In vivo measurements of neural stem and progenitor cells (NPCs) in patients with multiple sclerosis and normal controls, using MRS and LCModel

C. Schirda[1,2], C. Magnano[1], E. A. Yeh[2], B. Weinstock-Guttman[2], A. S. Drake[2], J. L. Cox[1,2], and R. Zivadinov[1,2]

[1]Buffalo Neuroimaging Analysis Center, Buffalo, NY, United States, [2]Department of Neurology, The Jacobs Neurological Institute, SUNY Buffalo, Buffalo, NY, United States

Introduction: Neural stem and progenitor cells (NPCs) have self-renewing capabilities and can produce neurons, astrocytes and oligodendrocytes, thus rendering them an attractive biomarker for monitoring repair of damaged nerve tissue. Recently [1], NPCs have been associated with the 1.28ppm resonance and MRS measurements in normal controls (NC) have been demonstrated, using a single value decomposition technique for quantification. We are presenting results of MRS *in vivo* NPCs measurements conducted in NC and multiple sclerosis (MS) patients at different ages and disease stages, using the well established LCModel [2,3] to quantify the 1.28 ppm biomarker.

Methods: Six NC (3 children, age range: 7 - 10 years and 3 adults, age range 21 - 25 years), 6 relapsing-remitting (RR) MS patients (3 children, range 8 - 13 years, 3 adults, range 28 - 35 years) and 2 secondary-progressive (SP) MS patients (aged 46 and 49) were scanned on a GE 3T scanner. Following acquisition of scout images, spectra from single voxels (SV) were placed on the left and the right hippocampus, and collected using an MRS sequence with parameters as previously [1] described (12x12x30mm^3 box, TR/TE=2s/30ms, 128reps, scan time 5:04). In addition, data from the same voxels were collected using an optimized MRS sequence (TR=1.2s and 256reps, scan time 5:34) that increased sensitivity up to 40% (Figure 1, plot on the right vs. the one on the left).. After each scan, scout images were reacquired, and the location of the spectroscopy voxel was compared on the scout images to determine if motion occurred. Data were processed using LCModel, and the weighted NPC average for each subject was calculated, with weights determined as the inverse of squared standard deviation (SD). The three young adults were scanned and re-scanned within a week to test reproducibility.

Results: The mean ±SD peaks for the pediatric NC were 5.14±1.02, and 7.41±2.68 for the pediatric MS patients. There was no difference between peaks in the young adult NC (2.66±0.22) and RRMS (2.69±2.03). SPMS patients showed (Figure 2) the highest peak (12.98±9.1). In MS patients there were significant peak level hemisphere differences (five fold or greater) not seen in the NC.

Discussion: When quantifying major metabolites (NAA, Cre, Cho) in brain, standard deviations less than 20% are widely considered acceptable [3] and viewed as a sign of a reliable measurement. They are marked automatically in blue on LCModel output (Figure 1,2). The 1.28 ppm resonance is generally weaker, resulting in larger SDs most of the time. For this reason, it's not uncommon to see 60-80% variations in scan-rescan reproducibility (defined here as difference/average of the two measurements) for a ~5 minutes sequence used. Therefore, for more reliable NPC quantification, multiple measurements would typically need to be averaged together.

Conclusions: The SPMS and pediatric MS patients exhibited higher levels of NPC peaks compared to age- and sex- matched NC groups. The hemispheric peak differences in MS patients may reflect greater neurological damage. Clinical and treatment related correlates of the current findings are under investigation in a larger group of NC and MS subjects in our department.

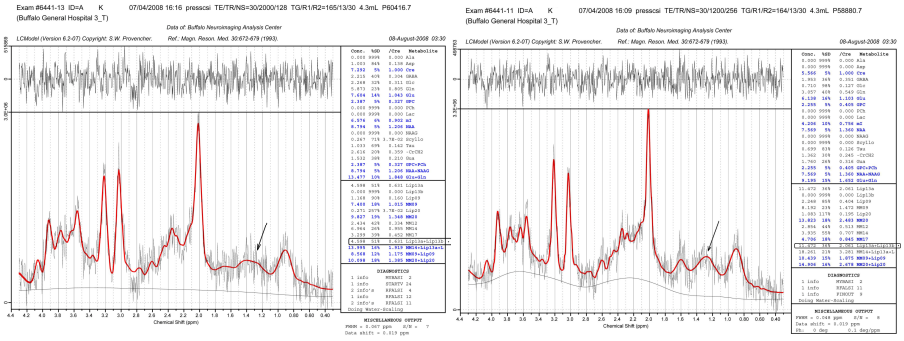

Figure 1: *LCModel one page output for the same voxel over the right hippocampus using the parameters in Ref [1]–left and the optimized sequence-right. The SNR increased from 7 to 8 and the SD for 1.28 ppm resonance decreased from 51% to 36%. Data from a 9yrs old NC.*

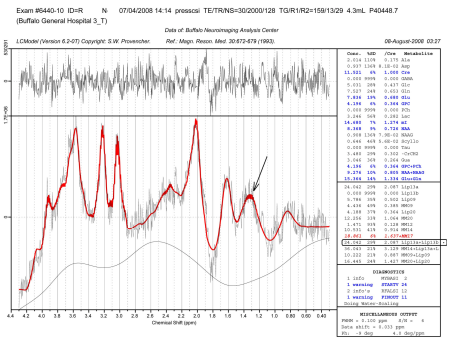

Figure 2: *LCModel processed spectrum for a 46 year old secondary progressive MS patient, collected in the left hippocampus*

References: [1] Curtis et al., Science, **315**(5816): p1243, 2007 [2] Provencher, MRM, **30**(6): p672, 1993 [3] Provencher, LCModel User's Manual, v. 6.2-0R 2008