Test-Retest Repeatability of Human Neurochemical Profiles Measured at 3 Versus 7 T

Melissa Terpstra[1], Uzay E Emir[1], Lynn E Eberly[1], and Gulin Oz[1]
[1]*University of Minnesota, Minneapolis, MN, United States*

Introduction: Increased precision of metabolite quantification by ^{1}H MRS at 7T relative to lower field strengths has been demonstrated[1,2] via lower Cramér-Rao lower bounds (CRLB). This project was designed to determine whether lower CRLB at 7T relative to 3T lead to greater inter-session test-retest repeatability, a critical factor when designing longitudinal clinical studies. The experimental approach was to use a large number of repeat scans, extensively optimized single-voxel MRS methodology and optimal hardware at both fields. This included commercially available components at 3T, while an in-house built coil together with B_1 shimming was utilized at 7T to optimize available B_1 and minimize chemical shift displacement errors.

Methods: Spectra were measured using body excitation and a 32 channel receive array coil at 3T and a 16-channel transceiver array coil[3] and B_1^+ phase shimming[4] at 7T. Four healthy participants were each scanned 4 times at 3T and 4 times at 7T on a weekly basis. Semi-LASER[5] and STEAM with VAPOR water suppression and outer volume suppression were used to measure spectra from 2 clinically relevant brain regions, the cerebellar vermis and posterior cingulate cortex. B_0 homogeneity[6] and B_1 amplitudes[4] were optimized for each voxel. Metabolite concentrations were quantified using unsuppressed water spectra and LCModel with a simulated basis set. They were reported when measured reliably (CRLB<50%, cross correlation coefficients r>-0.5) from more than ½ of the spectra at a given field strength. Test-retest coefficients of variance (CV) of metabolite concentrations were determined in each individual, and the inter-subject mean was calculated per field strength. CRLB and CV were compared at 3T versus 7T using a paired t test.

Results: For brevity, only data measured using semi-LASER in the cerebellum are shown. High quality, artifact free spectra with narrow line widths were acquired at both field strengths (fig. 1), which led to the quantification of 5 neurochemicals (NAA, total creatine, total choline, *myo*-inositol, glutamate) with CRLB *and* CV ≤ 6% at both field strengths (fig. 2). The CRLB were universally lower at 7T than at 3T ($p < 0.05$), while the CV were comparable ($p > 0.05$) at the two field strengths (fig 3). CRLB were representative of test-retest CV at 3T, while the CV tended to be higher than the CRLB at 7T (fig 2). Measured concentrations were comparable to those previously reported[7]. Findings using STEAM and in the posterior cingulate cortex were analogous.

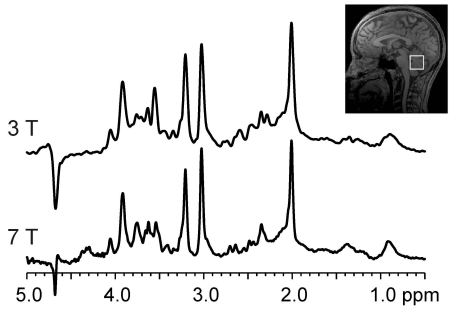

FIG. 1. Representative spectra (nt=64, TR=5s, TE=28 (3T) or 26 (7T) ms) measured from 1 subject during 1 scan session at 3T (90 cm bore Siemens TIM Trio) and 7T (90 cm bore Magnex magnet interfaced to a Siemens Syngo console). The image shows the 10x25x25 mm^3 voxel placement in the cerebellar vermis.

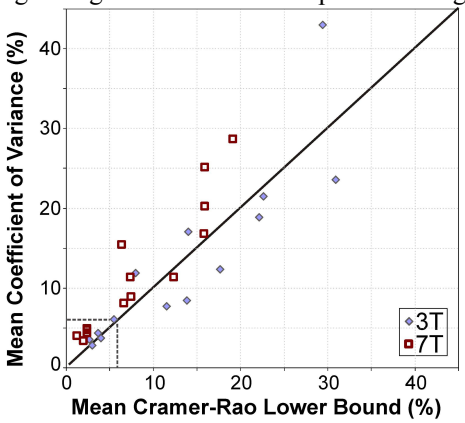

FIG. 2. Mean CV versus mean CRLB for each metabolite concentration at both field strengths. The dotted lines indicate 6% on both axes.

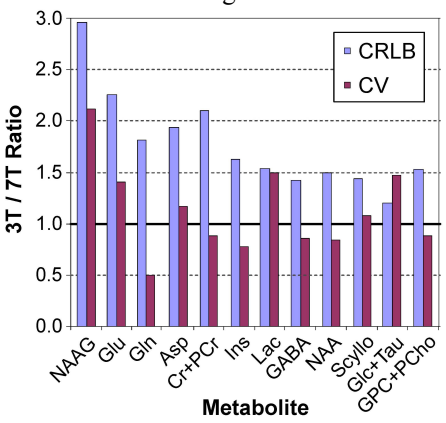

FIG. 3. Ratios of the CRLB and CV obtained at 3T vs. 7T for metabolites that meet inclusion criteria at both fields.

Discussion & Conclusions: Here we addressed reproducibility at 3T and 7T from a practical perspective, namely using the optimal hardware and methodology available to us. Hence, short-echo MRS pulse sequences implemented in-house and optimized to remove unwanted coherences were utilized on a clinical platform at both fields. RF coil designs were different at the two field strengths and no attempt was made to match all hardware components to isolate the effect of field strength on metabolite quantification reproducibility[2]. With these in mind, we conclude: **1)** Excellent spectral quality and reproducibility can be obtained at 3T using commercially available hardware on a clinical scanner and extensively optimized pulse sequence and parameters; **2)** at the current spectral quality and SNR, factors other than quantification precision (as measured by CRLB), such as reproducibility of subject placement and physiological variation, limit the achievable inter-session reproducibility at 7T**.** When CRLB are higher, i.e. at lower SNR (smaller volumes-of-interest or fewer number of acquisitions), we anticipate that CRLB will set the lower bound for test-retest reproducibility, thus rendering 7T advantageous over 3T.

References: [1]Mekle et al, MRM, 2009, 61:1279, [2]Tkac et al, MRM, 2009, 62:868, [3]Adriany et al, MRM, 2008, 59:5990, [4]Van de Moortele et al, MRM, 2005, 54:1503, [5]Oz & Tkac, MRM, 2011, 65:901, [6]Gruetter et al, MRM, 2000, 43:319, [7]Emir et al, NMR Biomed, 2011, DOI 10.1002/nbm.1727.

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