Robust Quantification of Contrast Agent Concentration with Magnetic Field Correlation Imaging

V. Patil[1], G. Johnson[1], and J. H. Jensen[1]
[1]Radiology, NYU School of Medicine, New York, New York, United States

Introduction: Estimation of gadolinum (or other contrast agent) concentration ([Gd]) is the essential first step in the measurement of a number of parameters, such as cerebral blood flow and volume and vascular transfer constant by contrast enhanced perfusion MRI. For this purpose a linear relationship between [Gd] and the change in relaxation rate, R, is generally assumed. However, this linear relationship is only valid in simple solutions and is invalid in tissues for R_2 and R_2^* and R_1 (1, 2).
The magnetic field correlation (MFC) is a measure of the average correlation between the magnetic field inhomogeneities experienced by a water proton as it diffuses through a tissue (3). Formally, it is defined by

$$\mathrm{K}(t) \equiv \gamma^2 \left\langle \delta B(\tau)\delta B(t+\tau) \right\rangle$$

where K is the MFC, γ is the gyromagnetic ratio and $\delta B(t)$ is the local magnetic field shift for a water molecule at time t. MFC may be measured using a sequence with spin echo sequence with a fixed echo time (TE) but asymmetric refocusing pulse shifts when the dependence of signal, S, on time shift, t_s, is given by (3)

$$S(t_s) = S_0 \exp\left(-2t_s^2 K\right).$$

Unlike relaxation rates, MFC is solely influenced by water diffusion and magnetic field inhomogeneities. Furthermore, MFC depends quadratically on [Gd] to a very good approximation. The purpose of this study was therefore to compare the accuracy of Gd-DTPA concentration estimates based on MFC and relaxivity measurements in yeast cell suspensions that simulate brain tissue.

Methods: Cell suspensions were prepared by mixing yeast, *Saccharomyces cerevisia*, in distilled water and allowing the mixture to settle for 48 hours at room temperature. After yeast activation the supernatant was removed and the concentrated yeast suspension was mixed and alloquated to six 60 mL plastic bottles. Gd-DTPA was added to each NMR bottle in varying amounts to yield concentrations of 0, 1, 2, 4, 7, and 10 mM. Six more 60 mL plastic bottles were filled with distilled water and the same concentrations of Gd-DTPA. Bottles were shaken vigorously before imaging to ensure homogeneous distribution of Gd-DTPA and cells. Six bottles at a time were imaged in a corn syrup bath that minimized susceptibility effects. Corn syrup was used because of its extremely short T_2 to eliminate any imaging artifacts and T_2 signals created by the bottles (3).
Imaging was performed on a Siemens 3 T Trio MRI scanner (Siemens Medical Solutions, NJ) with a multichannel head coil at room temperature with a single transverse slice positioned through the center of the array of bottles. MFC was measured with an asymmetric spin echo sequence with Hahn echo time of 24 ms, and refocusing pulse time shifts, t_s = 0, 1, 2, 3, 4, 5, 6, 7, and 8 ms. T2 was measured with spin echo sequences with echo times of 17, 27, 37, 47, 57, and 67 ms. T1 was measured with inversion recovery sequences with inversion times of 35, 55, 75, 95, 115, 200, 400, 600, 800, and 1000 ms. Segmented (multi-shot) EPI sequences were used to decrease imaging time. Common image parameters were as follows: TR 2000ms; FOV 200×200mm; slice thickness 1.7mm, matrix 128×128; EPI factor 13; NEX 1. MFC estimates and relaxation times were obtained by fitting the appropriate equations to the corrected signal intensities using non-linear least squares fitting routines.

Results: Figure 1 shows plots of MFC and relaxation rates plotted against Gd-DTPA concentration for both cell suspension and water phantoms. As expected relaxation rate varies linearly with [Gd] for the water phantoms (the dashed line gives the linear least squares fit). However, the response of the yeast phantoms is decidedly non-linear (the solid line is the fit through the first two data points for illustration). By comparison MFC depends quadratically on [Gd] to a very good approximation.

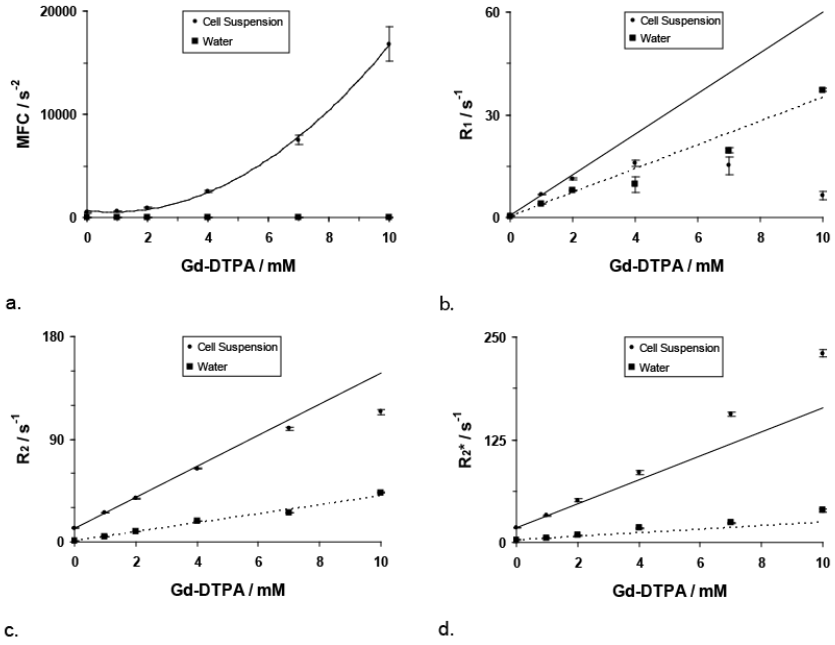

Figure 1. MFC and relaxation rates plotted against [Gd] for cell suspensions and water phantoms **a:** MFC, **b:** R_1, **c:** R_2, and **d:** R_2^*. Error bars indicate standard error

Discussion and Conclusion: Yeast cells range from 7 – 10 μm in diameter, similar to microglia and have R_1 (0.67 s^{-1}) and R_2 (12.3 s^{-1}) similar to brain tissues. We therefore expect the results of this study to be similar to those that would be found in the brain. This study suggests that estimates of [Gd] based on MFC may be more accurate than estimates based on relaxivity.

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References: 1. Kiselev VG: Magnetic Resonance in Medicine 2001; 46(6):1113-22. 2. Landis CS et al. Magn. Reson. Med. 2000; 44:563-574. 3. Jensen JH et al. Magnetic field correlation imaging. Magn Res Med 2006; 55(6):1350-61.