^{1}H Decoupling Significantly Improves the SNR in HP Dihydroxyacetone Analysis of Liver Metabolism

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Introduction

One of the many responsibilities of hepatic metabolism is whole body glucose homeostasis. A direct assessment of hepatic gluconeogenic capacity in humans could powerfully augment standard diagnostic paradigms for a variety of hepatic pathophysiologies. Hyperpolarized pyruvate cannot readily estimate hepatic gluconeogenesis, as the assignment of the apparent product of phosphenolpyruvate carboxykinase flux, HCO_3^-, is also produced by pyruvate dehydrogenase flux [1]. We have previously shown that hyperpolarized [2-^{13}C]dihydroxyacetone (DHA) is a superior agent for assessing hepatic gluconeogenesis and glycolysis [2]. Here we aim to initially duplicate the previous results at higher field (9.4 T vs 14.1 T), which should provide resolution sufficient to disambiguate multiple DHA metabolites. As compared to results from last year, we have implemented proton decoupling to simplify the spectra of metabolites produced from DHA.

Experimental

Mouse livers were perfused on a column purpose built for use in NMR systems. The perfused liver was placed in a 14.1 T NMR (Bruker Avance IIIHD) equipped with a 18 mm broadband probe (AMRIS, UF, Gainesville). Shimming the magnet was accomplished using ^{23}Na signal from the liver. After 30 minutes of perfusion, hyperpolarized [2–^{13}C]DHA (produced by Oxford HyperSense) was injected into the liver and ^{13}C NMR spectra was recorded with a 3 s repetition time. Proton decoupling of the carbon-13 spectra was accomplished using WALTZ-16 [3].

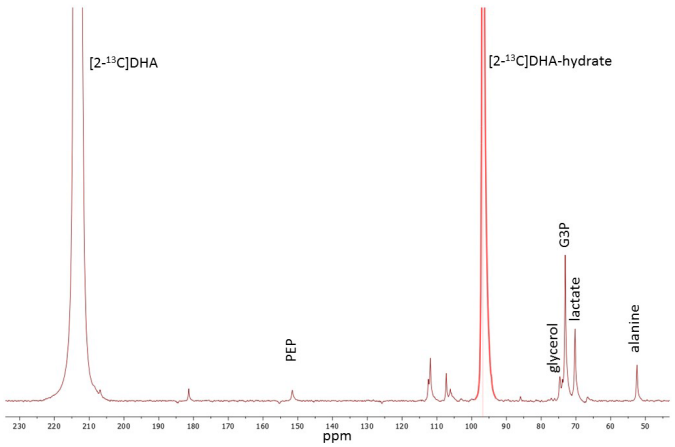

Fig.1 Sum spectrum of 25 individual scans from the perfused liver of a C57 BLKS mouse after injection with HP DHA. The spectral quality and the ability to assign peaks is significantly enhanced by the use of ^{1}H decoupling during the signal acquisition alone.

Results and Discussion

The spectra acquired with decoupling are significantly improved as compared to last year. We have become more proficient in the liver surgeries, and now readily also observe the [2-^{13}C]lactate and [2-^{13}C]alanine signals. Decouling removes the $^{1}J_{CH}$ that significantly reduced the detection limit for these metabolites prior to inclusion of the decoupling.

Conclusions

This project is being run by Alan Carter, a new masters student in my lab, and Dr. Ragavan, who has joined the BCH faculty at UF. Further testing of different metabolic conditions, including the addition of metformin to the perfusate, is funded by an NIH R01.

Acknowledgements

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References

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