Three-Dimensional Sel-MQC Mapping of Lactate and PUFAs in Human Breast Tissue at 2.1T by Hadamard Matrix Approach

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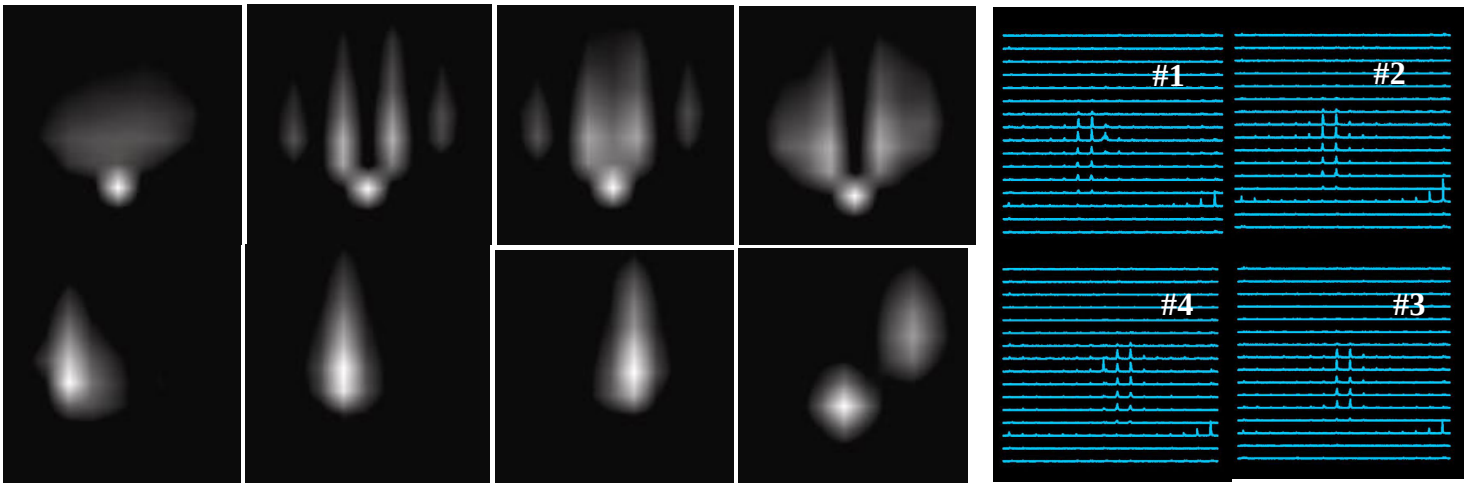
Introduction. The elevated levels of lactic acid in tumor cells even in the presence of oxygenation has fascinated researchers for 70 years since the Warburg's description of the effect.[1] Modern molecular biology studies have gradually revealed the genetic and biochemical basis of this abnormal metabolism. The same genetic and protein signaling alterations might also cause the altered lipid metabolism in tumors. For example, increased glucose uptake may stimulate transcription of genes encoding glycolytic and lipogenic enzymes, as shown in adipocytes and hepatocytes, through the carbohydrate response element (ChoRE).[2-5] Polyunsaturated fatty acids (PUFAs) are highly involved in the signaling network to regulate the tumor p53 pro-apoptotic signal, the anti-apoptotic signals Bcl-2 and superoxide dismutase SOD levels, telomere shortening, and tumor angiogenesis, mediated by the control of free radicals. Therefore, MR signals of lactate and PUFAs are potential tumor makers for non-invasive detection of breast cancer. We have developed the Sel-MQC (Selective Multiple-Quantum Coherence transfer) pulse sequences that eliminate lipid and water signals in a single scan to detect metabolites in breast tissues.[6] The same technique was applied to detect the PUFAs level changes in breast cancers.[7] As shown in other laboratories, Choline serves as a metabolic marker of breast cancer. Three-dimensional maps of these metabolites in breast tissues would improve the diagnostic specificity of breast cancer, especially for occult breast lesions that cannot be enhanced by the MR contrast agents (~5% of clinical cases). Here we report a successful 3D MRSI mapping of lactate and PUFAs on a 2.1T Bruker human MR spectrometer using Hadamard matrix approaches.

Methods. Two approaches can be applied for multiple slice imaging using the Sel-MQC sequence: the rf interleaving methods using spatial-spectral selective pulses and the Hadamard matrix approaches.[8] The conventional rf interleaving methods do not apply because the frequency-selective pulses are required for lipid suppression in the Sel-MQC methods. In the Hadamard spectroscopic imaging (HSI) approach,[9-11] the multi-slice selective Hadamard rf pulses simultaneously encode the spatial information of all slices. Spins in all slices will simultaneously go through the multiple quantum coherence transfer process when encountering subsequent frequency-selective pulses. The signals from different slices are separated by the inverse Hadamard transform during the post-processing stages of the MRSI data.

Results. A set of 4^{th}-order Hadamard 90^{o} pulses that localize four slices in the Sel-MQC experiment were implemented on a 2.1T human spectrometer for multi-slice Sel-MQC mapping of a lactate phantom (Fig. 1a) and PUFAs in the breast (Fig. 1b) of a human volunteer. Magnetization excited by the four Hadamard pulses creates four images of amplitude modulation (Fig. 1a upper panels) according to the fourth-order Hadamard matrix.[10] The inverse Hadamard transformation of the Hadamard matrix decodes the lactate (Fig. 1 lower panels) and PUFAs signals in human breast (Fig. 1b) in the four different slices. Complete lipid and water suppression achieved in a single scan was accomplished in all four images and thus, the summation and subtraction of the four different experiments in the inverse Hadamard transformation processes did not introduce lipid signals.



(a) *(b)*

Fig. 1 One-dimensional HSI Sel-MQC Chemical Shift Imaging obtained with the 4^{th} order Hadamard pulses from (a) the lactate signal in its aqueous solution and (b) unsaturated lipid signal from four adjacent sagittal slices from the human breast tissue of a normal healthy subject. In-plane phase encoding wass applied in the slice direction to show the effective of slice selection.

Conclusions. Multi-slice 3D Sel-MQC mapping of lactate and PUFAs in human breast tissue can be accomplished by the Hadamard matrix approach. We are designing the spatial-spectral selective pulses for fast Sel-MQC mapping of tissue metabolites in human breast cancer.

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