Absolute quantification of ^{1}H Magnetic Resonance Spectroscopy of human brain using qMRI

A. Tisell[1,2], O. D. Leinhard[1,2], M. Warntjes[1,2], J. West[1,2], and P. Lundberg[1,2]

[1]Department of medical and health sciences, Division of radiological sciences, University of Linkoping, Linköping, Sweden, [2]Center for Medical Image science and Visualization (CMIV), University of Linkoping, Linkoping, Sweden

Introduction

Absolute quantification (AQ) of MR-spectra is a useful tool for detailed studies of tissue metabolism *in vivo* in a non-invasive manner. Previously proposed methods have been based on additional spectroscopic measurements on the MRS VOI, and also on external references [1,2,3]. Thus time-consuming additional measurements must be performed for each individual VOI. In this work, a novel method was developed that uses the internal water signal as a reference. More specifically, the internal water was quantified using the quantitative imaging method QRAPMASTER [4]. The objective of this work was to develop a method that was rapid, easy and user independent.

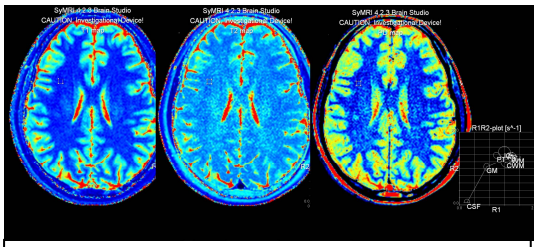

Figure 1. Quantitative T1, T2 and PD images

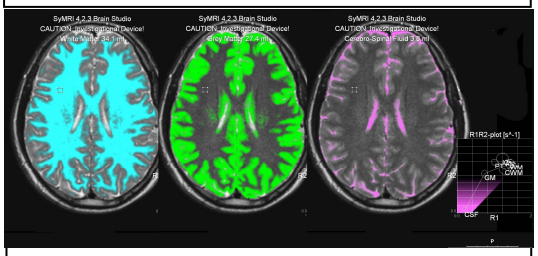

Figure 2. Tissue classification of WM,GM and CSF

Materials and Methods

Compartments: It was assumed that the VOI could be described using a three compartment model ('Intra Cellular fluid' (ICF), 'Extra Cellular Fluid' (ECF) and 'Solid Structures' (SS)). The SS was assumed to be invisible using our liquid-state NMR methods. Since essentially no metabolites are dissolved in ECF, the visible metabolites in NMR are limited to those that are dissolved in the ICF. Therefore an appropriate measurement of metabolite concentrations would be the determined amount of metabolites, divided by the volume of ICF.

Water scaling: Both a water suppressed MRS metabolite signal S_{met}, and an MRS signal using no water suppression S_{H2O} were obtained from the same VOI using the same preparation. Thus, S_{met} and S_{H2O} were affected by the same B0 and B1 inhomogeneities, shims, temperature, etc. Water scaling was 0btained by dividing S_{met} by S_{H2O}. Since S_{met} originates from the ICF compartment only, whereas S_{H2O} originates both from the ICF and the ECF compartments the water scaling was defined by Eq. 1. In this equation, C_{VOI} is a combination of factors affecting the signal level *e.g.,* coil loading, temperature, shims, pulse profile, etc. C_{VOI} was assumed to be equal for S_{met} and S_{H2O}, thus it cancels out in the water scaling. R_a^b describes the relaxation for signal a in compartment b. N_c^b were the number of protons of the substance c in compartment b. H_c is the number of protons in each molecule of substance c.

qMRI: QRAPMASTER which was proposed in [4], was used for covering the whole brain. The data were post processed using 'Brain Studio' (SyMRI, Sweden) resulting in quantitative T1, T2 and PD volumes see Fig. 1. The tissue classification was also performed using Brain Studio.

Validation experiments: Two separate validation experiments were performed using a 1.5 T Philips Achieva MR-scanner (Philips Medical Systems, The Netherlands). The first group included 17 healthy volunteers (8 males; 9 females). The Transmit/Receive quadrature spectroscopy head coil was used. In each subject, an SVS in parietal normal appearing white matter (NAWM) using PRESS (TE 30 ms, TR 3 s, NSA 80 and 8 NSA of the unsuppressed water signals). A 240 x 240 x 60 mm^3 QRAPMASTER volume with an resolution of 0.84 x 0.84 x 3 mm^3 were measured. In the other validation experiment repetitive measurements on a single subject were performed using an 8 elements SENSE head coil, and PRESS (TE 30ms, TR 3s, NSA 128, and 8 NSA unsuppressed water signals). QRAPMASTER (Volume 240 x 240 x 60 mm^3, res 0.84 x 0.84 x 3 mm^3). Two separate VOIs where placed in parietal NAWM. The experiments were repeated 4 times during two days. The MRS spectra were analyzed using LCModel (Provencher, Canada) using water scaling. The relaxation times of the internal water were calculated using the quantitative absolute T1, T2 and PD images. We assumed that the VOIs where positioned in pure NAWM, and that the ECF compartment was negligibly small.

Table 1	**Mean**		**SD**	**CV%**
tCr				
qrapSVS (n=15)	7.34	±	0.52	7.1
Rep qrapSVS (n=2*4)	7.26	±	0.23	3.1
Helms (n=11)	5.40	±	0.47	8.7
Danielsen (n=10)	5.79	±	0.66	11
Cho		±		
qrapSVS	2.78	±	0.29	10.5
Rep qrapSVS	2.72	±	0.15	5.3
Helms	1.46	±	0.15	10.3
Danielsen	1.32	±	0.14	11
Ins		±		
qrapSVS	6.81	±	1.54	22.6
Rep qrapSVS	5.57	±	0.45	8.1
Helms	-	±	-	-
Danielsen	4.14	±	0.62	15
tNAA		±		
qrapSVS	12.33	±	1.21	9.9
Rep qrapSVS	13.24	±	0.45	5.1
Helms	10.15	±	0.46	4.5
Danielsen	8.73	±	1.11	13

qrapSVS; group results measured with the proposed method. ***Rep qrapSVS***; results of the repetitive study
Helms; literature values of parietal WM [3]
Danielsen; literature values of parietal WM [1]

$$\frac{S_{met}}{S_{H_2O}} = \frac{C_{VOI}\, R_{met}^{ICF}\, N_{met}^{ICF}}{C_{VOI}\left(R_{H_2O}^{ICF} N_{H_2O}^{ICF} + R_{H_2O}^{ICF} N_{H_2O}^{ICF}\right)} = \frac{R_{met}^{ICF} V^{ICF} H_{met} [met]^{ICF}}{\left(R_{H_2O}^{ICF} V^{ICF} H_{H_2O} [H_2O]^{ICF} + R_{H_2O}^{ECF} V^{ECF} H_{H_2O} [H_2O]^{ECF}\right)} \quad \text{Equation 1}$$

Results and Conclusions

The determined absolute concentrations are shown in Table 1. The repetitive study showed standard deviations that can be fully accounted for by the standard deviation of the LCModel fit. Two volunteers were excluded due to movement during measurements. The standard deviations of the group results were comparable with literature value [1, 3] of metabolite concentrations in NAWM. This suggests that the method provided reproducible results. Our conclusion was that the method provides accurate MRS results, and also that the method is completely user independent.

References: *[1] Danielsen et al J Magn Reson B* ***106*** *(287-291), [2] Kreis et al J Magn Reson B* ***102*** *(9-19), [3] Helms NMRMB* ***13*** *(398-406), [4] Warntjes et al Magn Reson Med* ***60*** *(320-329).*