# Quantitative Susceptibility Mapping in the Basal Ganglia of Parkinson's Patients

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**Target audience:** Researchers interested in Parkinson's disease, neurodegeneration, susceptibility mapping and iron deposition.

**Purpose:** Parkinson's disease (PD) is a neurodegenerative disorder whose hallmark is the death of dopamine generating cells in the substantia nigra (SN). Abnormally increased iron levels in the basal ganglia is a frequent finding in most neurodegenerative disorders, including Alzheimer's disease and amyotrophic lateral sclerosis and is commonly considered reflective of the neurodegenerative process. However, while disease-related iron deposition in the SN of PD patients was continuously demonstrated and linked to the severity of motor symptoms [1,2], findings about an involvement of the basal ganglia structures are discussed conversely [2,3]. Quantitative susceptibility mapping (QSM) is a novel method for assessing the magnetic susceptibility and, thus, provides a fundamental biophysical property of tissue [4]. In recent post mortem studies, QSM and R2* relaxation rate mapping has been shown to be highly correlated to iron concentration in gray matter [5,6]. *In this work we aimed to quantitatively assess brain iron levels with QSM and R2* mapping in the basal ganglia in patients with PD and to relate these findings to healthy controls and to the clinical and neurocognitive status.*

**Methods:** Thirty-nine patients with PD (mean age 61.0 ± 6.0 years) and nineteen age-mated controls underwent quantitative MRI at 3T (TimTrio, Siemens Heathcare; 12 channel head coil). The entire cohort underwent a thorough diagnostic work-up including cognitive testing using the CERAD neuropsychological test battery for assessment [7]. The imaging protocol included a high resolution T1 weighted 3D MPRAGE sequence covering the entire brain with 1 mm isotropic resolution (TR/TE/TI=1900/2.19/900ms, FA=9°). A spoiled FLASH sequence was used for QSM and R2* mapping (TR/TE1=35/4.92ms, 6 echoes with inter-echo spacing=4.92ms, resolution 1x1x2mm$^3$, 64 slices). R2* maps were calculated by mono-exponential fitting of the magnitude signal decay and susceptibility maps were reconstructed using SHARP [4] and the HEIDI method [8]. Automated brain segmentation was carried out using FreeSurfer (http://surfer.nmr.mgh.harvard.edu/) and resulting subcortical maps were utilized to calculate regional QSM and R2* values for the basal ganglia (caudate nucleus, globus pallidus, putamen) and thalamus. Statistical analyses included t-tests to assess group differences between PD and controls and linear regression analysis to assess the relationship between iron deposition and clinical and cognitive scores. The study was approved by the local ethics committee and written informed consent was obtained from all subjects.

**Results**: Patients with PD showed significantly higher susceptibility values (more paramagnetic) in the putamen (p=0.03) when compared to healthy controls. In parallel, also the R2* rate was elevated in the putamen in PD (p=0.04). Other regions failed to show differences on a group level. All results of the regional analysis are summarized in Table 1.

R2* rates in the putamen of PD patients were negatively associated with constructional practice recall (r= -0.44, p<0.05) and constructional savings (r= -0.39, p<0.05). These correlations were lost with QSM.

| | Region | Controls | | Parkinson's disease | | p-value |
|---|---|---|---|---|---|---|
| | | *Mean* | *SD* | *Mean* | *SD* | |
| **R2*** | Caudate nucleus | 21.06 | ± 2.3 | 22.21 | ± 2.3 | 0.08 |
| | Globus pallidus | 36.98 | ± 4.7 | 38.02 | ± 4.9 | 0.45 |
| | Putamen | **24.59** | ± **3.1** | **26.41** | ± **3.1** | **0.04** |
| | Thalamus | 19.93 | ± 1.3 | 20.24 | ± 1.1 | 0.34 |
| **QSM** | Caudate nucleus | 0.039 | ± 0.014 | 0.046 | ± 0.015 | 0.10 |
| | Globus pallidus | 0.118 | ± 0.018 | 0.127 | ± 0.029 | 0.27 |
| | Putamen | **0.043** | ± **0.018** | **0.055** | ± **0.020** | **0.03** |
| | Thalamus | 0.002 | ± 0.011 | 0.005 | ± 0.014 | 0.35 |

**Table 1:** Regional R2* rates and susceptibilities (in mean ± standard deviation; R2* rates are given in $s^{-1}$ and susceptibility in ppm). Significant differences are marked in bold.

**Discussion and Conclusion:** QSM and R2* mapping, both indicated abnormally elevated iron levels in the putamen of patients with PD, which paralleled cognitive decline. The lack of correlations between QSM and cognitive scores might reflect the fact, that QSM is conversely impacted by myelin content than R2*. The cognitive domains most strongly correlated with R2* are in the field of visuo-constructional abilities. This finding is in contrast to healthy controls where increased iron deposition in the globus pallidus correlates with cognitive impairment during the process of normal brain aging [9]. Longitudinal studies are needed to determine the importance of iron accumulation as a predictor of mild cognitive impairment and dementia in Parkinson patients.

**References**

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