Partial Volume Correction Method for Improving Test-retest Repeatability of *In Vivo* Human Brain ^{1}H MRS and Quantification of Neurochemical Concentrations at 7T

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INTRODUCTION: Human brain ultra-high field (7T) ^{1}H-MRS is increasingly available in clinical research settings. It is advantageous because of increased sensitivity and specificity. Accurate quantification of single voxel spectra (SVS) is dependent upon appropriate consideration of partial volume contamination. A reliable technique for estimating the fractions of cerebrospinal fluid (CSF), gray matter (GM) and white matter (WM) (i.e., segmentation) in the presence of inhomogeneous B_1 is needed for accurate partial volume correction (PVC). For this purpose, we developed a segmentation approach for minimizing the effects of B_1 inhomogeneity, thus improving the efficacy and accuracy of image segmentation. Our hypothesis is that test-retest repeatability of metabolite concentrations quantified by *in vivo* ^{1}H-MRS spectra will be improved when the partial volume effect is corrected using this improved segmentation method.

METHODS: To assess test-retest repeatability, one human subject was scanned on four different occasions at 7T (Magnex/ Siemens) with a 16-channel transmit/receive head array coil. 3D-MPRAGE T_1, 3D-PD (proton density), and respective T_1/PD images (TR/TE/TI=2500ms/2.42ms/1500ms, 1mm^3 resolution) were acquired with an interleaved sequence [1] without B_1 shimming. ^{1}H MR metabolite and water spectra were measured from a posterior cingulate volume of interest (VOI; 20 x 20 x 20 mm^3) after localized B_0 and B_1 shimming using STEAM [2] (TE = 8 ms, TR = 5 s, TM = 32 ms, NEX = 64). 1st and 2nd order B_0 shims were adjusted using FASTMAP [3] and B_1 shims were adjusted using a B1$^+$ phase adjustment formalism[4]. Metabolites were quantified from spectra using LCModel [4] and a typical basis set of metabolites[5]. The exact VOI from which spectra were measured was segmented using the T_1/PD ratio image (Fig. 1). Histogram-based classification with Gaussian Mixture Modeling (GMM) was used to find the tissue type thresholds (Fig. 2). The tissue type fractions were incorporated into the metabolite quantification equation [6] according to:

$$Cmet = \frac{\mathrm{SI_{met}}}{\mathrm{SI_{H2O}}} \times [\mathrm{H_2O}] \times \frac{\left[f_{csf} \times 1 + (1 - f_{csf}) \times (f_{gm} \times 0.81 + f_{wm} \times 0.71)\right]}{1 - f_{csf}}$$

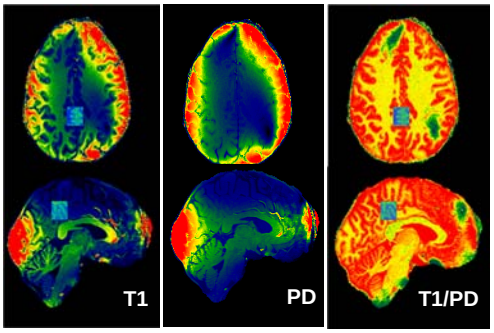

Fig 1. B1 inhomogeneity patterns of T1, PD and ratio (T1/PD) images, and VOI position. The ratio images show substantially reduced B1 inhomogeneity.

RESULTS & DISCUSSION: Figure 1 illustrates: the improvement in B_1 field and image intensity homogeneity that occurred when the T_1/PD ratio image was utilized (especially over the volume of interest), and improved brain tissue contrast. The ratio image also improved the histogram-based classification with GMM (Fig. 2) because the width of the spectrum for each tissue type was substantially narrower than that achieved using the T_1 image. No differences in tissue contents were observed among the retest occasions (Fig. 3), likely due to successful repositioning of the voxel during repeat scans, which is consistent with the similarity among the high quality spectra that were measured on all occasions (Fig. 4). Moreover, the test-retest repeatability of the partial volume corrected metabolite concentrations was better than that for the uncorrected data (Fig. 5). Whereas existing automatic whole brain and manual segmentation tools are time consuming, our method is fast and reliable for ultra-high field applications. This approach might also benefit surface RF coil applications. The improvement in the test-retest stability of metabolite quantification that was achieved will be important for monitoring treatment effects as well as for investigating aging and neurodegenerative diseases, whereby variation in CSF and tissue volume could otherwise confound findings.

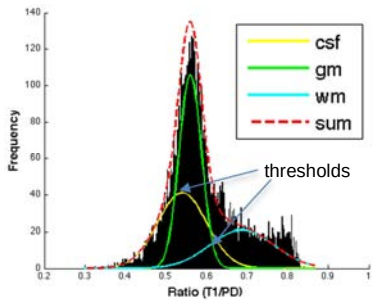

Fig 2. Histogram of signals in the VOI using the ratio image and GMM showing reliable separation of each tissue type.

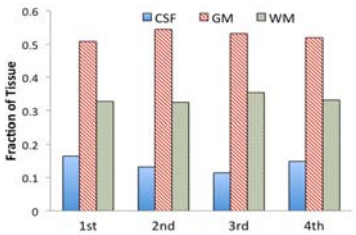

Fig 3. Results of GMM segmentation for the VOI used to measure spectra on each occasion (1st – 4th)

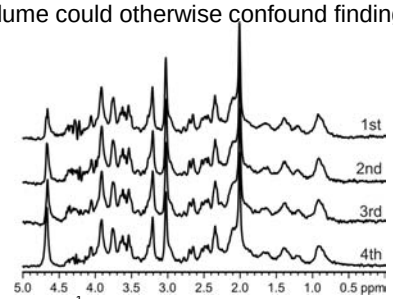

Fig 4. ^{1}H spectra measured from the same subject on four different occasions.

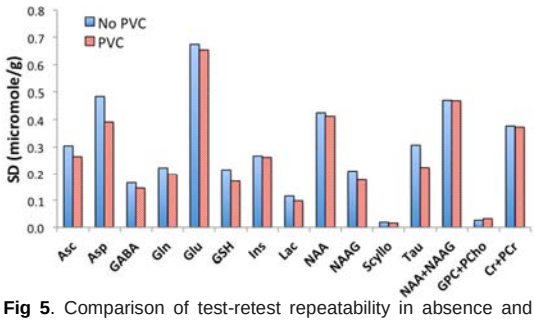

Fig 5. Comparison of test-retest repeatability in absence and presence of PVC for all metabolites via standard deviation (SD)

REFERENCES & ACKNOWLEDGEMENTS: [1]Van de Moortele et al. *NeuroImage* 2009; **46**:432, [2]Tkac et al. *Magn Reson Med* 1999; **41**:649, [3]Gruetter & Tkac *Magn Reson Med* 2000; **43**:319, [4]Van de Moortele et al. *Magn Reson Med* 2005; **54**:1503, [5]Provencher *NMR Biomed* 2001;14:260, [6]Emir et al. *NMR Biomed* 2011; 24:888, NIH R01AG039396, R21EB009133, NS057560, NS041262, NS070839, S10RR026783, P41 RR08079 & EB015894, P30 NS057091 & NS076408; and the WM KECK Foundation.