Parametric macromolecular baseline assessment using prior knowledge from inversion recovery signals measured at 9.4 T

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Introduction

Besides the metabolites, MR signals also contain macromolecules and lipids. At low magnetic fields, these macromolecule and lipid contributions are normally observed in the MR spectra in the frequency regions between 0.5 and 2 ppm, however, at high magnetic fields, numerous resonances appear along the whole spectrum band. In brain tumours and metabolic diseases, these contributions increase in concentration providing useful diagnostic information. On the other hand, in measurements close to the skull and the scalp, MR spectra from healthy tissue contain unavoidable high lipid contamination. In the frequency domain, they are observed as an underlying profile also known as baseline, which overlaps with the metabolite peaks and complicates quantification. Because there exist no exact chemical substances similar to macromolecules (i.e., to measure them in vitro), different studies focused on the detection, suppression, evaluation and modeling of this baseline. In the literature, several advanced acquisition techniques using inversion recovery, parametric and non-parametric methods [1,2,3,4] have been widely used. Here, we propose a parametric way of extracting characteristic information from a database of inversion recovery signals and include them in the quantification method as additional components.

Methods

Animals: Twelve wild-type mice were used for this study. Mice were anesthetized by using 1.25% isoflurane and their heads were immobilized during experiments. Body temperature was measured using a rectal thermometer and maintained at 37 ±1°C. **^{1}H MR Spectroscopy:** Single Voxel ^{1}H MR Spectroscopy (SVS) and inversion recovery signals were measured using a Bruker Biospec 9.4 T small animal MR scanner (Bruker BioSpin, Ettlingen, Germany). Short echo-time MRS parameters were: TR=4 s, TE=12 ms, SW=4 KHz and 256 averages. The *in vivo* spectrum from macromolecules was measured using a 1ms Hermitian inversion pulse. The inversion time and repetition time were 800ms and 3s, respectively, with 1024 averages. The inversion time was optimized experimentally (see Fig. 1). Spectra were corrected for B_0 eddy currents as well as B0 drift using the Bruker built-in routines. Shimming was performed using FASTMAP. SVS and FASTMAP VOIs were 3x1.75x1.75 mm^3. The linewidths of the unsuppressed water were between 20-25 Hz. **Data processing:** In vivo ^{1}H MRS signals were processed in jMRUI [6]. Preprocessing of data consisted in time circular shift, phase correction, water removal and normalization, which were performed in jMRUI. Then, the macromolecular resonances were identified at frequency locations around: 0.89 (MM1), 1.20 (MM2), 1.36 (MM3), 1.63 (MM4), 2.02 (MM5), 2.29 (MM6), 2.65 (MM7), and 3.03 (MM8), 3.21 (MM9), 3.75 (MM10), and 4.31 ppm (MM11) (see Fig. 2). These resonances are in accordance to literature [1,2] and extended with the MM7which appeared to be also present in all individual MM signals. AMARES [7] in jMRUI was used to compute individual spectral components. From the twelve available MM signals from different mice, the mean of amplitudes, frequency locations and linewidths were used to create individual macromolecule and lipid resonances that were further included in the basis set of AQSES [5]. It is important to notice that the model used in AQSES allows small parameter variations to better accommodate individual conditions of each signal under analysis. The estimated MM components are also subject to such corrections.

Results

Fig. 1 shows the spectra of both, the in vivo and the inversion recovery signals. Results of spectral fitting are shown in Fig. 2.

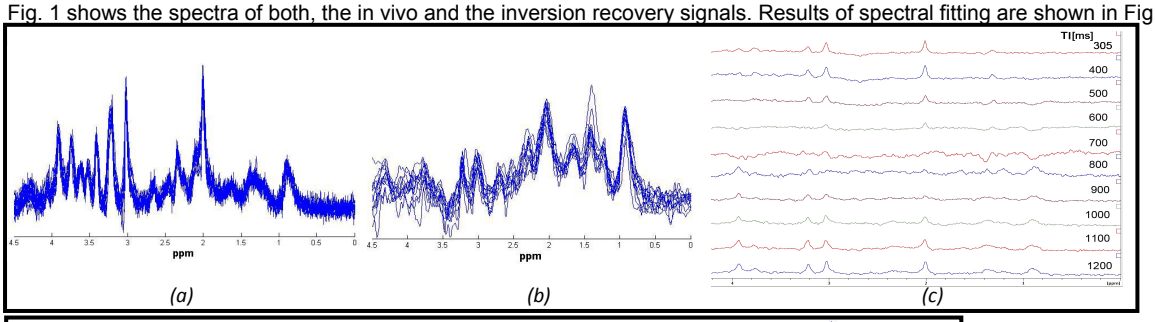

Fig. 1 SVS in vivo ^{1}H MR spectra of (a) in vivo MRS signals (b) macromolecular signals measured by inversion recovery at TI=800 ms, (c) MR spectra with different inversion times.

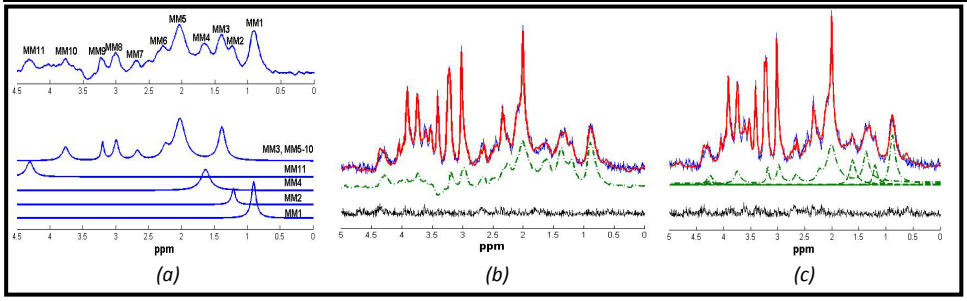

Fig. 2 (a) Real part of an in vivo metabolite-nulled MM spectrum together with the spectra obtained with AMARES using prior knowledge, (b) AQSES fit for the mean spectra quantified using the measured macromolecules and (c) AQSES fit for the mean spectra quantified using the individual macromolecule resonances computed via AMARES (Small variations are expected for different signals which are then corrected by AQSES.)

Discussion and Conclusion

Results obtained in this study show that a set of macromolecular and lipid resonances computed at high magnetic field can provide comparable satisfactory quantification results, as shown in Fig. 2 (b) and (c). Although the MM signal acquired by inversion recovery is known to provide a good approximation of the macromolecular contamination, it is also true that it requires a long acquisition time and is not reproducible when the conditions of the region of interest are affected by acquisition problems and various diseases. A promising new acquisition technique based on diffusion weighted spectroscopy has recently been proposed and was shown to be less contaminated by unsuppressed metabolites [8]. The location and characterization of all individual resonances in mice and human brain has been studied previously at various magnetic field strengths, (e.g., 8.4 T and 1.5 T [1,2]) and resonances similar to those observed in the mouse brains have been observed in the in vivo ^{1}H MRS spectra of human brain. To our knowledge, the use of an individually measured macromolecular background signal has not been presented using a series of inversion recovery signals measured at 9.4 T and we address the fact that good starting values and prior knowledge are advantageous for quantification methods, providing a strong motivation for using simulated macromolecular and lipid components. This approach is appropriate for decreasing the scanning time, reducing systematic errors and avoiding the non-parametric selection of baseline constraints.

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References: **[1]** K. L. Behar and T. Ogino., Magn. Reson. Med., 30(1):38–44, 1993. **[2]** U. Seeger et al., Magn. Reson. Med., 49(1):19–28, 2003. **[3]** J. Pfeuffer et al., J. Magn. Reson., 141(1):104 – 120, 1999. **[4]** L. Hofmann et al., Magn. Reson. Med., 46(5):855–863, 2001. **[5]** J-B. Poullet, et al., *NMR Biomed., 20(5):493 – 504, 2007.* **[6]** D. Stefan, et al., Meas. Sci.Technol., 20(10):104035(9pp), 2009. **[7]** L. Vanhamme et al., J. Magn. Reson., 129(1):35 – 43, 1997. **[8]** N. Kunz, et al., Magn. Reson. Med., 64(4):939–946, 2010.