# Cross-site reproducibility of $^1$H-MRS

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**Introduction:** Proton magnetic resonance spectroscopy ($^1$H-MRS) is a noninvasive technique for the detection of brain metabolites. MRS has wide spread applications in terms of studying neurological disorders such as multiple sclerosis and schizophrenia and has the potential to be an in-vivo marker for pathological changes that contribute to clinical disability and progression, as well as being used to assess treatment efficacy. Implementation of MRS in a standardized multi-site clinical trial setting is non-trivial and inter and intra-site reproducibility need to be considered. The present study aims to examine cross-site reproducibility of MRS data by determining the differences in metabolite concentrations measured on the same subjects at multiple sites.

**Methods:**

*Subjects*

Five healthy volunteers (3 female, 2 male; mean age 37 years (range 24-54 years)) were scanned twice within a 24 hour period at 6 different sites.

*MR Examinations*

All $^1$H-MRS examinations were performed on Philips 3T Achieva MR scanners. The single voxel $^1$H-MRS experiment consisted of a PRESS sequence (TR/TE=4000/36ms, voxel size = 65x45x18mm, 1024 samples) located just above the ventricles (Figure 1).

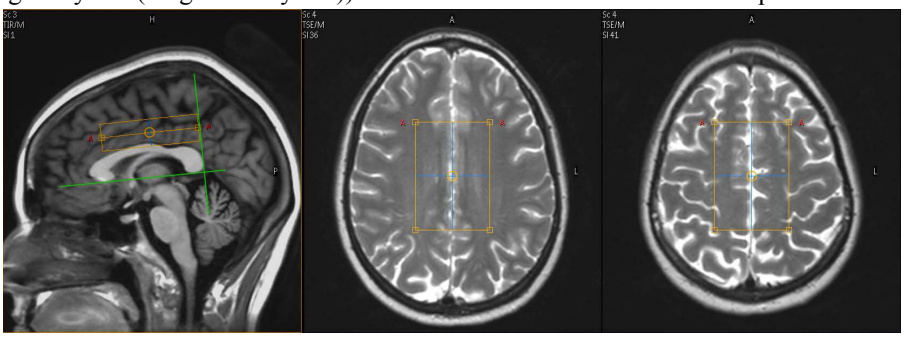

Figure 1: Location of MRS voxel

*Analysis*

Analysis of $^1$H-MRS data was performed using LCModel[1]. Water-scaling was used with the default white matter value, referencing the metabolite signal to the water signal in order to give absolute concentrations in millimolar (mM) for n-acetyl-aspartate (NAA), creatine (Cre), choline (Cho), myo-Inositol (mI) and glutamate and glutamine (Glx). For each site, mean intrasite percent differences were calculated for each metabolite from the two repeated scans done within 24 hours and then averaged over all volunteers. For each site, intersite percent differences were calculated averaged over volunteers for each metabolite. This was accomplished by first determining a mean metabolite concentration for each volunteer (avg[metabolite]$_{volunteer}$) by averaging all 12 concentrations from the 6 sites for each metabolite. Then the percent difference was determined between the metabolite concentration for each scan and avg[metabolite]$_{volunteer}$ (i.e. 60 percent differences were calculated). Finally, for each site a mean intersite percentage difference was determined by averaging over the 5 volunteers.

**Results:** Intersite and intrasite percent differences are shown in Table 1.

| *Site* | *Percent Differences (%)* | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **NAA** | | **Cho** | | **Cre** | | **mI** | | **Glx** | |
| | inter | intra | inter | intra | inter | intra | inter | intra | inter | intra |
| *1* | 2.6 | 2.8 | 3.0 | 1.6 | 4.8 | 2.0 | 5.0 | 7.2 | 13.8 | 4.6 |
| *2* | 4.5 | 3.3 | 4.2 | 5.1 | 2.0 | 3.8 | 4.7 | 9.2 | 3.5 | 6.3 |
| *3* | 3.9 | 5.5 | 4.8 | 6.4 | 3.7 | 6.5 | 4.6 | 8.9 | 7.7 | 13.0 |
| *4* | 5.9 | 9.5 | 5.1 | 8.0 | 4.5 | 6.8 | 6.2 | 9.5 | 9.5 | 15.9 |
| *5* | 2.6 | 2.9 | 4.6 | 3.3 | 3.6 | 2.0 | 5.3 | 4.6 | 4.6 | 5.3 |
| *6* | 3.4 | 6.0 | 2.5 | 4.4 | 3.9 | 4.5 | 6.5 | 4.2 | 11.6 | 20.8 |

Table 1: Intersite and intrasite percent differences averaged over the five volunteers for each metabolite and each site.

**Discussion:** The percent differences measured between the different sites were all below 10% except for glutamate and glutamine which was a bit higher due to the difficulty in separating the glutamate and glutamine peaks. All percent differences between sites were of a similar magnitude increasing confidence in comparing results from any of the sites. The percent differences measured here were lower than values reported previously[2,3], however, the previous studies were carried out at 1.5T with smaller voxels.

[1]SW Provencher (1993) Magn Reson Med. 30:672-9. [2]DT Chard (2002) JMRI 15:219-225. [3]RA Komoroski (2004) MRI 22:721-725.