# 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 for the label to be 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 shimming 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=4s/3.8ms, 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 dilatation 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 $B_{in}$, the variations $B_{out}$ induced by external sources and the field due to the mean brain susceptibility $B_{mean}$. From Maxwell equations, the Laplacians $\Delta B_{out} = \Delta B_{mean} = 0$ and $\Delta B = \Delta B_{in}$. Consequently, to isolate internal variations, the following WLS problem can be solved: $\min_{Bin} \|W_\Delta (\Delta B - \Delta B_{in}) \|^2$. The iterative conjugate gradients algorithm was used on the normal equation: $\Delta W_\Delta^2 \Delta B_{in} = \Delta W_\Delta^2 \Delta B$, in which $\Delta$ was approximated by the fast spatial calculation [-1 2 -1] for each second derivative operation. $W_\Delta$ is the error correlation matrix generated from W in this operation. Unwrapping was simply included by forcing the point by point difference between ]-π, π] when calculating $\Delta B$ from the phase map. Iterations were stopped when the relative norm was less than $10^{-3}$.

***Quantitative susceptibility maps*** $\chi$ were reconstructed from $B_{in}$ solving a constrained least-squares minimization problem (7): $\min_\chi \|W ( C\chi - B_{in}/B_0 ) \|_2^2 + \alpha^2 \| M\chi \|_2^2 + \beta^2 \| W_g G\chi \|_2^2$. The first terms is the squared distances between the measured field $B_{in}/B_0$ and the fitted ones $C\chi$, where $C$ is the linear transformation determining the field from $\chi$. The second and third terms are regularization terms on $\chi$ and its gradient ($G$), respectively. $W_g$ is a weighting term generated from $W$ enforcing $\chi$ to have a similar smoothness than $W$. The 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 injected volume as well as a lower natural contrast mainly due to veins within the brain. Susceptibility maps confirm the presence of iron in both striata with a larger quantity in the left. To assess the total quantity of iron, images were reformatted in axial view and summed over 10 slices including the striatum (e,f). The total magnetic moments inside regions of interest traced in each striatum were calculated and converted to iron mass (14 ppm L/g at 7T). From these images, 47 and 20 ng were measured in the left and right striata, respectively.

## DICUSSION AND CONCLUSION

Susceptibility maps were obtained in vivo on rat brain at 7T using QSM. Amounts of SPIO on the order of ~50 ng injected in the striata were detectable and generated a larger contrast than the paramagnetic veins in the background. The lower detected values (47 and 20 instead of 112 and 56ng) can be due to leakage of the contrast agent through the needle track, diffusion inside the parenchyma, and filtering effects in the reconstruction procedure. Using a left/right control as done here ensures that these effects are the same and a good relative quantification was obtained. The presented preliminary results illustrate the possibility of mapping paramagnetic contrast agents distribution at 7T using QSM in the rat brain. This approach could be used to quantify iron deposition in the brain or iron-oxides particle distribution used for cellular/molecular MRI.

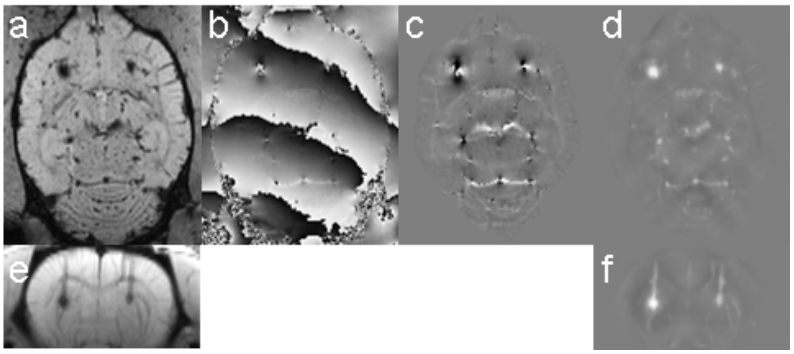


Fig. 1: Reconstructed signal intensity (a) and phase (b) maps in a selected horizontal slice through the striatum. The single step unwrapped and filtered phase map (c) showing dipolar effects in the striata. More iron is detected in the left striatum than in the right striatum on the susceptibility map (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 **4.** Kressler et al. IEEE TMI 2009 **5.** Liu et al., MRM 61p196 **6.** Shmueli et al., MRM 2009 **7.** de Rochefort et al., ISMRM 2008 p462; MRM *in press*.