# On the limitations of brain lesion characterization by direct assessment of MRI phase

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**TARGET AUDIENCE** – Researchers and clinicians interested in the differentiation between hemorrhagic and calcified brain lesions.

**PURPOSE** – Characterization of brain lesions as hemorrhages or calcifications is an important clinical neuroimaging task. The gold-standard technique for this is computed tomography (CT), on which both types of lesions appear hyper-dense, but calcifications have a higher CT number (HU>100). Major pitfalls of CT are the low sensitivity toward small hemorrhages and its use of ionizing radiation, which is generally to be avoided. Differentiation between calcifications and hemorrhages with magnetic resonance imaging (MRI) is a major challenge and has been subject to intense research over the past decade[1-3]. In the clinical community susceptibility weighted imaging (SWI) MRI phase images are often considered to be a viable source of information on the lesion type, on the basis that hemorrhages are more paramagnetic and calcifications more diamagnetic than surrounding parenchyma[2]. This results in opposed effects on the MRI phase[2,3]. Depending on the vendor of the MRI system[2] hemorrhages and calcifications are considered to have bright and dark phase values in their center[2,5], respectively, or the other way around. This approach is clinically established in many hospitals[2,5], although it is well-known that MRI phase only indirectly reflects tissue magnetic susceptibility because it critically depends on the geometric shape of susceptibility inclusions and on their orientation relative to the main magnetic field[7]. In this work we demonstrate the limitations of phase-based lesion characterization in a simple numerical model.

**METHODS** – *Numerical model:* We created a simple numerical model to illustrate the dependence of the lesion phase on the orientation of the lesion relative to the main magnetic field. A homogeneous ellipsoid with semi-major axis $(x,y,z)$ of 50, 30 and 10 voxels was created on a $256^3$ numerical grid in MATLAB (2013b, The MathWorks, Natick, MA). We chose an ellipsoid lesion shape because of its simplicity and because both elongated longitudinal lesions and spherical lesions are opposite extreme cases of an ellipsoid. The lesion was modelled relatively large with respect to the grid size to avoid discretization artifacts. The absolute lesion size is irrelevant for this simulation, because only the strength of the field perturbation due to a susceptibility inclusion scales with its size while the distribution pattern remains invariant. The ellipsoid's susceptibility was chosen to be +0.5 ppm (paramagnetic) relative to the surrounding tissue, a typical susceptibility value for hemorrhages in the human brain[8], while calcifications could be modeled as -0.5ppm (diamagnetic)[8]. We carried out the simulations only for a paramagnetic lesion and did not repeat the simulation for a diamagnetic lesion because the simulations are invariant with respect to the polarity of the susceptibility distribution. Results for a diamagnetic lesion can be directly obtained from the results of the simulation using the paramagnetic lesion by multiplication with -1.

*Experimental design:* The magnetic field perturbation due to the lesion was computed by fast forward field calculation[9] and converted to phase at 20 ms and 3 Tesla, typical for SWI experiments[10]. We successively repeated the phase computation for different orientations of the ellipsoid lesion relative to the main magnetic field, mimicking different orientations of an ellipsoid lesion in the brain. However, instead of rotating our lesion model, we rotated the magnetic field direction in steps of 2° from 0° to 180° around the $x$-axis, beginning with the magnetic field in the customary $+z$-direction. To compare simple direct analysis of the phase values to a comprehensive numerical analysis of the phase distribution pattern, each phase dataset was fed into a recently proposed method for quantifying the susceptibility from phase, quantitative susceptibility mapping (QSM)[8,11,12]. This technique has previously been used as a quantitative means to characterize lesions based on phase and has been validated by CT[8,11]. Here, we used the simplest QSM technique, thresholded k-space division (TKD; threshold 0.1)[12].

*Analysis:* We measured the mean phase and susceptibility values inside of the lesions as a function of the rotation angle.

**RESULTS** – **Figure 1** shows mean phase (left) and mean calculated susceptibility (right) inside the lesion as a function of the rotation angle for both a paramagnetic (black) and a diamagnetic (orange) lesion. A separation between hemorrhage and calcification is impossible due to the overlap of the curves. Calculated susceptibility values were clearly separated and, apart from minor deviations, were consistent with the model input magnetic susceptibility of ±0.5 ppm. The small deviations from ±0.5 ppm can be attributed to the simplicity of the QSM reconstruction algorithm (TKD)[12]. **Figure 2** shows phase and reconstructed susceptibility maps (QSM) for different orientations (indicated by the black arrows) of the paramagnetic model. As expected, both phase and magnetic susceptibility were constant throughout the lesions but the phase values inside the lesions depended on the orientation (red arrows). While the external magnetic field perturbation of the lesion changed with orientation, the polarity of the field was constant when assessed in the direction of the magnetic field (bright; blue arrows). This observation is important, as the slice orientation in SWI is usually chosen perpendicular to the main magnetic field[10], allowing assessment of the field perturbation of the lesion along the direction of the blue arrows in Figure 2.

**DISCUSSION** – Our simulation illustrated that a separation between paramagnetic and diamagnetic lesions is not possible based on phase values inside the lesion, due to the phase being dependent on orientation with the magnetic field. Consequently, the mean phase inside lesions must not be used as a criterion for differentiating between hemorrhages and calcifications. However, our results also indicate that if slices are oriented strictly perpendicular to the main magnetic field, a lesion may be characterized by observing its external field (Figure 2). While this strategy has been used heuristically in several studies[3], it should be noted that it is only valid for ellipsoid lesions and cannot be generalized to arbitrary shapes. Further research is required on the generalization of this observation to other lesion shapes, which has, to the best of our knowledge, not been carried out. Furthermore, in the clinical setting correct alignment of the imaging slab often cannot be guaranteed, potentially leading to false diagnosis even if a lesion has a perfectly ellipsoid shape. QSM has been shown in this and other studies[8,11] to overcome the non-locality and orientation dependence of MRI phase and to allow a specific differentiation of hemorrhagic and calcified lesion. QSM should generally be preferred over direct phase measurements for lesion characterization.

**CONCLUSION** – It is impossible to differentiate between hemorrhagic and calcified brain lesions based only on SWI phase values of voxels inside a lesion. This strategy should not be used in clinical routine imaging. QSM provides a means to objectively characterize lesions based on all available information.

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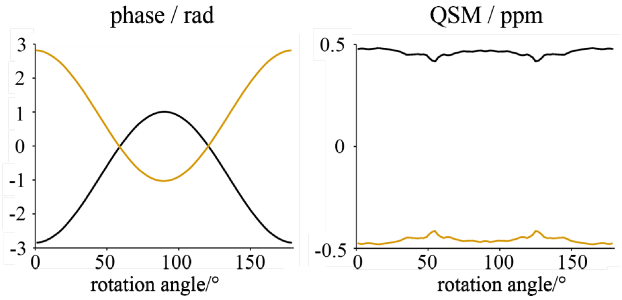


**FIGURE 1**. Mean phase (left) and susceptibility (right) inside of an ellipsoid lesion for different angles relative to the main magnetic field. The black lines represent the paramagnetic lesion, the orange lines the diamagnetic lesion (obtained by multiplication of the black line with -1). It is clear that the phases for the different lesions overlap near rotation angles 60° and 120°, obscuring differentiation (left), but this does not occur with QSM (right) for any orientation.

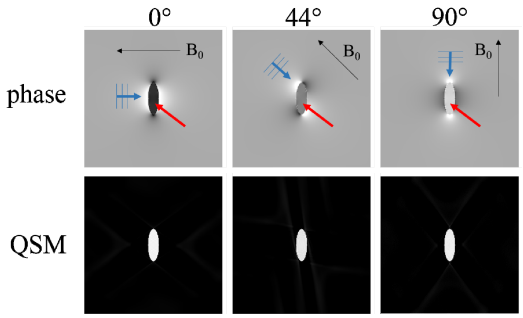


**FIGURE 2**. Illustration of the field patterns (top) and reconstructed susceptibility maps (bottom; contrast 0 to 0.5 ppm) for three different orientations (columns). Black arrows indicate the magnetic field direction, red arrows point to the orientation dependent phase inside the lesion, and blue arrows indicate the "viewing" direction when slices are located perpendicular to the main magnetic field.