Measuring the Concentration of Contrast Agent in Blood for DSC MRI from the Extra-Vascular Phase Shift

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Introduction: The large extra-vascular phase shifts associated with venous blood vessels have been exploited in Susceptibility Weighted Imaging (SWI) to enhance vessel contrast [1]. These phase shifts are a direct result of the large vessel/tissue susceptibility difference due to the paramagnetic deoxy-hemoglobin content of venous blood. Recently, it has been shown that the susceptibility of a uniform object with an arbitrary geometry can be quantified by least-squares fitting measured phase data to the simulated field-shift for that geometry [2]. The simulated field-shift can be created using a Fourier-based method [3]. It has also been shown that phase data from a single large artery of simple geometry (outside the brain) can yield an accurate measure of the concentration of paramagnetic contrast agent over the course of a Dynamic Susceptibility Contrast (DSC) experiment [4]. Here, we describe the implementation of a least squares fitting method to monitor the susceptibility of blood in the human brain from the extra-vascular field-shifts measured during a DSC experiment, and use this method to calculate the concentration of the contrast agent in the blood as a function of time.

Methods: The magnetic field perturbation, $\Delta B_z(\mathbf{r})$, due to an object with uniform susceptibility, χ, is given by, $\Delta B_z(\mathbf{r}) = \chi.FT^{-1}[B_0.FT[m(\mathbf{r})].(1/3-\cos^2\beta)]$, where B_0 is the main magnetic field, FT is a Fourier transform, β is the angle between the **k**-vector and B_o, and $m(\mathbf{r})$ is a mask of the object (1's for inside, 0's for outside). Hence if we have a mask for the object, and a measurement of the field perturbation, a simple least-squares fit can be used to estimate χ from, $\Delta B_z(\mathbf{r})=\chi.f[m(\mathbf{r})]$, where $f[m(\mathbf{r})]$ is the simulated, normalize field-shift for this mask. For the DSC experiment, phase images were acquired at 7T using a 16-channel head coil and a 3D segmented EPI sequence (EPI factor: 27; SENSE factor: 2) with TR/TE: 50/20ms, flip angle: 16^0, 1 mm^3 isotropic resolution, FOV: 208x168 mm^2. 16-25 volumes each consisting of 40 trans-axial slices were acquired per run, with an acquisition time of 11.1s for each volume. A dose of either: 0.2, 0.25, or 0.3 mmol per kg of ProHance (Gadoteridol;Gd) diluted in saline was administered manually at a time of about 44s after commencement of imaging in three female subjects. A control subject was scanned with no contrast agent injection. Phase data were unwrapped using FSL (FMRIB, Oxford), high-pass filtered to correct for large scale field variation, and scaled by $\gamma B_0 TE \times 10^{-6}$ to give a field perturbation map in ppm. Magnitude and phase data were motion corrected using AFNI (NIMH/NIH). Veins appear as regions of low intensity in the pre-Gd magnitude images due to dephasing caused by the presence of deoxy-hemoglobin. Appropriate thresholding of these images thus yields a venous vessel mask, $m_v(\mathbf{r})$. Both veins and arteries appear with low-intensity in the post-Gd magnitude images (Fig. 1B) due to the presence of the paramagnetic Gd, and after thresholding, these images yield a full vessel mask (Fig. 1D); $m_f(\mathbf{r})=m_v(\mathbf{r})+m_a(\mathbf{r})$, where $m_a(\mathbf{r})$ is the arterial mask. The pre-Gd phase data (Fig 1A) show the effect of field-shifts around the veins due to deoxy-hemoglobin, $\Delta B_z^{preGd}=\Delta B_z^{vblood}(\mathbf{r})$. The post-Gd phase data (Fig. 1C) also show the field-shift due to the deoxy-hemoglobin, but with the addition of the field-shift due to the Gd in both the veins and arteries, $\Delta B_z^{postGd}=\Delta B_z^{vblood}(\mathbf{r})+\Delta B_z^{Gd}(\mathbf{r})$. To calculate the susceptibility of venous blood, the pre-Gd images were used, giving $\Delta B_z^{vblood}(\mathbf{r})=\Delta\chi^{vblood}.f[m_v(\mathbf{r})]$. To calculate the susceptibility of the Gd, the pre-Gd phase must be subtracted from the post-Gd phase to give, $\Delta B_z^{postGd}-\Delta B_z^{preGd}=\Delta B_z^{Gd}(\mathbf{r})$ (Fig. 1E), and then incorporating the full vessel mask gives, $\Delta B_z^{Gd}(\mathbf{r})=\Delta\chi^{Gd}.f[m_f(\mathbf{r})]$ (Fig. 1F). For the least-squares fitting, only phase data from voxels with a high corresponding magnitude were used, as phase-noise scales inversely with the magnitude signal to noise ratio, thus the fitting is restricted to extra-vascular phase. In addition, only voxels with a high simulated field-shift, $f[m(\mathbf{r})]>0.001$, were considered in the fitting process to reduce errors. Gd concentrations could then be found by dividing the estimated susceptibility values by $\Delta\chi^{Gd}=3.4\times10^{-4}$ per mole per litre (SI units) [5].

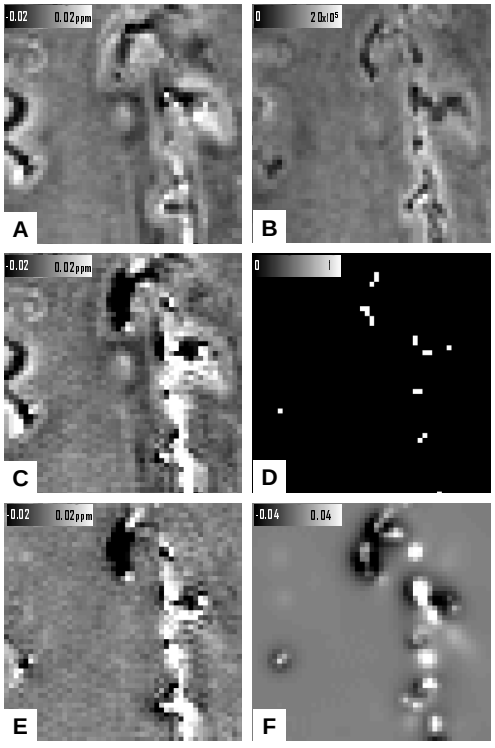

Fig.1-Pre-Gd phase(A), post-Gd magnitude(B), post-Gd phase(C), vessel mask from B(D), C-A=phase due to Gd(E), simulated field-shift using D (F).

Results: The calculated Gd concentration curves (Fig.2) show the expected bolus shape with a clearly visible 1st pass peak. The error bars represent the least-squares error. Although the peaks of the 0.2/0.25 mmol per kg doses overlap, this is probably a result of variable injection speed as the concentrations show the expected difference between doses after mixing. In the steady state regime after complete mixing, assuming a total blood volume of 4*l* for a 70kg woman, Gd concentrations of roughly 3.5, 4.2, and 5.3 mM are expected for 0.2, 0.25, and 0.3 mmol per kg doses respectively [6], in approximate agreement with the final measured concentrations of 2.9±0.4, 3.7±0.4, 5.4±0.2 mM. The average over the four subjects of venous blood susceptibility before administration of the contrast agent, $\Delta\chi^{vblood}$, was 0.4 ± 0.1 ppm (SI) in good agreement with the expected value of 0.36ppm (SI) (assuming HCT=0.4, fO_2=0.6,$\Delta\chi^{deoxy}$=2.26ppm (SI) [5]).

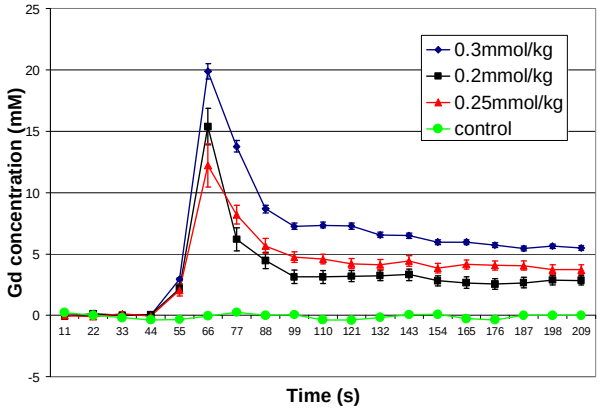

Fig.2- Gd concentration curves for DSC experiments.

Discussion and Conclusions: A robust method for directly calculating the susceptibility of blood in the human brain and its use in DSC MRI has been presented. More generally the potential of least-squares fitting methods for *in-vivo* susceptibility quantification from phase data has been highlighted. Although the blood $\Delta\chi$ measurement is global, sub-dividing the vessel masks to give a more local $\Delta\chi$ value is also feasible. Such an approach would have possible applications in the measurement of a local arterial input function, classification of MS lesions using Gd-enhanced phase data, or the quantification of Iron in brain tissues such as the substantia nigra. Further work is currently being carried out to validate and optimise the technique.

References: [1] Haacke et al. 2004. MRM 52:612-618. [2] Neelavalli et al. ISMRM, 2008, 3056. [3] Marques et al. 2005. Conc MR 25B:65-78. [4] Akbudak et al. 1996. MRM 36:809-815. [5] Weisskoff et al. MRM. 1992. 375-383. [6] Feldschuh et al. 1977. Circulation: 605-612.