Absolute Quantitative Spectroscopy through Internal Water Referencing with a One-Minute RRAMSC

Jack Knight-Scott[1]

[1]*Radiology, Children's Healthcare of Atlanta, Atlanta, Georgia, United States*

INTRODUCTION: In recent years, an increasingly greater number of studies depend on morphology-based image segmentation to obtain a water reference for quantitative spectroscopy. Although relaxometry-based segmentation/compartmentalization is the most accurate and precise method for separating brain tissue and cerebral spinal fluid (CSF) water signals in proton MRI and MRS[1-4], its long acquisition times make the technique one of rare use in quantitative neuro-spectroscopy. We recently presented an optimized ***R***apid ***R***elaxometry through ***A***cquisition of ***M***ultiple ***S***aturated T_2 ***C***urves (RRAMSC) technique capable of acquiring relaxometry data in approximately one minute[5]. Here, we use results of RRAMSC to calculate brain metabolite concentrations in molal units and compare results to previous studies.

METHODS: Ultra-short TE spectra (STEAM: TE/TM/TR=4/12/4000-ms, ~10 cm^3, 120 NEX, 24-step phase cycle, 2500 Hz SW, and 2048 pts) were acquired from the posterior cingulate gyri of five healthy female adults (mean age: 33.1 ± 16.4 years, 18-55) on a 3.0 T MRI system (Siemens Medical System, Erlangen, Germany). Each acquisition included a water spectrum for phase correction and an automated RRAMSC acquisition consisting of two curves: 13 echoes each (10 to 750-ms), logarithmically sampled, with delay times (TD=TR-TM-TE/2) of 1.03s and 2.75s. Water-suppressed spectra were phase corrected, and apodized. The RRAMSC data and water reference were phase corrected and their signal intensities measured in the time domain by a fit to the first 40 points in the FID. Fit of a bi-exponential model to the RRAMSC data allowed separation of the CSF and tissue water signals. Water references were scaled to yield the same intensity as the tissue water components from the RRAMSC fit. Scaled water references and corresponding water-suppressed spectra were then analyzed in LCModel with a GAVA[6] simulated nineteen-metabolite basis set. Group statistics included mean values and coefficient of variation (CV) values for metabolites with mean Cramer Rao Lower Bounds (CRLB) values or CVs of 20% or less.

RESULTS and DISCUSSION: Internal water referencing has long been an established method for quantitative spectroscopy. Relaxometry-based water referencing provides not only a means for separating the different water compartments, but also a stable reference. Through RRAMSC we provide a spectroscopy friendly, rapid relaxometry-based method by which to acquire this data (~ 1 min). RRAMSC might be especially suitable for high field 7T MRI systems with their very long T_1 relaxation times. In the current study, our metabolite concentrations are similar to 3T results reported by Mekle et al using[7], and while our CVs are on average lower than those of Mekle et al and our CRLB values are slightly higher. However, the latter is likely due to our use of apodized data. Other notable differences are our nearly double [Gln] and over 70% increased [PE]. Similar to other non-spectral edited experiments, quantifying [GABA] at 3T overestimates by approximately double its known value. GABA can be accurately identified and quantified without spectral editing at 7T, but at 3T, severe overlap with surrounding resonances yields a higher than normal [GABA]. Also comparable to other studies, the CV of tCho is relative high though its CRLB is consistenly low, suggesting choline variance is a normal phenomenom and likely indicative of natural physiological differences across the pool of participants.

We also quantified the macromolecules, but because of unreliable separation of the baseline and the macromolecule resonances, LCModel macromolecule concentrations were analyzed as peak areas including the spline baseline. As in previous studies, the macromolecule variance was greatest for the M4 peak at 1.63 ppm, and when analyzed as a function of age showed the following trend in Figure 2. The potenital high age-related sensitivty of this peak was first identified by Haley et al. in hippocampal studies of Alzheimers disease[8]. To our knowledge, these results represent the first data suggesting a clear age dependent trend throughout adulthood.

This limited study shows RRAMSC to be a robust method for separting the gross brain water compartments, and as a fast automated acquisition it can be employed in both clinical and research studies.

Concentration (μ mole/g) ± CV (%)		CRLB (%)
Asp	3.12 ± 5.9%	13%
GABA	2.76 ± 14.1%	14%
Gln	3.13 ± 16.3%	13%
Glu	10.94 ± 5.5%	5%
GSH	1.64 ± 11.2%	9%
mI	6.88 ± 7.6%	6%
NAA	13.04 ± 3.1%	2%
PE	3.78 ± 13.7%	12%
Tau	1.62 ± 7.9	31%
tCho	1.44 ± 14.2%	5%
tCr	10.01 ± 5.0%	2%
Macromolecules		
M1	487.7 ± 3.6%	13%
M2	296.4 ± 10.6%	23%
M3	413.8 ± 15.9%	25%
M4	*416.5 ± 19.5%*	*25%*
M5	638.9 ± 11.4%	17%

Macromolecule concentrations are in peak areas from LCModel fits and include spline baselines, while CRLB values are for macromolecule peaks alone

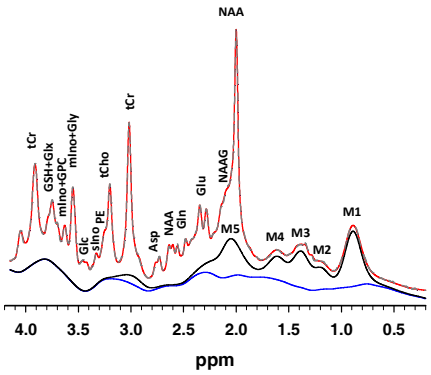

Figure 1. Averaged spectrum with LCModel fit results, 4ms TE, 12 ms TM, 4 s TR, 120 Nex

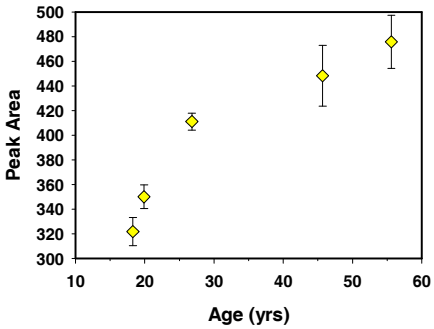

Figure 2. M4 peak area as a function of age over the five subjects in this study.

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