Quantum coherence spectroscopy to measure 1D ^{1}H-[^{13}C]-lipid signals

Lucas Lindeboom[1,2], Robin A de Graaf[3], Christine I Nabuurs[2,4], Matthijs KC Hesselink[4], Joachim E Wildberger[2], Patrick Schrauwen[1], and Vera B Schrauwen-Hinderling[1,2]

[1]*Department of Human Biology, Maastricht University Medical Center, Maastricht, Netherlands,* [2]*Department of Radiology, Maastricht University Medical Center, Maastricht, Netherlands,* [3]*Department of Diagnostic Radiology, Magnetic Resonance Research Center, Yale University School of Medicine, New Haven, CT, United States,* [4]*Department of Human Movement Sciences, Maastricht University Medical Center, Maastricht, Netherlands*

Target Audience

Researchers and clinicians interested in indirect ^{13}C spectroscopy (of lipids).

Purpose

Due to the low natural abundance of carbon-13 (^{13}C), and hence low incorporation in endogenous lipids, ^{13}C-enriched lipids are an excellent candidate to be used for *in vivo* tracer studies [1]. In order to enhance the detection sensitivity spectral editing techniques for the indirect detection of ^{13}C have been proposed. These techniques also offer the opportunity to use regular ^{1}H localization techniques. Gradient enhanced heteronuclear single and multiple quantum coherence spectroscopy (ge-HSQC or ge-HMQC respectively [2]) allows for acquisition of ^{1}H-[^{13}C] signals while simultaneously spoiling unwanted ^{1}H-[^{12}C] signals. Although intrinsically 50% of the ^{1}H-[^{13}C] signal is lost, this single shot acquisition technique may be preferable to subtraction-based editing methods (e.g. POCE [3]) for ^{13}C detection in tissues where movement artifacts and/or low ^{13}C fractional enrichments are expected. However, the large chemical shift of ^{13}C resonances of the lipid signal will lead to signal intensity loss and phase distortions when the conventional ge-HSQC and ge-HMQC sequences are applied as 1D editing technique. In this study we compared the use of modified ge-HSQC and ge-HMQC sequences, which were designed to refocus the chemical shift in the heteronuclear dimension to get 1D ^{1}H-[^{13}C]-lipid spectra.

Methods

Experiments were performed on a 3T clinical MR system (Achieva 3T-X, Philips Healthcare, NL) using a butterfly-loop ^{1}H TX/TR quadrature coil combined with two 16cm ^{13}C TX/TR surface coils in quadrature-mode for optimal ^{1}H receiving sensitivity (RapidBiomed, GE). The two sequences used are depicted in figure 1. For ge-HSQC, the sequence represents a modification of a recently described method [4], where the coherences are formed during the TM mixing period of a STEAM localization sequence. A single ^{13}C inversion pulse was inserted during the evolution period. Coherence selection gradients (length 1 ms) were used in a ratio of 2:-2:1. The duration of the hard ^{13}C excitation pulse was 340 μs, leading to an evolution period of 4.2 ms. For the ge-HMQC, the quantum coherence module was placed after PRESS localization. In this case, two additional ^{13}C inversion pulses were inserted to refocus ^{13}C chemical shift. Selection gradients (length 0.5 ms) were used in a ratio of 1:-1:-1:1:1, leading to an evolution time of 7.6 ms. Total TE was 29 ms. In both sequences, the first ^{13}C pulse was phase cycled to improve spoiling of unwanted coherences. Offset of the ^{13}C pulses was set at the midchain ^{13}C-CH_2 resonance (~29 ppm). Four different spectra were acquired, to compare HSQC versus HMQC and to show the effect of the extra inversion pulse(s) in both sequences. All experiments were acquired from a 20 x 40 x 40 mm volume, placed in a phantom filled with Intralipid (a stable emulsion with of 20% soybean oil, 1.1 % ^{13}C) with TR = 2000 ms, 1/2J = 3.95 ms and NSA = 128. A lipid reference signal was obtained by turning off the dephasing gradients and by setting the frequency of the ^{13}C RF pulses far off resonance.

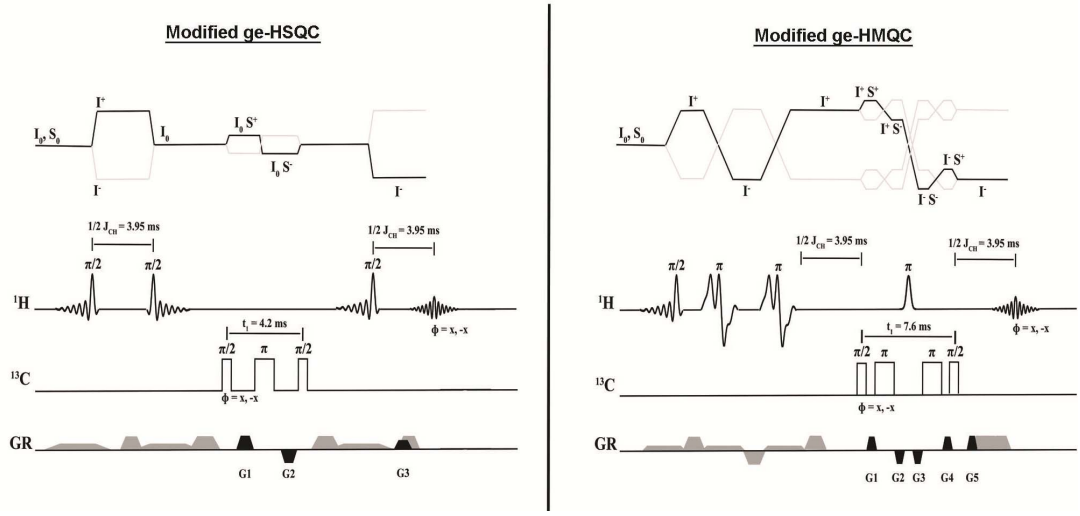

Figure 1. Modified ge-HSQC and ge-HMQC sequences as used in this study.

Results

The four different spectra acquired are depicted in figure 2. It is apparent that the insertion of the ^{13}C inversion pulses resulted in non phase distorted lipid signals with an increased signal intensity. The effective bandwidth of the ^{13}C refocusing pulse was sufficiently large for unambiguous detection of lipid methyl and methylene signals. The ^{1}H-[^{13}C]-CH_2 and –CH_3 signal is higher in the modified ge-HSQC sequence when compared to the modified ge-HMQC (calculated enrichment 0.9% vs. 0.6% respectively). The increased signal loss in ge-HMQC is likely due to the larger number of RF pulses as well as the non-refocused evolution of passive spin couplings in this sequence.

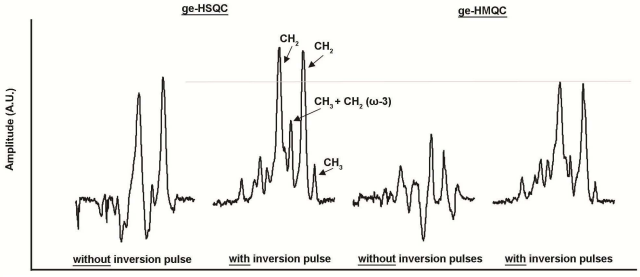

Figure 2. Comparison between the modified ge-HSQC and the modified ge-HMQC sequence, with and without additional ^{13}C inversion pulse(s).

Discussion and Conclusion

We have shown that the addition of ^{13}C inversion pulses to both the ge-HSQC and the ge-HMQC is essential to obtain ^{1}H-[^{13}C]-lipid signals without phase distortion. Due to the absence of ^{1}H-^{1}H couplings during the evolution time in the ge-HSQC, this sequence will yield higher signals than the ge-HMQC. The modified ge-HSQC sequence can be used in studies to follow the incorporation of ^{13}C lipid tracers.

References

1. Jonkers et al. MRM 2012. 2.Ruiz-Cabello et al. Journal of Magnetic Resonance, 1992. 3. Rothman et al., PNAS, 1985. 4. De Graaf et al. MRM (in press), 2014.

Acknowledgements

Funded by Top Institute Food and Nutrition (TIFN, WM003).