

# Quantitative intra-tumoral susceptibility signal in grading brain astrocytomas with susceptibility-weighted imaging

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## Introduction

Susceptibility-weighted imaging (SWI) is sensitive to paramagnetic substances such as deoxygenated hemoglobin and hemosiderin. Therefore, it became a useful tool to investigate the hemorrhage and vascularity, which usually exhibit low signal in SWI, in brain tumors.<sup>1</sup> The frequency of the low-intensity structures in the lesion, termed as intra-tumoral susceptibility signal (ITSS), was found to correlate tumor grade apparently, thus helping differential diagnosis.<sup>2,3</sup> However, most studies were performed using a qualitative or semiquantitative assessment on only one selected slice, in which subjective categorization is inevitable. In this study, a quantitative measurement was proposed to estimate the volumetric percentage of ITSS on subjects with brain astrocytomas.

## Materials and Methods

This study included 43 patients (23 male and 20 female; 13-88 years old) with brain astrocytomas. Final pathology results of all subjects were obtained by means of surgical specimens. Tumors were graded according to the standards described by the 2000 WHO classification of the central nervous system tumors, and in all cases of the brain astrocytomas were sorted to two groups: low-grade (grade I and grade II) and high-grade (grade III and grade IV) groups. Of the 43 patients, histopathological diagnoses were glioblastoma (n=32, WHO grade IV), anaplastic astrocytoma (n=3, WHO grade III), and diffuse astrocytoma (n=8, WHO grade II).

All patients underwent SWI and conventional MR imaging, including T1WI, T2WI, and T2-FLAIR, at a 1.5-T scanner (Signa HDx, GE Healthcare, Milwaukee, WI). To obtain SWI, a 3D flow-compensated gradient-echo sequence was conducted with TE/TR = 39/50 ms, flip angle = 18°, FOV = 22 cm, acquisition matrix = 288 x 256, and a 2.5-mm thickness. After processed by a high-pass Gaussian filter in a FWHM of 32, each axial SWI was reconstructed in 512 x 512. In addition, 3D contrast-enhanced (CE) T1WI was obtained after contrast injection by using IR-SPGR sequence with TE/TR/TI = 4.2/9.2/400 ms, flip angle = 20°, FOV = 24 cm, and a 1.2-mm thickness.

The region of lesion was manually delineated on CE-T1WI, which was automatically coregistered to SWI using a rigid-body model. Based on the concept of CNR, the normalized contrast (NC) was calculated on each pixel (with its intensity  $I_{SWI}$ ) of the lesion to detect the ITSS by

$$NC = (\mu_{\text{non-ITSS}} - I_{SWI}) / \text{STD}_{\text{NWM}}$$

where  $\mu_{\text{non-ITSS}}$  indicates the mean SWI intensity of non-ITSS voxels, which was estimated by averaging the class with higher mean after applying Otsu's thresholding<sup>4</sup> on the lesion. Besides,  $\text{STD}_{\text{NWM}}$  is the standard deviation of a manually selected normal white matter region, representing the signal fluctuation of SWI. Thus, regions with low gray levels, usually suspected as hemorrhage or venous blood, tend to present high NC values. As a result, the pixel is classified as the ITSS if NC is larger than a predefined threshold, and the volume of ITSS can be obtained once the determination is done on the whole lesion. Since the optimal NC threshold for tumor grading is unknown, various values, ranging from 4 to 20, were explored in this study. For each threshold, two-sample t-test was applied on the volumetric percentage of ITSS between low-grade and high-grade astrocytomas. Receiver operating characteristic (ROC) analysis was also performed to evaluate the differentiation.

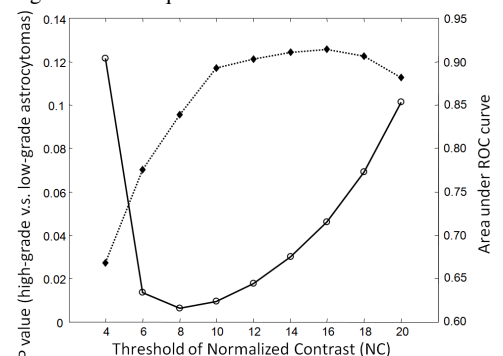
## Results

Figure 1 demonstrates the threshold dependency plot of p value (solid line with circle marks) and area under ROC curve (AUC, dotted line with diamond marks). Significant difference of ITSS percentage ( $p < 0.01$ ) was found when the threshold of NC was set as 8 or 10. The AUC was maximized at a threshold of 16 when the numbers obtained from 10 to 18 were close to each other. Therefore, a NC threshold of 10 was chosen for better differentiation in this study.

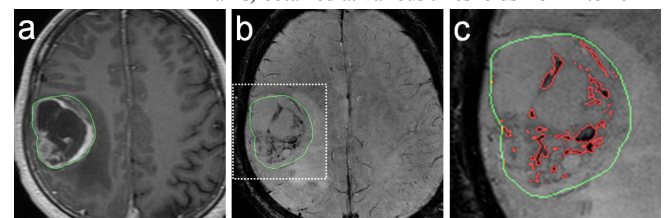
The average volumes of lesion and ITSS were 47.62 ml (range: 1.57 to 163.11 ml; std = 35.77 ml) and 5.35 ml (range: 0.01 to 48.00 ml) for high-grade lesions, and 62.52 ml (range: 14.19 to 104.53 ml; std = 38.14 ml) and 0.79 ml (range: 0.03 to 1.86 ml) for low-grade lesions. The coregistered CE-T1WI and SWI of a 51-yr male suffering glioblastoma (Fig.2, high grade) and a 39-yr male with diffuse astrocytoma (Fig.3, low grade) were shown. Zoomed SWI (Fig.2c and Fig.3c) clearly demonstrated the lesion (green line) and ITSS (red line). The ITSS region was found to match visual observation perfectly. Given ITSS percentage > 1.9% as positive event, the sensitivity and specificity of identification of a high-grade tumor were 80% and 100% respectively.

## Discussion

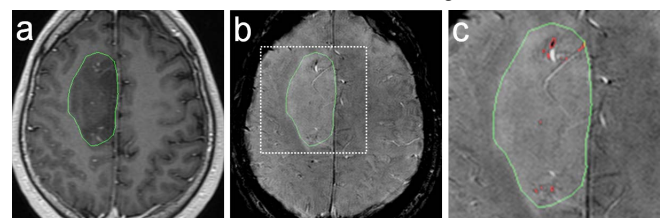
By using  $NC > 10$  for ITSS determination, significant difference between high-grade and low-grade astrocytomas was found ( $p < 0.01$ ) on the volumetric percentage of ITSS, and an AUC of 0.89 was obtained, rendering this quantitative index as a helpful classifier on discrimination of tumor grade. A larger threshold, such as 12 or 14, can still provide good identification of ITSS and similar capability of differentiation (not shown). Limitations of this study include relative small sample size of low-grade astrocytomas (n=8) and the interference of susceptibility artifacts around air-tissue interfaces, which was carefully excluded before evaluation of ITSS, resulting in possible underestimation of lesion volume. In conclusion, the quantitative measurement of ITSS percentage proposed in this study is able to provide useful information in grading of astrocytomas, which shows high potentials in differentiation of solitary tumors objectively.



**Fig.1** The p value (solid line with circle marks) and area under ROC curve (dotted line with diamond marks) obtained at various thresholds from 4 to 20.



**Fig.2** The CE-T1WI (a) and SWI (b) of a 51-yr male with a right parietal glioblastoma. Regions of the lesion and ITSS detected with a ND threshold of 10 were delineated in green and red in the enlarged SWI (c). Volumes of lesion and ITSS were 43.95 and 5.15 ml, leading to an 11.71% ITSS.



**Fig.3** The CE-T1WI (a) and SWI (b) of a 39-yr male with a right frontal-parietal diffuse astrocytoma (grade II). Regions of the lesion and ITSS (ND>10) were shown in green and red in the enlarged SWI (c). Volumes of lesion and ITSS were 76.34 and 1.26 ml, leading to a 1.65% ITSS.

**References:** 1. Sehgal V, et al. JMRI 2006; 24: 41-51. 2. Pinker K, et al. AJNR 2007; 28: 1280-6. 3. Kim HS, et al. AJNR 2009; 30: 1574-9. 4. Otsu N. IEEE T Sys Man Cyber 1979; 9: 62-66.