Diffusion-weighted Resting-state Functional MRI at 3T

Joe S Cheng[1,2], Iris Y Zhou[1,2], Hua Guo[3], Patrick P Gao[1,2], Russell W Chan[1,2], Queenie Chan[4], Henry Ka Fung Mak[5], Pek Lan Khong[5], and Ed X Wu[1,2]

[1]Laboratory of Biomedical Imaging and Signal Processing, The University of Hong Kong, Hong Kong, Hong Kong, [2]Department of Electrical and Electronic Engineering, Hong Kong, Hong Kong, [3]Biomedical Engineering & Center for Biomedical Imaging Research, Tsinghua University, Beijing, China, [4]Philips Healthcare, Hong Kong, Hong Kong, [5]Diagnostic Radiology, The University of Hong Kong, Hong Kong, Hong Kong

INTRODUCTION: Resting-state functional MRI (rsfMRI) using blood-oxygen-level-dependent (BOLD) contrast has emerged as a valuable tool for mapping functional connectivity in normal and diseased brains [1]. To date, most rsfMRI studies have used T2*-weighted gradient-echo (GE) echo planar imaging (EPI) due to its robust sensitivity [2]. Alternatively, spin-echo (SE) EPI provides better spatial specificity due to the elimination of static dephasing around large vessels [3]. At 3T, the benefit is however limited because of a nearly equal share of undesired intravascular (IV) contribution and well-localized extravascular (EV) contribution from capillary bed and smaller vessels [4]. IV components can be eliminated using small diffusion-weighted (DW) gradients [5]. DW gradients induce velocity-dependent phase shifts and thus reduce signal from blood due to inhomogeneous velocities within vessel and presence of vessels with different orientations in a voxel. In this study, we investigated rsfMRI connectivity spatially and spectrally using SE-EPI with moderate diffusion weighting at 3T to suppress the effect of EV and IV contributions from large vessels.

METHODS: **Participants:** Six right-handed subjects (F/M=3/3, median age =24 yrs) took part in the study. **Data acquisition:** MRI was performed on a 3T scanner (Achieva Philips) with an 8-channel SENSE head coil. High-resolution anatomical images were acquired using a 3D MPRAGE T1-weighted sequence with TR/TE= 7.1/3.2 ms, FA=8 ^{o} and 1.0 mm isotropic voxel. Resting-state images were acquired with the identical spatial resolution (3.75x3.75x4mm^3, slice gap =1mm) and geometry, and within 4 different acquisition sessions: (**1**) session #1 using GE-EPI with TR/TE = 2500/30ms, FA=90^{o}, number of slices (NSlice) =33 and number of dynamic scans (Ndyn) =120; (**2**) session #2 using DW SE-EPI with interleaving b-values of 0 and 200 s/mm^2 (b0b1) along slice direction, TR/TE = 2000/70ms, FA=90^{o}, NSlice =17 and Ndyn =240; (**3**) session #3 using SE-EPI with b=0 (b0b0); and (**4**) session #4 using SE-EPI same as session #3 but with b=200 s/mm^2 (b1b1). Sessions #3 and #4 were intended to examine whether the potential slow-decaying gradient eddy currents due to diffusion gradient switching in session #2 could affect the rsfMRI. **Data analysis:** First, for 3 SE-EPI sessions, interleaved datasets were separated into two sub-sessions (b0 and b1), resulting in an effective temporal resolution as 4s and Ndyn=120. For both the resulting 6 sub-sessions and GE-EPI session data, rsfMRI analysis was carried out using FSL 4.1.7 (www.fmrib.ox.ac.uk/fsl). Preprocessing included motion correction, skull removal, spatial smoothing with 5mm, deletion of the first 5 volumes and high-pass filtering with a 0.01Hz cutoff. EPI images of all subjects were registered together in two steps: EPI to T1 (DOF =7) and T1 to MNI standard (DOF=12). ICA implemented in MELODIC v3.10 was employed on each group of b0, b1 and GE-EPI [6]. The number of network components was set as 70 for b1, 20 for b0 and automatically estimated for GE-EPI. Then we used dual-regression to identify subject-specific temporal dynamics for power spectral density estimates and associated spatial maps. Spatial maps were z-transformed. Functional connectivity strength was calculated as the averaged z-scores within an ROI around the posterior component of default mode networks (center cluster coordinates in mm: x=4, y= -63, z=28 and cluster size = 90).To examine any contamination coming from the slow-decaying eddy currents associated diffusion gradient switching, we performed correlation between the interleaving b0b1 and b0b0 or b1b1 protocols. Correlation was also used to evaluate the interrelation between functional connectivity strength obtained by b0 and b1 of b0b1 protocol.

RESULTS: Fig.1 shows that functional connectivity strength of the b0 of b0b1 was comparable to 1st b0 of b0b0, and that the b1 of b0b1 was also comparable to 1st b1 of b1b1. These results indicated that any potential slow-decaying eddy current effects on rsfMRI coherence analysis were negligible (Spatial maps for GE-EPI, 1st b0 of b0b0, 1st b1of b1b1 are not shown). Fig. 2 shows the default mode networks (DMNs) maps derived from b0 and b1 of b0b1 method, covering medial parietal (posterior cingulate (PCC) and precuneus) and medial prefrontal cortex (mPFC). DMNs map from b1 data was generally of smaller spatial extent around PCC and lower z-scores. In addition, scatter plot of functional connectivity strength of b0 vs. b1 in b0b1 protocol confirmed that DMNs of b1 was of lower strength than b0. More interestingly, the power spectral density (PSD) of b1 DMNs shifted to higher frequency (Fig. 3). Note that SNR decreased less than 20% in b1 images when compared to b0.

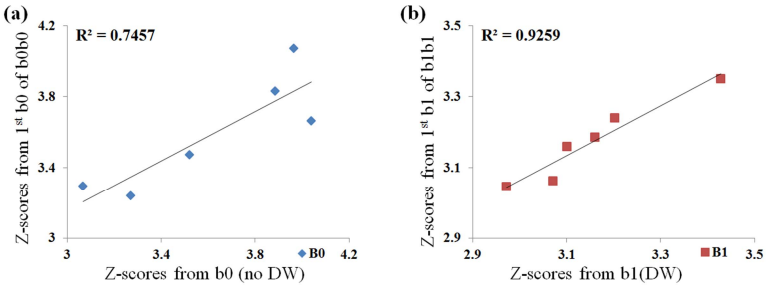

Fig.1: Scatter plot of functional connectivity strength (in z-scores) of b0 of b0b1 vs. b0 of b0b0 (a) and b1 of b0b1 vs. b1 of b1b1 (b). b0: no DW with b=0; b1: DW with b=200 s/mm^2.

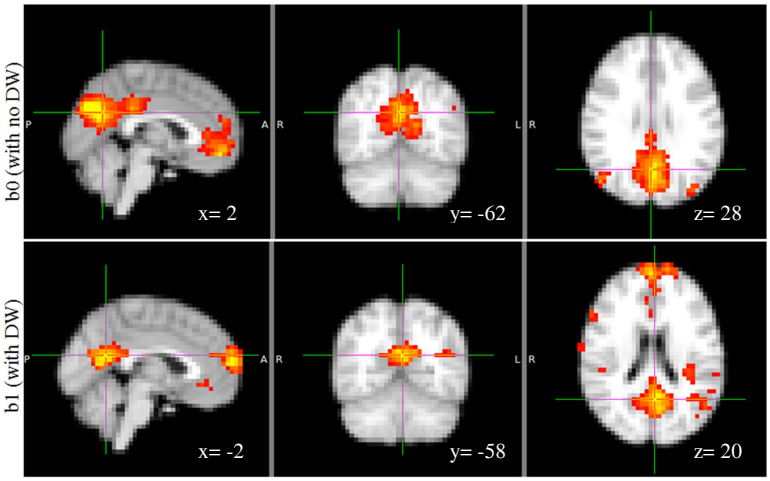

Fig.2: Group ICA identified DMNs spatial maps for b0 (no DW) and b1 (DW) datasets of b0b1 protocol. Z threshold =4. Crosses were placed on the z-scores' center-of-mass for the medial parietal cortex. The coordinates referred to MNI space

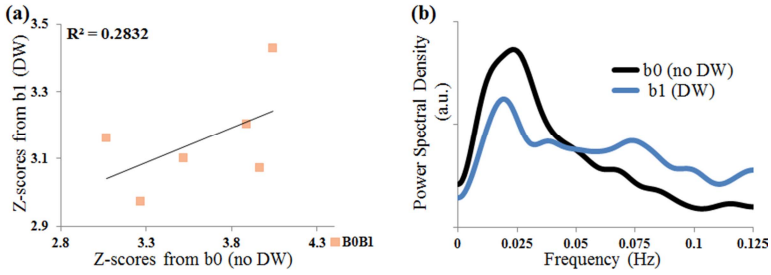

Fig.3: Spatial and spectral comparison between b0 (no DW) and b1 (DW) of b0b1. Scatter plot of DMN functional connectivity strength (in z-scores) of b0 against b1 indicated decreased strength in b1 DMN (a). Averaged power spectral density of b1 shifted to higher frequency when compared to b0.

DISCUSSIONS AND CONCLUSIONS: In this study, we eliminated the EV and IV contributions from large vessels to rsfMRI by implementing diffusion weighting. SE-EPI protocol with interleaving b=0 and b= 200 s/mm^2 (b0b1) identified DMNs with similar but different patterns in b1 when compared to those in b0. Spatially, although z-scores were lower (indicating lower sensitivity), b1 DMNs became more focused to PCC, a key hub for functional and structural connectivity with high baseline metabolic rates [7]. Spectrally, the difference observed in b0 and b1 power spectrum might be related to the frequency signatures of various components contributing to rsfMRI signal. We conjecture that in BOLD, small vessels contribute to higher frequencies more than large vessels, resulting in an overall up-shift in the spectrum. Future study combining higher resolution and diffusion weighting may enable us to probe rsfMRI connectivity networks with improved spatial specificity.

REFERENCE: [1] Fox M. D. and M. Greicius. Front Syst Neurosci 4:19. [2] D. G. Norris, Neuroimage 62, 1109-1115. [3] S. G. Kim and S. Ogawa. JCBFM 32, 1188-1206. [4]T. H. Jochimsen, et al. MRM 52, 724-732. [5]A. W. Song, et al. MRM 35, 155-158. [5] C. F. Beckmann, et al. Philos Trans R Soc Lond B Biol Sci 360, 1001-1013. [6]D. Tomasi and N. D. Volkow. PNAS 107, 9885-9890.