Non-CPMG Echo-Train Sequence for T_2 Mapping and Large SNR Gain in Hyperpolarized ^{13}C Imaging

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Introduction Previous studies showed long transverse relaxation times (T_2) of ^{13}C labeled metabolites in a transgenic mouse model of prostatic adenocarcinoma (TRAMP) [1] and hepatocellular carcinoma tumors [2], suggesting that T_2 of ^{13}C metabolites may be a promising metric for cancer diagnosis using hyperpolarized ^{13}C MR. The technique to measure T_2 of the non-recoverable ^{13}C metabolite signal was limited to a single voxel per injection and large voxel size (1.6 cc) [2]. To increase the diagnostic value of ^{13}C metabolite T_2, it is useful to map T_2 with good spatial resolution. Here we report a new MR pulse sequence for high-resolution T_2 mapping of multiple ^{13}C metabolites. The same sequence was also used to gain signal-to-noise ratio (SNR) by averaging the echo-train signals.

Method The pulse sequence was composed of a 90° spectral-spatial excitation RF pulse, followed by a train of spectrally selective, spatially non-selective 180° refocusing RF pulses with non-CPMG [3,4] phase schemes and EPI readouts. The sequence was used to acquire image of one slice from one ^{13}C metabolite at a time, which was then repeated with frequency offsets to acquire other ^{13}C metabolites of the same slice. The spectral selectivity was ±80 Hz and maximum B_1 0.2 Gauss for all RF pulses. Minimum slice thickness was 15 mm when using clinical gradients (40mT/m and slew rate 150mT/m/ms) but by using a high-performance gradient insert [5], 2 mm was achieved. The echo spacing was 60 ms and 32 echoes were acquired. The scan time was 2 s per metabolite. *In vivo* data were acquired on normal rat liver, TRAMP and rat glioma models, following IACUC approved protocols. 3 mL of 80 mM hyperpolarized [1-^{13}C]pyruvate was injected into normal rats, 0.3 mL of 80 mM into TRAMP mice and 3 mL of 125 mM into glioma rats. Scans started 24 s after the start of injection. All experiments were performed by using a custom-built $^{1}H/^{13}C$ quadrature coil [6] on a 3T clinical MR scanner (Signa™, GE Healthcare, Waukesha, WI). T_2 maps were obtained by fitting the echo-train magnitude images pixel-by-pixel with a mono-exponential decay curve after noise corrections were made [7]. SNR gain was estimated by comparing the SNR of the first spin-echo to both a linear sum of 32 echoes and to the sum of 32 echoes weighted by an exponential decay using the lactate T_2.

Results Large ^{13}C signals were observed for most metabolites and the quality of fit was good (Fig. 1). T_2 of healthy rat liver was consistent with the previous single-voxel results [1]. Heterogeneous T_2 values were observed from TRAMP tumor (Fig. 1), although it appeared homogeneous on proton image. The T_2 fitting errors were approximately ±200 ms (not shown). This sequence was also used to image SNR-challenging metabolites, such as ^{13}C bicarbonate in brain (Fig. 2). From a thin slice of 2.75 mm, SNR of 6:1 was obtained within the contralateral side, where bicarbonate signal was expected to be larger than that in glioma. On the contrary, lactate signal was larger in glioma than the contralateral side, in agreement with Warburg Effect. Compared to the first echo, linear sum over 32 echoes had an SNR gain of approximately 2.5 fold and weighted sum approximately 3 fold.

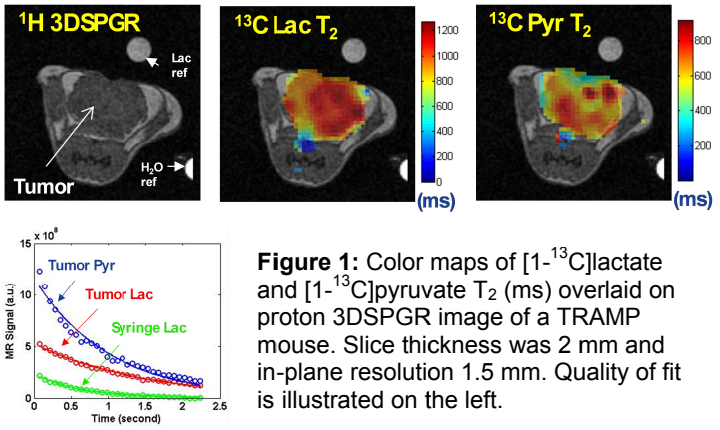

Figure 1: Color maps of [1-^{13}C]lactate and [1-^{13}C]pyruvate T_2 (ms) overlaid on proton 3DSPGR image of a TRAMP mouse. Slice thickness was 2 mm and in-plane resolution 1.5 mm. Quality of fit is illustrated on the left.

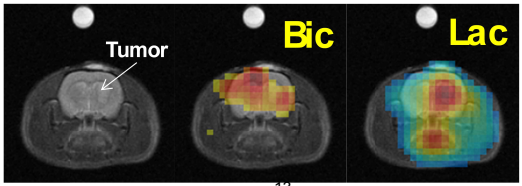

Figure 2: Good signal of ^{13}C-bicarbonate and [1-^{13}C]lactate on a rat glioma model acquired with isotropic resolution of 2.75 mm.

Conclusion This work reports a novel sequence for high-resolution T_2 mapping of multiple hyperpolarized ^{13}C metabolites in a single injection. It also has a large SNR advantage when summed over all echoes. Further studies are needed to understand physiological or physical basis for the T_2 variation in malignant tumors vs. normal tissues.

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Reference: 1) Y-F. Yen, et al., Proceedings of the 16th ISMRM, Toronto, Canada, 2008; p.1747. 2) Y-F. Yen, et al., NMR Biomed, 2010; 23(4):414-23. 3) P. Le Roux. J Magn Reson 2002; 155:278. 4) P. Le Roux, et al. ESMRMB 2009; p.114. 5) B. Chronik, et al. Magma 2000; 10(2):131-146. 6) K. Derby, et al. J Magn Reson 1990; 86:645. 7) R.M. Henkelman. Med. Phys. 1985; 12(2):232–233.