Improved diffusion measurement in heterogeneous systems using the new magic asymmetric gradient stimulated echo (MAGSTE) technique

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INTRODUCTION

Pulsed field gradient (PFG) NMR techniques have been applied to characterize structure information in complex systems such as the surface to volume ratio, tortuosity and diffusion restriction[1-3]. However, such systems are usually heterogeneous and comprised of regions of severe magnetic susceptibilities[4], which may introduce strong background gradients. Such gradients can be comparable to or even stronger than the laboratory gradients, and if not accounted for properly, may introduce complex artifacts in deducing diffusion and structure information. The recently proposed magic asymmetric gradient (MAG) technique suppresses the coupling between homogeneous laboratory gradients and the unknown susceptibility related gradients during the encoding and decoding interval independently, while the conventional bPFG technique can only suppress static/constant background gradients[5,6]. In this report, we compared the bPFG and MAG diffusion measurements in a microscopically heterogeneous system and showed that the MAG technique provided accurate measurements. In addition, we investigated the effects of background gradients upon NMR diffusion measurements, and by comparing bPFG and MAG measurements, the magnitude and correlation of the inherent gradients can be elucidated.

MATERIALS AND METHODS

Microspherical sodalime glass beads (Glen Mills, Clifton NJ) with mean sizes of 90μm (70-110μm) and 150μm (100-200μm) were acid cleaned, washed and transferred into 5 mm NMR tubes (Sigma Aldrich) filled up with 0.25 mM $CuSO_4$ solution. The NMR samples were then vortexed and vacuumed to remove residual air bubbles. A phantom containing 0.25 mM $CuSO_4$ solution was used as reference. All NMR experiments were conducted at 500 MHz Avance system (Bruker Biospin) using bPFG and MAG sequences with half sine shaped gradients (Temp=25^{0}C, TR=6 sec, DS=4, NA=8, gradient pulse duration δ= 3 ms, evolution time Δ varied from 8, 16, 32, 64, 128, 256 to 512 ms). In addition, the encoding time was varied from 6ms to 4ms to assess the sensitivity of both measurements to the diffusion encoding interval.

RESULTS & DISCUSSION

The spectral line-width of the 90, 150μm glass beads and reference phantoms were 1,130, 615 and 60 Hz, respectively, indicating strong susceptibility fields within the glass beads phantoms. For the reference phantom, the obtained diffusion rates were 2.24 ± 0.02 and 2.25 ± 0.03μm^2/ms (mean ± S.D.), identical for both the bPFG and MAG sequences (Fig.1, open marks). This equality was expected because the reference phantom was homogeneous and spins were under the influence of the applied laboratory gradients only. For glass beads phantoms, however, the bPFG measurements (blue solid circles, Fig. 1) showed less attenuation than the MAGSTE sequence (red solid squares, Fig. 1), especially at short diffusion times. This indicated that the diffusion rate obtained by bPFG sequence was less than that derived using MAGSTE method. Their difference reduced at longer evolution intervals and it can be observed that the measurements converged at diffusion time beyond 128 ms. Diffusion rates were obtained by fitting the echo attenuation of low b values (<1,000 s/mm^2) using a monoexponential function. Fig. 2 showed that the diffusion rates of glass beads phantoms were significantly reduced from those of the reference phantom, especially at long diffusion time, indicating restricted diffusion. The diffusion rate for 90 μm beads reached a plateau of 0.8μm^2/ms, in comparison with 1.2μm^2/ms for 150 μm beads and 2.2μm^2/ms for the reference phantom.

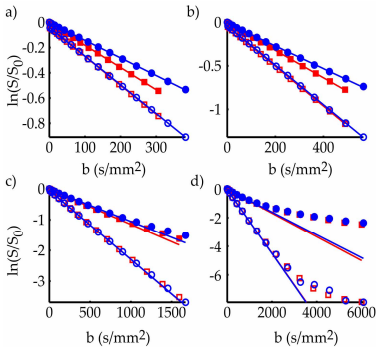

Fig. 1, Diffusion measurements using MAG & bPFG sequences for reference (open marks) and 90 um beads (filled marks), with the evolution time being 8, 16, 64 and 256 ms for a-d.

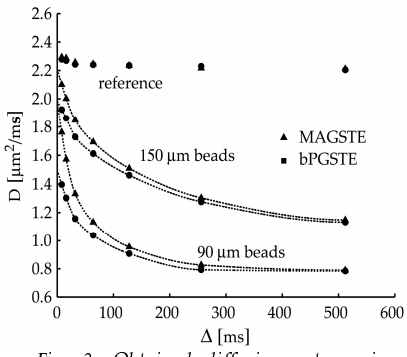

Fig. 2, Obtained diffusion rates using MAG & bPFG sequences as a function of evolution time. Measurements were identical for the reference phantom, while bPFG measurements were significantly lower than the MAG results.

When the bPFG and MAG measurements at equal diffusion times were compared, it showed that the bPFG measurements were consistently lower. For instance, the extrapolated MAG diffusion rates at zero evolution time were 2.0 and 2.2 μm^2/ms, while the bPFG rates were 1.5 and 2.0 μm^2/ms for the 90 and 150 μm beads phantom, respectively. As the diffusion rate shall be close to the free diffusion rate at very short evolution time, it showed that MAG technique provided improved measurements in heterogeneous systems over the conventional bPFG technique. When the encoding time was reduced from 6 to 4 ms, the bPGSTE measurements increased significantly by 16% and 6% for 90 and 150 μm beads phantoms, respectively, while only marginal change of the MAGSTE measurements were observed (Table 1). In sum, the MAG technique is a superior diffusion sequence than the conventional bPFG method and shall be used when characterizing complex structure with severe microscopic heterogeneities.

The study showed that the MAG and bPFG diffusion measurements are sensitive to heterogeneous gradients of a few G/cm with a temporal correlation time of ~10 ms. One potential *in vivo* application of these techniques is to study areas with severe microscopic susceptibilities, like blood vessels and tissue containing iron oxide nanoparticels.

Phantom	D_{bPGSTE} (μm^2/ms)		Change (%)	D_{MAGSTE} (μm^2/ms)		Change (%)
	τ=6 ms	τ =4 ms		τ =6 ms	τ =4 ms	
90 μm beads	1.50	1.74	16%	1.97	2.06	4%
150 μm beads	1.98	2.11	6 %	2.21	2.28	3%
Reference	2.24 ± 0.02			2.25 ± 0.03		

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