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A human-scale magnetic particle imaging system for functional neuroimaging

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Abstract

Non-invasive neuroimaging techniques have enabled a paradigm shift in the way neuroscientists study the human brain. However, the sensitivity limitations of existing methods are a barrier to the identification of differences in brain function in disease states in individuals, as required for clinical use. In contrast, conventional neuroscience studies can average across large cohorts (up to 100s of subjects) to discern significant differences. Magnetic Particle Imaging is naturally sensitive to changes in hemodynmaic blood volume associated with brain activation and may overcome the sensitivity barrier to clinical use. The sensitivity of MPI stems from the strong magnetic moment that induces the signal paired with an elimination of biological background signals and their associated biological nuisance fluctuations ("physiological noise"). However, MPI instrumentation is not widely available at the human scale, especially for the time-series imaging required for functional studies. Here, we demonstrate the sensitivity of a human-scale field-free line MPI system capable of long-term time series imaging at a 5 second temporal resolution and a spatial resolution of 6 mm, with a detection limit of 150 ng Fe (at SNR = 1). We hope this step toward human fMPI provides the sensitivity to enable new directions in neuroimaging, particularly permitting diagnostic functional neuroimaging of diseases states.

I. Introduction

Non-invasive neuroimaging techniques now dominate the way neuroscientists study the human brain. Before their advent, lesion studies (i.e. examining the loss of function after a localized lesion, such as a stroke) and autopsy were often the only way to connect brain and behavior. Now, techniques such as EEG, and MEG enable the localization of the electric/magnetic fields radiating from neuonal currents (limited by low spatial resolution), flourodeoxyglucose PET can localize the increased metabolic demand (limited by spatial resolution, temporal resolution, and radioactive tracer hazards), and Blood Oxygenation Level Dependent (BOLD) functional Magnetic Resonance Imaging (fMRI) localizes the local changes in blood oxygenation resulting from the hemodynamic changes induced by local metabolic demand. BOLD fMRI is the most common approach for functional

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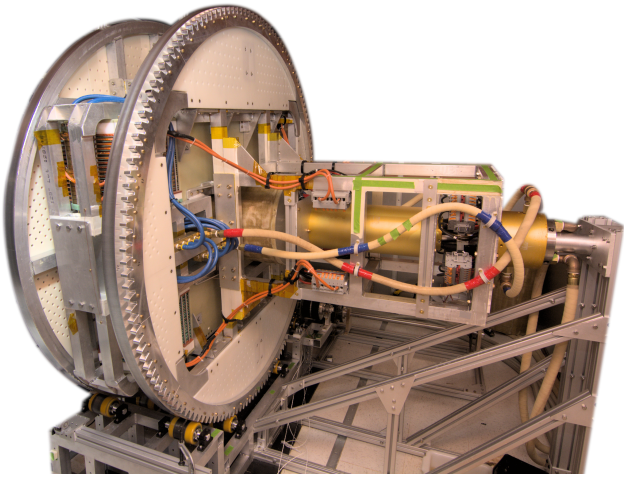

Figure 1: Photograph of the gantry from the service-end. The wheel is ∼2 m diameter

neuroimaging due to its non-invasive nature and reasonable spatial resolution (typ. smoothed to 4-12 mm[1]), however, the sensitivity limitations of BOLD typically requires averaging across large cohorts (up to 100s of subjects) to discern significant differences; an inconvenience for scientific studies, but a major barrier to its clinical diagnostic use. Magnetic Particle Imaging (MPI) may overcome this sensitivity limitation due to its very strong signal strength paired with an elimination of biological background signals and associated biological nuisance fluctuations (noise).

Previously, we built an MPI system for high-sensitivity functional neuroimaging of the rat brain [2] and used it in a hypercapnia trial to show up to 6× higher contrast to noise ratio (CNR) than 9.4T fMRI[3]. However, human-scale instrumentation is required to demonstrate clinical utility. So far, the only other human-size MPI systems developed at this scale are tailored for other applications [4, 5] and so have not prioritized the imaging FOV, temporal and spatial resolution, sensitivity, or long-term stability requirements of functional neuroimaging with MPI (fMPI). The imager photographed in Fig. 1 was designed and built for human functional neuroimaging trials with the following design requirements: i) Fit and image the 20 cm FOV of a human head, ii) Temporal resolution of ≤ 5 Sec.[3, 6], iii) Detect a 25% cerebral blood volume (CBV) change in brain parenchyma, and iv) Spatial resolution ∼ 6 mm.

II. Methods and materials

In order to maximize the sensitivity, a field-free line (FFL)-based design was preferred to a field-free point. The field-free line is generated by a pair of steel-backed NdFeB permanent magnets, and has a gradient of 1.1 Tm^{-1}. The shift coils are water cooled and capable of shifting the FFL ∼ ± 10 cm given a shift current of ± 200 A over long imaging runs. To achieve a 5 sec temporal resolution, the ∼ 1500 kg FFL and shift coil mass is rotated by a 3 HP (2.2 kW) motor (located outside of the shielded room). The FFL/shift assemblies have a 40 cm gap with a cylindrical copper shield housing the stationary drive and Rx coil.

To fit a human head, a receive coil was designed as an ellipse with a major radius of 118 mm, and minor radius of 80 mm. The receive coil is a two-part gradiometer where each half has 27 turns over 60 mm. The drive coil is a solenoid consisting of four modules each with 18 turns (72 turns total), and similar to the previously reported design in Ref. [7], with the notable exception that the "compensation assembly" was discarded because the large distance between the two halves limited its effectiveness. Additionally, the drive coil was made longer and optimized for homogeneity (including the effect of the shielding tube's eddy currents) along the center axis. The drive filter is similar to previously presented in Ref. [8] except the load impedance is half due to removal of the compensation assembly.

Following brain activation, the parenchyma's cerebral blood volume (CBV) changes by about 25 %[3, 6]. Given a 5 mg Fe/kg dose to an individual with 65 ml of blood per kg body mass, that corresponds to an iron-mass change of about 200 ng Fe in the 6 mm isotropic voxel (gray matter is about 5% blood). We test the scanners ability to detect this in a dilution series from 120 μg to 313 ng Fe. The image signal of each is compared to the noise of the empty bore data. The intercept of the best-fit signal-vs-mass line with the horizontal line marking the standard deviation of the empty bore image determines the SNR = 1 "detection limit".

The spatial resolution was measured using parallel ∼ 5 cm long × 2.5 mm diameter capillary tubes with 7 mm between the nearest surfaces. If the ratio of peak signal to minimum signal between peaks is less than 0.5, the samples are considered resolved. The reconstruction is a model based algorithm with a simulated 7 mm Gaussian FWHM kernel for the FFL.

III. Results

Figure 2 shows the results of the dilution series as well as the field of view letter phantom. The linear regression for SNR = 1 yields a detection limit of 150 ng Fe of Synomag. The current maximum field of view is limited by a broken shift amplifier channel to about 185 mm. Figure 3 shows the spatial resolution phantom. The lines with 7 mm between inner edges are clearly resolved indicating a spatial resolution better than 7 mm.

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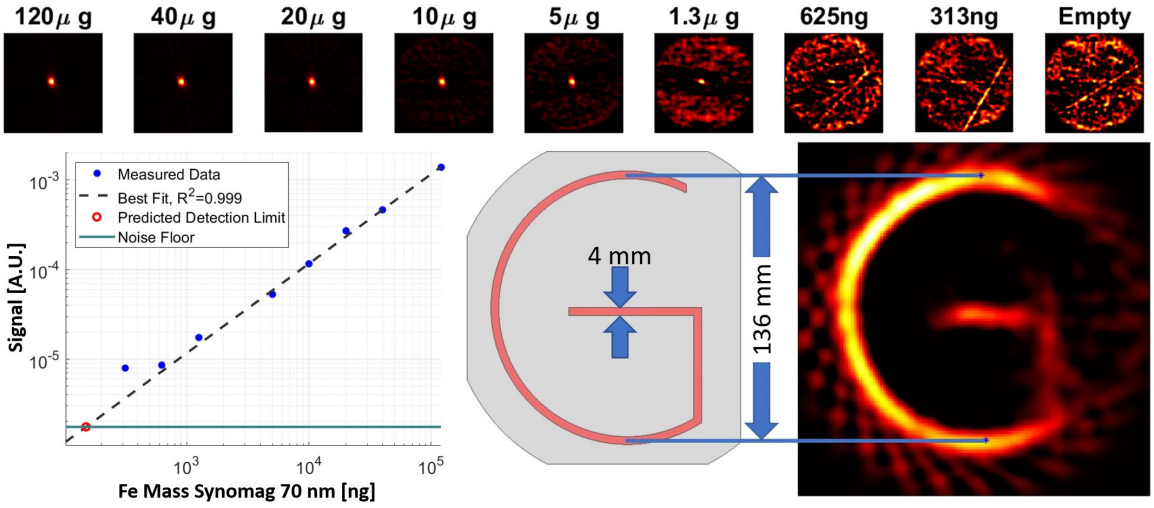

Figure 2: **Top:** Dilution series of Synomag from 120 μg to 313 ng Fe images where each image has a 180 mm diameter field of view and was acquired in 5 seconds. **Left**: Linear regression for the signal of each image compared to the noise floor. **Right:** A 'G' shaped phantom filled with 0.0625 mg Fe/ml of Synomag (approx. concentration of blood *in vivo*) where the center of the outer ring of the 'G' is 136 mm. This full field of view is 182 mm for 185 A_{Pk}

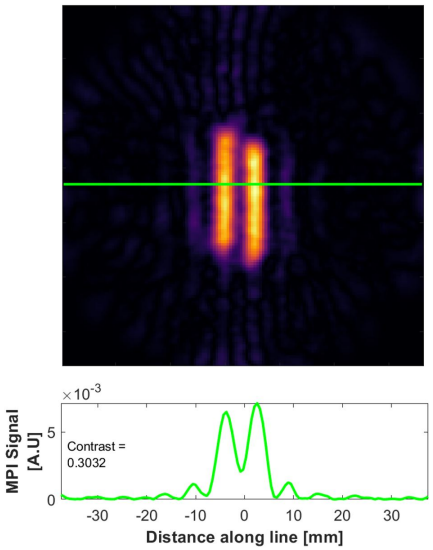

Figure 3: Resolution phantom: Two lines of undiluted Synomag where the spacing of the inner surfaces of the lines are 7 mm.

IV. Discussion and conclusion

Here, we show high sensitivity human-scale MPI images with a wide field of view in 5 seconds per image. The detection limit is 150 ng Fe for an SNR = 1, sufficient for changes in the gray matter SPION concentration in the human brain following activation given these acquisition parameters. The 185 mm diameter field of view is sufficiently large to encode a human brain, and in the future this is expected to be 250 mm (following shift amplifier repair). The spatial resolution is sufficient for many functional neuroimaging experiments, which currently often smooth the data to 4-12 mm FWHM [1]. The cooling scheme allows for continuous imaging, without the need for frequent cool-down breaks. Future tests are needed to verify cooling and other stability issues.

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Author's statement

Conflict of interest: Authors state no conflict of interest.

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