# Spectroscopic Imaging of Metabolites with 2D Heteronuclear Multiple Quantum Coherence in Mouse

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

**Purpose:** Magnetic resonance spectroscopic imaging (MRSI) using heteronuclear multiple quantum coherence (HMQC) or proton observed carbon editing (POCE) is used for imaging metabolites *in vivo*.[1] An increase of the spectral dimension from traditional 1D to 2D allows to identifying the multiple peaks. The purpose of this study is to investigate the feasibility of the HMQC MRSI, here the two spectral ($^1$H/$^{13}$C) and two spatial dimensions, for imaging metabolites.

**Methods:** A $^1$H-$^{13}$C HMQC MRSI was implemented for the whole-body acquisition of a nude mouse bearing tumor in the shoulder. The mouse was sacrificed at 30min post injection of a 300μL of 2.1M [U-$^{13}$C]glucose (Glc) in saline solution via the tail vein. MR scans of the postmortem mouse were performed on a Bruker 7T MR system (BioSpec 70/20 USR, Bruker BioSpin) using a double resonant $^1$H/$^{13}$C transmit-receive 72mm volume coil. The pulse sequence used in this study is shown in Fig.1. The gradient enhanced HMQC (ge-HMQC) based preparation[2] was incorporated into a standard chemical shift imaging (CSI) sequence. 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=8x4cm$^2$, coronal orientation without slice selection, 16 averages, and 1024 complex points with an $F_2$ bandwidth of 4000Hz ($^1$H direction). The second spectral dimension ($F_1$: $^{13}$C direction) was introduced by adding an incremental delay, $t_1$, between two $^{13}$C 90° pulses using 32 increments with spectral bandwidth of 8000Hz. 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 $S(F_2, x, y, F_1)$. The spectral peaks were identified using data from phantom experiments. The mapping of the peaks was implemented by calculating volume integrals for peaks identified in the 2D spectra.

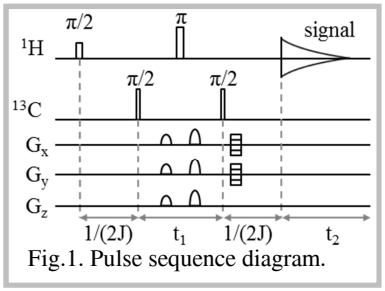

Fig.1. Pulse sequence diagram.

**Results and Discussion:** Figure 2b shows the spatially encoded 2D HMQC spectra. The multiple peaks were observed in $^1$H/$^{13}$C spectra (Fig.2c). The present study focused on the clearly recognized peaks of Glc, lactate (Lac), and fat (natural abundant $^{13}$C). By 2D HMQC, Lac signal could be distinguish from fat signal. Three peaks show the specific distribution throughout the mouse body. The fat signal distributed the specific regions according to the fat abundant site in mice, i.e. part of the neck and lower abdomen (Fig.2d) and the injected Glc showed strong signals throughout the whole body (Fig.2e). Lac signal, which is one of the metabolite from Glc, was clearly observed in the mouse (Fig.2f). In addition, the signal intensity ratio of Lac to Glc (Lac/Glc) was calculated and mapped (Fig.2g). The Lac/Glc map provided helpful information, that is, the increase of relative amount of Lac in the brain, tumor, and inferior limb (Fig.2g, yellow arrows). The accumulation of Lac in these regions would be caused by an anaerobic metabolism because of euthanization. Although the present study focuses on the three main peaks, this study can be expanded to a detail analysis of metabolites because there are still unidentified peaks in the present 2D HMQC measurements.

**Conclusion:** We have demonstrated the feasibility of the $^1$H-$^{13}$C HMQC MRSI for imaging metabolites. Although the long acquisition time is required for multidimensional MRSI, the fast acquisition strategy should overcome this disadvantage such as EPSI and/or compressed sensing.[3]

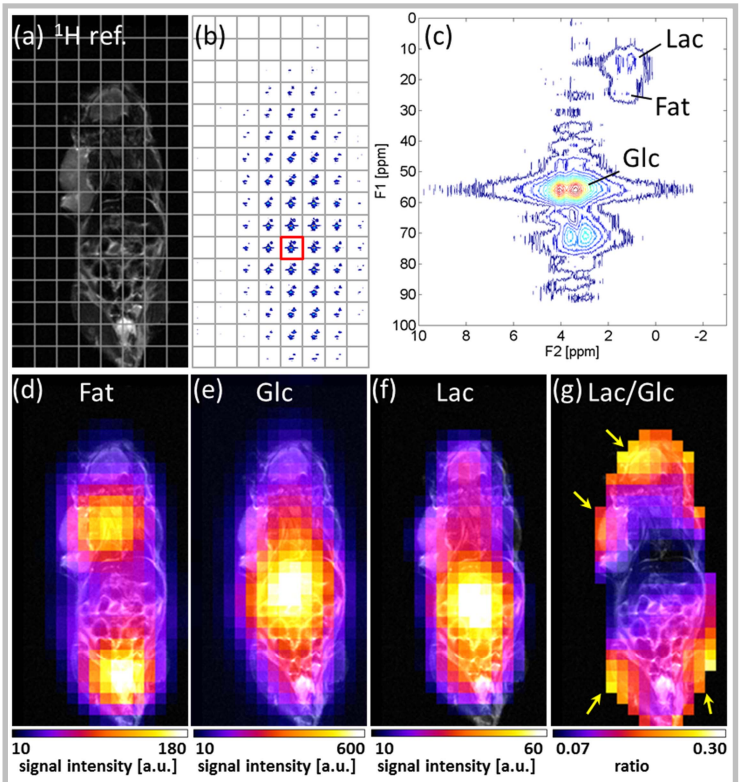

Fig.2. Obtained images and spectra from postmortem mouse. **a:** $T_2$ weighted $^1$H reference image (location being adjusted by phantom experiments), **b:** spatially encoded $^1$H/$^{13}$C HMQC spectra, **c:** $^1$H/$^{13}$C HMQC spectra from the voxel indicated by red square in (b), **d-f:** signal intensity maps calculated from (b), **g:** map of the signal intensity ratio of Lac to Glc.

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**References:** **1.** Hyder F, *et al*. Magn Reson Med 1999;42(6):997-1003. **2.** van Zijl PCM, *et al*. Magn Reson Med 1993;30(5):544-551. **3.** Furuyama JK, *et al*. Magn Reson Med 2012;67(6):1499-1505.