Sensitive J-coupled metabolite mapping using Sel-MQC with selective multi spin echo readout

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Introduction: The Selective Multiple Quantum Coherence (Sel-MQC) editing scheme proposed by He et al[1] enables editing of a single coupled metabolite with simultaneous suppression of water and other resonances in one scan. Especially partial hidden metabolites in extracranial tumor tissues with sufficient chemical shift between the coupling groups such as poly unsaturated fatty acids (PUFA, 2.8 ppm, 5.4ppm) or lactate (Lac, 1.3 ppm, 4.1ppm) are suited for this editing scheme. PUFAs, which are connected to apoptosis, show regions of ongoing cell death[2], and recent studies using quantitative bioluminescence methods on tumor models exposed that Lac accumulation correlates with the response to radiotherapy[3]. Mapping these metabolites in tumor tissues can be important for tumor characterisation and may help planning radiotherapy. In the last years several extensions were applied for the Sel-MQC sequence, such as volume selection[4], T_1/T_2 mapping[5] or spiral Sel-MQC[6]. Here we present a Sel-MQC editing version which **(1)** can be more sensitive than the conventional Sel-MQC Spin-Echo (SE) Chemical Shift Imaging (CSI) sequence, **(2)** suppresses artefacts which originate from higher order coherences of the water resonance using a 3-Point Dixon[7] method and **(3)** uses multiple spin echoes instead of gradient echoes and is therefore particularly suitable at higher magnetic fields where local and bulk magnetic susceptibility gradients are increased.

Material and Methods: Spectroscopic imaging using Echo-Time encoding[8] can increase the sensitivity Ω of an experiment compared to a classical spin-echo CSI, when the ratio of the spatial (N_x) to the spectral (N_δ) resolution becomes lager than the ratio of the spectral bandwidth $\Delta\delta$ to the bandwidth of the readout gradient Δf [9]:

$$\Omega_{\text{Echo-Time}} = \sqrt{\frac{N_X \cdot \Delta\delta}{N_\delta \cdot \Delta f}} \cdot \Omega_{\text{SE-CSI}} \qquad (1)$$

Optimal Sel-MQC edits one group of a J-coupling metabolite and suppresses all other resonances. A number of our phantom experiments have shown that some signal becomes detectable in the 4.7 ppm - 4.8 ppm area, which may originate from higher order coherences of the water resonance induced by the first slice selective pulse. A 3-Point Dixon editing scheme is able to separate the signals of the two resonances by shifting the Sel-MQC editing part about $d = \pi/2\omega_{cs}$ and 2d, where ω_{cs} is the chemical shift of the edited metabolite with respect to water. In Fig. 1 the theoretical sensitivity factor of the Echo-Time encoding compared to the classical SE-CSI against the bandwidth of the readout gradient is shown for four different spectral bandwidths (N_x = 18, N_δ = 3). Low bandwidth of the read gradient improves the sensitivity of the Echo-Time encoding method. The pulse sequence for Lac mapping is shown in Fig. 2 and consists of Sel-MQC preparing part (which can be shifted by d and 2d for the Dixon editing) and a multi spin echo readout. After the first echo acquisition (AQ1), selective pulses are placed on the Lac CH_3 group to acquire several echoes. Using frequency selective pulses, the J-modulation of a coupled spin system is not affected[10] and the inter-echo interval can be kept as short as possible, but does not necessarily have to be a multiple of 1/J. The multiple echoes enable determining T_2 of the edited metabolite and to improve the SNR by averaging the echoes or, if SNR is sufficient, a RARE readout can accelerate the measurement. As the Sel-MQC echo is asymmetric[1], only every second echo is used for RARE reconstruction resulting in an inter-echo time of 18 ms. For PUFA mapping only the timing and the selective pulses of the sequence must be adjusted to the J-coupling system. Experiments were carried out on a Bruker 17.6 T widebore spectrometer. The phantom consists of three 5 mm tubes (50 mM Lac, 100 mM Lac and sun flower oil (containing PUFAs)). The SNR of the sequence was compared to the SNR of conventional SE-CSI by using the same parameters and experiment duration (TR = 2 s, FOV = 20 x 20 mm^2, Matrix = 18 x 18, slice = 4 mm, RARE-Factor (RF) = 1, Δf = 12 kHz, $\Delta\delta$ = 4 kHz, total duration = 10 min 48 s). First in vivo experiments were performed for mapping Lac on a xenograft tumor model transplanted on the leg of a mouse (TR = 1.5 s, FOV = 16 x 16 mm^2, Matrix = 12 x 12, slice = 6 mm, RF = 1, Δf = 12 kHz, $\Delta\delta$ = 4 kHz, total duration = 10 min 48 s).

Results and Discussion: Fig. 3a shows a FLASH-reference image of the phantom. The PUFA resonance was edited with the Sel-MQC filter and mapped acquiring one echo (Fig. 3b). The arrows indicate artefacts. Using the 3-Point Dixon editing scheme, in-phase and opposite-phase image can be reconstructed: only the PUFA resonance (Fig. 3c) or the artefacts (Fig. 3d) are visible. Fig. 3e-g show editing of Lac with different RARE-Factors with identical total experiment duration. The SNR of Lac in the 50 mM tube acquired with the Echo-Time encoding experiment (RF = 1) was compared to that recorded with the conventional SE-CSI: $SNR_{\text{Echo-Time}}$ = 33.2 to $SNR_{\text{SE-CSI}}$ = 26.1. The experimental sensitivity factor ($SNR_{\text{Echo-Time}}$ / $SNR_{\text{SE-CSI}}$ = 1.27) for acquiring one echo in the current setup is slightly lower than the theoretical (1.41 - from equation *(1)*). In Fig. 3g the result of the in vivo experiment using the Sel-MQC with the selective RARE readout (RF = 1) is presented. Lac is visible in the inner tumor region, which was proven with the conventional SE-CSI Sel-MQC version (data not shown).

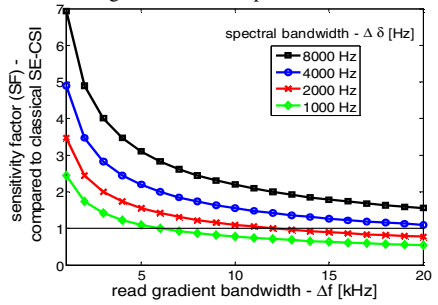

Fig.1. Theoretical sensitivity factor – compared to classical SE-CSI

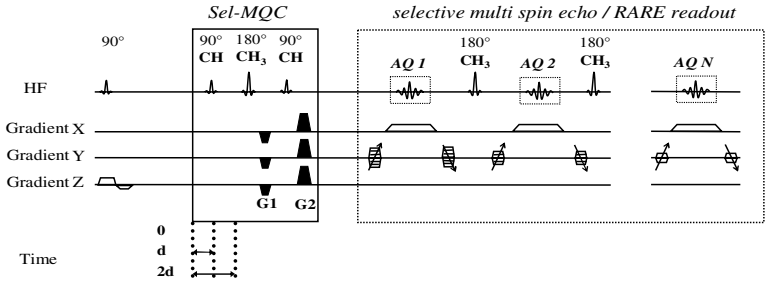

Fig. 2. Pulse sequence: Sel-MQC for Lac mapping with 3-Point-Dixon and selective RARE readout

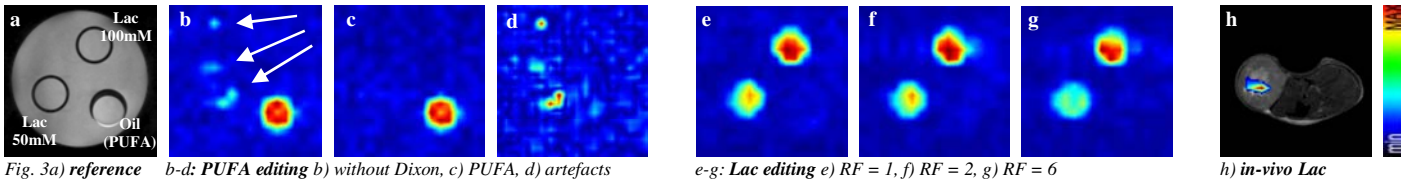

*Fig. 3a) **reference** b-d: **PUFA editing** b) without Dixon, c) PUFA, d) artefacts e-g: **Lac editing** e) RF = 1, f) RF = 2, g) RF = 6 h) **in-vivo Lac***

Conclusion: The Sel-MQC filter can be combined with a readout gradient for potential sensitivity improvement. Furthermore a Dixon editing scheme can be applied to suppress artefacts originating from higher order water coherences. Depending on T_2 of the edited metabolite the selective multi spin echo readout can further improve the sensitivity compared to multi echo CSI, because the inter-echo-time can be kept shorter than in conventional multi echo CSI where the acquisition time must be long enough to achieve adequate spectral resolution.

References: [1] He Q. J Magn Reson B 1996, 112: 18-25 [2] Hakumaki J.M. Nat Med. 1999 Nov; 5(11):1323-7 [3] Quennet V. Radiother Oncol. 2006 Sep 12 [4] Thakur. S.B. Proc Intl Soc Mag Reson Med 11 (2003) p1141 [5] Muruganandham M. Magn Reson Med. 2004, 52:902-906 [6] Zhu H. Proc Intl Soc Mag Reson Med. 14 (2006) p3051 [7] Glover G.H. Magn Reson Med. 1991, 18:371-383 [8] Sepponen R.E. Magn Reson Imag 1985, 3:163-167 [9] Pohmann R. J Magn Reson. 1997 Dec;129(2):145-60 [10] van de Ven F.J.M. New York: VCH, 1995