Using Spectral-Spatial Saturation RF Pulses to Remove Blood Signals in Hyperpolarized Carbon-13 Metabolic Studies

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INTRODUCTION Dynamic Nuclear Polarization (DNP) of metabolically active carbon13-labelled substance has been reported as a method of generating MR images of *in vivo* cellular metabolism [1]. Since aggressive tumours are known to have increased metabolism, this has the potential to be a method for detecting aggressive cancer [2]. By injecting active, hyperpolarized 13C metabolites such as pyruvate, it is possible to visualize its transformation to alanine, lactate and other products that have distinctive MRI frequencies. However, in addition to the metabolites that are transformed locally, there are also metabolic products generated elsewhere that enter the tissue of interest via the blood stream, complicating analysis of the local metabolism. One method to eliminate the signals of the washed-in metabolic product into the region of interest is by employing a spectral-spatial (sp-sp) saturation radiofrequency (RF) pulse [3] (fig1) that saturates alanine and lactate but leaves pyruvate undisturbed.

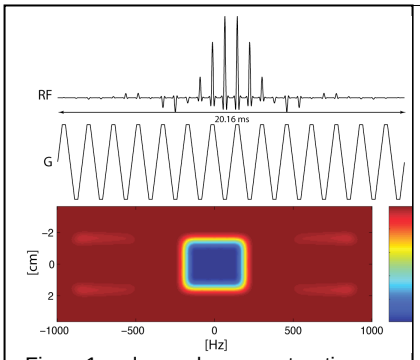

Figure1: pulse and sp-sp saturation profile. Longitudinal magnetization is null in the saturation band.

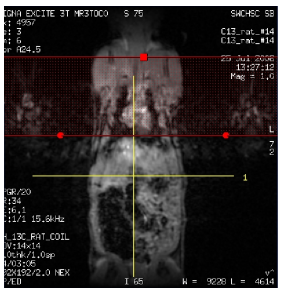

Figure2: Prescription of sp-sp saturation band red over the heart region on SPGR image (TRre34ms, TE6.1ms,flip angle 20deg)

METHODS Samples of [1-13C]pyruvic acid and 15mM trityl radical were hyperpolarized at 1.4K with a DNP hyperpolarizer (Oxford Instruments, Tubney Woods, UK). The sample was then rapidly dissolved with NaOH/Tris/EDTA buffer solution to a concentration of 80mM, and 2.5mL was injected into the tail vein of adult Sprague-Dawley rats (n=4) over 8 seconds. Data acquisition began at 6 sec after the start of injection. The experiments were performed on a GE Excite 3T MRI scanner with a dual-tuned transmit-receive rat birdcage coil. Twelve 15-mm thick slices were acquired using flyback echo-planar encoding with the 6th slice situated at the kidneys. The spectral-spatial saturation band was placed at the heart (fig2) to saturate alanine and lactate in the blood signal every TR (1s).

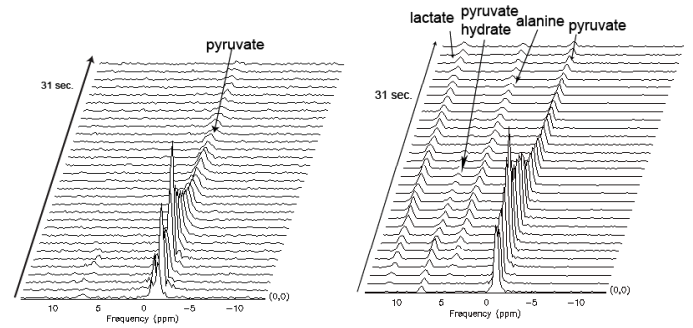

Figure3: Stacked spectral plot of heart slice with sp-sp saturation RF pulse (left) and kidneys' slice without the saturation pulse (right)

RESULTS The stacked spectral plots as a function of time at the saturated heart and unsaturated kidney slices are shown in figure 3. The 13C-labelled carbon signal transferred from the injected hyperpolarized pyurvate to lactate and alanine is eliminated in the saturated region that includes the heart. In the kidneys' slice, the lactate signal without the use of saturation band is 1.47+/-0.67 times of that with saturation (n=4). The signal for each metabolite and time point was computed by integrating the corresponding spectral line. These data were fitted to the modified Bloch equations for a three-compartment kinetic model:

$$dP/dt = -(k_{LP}+k_{AP}+k_{0P})P + R_A,\quad dL/dt = k_{LP}P - k_{0L}L,\quad dA/dt = k_{AP}P - k_{0A}A$$

Where P, L, and A denote the z-magnetizations of pyruvate, lactate and alanine, respectively; t is time, The peak integrals were least squares fitted to these equations with Matlab Mathworks to obtain the rate of pyruvate appearance R_A, conversion rate constants k_{LP} and k_{AP}, and the apparent spin lattice relaxation rates, k_{0P}, k_{0L} and k_{0A} (figure 4). The apparent pyruvate-to-lactate conversions, k_{LP} at the kidney slices are shown:

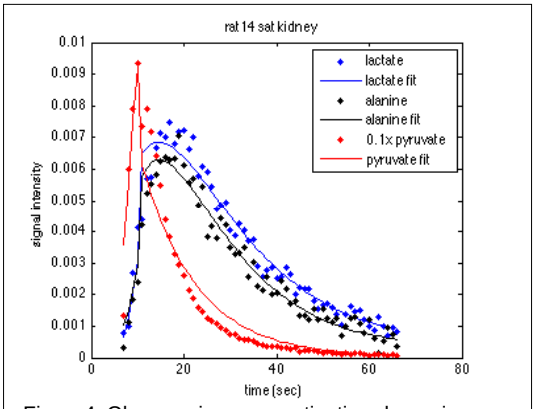

Figure4: Changes in z-magnetization dynamics fitted to a three-compartment kinetic model

Dataset	1		2		3		4	
Heart SAT	No	Yes	No	Yes	No	Yes	No	Yes
k_{LP} (s^{-1})	0.0142	0.013	0.0162	0.0136	0.0162	0.0141	0.0160	0.0180
R^2	0.9699	0.9848	0.9735	0.9508	0.9735	0.9788	0.9811	0.9661

DISCUSSIONS Using spectral-spatial saturation RF pulse, we observed a lower lactate peak integral curve at the kidneys because lactate that was produced at other sites and carried by the blood was saturated at the heart. This way, we can quantify the metabolites that were transformed locally, without signal contamination of washed in products. Fitting the data to the kinetic model described above (figure 4) revealed a difference in k_{LP}, the apparent local pyurvate-to-lactate conversion rate. Without saturation at the heart, k_{LP} values were contaminated by contribution of lactate washed into kidneys.

References: [1] Golman K et al., Proc. Natl. Acad. Sci. USA 2006,103:11270 [2] Golman K., Cancer Res 2006,66:10855 [3] Cunningham C., JMR 2008,193:146