

ORAL PRESENTATION

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Myocardial fatty acid metabolism probed with hyperpolarized [1-¹³C]octanoate

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From 18th Annual SCMR Scientific Sessions
Nice, France. 4-7 February 2015

Background

The heart normally derives most of its energy from the oxidation of fatty acids. Myocardial metabolism can be monitored non-invasively by MRS using hyperpolarized (HP) ¹³C-labelled compounds; however, the vast majority of studies reported have used HP pyruvate and did not measure fatty acid catabolism. The myocardial metabolism of HP [1-¹³C]butyrate and [1-¹³C]acetate has been reported. The conversion of these short-chain fatty acids to acetyl-CoA does not involve successive rounds of beta-oxidation, as is the case for longer chain fatty acids, which are a more important source of cardiac energy. In this study we examined the applicability of hyperpolarized [1-¹³C]octanoate, a medium-chain fatty acid, as a probe of myocardial metabolism.

Methods

[1-¹³C]octanoic acid (4 M in DMSO, doped with stable trityl radical) was polarized by microwave irradiation (196.8 GHz) at 7 T & 1 K. After dissolution with superheated buffered D₂O, ~0.04 mmol was infused via a femoral vein catheter into anesthetized Wistar rats in a 9.4 T horizontal bore scanner (Varian) and a series of single pulse (BIR-4, 300, TR ~3 s) gated ¹³C MRS acquisitions was performed with a surface coil positioned over the heart. To aid metabolite identification, HP [1-¹³C]acetate and/or ¹³C-urea were coinfused in several experiments.

Results

After dissolution, [1-¹³C]octanoate polarization level and T₁ relaxation rate were ~11% and 29 ± 3 s, respectively. In vivo, the octanoate signal decayed rapidly and was no

longer measurable 20-36 s after the start of infusion. Interactions with blood proteins such as serum albumin are likely responsible for the rapid loss of signal, and the T₁ in blood ex vivo was ~9.6 ± 0.5 s. One metabolite peak at 175.4 ppm, was consistently observed (Fig 1). Summing the FIDs where octanoate was present and integrating the peaks, the metabolite had 1.49 ± 0.20% the area of octanoate C-1 (n=5). The chemical shift of the metabolite was assigned to [1-¹³C]acetylcarnitine. This was confirmed by infusing HP [1-¹³C]acetate and observing [1-¹³C]acetylcarnitine with the same chemical shift, as well as coinfusing HP [1-¹³C]acetate and [1-¹³C]octanoate and observing a single metabolite peak for [1-¹³C]acetylcarnitine.

Conclusions

This study demonstrates that in-vivo dissolution DNP metabolic experiments can be performed with ¹³C-labelled medium-chain fatty acids. Sufficient ¹³C polarization in octanoate survives circulation, tissue uptake, mitochondrial transport and conversion by beta-oxidation to acetyl-CoA to be detectable in the acetylcarnitine pool. HP octanoate can be used to directly probe the beta-oxidation of metabolically important fatty acids in the heart.

Funding

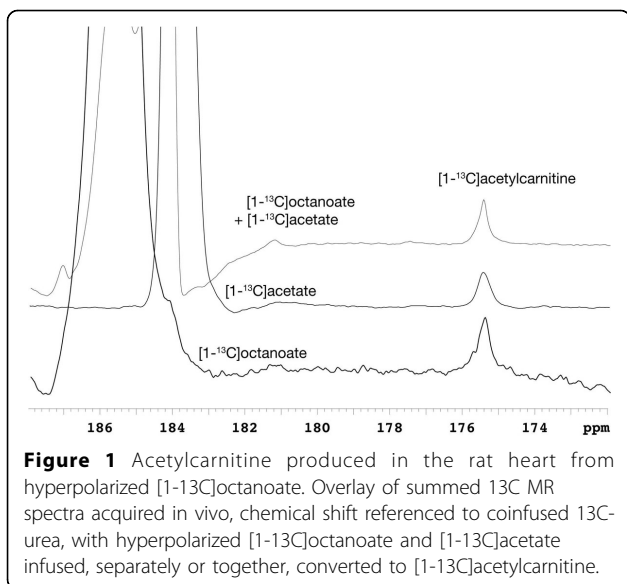
Work supported by the Swiss National Fund (grants #138146 & PPOOP1_133562).

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Published: 3 February 2015

doi:10.1186/1532-429X-17-S1-O101

Cite this article as: Yoshihara *et al.*: Myocardial fatty acid metabolism probed with hyperpolarized [1-¹³C]octanoate. *Journal of Cardiovascular Magnetic Resonance* 2015 **17**(Suppl 1):O101.

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