Validation of MRI Mn Concentration Mapping in the Rat Brain

Geoffrey Topping1, Andrew Yung2, Paul Schaffer3, Cornelia Hoehr1, Thomas Ruth1, Piotr Kozlowski2, and Vesna Sossi1

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

Target Audience
This work will be of interest to researchers planning MRI studies using Mn2+, and possibly other paramagnetic ions, as a contrast agent in the brain of small animals.

Purpose
Mn2+ is used as a contrast agent in MRI, which increases the R1 relaxation rate, roughly proportional to its concentration, and accumulates in regions of neuronal activity[5]. Mn imaging studies generally report R1-weighted signal changes or probability maps[4,5] of likely locations of Mn accumulation. Region-of-interest (ROI) averaged relaxation rate changes have been reported[6], and converted to Mn2+ concentration using a calibration factor, without details of the Mn2+ distribution. We have previously reported initial results of Mn imaging in the rat brain with MRI relaxation rate changes, and with positron emission tomography (PET) and autoradiography (AR)[5]. In this work, we validate the use of relaxation rate changes to estimate Mn2+ concentration in the brain of live rats at a per-voxel level. This technique offers potential much greater experimental power than ROI-averaged or probabilistic results, and should facilitate study activation-induced Mn uptake by revealing variation in its strength and distribution in response to varying strength and type of stimuli, which cannot be assessed with previous methods.

Methods

\[ ^{52}\text{Mn} \text{ was produced by irradiating natural Cr foil with 12.5 MeV protons (} ^{52}\text{Cr(p,n)}^{52}\text{Mn})[6]. \]

Mn was separated from Cr by column chromatography and redissolved in phosphate-buffered saline. Additional non-radioactive MnCl2 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}\text{Mn}) by stereotaxic surgery. MRI R1 maps were acquired at baseline and post-injection with a 7 T small animal MR system (Bruker, Germany) using a sagittal multi-slice FLASH-based Look-Locker sequence[7] (Parameters: TR=10 s, TE=3 ms, inter-excitation time=150 ms, 40 images per inversion, excitation angle=20 deg, matrix size 128x72, FOV=4x2.25 cm², slice thickness 625 µm, 17 slices, and acquisition time 12 min.) PET data was acquired on a 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 0.433x0.433x0.796 mm³ voxels. Autoradiographs (AR) were acquired by slicing frozen brain tissue into 20 µm segments onto slides and placing against radiosensitive phosphor screens for 3 days. Screens were read on a storage phosphor system (Cyclone), producing images with 43.2 µm pixels. A Mn concentration to R1 change calibration constant was measured by non-imaging inversion recovery on prepared Mn solutions in saline.

Analysis

MNI R1 maps were coregistered and subtracted to produce maps of R1 change, and converted to concentration using the calibration constant 4.2 mM⁻¹⋅s⁻¹. AR slice images and PET images were coregistered to the MR image. The MR concentration image was smoothed with a 2 mm FWHM Gaussian kernel convolution to match the PET image spatial resolution. Scatter plots of unsmoothed MR against AR, and smoothed MR against PET concentration were fit with linear least squares models. Excellent quantitative agreement is seen between MRI-derived relaxation rate change or Mn concentration, and PET and AR concentrations in images of the same animals. This validates the use of MR relaxation rate change to measure Mn accumulation in the rat brain. Mn concentration mapping with MRI is a potentially useful tool to improve the experimental power of Mn-uptake imaging to assess neuronal activation.

Conclusion

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[5] Topping GJ et al., 2013, ISMRM Poster 1265