Detection of 2-Deoxy-D-Glucose in Tissues By $T_{1\rho}$ Relaxometry

John Thomas Spear[1,2], Zhongliang Zu[2,3], and John C. Gore[2,4]

[1]*Physics & Astronomy, Vanderbilt University, Nashville, TN, United States,* [2]*Institute of Imaging Science, Vanderbilt University, Nashville, TN, United States,* [3]*Radiology, Vanderbilt University, Nashville, TN, United States,* [4]*Biomedical Engineering, Vanderbilt University, Nashville, TN, United States*

Target Audience: Scientists interested in chemical exchange saturation transfer or spin-locking based MR experiments and the potential for measuring glucose analogues in tissue.

Purpose: MRI detection of 2-Deoxy-D-Glucose (2DG) in tissues has the potential to allow imaging of regional metabolism as 2DG is taken up like glucose and, after phosphorylation, accumulates within the cells. Previous studies have used chemical exchange saturation transfer (CEST) to detect 2DG in live animals.[1] Here we explore the feasibility of detecting 2DG using measurements of the dispersion of $R_{1\rho}$ (the spin-lattice relaxation rate in the rotating frame, $R_{1\rho}=1/T_{1\rho}$) at different locking fields. We have previously shown that at high fields, $R_{1\rho}$ dispersion is dominated by exchange effects, and that by appropriate analysis of the dispersion data, images may be produced that are sensitive to the presence of compounds with specific exchange rates.[2,3] We have therefore performed preliminary computer simulations and in vitro experiments to assess the feasibility of detecting 2DG by spin-locking methods. The technique relies on being able to detect changes caused by exchanging hydroxyl protons in 2DG against the natural background of intrinsic compounds.

Methods: The behavior of $R_{1\rho}$ over a relevant range of locking fields was simulated using finite difference Bloch-McConnell simulations of two and three-pool systems of small pool fraction sizes undergoing exchange to demonstrate how $R_{1\rho}$-dispersion curves add almost independently (results not shown). $R_{1\rho}$ dispersions were subsequently measured in tissue homogenates. The brains of freshly sacrificed healthy Sprague-Dawley rat's were immediately removed, washed, and placed in ice cold isotonic PBS. The PBS to tissue mass ratio was 3, and four different samples were made with the addition of 0, 10, 50, 100 mM 2DG. The tissues were homogenized, then $R_{1\rho}$-dispersions were measured using spin-lock amplitudes varying from 50-10,000 Hz and $R_{1\rho}$ values were calculated using a mono-exponential fit to five different locking times. The dispersion curves were then fit in a least squares manner to the theoretical model of Chopra et al. $R_{1\rho} = \left[\frac{R_2 + {R_{1\rho}^{\infty}\omega_1^2}/{S_\rho^2}}{1 + {\omega_1^2}/{S_\rho^2}}\right]$ where R_2 is the system's low amplitude relaxation rate, $R_{1\rho}^{\infty}$ is the high amplitude relaxation rate, and S_ρ is a parameter used to estimate the system's average exchange rate.[4] Exchange Rate Contrast (ERC) Images were calculated using $ERC = 4\frac{(S(\omega_1=0)-S(\omega_1))(S(\omega_1)-S(\omega_1=\infty))}{(S(\omega_1=0)-S(\omega_1=\infty))^2}$, where $S(\omega_1)$ is the signal at the corresponding locking field, to generate signal intensity between 0 and 1 that will be scaled by the concentration of 2DG when the intermediate ω_1=800 Hz based on phantom experiments. Mean signal intensities were compared as a function of 2DG concentration.

Results: Figure 1a shows the $R_{1\rho}$ map for the four homogenate samples at 80 Hz. Each corresponding measured dispersion curve is shown in figure 1b. The dispersion magnitude increases with 2DG concentration and the inflection amplitude moves to lower frequencies. Figure 1c shows the mean exchange rates of the homogenates estimated from the dispersion data. Figure 2 shows the mean ERC signal as a function of 2DG concentration.

Discussion: The Bloch-McConnell simulations show the exchange effects add almost completely independent of each other. This suggests that a change in dispersion caused by an injected species can be detected. The $R_{1\rho}$ map shows the low spin-lock amplitude relaxation rates, which should be very close to R_2 values, but the dispersions of $R_{1\rho}$ taken at different spin-lock amplitudes allows for quantitative analyses of the changes in mean exchange rates within the tissue. The addition of 2DG shifts the mean exchange rate in the homogenates to lower frequencies and the mean ERC to higher intensities in a dose dependent manner.

Conclusion: Multiple factors contribute to $R_{1\rho}$ dispersion in tissues, but adding an exogenous agent can be detected via appropriate analysis against the intrinsic background if it is characterized by a specific exchange rate. Simulations show that exchange contributions add roughly independently for small pool fractions. Exchange rate contrast analysis emphasizes specific exchange rates using parametric images, which produces intensity that scales as a function of concentration in the present case. In vivo rat studies show that relatively high concentrations of 2DG can be achieved in e.g. brain and tumors, and $R_{1\rho}$ approaches have the potential to improve detection over CEST methods.

References: [1] Fatima et al. J Cereb Blood Flow Metab 33:1270-1278, 2013. [2] Cobb et al. Magn Reson Med 66:1563-1571 [3] Cobb et al. Magn Reson Med 67:1427-1433, 2012. [4] Chopra et al. J Magn Reson 59:361-372, 1984.

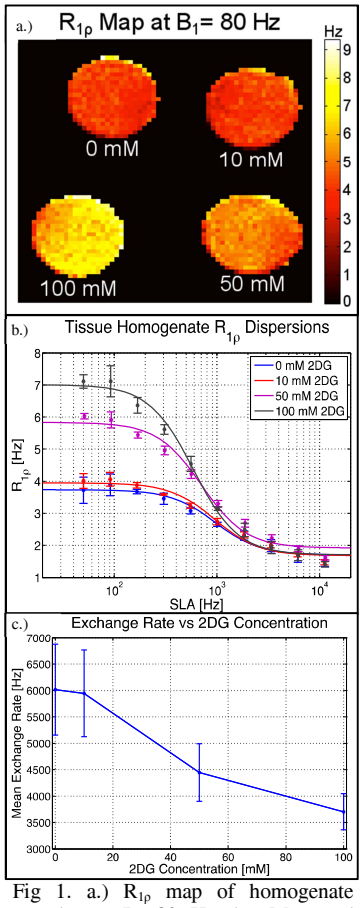

Fig 1. a.) $R_{1\rho}$ map of homogenate samples at B_1=80 Hz. b.) Measured dispersion curves with fits to Chopra model. c.) Average exchange rate calculated from dispersion curve fits. Error bars display 1 standard deviation.

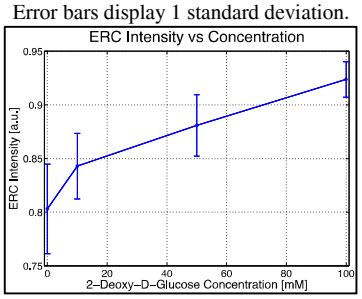

Fig 2. Mean ERC image intensities calculated at B_1= 800 Hz.The errorbars represent 1 standard deviation.