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 13C 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 13C, exogenous 13C-glucose labeling was needed to detect 13C 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 13C-enrichment while also conserving efficiency of localization and, 2) follow up changes in glycogen signals after a delivery of 1-13C 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 13C coil and a 3.2 cm square butterfly 1H MRI coil for anatomic localization (for the liver) and proton decoupling. The B1 fluxes of the two coils are perpendicular to facilitate efficient 1H-13C 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 1-13C-acetate 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 (1H)13C 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 1H 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 13C coil relative to the liver. Figure 2 shows the C-1 glycogen peak before any enrichment of exogenous 13C-labeled acetate. Figure 3 shows glycogen C2-5 enriched by i.p. delivery of 1-13C-acetate after 6 days (top spectrum) in contrast to the natural abundance 13C-1 glycogen resonance without any 13C labeling. To our knowledge, this is the first demonstration of 13C glycogen in rat liver without exogenous 13C 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 conclusion, using 1-D 13C SI with Gaussian-weighted phase-encoding at 9.4T, we were able to observe natural abundance 13C-1 glycogen resonance without any 13C labeling. To our knowledge, this is the first demonstration of 13C glycogen in rat liver without exogenous 13C labeling.

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