Improved Measures of Renal Pyruvate-to-Lactate Conversion using Diffusion Gradients

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INTRODUCTION

The rapid conversion of [1-^{13}C]pyruvate into lactate, alanine and bicarbonate has been used as a marker to assess a number of metabolic abnormalities, chief among them being cancer [1]. Dynamic imaging with pyruvate therefore holds potential for quantitative measurements of metabolism. However, in hyperpolarized ^{13}C experiments, signal from the vasculature often corrupts metabolite data due to flow and the large vascular pyruvate concentration interferes with modeling of kinetic parameters. In this work, we investigate the use of bipolar gradients to crush the signal contribution from vascular spins.

MATERIALS AND METHODS

Bipolar gradients were inserted into a spiral sequence developed for use on a 4.7T small animal scanner (Agilent, Palo Alto, CA, USA). Prior to ^{13}C experiments, ^{1}H images were acquired with multiple b-values by varying the diffusion gradient strength while holding the pulse timing constant. An optimal b-value was subsequently determined as the lowest value sufficient to crush the vascular signal. Scan parameters were TR/TE = 30/6.9ms, bipolar gradient duration δ = 2ms, G_{diff} = 0-28 G/cm. The b-values ranged from 0-52 s/mm^2 and were calculated as in [2].

For hyperpolarized studies, 30μL samples of [1-^{13}C]pyruvic acid/15mM trityl radical (OX63, GE Healthcare) were polarized for one hour (Tubney Woods, Abingdon, Oxfordshire, UK). Samples were subsequently dissoluted with 4mL of 100mM NaOH/Tris and 250mg/L EDTA. [1-^{13}C]pyruvate was drawn off and 10μL/g was rapidly injected into healthy ICR mice via tail-vein cannulation. ^{13}C data were acquired using a spiral readout with one echo per excitation, a readout duration of 41 ms, 5 echoes per dataset, and a voxel size of 2x2x10mm. A ΔTE of 1.19ms was chosen from NSA analysis. In-vivo experiments were performed with (TR/TE$_1$ = 55/7.0 ms) and without (TR/TE$_1$ = 55/0.55ms) diffusion gradients (G_{diff} = 36 G/cm, δ = 3.1ms) on all three axes. ^{13}C data were subsequently reconstructed with a least-square estimation technique [3].

RESULTS AND DISCUSSION

Coronal ^{1}H images of the kidney (**Fig. 1**) indicate that b = 17 s/mm^2 is sufficient to null signal from flowing spins in the renal and segmental arteries. Higher b-values were found to have a minimal effect on the vasculature while further attenuating static signals. Utilizing this diffusion weighting for in-vivo ^{13}C imaging of renal metabolism leads to a substantial decrease in vascular signal (**Fig. 2**), which is most evident when observing pyruvate (**Fig. 2A vs C**). SNR measurements of lactate in the kidney are similar for both experiments (42 and 40), indicating that the diffusion gradient has a minimal effect on static spins. Metabolite data fit to the two-site exchange model [4] show substantially different K_{PL} values, with whole kidney values of K_{PL} = 0.012 s^{-1} and 0.02 s^{-1} with and without diffusion gradients, respectively. We attribute this difference to reduced partial-volume contamination from vascular pyruvate.

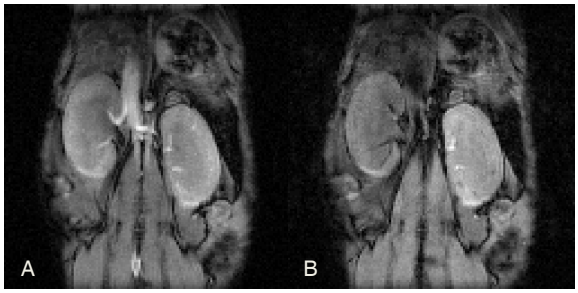

Figure 1. Coronal ^{1}H images in the absence (A) and presence (B) of bipolar diffusion gradients. Note the signal loss from the aorta, renal and segmental arteries that occur with a b-value of 17 s/mm^2.

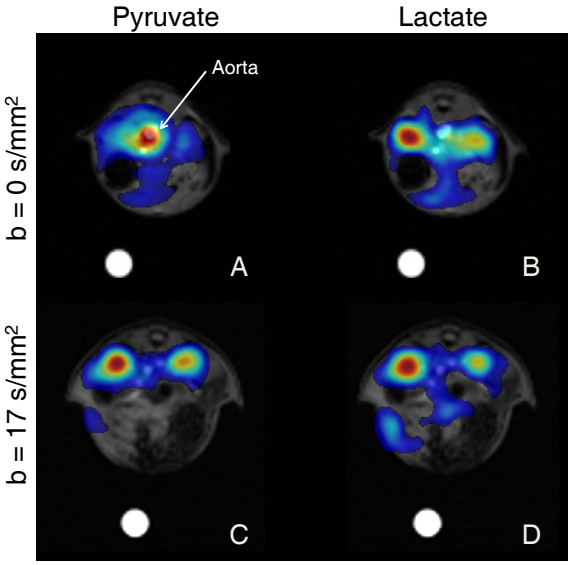

Figure 2. The effect of bipolar gradients on renal metabolism. The strong vascular pyruvate (A) and lactate (B) signals from the aorta lead to partial-volume effects with kidney voxels. The application of a bipolar gradient nulls the vascular pyruvate (C) and lactate (D) signals, increasing kidney conspicuity and mitigating partial-volume effects. Lactate images (B, D) remain relatively unaffected (SNR = 42 and 40, respectively), while kinetic rates are substantially changed. Metabolite maps are thresholded to 15% of maximum signal intensity.

CONCLUSION

In hyperpolarized ^{13}C experiments, accurate measures of metabolite dynamics are critical to assessing the disease state and health of the tissues of interest. However, accurate kinetic modeling can be corrupted by outside vascular signal that doesn't contribute to metabolism. By applying a bipolar gradient following excitation, flowing spins are nulled, removing contaminating signal from the vasculature and enabling a more accurate measure of metabolism. While the insertion of bipolar gradients leads to an increase in echo time, signal loss is mitigated by the long T_2^* of the hyperpolarized spins labeled in the C1 position.

ACKNOWLEDGEMENTS

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REFERENCES

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