Probing Short Diffusion Time Behavior by Oscillating Gradient Spin Echo Sequences

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Introduction: Measurements of diffusion rates may provide important information on tissue structure in brain and other organs. However, due to hardware limitations, typical diffusion times used in practice are relatively long and the signal is greatly influenced by diffusion boundaries on different scales. It is difficult to obtain information at or below the cell length scales. One approach to reduce the diffusion time is the oscillating gradient spin echo (OGSE) method. Studies have previously been performed on a model system of packed microspheres (1) and rat brain (2) which show the feasibility of OGSE. To better understand the characteristics of the diffusion attenuated MR signal obtained by OGSE from a whole complex tissue, the spatial distribution of magnetization inside a single cell-like compartment has been studied in this work. Compared with results from the pulse gradient spin echo (PGSE) method (3), it has been shown that the OGSE sequence reduces edge enhancement effects significantly, especially for applied gradients with high frequencies. In the presence of barriers, the PGSE signal vs. b-factor decay is not mono-exponential. The decay is often approximated as the sum of two components of different intrinsic diffusion rates. Here we explore how these two components change with choice of gradient frequencies using the OGSE method.

Methods and Results: By considering a general finite-duration gradient as a series of short gradients, a quasi-analytical expression for magnetization distribution at the echo time can be written as (3,4)

$$m(x,t_{TE}) = \int dx_1 \cdots \int dx_N \rho(x_1)\exp(-iq_1x_1)\exp(-\Delta t/T_2(x_1))P(x_1 \mid x_2,\Delta t)\exp(-iq_2x_2)\exp(-\Delta t/T_2(x_2))P(x_2 \mid x_3,\Delta t)\cdots\exp(-iq_Nx_N)\exp(-\Delta t/T_2(x_N))P(x_N \mid x,\Delta t)$$

where ρ is the spin density, $P(x_1 \mid x_2, \Delta t)$ is the conditional probability, $q_n=\gamma g_n \Delta t$, $n=1 \ldots N$, g_n is the gradient at time t_n , Δt is the time step and echo time $t_{TE}=N\Delta t$, N is the total number of time steps. The explicit functional forms for conditional probabilities for some simple geometry structures can be found in Ref.5. For simplicity, only diffusion between two infinite impermeable planes is considered below but it is sufficient to show important characteristics of the MR signal detected by OGSE. Only cosine-modulated waveforms OGSE were used in this work and all pulse sequences used have a fixed b value as $bD_0=1$ (D_0 is the intrinsic diffusion coefficient). Fig.1 shows the comparison of the echo magnetization distribution (normalized by the free-diffusion results) obtained by PGSE and OGSE, respectively, with respect to different echo times (denoted by a dimensionless parameters $\alpha=(D_0t_{TE})^{1/2}/a$, where the distance between planes is 2a). OGSE has applied gradients with a frequency of 1kHz. Although the edge enhancement effect has been remarkably reduced compared with PGSE, the OGSE still shows strong magnetization inhomogeneity (boundary influence) for long echo time ($\alpha>1$) with a low frequency (1kHz). However, if the frequency of the applied gradients increases, the edge enhancement effect decreases steeply for the same echo time. Fig.2 shows this effect with a certain echo time ($\alpha=1$). For a restricted diffusion system, the net signal is often considered as a quasi-two-diffusion-compartment system and can be approximated in the form of a bi-exponential function $E(b)= \xi \exp(-bD_1)+(1-\xi)\exp(-bD_2)$, where D_1 is the fast-diffusion coefficient, D_2 slow diffusion and ξ the volume fraction of the fast diffusion component. Fig.3 shows the bi-exponential function fits the signal detected by OGSE quite well for a fixed relatively long echo time ($\alpha=1$). For a low frequency 1kHz, D_1 has about 15% difference with the intrinsic diffusion coefficient and it drops to less than 10% error when frequency increases to 5kHz and 5% when f=10kHz. The corresponding fast-diffusion component volume fractions are >70%. The slow diffusion component D_2 increases rapidly as the gradient frequency increases. This is associated with the magnetization inhomogeneity. A decrease of the effective diffusion time occurs at frequencies >25kHz causing a collapse of the two diffusion compartments into a single one.

Discussion: Sukstanskii *et al.* has studied the same structure with the conventional PGSE method, showing that the bi-exponential fit only works for very short diffusion times and it gives 20% errors of D_1 compared when the intrinsic diffusion coefficient when $\alpha=0.3$ (3). Therefore, to study the intrinsic diffusion of tissues with cell size of 4μm, a diffusion time of less than 1ms is needed, which is very difficult to implement in practice. In contrast, in despite of a relatively long echo time (such as $\alpha=1$ in this work), OGSE can remarkably reduce the edge enhancement effect and the magnetization inhomogeneity by increasing the gradient frequency. In addition, the bi-exponential fit works well for long echo time for OGSE and the fast-diffusion coefficients are very close to the intrinsic values at high frequencies. This feature provides a means to study intrinsic diffusion behavior and probe intracellular structure.

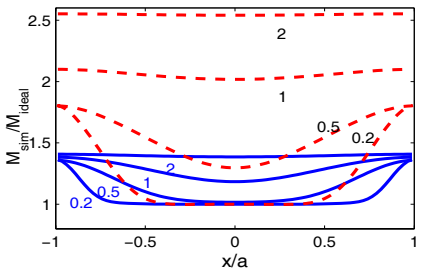

Fig.1 The comparison of the spatial magnetization distribution obtained by PGSE(red) and OGSE(blue) with respect to different echo times.

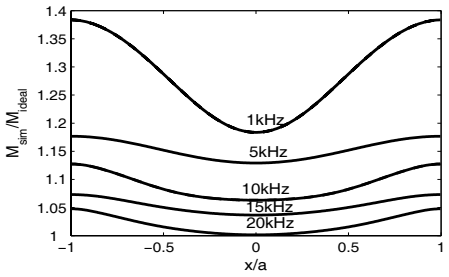

Fig.2 The edge enhancement effect is reduced by OGSE with the increase of the applied gradient frequency.

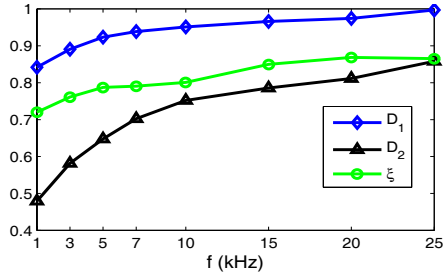

Fig.3 The calculated ADCs and the fast-diffusion coefficients obtained by bi-exponential fits change with the applied gradient frequencies. The echo time keeps fixed ($\alpha=1$).

References: (1)Schachter, JMR, 2000 (2)Does, MRM, 2003 (3)Sukstanskii, MRM, 2003 (4)Callaghan, JMR, 1997 (5)Callaghan, JMR, 1995