Imaging of the nigrosomes of the substantia nigra at 3T

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Introduction Nigrosomes are substructures of the substantia nigra (SN) that are clinically important due to their high vulnerability to dopaminergic cell loss in Parkinson's disease (PD) [1]. High resolution T2* weighted (T2*w) images obtained at 7T allow *in vivo* detection of the largest nigrosome (N1) and therefore can potentially provide a marker of PD. However, since 7T scanners are not widely available, it is important to determine whether, based on information gained at 7T, nigrosome 1 can now be detected at 3T. **Aim**: to compare different 3T scans in terms of their ability to visualise nigrosome 1.

Methods Eight healthy subjects (Age: 33±11y.o., F/M=4/4) were scanned on a 3T Philips Achieva scanner using four different sequences: (i) high resolution T2* weighted (T2*w), (ii) Fast Field Echo (FFE), (iii) PRESTO and (iv) T1 weighted scans with off resonance MTC sensitive to neuromelanin (NM) [3] (Table 1). One dataset was excluded from the analysis due to insufficient coverage. Figure 1 shows example images for one subject, including the filtered phase image from the T2*w scan. Two neuroradiologists independently rated the images using two scales: *nigrosome visibility*, 1-3 (definitely not visible - definitely visible) and *image quality*, 1-5 (very low - very high, equal to the quality of the T2*w image obtained at 7T). The NM scan specifically highlights the high NM area which extends beyond the nigrosome, so delineation of the nigrosome 1 is not generally possible and therefore for this scan *nigrosome visibility* is interpreted as 'high NM in the region corresponding to nigrosome 1'. For quantitative comparison, all images were co-registered to the PRESTO data using FLIRT (FSL). For each dataset two slices of the T2*w image, in which nigrosome 1 was clearly visible, were used to define circular regions of interest (ROIs): 4 voxel diameter for nigrosome, 8 voxel diameter for remainder of SN and for a reference region in the brain stem (care was taken to avoid small veins). These are shown in Fig 2. ROIs were used to calculate the relative contrast between nigrosome and the SN, as well as the contrast-to-noise ratio (CNR), formed by dividing the contrast by the standard deviation of the signal in the reference region. One-way ANOVA test with Tukey-Kramer correction for multiple comparisons was performed to examine differences between the contrast and CNR of the images.

name	resolution	slices	TR/TE	FA	additional	time
T2*w	0.43x0.43mm^2	8 x 1.5mm	300/50ms	42°	NSA=5	9:57
FFE	1.0x1.0mm^2	40 x 1.0mm	100/35ms	10°	EPI=3	5:06
PRESTO	1.0x1.0mm^2	200 x 1.0mm	15/21ms	10°		4:34
NM	0.6x0.6mm^2	8 x 2.5mm	699/9ms	90°	NSA=4, MTC=off	9.23

Table 1. Summary of the scanning parameters.

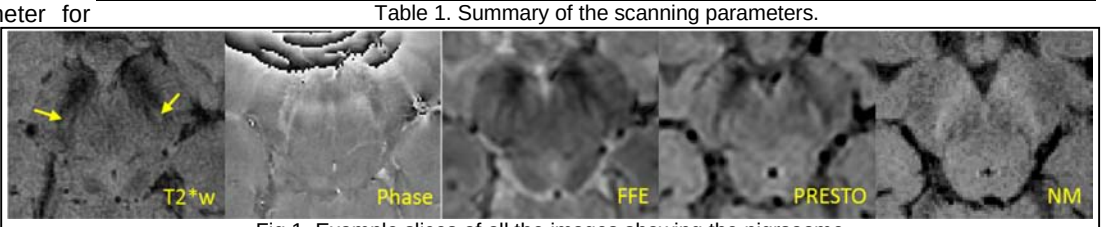

Fig 1. Example slices of all the images showing the nigrsoome

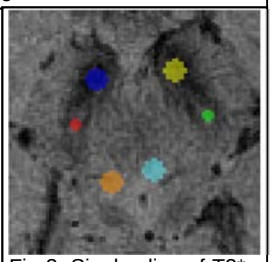

Fig 2. Single slice of T2*w image with ROIs: SN (blue, yellow, nigrosome (red, green), reference region (orange, cyan).

Results Averaged scores of *nigrosome visibility* and *image quality* from the two neuroradiologists are plotted in Fig. 3, with error bars calculated by propagating standard deviation in cross subject measurements for each observer. FFE and PRESTO provided the best images for nigrosome detection (*nigrosome visibility*=2.9) and also achieved high *image quality* scores (2.7 and 3.0), while the NM scans obtained the highest *image quality* value (3.2). T2*w images had significantly higher contrast between nigrosome and the SN than all of the other images, except the FFE, FFE significantly higher than phase and NM and PRESTO than NM ($p<0.01$). There was no significant difference between CNR values for T2*w, phase, FFE and PRESTO images ($p<0.01$). Contrast and CNR values are plotted in Fig 4 with error bars corresponding to the interquartile range (IQR).

Discussion 7T T2*w images have previously been shown to allow detection of nigrosome 1. Here we show that nigrosome 1 can also be detected at 3T, and PRESTO and FFE images were preferred by the neuroradiologists for this identification task. T2*w images provided the greatest contrast between nigrosome 1 and surrounding tissue. The CNR values of FFE and PRESTO images were similar to T2*w, which in combination with the short scanning (~5min) make them potentially clinically useful. Susceptibility weighted images (SWI) created by multiplying the T2*w modulus image by a phase mask did not yield improved results. The low contrast and CNR values of the NM scan are explained by its specificity to NM, which is high in the nigrosome1 area and much of the rest of the SN.

Conclusion Nigrosome 1 can be detected at 3T in clinically useful imaging times using an FFE or PRESTO scan.

References [1] Damier et al., *Brain* 1999, 122:1421-36; [2] Blazejewska et al., ISMRM 2013; [3] Schwarz et al., MDS 2011, 26:1633-8.

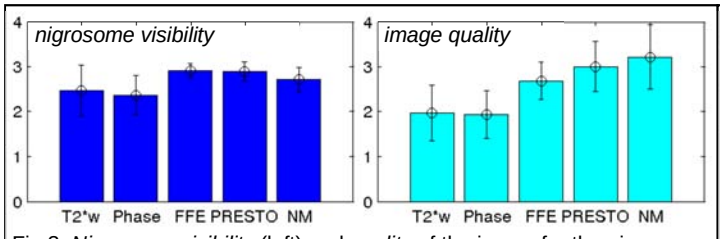

Fig 3. *Nigrosome visibility* (left) and *quality* of the image for the nigrosome delineation (right), average scores from two neuroradiologists

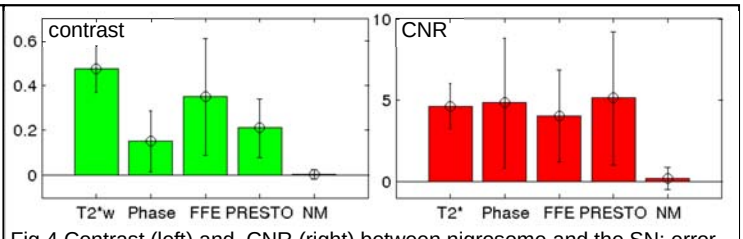

Fig 4.Contrast (left) and CNR (right) between nigrosome and the SN; error bars represent IQR values.