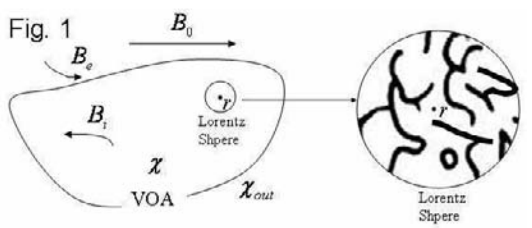
Physical source of fMRI signal phase change: theory and simulation

F. Zhao[1,2], P. Wang[2], T. Jin[2], X. Hu[1], S-G. Kim[2]

[1]Biomedical Engineering Department, Emory / Georgia Tech University, Atlanta, GA, United States, [2]Neurobiology Department, Pittsburgh University, Pittsburgh, PA, United States

INTRODUCTION: Most of the previous functional studies focus on the magnitude change of the MR signal. However, as well as the magnitude change, the phase change of the BOLD fMRI signal [1-3] and the frequency shift of the functional MR signal [4] have also been detected in human. Since no fMRI signal phase change should be detected if the fMRI signal is only consisted of extravascular signal and the blood vessel is modeled as the infinite cylinder [5, 6], the observed phase change and frequency shift were attributed either to the phase change of intravascular signal [3], or to the tissue water's frequency shift caused by local brain temperature change after long stimulation of several minutes [4]. 'Lorentz Sphere' concept was introduced for estimating the local magnetic field at the nucleus of interest [7-9]. This 'Lorentz Sphere' concept has been applied to calculate the magnetic field distribution in heterogeneous blood which consists of high magnetic susceptibility red blood cell and plasma to study blood transverse relaxation rate [10] or hyperpolarized ^{129}Xe frequency shift in blood [11]. In this work, the 'Lorentz Sphere' concept was extended to calculate the magnetic field distribution in the heterogeneous tissue which consists of extravascular water and high magnetic susceptibility intravascular blood. After the Lorentz Sphere effect was accounted for, the frequency shift of the extravascular water could not cancel out, mostly because of the magnetic field contribution from the surface of the Lorentz Sphere. Theory of using the 'Lorentz Sphere' concept to describe the magnetic field inhomogeneity of the heterogeneous cortex was provided. To further examine the theory, a simulation based on the real fMRI data and the approximated cat visual cortex anatomical structure was conducted. It is proved that the volume-averaged magnetization change during the stimulation and its demagnetization effect is most likely the sources of the detected fMRI signal phase change.

THEORY: A two-component model was used for analysis of the local magnetic field experienced by proton [12]. In this model the magnetized blood vessels are embedded in a given extravascular tissue. In each imaging voxel, the volume-averaged magnetic susceptibility χ can be calculated from the local volume magnetic susceptibilities of the extravascular tissue χt and the intravascular blood χb: $\chi = f\cdot\chi b + (1-f)\cdot\chi t$. Where f is blood volume. In an external magnetic field B_0, the volume-averaged magnetization for a voxel at position **r** is then given by: $\mathbf{M(r)} = \chi\cdot(\mathbf{r})\cdot\mathbf{B_0}/\mu_0$. Here μ_0 is the magnetic permeability of vacuum. By defining a volume of activation (VOA) where the blood susceptibility and/or the blood volume would change during the brain activation, a Lorentz sphere can be drawn around a particular position **r** within the VOA (Fig.1). The size of the sphere (sub-millimeter to millimeter scale, comparable with imaging-voxel size) is so large comparing with the size of vessel segment (the size of the microvascular segment is ~0.1 mm [13]) that local field contributions at **r** from vessel segments outside the sphere can be modeled as the random distributed magnetic dipoles. The magnetic field **B(r)** at **r** can be written as [9, 10, 14]:



$$\mathbf{B(r)} = \mathbf{B}_0(\mathbf{r}) + \mathbf{B_e(r)} + \frac{\mu_0}{3}\mathbf{M(r)} + \sum B_b(r) + \mathbf{B_i(r)}$$

$\mathbf{B_0(r)}$ is the magnetic field at position **r** originated from the magnet; $\mathbf{B_e(r)}$ is the magnetic field at position **r** originated from the external demagnetizing field projected to **r** by the magnetic moment distributions in regions outside the VOA; **M(r)** is the volume-averaged magnetization at position **r**; $\mathbf{B_b(r)}$ is the magnetic field generated by the blood vessels within the Lorentz sphere, which is used to calculate the fMRI signal change [6, 12]; $\mathbf{B_i(r)}$ is the self-demagnetizing field generated by the magnetic moments within the VOA (but excluding the Lorentz sphere) at position **r** and can be expressed as:

$$\mathbf{B_i(r)} = \frac{\mu_0}{4\pi}\iint_S \frac{(\chi(\mathbf{r'}) - \chi_{out}(\mathbf{r'}))(\mathbf{B_0}\cdot\mathbf{n})(\mathbf{r}-\mathbf{r'})}{|\mathbf{r}-\mathbf{r'}|^3}ds' - \frac{\mu_0}{4\pi}\iiint_{VOI}\frac{div'\mathbf{M(r')}(\mathbf{r}-\mathbf{r'})}{|\mathbf{r}-\mathbf{r'}|^3}dv'$$

in which S is the surface of the VOA; $\mathbf{r'}$ is the position on the surface for the surface integration term or within the VOA (excluding the Lorentz sphere) for the volume integration term based on which integration is calculated; $\chi(\mathbf{r'})$ is the volume-averaged susceptibility inside the surface at position $\mathbf{r'}$; $\chi_{out}(\mathbf{r'})$ is the volume-averaged susceptibility outside the surface at position $\mathbf{r'}$; **n** is the unit normal vector of surface at position $\mathbf{r'}$; *div* is the divergence operator.

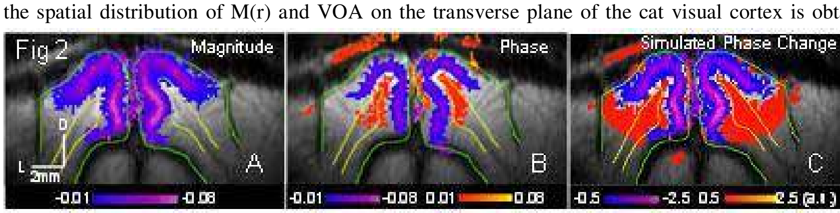
During the brain activation, either the blood susceptibility is changed by the BOLD effect, and/or the high susceptibility blood volume is changed by vessel dilation. Since such changes only happened in the VOA according to our definition, the $\mathbf{B_e(r)}$ term in above equation does not change. The magnetic field change is:

$$\Delta\mathbf{B(r)} = \Delta\mathbf{B_i(r)} + \frac{\mu_0}{3}\Delta\mathbf{M(r)} + \sum \Delta B_b(r)$$

$\Delta\mathbf{B_i(r)}$ is the demagnetization field change caused by susceptibility change on the surface of the VOA and magnetization distribution change within the VOA. $\Delta\mathbf{B_b(r)}$ is the local magnetic field change from the blood vessels and its contribution to the fMRI phase change is zero as the blood vessels are randomly distributed [5, 6].

For the CBV-weighted fMRI, the blood susceptibility is so high that the blood volume change (Δf) during the brain activation is the main source of fMRI signal. If the phase change is mainly caused by the volume-averaged magnetization change rather than the demagnetization effect, a negative phase change should be expected to dominate in the area where the blood volume change is the highest, i.e. the middle cortical layer of the cat visual cortex [15]. The positive phase change can be detected in the surrounding tissue area due to the demagnetization effect.

SIMULATION and RESULTS: Assuming the detected fMRI magnitude change is proportional to ΔM(r) [6], based on the results from the CBV-weighted fMRI the spatial distribution of M(r) and VOA on the transverse plane of the cat visual cortex is obtained. The cat visual cortex in the anterior-posterior direction can be further assumed to be parallel to the $\mathbf{B_0}$ with size of 1 cm, the $\Delta\mathbf{B}$(r) caused by $\Delta\mathbf{M}$(r) and demagnetization effect can be calculated by the above equations. Fig.2 shows the detected CBV-weighted fMRI magnitude change (A), phase change (B) and the simulated phase change (C). Taking the product of simulated phase change and baseline image intensity as CNR, then CNR-adjusted simulated phase is shown in Fig. 2C. Comparing the Fig. 2C and 2B, the spatial pattern of negative phase response is very similar, indicating that the functional volume-averaged magnetization change dominates the phase response of the middle cortical layer. For the positive phase response in Fig. 2C, it is also roughly similar as the detected positive phase change in Fig. 2B, which is caused by the demagnetization effect. It is proved that the volume-averaged magnetization and its demagnetization effect are most likely the sources of the fMRI signal phase change.



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