QUANTIFICATION DIFFERENCES OF \(^1\)H SPECTRA IN HUMAN BRAIN AT 3 TESLA USING THE ACQUIRED MACROMOLECULE BASELINE OR THE BUILT-IN LCMODEL SPLINE BASELINE

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Introduction: The improved spectral resolution of \(^1\)H spectroscopy at high field [1] is of great importance for a precise understanding of brain metabolism. However, the accuracy of the metabolite quantification of short echo time is challenged by a baseline of broad resonances underlying the whole \(^1\)H spectrum, identified as macromolecules (MM) and characterized by short \(T_1\) and \(T_2\). At high field (>3 Tesla), the in-vivo acquisition of the MM baseline is required for an accurate quantification of the metabolites [3]. However, at fields lower than 3T, MM are estimated mathematically using splines and then included in the basis sets. Inaccuracy in the MM baseline might lead to a poor estimation of the metabolite concentration [4]. Thus, at 3T, the influence of the choice of the baseline on the quantification is crucial and has not been previously investigated with LCModel. To further understand its effect on the quantification, macromolecule signal has been acquired with the SPECIAL (SPin Echo full Intensity Acquired Localized Sequence) [5] preceded by an inversion pulse. The aim of this study was to investigate the effect of the choice of the baseline, the in-vivo acquired macromolecule baseline or spline-baseline, on the metabolite quantification at 3T.

Materials and Methods: Four healthy subjects (4 men, aged 25 to 30 years) gave informed consent according to the procedure approved by the local ethics committee. A TEM transmit/receive volume RF coil was used to measure \(^1\)H spectra in a 3T Siemens Trio scanner. The voxel (VOI=20×20×25mm\(^3\)) was placed in the frontal lobe (fig. 1). First and second order shims were adjusted using FASTMAP. A preliminary experiment with a series of different inversion times (TI=650ms, 700ms, 750ms, 800ms) was used to determine the optimum TI for the acquisition of the MM spectra. The latter were acquired for three subjects using the IR SPECIAL sequence (TR/TE=4000/750/6ms, BW=2000Hz, vector size=2048 pts, 32×4 scans) employing VAPOR water and outer volume suppression [6]. In-vivo \(^1\)H spectrum was acquired with SPECIAL (TR/TE=4000/6ms, 16×4 scans, no inversion). The individual \(^1\)H MR spectra were frequency and phase corrected before averaging, using Matlab. Correction of the MM spectrum was performed with jMRUI using AMARES by fixing the linewidth, the frequency, the phase and the amplitude of the Lorentzian functions. Metabolites were quantified using LCModel (S. Provencher Inc., USA) with basis sets of simulated spectra of 21 metabolites and using the corrected in-vivo macromolecule baseline or the spline-baseline. A concentration of Creatine of 8.5µmol/g was used as an internal reference. Statistical test were based on a two-way ANOVA, testing for the influence of the baseline on the LCModel quantification.

Results and Discussion: Shimming resulted in typical water linewidths of 6.3±0.1Hz (mean±SD). In-vivo \(^1\)H NMR spectra were judged to be overall of high quality based on the high sensitivity (SNR=22.5±0.5, mean±sd, n=3, 32 averages) of the spectra and the absence of lipid contamination. The location of the voxel and the placement of OVS bands were carefully set to minimize lipid contamination. Based on the preliminary IR experiment, a TI of 750ms was set for the MM baseline acquisition since it contains the smallest metabolite residuals (due to the heterogeneity of the \(T_1\) of the metabolites). Metabolite residuals were observed on the measured MM baseline with two inverted peaks assigned to NAA (2.01ppm) and Creatine (3.01 ppm) and a positive peak of Creatine (3.9ppm) in agreement with \(T_1\) values reported at 3T [7]. Removal of the residual metabolite and water signals was performed with jMRUI (AMARES) providing a metabolic-nulled MM baseline (fig. 2.B, middle). The small standard deviation of the measured MM baseline illustrates the overall stability and reproducibility of the experiment. The two MM baselines, spline baseline (fig. 2.A) and corrected MM (fig. 2.B), were then integrated as prior knowledge in the LCModel basis sets and their effect on the metabolite quantification is shown in figure 3 (only metabolites with CRLB<20%). Changes in metabolite concentration of Ins and PCr were slightly higher (15-25%) and Cr and Glu were slightly lower (8-15%) using the in-vivo acquired macromolecules in agreement with previous study [4]. Although, they are relatively small changes (within the standard deviation), they are systematic and thus highly significant (with p values from 0.05 to 0.001). Other small concentrated metabolites, such as GABA, PE and GPC, revealed big changes (36-68%) (p<0.001). The results in the aforementioned concentration changes are directly related to the difference in the shape of the spline baseline and the acquired MM baseline in the region 2.1-3.5ppm (fig. 2). We conclude that, given the small changes (fig. 3), the spline is an overall good approximation of the MM baseline at 3T, however substantial differences in the quantification remain due to an underestimation of the macromolecules signal around 2-3.5ppm.