STEAM-MiTiS: a new spectral editing method for the detection of scalar coupled metabolites and its application for the detection of Glutamate at 7T

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Target audience: Scientists and clinicians interested in revealing scalar coupled metabolites using magnetic resonance spectroscopy (MRS).

Purpose: MRS has already proven to be a reliable and non-invasive technique for the detection of brain metabolites, however many metabolites consist of coupled spin systems, and often overlap with much stronger singlet signals. Traditionally, editing approaches for the detection of these metabolites are based on TE optimization, multiple quantum filtering, J-resolved spectroscopy, or other 2D NMR techniques[1]. We propose a novel method called STEAM-MIxing TIme Subtraction (STEAM-MiTiS) based on the time evolution of scalar coupled metabolites at different mixing time (TM) and constant echo time (TE). The method is capable of completely cancelling out all the strong singlet lines and, possibly, macromolecules, and leave the scalar coupled metabolites signals, only. Therefore, it strongly simplifies the edited spectra, but also retains the complete spectral information of the traditional STEAM acquisition. A somewhat similar approach has been proposed and implemented with the PRESS localization technique[2,3], only, but we apply it to STEAM and extend the analysis to the whole TM-space combinations to completely exploit the potentialities of the method. The sequence design is simple and can be implemented with any standard STEAM sequence even without sequence programming.

Methods: The method consists in acquiring two different STEAM spectra with same TE, but different TMs peculiar for each J-coupled metabolite. The sum of the two spectra gives the complete STEAM spectral information at that specific TE, but the difference of the two acquisitions perfectly cancels out the singlets contribution leaving only the information of scalar coupled metabolites. We optimized the method for the detection of Glutamate (Glu) in the human brain while minimizing Glutamine (Gln) contamination.

Simulation and optimization of the parameters: Density matrix simulation at various TE and TM were performed with the VESPA package and the following analysis was performed with a homemade routine in Matlab (MathWorks, Natick, USA). For every TE we built a TM-TM map with the editing efficiency (calculated as the maximum subtracted intensity divided by the maximum peak at every TE) plotted in color. The map easily identifies the TM_i-TM_j combination that maximizes the editing efficiency, and the comparison of the maps at various TEs gives the best combination of all the parameters. The maximum editing efficiency for Glu in the 2.25-2.4 ppm range was found at TE=65ms. Fig. 1 shows the TM-TM map for Glu at TE=65ms and TM ranging from 12 to 35ms with 0.1ms steps. The map is symmetric and presents a sharp periodic modulation (0.9ms period) of the editing efficiency as a function of TM, as expected for strongly coupled metabolites. The maximum efficiency is 1.18 and is reached for subtraction of TM_1=13ms and TM_2=31.5ms spectra. We performed the same simulation for Glutamine and observed that the residual Gln contamination at the optimal Glu parameters is around 10% and that the maximum editing efficiency for Gln at TE=65ms occurred at completely different mixing times (TM_1=15.4ms, TM_2=21ms).

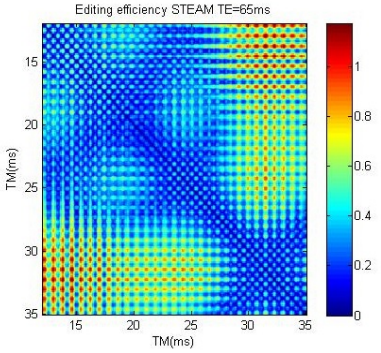

Fig. 1: TM-TM map for Glu

In-vitro experiment: We used the optimized parameters for acquisitions on homemade phantoms containing 10mM of Creatine (Cr), and various concentration of Glu and Gln (10.5mM, 8.2mM, and 5.1mM). The single voxel STEAM sequence was modified for acquiring two different FIDs in interleaved fashion with identical parameters (TR=2000ms, TE=65ms, spectral width=5000Hz, number of points=4096, averages=64, NEX=8, voxel size 2X2X2cm^3) and two different TMs (13ms and 31.5ms).

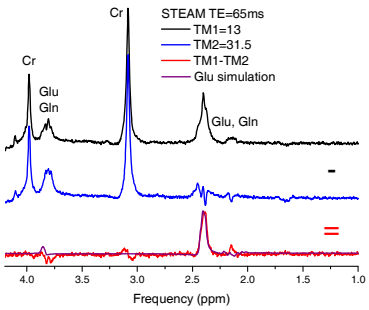

Fig. 2: in-vitro spectra

In-vivo experiment: Spectra were acquired on four normal volunteers, who gave informed consent in accordance with procedures approved by local institutional review board. VOI was located in the left primary motor cortex (M1). The STEAM sequence was performed with the same parameters used for phantom acquisitions, except for 80 averages for a total acquisition time=6min and 40s. Data analysis was performed with a home-made routine in Matlab (MathWorks, Natick, USA), and consisted in zero filling, coil combination, Gaussian apodization (1.25Hz for in-vitro and 4Hz for in-vivo acquisitions), frequency alignment of the water line (for in-vivo acquisitions, only), frame average, Fast Fourier Transform, residual water subtraction, and DC correction.

All experiments were performed in a GE MR950 7.0 T human system (GE HealthCare, Milwaukee, WI, USA) using a Qd Tx - 32 Channel Rx head coil (Nova Medical USA).

Results: Fig. 2 and 3 show typical phantom and in-vivo acquisitions, respectively: the two top lines are the spectra acquired at different TMs; the bottom spectrum is the subtraction of the two with the simulated result superimposed. In the subtracted spectrum, both in-vitro and in-vivo, we obtained almost perfect cancellation of the singlet signals and macromolecules, while retaining the spectral information of the scalar coupled metabolites. The simulation is in good agreement with experimental results. Moreover, the in-vitro calibration yielded a linear dependence of the peak intensity as a function of Glu concentration. In addition, the sum spectrum contains all the spectral information of singlets and scalar coupled metabolites altogether and can be used for quantification, as well.

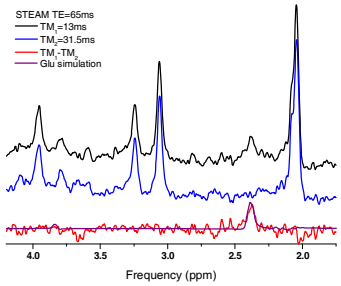

Fig. 3: in-vivo spectra

Discussion and conclusion: The STEAM-MiTiS method has been optimized for the in-vivo detection of Glu. Simulation results yielded the optimum parameter values that were used for in-vitro and in-vivo validation. Experiments indicated an almost perfect cancellation of singlet and macromolecule signals, and resulted in clear editing of the Glu peak. In-vitro calibration confirmed a linear dependence of the residual Glu line with concentration. Therefore, the method demonstrated good spectral editing performance for the detection of Glu at 7T. The method is simple, easily implementable on MR systems without sequence programming, and can be easily generalized for the detection of other scalar coupled metabolites. Moreover, the same acquisition retains all the spectral information of a usual STEAM acquisition, when used in 'added' mode; therefore, it also permits the quantification of all the singlets and the other metabolites.

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