Imaging of Tumor Glycolysis with 2D Heteronuclear Multiple Quantum Coherence: Accelerated Acquisitions using Compressed Sensing

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Target audience: Researchers interested in the study of metabolism.

Purpose: We reported MRSI combined with 2D ^{1}H-^{13}C heteronuclear multiple quantum coherence (HMQC) for imaging glucose metabolism in the tumor.[1] Although this technique has a potential to provide rich information about *in vivo* metabolism, the extremely long acquisition time is a major drawback. The purpose of this study is to image metabolic dynamics with 2D-HMQC MRSI accelerated by using compressed sensing (CS).

Methods: Our objective is to estimate spatio-temporal changes in densities of substances via 2D-HMQC MRSI. Ideally, the spectrum at spatial position (x, y) at time t is a linear combination of the spectra of the substances, as

$$D_0(F_1, F_2, x, y, t) = \sum_{p=1}^{P} \Phi_0(F_1, F_2; p) S_0(x, y, t; p)$$

where P is the number of different types of substances to be considered, Φ_0 is the spectrum of substance p at (F_1, F_2), and S_0 denotes the density of substance p at spatial position (x, y) at time t. We write this relation abstractly as $D_0 = \Phi_0 S_0$. The whole data acquisition process, including the undersampling as well as noise, is represented abstractly as $K = U\mathcal{F}(\Phi_0 S_0) + W$, where K is the actually acquired data contaminated by measurement noise W, U is the undersampling operator, and $\mathcal{F}$ denotes the discrete Fourier transform operator. CS allows us to estimate S_0 from K via solving the minimization problem

$$\min_{S_0}(\|K - U\mathcal{F}(\Phi_0 S_0)\|_2^2 + \lambda_{\mathrm{s}}\|S_0\|_1 + \lambda_{\mathrm{fd}}\|DS_0\|_1)$$

where λ_{s} and λ_{fd} are regularization parameters, D is an operator which calculates differences between adjacent time frames, and $\|X\|_{\mathrm{n}}$ is the l_{n} norm. To alleviate computational difficulty in solving this problem, we used a heuristic algorithm based on a modified version of complex approximate message passing (CAMP).[2] The MR scans were performed on a Bruker 7T MR system (BioSpec 70/20 USR) using a double resonant ^{1}H/^{13}C transmit-receive volume coil. A standard chemical shift imaging (CSI) combined with the gradient enhanced HMQC based preparation was used as a basic pulse sequence.[1] The following experimental parameters were used: TR/TE=990/9.6ms, 8 and 16 phase encoding steps for k_x and k_y dimensions, respectively, FOV=4×8cm^2, coronal orientation without slice selection, 256 complex points with an F_2 bandwidth of 2000Hz (^{1}H direction), 32 points with an F_1 bandwidth of 8000 Hz (^{13}C direction), and 4-step phase cycling. This pulse sequence requires ~4.5hr to acquire 4096 FIDs, which constitute of fully sampled data set $K_0(t_2, k_x, k_y, t_1)$. In this study, the k_x, k_y, and t_1 dimensions were undersampled according to the sampling pattern determined by a Sobol sequence.[3] The MRSI was performed for the tumor-bearing mice after intraperitoneal bolus injection of [U-^{13}C]glucose solution. Data acquisition was continued until 2048 FIDs were collected, which took ~2.3hr. As a reference for metabolic dynamics, non-localized whole-body 2D-HMQC spectra were acquired before, after and at the middle of MRSI measurements (scan time ~1min, 2-step phase cycling). We divided the acquired data set into 4 time frames and estimated the time variation of S_0 for glucose, lactate, and fat, and then mapped them. Prior to estimation, the substance basis Φ_0 was identified from 2D-HMQC spectra acquired additionally from the mouse after the MRSI measurements (scan time ~2min, 4-step phase cycling).

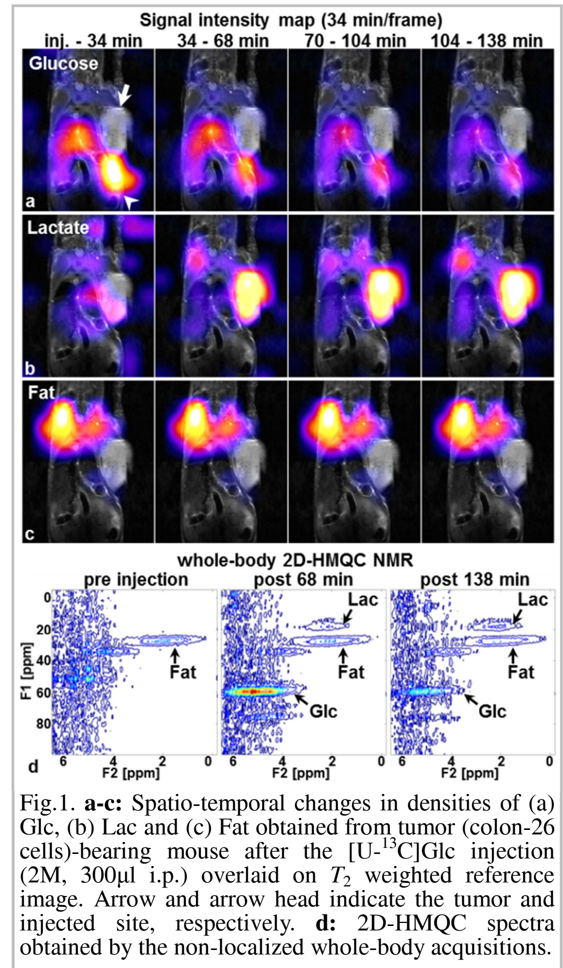

Fig.1. **a-c:** Spatio-temporal changes in densities of (a) Glc, (b) Lac and (c) Fat obtained from tumor (colon-26 cells)-bearing mouse after the [U-^{13}C]Glc injection (2M, 300µl i.p.) overlaid on T_2 weighted reference image. Arrow and arrow head indicate the tumor and injected site, respectively. **d:** 2D-HMQC spectra obtained by the non-localized whole-body acquisitions.

Results and Discussion: The estimated results are shown in Fig.1a-c. Glucose map at the first time frame shows that the glucose was measured at the injection site with high signal intensity and distributed at the liver, and then decreased gradually with time (Fig.1a). 30min after the injection, the lactate was specifically measured at tumor, and then its signal intensity was increased with time (Fig.1b), reflecting the accumulation of lactate as a result of Warburg effect.[4] On the other hand, the fat was shown in the lipid abundant region of the mouse and its signal intensity was constant over time (Fig.1c). The tendency of these dynamics was consistent with the one obtained by the whole-body 2D-HMQC spectra (Fig.1d).

Conclusion: The application of CS to 2D-HMQC MRSI provided an 8-fold acceleration factor and made it possible to image tumor glycolysis *in vivo*.

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References: **1.** Imai H, *et al*. In: Proc ISMRM 2013, p1962; ISMRM-ESMRMB 2014, p2918. **2.** Maleki A, *et al*. IEEE Trans Inf Theory 2013;59(7):4290-4308. **3.** Sobol' IM. USSR Comput Maths Math Phys 1967;7(4):86-112. **4.** Heiden MGV, *et al*. Science 2009;324:1029-1033.