Hepatic glycogen signal detection in rats using Gaussian-weighted phase encoding C-13 MR spectroscopic imaging

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Introduction: In mammals, carbohydrates are primarily stored in the form of hepatic glycogen. The content and synthesis/breakdown rates of hepatic glycogen in animal models can provide crucial information for diabetes research as well as a potential marker for the vitality of hepatocytes (e.g. after hepatocyte transplantation). In order to detect the 13C glycogen signal, Jucker et al. and Choi et al utilized single voxel, or 1-dimensional [1-D] ISIS to localize hepatic glycogen for ^{13}C MR spectroscopy in rodents [1,2]. Due to the very small object size as well as low signal-to-noise ratio (SNR) at natural abundance of ^{13}C, exogenous ^{13}C -glucose labeling was needed to detect ^{13}C glycogen in rodents [1,2]. Thus, the goal of our work was to develop a 1-D Gaussian-weighted *k*-space encoding SI in order to improve SNR for glycogen detection in rats so that we could, 1) detect glycogen signal *without* any exogenous ^{13}C-enrichment while also conserving efficiency of localization and, 2) follow up changes in glycogen signals after a delivery of 1-^{13}C acetate in order to set up a method for future dynamic studies.

Methods: Instrumentation: 9.4 T Varian horizontal bore, animal MR spectrometer. RF coils: A home-built, 2-cm circular ^{13}C coil and a 3.2 cm square butterfly ^{1}H MRI coil for anatomic localization (for the liver) and proton decoupling. The B1 fluxes of the two coils are perpendicular to facilitate efficient ^{1}H-^{13}C decoupling.
Gaussian-weighted phase-encoded CSI: As a first step, before implementation of the SI method, we evaluated the spatial localizing efficiency by comparing the point spread functions (PSF) of Gaussian-weighted and conventional encodings. For the Gaussian-weighted sampling scheme, a total of 137 encoding steps were used over 16 *k*-space values. The resulting PSF for Gaussian-encoding showed very little contamination outside the slice of interest.
Animal experiment: A total of 5 rats were studied with a slow 1-^{13}C-aectate i.p. delivery by a bolus injection by a syringe or a pump. A normal Sprague-Dawley rat (~300g) was intubated and anesthetized with isofluorane through a respirator. Both coronal and transverse images gradient echo images [TE=6 msec] were acquired to confirm liver position. The repetition time of the images were gated by respirator to remove breathing motion artifact. The {^{1}H}^{13}C MR SI sequence was performed using a repetition time of 0.9 sec, 100 μsec non-selective excitation pulse, 30K Hz sweep width and 4096 complex points. The CSI was both obtained before and after the delivery of 1-13C-acetate. Proton-decoupling was performed using the WALTZ-16 centered at ~5.2 ppm in ^{1}H spectra. A field of view of 6.4 cm with 16 phase-encoding steps resulted in a 1-D nominal voxel resolution of 0.4 cm (equivalent to the slice thickness).

Results and Discussion: Figure 1 shows coronal and transverse images of the liver obtained by the surface coil. The dashed circle indicates the actual size and position of the ^{13}C coil relative to the liver. Figure 2 shows the C-1 glycogen peak before any enrichment of exogenous ^{13}C-labeled acetate. Figure 3 shows glycogen C2-5 enriched by i.p. delivery of 1-^{13}C-acetate after 6 days (top spectrum) in contrast to the natural abundance C2-5 region of glycogen (bottom spectrum). In conclusion, using 1-D ^{13}C SI with Gaussian-weighted phase-encoding at 9.4T, we were able to observe natural abundance ^{13}C-1 glycogen resonance without any ^{13}C labeling. To our knowledge, this is the first demonstration of ^{13}C glycogen in rat liver without exogenous ^{13}C labeling. The SNR of C-1 glycogen at 100.5 ppm from one extracted spectrum [Figure 2] was ~10:1, and approximate localized volume was ~0.5 cc. In addition, increased signal intensities in the C-1 and C2-5 region of glycogen signals after labeling were detected.

Refs 1. Jucker BM et al, J Biol Chem, 15: 12187-94,1998, 2. Choi IY et al Eur J Biochem, 269:4418-26,2002.
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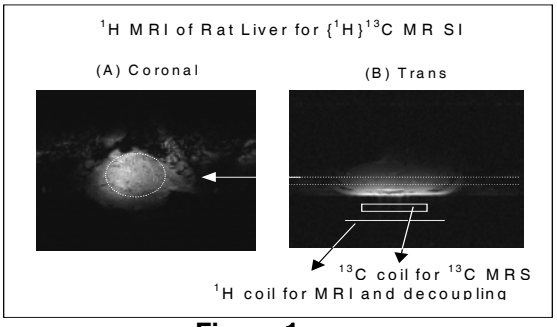

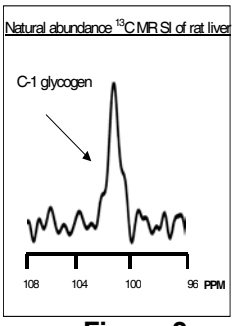

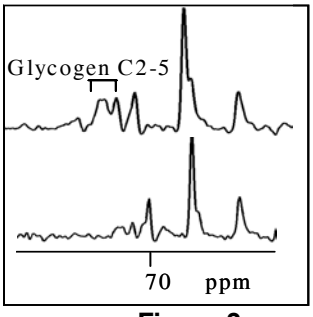

Figure 1 **Figure 2** **Figure 3**

Figure 1: Representative coronal and axial proton images of rat liver showing relative size and position of surface coils.
Figure 2. Natural abundance 1-13C glycogen spectrum from rat liver. Figure 3. The comparison of C2-5 region of glycogen before and after 1-13C-acetate.