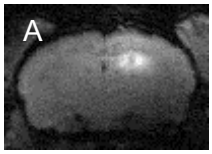
Manganese Detection by MRI Relaxation Ratio Mapping

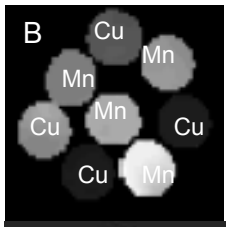
Loredana Sorina Truica[1], Keiko McCreary[1], and Albert Cross[1]
[1]*Neuroscience, Canadian Centre for Behaviour in Neuroscience, Lethbridge, Alberta, Canada*

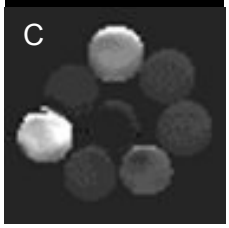
Introduction: Manganese enhanced magnetic resonance imaging (MEMRI) is becoming widely used as a neuro-anatomical and functional tool in studies of animal models. By administering a solution of manganese chloride ($MnCl_2$)[1,2] contrast is achieved by the entry of the Mn^{2+} ions into the neurons through calcium (Ca^{2+}) channels. Most studies using manganese as contrast agent investigate longitudinal relaxation (T_1) changes. Figure 1A shows a T1 weighted images of a Mn infusion into the brain of a rat. The contrast change at the location of the cannula is obvious; however, changes in the transport and distribution of the Mn that relate to changes in experience will be quite small. To quantify the Mn distribution and improve the sensitivity, T1 mapping is normally used[2]. It is known that the paramagnetic relaxation properties of manganese in solution are unique[3] with an unusually large ratio of T_1 to T_2. This study investigates the addition of T_2 mapping to the detection of low-level changes of manganese and demonstrates how T_1/T_2 ratio mapping may be used to reveal contrast specific to manganese.

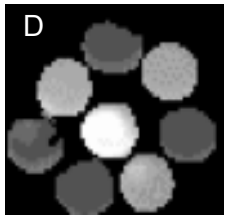
Methods: Imaging data was acquired using a Magnex (Abingdon, UK) 3T 800 mm bore magnet, with a MR6000 console (Surrey UK). For the phantom study the samples were composed of solutions of manganese chloride (0.1, 0.2, 0.05 and 0.045 mM) or copper sulphate (11, 10, 2.2 and 1 mM) The image slice thickness was 2 mm, FOV 128mm (128x128). T_1 data was taken with a saturation recovery spin-echo pulse sequence (10 saturation delays: 50, 200, 400, 500, 700, 900, 1500, 2000, 3000 and 4000 ms) in a random order. T_2 data was taken with a 32 echo spin-echo pulse sequence with a TE of 20 ms. All 8 samples were imaged together in a home built coil (80 mm diameter and 100 mm length). A uniform tip angle map was obtained by T_1 fitting indicating that B_1 field variation was minimized.
The simulations were done using Origin and the input data for simulations was a typical relaxation parameter for rat brain with a T_1 of 1500 ms and T_2 of 150 ms. The relaxivity enhancement was based on data taken for solutions of $MnCl_2$ in water. Mn relaxivity values of 6.7 and 133 $ms^{-1}mM^{-1}$ were used for T_1 and T_2 respectively. T_1/T_2 ratios were simulated for both small concentration changes (1%, 2%, 3%, 4%, 5%) as well as large ones (10%, 20%, 30%, 40%, 50%). The ratio contrasts expected for the regions that have the above mentioned elevated uptake of manganese compared with surrounding tissue were calculated and the rate change with concentration were plotted (see Figure 2).



Results and Discussion: Phantom measurements as well as image contrast simulations were performed to assess the sensitivity to concentration (activity) changes. At first, the ratio behaviour was investigated in water. The water phantom experiments show that T_1 and T_2 maps do not uniquely distinguish the manganese tubes from the copper tubes (see Figure 1 B) and C)). Conversely the ratio map (Figure 1, D) clearly shows 4 brighter tubes, which indeed are the 4 manganese tubes imaged. The samples were specifically selected to have 2 samples (Mn and Cu) with the same T_1 and 2 other with the same T_2. The other 4 samples tested the ability to detect a change in concentration. The phantom experiment demonstrates the use of the ratio contrast; however, when infusing Mn into an animal, there may be different environments for it, but there is only one paramagnetic species. The results in figure 1D used relaxivities for Mn in water. The literature[4,5] indicates that these relaxivities further translate to tissue. We therefore simulated an infusion of a base concentration on Mn and looked at the effect of a small increase in concentration on the ratio. The background relaxation properties of tissue are different than water and partially mask the effect of manganese. Taking the tissue relaxations into account, Figure 2 shows the change in ratio versus base concentration for varying elevated uptakes. The highest rate of change occurs at low concentration with a peak change at 0.1 mM. In manganese imaging of an animal, toxicity is an issue. The simulations indicate that the highest sensitivity to the ratio change occurs at low concentrations. This is favourable to the toxic effect on the animal.



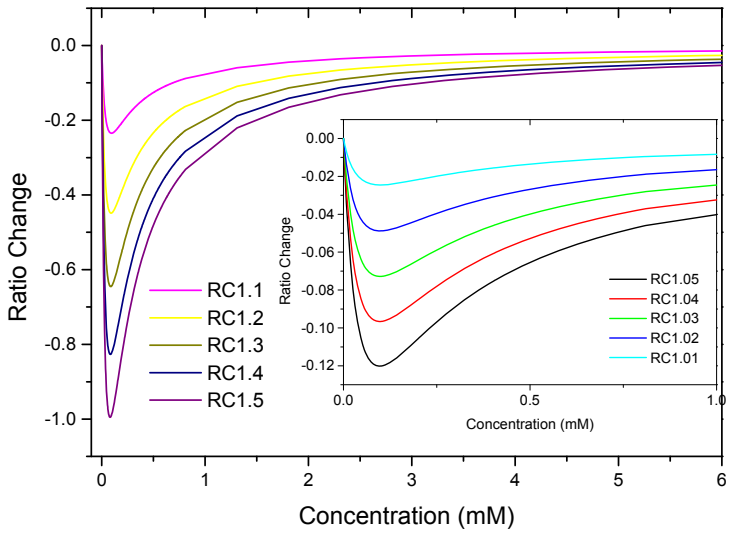




Conclusion: The water phantom study shows that the information in a T_1/T_2 ratio map can be used to identify contrast specific to manganese. The simulations show that the highest sensitivity to changes in the ratio, occur at low concentrations. This is compatible with the manganese infusion into animals (has already been proved toxic) and it is necessary to keep the concentration as low as possible. Ratio mapping could therefore be a useful tool in the detection of small concentration changes in manganese enhanced MRI.

Figure 1. A) Day 10, SE image (700/13) of a rat brain. The bright region is centered around the tip of a cannula infusing Mn via an osmotic pump (28 day, 0.25 ul/hr 200ul 100 mM of $MnCl_2$); 8 tube phantom B) T1 map, C) T_2 map and D) Ratio T_1/T_2 map.

Figure 2. Ratio T_1/T_2 change (contrast) between tissue with a higher manganese uptake compared with surrounding tissue. The plots shown correspond to activity changes from 1% to 5% (inner graph) and from 10% to 50% (outer graph).



References: 1. Y-J. Lin and A.P. Koretsky, Mag. Res. Med. 38, 378-388, (1997). 2. A.C. Silva, J.H. Lee, I. Aoki and A.P. Koretsky, NMR in Biomed, 17, 532-543, (2004). 3. N.J. Bloembergen, J. Chem. Phys, 27, 572, (1957). 4. S. Huang et al. NeuroImage, 46, 589 (2009). 5. C.H. Liu, H.E. D'Arceuil and A.J. de Crespigny, MRM, 51, 978 (2004).