Comparison of QSM, T2-Relaxometry and T2-Weighted Imaging at 7T for Assessment of Basal Ganglia Iron in MS Patients

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Target Audience: Researchers and clinicians interested in using advanced MRI as biomarker in Multiple Sclerosis

Purpose: The basal ganglia in MS patients show higher iron compared to healthy control subjects. In early studies this finding resulted from comparing CSF-normalized hypointensity in conventional T2-weighted images and T2 hypointensity correlated to atrophy [1], clinical outcome measures [2-4] and cognition [5], and it was suggested that BG hypointensity might serve as a predictor for MS disease progression [6]. More recent quantitative MRI studies including T2 relaxometry [7], T2* [8], filtered phase imaging [9,10] and QSM [11] have confirmed the iron increase in MS patients. However, to the best of our knowledge, direct comparison between T2 and QSM has not yet been published. The purpose of our study is to evaluate the relationships between CSF-normalized T2 hypointensity (T2w), T2 relaxometry (qT2) and QSM at 7T with respect to their measurement variability, correlation to each other, and correlation to demographics in RRMS patients.

Methods: Twenty-nine RRMS patient age 30-60y (43.9±9.7), disease duration 0.3-23.6 years (6.5±5.5), EDSS 0 to 6.0 (3.0±1.5) were scanned at 7T using a head volume transmit/16-channel receive coil to acquire 3D-Gradient Echo: (TR/flip=24ms/5 degrees, 4 echoes TE=4-20ms bipolar, voxel size 0.5mm^3, scan time 9 min) and T2 (single echo-multishot EPI (TR=5000, TE=13.5,21,36,50ms, 1x1x2mm, , scan time 4x1min). For QSM, complex data were saved, the echo1/echo3 ratio was phase unwrapped using FSL prelude, background field was removed using PDF [13], and QSM was computed using Wiener filter deconvolution [13]. ROIs in the right and left Globus Pallidus, putamen and caudate were manually traced on 10 slices on QSM and 2 on T2. Care was taken to stay within the area of the structure. Linear regression was used for statistical analysis.

Results: Significant signal variability within each structure (GP, put, cau) was observed consistently on T2, T2* and QSM (**Fig 1**). This indicates that variability is not due to SNR, but reflects true within structure differences. Most prominently, we observed higher iron in the posterior compared to anterior putamen, and high iron foci in the GP, as well as vascular structures. As a consequence, measurement variability (quantified by the coefficient of variation CV) within ROIs encompassing the entire structure was fairly high for all methods (average CV T2w: 20%, T2: 14% for pixel-wise T2 fit followed by averaging, 3% for signal averaging followed T2 fitting, QSM: 11.5 %). High variability for CSF-normalized T2w results from significant within structure signal variability and error propagation due to normalization, whereas effects from local signal variability are reduced by averaging prior to T2-fitting. CV for QSM is high because local differences in magnitude images are amplified by QSM processing. All three measurements strongly correlated with each other for each traced structure separately, and all structures combined ($p<10E-6$, **Fig 2**). Regressional statistics for MRI and patient demographics is listed in **Table 1**. Only putamen changed with age; this is consistent with studies of healthy subjects [14] in the age range of our MS patients (30-60y).

Discussion: ROI selection of an entire BG structure leads to large variability with T2w, T2 relaxometry and QSM. Given our initial analysis approach, this may account for the modest correlation between EDSS and disease duration. Our observations are, however, consistent with prior studies in healthy aging noting regional changes within the putamen and GP in filtered phase [15] and T2* [16]. Such regional variability may not have been apparent with early low resolution T2w studies [1], but was taken into account in the analysis of filtered phase that defines "areas of highest iron" and uses the phase and volume of these areas to differentiate MS from controls. [9,10]. Most notably, regional variability is also expected from functional anatomy studies in primates delineating different functional areas e.g. within the GP for motor vs cognitive pathways [17].

Conclusion: Our study shows that similar results regarding iron content in the BG can be achieved with T2 or QSM methods at 7T. Most notably, future analysis has to take into account regional variability within structure, and high resolution 7T MRI may allow for functional differentiation of deep gray matter, and its relation of local iron accumulations and functional deficits in MS.

Table 1: p-values from univariate linear regression

	Demographics		QSM			1/qT2		
	EDSS	duration	GP	put	cau	GP	put	cau
age	0.12	0.11	0.051	**0.004**	0.059	0.10	**0.007**	0.09
EDSS	-	**0.001**	0.62	0.09	0.064	0.38	**0.013**	**0.0034**
duration	-	-	0.92	0.9	**0.044**	0.80	0.65	0.34

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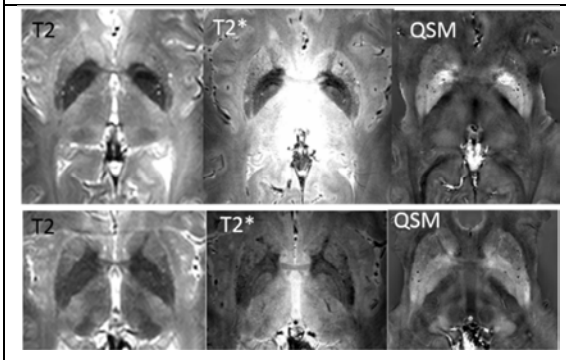

Fig 1: Example images for 2 female patients (top:50y; bottom:48y)

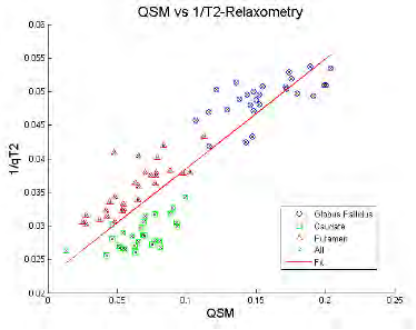

Fig 2: linear regression of QSM with 1/qT2**,** note that putamen and caudate date from separate clusters indicating differences in QSM vs T2