The role of intravascular effects in phase contrast between Gray and White Matter

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Introduction: Recent studies have shown dramatic contrast between gray (GM) and white (WM) matter in MR phase images [1-3]. Several sources for this contrast have been proposed including tissue iron concentration, myelin, water-macromolecule interaction, and deoxy-hemoglobin [1-3], but the issue remains under investigation. Here we examine the contribution of blood-related sources to this contrast by modulating the blood susceptibility with a gadolinium-based contrast agent during time-series phase imaging.

Methods: Time courses were acquired at 7T using a 16-channel RF head coil (Nova Medical, MA) and a flow-compensated 3D segmented EPI sequence (EPI factor = 27; SENSE factor = 2) with TR/TE: 50/20ms, flip-angle: 16^0, FOV: 208x168mm, $1mm^3$ isotropic resolution. 16-25 volumes consisting of 40 axial slices spanning the corpus callosum were acquired per experiment, with an acquisition time of 11.1s per volume (~178-278s/experiment). A dose of either: 0.2, 0.25, or 0.3 mM/kg of ProHance (Gadoteridol; Gd) diluted in saline was administered manually appx. 44s after the start of scanning, in 3 subjects. Two control subjects were also scanned with no injection of contrast agent. Phase data were unwrapped using FSL (FMRIB, Oxford) and then high-pass filtered to eliminate large length-scale field variation. Subsequently, both magnitude and phase data were motion corrected and further processed using AFNI (NIMH/NIH). The contrast between GM and WM was computed for ROIs obtained in pure GM (away from large vessels) and proximal WM (~2-3mm separation) in the frontal, motor and parietal areas, for each time-point. Three pairs of GM/WM ROIs (5 voxels/ROI) were assessed per subject. Phase values were scaled by $2\pi TE$ to convert to field offsets in Hz.

Results: The GM/WM phase difference ($\Delta\phi_{GW}$) time courses for each subject, averaged over the 3 pairs of ROIs, are shown in Figure 1. The pre-Gd-injection $\Delta\phi_{GW}$ across subjects was 3.75±0.44Hz consistent with published results [1-3]. The $\Delta\phi_{GW}$ increased significantly during the first-pass of the Gd-bolus through the vasculature, showing a change that increased with Gd dose, but showed only a small deviation from pre-Gd values after recirculation and mixing. The difference in $\Delta\phi_{GW}$ between the post-Gd and pre-Gd values, over the 3 pairs of ROIs, was 0.4±0.4Hz, 0.95±0.3Hz, and 1.35±0.88Hz for the 0.25, 0.25 and 0.3 mM/kg dose respectively. During the first-pass of the Gd-bolus there was a reduction in the magnitude signal from GM, and a smaller reduction persisted after mixing. The signal plots from the control subjects indicate the stability of the data. Figure 2 shows phase images obtained before and after Gd injection, and at the Gd-bolus curve peak, along with the post/pre difference image, for the 0.25mM/kg dose. A line profile showing the phase variation across a sulcus is shown in E. This indicates again that $\Delta\phi_{GW}$ is slightly increased from the pre-contrast value after the first-pass of the Gd-bolus, while the phase difference between the GM and central CSF/veins remains significantly elevated after mixing.

Discussion: The finding that the $\Delta\phi_{GW}$ returns to a level similar to the pre-contrast value after mixing, while the phase difference between GM and the vasculature remains enhanced, indicates that the elevated susceptibility of blood due to the "steady state" (≥200s) concentration of contrast agent is not large enough to perturb the GM/WM susceptibility difference significantly. Based on the subject's weight we estimate that the Gd concentration in the blood in the steady state is about 4.2 mM for the 0.25 mM/kg dose, which yields a blood susceptibility change due to Gd of 1.4 ppm, assuming that $\Delta\chi_{Gd}= 3.4x10^{-4}$ per mole/l (SI units) [4]. This change is more than three times larger than the susceptibility difference between venous blood and tissue, estimated as 0.36 ppm [4]. Increasing the susceptibility difference between venous blood and tissue by more than a factor of three (and that of arterial blood and tissue by a much greater factor) can thus be seen to have no significant effect on the GM/WM susceptibility difference, and therefore it can be stated that the measured difference of susceptibility in these tissues is not explained by the effect of deoxyhaemoglobin in blood.

References: [1] JH Duyn et al. PNAS 104(28): 11796-801, 2007; [2] K Zhong et al. NeuroImage 40: 1561–1566, 2008; [3] Haacke et al. MRM 23:1-25, 2005; [4] Weisskoff et al. MRM 24:375-383, 1992. *The 7T programme is funded by the MRC and Wellcome Trust*

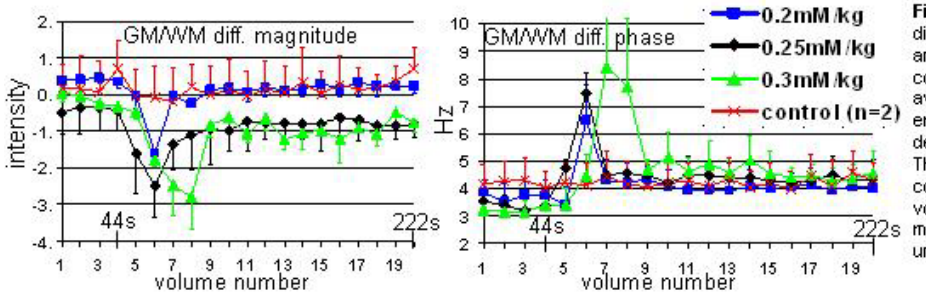

Figure 1. Time courses of the difference in contrast between GM and WM for each subject (n=5, 2 controls). Time courses are the average over the three ROI pairs; error bars show the standard deviation across ROIs per volume. The average time course between the control subjects (n=2) is shown. Each volume was acquired over 11.1s. Left: magnitude data (yaxis in arbitrary units), Right: Phase data.

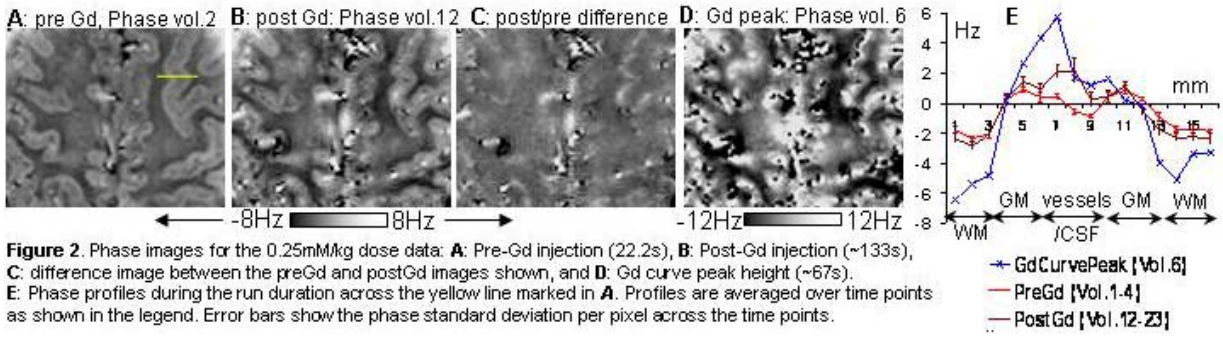

Figure 2. Phase images for the 0.25mM/kg dose data: **A**: Pre-Gd injection (22.2s), **B**: Post-Gd injection (~133s), **C**: difference image between the preGd and postGd images shown, and **D**: Gd curve peak height (~67s). **E**: Phase profiles during the run duration across the yellow line marked in ***A***. Profiles are averaged over time points as shown in the legend. Error bars show the phase standard deviation per pixel across the time points.