Chemical Shift Enhanced Acquisition of in vivo Hyperpolarized 13C Metabolism in 9.4T

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Introduction Hyperpolarized ^{13}C metabolic imaging and spectroscopy has been widely used to acquire metabolism kinetics between injected substrates and their downstream metabolites[1]. Many studies focused on imaging the signal *in vivo*, thereby providing spatially varying metabolite images depending on tissue/tumor type, etc[2-4]. At very high field strengths (beyond 3T) however, common imaging methods such as chemical shift imaging (CSI) is much more vulnerable to increased chemical shift displacement artifact resulting from wider spectral dispersion of the resonances, which results in severe chemical shift displacement artifact during slice-selective acquisitions. To overcome this, an acquisition method which instead utilizes the increased spatial displacement as the source of selectivity of substrate and downstream metabolites is presented. The amount of spatial shift was designed to push the excitation band out of the subject. Initial experiment was performed for ^{13}C metabolic imaging of *in vivo* mouse kidney in 9.4T.

Methods All experiments were performed on a 9.4T Bruker BioSpec 94/20 USR small animal imaging system (Bruker BioSpin MRI GmbH, Ettlingen, Germany) equipped with ^{1}H-^{13}C dual-tuned rat volume transmit/receive coil. For our proposed chemical shift 'enhanced' acquisition, slice-selection gradients were modified as shown in Fig 1 from conventional 3D chemical shift imaging (CSI) sequence. By using an elongated and polarity-switched slice-selection gradient, spatial chemical shift created by frequency difference between the metabolites can be alternately extended outside the subject, as shown in Fig 2. Frequency-selective metabolic images can then be acquired in an interleaved manner while exciting the target slice and the slice outside subject alternately. The amount of spatial displacement required to push the excitation band out of the subject was calculated from an axial reference ^{1}H image. To achieve 10mm displacement with 5mm slices and Δf of ~1.4kHz (pyr to lac), the required bandwidth was around 700Hz, which could be covered by a ~4.4ms Gaussian RF pulse.

For *in vivo* experiment, [1-^{13}C] pyruvic acid doped with 15mM Trityl radical and 1.5M Dotarem was polarized using HyperSense DNP polarizer (Oxford Instruments, Molecular Biotools, Oxford, UK). After dissolution into aqueous state, healthy balb/c nude mouse was injected with approximately 350ul of the hyperpolarized pyruvate solution through a tail vein catheter. All animal procedures were approved by the local Animal care and Use Committee. For anatomical localization, turbo-RARE ^{1}H MR images in the axial plane were acquired. Additional coronal slice through the kidneys were also acquired for overlaying the metabolic images. Chemical shift-'enhanced' ^{13}C CSI data were acquired using a TR of 100ms (50ms between pyruvate / lactate), with an in-plane resolution of 5mm (16x8 matrix), 5mm slice thickness and 10mm separation between slices. The CSI acquisition was started 13s after the start of pyruvate bolus injection, and the time between dissolution to beginning of injection was approximately 15s. The first excitation was targeted for lactate band placed through the target slice with 10° flip angle, and then pyruvate band was acquired in an interleaved manner with 5° flip angle. Centric phase encoding was applied for both kx and ky directions. The metabolite maps were generated by integrating respective spectral peaks using ±40 Hz of the phased real spectrum for lactate, and ±30 Hz for pyruvate, followed by bicubic interpolation. The same threshold level was applied for both lactate and pyruvate.

Results and Discussion Results of CSI acquisition shown in Fig 3 shows that the spectral selectivity of the proposed method is valid. Signal from lactate and other metabolites were completely suppressed in the pyruvate spectrum. In the case of lactate, small residual signal from pyruvate-hydrate (<7% of peak lactate) and pyruvate (<5% of peak lactate) can be observed. This may be the result of sidelobe contamination from the excitation RF pulse, which can be overcome during RF pulse design. Anatomical localization can be easily observed in interpolated metabolite maps as shown in Fig 4. Signal from lactate were primarily localized to kidney areas (Fig 4, left), whereas pyruvate displayed relatively more dispersed appearance over other regions (Fig 4, right). Although the resolution for CSI acquisition was limited to 5mm in this initial work, increasing the in-plane resolution can be achieved along with application of various fast imaging methods means such as elliptical k-space sampling or faster readouts such as spiral or radial. Using fast readout can allow actual imaging of ^{13}C metabolites, which remains as future work. Also, the proposed method can be applied to any slice-selection direction provided that the target slice is sufficiently close to the subject border to allow spatial displacement to be extended outside the subject. Potential application of this method therefore can be metabolic imaging in the brain, using axial slices. Lastly, the number of observable resonances with this method can be increased by choosing multiple slice-selection gradient duration / polarity combinations.

Conclusion A simple method for frequency selective acquisition of hyperpolarized ^{13}C metabolism *in vivo* for high field strength is presented. By utilizing the spatial displacement of resonances induced by the slice selection gradient, excitation bands of metabolites of interest can be alternately pushed out of the subject, thereby creating frequency selective images. Application of suggested method to conventional CSI sequence allowed effective signal suppression from neighboring frequency bands during the acquisition of single resonance, while providing sufficient spatial resolution to differentiate major signal sources of each metabolite.

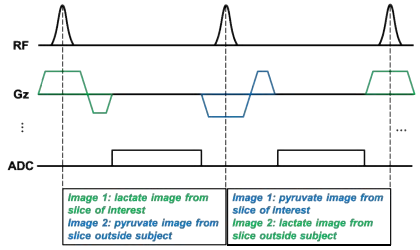

Figure 1: Pulse sequence diagram of proposed chemical shift enhanced acquisition scheme. Excitation bands of neighboring resonances are alternately pushed in and out of the imaging subject, acquiring 2 images each from 2 different slices.

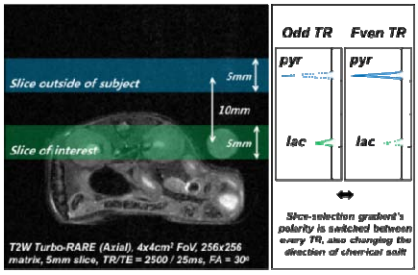

Figure 2: Slice positions and corresponding excitation band of metabolites. Lactate band is placed inside the subject at odd TRs, whereas pyruvate band is placed inside at even TRs.

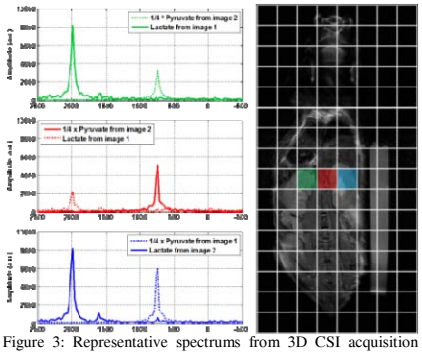

Figure 3: Representative spectrums from 3D CSI acquisition (magnitude). Highest lactate signals were observed at the kidneys, while highest pyruvate was seen from the vasculature.

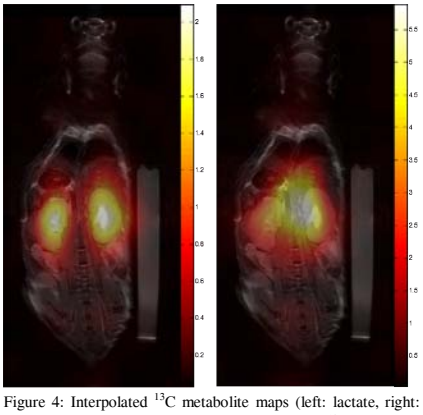

Figure 4: Interpolated ^{13}C metabolite maps (left: lactate, right: pyruvate) from injection of hyperpolarized [1-^{13}C] pyruvate overlaid on coronal ^{1}H MR image.

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