Quantitative Susceptibility Mapping In Vivo in the Rat Brain

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INTRODUCTION
Molecular and cellular imaging is seeing a growing interest, but their applicability to MRI relies on the ability to label the images to specific, sensitive enough and quantifiable via adapted imaging methodologies. Superparamagnetic iron oxides (SPIO) are good candidates as they can be functionalized or used to label cells (1). More recently, it was shown that they could be directly produced by the cells through genetic engineering (2). When accumulating, SPIOs produce locally a strong magnetic field that creates signal voids in gradient echo images. This contrast is not specific as veins generate the same effects, and it is not quantitative without further analysis. Quantitative susceptibility mapping (QSM) additively uses the magnetic field to quantify the magnetic sources (3-7). In this study we apply QSM in the preclinical context of the rat brain using a reconstruction algorithm that includes the 3 challenging steps of unwrapping, removing background effects and inverting the field map. The technique demonstrates its ability to quantify SPIO amounts injected in the brain.

MATERIAL AND METHODS
MR system
Experiments were performed on a horizontal 7T/40cm system (Varian, Palo Alto, CA) equipped with a 12cm ID gradient coil (700 mT/m). A 4-channel receive brain surface coil and an actively decoupled volume transmit coil were used.

Animal handling
A 300g male Sprague Dawley rat was anesthetized by i.p. injection of Ketamine Domitor and immobilized in a stereotaxic frame. An injection pump was used to precisely inject in the left and right striata 2uL of Endorem solutions (Guerbet) diluted by a factor 200 and 400 in saline corresponding to 112ng and 56ng of iron. The rat was then immobilized in the magnet using ear rods and tooth bar. After chopping and scout imaging, 33 2D horizontal slices were acquired with a multi-echo gradient-echo sequence for 6 different echo times. Parameters were: 200µmx200µm in plane resolution (38.4x38.4mm FOV, 192x192MTX), 300µm slice thickness, 50 kHz SW, TR/TE=4x3.8ms, echo spacing 6.5ms, flip angle 90°.

Image reconstruction
k-space signals from each coil were zero-filled to 256x256 and Fourier transformed (FFT). Coil images were combined with weighted linear least-squares (WLS) for which the relative complex weights were generated from low resolution images (gauss filtered central echo images). A FFT along the gradient-echo time was performed on 256 points and the largest spectrum component (W) and the corresponding mean frequency (F) for each pixel were kept. Images were then cropped down to a 192x128 matrix including the entire brain and W was normalized to the noise mean estimated in a region void of signal. The brain region M was segmented using a connected component analysis based on a mask (W>3) combined with dilation and erosion operations. W was then masked to the brain region.

Unwrapping and background filtering
were treated simultaneously. The field B inside the brain was decomposed as the sum of the internal variations Bint, the variations Bext induced by external sources and the field due to the mean brain susceptibility Bmean. From Maxwell equations, the Laplacians ΔBint = ΔBext = 0 and ΔB = ΔBw. Consequently, to isolate internal variations, the following WLS problem can be solved: min∥Bint - ΔBw∥22 + α∥M∥22 + β∥W∥22. The iterative conjugate gradients algorithm was used on the WLS problem (7). A CG algorithm was used to perform the regularized inversion.

RESULTS
Strong T2* effects can be seen in both striata with larger effects in the left as expected (Fig.1a). The internal effects (c) showed a clear dipolar pattern around the injection sites. The single step unwrapped and filtered phase map (e) showing dipolar effects in the striata. More iron is detected in the left striatum than in the right striatum on the susceptibility map (d). Reformatted axial signal intensity (e) and susceptibility (f) images showing the injection sites.

Fig. 1: Reconstructed signal intensity (a) and phase (b) maps in a selected horizontal slice through the striatum. The single step unwrapped and filtered phase map (c) showing dipolar effects in the striata. More iron is detected in the left striatum than in the right striatum on the susceptibility map (d). Reformatted axial signal intensity (e) and susceptibility (f) images showing the injection sites.

REFERENCES
1. Sun et al., Advanced drug delivery reviews 60p1252.
2. Zurkiya et al., MRM 59p1225.
3. de Rochefort et al., MRM 60p1003
5. Liu et al., MRM 61p196
7. de Rochefort et al., ISMRM 2008 p462; MRI in press.