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Measurement of cerebral blood volume modulation in non-human primates

Alex C. Barksdale[1,2,*]· Frauke H. Niebel[2,3,4]· Jorge Chacon-Caldera[2,5]· Monika Śliwiak[2]· John M. Drago[1,5,7]· Eli Mattingly[2,7]· Matthias Graeser[3,6]· Hong P. Deng[2]· Joseph B. Mandeville[2,5]· Lawrence L. Wald[2,5,7]

[1]Department of Electrical Engineering and Computer Science, MIT, Cambridge, MA, USA
[2]Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, USA
[3]Fraunhofer Research Institution for Individualized and Cell-Based Medical Engineering IMTE, Lübeck, Germany
[4]Institute of Medical Engineering, University of Lübeck, Lübeck, Germany
[5]Harvard Medical School, Boston, MA, USA
[6]Chair of Measurement Technology, University Rostock, Rostock, Germany
[7]Harvard-MIT Division of Health Sciences & Technology, Cambridge, MA, USA
*Corresponding author, email: alexbark@mit.edu

Abstract

MPI offers a promising alternative to fMRI for detecting changes in cerebral blood volume (CBV) during brain activation, potentially enabling single-patient functional brain mapping. We assess our human-scale MPI brain scanner by imaging anesthetized non-human primates, achieving continuous imaging with 5 s temporal and 7 mm spatial resolution. We successfully detect CBV modulations during alternating cycles of hypercapnia and normocapnia, achieving a CNR of up to 7.9 following activations in the brain region.

I. Introduction

MPI [1] is well-suited for CBV-based neuroimaging, directly measuring superparamagnetic iron oxide nanoparticle (SPION) concentrations. Blood-pool confinement allows for a direct correlation with CBV [2] and potentially enhances sensitivity compared to fMRI. In rat hypercapnia studies, functional MPI (fMPI) achieved a CBV contrast-to-noise ratio (CNR) up to six times greater than fMRI at 9.4T [3]. As human-scale MPI brian scanners develop [4–8], the lack of a clinically approved SPION tracer for MPI necessitates testing in non-human primates to explore clinical viability. This work presents the first images and preliminary hypercapnia time-series measurements of CBV changes in the primate brain using a human-capable MPI scanner [5].

II. Materials and Methods

Details of our human-capable MPI scanner can be found in [5]. Our FFL rotates at 0.1 Hz, yielding a 5 s temporal resolution. The system has a 7 mm spatial resolution, and a 65 ng Fe detection limit at SNR = 5 in a 5 s phantom image. Images are formed using iradon reconstruction, and smoothed to the native 7 mm resolution using a gaussian kernel. We acquire images in a psuedo-continuous manner, capturing 5 images followed by a 1 image pause.

After protocol approval from our Institution's animal ethics committee insuring adherence to ARRIVE guidelines, we studied an adult rhesus macaque weighing 7 kg over two sessions. Anesthesia was induced with ketamine/xylazine and maintained using 1% isoflurane after xylazine reversal. The NHP was placed on

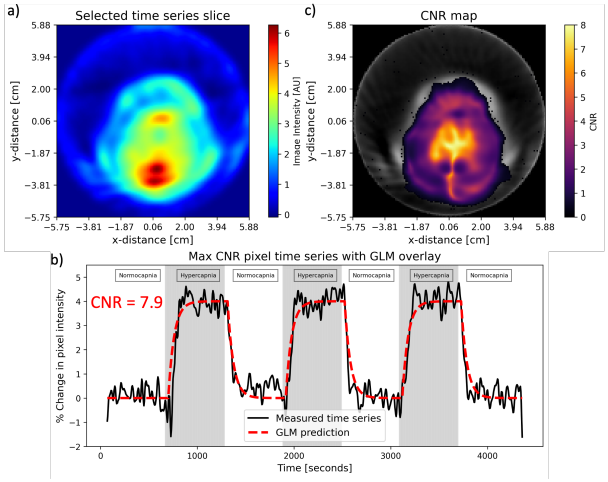

Figure 1: (a) Slice chosen for hypercapnia time series acquired as a 5s image. (b) Percent change in pixel over time series, with cubic order polynomial baseline subtracted. (c) CNR map overlaid on average time series image for individual pixels.

a heated removable bed where they remained for the duration of the experiment. Physiological monitoring included blood pressure, pulse oximetry, respiration, and end-tidal CO2. We slowly injected 10 mg Fe/kg dextran/PEG-coated Synomag-D 70nm SPIONs (Micromod, Germany, Lot # 18224104-01) followed by a saline flush. Under hypercapnia, the macaque was venitlated with 5% CO_2, 30% O_2, (balance N_2), while normocapnia used 30% O_2, (balance N_2).The experiment included three cycles of alternating normocapnia and hypercapnia, each lasting 10 minutes, totaling 70 minutes.

III. Results

Figure 1a illustrates the slice chosen for the hypercapnia time series acquired in a single 5s image. In our preliminary analysis, we fit a generalized linear model (GLM) with a cubic polynomial baseline and an exponentially ramped binary activation function shown in Figure 1b. We detected hypercapnia activation with a CNR of up to 7.9 within the brain region. CNR is computed as signal change from hyper/normo capnia divided by the GLM residual standard deviation. Finally, we construct a CNR map overlaid on the average time series image by fitting the GLM pixel-wise in Figure 1c.

IV. Discussion and conclusion

This study presents preliminary in-vivo brain imaging measurements capturing hemodynamic changes in the non-human primate brain under hypercapnia, the first functional time series using MPI. We successfully tracked CBV modulations with good contrast-to-noise ratio (CNR) although further noise-source elimination and processing enhancements could improve CNR and temporal SNR. Additionally, MPI images benefit from coregistration with MRI or other anatomical context, since the spatial resolution (7 mm) is relatively low. Despite these limitations, our findings represent a crucial step toward using MPI for functional brain imaging and advancing single-patient imaging in clinical neuroscience.

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Author's statement

Conflict of interest: Authors state no conflict of interest.

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