

Selective Zero-Quantum Coherence Transfer (Sel-ZQC) Method for High-Resolution Metabolite Imaging at Ultrahigh Field without Inhomogeneous Broadening and Susceptibility Artifacts

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Introduction: Magnetic resonance spectroscopic imaging in human scanners at ultrahigh magnetic field encounters numerous technical challenges. For example, gradient hardware for whole-body shimming adjustment of magnetic field inhomogeneity is not yet available at human 7T and 9.4T scanners, which limits our ability to generate high quality NMR spectra in extracranial organs *in vivo*. Here we report a novel zero-quantum spin editing method for high-resolution spectroscopic imaging of metabolite distributions in a poorly shimmed magnet, as a modification of our previous selective multiple quantum coherence transfer (Sel-MQC) techniques [1,2]. In Sel-ZQC experiments, the ZQ-spectra of metabolites are not subject to magnetic susceptibility artifacts with ultrahigh field human MRI scanners. Using a double quantum filter (DQF), the superior power of complete lipid and water suppression can be maintained in the Sel-ZQC sequence. The Sel-ZQC method will be applied to study human breast cancer and other extracranial human diseases *in vivo* at ultrahigh magnetic field.

Method: The Sel-ZQC pulse sequences for acquiring the high-resolution ZQ-NMR spectra and imaging metabolite distributions are shown in Fig. 1 and 2, respectively. Since ZQ-coherences are not sensitive to magnetic field inhomogeneity or magnetic susceptibility effect, these sequences can be employed to measure spectra of biochemicals in human tissues *in vivo* with high field magnets (e.g., 7T and 9.4T human MRI scanners), which are not yet equipped with whole-body shimming hardware. For example, in lactate detection using Sel-ZQC method, the lactate CH₃ protons at 1.3ppm are selectively excited by the first 90° pulse in channel I, which also excites lipid at 1.3ppm. In channel S, the selective 90° pulse excites the lactate CH at 4.2ppm and water protons at 4.7ppm after the MQ-preparation period $\tau = 1/2J$ and converts the lactate anti-phase magnetization into the MQ-modes. In the subsequent ZQ-evolution period, t_1 , zero-quantum coherences of lactate are selected by the ZQ-gradient, g_{ZQ} , which dephases other spin coherences of lactate, SQ-magnetizations of lipid and water. The selective 180° pulse on lactate CH₃ converts the ZQC into the DQC of lactate, and the final CH-selective 90° pulse converts the lactate DQ coherence into the detectable single-quantum (SQ) magnetization. Water and lipid suppression is accomplished by a pair of double quantum filter (DQF) gradients ($g_1: g_2 = -1:2$). In a poorly shimmed magnet, although the directly detected signal in F_2 dimension is sensitive to the magnetic field inhomogeneous broadening and susceptibility distortions with a total B_0 field shift of ΔB , the ZQ resonances in the indirectly detected dimension F_1 occurring at the chemical shift differences between spin I and S, $\Omega_I - \Omega_S = (\omega_I + \gamma\Delta B) - (\omega_S + \gamma\Delta B) = \omega_I - \omega_S$ are not affected. Therefore, the frequency shifts (i.e., $\gamma\Delta B$) for both spin I and S in inhomogeneous field are cancelled for ZQCs in F_1 dimension. In the Sel-ZQC imaging experiments, a frequency-encoding and a phase encoding gradient are applied to map metabolite spatial distributions (Fig. 2). Different from the chemical shift imaging (CSI) experiments, the chemical shift information of the tissue metabolites are obtained in the indirectly detected ZQ-dimension by t_1 incrementation. All experiments were performed on a horizontal bore Varian 9.4T MR spectrometer for small animal imaging and spectroscopy. A two-compartment phantom containing pure vegetable oil in the inner 10mm NMR tube and 100 mM lactate in saline solution in an outer 20mm NMR tube (Fig. 3) was used for 2D Sel-ZQC spectral acquisition to demonstrate the feasibility of the Sel-ZQC spectroscopic imaging technique. The magnetic field was de-shimmed to produce a broadened water peak of 280 Hz line-width.

Results and Discussion: In the 2D Sel-ZQC spectra, a ZQ cross peak of lactate (F_1, F_2)

$= (-2.8\text{ppm}, 1.3\text{ppm})$ was detected (Fig. 4) at the difference frequency of lactate $\text{CH}_3 = (-2.8\text{ppm}, 1.3\text{ppm})$ and CH proton chemical shifts at 1.3 and 4.1 ppm, respectively. The strong water and lipid signals were completely suppressed by the DQF gradients. The projected 1D ZQ lactate spectrum in the F_1 dimension showed a sharp narrow peak without being affected by inhomogeneous broadening, although it had a broadened lactate peak of 280Hz line-width in F_2 dimension. The intermolecular multiple-quantum coherences (iMQCs) were reduced by applying the gradients in the magic angle direction [3-5]. In conclusion, the Sel-ZQC technique is an effective method to study metabolism *in vivo* in extracranial organs, including breast cancer, that contain high fat content, at ultrahigh magnetic field without subjecting to B_0 field inhomogeneity and magnetic susceptibility signal distortions.

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References : [1] He Q., et al., *J. Magn. Reson. B*, 106:203, 1995. [2] He Q., et al., *Magn. Reson. Med.*, 58:1079, 2007. [3] He Q., et al., *J. Chem. Phys.*, 98:6779, 1993. [4] Warren W.S., et al., *Science*, 262:2005, 1993. [5] Richter W., et al., *Science*, 267:654, 1995.

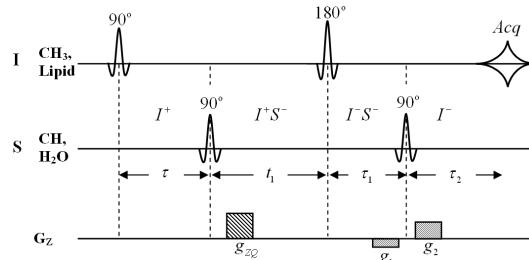


Fig. 1 The Sel-ZQC pulse sequence to obtain high-resolution NMR spectra of metabolites *in vivo* in inhomogeneous magnetic fields.

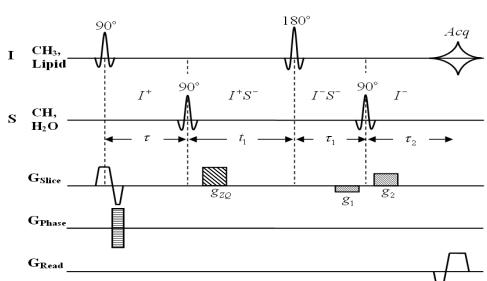


Fig. 2 Sel-ZQC imaging sequence.

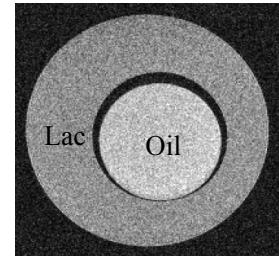


Fig. 3 The GRE image of phantom.

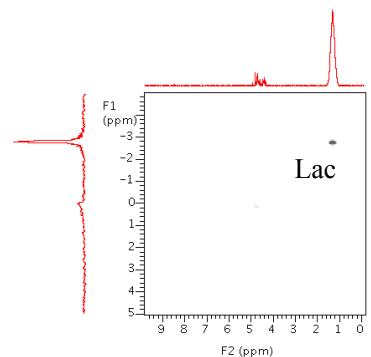


Fig. 4 The 2D ZQ-spectrum of lactate with complete lipid and water suppression.