Clinical 3.0 T ^{13}C MRS: Net Hepatic Glycogen Breakdown during 19 hr Fast

Paul Begovatz[1], Sabine Kahl[1], Bettina Nowotny[1], Juergen Bunke[2], Michael Roden[1,3], and J.-H. Hwang[1]

[1]*Institute of Clinical Diabetology, German Diabetes Center, Duesseldorf, Germany,* [2]*Philips Healthcare, Hamburg, Germany,* [3]*Department of Metabolic Diseases, University Clinics, Heinrich Heine University, Duesseldorf, Germany*

Introduction:

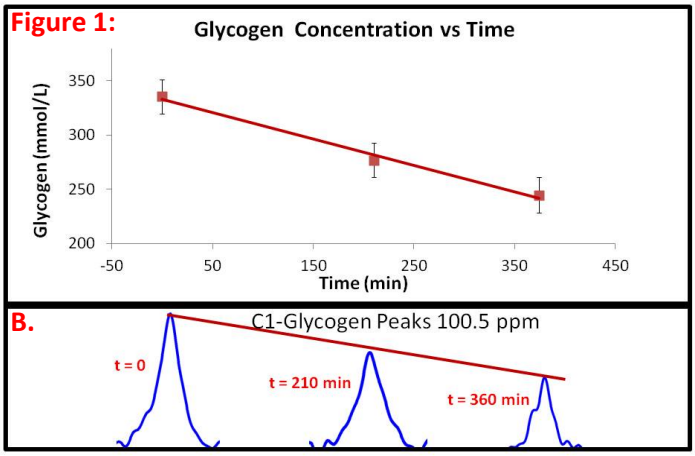
The assessment of hepatic glycogen fluxes is of great interest regarding the pathophysiology of metabolic diseases like type 2 diabetes [1]. ^{13}C MRS is the only method to non-invasively measure changes in net hepatic concentrations, with experiments traditionally conducted on MR-systems designed for spectroscopy [2]. Results with clinical scanners prove more challenging due to limited ranges of sequence parameters and RF pulses. However, the expansion to FDA approved scanners could play a vital role in clinical research [3]. Therefore, the goal of this study was to develop a robust ^{13}C MRS method to detect net hepatic glycogen breakdown on a 3.0 T clinical scanner.

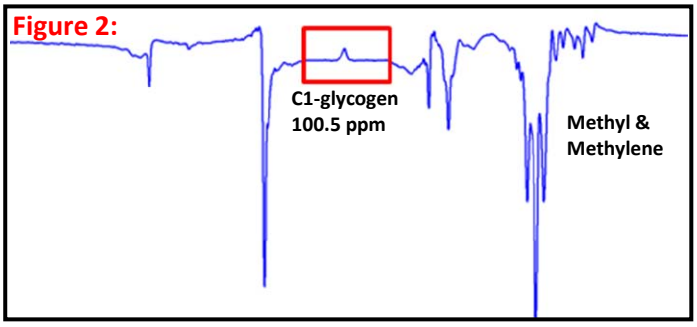
Subjects:

Healthy, lean volunteers (n = 7, Age: 26±1 yr, BMI: 21.9±0.8 kg/m^2), maintained a diet of 60% carbohydrates for three days prior to the study. On the night before the 19 hr fast, a 800 kcal meal was consumed.

Materials and Methods:

^{13}C liver glycogen MRS measurements were made the next morning at 13 hr (Figure 1: t = 0), 16.5 hr, and 19 hr into the fast. A 7 cm ^{13}C coil with ^{1}H decoupling (PulseTeq, UK) was positioned over the liver and verified with scout images. Pulse acquire measurements (TR: 230 ms, BW: 8 KHz, NSA: 4000, decoupling: CW, scan time: 15 min) with a COV = 12% [4] were acquired on a 3.0 T Achieva MRI (Philips Healthcare, The Netherlands). Coil loading was corrected via integration of the right most peak of a ^{13}C enriched sample of formic acid placed in the coil housing. Glycogen concentration was determined from the integration of the C1-glycogen resonance after the addition of two scans (2 x 4000) (NUTS, Acorn NMR Inc, USA). The glycogen signal was corrected for distance, and quantified via aqueous glycogen phantom measurements of 70 and 140 mM measured at a distances of 15-37 mm. Corrections for liver volume were made with a high resolution T2 weighted turbo spin echo sequence.





Results:

A ^{13}C MRS spectrum with the proton decoupled C1-glycogen peak (Figure 2) is shown along with the inverted methyl and methylene peaks from adipose tissue. Examples of typical glycogen peaks are depicted in Figure 1B. Glycogen concentrations were detected with SNRs ranging from 32:1 at 514 mM, to 5:1 at 106 mM (Figure 1), with an average linewidth of 58.77±6.98 Hz. Liver volume corrected rates of net hepatic glycogen breakdown were 5.53±0.22 µmol/kg$_{BW}$/min (mean ± SEM), with a range of 3.16-7.44 µmol/kg$_{BW}$/min.

Discussion:

A method for accessing net hepatic glycogen breakdown through ^{13}C MRS on a 3.0 T clinical scanner is shown. In vivo hepatic glycogen peaks were measured at SNRs that allowed for reproducible and accurate absolute quantifiaction. Results of net hepatic glycogen breakdown, corrected for liver volume and body weight, were also consistent with previous studies [1,5]. These findings prove that methods outlined here can be implemented for use in clinical studies, to detect changes in the rate of net hepatic glycogen breakdown caused by intervention in healthy lean subjects.

References:

1. Kacerovsky M et al, Diabetes (2011). 2. Rothman DL et al, Science (1991). 3. Flück C et al, Pediatric Diabetes (2003).
4. Begovatz P et al, ESMRMB abstract #92 (2012). 5. Bischof M et al, Diabetes (2002)