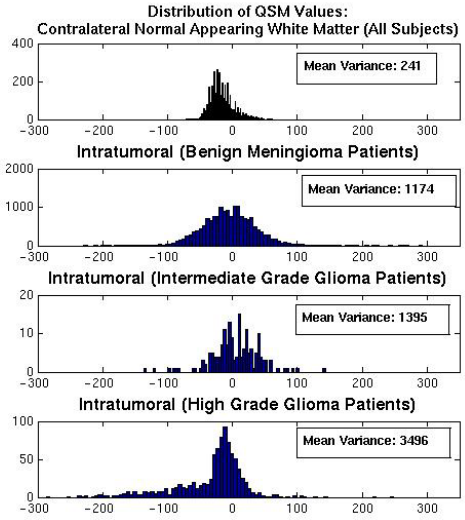
Quantitative Susceptibility Mapping of Intracranial Tumors: Correlation with Histologic Grade

K. Surapaneni[1], C. Horenstein[1], T. Liu[2], C. Wisnieff[2], Y. Wang[3], and R. DeLaPaz[1]
[1]Radiology, Columbia University, New York, NY, United States, [2]Biomedical Engineering, Cornell University, Ithaca, NY, United States, [3]Radiology, Cornell University, NY, NY, United States

Introduction: Prior work using T2* weighted gradient echo and susceptibility weighted MR imaging (SWI) have shown correlations between histopathologic tumor grade and intratumoral susceptibility from elevated levels of ferritin and transferrin receptors, intra-lesional hemorrhage, and microvascularity within brain tumors (1-3). Higher grade tumors are associated with neovascularity and an increase in intratumoral microhemorrhages, which can be evaluated with SWI techniques due to the paramagnetic effects of blood breakdown products and deoxyhemoglobin. The susceptibility distribution can be further calculated by quantitative susceptibility mapping (QSM), a technique that incorporates anatomic information from the SWI magnitude image and overcomes the ill-posed magnetic field to susceptibility source inverse problem (4). The purpose of this study was to determine if intrinsic tissue susceptibility differences calculated by QSM correlated with higher tumor grade. Correlation between intratumoral SWI signal intensity, apparent diffusion coefficients (ADC), and QSM-derived susceptibility values were evaluated to assess if intratumoral susceptibility values offer additional complementary information of the tumor microenvironment.

Materials and Methods: *Data Acquisition.* MR imaging and patient demographic data were retrospectively reviewed in a HIPAA compliant manner and with IRB approval. Ten patients with pathologically proven brain tumors were analyzed. Patients were categorized into three groups for analysis: 1) benign tumors (4 meningiomas), 2) intermediate grade tumors (1 recurrent grade II oligodendroglioma, 2 grade III astrocytomas) and 3) high grade tumors (3 recurrent grade IV glioblastomas). MR imaging was performed on a 3T GE scanner with an 8 channel birdcage head coil. A multiecho spoiled gradient echo sequence with 7 TEs was acquired without contrast; uniform TE spacing= 5 ms and TR=42.1 ms; flip angle=15 degrees; bandwidth=62.5kHz; FOV=22cm; slice thickness=3mm (ZIP2 to an effective thickness of 1.5mm); acquisition matrix size=320 x 224; image acquisition time=2:33 min. Diffusion weighted imaging was performed using a spin echo echoplanar sequence with b=1000; TR/TE=7000/72; and 5 mm slice thickness. *Data Analysis*. Susceptibility maps were generated using a morphologically enabled dipole fitting (MEDI) technique. The MR sequences were co-registered into MNI space using FLIRT. Regions of interest (ROI) were drawn in AFNI by a neuroradiologist on enhancing tumor tissue on T1 post-contrast sequences; ROIs were drawn on non-enhancing tumors based on either 1) regions of restricted diffusion confirmed on ADC maps with corresponding elevated rCBV in 2 cases of recurrent grade IV glioblastoma and 2) FLAIR signal abnormality in regions of elevated rCBV in a case of recurrent grade II oligodendroglioma. Additional ROIs were drawn 2-3 mm immediately adjacent to the tumor in normal appearing white matter (NAWM) to determine changes in local tissue susceptibility in peritumoral regions. An ROI of similar size to the tumor was placed in contralateral normal appearing white matter (CNAWM), with additional adjacent ROIs placed within 2-3 mm of the CNAWM to serve as internal reference standards. Two-tailed t-tests were performed in MATLAB between intratumoral susceptibility values and histopathologic tumor grade to assess for statistically significant differences.

Results: In all 4 patients with benign meningiomas, QSM showed a relative increase in intratumor susceptibility, compared to CNAWM [range: 6.7 to 20.3 ppm; mean: +11.3; sd: 6.16]. The ratio of SWI signal intensities between benign tumors and CNAWM ranged between 0.99 and 1.14 (mean: 1.1). Three of 4 patients with meningiomas had DWI; the ratio of ADC values between tumor and CNAWM was similar in 2 patients (range 1.03-1.12) and was markedly increased in the third patient (2.02). In 2 of the 3 patients with intermediate grade gliomas, QSM showed a relative decrease in susceptibility within the tumor (range -2.2 to -3.5 ppm), while the third patient had a relative increase in susceptibility equal to 27.5 ppm; overall the mean change in intratumoral susceptibility for this cohort was +7.3 ppm (sd: 17.5). The ratio of SWI signal intensity between intermediate grade tumors and CNAWM ranged from 1.09 and 1.19 (mean: 1.13, sd: 0.06). Only one patient with intermediate grade glioma had DWI; the ADC ratio b/w the tumor and CNAWM was 1.71. In all 3 patients with recurrent grade IV glioblastoma, QSM showed a relative decrease in intratumor susceptibility, compared to CNAWM [range: -1.71 to -63.1 ppm; mean: -24.4; sd: 33.7]. The ratio of SWI signal intensity between high grade tumors and CNAWM ranged b/w 0.9 and 1.06 (mean:0.96, sd:0.09). The ADC ratio b/w high grade tumor and CNAWM was similar in 3 patients (range 1.1-1.4; mean:1.2, sd:0.17). For all 11 patients, the relative QSM phase shift in the tumor compared to CNAWM was significantly correlated to tumor grade (r= -0.66, p=0.03). There was no correlation between tumor grade and SWI signal intensity (r=-0.27, p=0.42) or ADC (r=-.11, p=0.8) values. Additionally, it was observed that the variance of intratumoral QSM values was increased relative to the variance of QSM values in the contralateral white matter (figure). The mean subject variances were 241 +/- 103 (CNAWM), 1174 +/- 486 (meningiomas), 1395 +/- 1093 (intermediate grade gliomas) and 3496 +/- 2637 (grade IV gliomas). There was a trend towards a significant correlation between intratumoral QSM variance and tumor grade (r=0.57, p=0.07).



Discussion and Conclusion: Relative changes in intratumoral susceptibility obtained by QSM significantly correlated with histopathologic grade of intracranial brain tumors in this small pilot study. The variance of QSM values inside the tumors is also increased relative to CNAWM, and may better reflect the characteristic tissue heterogeneity of malignant brain tumors as compared to conventional MRI sequences. By calculating the intrinsic tissue susceptibility, quantitative susceptibility mapping may offer a non-invasive evaluation of the tumor microenvironment without the need for contrast agents. Further validation of these findings and correlation with additional parameters such as MR perfusion data is needed.

Ref: 1. Recht L, J Neurosurg 1990; 72:941-945. 2. Bagley L, Radiology 1997;202: 511-516. 3. Christoforidis GA, AJNR 2004; 25:756-760. 4. Liu T, ISMRM Proc 2010:4996.