Fast Chemical Shift Imaging of Hyperpolarized ^{13}C Substrates

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Introduction: While ^{13}C-labelled substrates such as glucose and acetate have been helped to elucidate cellular metabolism across a wide range of diseases using proton-decoupled ^{13}C spectroscopy [Ross, NMR Biomed 2003], its application is limited by a low Boltzman distribution. The use of hyperpolarized ^{13}C reagents via parahydrogen induced nuclear alignment (PASADENA-PHIP) [Bowers, Phys.Rev.Lett 1986; Golman, MRM 2001] has demonstrated 26,000 times increases in SNR [Bhattacharya, MAGMA 2005] however have a signal relaxation of 5x T1. The aim of this study is to utilize fast spectroscopic imaging pulse sequence to take advantage of this short-lived gain in SNR in *in vitro* and *in vivo* experiments.

Methods: A free induction decay ^{13}C chemical shift imaging pulse sequence (fastCSI) using spectral width of 5 kHz, 256 spectral points and repetition time of 85ms for a total scan time of 24 seconds for 16 encoding steps in a 16 cm^2 field of view. All data was acquired on a clinical 1.5T MR scanner (GE LX 9.1) equipped with a broadband amplifier. Initial chemical shift tests were made with solutions of 1-^{13}C-labelled glucose, acrylate and acetate. ^{13}C fastCSI was acquired *in vitro* and *in vivo,* of ^{13}C-labelled hyperpolarized hydroethyl propionate (HEP) with a 3M acetate phantom as a chemical shift reference.

Results:

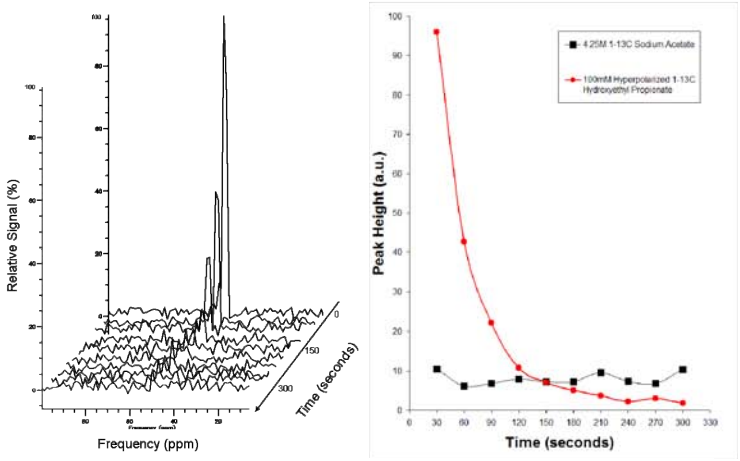

Figure 1. *Time Course of ^{13}C CSI of Hyperpolarized ^{13}C reagent. ^{13}C CSI readily demonstrates acquisition of the hyperpolarized signal with correct chemical shift, as shown in the stack plot of CSI spectra on the left, and demonstrable increase in SNR (right).*

Both 2D spectral reconstruction and metabolic maps were generated from the carbon-13 data acquisitions demonstrating accurate spatial and spectral reconstruction of phantom solutions (not shown). By repeated acquisitions of ^{13}C fastCSI, signal from propionate could be measured for up to 5 minutes post-hyperpolarization as shown in Fig 1. This demonstrates significant gains in sensitivity when compared to ^{13}C MRI that observed signal from the same experimental parameters for 30-60 seconds. Furthermore, ^{13}C CSI also distinguishes chemical shift as demonstrated in a dual infusion of both hyper-polarized ^{13}C propionate and ^{13}C cis-fumerate as shown in Figure 2.

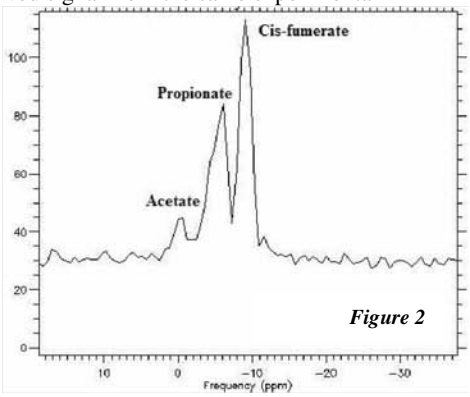

Figure 2

Preliminary results were achieved in *in vivo* rat studies with fast^{13}C CSI. Signal from the hyperpolarized reagent can be observed in the CSI reconstriction from the reference phantom and from the vena cava of the rat (Fig 3, left). Furthermore, due to the fast data acquisition times, we can also measure signal repeatedly *in vivo* thereby providing dynamic time courses (Fig 3,right).

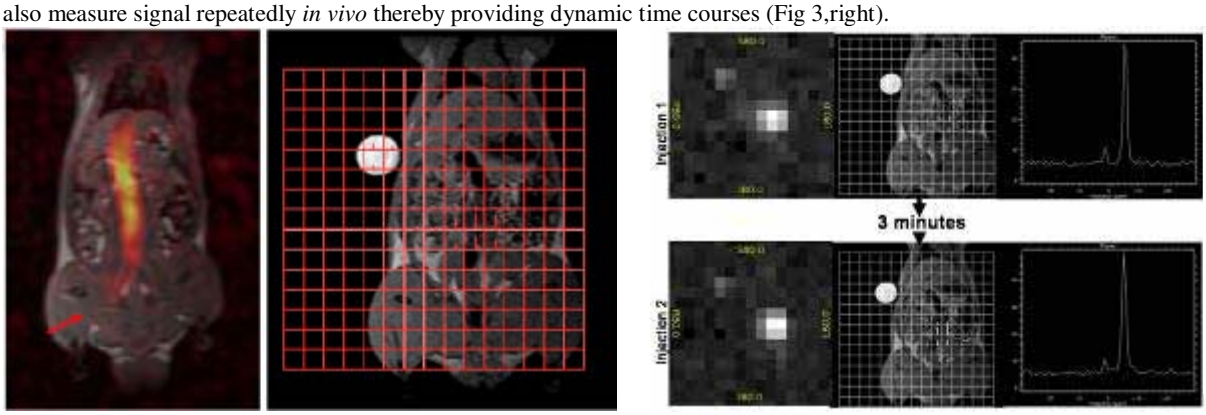

Figure 3. Left: *^{13}C MRI of hyperpolarized ^{13}C reagent..**Middle:** ^{13}C CSI of the same experiment. The CSI grid is overlaid over ^{1}H image. **Right:** ^{13}C CSI acquired with 1st injection (top) and 2nd injection three minutes later (bottom).*

Conclusion: Successful development of fast 13C CSI pulse sequence that can accurately detect ^{13}C a) signal intensity, b) anatomical location, c) chemical shift d) dynamic and repeatable time course. To our knowledge, this work is the first observation of PASADENA in vitro and in vivo using fastCSI on a GE 1.5T system. Observation of prolonged polarization with 13C CSI will permit metabolic flux measurements that were previously beyond detection

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