

Time Course Study on Glucose Metabolism in Mice by Spectroscopic Imaging with 2D Heteronuclear Multiple Quantum Coherence

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Target audience: Target audience is the researchers interested in the study of metabolism.

Purpose: We reported MRSI combined with 2D ^1H - ^{13}C heteronuclear multiple quantum coherence (HMQC) for imaging metabolites, where it was shown that the ratio of lactate (Lac) to glucose (Glc) after the $[\text{U}-^{13}\text{C}]$ Glc injection provided helpful information, that is, the increase of relative amount of Lac in the brain, tumor, and inferior limb.¹ The purpose of this study is to investigate the feasibility of the Lac/Glc map for imaging metabolite dynamics.

Methods: Four male BALB/c mice aged 8 weeks were transplanted with murine colon carcinoma cells (Colon 26, 1×10^6 cells/15 μL) into subepidermal tissues near the right shoulder two weeks prior to the MR experiments. A 300 μL of 2M $[\text{U}-^{13}\text{C}]$ Glc in saline solution was injected via the tail vein. After 5min, 8min, 30min, and 20hr post injection, mice were sacrificed, and then ^1H - ^{13}C HMQC MRSI was performed for the whole-body acquisition of the postmortem mice. MR scans were performed on a Bruker 7T MR system (BioSpec 70/20 USR, Bruker BioSpin) using a double resonant ^1H / ^{13}C transmit-receive 72mm volume coil. A standard chemical shift imaging (CSI) sequence combined with the gradient enhanced HMQC (ge-HMQC) based preparation² was used. 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 \times 8cm 2 , coronal orientation without slice selection, 16 averages, 1024 complex points with an F_2 bandwidth of 4000Hz (^1H direction), and 32 points with an F_1 bandwidth of 8000 Hz (^{13}C direction). Total scan time was approximately 18 hours. Raw data set $s(t_2, k_x, k_y, t_1)$ was processed by a MATLAB (The MathWorks) to yield the spectral and spatial data set $S(F_2, x, y, F_1)$. A shifted sine-bell squared filter was apodized to the time dimensions t_2 and t_1 , followed by zero-filling by a factor of two. A spatial Hamming filter was applied to the dimensions k_x , and k_y , followed by zero-filling by a factor of two. The data set was then subjected to 4D FFT reconstruction. The final data set were plotted in the magnitude mode. The mapping of the peaks was implemented by calculating volume integrals for $[6-^{13}\text{C}]$ Glc and $[3-^{13}\text{C}]$ Lac peaks identified in the 2D spectra. The signal intensity ratio, Lac/Glc, was calculated pixel-by-pixel basis and mapped.

Results and Discussion: The Lac/Glc maps show the specific distribution throughout the whole body depended on the time between Glc injection and scarification (Fig.1a). When focusing on the tumor region, the Lac/Glc value increased with time (Fig.1b), reflecting the accumulation of Lac as a metabolic end product from Glc in the tumor. The Lac/Glc value could be derived even in the lipid (Lip) abundant region by means of 2D HMQC, which has an ability to clearly distinguish Lac signal from Lip signal (Fig.1c). This ability would be useful for not only monitoring the tumor metabolism but also detecting the necrosis, where Lip signal increased.

Conclusion: We have demonstrated the feasibility of the ^1H - ^{13}C HMQC MRSI for imaging Lac accumulation in the tumor. In the present study, although the imaging method was applied to postmortem mice, introduction of the fast acquisition strategy into this method would make it possible to image metabolic dynamics *in vivo* on the same animal.

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References: 1. Imai H, *et al.* In: Proc ISMRM 2013;21:1962. 2. van Zijl PCM, *et al.* Magn Reson Med 1993;30(5):544-551.

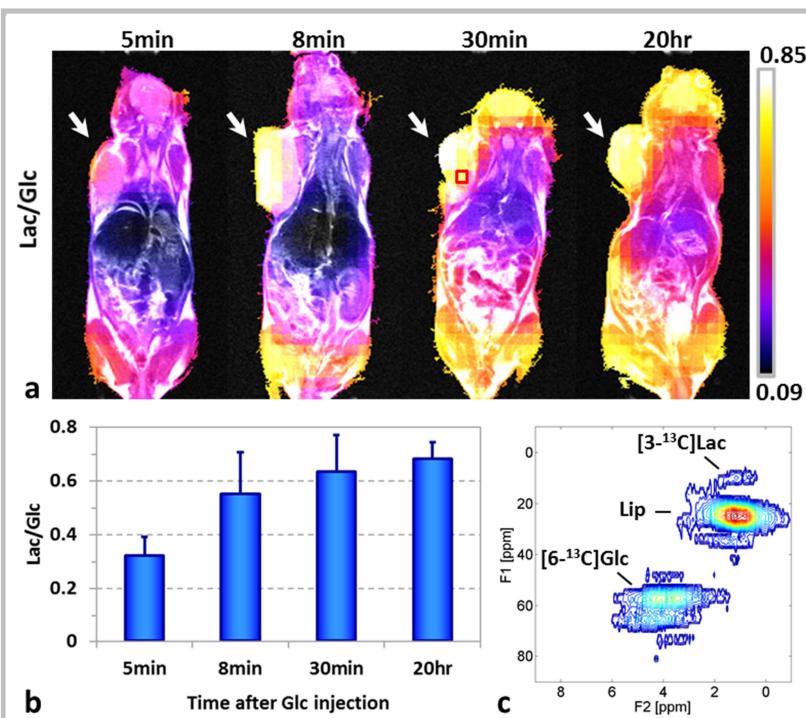


Fig.1. **a:** Lac/Glc maps obtained from postmortem mice overlaid on T_2 weighted reference image. Arrows indicate tumors. (from left to right: a mouse sacrificed at 5min, 8min, 30min, and 20hr after the $[\text{U}-^{13}\text{C}]$ Glc injection), **b:** Lac/Glc values in the tumor regions. Data are mean values calculated from whole-tumor regions with standard deviation displayed as an error bar, **c:** ^1H - ^{13}C HMQC spectra from the voxel indicated by red square in **a** (a part of the tumor region of a mouse sacrificed at 30min post injection).