

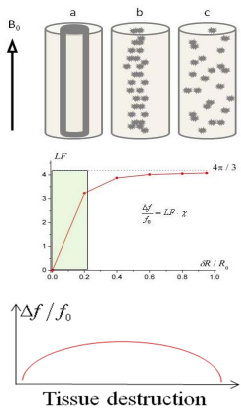
On the Nature of Phase Contrast in Multiple Sclerosis Lesions

Dmitriy A. Yablonskiy¹, Jie Luo¹, Aditi Iyer¹, Alexander L. Sukstanskii¹, and Anne H. Cross²

¹Radiology, Washington University, St. Louis, Missouri, United States, ²Neurology, Washington University, St. Louis, Missouri, United States

Introduction: Phase images obtained by gradient echo (GE) MRI provide image contrast distinct from T1 weighted (T1W) and T2 weighted (T2W) images. One of the emerging applications in phase imaging is studying multiple sclerosis (MS) [1, 2]. Herein we provide theoretical explanation of the phase contrast in MS lesions based on the mechanism that relates MRI signal phase not only to tissue magnetic susceptibility but to tissue microarchitecture at the cellular and sub cellular levels [3].

Theory: Tissue magnetic properties are usually defined in terms of magnetic susceptibility χ that has contributions from magnetic susceptibility inclusions such as proteins, lipids, deoxyhemoglobin, iron, etc. In the presence of external magnetic field, magnetic susceptibility inclusions become magnetized and induce their own magnetic field that shifts Larmor resonance frequencies of neighboring water molecules. This shift Δf is usually described in terms of a Lorentzian sphere: $\Delta f/f_0 = (4\pi/3) \cdot \chi$, where f_0 is the

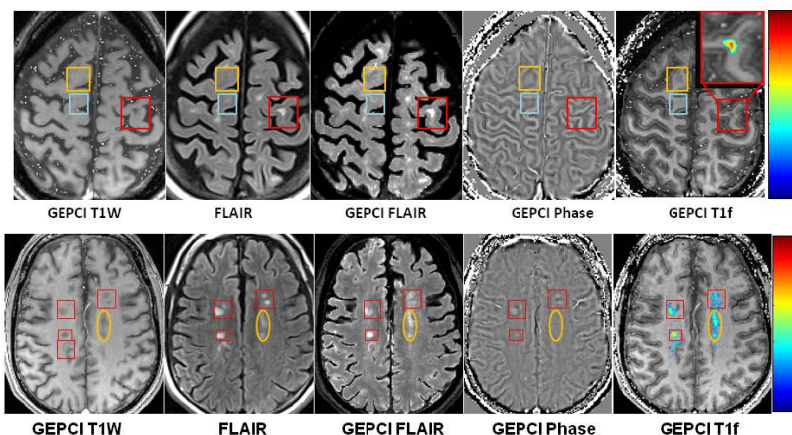


base Larmor resonance frequency. However, as it was demonstrated in [3], for white matter, where the distribution of induced magnetic fields is mainly determined by magnetic susceptibility of myelin sheath and intra-axonal filaments that run mostly parallel to axonal axis, the Generalized Lorentzian approach rather than Lorentzian sphere approximation should be used to describe susceptibility induced MR signal frequency shift. Herein we demonstrate that this mechanism can explain most of the phase lesions in MS. Figure at left shows our theoretical result derived from computer Monte-Carlo simulations of the effect of increasing axon damage on phase/frequency of MR signal. a) Schematic of an intact axon (internal cylinder) covered by myelin sheath (bold outline of the internal cylinder) in an extra-cellular space between bold and outer cylinder with radius R_0 . b) "mildly" damaged axon – fragments of the original myelin sheath are slightly scattered. c) "severely" damaged axon - fragments of the sheath are scattered randomly. Middle panel -- dependence of the Lorentzian Factor (LF) in the MR signal frequency shift $\Delta f/f_0 = LF \cdot \chi$ on a "level of distraction" (δR – average fragments' distance from the center). Note that for intact axon $LF=0$ (no phase contrast). Our theory indicates that phase contrast appears abruptly with minor injury, when LF rapidly grows from zero to almost $4\pi/3$ (shaded green zone). Importantly, the phase contrast can disappear with extreme tissue destruction (lower panel) because the frequency shift is a product of LF and magnetic susceptibility χ : even though LF grows,

$\chi \rightarrow 0$ when tissue loses its cellular content.

Methods: Three RRMS and three SPMS patients were imaged using a Siemens 3T Trio MRI scanner. Three dimensional (3D) version of the GEPCI technique [4] was used to generate frequency and $R2^*$ maps along with GEPCI-FLAIR, GEPCI T1f and T1w images [5]. Lesion severity was assessed based on the lesion Tissue Damage Score (TDS) introduced in [4].

Results and Discussion: Upper panel – data obtained from a subject with SPMS. GEPCI-FLAIR image is T2* map with suppressed CSF signal. GEPCI T1f image has superior contrast between GM and WM. Rectangles outline MS lesions. Orange rectangle represents example of MS lesion that is seen only on phase image (bright contrast) and GEPCI T1f image with negative dark contrast.



Blue rectangle outlines small MS lesion that is barely seen on FLAIR and GEPCI-FLAIR but is well visible on phase image. Red rectangle outlines severe MS lesion (very high, red, TDS score) that is seen on T1W, FLAIR and GEPCI FLAIR but does not have a footprint on phase image. A magnified view of this lesion is shown in inset upper right of GEPCI T1f image along with overlaid GEPCI TDS score (shown as a color bar).

Lower panel - data obtained from a subject with RRMS showing multiple lesions (red rectangles) with intermediate TDS scores (color overlaid on GEPCI T1f image). Here, lesions seen on FLAIR are also seen on GEPCI Phase. Area within orange oval corresponds to partial volume effect from the ventricle in the adjacent slice.

Conclusion: We have proposed theory of phase contrast in MS. Our theory predicts that the phase contrast in MS lesions could appear because of the well known MS pathology affecting white matter integrity, such as injury to the myelin sheath, even without its removal from the affected area, thus preserving tissue magnetic susceptibility. Contrary to an expectation that the phase contrast in MS lesions should always increase in magnitude with lesion worsening (as happens for all known MR magnitude imaging contrast mechanisms), our theory and results demonstrate that phase contrast can actually disappear with extreme tissue destruction.

References: 1. Hammond, K.E., et al., Ann Neurol, 2008; 64: 707. 2. Haacke, E.M., et al., J Magn Reson Imaging, 2009; 29: 537. 3. He, X. and D.A. Yablonskiy, PNAS, 2009; 106: 13558. 4. Sati, P., et al., Neuroimage, 2010; 51: 1089. 5. Luo, J., et al, in Proc. ISMRM-2011: Montreal, CA.