

## <sup>31</sup>P-MRSI at 7T in Parkinson's Disease

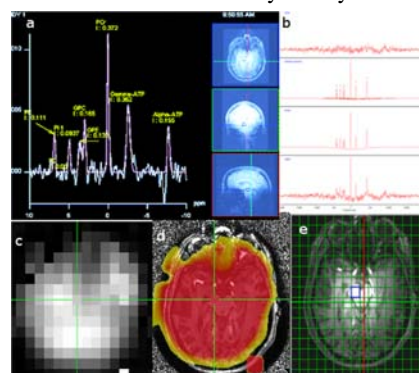
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**TARGET AUDIENCE**—Clinicians interested in neurodegenerative disorders, spectroscopy physicists, neuroscientists.

**PURPOSE**—Parkinson's Disease (PD) is caused by loss of dopaminergic neurons in the substantia nigra (SN). Impaired mitochondrial function is one of the suspected etiological factors in PD which might contribute to dopaminergic cell degeneration. Phosphorus spectroscopy imaging (<sup>31</sup>P-MRSI) allows *in-vivo* measure of energy and phospholipid metabolism with signals from phosphocreatine (PCr), inorganic phosphate (Pi), and ATPs and from (glycero-)phosphoethanolamine (GPE) and (glycero-)phosphocholine (GPC). The precise role of mitochondrial dysfunction in PD or how it is influenced by treatment, disease duration or disease severity is still unclear. Understanding mitochondrial involvement in PD may therefore be valuable in developing new therapeutic targets. This study evaluates the use of 7T <sup>31</sup>P-MRSI as a biomarker for Parkinson's disease.

**METHODS**—Seventeen subjects (7 healthy volunteers (HV), 6 PD patients with Hoehn and Yahr scores of 2 and 2.5, and 4 patients with parkinsonism syndromes (PS) (not classic PD) participated in a <sup>31</sup>P MRSI study conducted in an active-shielded 7T whole body MR system (Magnetom 7T, Siemens Healthcare, Erlangen) using a dual-transmit-receive coil assembly of a <sup>1</sup>H and <sup>31</sup>P birdcage coil (Quality Electrodynamics LLC, Mayfield Village, Ohio, USA). After a quick localizer, anatomical imaging was performed using MPRAGE with 1mm isotropic resolution. After shimming, the <sup>31</sup>P RF power level was calibrated for each volunteer as previously described in [1]. 3D <sup>31</sup>P-MRSI with a spatial resolution of 17.28 cc (FOV=200 x 180 x 180 mm<sup>3</sup>, matrix=12 x 12 x 12) was acquired with Nuclear Overhauser Enhancement (NOE) (rectangular, count 10, duration 98 ms, pause 2000ms, flip angle 90, hard pulse excitation 300ms) and TR 1550ms, TE 0.1ms, flip angle 45, avg time 4 for a total scan time ~21 min. A representative spectrum is shown in fig 1a. As illustrated in fig 1b, data processing was performed using JMRUI software [2]. After apodization (20 Hz Gaussian), eight peaks (PE, PC, GPE, GPC, Pi, PCR and gamma and alpha ATP) were estimated using AMARES (2). PCr line width was determined by AMARES algorithm; line widths for low energy peaks were matched to PCr. All peak shapes were set as Gaussian. Zero order phase was estimated from -180.0 to -90.0 deg with a starting value of -156.0 deg. The output file from AMARES was then converted to a nifti file using Matlab (fig 1c). Using headers information from the MRSI and MPRAGE, data were overlaid (fig 1d) and four voxels-of-interest were defined bilaterally in substantia nigra (fig 1e) and putamen. Ratio of high energy phosphates (HEP) (defined as the sum of PCr and gamma and alpha ATP) over Pi was computed for each region in the affected and non affected side using AFNI [3]. Differences between the affected and non-affected side of patients were tested. As a control, right-left differences in patients and in the HV group were also tested.



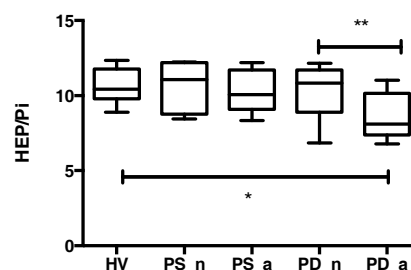
**Figure 1.** a) Representative <sup>31</sup>P spectrum using scanner viewer. b) Spectra processed and fitted under JMRUI. c) Output processed MRSI data. d) MRSI data overlaid on coregistered MPRAGE image. e) Typical voxel selection for SN.

**RESULTS**—As illustrated in Figure 2, HEP/Pi values in substantia nigra were significantly different between the affected (PD\_a) and non-affected side (PD\_n) of the patients (p=0.0121). The more affected PD side was significantly decreased compared to the normal values measured in HVs (p=0.022). For PS patients, HEP/Pi values for the affected side (PS\_a) were in between HVs and PDs. No differences were observed for the metabolites reflective of amount of membrane (GPE and GPC). No differences were observed for voxels located in the anterior putamen.

**DISCUSSION**—This is the first study of 7T <sup>31</sup>P-MRSI in PD and PS. A previous study performed on PD patients at 3T found decreased HEP in the SN and putamen of patients [3]. This is consistent with our study, which showed a decreased HEP/Pi ratio in the most affected SN areas of patients, suggesting that this measure reflects neurodegenerative processes. HEP is an indicator of mitochondrial function, which is presumed damaged in the SN in PD patients. All patients were in early stages of the disease. Follow-up measures from this cohort and larger number of subjects are underway to further establish the relationship between mitochondrial dysfunction and PD progression.

**CONCLUSION**—<sup>31</sup>P MRSI measurement at 7T has the potential to become a relevant marker for differential diagnosis in PD. In this pilot study, we were able to detect changes limited to the areas where the disorder is believed to start. Larger populations and longitudinal studies will be needed to confirm this measure as a reliable biomarker.

**REFERENCES**—[1]Scheenen et al. ISMRM 2013. 4489. [2]Stefan, D., et al. Quantitation of magnetic resonance spectroscopy signals: the jMRUI software package. Measurement Science and Technology 20:104035 (9 pp), 2009. [3]Cox et al 1996. <http://afni.nimh.nih.gov> [4] Hattinen et al. Brain, 132:3285, 2009.



**Figure 2.** HEP/Pi ratio in the substantia nigra of HVs, PS and PD patients.