2D iZQC *in vivo* Spectroscopy with Optimized Pulse Sequences: Water Suppression and Localization

D. Balla[1], C. Faber[1]

[1]Experimental Physics 5, University of Würzburg, Würzburg, Bavaria, Germany

Introduction

A major limitation of *in vivo* spectroscopy in inhomogeneous tissue is linebroadening. Techniques based on long range intermolecular dipolar interactions were reported to give high resolution in the indirect dimension of 2D spectra independent of the field homogeneity in the sample[1,2]. The possibility to enhance the resolution in *in vivo* spectroscopy with this technique has recently been demonstrated by our group[3]. Here, we present optimizations of the intermolecular zero-quantum coherence (iZQC) pulse sequence for *in vivo* spectroscopy.

Theory and method

The development of the MR signal originating from intermolecular dipolar interactions can be described in a theoretical framework employing intermolecular multiple-quantum coherences. The multiple-quantum signal has two major properties rendering it interesting for *in vivo* applications. First, it builds up on a time scale of $\tau_D=(\gamma M_0\mu_0)^{-1}$ (about 70 ms under *in vivo* conditions at 17.6 T), where M_0 is the equilibrium magnetization of water. Second, it arises due to interactions of spins within a correlation distance $d_C=\pi(\gamma GT)^{-1}$, where G and T are the strength and duration of the gradient pulse, making it insensitive to long range field variations[1,4]. Zero-quantum pulse sequences are, in addition, insensitive to short range inhomogeneities caused by air-tissue interfaces and thus well suitable for application in inhomogeneous tissues[4]. However, the problems of strong residual water signal and/or strong axial peaks remains. We have applied a pulse sequence (Figure 1) derived from the HOMOGENIZED sequence[1]. Alterations of the mixing pulse were used to influence the build-up of the signal and to suppress axial peaks or for selection of one coherence order. To suppress the residual water, a frequency selective refocusing module[5] immediately prior to the acquisition was combined with the iZQC sequence. Since the detectable metabolite signal is built up by the dipolar couplings between solvent and solute, a water suppression with presaturation is not applicable.

Experiments and Results

Spectra were acquired on a Bruker 17.6T widebore spectrometer. Imaging resonators for rodents were used to simulate experimental *in vivo* conditions with limited B_0 and B_1 homogeneity. The spoiler gradients (S) for the water suppression module (WS) were applied at the magic angle and were smaller than 40 % of the coherence selection gradient (CSG), to avoid refocusing of unwanted coherences. We have performed experiments on a 1:1:1 mixture of water:DMSO:acetone, on agarose gel phantoms containing 9 major brain metabolites at their *in vivo* concentration, and on a female Fisher rat anesthetized with isoflurane. Application of a 90° (instead of 45°) hard pulse as mixing pulse resulted in an increase in SNR of 10 % after adding positive and negative frequencies along the indirect dimension. A 90°-pulse selective on water reduced axial peaks and allowed the selection of one order of coherence resulting in an increase in SNR of about 20 %. With an excitation scultping WS the water signal was suppressed by up to 90 % in the concentrated sample. A water suppressed spectrum of the brain phantom is shown in Figure 2. Observing the water frequency in F2 at -500 Hz one can realize that the remaining - mainly off resonant - signal is due to the inhomogeneity of the *in vivo* probehead.

A first localization of an iZQC spectrum of the rat brain was achieved by use of a surface coil (Figure 3). Three major metabolites could be identified in five minutes scan time. Because of the well known B_1 inhomogeneity of the surface coil, the straightforward use of the WS, as in Figure 1, was not efficient.

Conclusion

Optimized iZQC spectroscopy sequences allow to obtain metabolic information in only a few minutes under *in vivo* conditions. The low sensitivity to field inhomogeneities, to short relaxation times and to huge water signals makes this technique a promising tool for future applications in inhomogeneous organs such as the heart or the lung.

Acknowledgement

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References

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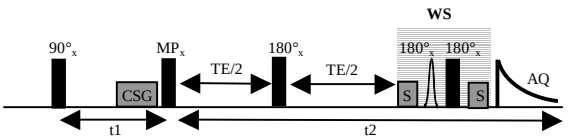

Figure 1: 2D iZQC pulse sequence with integrated excitation sculpting water suppression module (WS). IZQCs produced by the first pulse are transformed into two-spin-one-quantum operators by the mixing pulse (MP). Dipolar couplings create observable magnetization. Frequency-selective-refocusing WS with spoiler gradients (S) only eliminate observable water signal.

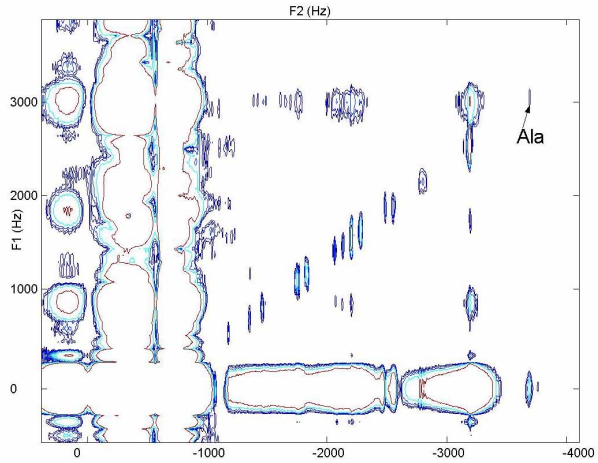

Figure 2: Water suppressed iZQC spectrum of a brain phantom (TR=4.4s, CSG=40G/cm, MP=45°, TE=210ms, WS=excitation sculpting, scan time:5min). Residual water and axial signals do not overlap with metabolite peaks which are seen as a diagonal in the spectrum. Metabolites are detected down to concentrations of 1.4 mM (Alanine). Off-diagonal peaks are artefacts partly due to imperfections of the WS.

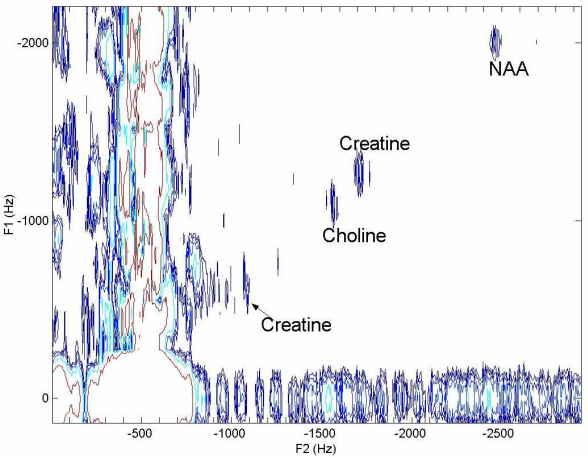

Figure 3: iZQC spectrum of the rat brain *in vivo* localized with a surface coil, acquired in 5 minutes. 64 t1 increments, TR=4.4s, CSG=40G/cm, MP=90°, TE=210ms.