Delta relaxation enhanced magnetic resonance (dreMR) imaging of a healthy mouse for determination of spin-lattice relaxation rates and R_1 dispersion at 1.5 T

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Target Audience – Researchers and clinicians interested in quantitative relaxometry, field-cycled MRI, molecular imaging, and dreMR contrast.

Purpose – Recent technical advances in quantitative relaxometry magnetic resonance imaging (MRI) at clinical field strengths have attracted interest for *in vivo* studies and quantification of biological tissues.[1,2,3] The ability to exploit spin-lattice relaxation rates (R_1) and their associated dispersion over a range of magnetic field shifts (ΔB_0) is an attractive tool to differentiate between normal and abnormal tissues. Molecular interactions can be further probed with administration of targetable T_1 contrast agents, from which only tissues from the targeted (or bound) portion of the agent demonstrate significant R_1 magnetic field dependence.[3] Herein, we present *in vivo* whole-body relaxometry quantification using delta relaxation enhanced magnetic resonance (dreMR) imaging. dreMR is a novel field-cycling imaging technique that is capable of exploiting the R_1 magnetic field dependence using an auxiliary insertable magnet within a clinical MRI scanner.[4]

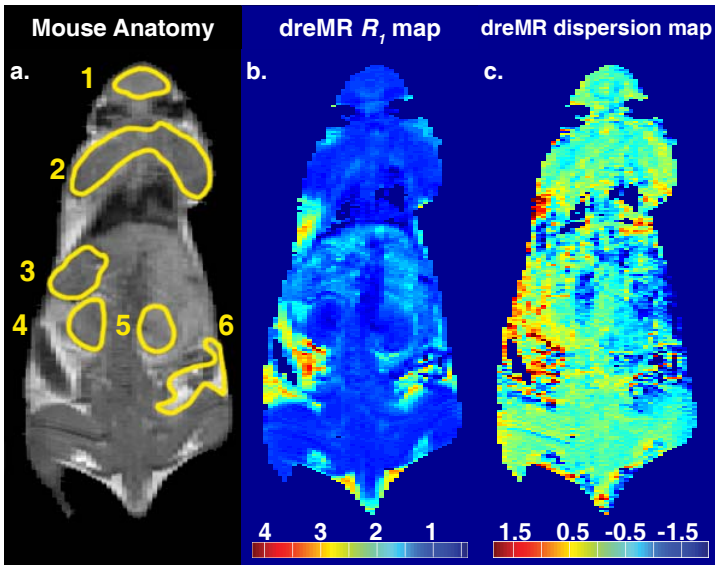

Figure 1. **[a]** Anatomical T_1-weighted MRI highlighting ROIs of selected tissues. **[b]** dreMR R_1 [s^{-1}] map at 1.5 T in false colour. **[c]** R_1 dispersion dreMR map, $\Delta R_1/\Delta B_0$, [s^{-1}/T] at 1.5T.

Methods – Imaging was performed on a 1.5 T GE CVMR system (WI, USA) outfitted with a dreMR field-cycling coil to dynamically control B_0 prior to imaging.[4] Three coronal dreMR images were acquired using a field-cycling T_1-weighted fast spin-echo inversion recovery pulse sequence[3], where ΔB_0 was modulated for a duration of relaxation times (Δt_R) prior to imaging. dreMR T_{1+} (+0.11 T field shift), T_{1-} (-0.11 T field shift), and T_1 (0.0 T field shift) images were acquired with varying Δt_R times (50, 75, 100, 125, 150, 200, 400, 750, 1000, 1500, 2000, 3000, 5000, 8000 ms). Prior to each magnetic field shift, the sample was allowed to polarize for 2000 ms at the clinical field strength of 1.5 T followed by a 180° inversion radiofrequency (RF) pulse, after which the dreMR magnetic field shift was applied (ramp time=10 ms, 6 ms delay before imaging). The remaining sequence parameters were as described (TE=14.2 ms, NEX=2, matrix=320x128, FOV=12.0x4.8 mm^2, slice thickness 2.0 mm, 4 echoes). The repetition time, TR, was minimized to the sum of the polarization, relaxation and imaging times over the course of the dreMR imaging. A healthy female NU/NU mouse (26g) anesthetized with 2% isofluorane was placed on a custom water heated (37°C) bed in a Tx/Rx birdcage RF coil within the dreMR coil for imaging.
R_1 maps at 1.61 T, 1.5 T, and 1.39 T were produced from the dreMR images using a 3-parameter non-linear fit for spin-lattice relaxation (R_1, amplitude & background parameters) on a pixel-by-pixel basis.

Tissue Type	$\Delta R_1/\Delta B_0$ ± SD
1 - Brain	-0.21 ± 0.091
2 - Limb Muscle	-0.13 ± 0.023
3 - Liver	-0.57 ± 0.28
4 & 5 - Kidneys	-0.24 ± 0.79
6 - Mammary fat	-0.045 ± 0.77

Table 1. ROI analysis of selected tissues for R_1 dispersion. R_1 values were calculated at each field strength (1.61 T, 1.5 T, 1.39 T). A linear regression analysis provided the dispersion slope ($\Delta R_1/\Delta B_0$) ± one standard deviation [s^{-1}/T].

Results – On the T_1-weighted MRI, regions of interest were drawn for the brain, liver, kidneys, mammary fat, and limb muscle (Fig. 1.a). R_1 maps were produced across the whole-body of the mouse at 1.61 T, 1.5 T (Fig. 1.b), and 1.39 T magnetic field strengths. ROIs analysis of the tissues showed little dispersion, $\Delta R_1/\Delta B_0$ (Table 1), across a dreMR field shift of ±0.11 T about 1.5 T. Figure 1.c shows the dreMR R_1 dispersion map calculated from a total dreMR magnetic field shift of 0.22 T.

Discussion – *In vivo* whole-body spin-lattice relaxation rates (R_1) and dispersion maps of protons at 37°C for a healthy mouse have been quantified for a dreMR magnetic field of shift of ±0.11 T about 1.5 T. ROIs of selected tissues from the dreMR R_1 maps displayed little dispersion among the magnetic field changes, confirming previous published *ex vivo* NMRD reports.[5] Current capabilities to safely extend to larger ranges of dreMR magnetic field shifts of ±0.22 T will further exploit the dispersion R_1 magnetic field dependence enabling quantification of targetable contrast agents.[6] *In vivo* whole-body imaging of small rodents presents challenges with respect to breathing and motion artifacts so that gating techniques are under investigation to minimize the artifacts while maintaining reasonable scan times.

Conclusion – These preliminary findings emphasize the R_1 magnetic field dependence of tissues at clinical field strength of 1.5 T over a range of ±0.11 T, presenting a basis for investigations of cancerous and abnormal tissues, with administration of targetable and non-targetable contrast agents.

References – **[1]** Lurie D.J., *et al.*, C. R. Physique (2010);11:136-148. **[2]** Hoelscher, U.C., *et al.*, Magn Reson Mater Phy (2012);23:223-231. **[3]** Alford, J.K., *et al.*, MRM (2009);61:796-802. **[4]** Alford, J.K., *et al.*, Con Mag Reson Part B (2009);35B(1):1-10. **[5]** Koenig, S.H., *et al.*, Invest Radiol (1984);19:76-81. **[6]** Martinez-Santiesteban, F.M., *et al.*, Proc. Intl. Soc. Mag. Reson. Med. 21, abstract 0560 (2013)

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