Functional Blood Volume Imaging (fBVI) using Blood Pool Gadolinium Contrast Agent Gadofosveset Trisodium

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Introduction:
T2*-based BOLD (Blood Oxygenation Level Dependent) imaging is the commonly used functional MRI (fMRI) technique, which depends on complex interactions between multiple physiological processes and has inherent resolution limits due to sensitivity to large veins. Gadofosveset trisodium is a blood pool T1 contrast agent with a relatively long plasma half-life). During brain activation, the cerebral blood volume changes in response to stimuli [2]. With a persistent blood pool T1 contrast agent, changes in blood volume in response to functional activation leads to signal changes on T1-weighted images. T1-weighted based functional Blood Volume Imaging (T1-fBVI) has the potential advantage of achieving high-resolution and relatively distortion-free activation maps without the common T2*-weighted artifacts. Here, we demonstrate the first proof-of-concept of the use of T1 blood pool contrast agent for fBVI in a human subject.

Materials and Methods:
This study was approved by the local Institutional Review Board. MR imaging was performed at 3T with an 8-channel head coil (MR750, GE Healthcare, Waukesha, WI). Subjects were scanned after informed consent with the following protocol: A 3D T1-weighted inversion recovery spoiled gradient echo (SPGR) sequence covering the entire brain was acquired. Five minutes after the injection of Gadofosveset Trisodium (Ablavar, Lantheus Medical Imaging, Inc., USA) (20ml, body weight = 84kg), T1-fBVI was performed using a new high spatio-temporal resolution 3D dynamic SPGR technique [3] called DISCO (DIfferential Sub-sampling with Cartesian Ordering) that uses a pseudo-random variable density k-space segmentation and a view sharing reconstruction to provide high spatial resolution images with a temporal resolution of ~3.5s (TR = 4.4ms, TE = 1.2/2.2ms, FOV = 22cm, in-plane resolution = 1.7x1.7mm, 32 slice thickness of 4mm, BW=166.7khz, Flip angle = 45 degrees, ARC factor = 2). Subjects performed 3 epochs of 48s of right hand finger tapping and 4 epochs of 48s of rest in alternation. The T1-fBVI images were processed using FSL. They were registered to correct for subject motion effects and smoothed with a Gaussian kernel with a full-width half height of 5mm. Independent Component analysis (ICA) was performed for model free analysis of the T1-fBVI data. The components were sorted according to the correlation coefficient of the time course/mixing matrix with the boxcar function of the paradigm.

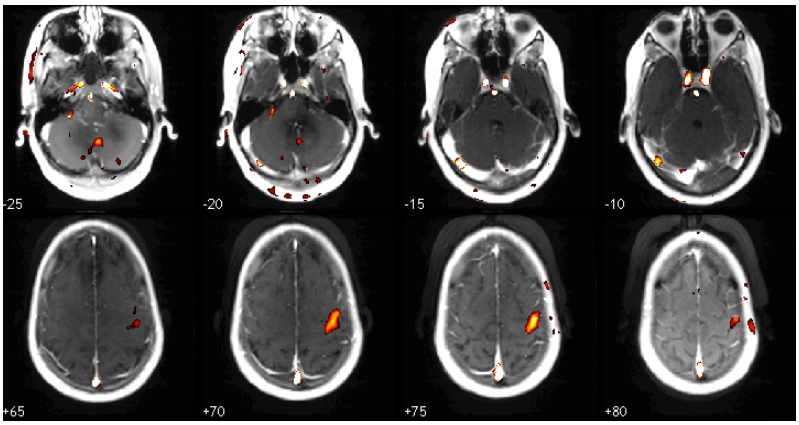

Fig 1: Activation map overlaid on the mean source DISCO image.

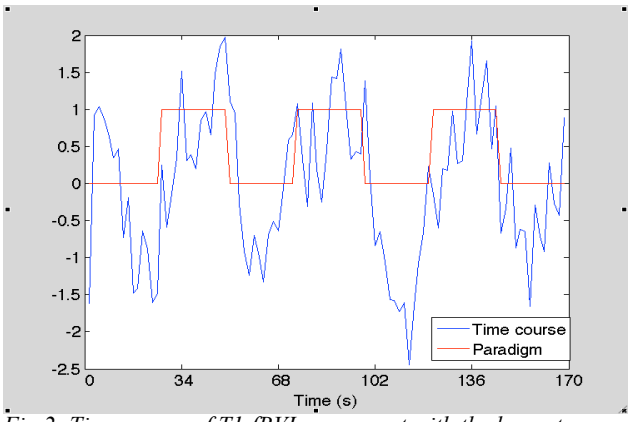

Fig 2: Time course of T1-fBVI component with the largest correlation coefficients with the paradigm boxcar function.

Results:
Nineteen independent components were identified. The largest correlation coefficient of the time courses with the paradigm boxcar function was 0.51. The corresponding spatial maps and time course are shown in Figures 1 and 2 respectively. The expected activation of the left motor cortex was observed. There is also activation in the cerebellum. Interestingly, strong activation in the feeding arteries and the sagittal sinus was also found. The fluctuations in the arterial supply and venous drainage may lead to a better future understanding of the hemodynamics in fBVI.

Discussion and Conclusion:
To our knowledge, this is the first study demonstrating the feasibility of using T1 blood pool contrast agents for CBV-based fMRI imaging. Activation was observed in the expected motor cortex of the brain. The cause of activation of arteries and veins is not currently understood. In the current technique, volumetric excitation was used, which eliminates the in-flow based effects that could also be used for functional mapping [4]. Further developments are underway to improve the contrast to noise ratio of T1-fBVI, which would enable a more precise mapping of brain function with high spatial resolution and reduced distortion.

References: [1] Ogawa, S. 1990. MRM. 14: 68–78. [2] Lu H. 2003. MRM. 50:263-274 [3] Saranathan M. 2011. Proc ISMRM, p2941. [4] Kwong K. 1992. PNAS. 89:5675-5679.

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