Assessment of Intratumoral Susceptibility Signals (ITSS) in Patients with newly diagnosed Glioblastoma using Quantitative Susceptibility Mapping (QSM)

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INTRODUCTION – Susceptibility weighted imaging (SWI) is a non-quantitative MRI technique that employs phase images to enhance small susceptibility variations on magnitude images [1,2]. SWI may be applied to assess the grade of tumors by analyzing the presence of intratumoral susceptibility signals (ITSS). Based on SW images, these ITSS are defined as fine linear or dot-like structures with low signal intensity that are not discernable on conventional MR images (T_1-w, T_2-w, T_2^*-w, diffusion weighted, and contrast-enhanced T_1-w images with slice thicknesses of typically 5 mm) [3]. On SW images glioblastoma usually exhibit a large amount of ITSS, thus enabling differentiation from other enhancing brain lesions, such as lymphoma, that rarely present ITSS [3]. However, the source of ITSS in glioblastoma is still unknown because both calcium and blood products appear hypointense on SW images, thus impeding further differentiation. Quantitative susceptibility mapping (QSM) represents a non-invasive approach to characterize arbitrarily shaped brain lesions as blood product or calcium deposits [4]. This novel approach converts susceptibility-weighted phase images into quantitative maps of magnetic susceptibility [5]. This contribution aims to determine the underlying biophysical sources of ITSS in glioblastoma with quantitative susceptibility maps.

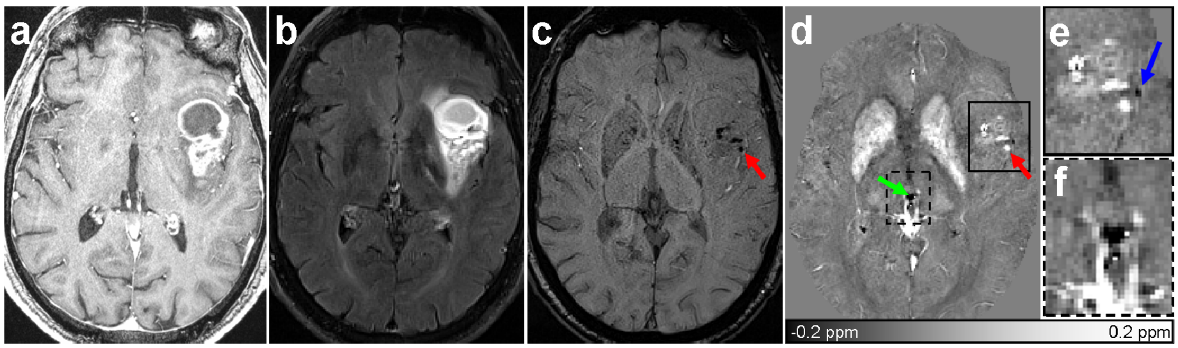

Figure 1: *MR images of a 68-year-old man with a left temporal glioblastoma. ITSS are marked by the red arrow on the SW image (c) and quantitative susceptibility map (d). The contrast-enhanced T_1-w and FLAIR images, presented in (a) and (b), respectively, do not show any correlates of the ITSS. Enlarged sections of susceptibility images showing the glioblastoma (solid rectangle) and the glandula pinealis (dashed rectangle) are illustrated in (e) and (f), respectively. The blue arrow indicates a hypointense susceptibility region due to the phase shift induced by pulsatile arterial blood flow.*

MATERIAL AND METHODS

***Data Acquisition*:** Images were acquired in a routine clinical workup from 9 patients with newly diagnosed and histologically proven glioblastoma before surgery using a 3 T MR system (Magnetom Tim Trio, Siemens Healthcare, Erlangen, Germany) with a 12-channel head-matrix coil. SWI data were recorded with a 3D fully flow-compensated gradient-echo (GRE) sequence (TE/ TR/FA/BW=19.7ms/27ms/ 15°/140 Hz/px, voxel size 0.72×0.72×2.5mm³, GRAPPA [acceleration factor = 2, 32 reference lines]). For comparison contrast-enhanced MP-RAGE (TI/TE/TR/FA/BW=1100ms/4ms/1710ms/ 15°/130 Hz/px, voxel size 0.5 × 0.5 × 1.3 mm³) and FLAIR sequences (2D turbo-inversion recovery sequence, TI/TE/TR/FA/BW=2400ms/ 135ms/8500ms/170°/150 Hz/px, voxel size 0.9 × 0.9 × 5 mm³) were applied.

Data Processing: Multi-channel SWI magnitude images were reconstructed using the sum-of-squares (SoS) method [6], whereas multi-channel SWI phase images were combined by taking into account the channel-dependent phase offset, which was estimated from the single channel images within the same homogenous region of interest [7]. Phase aliasing in the combined phase images was resolved by 3D phase unwrapping [8] and background phase contributions were eliminated with the SHARP method [5]. Background-corrected phase images were then supplied to a novel susceptibility mapping algorithm (homogeneity enabled dipole inversion, HEIDI [submitted to ISMRM 2012]) to yield quantitative susceptibility maps without streaking artifacts. Finally, the combined magnitude and phase images were converted into SW images according to [2]. All processing was performed fully automatically with the MeCS-framework [9]. T_1-weighted and FLAIR images were reconstructed by the MR scanner software.

Data Analysis: Two experienced neuroradiologists (M.B. and A.R.) graded ITSS on the acquired susceptibility maps as either 1) 80-100 % hypointense, 2) 60-80 % hypointense, 3) indifferent, 4) 60-80 % hyperintense, 5) 80-100 % hyperintense. Discrepancies were resolved by consensus reading. Additionally, typical locations for calcifications, such as glandula pinealis and plexi choroidei were graded according to the introduced scale.

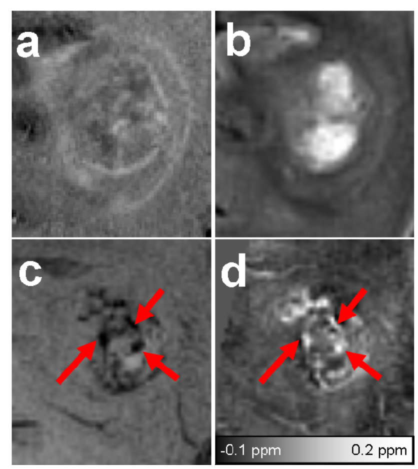

Figure 2: *Corresponding sections of MR images of a 72-year-old man with a right temporal glioblastoma. The contrast-enhanced T_1-w, FLAIR, SW, and susceptibility images are shown in (a), (b), (c), and (d), respectively. Arrows indicate ITSS.*

RESULTS – All glioblastoma presented multiple ITSS. In 8 glioblastoma ITSS were classified as grade 5, whereas in one glioblastoma ITSS were classified as grade 4. In contrast, the glandula pinealis and plexus choroidei were classified as grade 1 in all patients. One representative example of a patient with glioblastoma multiforme is demonstrated in Fig. 1. ITSS are clearly seen on SWI, but do not show any correlates on FLAIR or contrast-enhanced T_1-w images. The ITSS (red arrow) and the calcification in the glandula pinealis appear hypointense on the SW image. In contrast, the ITSS is hyperintense on the susceptibility map and can thus be differentiated from the calcification in the glandula pinealis that is hypointense. Another example which reveals the sources of ITSS as blood products is shown in Fig. 2.

DISCUSSION – We have demonstrated for the first time that QSM is able to differentiate between calcium and hemorrhage in glioblastoma and that ITSS in untreated glioblastoma originate from blood products. This finding improves the understanding of the pathophysiology of glioblastoma. It is anticipated that quantitative susceptibility mapping will influence progression-assessment and daily clinical decision making, as recent studies suppose calcifications to be an imaging biomarker for response and outcome in the treatment of glioblastoma [10].

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