Use of High Efficiency 20 mm NMR Probe for Studying Metabolism in Perfused Mouse Livers

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Introduction

Hyperpolarized (HP) dihydroxyacetone (DHA) has been shown to be a superior agent to probe hepatic metabolism using murine models [1]. Since DHA has several different metabolic fates, we have been using higher magnetic field (14.1T vs 9.4T) to better resolve the metabolites produced from DHA. Here, we describe preliminary results from the setup of a high efficiency 20 mm broadband probe to observe metabolism following injection of HP DHA.

Experimental

A 20 mm broadband probe was purchased from QoneTec (Switzerland) and installed in a 14.1 T NMR magnet equipped with Bruker Avance IIIHD console (AMRIS, UF). For the purposes of probe setup, a sample containing 40 mM each of [U-^{13}C] acetate and [U-^{13}C] glucose was used.

Results and Discussion

The QoneTec 20 mm probe showed increased efficiency on both ^{13}C and ^{1}H RF channels (^{13}C 90° pulse length of 65 µs at 73 W compared to 200 W needed for the currently used probe). Since we use a 45° {x, -x} binomial pulse for detection of metabolism, we tested the excitation profile using a test sample as shown in Figure 1. It can be seen that there is no change in intensity of glucose resonances between the two traces indicating a uniform excitation profile obtained from probe matching calculated profiles. In addition to ^{13}C, we have also measured satisfactory ^{23}Na and ^{31}P spectra using this probe.

We are now able to use this setup to record preliminary spectra of liver metabolism following injection of hyperpolarized dihydroxyacetone.

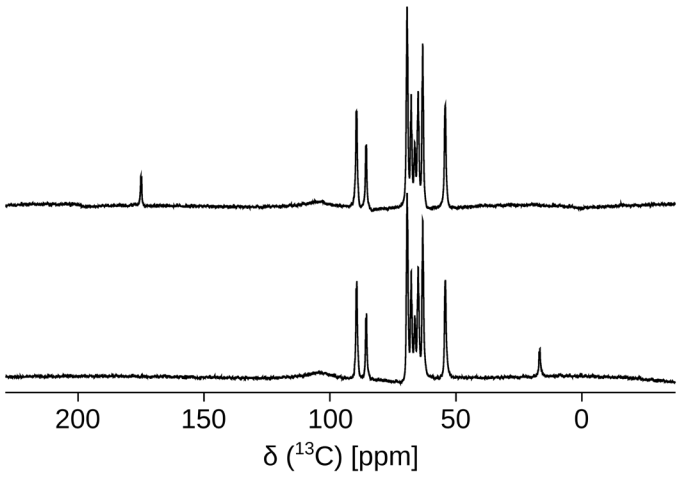

Figure 1: Performance of a 45° {x, -x} binomial pulse centered at C-1 of acetate (181 ppm; bottom trace) and C-2 of acetate (21 ppm; top trace). 90° pulse length was 65 µs at 73 W. ^{13}C spectra were acquired with ^{1}H decoupling (WALTZ-16) during acquisition.

Conclusions

The performance of the new 20 mm NMR probe offers promise to study hepatic metabolism. The higher sensitivity on offer will likely enable to us to record and identity low abundance metabolites in these studies. Utilizing a 20 mm probe is beneficial in ensuring the integrity of the perfused livers since larger diameter tubes does not physically constrain the tissue.

Acknowledgements

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References

[1] Karlos X. Moreno, Santhosh Satapati, Ralph J. DeBerardinis, Shawn C. Burgess, Craig R. Malloy, and Matthew E. Merritt. 2014. Real-time Detection of Hepatic Gluconeogenic and Glycogenolytic States Using Hyperpolarized [2-13C] Dihydroxyacetone. *J. Biol. Chem.* 289, 52, 35859–35867.