Hyperpolarized ^{13}C 3D Metabolic Imaging with Stimulated Echoes for Flow Suppression

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Introduction: The Dynamic Nuclear Polarization (DNP) method for dissolution of hyperpolarized compounds has allowed for in vivo metabolic imaging, primarily done with hyperpolarized [1-^{13}C]-pyruvate [1]. One shortcoming of current hyperpolarized MRSI methods is that they do not distinguish between in-flowing labeled-metabolites and those generated within the region of interest. By using a stimulated echo (STE) [2], the magnetization can be stored longitudinally with spatial encoding, which is followed by a mixing time (TM) during which the spins can move and evolve before data acquisition. We are presenting a new stimulated echo method to isolate the source of metabolite conversion and increase the contrast for highly metabolically active tissues such as cancer.

Methods: Figure 1 shows graphically the STE pulse sequence. A 90º-90º and gradients first encode the magnetization longitudinally, and the crusher dephases any remaining transverse components. Some mixing time allows the spins to evolve, and then a progressive flip angle readout is used (for complete magnetization usage [3]) with an echo-planar spectroscopic imaging (EPSI) gradient (for rapid imaging) to acquire a 3D MRSI. Spins that move in any direction during the mixing time are not properly rephased and therefore do not significantly contribute to the image.

Animal experiments were performed on a transgenic mouse prostate cancer model with hyperpolarized [1-^{13}C]-pyruvate polarized using DNP in an Oxford Instruments Hypersense and imaged with a dual-tuned mouse coil in a GE 3T scanner. The STEAM dephasing gradients resulted in a spatial period of 1.25 mm in the longitudinal encoding, and this determines the flow sensitivity. The images were acquired 35 s after the start of injection with concentric k-space encoding, TE = 20ms, TM = 1 s, TR = 130 ms, 8x8x16 (EPSI) matrix, 7.5x7.5x7.5 mm resolution, and a 9 s acquisition time. The control 3D acquisition was the same except without any encoding STEAM gradients or 90º-90º pulses.

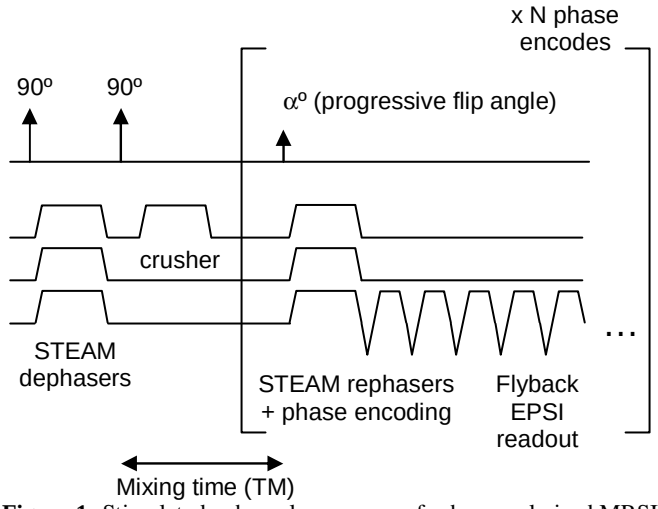

Figure 1: Stimulated-echo pulse sequence for hyperpolarized MRSI.

Results and Discussion: Figures 2 and 3 compare spectra acquired with and without a STE. There is an inherent SNR reduction of 29.3% due to the STEAM modulation, but the metabolite ratios were also significantly different between the experiments. This is most obvious in hyperpolarized pyruvate, due presumably to the fact that it is injected into the bloodstream and flows into the tissues of interest. In Fig. 2, hardly any metabolites in the STE acquisition were the seen in the chest slice (left), likely due to motion and flow in and around the heart. In the kidney voxels, which are accumulating and filtering fluids from throughout the body, pyruvate was reduced by 89.6%, while alanine and lactate were reduced by 53.1% and 66.2% respectively. The reductions were similar in the liver: pyruvate by 91.8%, alanine by 52.9%, and lactate by 65.8%.

The reduction in lactate was only 28.9% in the tumor voxels shown in Fig. 3, which is approximately the expected STEAM loss, but there was a 71.4% reduction in pyruvate. This implies that the ^{13}C-lactate is primarily generated in the tumor not from in-flow, while the reduction of pyruvate suggests the tumors have high vascular perfusion. These results demonstrate the ability of this method to increase the detection of metabolism differences between tumor and normal tissues, which could be of great future clinical value.

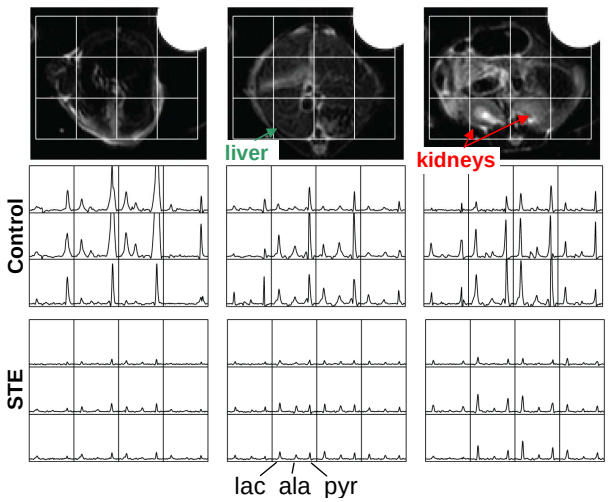

Figure 2: Phased spectra in slices from chest (left), liver (middle) and kidney (right).

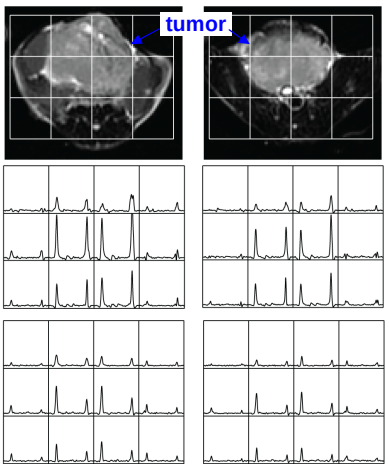

Figure 3: Slices in the prostate tumor. The lactate is relatively similar within the tumor, suggesting that it is better retained in tumor than in other tissues.

References:
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