A Multi-compartment Phantom for Controlled and Heterogeneous Conversion of Hyperpolarized [1-13C]-Pyruvate to Lactate

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Target Audience

Investigators focused on quantitative imaging of hyperpolarized (HP) agents, including sequence design, optimization and validation.

Purpose

Assessment of HP metabolites like [1-^{13}C]-pyruvate by magnetic resonance shows tremendous promise as a powerful method to probe cellular metabolism *in vivo*. Advanced imaging and reconstruction techniques[1,2] have been proposed to extract as much information as possible given limitations inherent to the observation of HP agents[3]. However, for HP agents to achieve maximal impact imaging studies must accurately reflect the underlying processes being probed. A robust platform is necessary for efficient development, characterization, optimization, and validation of complex acquisition strategies. We recently characterized the repeatability of a single enzyme phantom for use as a reference standard for spectroscopic measurements of HP[1-^{13}C] pyruvate and its subsequent conversion to lactate [4]. While this model had many benefits for spectroscopic measurements, it lacked the spatial variability required to properly characterize imaging sequences and their ability to accurately detect spatially heterogeneous differences in activity. In this work, multiple compartments were used to provide dynamic signal evolution that is spatially and chemically heterogeneous.

Methods

Phantom Preparation: A mixture of 13 mg pyruvic acid containing 0.22 mg OX063 (GE Healthcare) and 0.03 µL ProHance was polarized using a HyperSense DNP system (Oxford Instruments). 0.3 mL of 40 mM HP [1-13C]-pyruvate was injected into each of two distinct phantom chambers. Regions of low and high relative activity were realized using a mixture containing 4.6 mM NADH, 203.3 mM Tris pH 7.6, 81.3 mM NaCl (Sigma) and either 2 U/mL or 7 U/mL lactate dehydrogenase (Worthington), respectively.

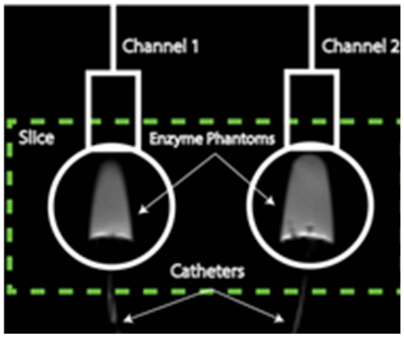

Figure 1: Schematic of spectroscopic acquisition.

***Imaging*:** Scanning was performed on a 7T/30cm Biospec system (Bruker Biospin MRI), with an actively decoupled dual tuned 1H/13C volume coil and two custom ^{13}C surface coils. Dynamic data was acquired simultaneously from both phantom chambers in the configuration outlined in Figure 1. A slice-selective pulse-acquire sequence (TR = 2 s, 10-deg flip angle, 4960 Hz BW, and 100 repetitions) was used for data acquisition. Spatial localization was achieved by the distinct coil sensitivities of two actively-decoupled 15-mm surface coils tuned to 13C. Each coil was connected to an independent channel of a custom broadband receiver. The volume coil was used for 1H imaging and 13C excitation. Imaging data was acquired with a similar setup, but with a volume coil instead of dual surface coils. Data was acquired with a 2D radial multiband frequency encoding sequence (TE/TR = 21.1/1000 ms, 200 projections, 15-deg flip angle, 12 readout points per band, 15-mm slice thickness[3]. Cumulative images were formed using filtered back projection.

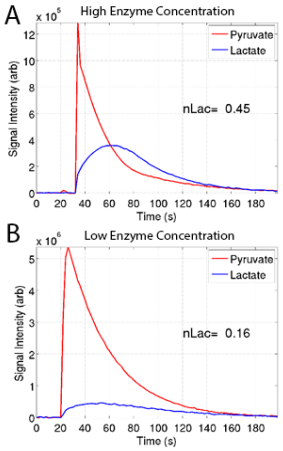

Figure 2: Time course spectral data from both High (A) and Low (B) enzyme concentration, corresponding to channel 1 and 2 in Figure 1 respectively

Results

HP lactate was detected in both compartments using dual surface coils. The size of the normalized lactate signal was a factor of 2.8 larger in the compartment designed to exhibit high activity. Imaging performed with the volume coil is shown in Figure 3. Again, strong lactate signal is imaged in one compartment which correlates with a weaker pyruvate signal. In the low enzyme compartment almost no lactate is observed, highlighting the potential for the threshold of detectability to be influenced by acquisition strategy.

Discussion

By utilizing multiple isolated compartments, different tissue types or stages of disease can be simulated using this enzyme phantom system. This design can mimic in a controllable manner some of the distinct spatial and kinetic properties seen *in vivo*.

Conclusion

This phantom model has many advantages for imaging sequence design, optimization, and validation. This system preserves the practical advantages of a tunable rate of conversion while creating a known spatial variability. Future improvements will include the inclusion of spatial structures within compartments to allow more precise characterization of measurements.

References

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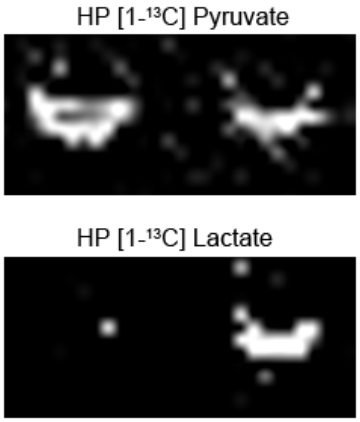

Figure 3: Average Pyruvate and Lactate signal for two compartments containing different LDH concentrations,