Magnetic Particle Imaging (MPI) for functional brain imaging; rodent and human-scale devices

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Magnetic Particle Imaging (MPI) forms images of the cerebral blood pool by detecting the non-linear magnetization of injected superparamagnetic iron oxide nanoparticles (SPIONs). Its lack of biological background, fast imaging, and high sensitivity make it an attractive potential modality for human functional neuroimaging. We report the first use of MPI for imaging hemodynamic modulation of Cerebral Blood Volume (CBV) in a study of rats undergoing a hypercapnia activation paradigm, expanding on our preliminary detection [1] and imaging [2] experiment. We show that fMPI has up to 6-fold higher CNR than 9.4T BOLD fMRI in the same hypercapnic paradigm. We also report the first phantom images and sensitivity measures in an MPI scanner constructed for human functional brain imaging.

The rodent hypercapnia studies used an in-house built rotating field-free line (FFL) imaging system with a spatial resolution of 3 mm and 5-second temporal resolution. We scanned 5 rats with alternating hyper-/hypocapnia periods to modulate CBV and imaged the blood-pool agent Synomag-D 70 nm (Micromod, Germany) The analyzed fMPI time-series data showed a high CNR hemodynamic functional CBV response; up to 6 fold higher than observed in BOLD fMRI at 9.4T. Figure 1 shows the rodent fMPI hypercapnia results.

The human-scale rotating FFL functional MPI scanner is the first of its kind and uses a 1 T/m gradient on a mechanically rotating gantry (~2 tons of rotating mass). The system is also designed for 5 s temporal resolution but with a 40 cm diameter bore to enable human head studies. The first images were acquired in phantoms at realistic human blood-Fe concentrations at an in-plane resolution of 6.6 mm.

Conclusions: We report the first *in vivo* fMPI time-series images of hemodynamic modulation and characterize their signal and noise levels and the modalities' sensitivity to CBV changes induced by a hypercapnic challenge in a rodent model. In these trials, we see up to a 6x increase in CNR compared to 9.4 T BOLD fMRI. The activation was localized to the animal's brain and showed a 25% CBV change on average consistent with the physiological expectation for the hyper-/hypocapnia challenge. The human-scale fMPI system shows promise for translating this modality to NHP and human studies at a resolution sufficient for many functional neuroimaging studies.

References & Acknowledgements

1) NIBIB Brain Initiative grant: U01EB025121-02
2) Mason EE, Cooley CZ, Cauley SF, Griswold MA, Conolly SM, Wald LL. Design analysis of an MPI human functional brain scanner. Int J Magn Part Imaging. 2017;3(1): PMCID: PMC5526464.
3) Mason EE, Mattingly E, Herb K, Cauley SF, Sliwiak M, Drago JM, Graeser M, Mandeville ET, Mandeville JB, Wald LL. Functional magnetic particle imaging (fMPI) of cerebrovascular changes in the rat brain during hypercapnia. Phys Med Biol. 2023. Epub ahead of print. PMID: 37531961.

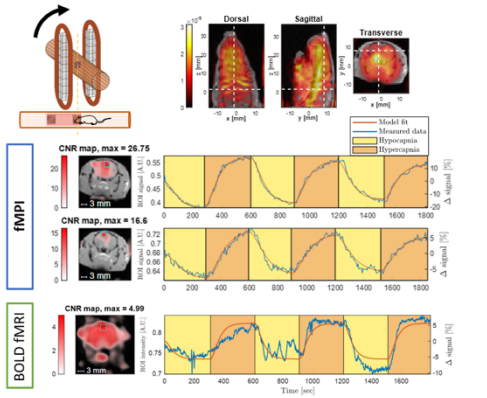
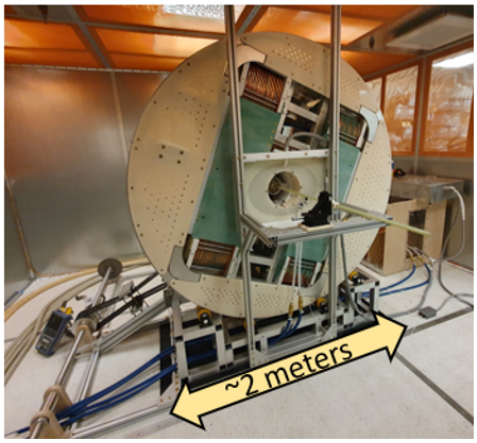
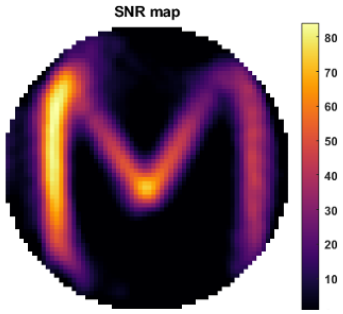


Figure 1: *Top left:* Illustration of the hardware configuration for the MPI experiments (described further in ref. 3). *Top right:* 3D reconstruction of the rat MPI data superimposed on MRI scans of the same rat. The 3D MPI volume was formed by stacking 72 transverse slices together. *Middle:* Time series from the first two of 10 rat experiments. On the left is the MPI CNR map overlaid on MRI with a transparency weighted by CNR. The cyan rectangle represents the maximum CNR, and the data from within is plotted on the right. Blue trace is the measured data with drift terms subtracted, and red is the model fit. *Bottom:* BOLD fMRI data with the same protocol, smoothed by the same 3 mm FWHM kernel. The model was identical except there was no particle decay term in the fMRI regression model.



Photograph of the human imaging system. A welded aluminum frame holds the magnet assemblies and rotates around the human head-sized bore at 6 RPM



The 54.4mm x 59mm "M" phantom filled with 0.125 mg Fe/ml of Synomag-D, at roughly the concentration of blood given a 10 mg Fe/kg of body mass (the expected dose for humans). **Bottom)** The signal-to-noise ratio (SNR) of the resulting image. The signal is the image intensity of each voxel, and the noise is the standard deviation of all voxels from an empty bore image taken immediately prior and processed identically.