DIFFERENTIATING MICROSCOPIC FIELD INHOMOGENEITY INDUCED RELAXATION FROM R_2 AND R_2* RELAXATIONS WITH MAGNETIC FIELD CORRELATION IMAGING

Chu-Yu Lee[1,2], Xingju Nie[1,2], Jens H Jensen[1,2], Vitria Adisetiyo[1,2], Qingwei Liu[3], and Joseph A Helpern[1,2]

[1]*Department of Radiology and Radiology Science, Medical University of South Carolina, Charleston, SC, United States,* [2]*Center for Biomedical Imaging, Medical University of South Carolina, Charleston, SC, United States,* [3]*Neuroimaging research, Barrow Neurological Institute, Phoenix, AZ, United States*

Target audience: Scientists and clinicians interested in relaxometry and quantitative biomarkers.

Purpose: In biological tissues, the presence of iron-rich cells, deoxygenated red blood cells or a paramagnetic agent generates micron-scale variations of magnetic susceptibility,[1-3] resulting in microscopic magnetic field inhomogeneities (μMFI). Therefore, it is possible to characterize in vivo tissue properties through quantifying the μMFI. The relaxation rates R_2, R_2*, and R_2' have been previously used to quantify the relaxation due to μMFI.[4,5] An alternative approach is magnetic field correlation (MFC) imaging,[6] where the measured MFC is closely linked to the μMFI. MFC has been shown to effectively reflect iron depositions in the brain during normal aging and disease processes.[7-12] A prior study compared MFC, R_2, and R_2* for cell suspensions with different Gadolinium (Gd) contrast agent concentrations.[13] However, the distinction between these measures has not been investigated with structure-induced variable μMFI. In this work, we investigate how MFC, R_2, R_2*, R_2' change in phantoms with distinct μMFI properties.

Methods: Phantom preparation: We generated μMFI using a mixture of water and Sephadex (G-25; Sigma, St. Louis, USA), because water and dextran have different magnetic susceptibilities.[14] To vary the μMFI properties, Sephadex with three median bead sizes: superfine (52 μm), fine (88 μm), and medium (140 μm) were prepared in separate tubes, and these were fully saturated in water with similar water content (79-83 % in volume). Thus, given the similar concentration of dextran, the μMFI length scale is expected to increase with the larger bead size. For comparisons, two additional homogenous tubes were prepared without μMFI but with different dipole-dipole interactions induced by varying concentrations of agarose (1.5% and 8%). The two tubes also contained identical concentrations of Gd (50 μmol/L) to adjust the T_1 values. Five tubes were placed in a container and were surrounded with a corn syrup bath (Fig. 1a). MR experiments: The experiments were performed in 7T Bruker Biospec scanner. MFC images were acquired with an asymmetric spin echo sequence, where the 180° RF refocusing pulse was shifted with a fixed TE of 30 ms to specifically sensitize the signal to the μMFI. The time shifts were 0, ± 2, ± 4, and ± 6 ms. Other parameters were: TR = 2000 ms, FOV = 40 × 40 mm^2, isotropic voxel sizes: 0.625^3 mm^3, and NEX = 5. R_2 and R_2* images were acquired using the identical TR, slice coverage, and NEX as the MFC images. R_2 images were acquired with the CPMG sequence with TE = 11, 22, 33, 44, and 55 ms. R_2* images were acquired with the multiple gradient echo sequence with min/max TE = 2.6/22.5 ms and echo spacing = 2.2 ms. Model fits: The MFC images with different time shifts were fitted with the model [6]: $S(t_s) = S_0 \exp(-2 \times MFC(TE/2) \times t_s^2)$, where t_s is the time shift of the 180° RF refocusing pulse. MFC is the correlation function of the μMFI, defined as $MFC(t_1 - t_2) = \gamma^2 \langle \Delta B(t_1)\, \Delta B(t_2) \rangle$. Here, $\Delta B(t)$ is the magnetic field shift experienced by a water molecule, and γ is the gyromagnetic ratio. It is time-dependent because of water diffusion. MFC(0) is the variance of the μMFI. The R_2 and R_2* images were fitted with the monoexponential model: $S(t) = S(0) \exp(-R \times t)$, where R is the measured relaxation rate. R_2' was computed as $R_2^* - R_2$. All the signals were corrected for rectified noise[13] prior to the fittings, which were performed using the Levenberg-Marquardt algorithm in Matlab (Mathworks, Inc.).

Results: The measured R_2, R_2* and MFC values of the five tubes (Fig. 2) were within the range of in vivo measurements; measured MFC values in 3T [8-12] range from 0 to 1200 s^{-2}, and these are expected to increase quadratically with the applied field. The different dipole-dipole interactions induced by the two concentrations of agarose were only revealed by the measured R_2 and R_2* (Fig. 1 and 2). Nonetheless, R_2*, R_2' and MFC values were elevated by the generated μMFI in the mixtures of water and Sephadex. Interestingly, only the MFC values clearly distinguished all three bead sizes.

Discussion: R_2 and R_2* were sensitive to the dipole-dipole interactions and the μMFI. R_2' and MFC values were specifically sensitive to the μMFI, but only MFC differentiated the μMFI induced by all three bead sizes. This may be related to the fact that MFC has a well defined relation with μMFI, whereas the relation between R_2' and μMFI is less straightforward.[15,16]

Conclusion: We varied μMFI with different Sephadex bead sizes in phantoms over the range of in vivo measurements. We demonstrated that MFC better characterized the variation of μMFI compared to R_2, R_2*, and R_2'. This distinct contrast provided by MFC may be useful in assessing μMFI changes associated with pathology.

References: [1]. Connor JR, et al, J Neurosci Res (27), 595-611, 1990. [2]. Brooks RA, et al, Med Phys (14), 903-13, 1987. [3]. Mathur-De Vre R, et al, Br J Radiol (68), 225-47, 1995. [4]. Ordidge RJ, et al, MRM (32), 335-41, 1994. [5]. Ma J, et al, JMR B (111), 61-9, 1996. [6]. Jensen JH, et al, MRM (55), 1350-61, 2006. [7]. Ge Y, et al, AJNR (28), 1639-44, 2007. [8]. Jensen JH, et al, MRM (61), 481-5, 2009. [9]. Raz E, et al, AJNR (32), 1851-6, 2011. [10]. Dumas EM, et al, Neuroimage (61), 558-64, 2012. [11]. Adisetiyo V, et al, JMRI (36), 322-31, 2012. [12]. Adisetiyo V, et al, Radiology (272), 524-32, 2014. [13]. Patil V, et al, MRM (62), 1002-6, 2009. [14]. Kuznetsov OA, et al, Adv Space Res (28), 651-8, 2001. [15]. Yablonskiy DA, et al, MRM (32), 749-63, 1994. [16]. Jensen JH, et al, MRM (44), 144-56, 2000.

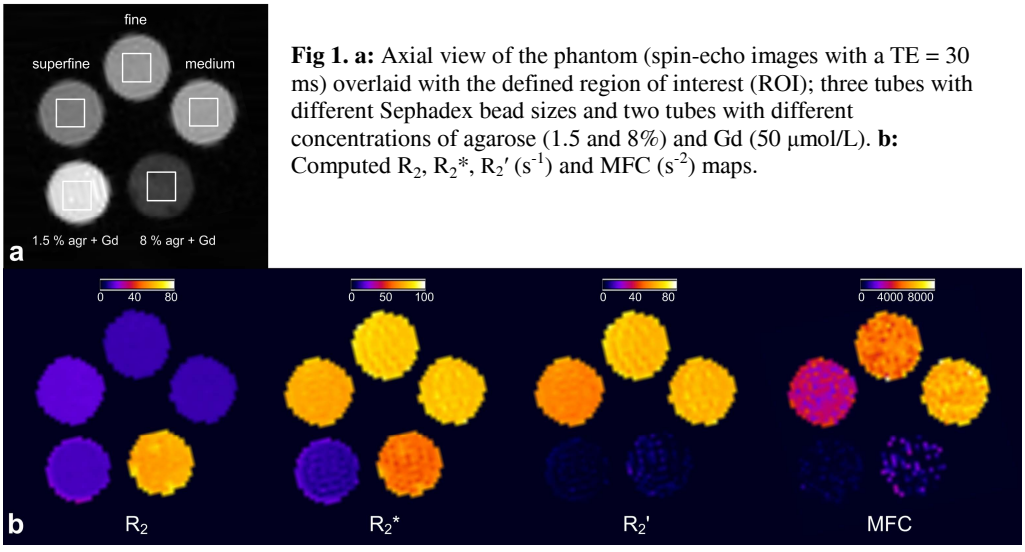

Fig 1. a: Axial view of the phantom (spin-echo images with a TE = 30 ms) overlaid with the defined region of interest (ROI); three tubes with different Sephadex bead sizes and two tubes with different concentrations of agarose (1.5 and 8%) and Gd (50 μmol/L). **b:** Computed R_2, R_2*, R_2' (s^{-1}) and MFC (s^{-2}) maps.

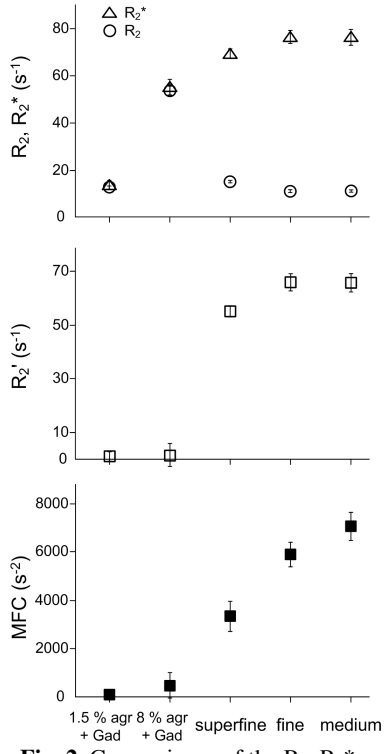

Fig. 2. Comparisons of the R_2, R_2*, R_2' and MFC values derived from the ROI in Fig. 1. Error bars indicate SD.