Detection of brain macromolecules using double inversion recovery ultra-short acquisition delay ^{1}H MRSI at 7 Tesla

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Target audience: Scientists interested in brain MRSI techniques and macromolecules detection.

Purpose: Brain short-echo time (short acquisition delay) ^{1}H MRS spectra contain resonances of low molecular weight metabolites superimposed on signal of high molecular weight macromolecules[1] (MM). This MM contribution is even more enhanced at ultra-high fields, due to increased spectral resolution of the MM components. Therefore for reliable quantification of brain metabolites, the MM need to be considered in the prior knowledge. Consequently, an error in the MM estimation can lead to substantial errors in the obtained metabolite concentrations[2]. Several groups have identified the human macromolecular background utilizing ultra-short echo-time single voxel spectroscopy, however the studies [3,4] were carried out with echo time TE > 10ms and fully relaxed conditions. We aimed to adapt an FID-based ^{1}H MRSI sequence to measure macromolecular signal by double inversion nulling of metabolites with ultra-short acquisition delay of only 1.3ms.

Methods: The inversion recovery is usually the method of choice for metabolite nulling, however the situation is different at ultra-high fields and sequences with very short repetition time. The short TR combined with spatially variable excitation flip angle leads to spatial differences in saturation behavior. This makes TIs for optimal suppression spatially dependent. In addition, not using a 90° excitation leads to signal loss. The double inversion improves the nulling efficiency as it is less sensitive to B_1^+ inhomogeneities. Therefore double inversion recovery pulses (TI1 – time between first and second inversion pulse, TI2 – time between second inversion pulse and excitation pulse) were implemented into an FID-based 2D ^{1}H MRSI sequence[5] to obtain metabolite-nulled spectra. To find the optimal inversion time (TI1) to null the metabolite signal, two volunteers were scanned with fixed TI2 =1ms and TI1s of 300, 400, 500, 550, 570, 600 and 700ms (Fig. 1). Simulations were carried out beforehand the actual measurement (T_1s of metabolites and macromolecules used for simulations were adapted from [6]) to find the approximate optimal TI1. Metabolite-nulled spectra from 4 healthy volunteers were measured with a Magnetom 7T (Siemens Healthcare, Erlangen, Germany) scanner with following parameters: TR = 900ms, TI1 = 1ms, TI2 = 570ms, FOV = 180mm, 32x32 matrix, 12 mm slice thickness, 55° flip angle, elliptical phase encoding and WET water suppression. All inversion pulses were Wurst pulses with 40ms duration and sufficiently high bandwidth to invert all resonances from water to lipids (i.e., 2 kHz bandwidth). Raw data were exported and processed using a home-written script. All data were coil combined and automatically phase corrected based on reference data[7], afterwards Hamming filtered, and masked. Since small regional differences in MM basis set spectra do not affect the metabolite quantification significantly[3], an ROI (10x10 voxels) was drawn and corresponding spectra were frequency aligned and summed in jMRUI (jMRUI 3.0) to improve SNR. The residual metabolic signals of creatine at 3.9ppm (shorter T_1 than other major metabolites) and choline were removed after careful setting of parameter constraints in AMARES (jMRUI 5.0). The MM baseline with the narrowest linewidth was included into the LCModel basis set. Non-IR datasets from four healthy volunteers were then quantified by LCModel (v 6.3) using two different datasets – (1) containing metabolite resonances only, (2) containing the same metabolites+MM baseline. The fitted results were compared using paired t-test (SPSS 22).

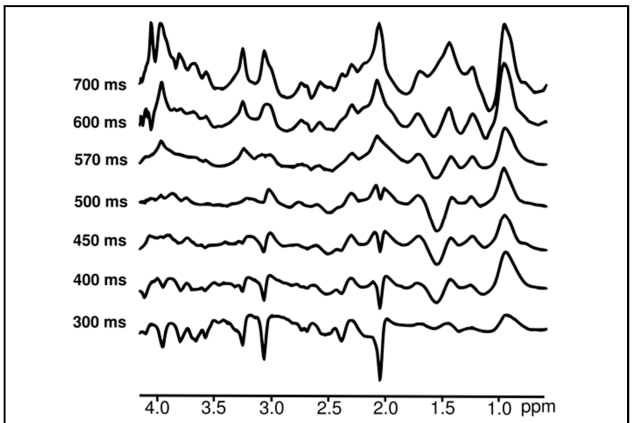

Fig. 1 – Inversion recovery experiment, 1st order phase corrected. Optimal nulling of metabolites was found at TI1=570ms

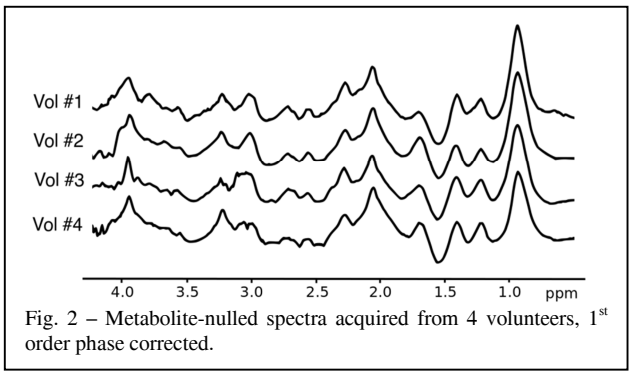

Fig. 2 – Metabolite-nulled spectra acquired from 4 volunteers, 1st order phase corrected.

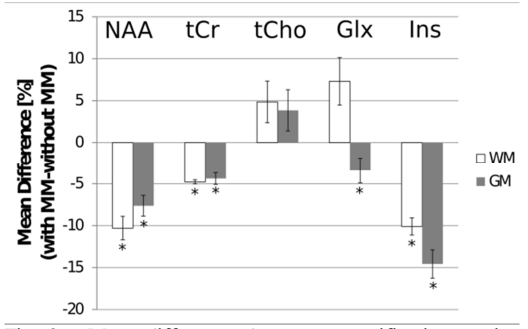

Fig. 3 – Mean differences between quantification routine with and without MM in basis set. * - significant difference in paired t-test, p<0.001, WM-white matter, GM-grey matter

Results & Discussion: The optimal nulling for metabolites was found at TI=570ms, which corresponded to theoretical calculations (Fig 1). Overall consistent quality of metabolite-nulled spectra was achieved for all four volunteers (Fig. 2). The relative concentrations of NAA, total creatine and inositol showed a significant difference (p<0.001) between two quantifications for both white and grey matter, glutamine and glutamate levels were significantly different for grey matter (Fig. 3). The CRLB values remained unchanged after MM incorporation.

Conclusion: We have developed and optimized a method of detecting macromolecules with ultra-short acquisition delay and short repetition time at 7T, which is not possible to obtain using any single voxel spectroscopy approach. In addition, we improved the accuracy of our quantification routine by taking the MM contribution into account. The sequence might be also further utilized to study regional differences in MM signals in diseased brain tissue.

References: [1] Cudalbu et al., J. Alzheimers Dis., 2012;31:5101-15. [2] Pfeuffer et al., JMR,1999;141:104-120 [3] Schaller et al. MRM, 2014;72:934-940 [4] Penner et al. MRM, 2014; [5] Bogner et al., NMR Biomed., 2012;25:873-882 [6] Xin et al., MRM, 2013;69:931-936 [7] Strasser et al., NMR Biomed, 2013;26:1796-1805