Comparison of quantification strategies for clinical 1H-MRS using a large spectroscopy database

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1. Introduction.

Proton magnetic resonance spectroscopy (1H-MRS) is a promising method to track the progression and treatment of neurodegenerative diseases. Several studies have shown that the NAA/mI ratio represents a useful diagnostic measurement for differentiating cognitively normal subjects from those with Alzheimer's disease ([1]). More recently this methology has been applied also in subjects with mild cognitive impairment (MCI), in which an increase of mI was observed in the paratrigonale area ([2]) and in the posterior cingulate gyrus([3]). The aim of this study was to compare the results of processing a large database of spectra (72 subjects, 142 spectra) with two different analysis methods. The first method is a widely used fully automatic MRS reconstruction technique that works on the host MRI computer and is routinely applied in clinical practice (PROBE-q), while the second method is the more sophisticated LC Model technique ([4]).

2. Patients, materials and methods.

We studied 74 subjects: 24 healthy controls (CTL), 25 subjects fulfilling Petersen's criteria for amnestic mild cognitive impairment (aMCI) ([5]) with a slight impairment in memory function as evaluated by the Babcock recall story test, and 25 patients fulfilling the NINCDS-ADRDA diagnostic criteria for probable Alzheimer's disease (AD) ([6]) (see table 1). All subjects were enrolled in the AddNeuroMed study ([7]) and examined twice, at baseline (T0) and 12 months later (T12). We used a PRESS pulse sequence with TE = 35 ms, TR = 2000 ms, number of data points = 4096, number of averages = 128, bandwidth = 2500 Hz. The VOI was located in the left peritrigonal white matter (volume = 20x20x20 mm). The spectra were reconstructed using two methods. The first was the fully automatic PROBE-q (PROton Brain spectroscopy Exam - quantitation) ([8]) MRS reconstruction routine, and the second LC Model ([9]). All spectra showed a good quality: FWHM of unsuppressed water peak < 5 Hz, residual water signal < 1%, no evident baseline distortion, no evident fat contamination and SNR with respect to the Cr+PCr total peak > 25.

Tab. 1	CTL (n=24)	aMCI (n=25)	AD (n=25)
Age (y)	72.67±5.25	75.52±5.00	76.4±5.33
sex	M: 54.2% F: 45.8%	M: 60% F: 40%	M: 28% F: 72%
MMSE T0	28.96±1.23	27.04±1.8	21.92±4.02
MMSE T12	28.71±1.60	25.96±3.2	20.72±4.51

The basic PROBE-q reconstruction uses unsuppressed water reference frames to correct metabolite spectra (the scanner acquires a series of water reference scan followed by 8*16 blocks of water suppressed data) PROBE-q reconstruction consists of the following steps: internal water reference correction (the algorithm choice operates on one frame of the data at a time using the frame's residual water signal to correct for phase, frequency, and residual eddy current distortion), zerofilling to 8192, linear baseline correction, convolution filtering, apodization (Gaussian with 1.25 Hz FWHM), FFT and Marquardt fitting.

In the second method 1H-MRS concentrations were derived using LC Model on a Sun SPARC-10 workstation (Sun Microsystems Inc, Mountain View, Calif). LCmodel uses a linear combination of model spectra of metabolite solutions in vitro to analyze the major resonances of in vivo spectra. A basis set of concentrations of alanine, aspartate, creatine, {gamma}-aminobutyric acid, glutamine, glutamate, glycerophosphocholine, myo-inositol, lactate, NAA, N-acetyl-aspartylglutamate, scyllo-inositol, and taurine, together with a baseline function, were used for analysis. As expected, many of these metabolite peaks that were included in the LC Model did not reach statistical significance when fitted. However, myo-inositol, NAA, Cr + PCr, and Cho concentrations concentrations were therefore derived from these metabolite peaks. Statistical analysis was performed using the Mann-Whitney test and correlation with the Spearman test.

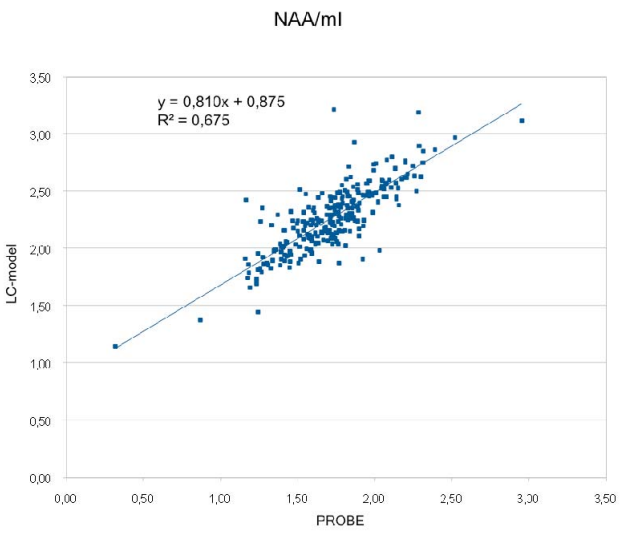
3. Results.

Figure 1 shows that the NAA/mI ratio evaluated with the PROBE-q software is constantly higher than the ratio calculated with LC Model. This result is also confirmed by computer simulation using synthetic data. PROBE-q demonstrated a smaller percentage standard deviation than LC Model. Table 2 shows the results of the statistical analysis, with LC Model demonstrating a more statistically significant difference ($p<0.001$) between the MCI and CTL groups and between the AD and CTL groups. The same comparisons show less differences for PROBE-q, where a statistically significant difference ($p=0.039$) was only observed between the AD and CTL groups.

Tab. 2: NAA/mI mean±SD (SD%)	CTL	aMCI	AD	p
PROBE	2.29±0.22 (9.60%)	2.30±0.30 (13.04%)	2.18±0.36 (16.51%)	0.069 MCI vs AD 0.039 CTL vs AD
LCmodel	1.54±0.23 (14.93%)	1.53±0.27 (17.64%)	1.36±0.30 (22.05%)	<0.001 MCI vs AD <0.001 CTL vs AD

4. Conclusion.

To our opinion the PROBE method is very useful in the clinical setting when the radiologist aims to get peaks easily evaluable at glance (for example for the diagnosis of brain tumors) but it is less sensitive and specific than the LC model for more sophisticated research studies, such as the diagnosis of MCI. For this reason it is important to modify the PROBE software parameters according to the aim of each study.



5. References

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