Intramolecular zero-quantum-coherence 2D NMR spectroscopy of lipids in human breast tissue at 7 T

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Introduction – The lipid composition in human breast tissue is related to diet and fat consumption and may play a role in the pathogenesis of breast cancer. Recently [1], ^{1}H NMR spectroscopy at high magnetic field strength has been shown to provide a detailed and non-invasive characterization of breast lipid composition. As the characterization relies on the detection of multiple spectral lines, the robustness of the method is only maintained in the absence of strong magnetic field inhomogeneity. Unfortunately, depending on the location in the breast, local magnetic field inhomogeneity can be extremely severe due to abundantly present water-lipid susceptibility transitions. Here we present a novel lipid detection technique based on the indirect detection of intramolecular zero-quantum-coherences (ZQCs), which are intrinsically insensitive to magnetic field inhomogeneity [2].

Methods – All experiments were performed on a whole body 7 T MR system (Philips, Cleveland, OH, USA) using a home-built unilateral breast transceiver coil consisting of two orthogonal loops (19 cm diameter) driven in quadrature. The MR pulse sequence is essentially composed of a 3D localized STEAM method. To increase the robustness of the method an additional non-selective excitation pulse and appropriate crusher gradients were placed in the mixing (TM) period to create a double-quantum filter (DQF). 2D DQF-ZQC MR spectra (TE = 70 ms) were acquired in circa 9 min as 192 t_1 increments of 0.71 ms, giving an indirect spectral width of 1.4 kHz. Cardiac triggering and voluntary synchronized breathing were used to minimize temporal B_0 variations. In addition, by appropriate gradient selection a navigator echo was created prior to DQF-ZQC signal acquisition and was used to correct phase and frequency variations.

Results – Figs. 1A/B show STEAM and 2D DQF-ZQC MR spectra from a relatively homogeneous area in the breast of a healthy volunteer (left voxel, Fig. 1C). As reported previously [1], the STEAM spectrum contains ten distinct spectral peaks from which the fractions of poly-unsaturated (PUFA), mono-unsaturated (MUFA) and saturated (SFA) fatty acids can be determined. The information content of the 2D DQF-ZQC spectrum is similar, with the main difference that the spectral resolution in the second, indirect dimension is independent of the magnetic field homogeneity. This is especially important in breast regions with poor magnetic field homogeneity, as shown in Fig. 1D/E (right voxel in Fig. 1C). Whereas the spectral resolution in the STEAM spectrum (Fig. 1D) is insufficient for quantitative analysis, the peak separation in the 2D DQF-ZQC spectrum (Fig. 1E) is adequate for quantitative PUFA, MUFA and SFA determination. The average levels of PUFA/MUFA/SFA in breast tissue as determined by 2D DQF-ZQC NMR were 20 ± 4 %, 65 ± 4 % and 15 ± 4%, in agreement with previously published results [1].

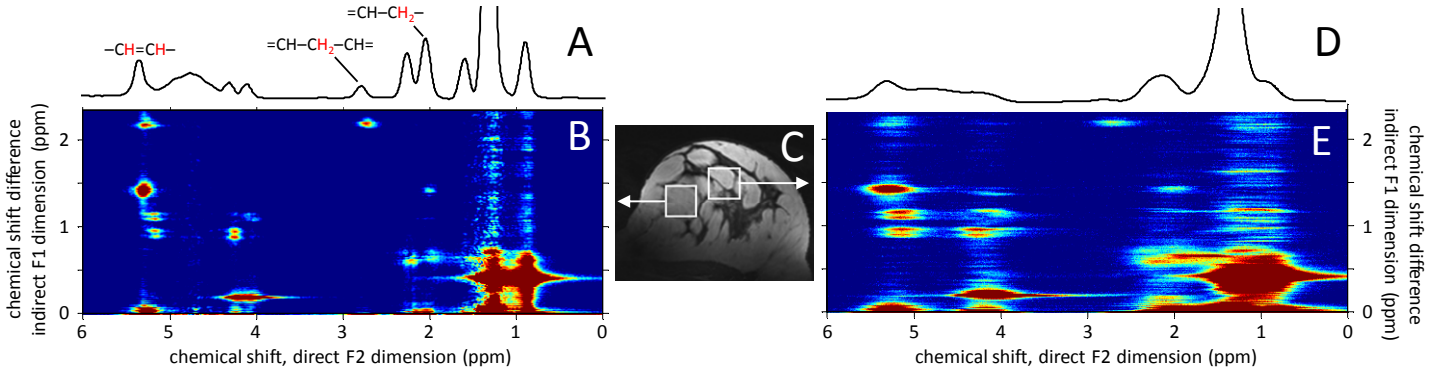

Figure 1: (A) STEAM and (B) 2D DQF-ZQC spectra from the human breast at 7 T (27 mL, left voxel in (C)). The resonances that are important for PUFA, MUFA and SFA determination are indicated. (B) The 2D peaks appear at the chemical shift *difference* between two scalar coupled spins. Note that some 2D peaks are aliased due to the limited spectral width in F1. (D) STEAM spectrum from a second volunteer in which water-lipid susceptibility transitions cause severe magnetic field inhomogeneity (right voxel location in (C) is representative). Most signals are no longer resolved, making lipid characterization difficult. (E) While the cross peaks in the 2D DQF-ZQC spectrum have broadened in the direct, F2 dimension, they retain their narrow lines in the indirect F1 dimension. As a result, the relevant cross peaks can still be separated and quantified. Phase and frequency instabilities between subsequent t_1 increments lead to t_1-noise for the large methylene signals at F2 ~ 1.4 ppm. However, triggering and navigator echo acquisition has reduced t_1-noise for the smaller cross peaks to the noise level.

Discussion – Here we have presented a novel technique for lipid detection and characterization in the presence of severe magnetic field inhomogeneity. While the simplicity and sensitivity of STEAM are preferable when the magnetic field homogeneity is adequate, the 2D DQF-ZQC method provides a viable alternative. The combination of cardiac and respiratory triggering and navigator echo-based post-acquisition correction is sufficient to provide high-quality 2D NMR spectra of the human breast at 7 Tesla.

[1] I.E. Dimitrov et al, MRM 67, 20 (2012) [2] R.A. de Graaf et al, JMR 187, 320 (2007)