

# Quantitative Susceptibility Mapping to assess Iron Levels in Rat Brain Tumors

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**Target Audience:** Neuro-oncologists, neuroradiologists, neurosurgeons, clinicians and scientists in susceptibility imaging

**Purpose:** The purpose of this study was to pursue quantitative susceptibility mapping (QSM) as a means to quantify and assess iron levels in brain tumors. Altered iron uptake, storage, efflux, and metabolism have been found to play a critical role in the growth and metastases of cancer<sup>1</sup>. The ability to non-invasively quantify these altered iron stores may provide valuable insight about tumor type, grade, and physiology. Traditional iron imaging techniques involve measuring the relaxation properties of T2 and T2\*. However, these signals are affected by calcification and bound water effects on the signal<sup>2,3</sup>. QSM is a recently identified post-processing technique that measures bulk tissue susceptibility from the signal phase<sup>4</sup>. QSM is routinely used to accurately measure iron concentrations in different brain regions<sup>2</sup>, yet very few studies have addressed susceptibility and iron in brain tumors<sup>5</sup>. The goal of this study is to determine if QSM will provide a novel means to detect and quantify iron in brain tumors. To address this, QSM maps were created and analyzed in a rat brain tumor xenograft model.

**Methods:** A retrospective study was completed on imaging data from sixteen athymic rats that were inoculated with U87 cells. A multi-echo gradient echo (MGE) imaging sequence acquired images on a 9.4T Bruker scanner (BioSpin, Billerica, MA, USA) on days 8 and 18 following inoculation with the following parameters; FOV=30x30x5 mm<sup>3</sup>, MAT=256x256x5, TR/TE<sub>1</sub>=1500/4ms,  $\Delta$ TE=6ms, Echos=8, Averages=3. Phase images were extracted from the raw signal, unwrapped using FSL PRELUDE<sup>6</sup> and background phase was removed using a Gaussian low-pass-filter (radius=4 pixels). A closed form, l2-regularization dipole inversion technique<sup>7</sup> was used to create the susceptibility maps from the tissue field using MATLAB (MathWorks, Natick, MA, USA). This technique was implemented on a slice-by-slice basis, so susceptibility contributions in the slice-select dimension are ignored. Masks were manually drawn around the white matter (WM), gray matter (GM), and tumor, from which susceptibility values were extracted and averaged from the first and second echo time (TE=4,10ms). These values were referenced to white matter to create relative susceptibility maps ( $\Delta\chi$ ). A paired t-test was used for statistical testing to compare  $\Delta\chi_{GM}$  to  $\Delta\chi_{Tumor}$  for each rat dataset.

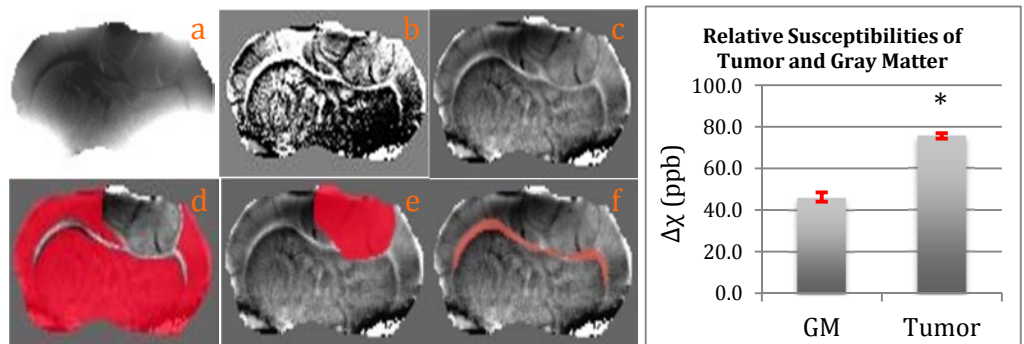
**Results:** Phase, tissue field susceptibility, and masks of the white matter and tumor of the rat brain are shown in **Figure 1**. In the rat brains, a statistically significant increase in susceptibility ( $p=0.012$ ) was found in tumor ( $\Delta\chi_{Tumor}=75.6\pm2.5$  ppb) relative to gray matter ( $\Delta\chi_{GM}=46.2\pm4.3$  ppb), shown in **Figure 2**.

**Discussion:** This study provides initial results demonstrating the feasibility of noninvasively measuring iron stores in brain tumors using QSM, which are critical to cancer cell metabolism.

Accurate quantification of iron type and content may be a vital clue for treatment efficacy, specifically for chemotherapy drugs that target iron-related components of the cell. QSM has also been shown to distinguish calcifications from blood depositions in GBM patients<sup>5</sup>, which is important for monitoring treatment response. QSM alone may not provide all the means to separate and quantify different types of iron stores in brain tumors. Therefore, we believe that QSM in combination with alternate iron imaging modalities, such as qualitative susceptibility weighted imaging (SWI), T2\*, and T2', will provide as a robust iron quantification technique. In conclusion, increased susceptibility in the tumor relative to gray matter in the rat brain supports the hypothesis of elevated iron levels in tumors. Phantom imaging, histological processing, and implementation of a flow compensated susceptibility sequence are ongoing to verify these results and their relationship to iron.

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**References** [1] Torti SV, et al. Nature Rev. Cancer 2013;(5):342-55. [2] Langkammer C. et al. Neuroimage 2012;(62):1593-1599. [3] Ordidge RJ, et al. MRM. 1994;(32):335-41. [4] Li L, et al. MRM 2004;(51):1077-1082. [5] Deistung A, et al., PLoS 2013;8(3):e57924. [6] Jenkinson M. MRM. 2003;49:193-197. [7] Bilgic, B, et al. Proc. Intl. Soc. Mag. Reson. Med. 21 (2013).



**Figure 1:** Unwrapped phase (a), Tissue Field (b), QSM (c), and ROIs surrounding the Gray Matter (d), White Matter (e), and tumor (f) in a rat brain dataset.

**Figure 2:** Quantified relative susceptibility values in the tumor and gray matter (\* $p=0.012$ )