Mn Concentration Mapping with MRI: Comparision with Autoradiography and PET

Geoffrey Topping[1], Andrew Yung[2], Paul Schaffer[3], Cornelia Hoehr[3], Thomas Ruth[3], Piotr Kozlowski[2], and Vesna Sossi[1]

[1]Physics and Astronomy, University of British Columbia, Vancouver, British Columbia, Canada, [2]MRI Research Centre, University of British Columbia, Vancouver, BC, Canada, [3]Nuclear Medicine, TRIUMF, Vancouver, BC, Canada

Introduction

Manganese-enhanced MRI (MEMRI) is used to study neuronal activity by detecting Mn accumulation in cells via voltage gated calcium channels[1]. Mn accumulation is assessed with statistical test maps, or simple observation of image contrast changes. Concentration maps give additional information about the amount of Mn present, which may greatly increase the power of stimulus-induced Mn accumulation imaging. In this work, we generate Mn concentration maps in rats from MRI relaxivity maps, and compare with ^{52}Mn PET and autoradiographic images of the same animals in order to assess quantitative reliability.

Methods

^{52}Mn was produced by irradiating natural Cr foil with 12.5 MeV protons (^{52}Cr(p,n)^{52}Mn). Mn was separated from Cr by column chromatography and redissolved in phosphate-buffered saline. Additional non-radioactive Mn was added to provide MR contrast. Healthy Sprague-Dawley rats received single injections: direct intracerebroventricular (ICV) (30 µl, 0.2 µmol Mn, 282 kBq ^{52}Mn) by stereotaxic surgery, or intraperitoneal (IP) (2 ml, 40 mg/kg $MnCl^2$, 14.7 MBq ^{52}Mn). Baseline MRI T1 maps were acquired prior to injections. On multiple days post-injection, T1 maps and PET data were acquired on each animal. MRI was acquired with a 7 T small animal MR system (Bruker, Germany) using a sagittal multi-slice FLASH-based Look-Locker sequence[2] with volume-coil transmit and surface coil-receive, TR=10 s, TE=3 ms, inter-excitation time=150 ms, 40 images per inversion, α=20 deg, inversion delay=18 ms, matrix size 128x72, FOV=4x2.25 cm^2, slice thickness 625 µm, 17 slices, and acquisition time 12 min. Voxel Mn concentrations were calculated from change in R1 and a calibration constant (4.2 mMs) derived from MR inversion recovery of saline Mn dilutions. PET data was acquired on Focus 120 small animal microPET system (Siemens, Germany) with a 450-600 keV energy window, and reconstructed by filtered back projection with cascade, scatter, and attenuation corrections, into single frame images with 0.433x0.433 mm^2 pixels, 0.796 mm slice thickness, 128x128x95 voxels, 76 mm axial FOV, and 55x55 mm^2 in-plane FOV. Autoradiographs (AR) were acquired by slicing frozen brain tissue into 20 µm segments onto slides and placing against radiosensitive phosphor screens for 1-3 days. Screens were read on a storage phosphor system (Cyclone), producing images with 43.2. µm pixels

Results

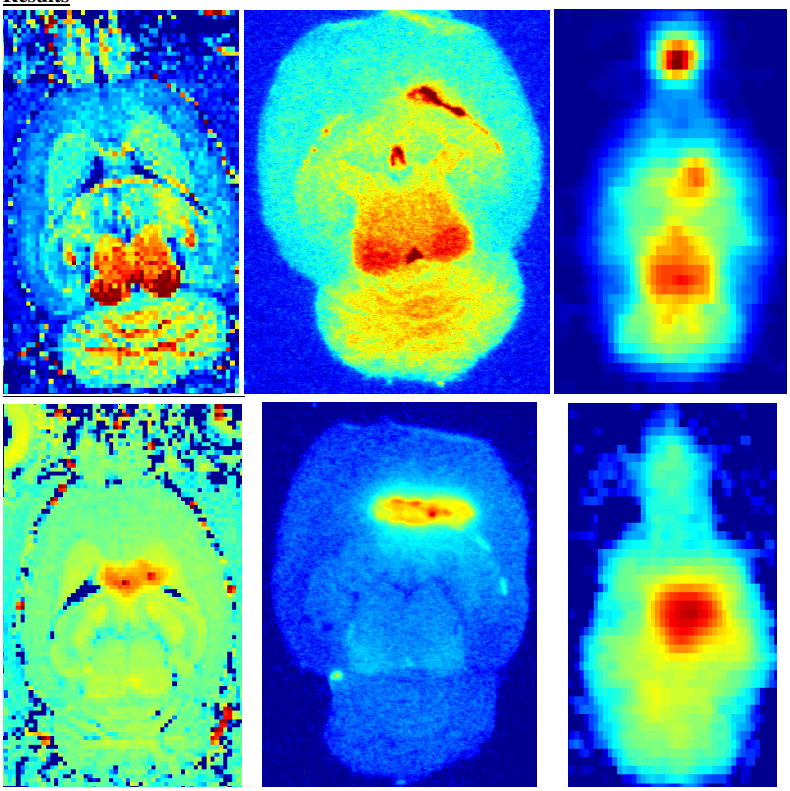
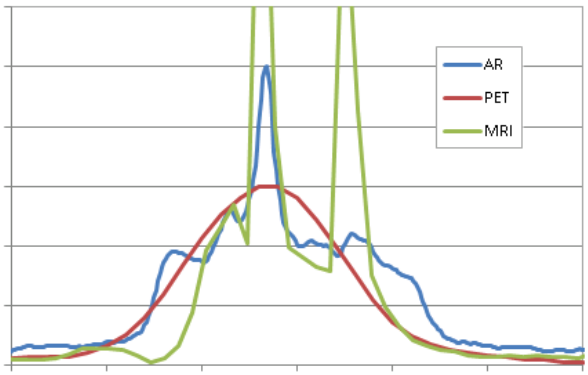


Fig. 1 - (top row left to right) MRI, autoradiography (AR,) and PET Mn concentration images in rat brain after ICV injection of Mn. Image colour scale is linear from blue (0 Mn) to red (MRI: 3 mM, PET: 18 kBq/cc, AR: uncalibrated). MRI was acquired 4 days post-injection, and PET was acquired and animal sacrificed 5 days post-injection. In all modalities, Mn has spread throughout the brain (cyan regions), with large accumulation visible in the inferior colliculus. PET and autoradiography show large accumulation near the injection site (right ventricle), while MRI and AR show large accumulation in the cerebellum which is less apparent in PET. PET also shows a large accumulation in the olfactory bulb or adjacent tissue, and some lesser accumulation is seen in this region in MRI. The AR image slices do not include the olfactory bulb due to the manner in which the brain was extracted and sliced.

Fig. 2 - (bottom row) Mn concentration images in rat brain after misplaced ICV-targeted injection of Mn. Image colour scale is logarithmic due to large dynamic range of concentrations between the peak and other visible structure, from blue (0 Mn) to red (MRI:100 mM, PET: 100 MBq/cc, AR: uncalibrated). MRI and PET were acquired and animal sacrificed 8 days post-injection. Mn is highly concentrated at the injection site, and appears in much lower levels elsewhere in the brain.

Fig. 3 - (below) Horizontal profiles were placed through images in Fig. 2 and are plotted with arbitrary vertical scaling and pixel-size proportional horizontal scaling for each modality. Large spikes are seen in the MRI profile, corresponding to voxels in which the R1 fitting procedure failed to produce reasonable values, leading to unreasonably high Mn concentration estimates.



Discussion / Conclusion

Localized differences are seen between MRI and AR, particularly where Mn is present at concentrations on the order of 100 mM and the Look-Locker MRI sequence unable to reliably determine the R1, leading to inaccurate large spikes or voids in Mn concentration maps. This is likely due to a combination of insufficient temporal resolution of sampling of the inversion recovery curve, and the impact of T2* effects on the signal from these voxels. Compared with PET, the spatial resolution of MRI is vastly superior; small details of the anatomy and Mn accumulation pattern may be seen in the MRI, while PET shows only general structural locations, or has structure obscured by blurring from an adjacent peak region. The distributions seen in MRI, PET and AR are broadly similar, however, confirming that change in R1 relaxivity is concentration dependent and at least roughly proportional in vivo. *In vivo* MRI Mn concentration mapping is a potentially useful technique for small animal brain imaging studies.

[1] Lin Y-J and Koretsky AP. 1997, MRM 38:378-388
[2] Chuang K-H and Koretsky A. 2006, MRM 55:604-611