Assessment of Magnetic Resonance Spectroscopy variability across metabolites and field strengths

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BACKGROUND

Magnetic Resonance Spectroscopy (MRS) is a non-invasive technique assessing the concentration of various metabolites within the brain, both cross-sectionally to characterize disease type and severity, and longitudinally to assess disease progression and potential treatment efficacy in the context of disease-modifying interventions. In such context, the involvement of multiple imaging facilities inevitably introduces variability, whose amount must be known to inform on comparability between sites and sensitivity to change.

Our objective is to study variability in the concentration of various brain metabolites using a dedicated MRS phantom and assess impact of field strength.

METHODS

Data

19 sites were qualified to participate in a clinical trial in metachromatic leukodystrophy. Site qualification mandated the scanning of a dedicated MRS phantom.

For that purpose, a series of SPECTRE (SPECtroscopy Reference, see Fig. 1) phantoms was developed by Gold Standard Phantoms (London, UK) to replicate the brain's metabolite concentrations. The phantoms used HD-polyethylene spheres and were simultaneously manufactured and filled with the same mixture of chemicals mimicking the most important brain metabolites in the appropriate nominal concentrations: N-Acetyl-L-aspartic acid (NAA) [12.5 mM], Creatine (Cr) [10.0 mM], Choline Chloride (Cho) [3.0 mM], Myo-inositol (mI) [7.5 mM], Glutamate (Glx) [12.5mM] and Lactic acid (Lac) [5.0 mM]. Importantly, all phantoms were filled out of the same batch, ensuring thereby that each phantom had the exact same metabolic profile.

From the 19 sites, 22 scanners were qualified (6 1.5T scanners and 16 3T).

All sites implemented a standardized single-voxel MRS sequence (TR=3000 ms, TE=35 ms, Voxel size = 15x15x15 mm^3, Water-suppressed averages = 96, Water-reference averages = 8). MRS voxel was placed within the phantom and acquisition repeated 3 times.

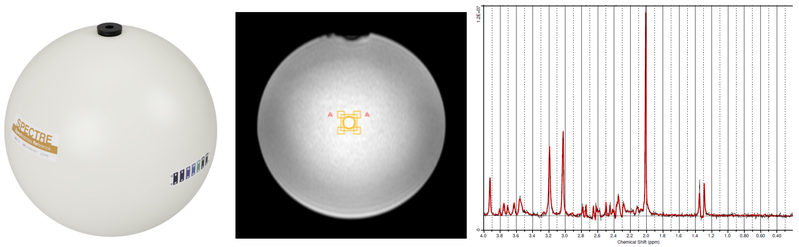

Figure 1 - SPECTRE phantom, voxel positioning and resulting spectrum

Analyses

Spectra were centrally analyzed using LCModel v6.3 [1] and quality controlled by Bioclinica. Repeat acquisitions were requested for parameter deviations, voxel positioning and/or shimming issues. Results only include passing datasets.

Coefficient of Variation (CV) was calculated for NAA/Cr, Cho/Cr, mI/Cr, Glx/Cr and Lac/Cr ratios for each scanner and overall. LCModel quality metrics (FHWM and S/N) were also extracted to assess spectra quality. Comparison between field strengths was carried out using t-tests.

1. Provencher, *Estimation of metabolite concentrations from localized in vivo proton NMR spectra*, Magn Reson Med 1993

RESULTS

Average CV by site was 2.0% for NAA/Cr (2.2% at 1.5T and 2.0% at 3T), 2.1% for Cho/Cr, 3.0% for mI/Cr, 4.3% for Glx/Cr and 5.6% for Lac/Cr.

CVs were generally lower at 3T (except for Lac/Cr) although difference was not significant (except for Glutamate).

As expected, Signal-to-Noise was much higher at 3T for most scanners but not statistically significant overall.

Overall CV by metabolite across scanners was much higher (ranging from 4.2% for NAA/Cr up to 12.5% for Lac/Cr).

CONCLUSION

MRS measures of metabolite concentrations have low variability at scanner-level, with minimal impact of field strength. Nevertheless, variability across scanners is much higher and would require, if possible, cross-calibration. These phantom data make such calibration possible and will improve sensitivity of subject data analyses.

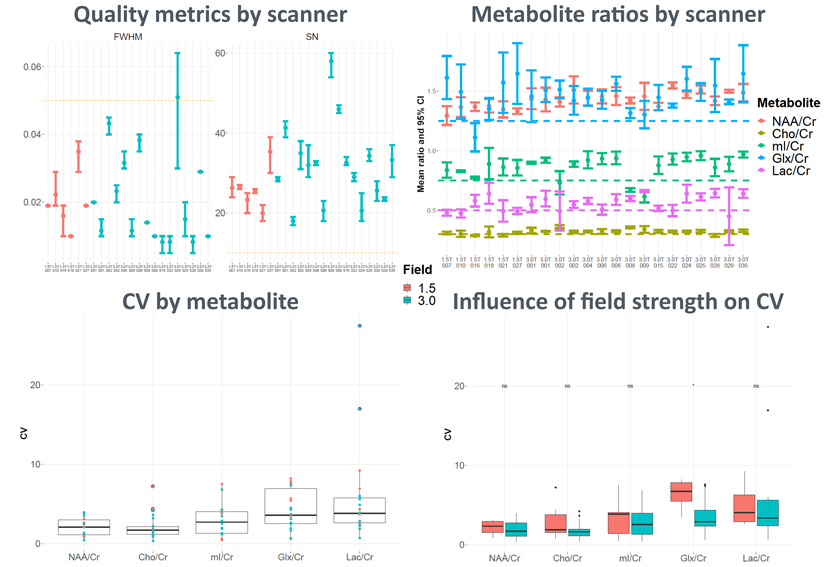

Figure 2 - Analysis results

Top left: FHWM and SNR by scanner (dashed lines: optimal values) - Top right: Metabolite ratios by scanner (dashed lines: expected values) Bottom left: Scanner CV by scanner for each metabolite ratio - Bottom right: Influence of field strength on CV for each metabolite