^1H_2O MR Relaxography of the Perfused Rat Heart

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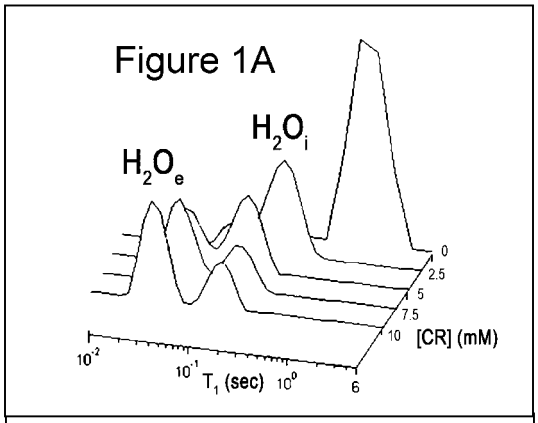
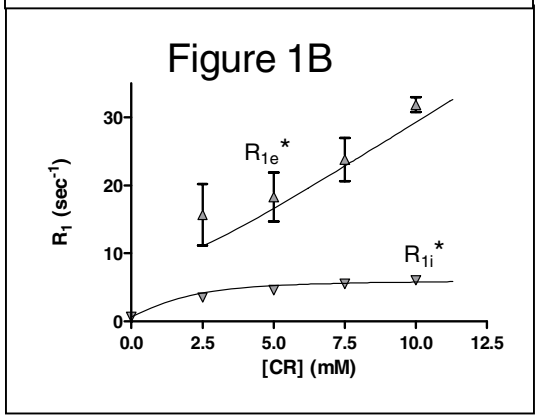
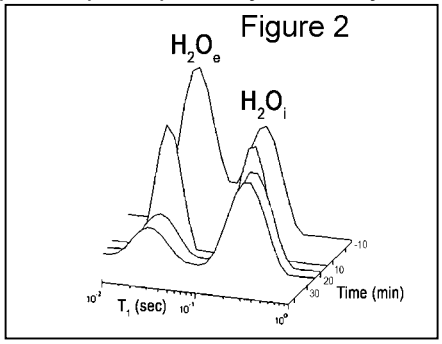
Introduction: Knowledge of the intracellular water volume is essential for the measurement of intracellular ion and metabolite concentrations. Extracellular and intracellular water volumes are difficult to measure. Use of a contrast reagent (CR) in combination with relaxographic analysis of the H_2O T_1 relaxation decay allows discrimination of the $^1H_2O_i$ and $^1H_2O_e$ T_1 and population values (1). Analysis with the Bloch equations modified for two site exchange (2SX) reveals the intracellular (p_i) and extracellular (p_e) water populations, which reflect the tissue water volume fractions. 2SX analysis also yields the average lifetime of intracellular water molecules (τ_i). This study measured the ^1H_2O T_1 relaxation times of isolated rat hearts perfused with steady-state CR concentrations ([CR]).





Methods: Isolated rat hearts were perfused with Krebs-Henseleit (KH) buffer. $GdDTPA^{2-}$ was the CR. KH buffer with [CR] values of 0, 2.5, 5, 7.5 and 10 mM were used. The isolated hearts were suspended 20 mm NMR tubes but not submerged in the effluent, which was drained away to remove the ^1H_2O signal outside the heart. ^1H NMR data were acquired at 398.8 MHz using a Varian Inova spectrometer. T_1 Inversion Recovery (IR) measurements used a composite 180° pulse. The H_2O free induction decay (FID) amplitudes were quantified using Bayesian Analysis Software. An Inverse Laplace Transform (ILT) analysis (magritek Ltd Wellington, NZ) of the IR ^1H_2O FID amplitudes yielded the T_1 distribution (relaxogram) for each IR data set. The T_1 and the peak area values were measured using Gaussian fittings.

Results: Figure 1A displays a stacked plot of ^1H_2O relaxograms from a heart perfused with 0, 2.5, 5.0, 7.5 and 10 mM [CR]. The relaxographic H_2O_e and H_2O_i peak areas approach p_e and p_i, respectively as the system approaches the slow-exchange-limit (SXL), which occurs near 7.5 mM [CR]. The relaxivity plot (Fig. 1B) shows the [CR]-dependence of the reciprocals (R_1) of the apparent T_1* values for H_2O_e (R_{1e}*) and H_2O_i (R_{1i}*) (mean ± SD). 2SX analysis fitting (solid lines) of the R_{1e}* and R_{1i}* yields a τ_i = 0.184 ± .007 sec and p_i = 0.24 ± .03. Relaxograms were obtained during no flow ischemia (Figure 2). At the rear is the 10 mM relaxogram from the well perfused heart (Fig. 1A). Ischemia began at t = 0; three relaxograms were obtained after 10, 20 and 30 mins of ischemia. Vascular collapse and loss of $^1H_2O_e$ reduced the area of H_2O_e from 0.59 before ischemia to 0.22 (10 min), 0.11 (20 min) and 0.08 (30 min).The τ_i was 0.28 ± .02 sec during ischemia.



Conclusions: Relaxographic analysis measured reasonable values for the p_i and p_e of the perfused heart (2). The τ_i was < 0.2 sec in the oxygenated perfused heart at 37°C. This is much lower than τ_i = 10 sec reported for excised heart tissue in which Mn^{2+} acted as an intracellular CR (3). ^1H_2O relaxography can be used to measure intra- and extracellular volumes and water lifetimes during normal and disease states in the heart.

References: (**1**) Labadie, C., J.H. Lee, G. Vetek, and C.S. Springer, Jr. J Magn Reson Series B, 1994. 105(2) p. 99.
(**2**) Clarke, K., R.E. Anderson, J.F. Nedelec, D.O. Foster, and A. Ally, Magn. Reson. Med., 1994. **32**(2): p. 181.
(**3**) Nordhoy, W., H.W. Anthonsen, M. Bruvold, P. Jynge, J. Krane, and H. Brurok, , 2003. **16**(2): p. 82.