A Multiple Field Study of Permeability Difference Between Gray and White Matters

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Introduction: Phase maps have been applied in susceptibility weighted imaging (SWI) (1) to enhance the blood/tissue contrast. Recently, there were several reports that demonstrated direct tissue contrast in gray/white matter (GM/WM) from phase maps acquired at 7 Tesla. It was further suggested that such phase contrast could be utilized as a novel contrast mechanism at high field to separate different tissues. Previous studies (2) showed correlation between phase shift and regional iron concentration, and it is known that iron deposition in the brain increases with age (3). However, there is up-to-date no mechanism or physiological basis to explain the observed phase difference between gray and white matter. Therefore, we hypothesize that the phase contrast observed at high field could be due to the tissue permeability difference (most likely from blood volume / capillary density in GM/WM). Such difference would be field-independent and should manifest itself at different magnetic field strengths. In order to verify this assumption, a set of experiments was performed at different magnetic field strengths ranging from 1.5 to 7 Tesla.

Methods: Experiments were carried out on three scanners: Siemens Sonata (1.5 T), Siemens Trio (3 T) and Siemens MAGNETOM 7 T. Eight channel phase arrays were used to acquire all images at different field strengths. A modified echo-shifted FLASH 3D sequence was used to acquire the phase maps. Image matrix size was 208x256x64 with 0.8 mm^3 isotropic resolution. The echo times for different field strengths were adjusted (Table 1) to obtain large phase-shifts at high SNR. 3D-MPRAGE images (256x256x160, 1 mm^3 isotropic) were also acquired for co-registration. MATLAB and SPM5 were used for data processing. Phase map unwrapping was performed within the FSL software package. Magnitude images (with skull tissue signals removed) were used to generate image masks that were applied to the phase images. The masked phase images were subsequently unwrapped to remove the $\pm\pi$ phase discontinuities. A high-pass filter was applied on the unwrapped phase images to remove field inhomogeneity induced phase shifts. Finally, the phase maps were normalized to the field strength and the echo time. Thus, the observed phase shifts are expressed in absolute units of part-per-million (ppm).

Table 1: Echo times used

B_0 (MHz)	TE (ms)
63.69	60
123.24	40
297.14	25.7

Result and Discussion: Normalized phase maps from different field strengths are shown in Figure 1. Phase maps from the three field strengths showed similar features. The 1.5 T phase map had lower SNR. This is due to the factor that the phase resolution is proportional to 1/SNR. There were some artifacts present in the 7 T phase maps which might be due to B1 inhomogeneity problems of the multi channel coil at this field strength. Overall, the 3 T and 7 T phase maps showed more details compared to 1.5 T, and 7 T phase map showed finer details compared to 3 T due to better phase resolution. The similarities between the phase maps at different field strengths were further confirmed by comparison of their corresponding histograms (Figure 2). Normalized phase maps showed essentially the same distribution at different field strengths. In order to determine the permeability difference between GM and WM, WM and GM masks derived from segmented MPRAGE images were used to obtain the phase histograms of WM and GM tissues (Figure 3). The histograms showed clear GM/WM separation. The estimated WM/GM separation is approx. 0.0038 ppm, fitted by a Gaussian function. Phase dispersion was also observed in Fig.2 (from 0.06 to 0.1 ppm) which might reflect the local field inhomogeneity in slices close to the brainstem or sinus. This effect can also be observed in Fig.3 from the extra peaks of WM (0.055 ppm) and GM (0.08 ppm) which are likely to arise from the high phase shift in frontal cortex (Fig.1). It remains to be clarified if the permeability separation between GM/WM arises mainly from blood volume differences. For 50% oxygenated blood with a hematocrit level of 0.4, the blood susceptibility is around 0.04 ppm (4). Typical blood volume in tissue is around 2-5% and therefore gives an upper limit for GM/WM blood volume difference of 3%. This corresponds to a permeability difference due to the intravascular volume fraction of 0.0012 ppm. This is only one third of the observed GM/WM separation. Thus, the blood volume difference along can not explain our findings. Another possible explanation for the WM/GM phase separation would be a difference in capillary density and its micro-network structure. Traditional micro-vascular models use long cylinders to simulate capillary vessels. However, the net extravascular phase shift is zero for a cylindrical vessel. Therefore, our findings suggest that the curvature of the capillaries might be significant on the voxel scale and should be taken into consideration to address the permeability differences in GM/WM tissues and a formal theoretical treatment is required.

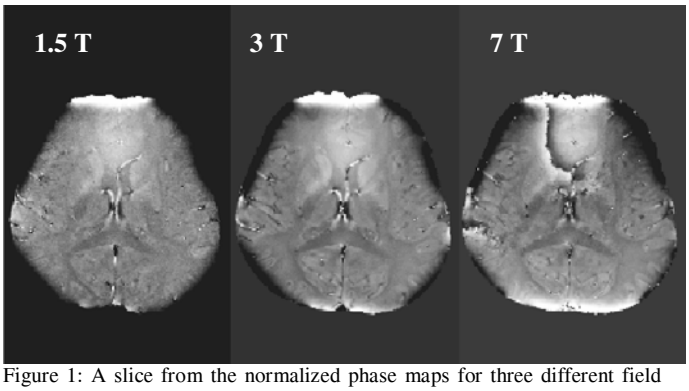

Figure 1: A slice from the normalized phase maps for three different field strengths. The artifact at 7 T is caused by B1 inhomogeneity. Phase maps at high field show more details due to higher phase resolution and SNR.

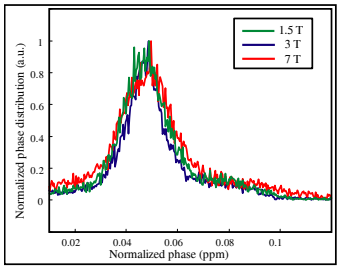

Figure 2: Histogram from slice in Fig.1 for all three field strengths. The histograms showed essentially the same normalized phase distribution at all field strengths.

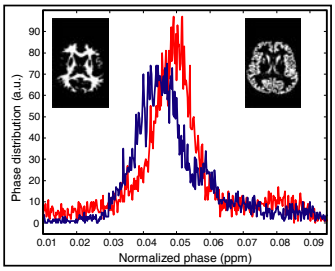

Figure 3: Histograms of WM (blue) and GM (red) tissue from the corresponding WM/GM masks (from MPRAGE). The approx. separation between WM and GM is 0.0038 ppm, using a Gaussian fit.

Conclusion: Normalized phase maps acquired at different field strengths showed similar contrast for WM/GM. The permeability difference between WM/GM is field independent and is around 0.0038 ppm. The result is consistent with our hypothesis that the WM/GM phase contrasts are caused by permeability differences in capillary density. The permeability difference could be utilized to further understand the capillary structures in vivo.

References:

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