Non-linear Phase Evolution: The Dominant Source of the Average Frequency Difference between Grey Matter and White Matter in Gradient Echo MRI?

Samuel James Wharton[1], and Richard Bowtell[1]

[1]*Sir Peter Mansfield Magnetic Resonance Centre, School of Physics and Astronomy, University of Nottingham, Nottingham, United Kingdom*

Introduction: Phase images acquired using gradient echo (GE) based techniques show excellent tissue contrast at high field strengths [1]. Investigation of the source of the observed frequency difference between grey matter (GM) and white matter (WM) in the human brain is a particularly active area of research. Several contrast mechanisms have been considered, including susceptibility, exchange, and NMR invisible inclusions [1-3]. Recently, Schweser et al. [4] showed that at 3 T the evolution of the phase with echo time in the WM of the optic radiations is non-linear. They postulated that this was due to a small rapidly decaying signal contribution with a high associated frequency offset. Here, we assess the contribution of non-linear phase evolution to the average GM/WM frequency difference at 7 T. The results show that non-linear phase effects may be the dominant source of the mean offset observed between GM and WM in phase images acquired using long echo times (TE > 15ms).

Methods: Three healthy male subjects aged 23-27 were imaged on a Philips 7 T scanner equipped, with a 32 channel receive-only head coil, using a flow-compensated spoiled 3D GE sequence with in plane resolution of 0.6×0.6mm^2, slice thickness 1.2mm, FOV = 230×230×50mm^3, TR=22ms, SENSE factor = 1.2, scan time = 5min. Four scans were acquired with associated TE values of 5, 9, 13, and 17ms. The phase images at each TE value were unwrapped and high-pass filtered using the SHARP method [5], with a kernel radius of 2.4mm to remove phase effects due to field sources outside the brain. Maps showing the spatial variation of frequency, f_{TE}, were created by scaling the filtered phase by the associated TE-value (Fig.1 A-D). Regions of interest (ROI) were drawn in cortical GM and nearby WM throughout the image volume using the magnitude data acquired with TE = 5ms as a guide (Fig. 1E). The mean GM-WM frequency difference was then calculated for each echo time. Maps of the frequency difference, Δf, were created by subtracting the $f_{TE=5ms}$ map from the frequency maps measured at longer TE (Fig. 1F-H). Since phase is expected to evolve linearly with TE in the CSF compartment, frequency offsets at each echo time were measured relative to the average frequency in CSF.

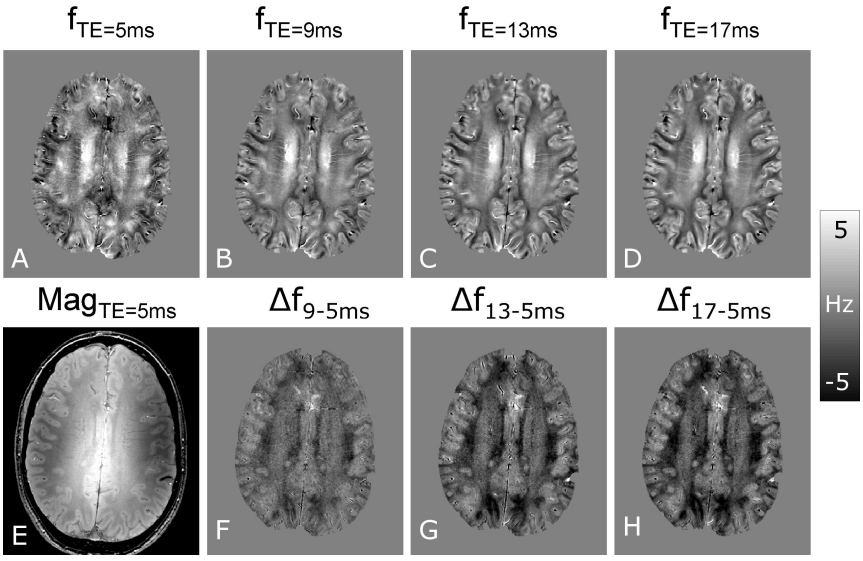

Fig.1 (A-D) Representative frequency maps for each TE value. (E) Magnitude data for TE=5ms. (F-H) Frequency difference maps for each TE value relative to $f_{TE=5ms}$.

Results: Comparison of the frequency maps measured at different echo times (Fig. 1A-D) indicates that the GM-WM frequency offset is highly dependent on TE and as a consequence the GM-WM contrast increases as TE increases from 5 to 17 ms. The frequency difference maps (Fig. 1F-H) confirm that the dominant frequency changes occur in WM. Larger differences were found to occur in the fiber tracts as previously observed in the optic radiations [4]. The mean cortical GM-WM frequency difference in the three subjects is plotted versus TE in Fig. 2. The plot indicates that the average GM-WM frequency offset is approximately zero (0.093 ± 0.085 Hz) at TE = 5ms, but then increases monotonically with TE to a value of 1.66 ± 0.084 Hz at TE=17ms. Fitting these data using a simple two compartment model for the white matter yielded the frequency differences shown by the gray dashed line in Fig. 2. The best fit was achieved when the signal from one WM compartment generating 12% of the signal at TE=0, decayed with $T_2^* \approx 6$ms and had a frequency offset of +27 Hz relative to GM. The fit suggested a frequency offset of -1.66 Hz for the larger WM compartment (88 % of signal at TE=0) relative to GM.

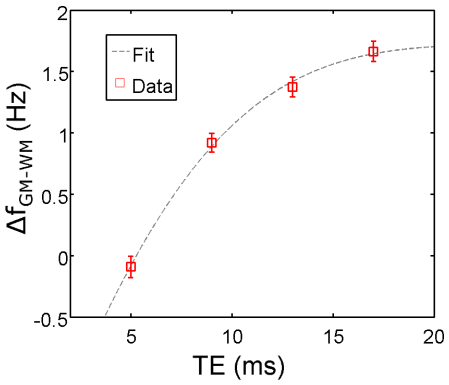

Fig.2 Plot of mean GM-WM frequency difference against TE.

Discussion: The results of this study show that GM-WM phase contrast is strongly dependent on TE for values in the range 5-17 ms. One possible reason why this effect has not been clearly observed in phase data before, is that the underlying frequency changes occur at times shorter than the TE values (> 17 ms) that are commonly used for phase imaging at 7 T. The results also show that non-linear phase evolution occurs mainly in WM. This suggests that myelin-water [6] is the source of the rapidly decaying signal component which gives rise to this effect. The fitted T_2^*-value of 6 ms is consistent with the work of van Gelderen et al. [7] who identified a rapidly decaying WM signal component based on the evolution of signal magnitude with TE at 7 T. Our results indicate that phase images acquired at long echo times may not accurately represent local field offsets. Indeed, the fitted curve from Fig. 2 suggests that at very short echo times (TE<5ms) the mean GM-WM phase difference may be reversed relative to that found at long TE. This observation implies that non-linear phase effects should be properly accounted for before quantitative information about differences in GM-WM tissue composition, such as differences in iron and myelin content, can be inferred from phase images acquired at high field strengths.

References: [1] Duyn et al. 2007. PNAS. (104) 11796-11801; [2] Shmueli et al. 2010. MRM. (65) 35-43; [3] He et al. 2009. PNAS. (106) 13558-13563; [4] Schweser et al. 2011. Proc of ISMRM. 1428; [5] Schweser et al. 2010. Neuroimage. (54) 2789-2807; [6] Mackay et al. 1994. MRM. (31) 673-677. [7] van Gelderen et al. 2011. MRM. DOI: 10.1002/mrm.22990.