Short Echo Time H^1 Chemical Shift Imaging data quantification in the mouse brain at 11.7T using a constrained parametric macromolecular model

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Introduction

Short echo time chemical shift imaging (SE-CSI))of the mouse brain at 11.7T is technically challenging due to important magnetic field inhomogeneity effects [1] on the quality of the water suppression and spectral resolution and due to the small size of the volume of interest. Working at very high field help to increase signal to noise ratio but the quantification of metabolite concentration still needs to accommodate for more complicated baselines than in 1D MRS. This later is composed of 1) important residual water and 2) macromolecular (MM) contamination varying from voxel to voxel. We propose to derive from macromolecular CSI acquisition a constrained parametric macromolecular model which is incorporated as strong prior knowledge into the fitting of SE-CSI data. Applicability on *in vivo* data is demonstrated and discussed.

Material and Method

MR acquisitions: Experiments were performed on Swiss mice strain on a vertical 11.7T wide-bore system using a 25 mm micro probe (Bruker Biospin). Two chemical shift imaging (CSI) sequences were used to acquire the spatial distribution of 1) short-echo time signals (TE=6.5ms) 2) macromolecular signal. Macromolecular editing sequence was based on an inversion recovery preparation placed ahead of a k-space weighted spin-echo sequence (TR/TE = 2500/6.5 ms, 20x20x2 mm^3 FOV, 21x21 in-plane CSI matrix, 512 data-points, bandwidth of 8 kHz, Tacq = 40 min.) combined with diffusion-weighted spectroscopy to eliminate residual metabolite contributions [2]. Inversion recovery was performed using a secant hyperbolic RF pulse (4ms, 4.5kHz Band Width) with an inversion time of 700ms. Diffusion weighting was applied with a $\bar{\delta}/\Delta$= 1.5/4 ms and the equivalent gradient strength was set to 770 mT/m giving a b-value of 338 s/mm^2. Short echo time acquisition used the same TR, TE and FOV as for the macromolecule acquisition (Tacq = 40 min). Signal from the outer volume was suppressed by six bands of spatial saturation pulses interleaved in the water suppression pulses (VAPOR). Care was taken to preserve the same saturation band prescriptions on the two acquisitions. First and second order shimming were adjusted using FASTMAP. The mice were anaesthetized by inhalation of isoflurane (1%) and monitored for their respiration during the acquisitions.

Quantification procedure: The macromolecular spectra were considered as a density probability function and decomposed into a mixture of Gaussian lines using the Expectation Maximization (EM) algorithm. Twelve macromolecular components (MM_i , i=1 to 12), were derived by grouping Gaussian components around the following chemical shift: 0.88, 1.2, 1.4. 1.7, 1.9, 2, 2.2, 2.8, 3, 3.2, 3.6, 3.9ppm. (see figure 1)

Preprocessing of short-echo time signals included frequency alignment, phasing and residual water suppression using HLSVD. Short-echo time signals within each voxel were fitted using a non linear optimization which employs a metabolite basis set as prior knowledge [3-5]. These metabolite basis signals were adjusted to actual data according to the time domain approach developed in QUEST[3] using Gaussian apodization, frequency shifts, and amplitude multiplicative factor. Macromolecular model can be incorporated as prior knowledge into the model function either as

A) A whole rigid signal. In this case, it is adjusted the same way as the other metabolite signals as employed in 1D MRS [6].
B) Individual components. Here, each MM component are adjusted during the fitting procedure according to constraints applied on their amplitudes (A_{MMi} and frequency shifts f_{MMi} and expressed as follow:

$A_{MMi}=r_i A_{MM1}$ with $0.6\leq r_i\leq 1.4$ and $f_{MMi}= f_{MM1}+\delta f_i$ with $-8Hz\leq\delta f_i\leq 8Hz$ and i=2…12, MM_1 corresponding to the resonating group at 0.88 ppm

These constraints were chosen to allow little flexibility in the macromolecular modeling and to account for voxel to voxel variation or within subject variations

Comparative study: We have compared the two approaches (A and B) on the acquired in vivo data of one mouse brain by using as prior knowledge the macromolecular model computed from a second mouse CSI-macromolecular acquisition for which 4 voxel spectra were averaged.

Results: Figure 1 is displayed an example of a derived MM model. On Figure 2, mean estimated metabolite concentrations (averaged on 8 voxels) for the two approaches are represented for metabolite with estimated Cramèr Rao Lower Bound (CRLBs) below 50%. In the B option, the fit of individual components increases the number of parameters in the model function and results in a general increase by 5 to 10 % for the CRLB. On the other side, employing constrained MM parametric model (B) reduced the mismatching between the model function and the data resulting in a flat residue, closer to random Gaussian noise (see Figure 3).

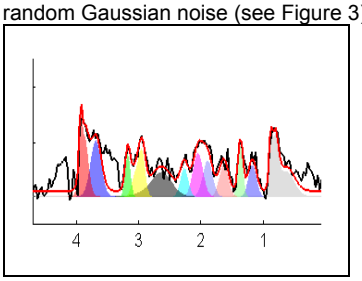

Figure 1: EM -MM model displayed as a whole rigid spectrum (red),and 12 MM components (colors) overlayed on the original macromolecules from one voxel of the CSI acquisition, in red

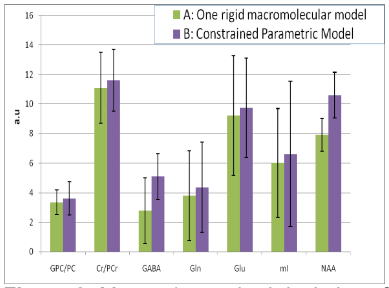

Figure 2: Mean +/- standard deviation of the Metabolite Concentration obtained for A and B MM kind of prior knowledge , obtained by averaging quantification results of the 8 voxels displayed figure 3. Systematic differences are observed for GABA and NAA.

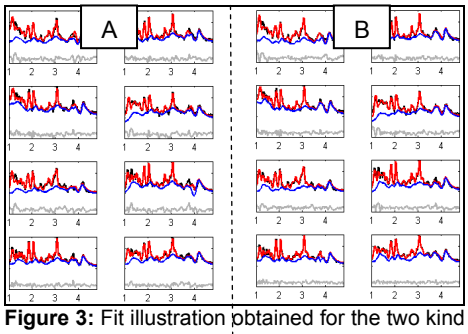

Figure 3: Fit illustration obtained for the two kind of MM prior knowledge **A** (left) and **B** and 8 central voxels. In black original spectra, in red the estimated spectra(metabolite+MM), in blue the fitted MM, in light grey the residual.

Conclusion:

In this work, macromolecular models have been generated in an automated way and introduced as strong prior knowledge into the model function used for fitting in vivo SE-CSI data in the mouse brain. Besides the fact that similar results were obtained between rigid and constrained parametric macromolecular model, the flexible approach is expected to accommodate for presumable macromolecular changes in pathological conditions, in which case rigid model is unsuitable.

References:

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