

## Magnetic Resonance Imaging at 7T enables the diagnosis of Parkinson's disease

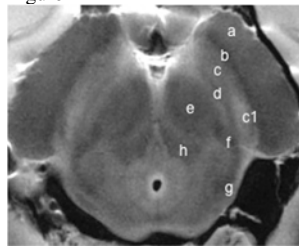
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**Target Audience:** Neurologists and neuroradiologists interested in employing ultra-high field magnetic resonance imaging (UHF-MRI) in clinical practice for diagnosing Parkinson's disease (PD), as well as researchers who study deep gray matter brain structures.

**Purpose:** The pathological correlate of dopaminergic depletion in PD is the neuronal loss in the pars compacta of substantia nigra (SNpc). At present, there is no established MR marker that can be exploited on a single-subject basis in the clinical practice to diagnose PD. The purpose of this contribution was twofold: *i*) to evaluate the normal anatomy of the SN by means of UHF-MRI and *ii*) define the accuracy of UHF-MRI targeted imaging in distinguishing PD patients from healthy subjects (HS).

**Methods:** At present, 21 HS and 17 PD patients in the early stage of disease participated to the study. A multi-parametric imaging protocol targeting the SN was set up on a 7T scanner (GE Healthcare) equipped with a 2ch-transmit/32ch-receive head coil (Nova Medical). Image sequences relevant to this contribution consist of: 2D dual echo gradient echo (GRE) acquisitions (TR=500ms, TEs=10 and 22ms, slice thickness=2mm, FOV=10cm, matrix size=512x512, in plane resolution=200 $\mu$ m); 2D Fast Spin Echo (FSE) acquisitions (TR=800ms, echo train length=3, effective TE=7ms, slice thickness=2mm, slice spacing=1.5mm, FOV=12cm, matrix size=256x256, in plane resolution=469 $\mu$ m); 3D "SWAN" multi-echo GRE acquisitions (TR=55.7ms, TEs=5.57ms, 10.7ms, 15.84ms, 20.97ms, 26.1ms, 31.23ms, 36.36ms, 41.5ms, thickness=1.2mm, FOV16cm, in plane resolution=312 $\mu$ m). Prescriptions were pseudo-axial, perpendicular to the floor of the fourth ventricle. Data obtained from each echo of the SWAN images was used to produce T2\* maps by exponential curve fitting. The SN was examined also ex-vivo, using a brain specimen from a cadaver of a 67 year-old woman with unremarkable neurological and psychiatric history, which besides the sequences above, underwent also a spin echo proton density (SE-PD) scan (TR=1200ms, TE=20ms, thickness/spacing=1/1.5mm, FOV=10cm, in plane resolution=190 $\mu$ m). The normal anatomy of SN was evaluated on the ex-vivo sample and on 8 HS. The diagnostic power of UHF-MRI for PD in terms of sensitivity, specificity and diagnostic accuracy with respect to clinical diagnosis was tested on the remaining 13 HS and 17 PD patients, by presenting the images in a blinded and randomized manner to two experienced neuroradiologists.

Figure 1:



**Results:** Figure 1, left, depicts the GRE image of the ex-vivo sample, which demonstrates that UHF-MRI allows a precise representation of the fine anatomy of the brain-stem [a: crux cerebri; b: SN pars reticulata (pr); c: ventral component of the SNpc; c1: nigrosome formation; d: dorsal component of SNpc; e: brachium conjunctivum; f: medial lemniscus; g: lateral lemniscus; h: central tegmental tract]. SWAN images in HS

(Figure 1, center) are characterized by a clear pattern of hypointense (SNpr), hyperintense (vSNpc+nigrosome), hypointense (dSNpc) representation of the SN, which is lacking in PD (Figure 1, right). The pattern of intensity of SN is shown in Figure 2 for three representative HS (left), where the hyperintense vSNpc is highlighted by red ovals, and three representative PD patients (right), where the whole SN is hypointense. The difference between these two patterns is in the representation of the ventral component of the SNpc, which correlates with neuronal loss in this area in all parkinsonian disorders. This short sequence (only 4'02'') allowed two neuroradiologists to independently discriminate HS and PD with 100% sensitivity (all PD patients were correctly identified) and 92.3% specificity (one of the two neuroradiologists classified one HS as PD).

The same sequence allowed the computation of T2\* maps: as opposed to SWAN images, T2\* maps of both HS and patients did not represent the three main compartments of SN, which all appear to be characterized by similar T2\* values (24.8 $\pm$ 3.4ms, mean  $\pm$  standard deviation). This observation suggests that the disappearance of the hyperintense representation of vSNpc in patients does not reflect abnormal increment of high-T2\* deposits (e.g. iron), but, rather, reflects the atrophy of structures that are visible in SE-PD and T1-weighted images of brains not affected by the disease (images from one typical HS are displayed in Figure 3).

**Discussion and Conclusion:** The results reported in this contribution demonstrate that UHF-MRI allows a precise characterization of SN and the visualization of its inner organization. Most importantly, SWAN images were sufficient to accurately differentiate HS from PD patients providing novel diagnostic opportunity. Considering the limited cooperativeness of PD patients, the possibility to reach a diagnostic result by using a short (4'02'') single targeted SWAN sequence with an excellent inter-observer agreement was an important goal of 7T-MRI. The demonstration this potential clinical use of 7T MRI may favour its acceptance and future employment in the medical community.

Figure 2:

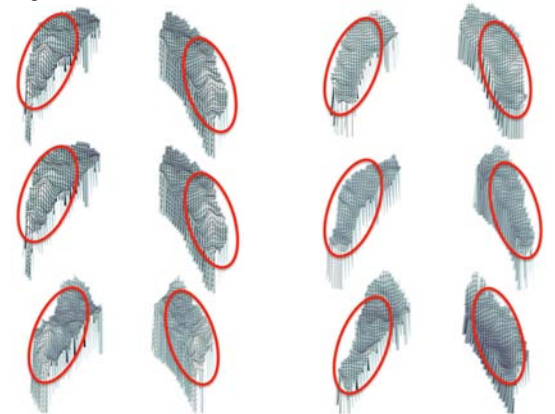
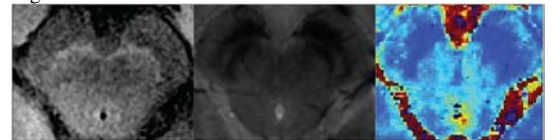


Figure3:



left: FSE; center: SWAN; right: T2\*-map (scale: 0:130ms)