Hyperpolarized C-13 MRSI data of Dog Prostate at 3T

S. J. Nelson[1], A. P. Chen[1], R. Bok[1], M. Albers[1], M. L. Zierhut[1], J. Kurhanewicz[1], D. B. Vigneron[1], S. Kohler[2], Y-F. Yen[2], J. Tropp[2], A. Gram[3], J. Wolber[3], H. Dirven[3], and R. E. Hurd[2]

[1]University of California, San Francisco, CA, United States, [2]GE Healthcare, Menlo Park, CA, United States, [3]GE Healthcare-Europe

The increased sensitivity of hyperpolarized C-13 labeled pyruvate was used to obtain non-invasive MR measurements of metabolic activity in the dog prostate. These included an evaluation of the temporal changes in pyruvate and its conversion to lactate, alanine and bicarbonate following a bolus injection of the agent and an analysis of the spatial changes in levels of these metabolites using 2-D CSI and 3D EPSI pulse sequences. The signal to noise ratio of lactate in the metabolite maps that were acquired in less than 20 seconds at a spatial resolution of 0.125ml was in the range of 25:1 to 67:1.

Introduction: Hyperpolarized C-13 pyruvate has been used to image metabolism in pre-clinical experiments within rodents and other small animals. Products that have been monitored following injection of this agent include lactate, alanine and bicarbonate. The objective of this study was to perform experiments that would evaluate the feasibility of observing changes in hyperpolarized C-13 pyruvate and its products using in vivo MR spectroscopic imaging techniques. The choice of a dog model was dictated by the fact that the anatomy of its prostate is similar to humans. This meant that the coil geometry and data acquisition parameters used would provide a realistic test of the methodology. Specific goals of the study were to test the radiofrequency coils and pulse sequences being developed, to determine the dynamics of arrival of the pyruvate bolus, to evaluate the signal to noise of pyruvate in healthy dog prostate and to see whether its metabolic products could be observed using a 3T MR scanner.

Methods: Six dogs were sedated and maintained under anesthesia with 2% isoflurane and oxygen flow of 1 liter/min, allowing spontaneous respiration. A carotid artery catheter was placed aseptically over the tracheal area and secured with sutures. The animal was transported to the MR suite, located in a supine position and kept at 37° C with a heating blanket. A volume C-13 transmit coil and endorectal C-13/H-1 receive coil (Tropp et el, ISMRM 2006) were positioned and the animal was advanced into the bore of the 3T scanner. Polarizations were performed using the system developed at GEH and installed in a room adjacent to the 3T MR scanner. The amount of C-13 labeled pyruvate for each dog was calculated based upon delivery of 250 mM at a dose volume of 1.4ml/kg body weight. A 10 ml saline flush was used to ensure that the infusion line was emptied of pyruvate solution. Polarization was estimated at 19.7% ±1.4%. The injections were done automatically using an Ulrich Mississippi power injector. The MR protocol comprised 4 components: conventional fast spin echo imaging to define the anatomy; non-localized dynamic C-13 spectroscopy; 2-D C-13 spectroscopic imaging with conventional phase encoding (FastCSI) and 3-D C-13 echo planar spectroscopic imaging (3D EPSI).

Results: The endorectal coil provided excellent soft tissue contrast. Dynamic data comprised free induction decays with a sweepwidth of 5000Hz, 2048 points per FID, TR of 3 seconds, rectangular rf pulse with flip angle 5 degrees and 64 time points. The Figure on the left shows an example of the data acquired. The FastCSI data were acquired from six dogs as follows: 10mm axial slice, sweepwidth 5000Hz, 256 points per FID, TR 80ms, 8 cm field of view, 16x16 phase encode matrix, with centric encoding, variable increasing flip angle and total acquisition time of 17.1s. The FastCSI pulse sequence was used to obtain a single 10mm slice with 5mm x 5mm in plane resolution, with a matrix of 18x16x8. Conventional phase encoding was used in anterior-posterior and superior-inferior directions and echo planar encoding in the right-left direction. The k-t space trajectory gave a spectral bandwidth of 493Hz with 32 time points. Variable flip angles were used with centric phase encoding, TR 90ms and total acquisition time of 12s. The reconstruction and analyses of the C-13 MR data were performed using the SAGE package from GE Healthcare and a software package developed at UCSF Although some features needed to be adapted to accommodate the rapid acquisition and specialized features of the C-13 experiments, the basic architecture and display features of these packages were as described previously (Kohler et al, ISMRM 2006). The lactate peak occurred, on average, 14s later than the pyruvate peak. The average arrival time for the pyruvate was 26s. If these values were corrected for the time that it takes to clear saline from the injector, the arrival time would be 14s after injection and the peaks of pyruvate and lactate would be at 41s and 46s respectively. There were relatively low levels of alanine and bicarbonate in all dogs studied. The SNR for the FastCSI data varied from 154:1 to 361:1 for pyruvate and 25:1 to 67:1 for lactate. As expected the use of the fly-back trajectories provided a loss in signal to noise ratio of the order of 42-50% but the spectral quality was still excellent and they provided volumetric coverage.

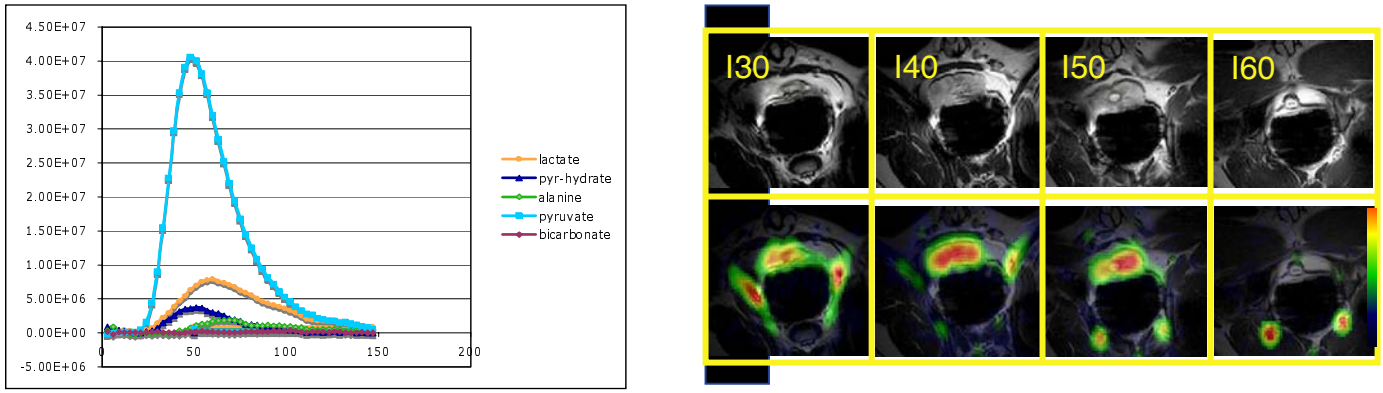

Figure: Dynamic curves of metabolite intensity obtained from a slice through the prostate and metabolite maps of pyruvate obtained using 3D EPSI.

Discussion: These studies have provided strong evidence for the feasibility of the hyperpolarized C-13 technology for evaluating in vivo metabolic processes in the prostate. FastCSI and 3D EPSI data show that pyruvate is taken up in the dog prostate and that some of it is converted into lactate. The observed levels of lactate are significantly lower than previously seen in studies of the rat kidney but were still detected by the 3D EPSI sequence with an isotropic spatial resolution of 0.125cc. Levels of alanine in the dog prostate were relatively low, which is consistent with previous measurements in human biopsies from normal, healthy prostate tissue. Further improvements in the MR data acquisition techniques, in conjunction with more sophisticated post-processing algorithms are likely to provide data with improved coverage and/or finer spatial resolution.

References: 1. Golman, K. et al. Proc Natl Acad Sci U S A 2006; 103:11270-11275., 2. Chen AP. et al. Proc., ISMRM, 14th Annual Meeting, #587., 3. Kohler S. et al, Proc., ISMRM, 14th Annual Meeting,, 4. Tropp et al, Proc., ISMRM, 14th Annual Meeting,.