this probe, a 4-channel torso coil was used for ^{1}H MRI. Extensive deployment of radiofrequency trap circuits in all these coils helps alleviate inter-channel cross-talk. A prior version of the hardware configuration was tested in canines [4].
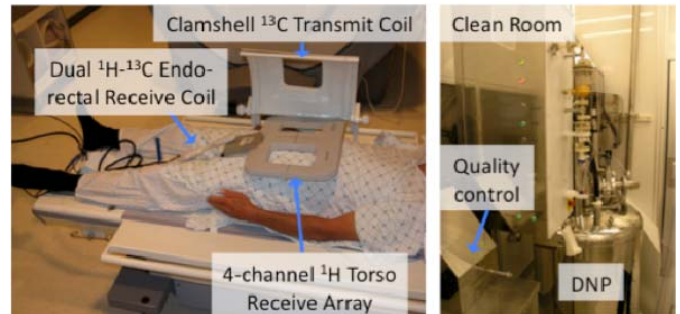

Figure 1: Coil setup (left) and clean room dissolution DNP (right).

Pulse Sequences: SPGR and FSE ^{1}H imaging sequences were used to test the proton coils, confirming the trap circuit effectiveness and coil sensitivities. They are also used to provide an anatomical reference for the ^{13}C imaging. The ^{13}C coils were tested and calibrated on the ^{13}C-urea insert using a non-localized pulse-acquire pulse sequence. Specialized sequences were developed for either 1-D dynamic or 3-D MRSI hyperpolarized acquisitions, which were also tested with the hardware setup. The dynamic 1-D MRSI data is acquired every 3s using a S/I slab excitation and will be resolved in the sagittal dimension with an echo-planar spectroscopic imaging (EPSI) gradient trajectory that simultaneously acquires both spectral and spatial data during each readout. With this sequence, we will determine the timings of contrast delivery and metabolic conversion relative to the injection. A 3-D MRSI pulse sequence will be used for finer localization of the metabolism. It is acquired using an adiabatic double spin-echo [5] with low peak power HSn pulses [6] to provide B1-insensitivity and an EPSI readout to accelerate the acquisition. This 14-21 sec (depending on matrix size) acquisition will be delayed from the start of injection based on the 1-D dynamic data. For both sequences, the EPSI trajectories were designed with a 580-Hz/18-ppm spectral bandwidth to cover from [1-^{13}C]-lactate to [1-^{13}C]-pyruvate with a 4.5 mm minimum resolution.

DNP Clean Room: A proof-of-concept Dynamic Nuclear Polarization (DNP) polarizer has been installed into a clean room adjacent to the scan and console rooms. It meets clean room specifications and includes quality control systems to validate the temperature, pH, purity, and polarization of the hyperpolarized pyruvate solution prior to injection.

Discussion: The specialized MR coils and sequences were tested in over 25 prostate cancer patient research MRI/MRSI studies. Clinical quality anatomic ^{1}H images (Fig. 2) and 3D ^{1}H MRSI were obtained. Figure 3 shows ^{13}C spectra with the ^{13}C-urea insert reference using the calibration, 1-D dynamic, and 3-D pulse sequences. Using the ^{13}C-urea reference, we measured maximum achievable RF amplitudes of 0.83±0.33 G and established the frequency and SNR values for ^{13}C MRSI prescan procedures. Using these SNR values, we estimated the high-resolution 3-D sequence will detect ^{13}C metabolite levels >0.13 mM with SNR ≥ 5, assuming 2.5% polarization at the time of imaging.

We have developed and tested custom hardware and methods including ^{13}C coils for prostate imaging, clean room dissolution DNP system, and hyperpolarized ^{13}C pulse sequences for future prostate cancer patient studies.
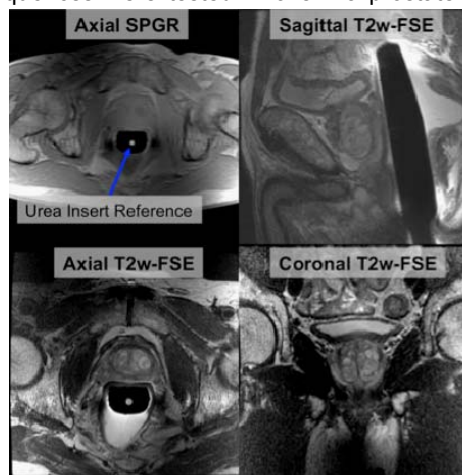

Figure 2: ^{1}H images acquires with our custom configuration. The images are intensity-corrected based on the coil sensitivity profile.
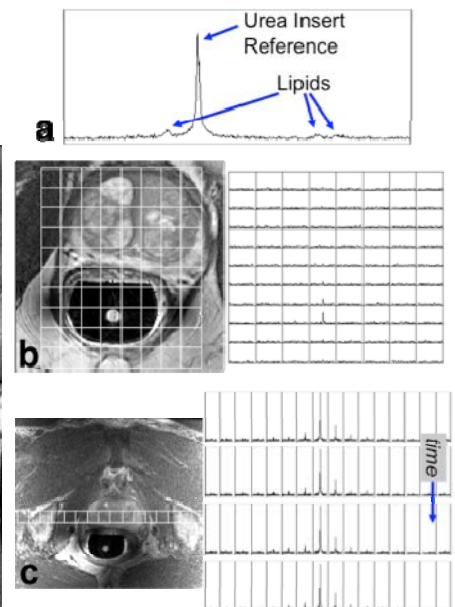

Figure 3: Spectra of the ^{13}C-urea syringe using: a) pulse-acquire, b) 3-D MRSI, and c) 1-D dynamic MRSI as described.

References: [1] Golman K, et al. PNAS 103(30): 11270-5 (2006). [2] Albers MJ, et al. Cancer Res 2008; 68:8607–8615. [3] Tropp J et al, Proc 14th ISMRM 2006, p. 501. [4] Nelson SJ, et al. Proc 15th ISMRM 2007, p. 536. [5] Cunningham CH, et al. JMR 2008; 193:139–146. [6] Hu S, et al. Proc 17th ISMRM 2009, p. 333.