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Functional MPI (fMPI) of hypercapnia in rodent brain with MPI time-series imaging

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Abstract

MPI has been proposed as an alternative to fMRI for detecting cerebral blood volume (CBV) changes associated with brain activation due to potentially higher sensitivity, possibly enabling single-patient studies. In this work, we show preliminary neuroimaging data of CBV modulation with hypercapnia acquired in vivo on a rodent MPI scanner designed for time-series imaging. This continuously rotating 2D projection field free line (FFL) imager enables time-series imaging with temporal resolution of up to 3 seconds. As a first demonstration of "fMPI", we acquire time-series images of a rodent brain with 5 second temporal resolution with the animal undergoing alternating 3-minute periods of either hyper- or hypocapnia. Image intensity changes from CBV modulation of the injected SPIONs concentration were detected with a CNR of up to 14 in brain pixels.

I. Introduction

MPI is a high-sensitivity imaging modality with short scan times [1,2]. Together with its ability to directly measure the blood plasma tracer concentration and thus cerebral blood volume (CBV), these features make MPI a promising technology for functional neuroimaging based on CBV contrast [3]. MPI's direct detection of high magnetic moment tracers with no background signal promises high sensitivity. Sufficient sensitivity increases over other modalities could potentially allow the study of functional neuroactivation on a single-patient level – a crucial step toward clinical diagnostic application of functional neuroimaging. Spectroscopic detection of global CBV changes in rodents undergoing a similar hyper-/hypocapnia challenge has been previously shown with a single-sided magnetic particle detector [4]. Here, we present preliminary in vivo imaging data showing CBV modulation from a hyper¬capnia challenge in a time series of images.

II. Experimental apparatus

The overall system concept for the imager has been pre¬viously described [5,6]: NdFeB permanent magnets produce the FFL (gradient ~2.8 T/m) and diamond-

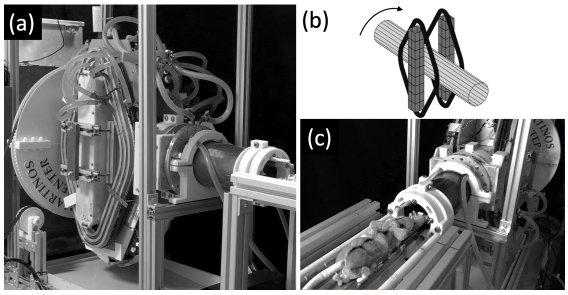

Figure 1: (a) The rotating part of the FFL imager setup. Note the slip rings close to the front part of the frame. (b) Illustration of the imager showing the copper bore, the magnets and shift coils. (c) Demonstration of rat setup with a toy rat model.

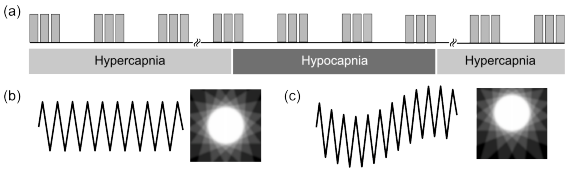

Figure 2: (a) A block diagram of the experiment sequence. Hyper- and hypocapnia periods are periodically alternated during imaging with a duty cycle of 50 %. (b) Traditional shift current waveform with simulated sensitivity map of the 2D slice. (c) Shift waveform with low-frequency modulation as described in the main text and the shifted sensitivity map.

shaped, water-cooled shift coils sweep the FFL across the projection axis, c.f. Fig. 1a-b. The Litz-wire solenoid applies a 25 kHz drive field colinear with gradiometer receive coils inside a stationary copper tube bore. The rotary position is tracked by an absolute rotary encoder. Power and water are applied to the shift coils using slip rings to enable continuous rotation and thus continuous time-series imaging.

The drive signal is produced by an NI PXI DAQ system, amplified by an AE Techron 7548 power amplifier, and filtered by a custom high-power low-pass filter. Unlike most MPI systems, the current implementation detects only on $3f_0$.

The experiment is controlled by custom software implemented in LabVIEW (National Instruments, Austin, TX). The highly parallelized architecture allows real-time image reconstruction and post-processing of the acquired projection data during imaging. The system enables continuous imaging with temporal resolution of less than 3 sec without pausing the data acquisition between images. The system is able to detect 100 ng Fe Vivotrax (Magnetic Insight, Alameda, CA) with an average SNR of 5:1 in 5 sec. The animal is placed on a home-built 3D-printed bed as seen in Fig. 1c. A stepper motor allows a precise and reproducible positioning. The rat bed includes water-tubing for heating the animal under anesthesia and manages the necessary breathing tubes, intravenous and arterial lines.

III. Experiment sequence

The imaging sequence is shown in Fig. 2a: Three 5 sec images were acquired followed by a cooling pause of 15 sec to allow air-cooling of the drive coil. This sequence was repeated throughout the hyper-/hypocapnia alternations. The gantry rotated continuously every 10 sec producing a ∼35 mm FOV image every $\frac{1}{2}$ cycle, and the triangular waveform current applied to the shift coils had a frequency of 2.7 Hz yielding 27 projections per cycle.

The animal preparation followed our previous work [7,4]. Two Sprague-Dawley rats were imaged. Anesthesia was induced using 3 % isoflurane for surgical implantation of femoral venous and arterial catheters and a tracheostomy fitting for ventilation. During imaging, anesthesia was maintained by 1-1.5 % isoflurane. Hyper- and hypocapnia were induced manually every 3 min and time stamps were recorded in synchronization with the image acquisition. Hypocapnia was induced with hyperventilation of normal air by raising the respiration rate to 55 breaths per minute (BPM). Hypercapnia was induced with ventilation of a 5 % CO_2 air mixture at a moderately depressed respiration rate of 35 BPM. A 25 nm core PEG coated SPION was used (Ocean Nanotech, SP-025, San Diego CA USA) and injected shortly before the sequence. The injected dose was typically around 30 mg/kg and the injection rate ∼40 ml/hr.

Because the rodent brain is relatively high in the imaging bore, a FOV translation was introduced by adding a very low-frequency sinusoidal modulation to the shift current frequency-matched to the rotation with a phase chosen to shift the FOV in the desired direction in the xy plane, cf. Fig. 2b-c. In the stationary reference frame of the sample, this low-frequency component appears as a DC FFL shift.

IV. Results and discussion

To reconstruct the imaging data, we use a model-based preconditioned conjugate gradients minimization instead of a simple filtered back-projection. The model utilizes the measured angular position and shift current waveform to account for experimental deviations. The FFL was convolved with a Gaussian profile to give it a finite width. To stabilize the reconstruction, a Tikhonov regularization is applied to penalize noisy solutions. In addition, the Tikhonov matrix incorporates the weighted sensitivity profile to suppress solutions with large signal contributions from pixels where the sensitivity is expected to be small.

For the time-series analysis of each image pixel, we implemented a generalized linear model (GLM) of the acquired time-series signal, which includes a hemodynamic response function, constant and linear signal drift terms, and nanoparticle clearance/uptake. The latter is

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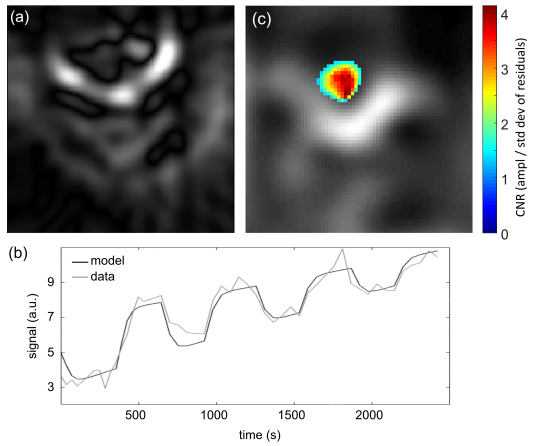

Figure 3: (a) A single MPI image from the time series. The slice is acquired approximately 2 mm ventral of bregma. (b) Signal intensity together with the GLM for a single voxel in the brain region. (c) Contrast-to-noise ratio map for the GLM fit. The functional activation of the brain region is clearly visible.

described by two exponential decay rates, τ_1 for the impulse response and τ_2 for the overall signal decay due to SPION clearance. The GLM is fit voxel-wise to the signal intensity time-series (Fig. 3b) yielding a map of the CBV response, c.f. Fig. 3c.

V. Conclusions

The presented work shows in vivo brain imaging of hemodynamic modulation in the rodent brain using MPI with relatively high CNR and temporal SNR sufficient to track dynamic changes in CBV. Further improvements can be performed and are underway, e.g. better cooling of the coil systems is needed to increase the imaging duty cycle (potentially doubling the number of images per hypercapnia cycle) and co-registration with CT or MRI images will provide anatomical information important in the interpretation of the MPI images. Nevertheless, the data presented here demonstrate the potential for MPI as an imaging modality for studying in vivo brain activity, advancing toward our goal of single-patient sensitivity.

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Author's Statement

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