ESTIMATED METABOLITE CONCENTRATIONS IN THE RAT BRAIN WITH QUEST:A COMPARISON BETWEEN IN VITRO AND SIMULATED BASIS SETS

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INTRODUCTION

Localized brain proton Magnetic Resonance Spectroscopy (MRS) can non invasively provide - by quantitation of brain metabolites - biochemical information from distinct regions of the brain. Quantitation of short echo-time signals is usually based on a metabolite basis set. The basis set can be obtained either by quantum mechanically simulating the theoretical metabolite signals, or by measuring signals of metabolite aqueous solutions. The purposes of the present study are: 1) to compare the influence of the basis set on the quantitation results; and 2) to estimate the metabolite concentrations in the central region of the rat brain. Short echo-time *in vivo* signals of rat brains were acquired at 7 Tesla from the central region of the brain. Brain metabolites were quantitated with the method QUEST [1]. Estimated brain metabolite concentrations are compared for the two basis sets and to previously reported results.

METHODS

The experiments were performed on a 7T Biospec BRUKER system using a bird cage coil for excitation and a receiver surface coil. Fifteen signals from eight healthy adult rats (Sprague-Dawley) were acquired using a short echo-time PRESS sequence (TE=20ms, TR=5s, SW=4kHz, 4096 data-points, 128 averages) combined with outer volume suppression. All first- and second- order shim terms were adjusted using FASTMAP for each voxel of $(3.5mm)^3$ positioned in the center of the rat brain. The *in vivo* signals were processed using the jMRUI software [2]. Removal of residual water components was performed in a preprocessing step using HLSVD.

Quantitations were performed with QUEST combined with the 'Subtract' approach for background modeling [1] (see Figure I). The numerical time-domain model functions of eleven metabolites [Aspartate (Asp), creatine (Cr), choline (Cho), γ-Aminobutyric acid (GABA), glucose (Glc), glutamate (Glu), glutamine (Gln), N-Acetylaspartate (NAA), taurine (Tau), lactate (Lac) and myo-inositol (Ins)] were used as prior knowledge in QUEST. To set up the *in vitro* metabolite basis set, the eleven metabolites were dissolved separately in aqueous solutions (100mM, pH=7.0±0.1, 10ml). The *in vitro* signals were measured using identical acquisition parameters as the *in vivo* ones. The eleven metabolites signals of the simulated basis set were quantum mechanically simulated for the *in vivo* experimental protocol (PRESS sequence, TE=20ms, bandwidth of 4 kHz, 4096 data points) with NMR-SCOPE [3]. Since the *in vitro* basis set takes into account the *in vitro* spin-spin relaxation time effects, for comparison, the simulated basis set signals need to be corrected for the spin-spin relaxation time effects too. The latter were corrected using the metabolite *in vitro* relaxation times given in [4]. The reliability of metabolite quantitation was assessed using the Cramér-Rao lower bounds. An estimate was considered as relevant when the corresponding bound was found below 15% of the estimate.

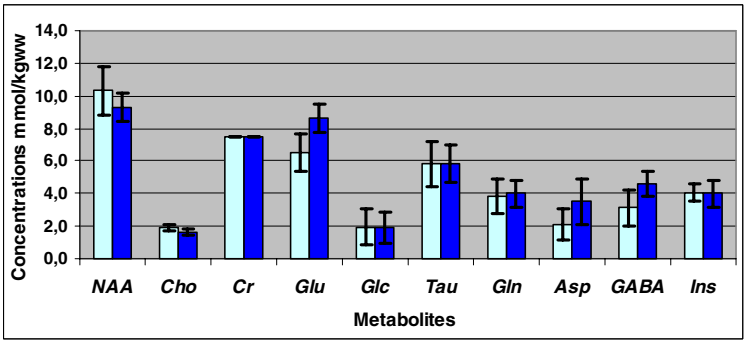

Figure II: Mean values and corresponding standard deviations of the metabolite concentration estimates obtained from fifteen signals of rat brains quantitated using QUEST and an *in vitro* metabolite basis-set (light blue bars), and theoretical quantum mechanically simulated basis-set (dark blue bars).

RESULTS

For the two basis sets, the mean values and the corresponding standard deviations of the estimated metabolite concentrations obtained from the fifteen signals were computed from the relevant estimates (Figure II). For the sake of comparison, metabolite concentration estimates were set proportional to the total creatine (Cr + PCr) concentration, used as an internal reference, which was supposed to be 7.5 $mmol/kg_{ww}$. Results are of comparable quality, as can be seen in Figure II.

Both basis sets have advantages and drawbacks:

- ***In vitro* basis set:**
  - ☺ The experimental conditions are automatically taken into account.
  - ☺ The metabolite concentration estimates are automatically and partially compensated for the spin-spin relaxation effects.
  - ☹ A new basis set must be acquired for any new experimental protocol, and tedious and time consuming experimental work is needed for acquiring signals of *in vitro* metabolite solutions.
- ***Simulated* basis set:**
  - ☺ The basis set can easily and quickly be simulated for any experimental protocol.
  - ☹ The metabolite concentration estimates may need to be compensated for the spin-spin relaxation effects.

CONCLUSIONS

- ✓ The central region of the brain from healthy rat brains was investigated at 7Tesla.
- ✓ Metabolites were well identified and successfully quantitated using QUEST.
- ✓ Influence of *in vitro* and simulated metabolite basis sets on QUEST quantitation results, was compared.
- ✓ The concentration estimates using the two basis sets are not significantly different and are in good agreement with the values from the literature [5].

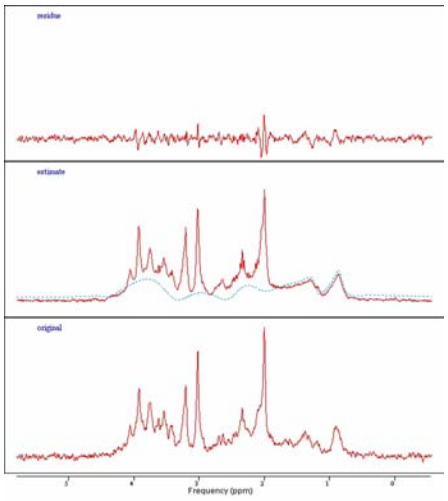

Figure I: QUEST Quantitation results. From bottom to top, original spectrum of a rat brain acquired *in vivo* at 7T in the center of the brain; estimated spectrum and background (dashed line); and residue.

REFERENCES:

[1] H. Ratiney, et.al., *NMR in Biomedicine,* 18 (2005), 1. [2] http://www.mrui.uab.es/mrui/ [3] D. Graveron-Demilly, et. al., *JMR,* A101 (1993), 233. [4] C. Cudalbu, et. al., *MAGMA,* 17, supp1 (2004), 337. [5] J. Pfeuffer, et. al., *JMR,* 141 (1999), 104.