Reproducibility of Short Echo Time MRSI of the Human Brain at 3T using a semi-LASER Approach.

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Introduction:
In this work we investigated the reproducibility of ^{1}H-MRSI of the normal human brain as obtained by the semi-LASER sequence at 3T. This sequence was recently developed and overcomes the chemical shift displacement error problem at 3T to a level, which is even better than in regular PRESS at 1.5T (1). The semi-LASER sequence uses adiabatic refocusing pulses with bandwidths of 5 kHz, retaining a short echo time of 30ms. The adiabatic refocusing pulses make the sequence more tolerant to B_1 inhomogeneieties. Knowledge of the reproducibility of the MRSI method and of the within and between subject variability is essential in interpreting MRSI spectra of brain disorders.

Methods:
Six healthy volunteers were examined twice with the semi-LASER MRSI pulse sequence in a 3T whole body MR system (Magnetom TRIO, Siemens Medical Solutions, Erlangen). The MRSI matrix (20x20) was positioned in an axial plane of the brain parallel to the Corpus Callosum. The measurement parameters were: TR of 2 s, TE of 30 ms, nominal resolution of 8x8x10 mm, spectral resolution of 2 Hz/point, carrier frequency was set to 2.2 ppm, elliptical weighted k-space acquisition with 2 averages, and acquisition time of 11 minutes. All MRSI data were filtered in the two spatial dimensions with a 100% Hanning filter. Before Fourier transformation the data was zerofilled to a 32x32 matrix. The combination of the weighted acquisition and the filtering of the k-space reduces contamination from neighboring voxels, however it increased the real voxel size by a factor of 1.7 in both spatial directions. The real voxel size is best approximated by a circle with a diameter of 8*1.7mm in a slice of 10mm thickness (white circles in figure1). Also one k-space acquisition of an unsuppressed ^{1}H-MR spectrum was obtained as a water reference file.
To determine the reproducibility of the repeated MRSI measurement, the metabolite concentrations were determined using LCModel (2) in three ROIs; parietal white matter in the Gyrus Cinguli (PWM), frontal white matter in the Gyrus Cinguli (FWM) and parietal gray matter (PGM) (figure 1). The LCModel basis set of 22 common brain metabolites and macromolecules was simulated with NMRSIM (3) on the basis of the semi-LASER pulse sequence. The within subject variability is defined as the standard deviation of the differences between the first en second measurement. The between subject variability is defined as the standard deviation of the mean value of the first and second measurement (4). We also determined the Coefficient of Variation (CoV), defined as the standard deviation of differences between the first and second measurement divided by the mean values of all measurements, for each metabolite in each ROI. This means that the between subject variability is included in the CoV.

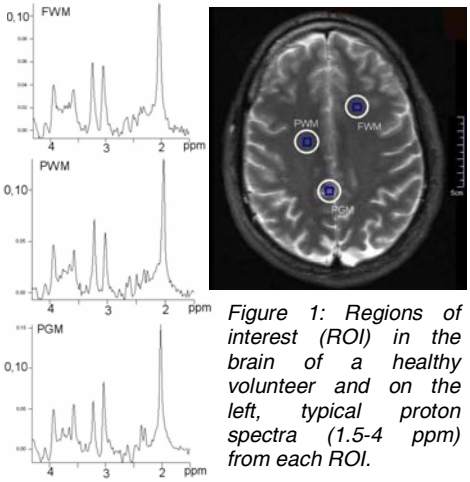

Figure 1: Regions of interest (ROI) in the brain of a healthy volunteer and on the left, typical proton spectra (1.5-4 ppm) from each ROI.

Results and Discussion:
Results from LCModel fits of the total Choline (tCho) concentration (Cho+GPC) from each ROI of all subjects are plotted for the two measurements in figure 2. From this it becomes clear that regional differences in tCho exist because all values for PGM are concentrated around 1.5 and the tCho values in FWM and PWM are concentrated around 2.2. The reproducibility of metabolites, for example NAA+NAAG, can better be represented as in figure 3. The green line is the mean difference of the first and second measurement, the red lines represent the 95% confidence intervals of the within subject variability (mean +/- 2*sd of the difference between the measurements). The between subject variability can be seen along the x-axis. The data as presented in figure 3 is summarized in table 1 together with the values obtained for total Creatine (Cr+PCr), tCho and myo-inositol (mI) in each ROI. Also the mean values of metabolite concentrations and the CoV are given in table 1. The metabolite concentrations correspond to previous reported values (5,6). The within and between subject variability vary with ROI and metabolite and range between 5% and 15% of the mean metabolite value. Also, in some ROIs the within subject variability is larger than the between subject variability. This can be assigned to the fact that we only repeated the measurement once. Although the CoV is not a real measure for the reproducibility (4), this parameter is often used in reproducibility studies and the values for CoV we found are smaller or comparable to values found by other research groups (7,8).

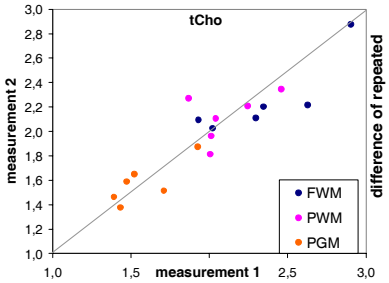

Figure 2: Graph of tCho concentrations in the first (y-axis) and second (x-axis) measurement the 3 ROIs of each volunteer.

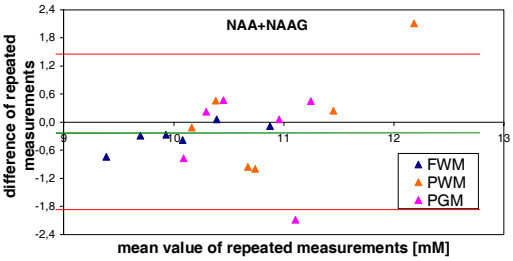

Figure 3: Graph of the reproducibility of the concentration NAA+NAAG in the 3 ROIs of each volunteer. Red lines indicate the mean +/- 2sd of the difference of the repeated measurement. The mean value (green line) of the difference deviates not significantly from 0.

Table 1: Reproducibility results.

	NAA+NAAG	Cr+PCr	Cho+GPC	mI
mean values [mM]				
FWM	10.06	6.69	2.30	6.21
PWM	10.93	5.96	2.11	5.75
PGM	10.69	8.34	1.58	6.73
within subject sd [mM]				
FWM	0.27	0.56	0.20	0.37
PWM	1.15	0.62	0.21	0.47
PGM	1.00	0.70	0.13	0.46
between subject sd [mM]				
FWM	0.52	0.24	0.33	0.87
PWM	0.75	0.36	0.18	0.67
PGM	0.47	0.51	0.18	0.23
CoVariance [-]				
FWM	2.7	8.3	8.5	5.9
PWM	10.5	10.5	9.9	8.2
PGM	9.3	8.4	8.0	6.8

Conclusion:
The semi-LASER MRSI sequence is a robust method for short echo time MSRI of the human brain at 3T. Although differences between ROIs and metabolites exist a manageable within subject variability of 10% and a between subject variability of 15% can be used over the brain for all main metabolites. Therefore larger deviations in metabolite concentrations, obtained from MRSI in patients, can be addressed to brain abnormalities.

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