Investigation of fMRI Induced Resonance Frequency Shifts at 7T

Marta Bianciardi[1,2], Peter van Gelderen[1], and Jeff H Duyn[1]
[1]*Advanced MRI Section, LFMI, NINDS, National Institutes of Health, Bethesda, MD, United States,* [2]*A.A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Charlestown, MA, United States*

Introduction: Resonance frequency shifts observed from the phase (Φ) of fMRI signals may report on susceptibility changes due to variation in blood volume and oxygen extraction fraction, and therefore may provide information complementary to magnitude signals. Nevertheless, the use of Φ fMRI signals during functional tasks and at rest has been very limited so far compared to the use of magnitude (M) signals because of the large contribution of physiologic and instrumental noise. In previous work at low fields, fMRI Φ maps generally display only few sparse voxels representing the largest veins, or are very noisy [1-2]. We investigated whether Φ could be detected more sensitively when using advanced technology (7T scanner, array detectors) and optimized processing methods to remove noise contributions.

Methods: 8 subjects (4m/4f, age 30±3) participated in the IRB-approved study. Multi-echo GE-EPI SENSE-rate3 BOLD-fMRI was performed at 7T (GE-Medical-Systems) using 32 receive-only coil elements and parameters: echo-time = 31.5 ms, repetition time = 2.3 s, flip angle = 65°, number of slices = 4, voxel-size = 2.5x2.5x2.5 mm^3, number of scans: 158. Two conditions were investigated: 1) visual fixation on a central dot during presentation of a visual stimulus (B/W checkerboard, flickering at 7.5Hz, block-design: 34.5s OFF/34.5s ON cycle); 2) resting with the eyes closed. For each time-point and voxel, the Φ fMRI images were pre-processed as follows: subtraction of the first Φ time-point; removal of phase wrap from time-course signals, and removal of linear drift over time. The background spatial low-frequency Φ variations were fitted for each slice and time point with a 4^{th} order polynomial function. These signal fluctuations appeared to be correlated to the respiratory chest motion and were employed, on a voxel-by-voxel basis, as physiological noise regressor (Φnoise-regressor) for both M and Φ fMRI data. Physiological and instrumental noise correction [3] was applied on both M and pre-processed Φ fMRI images. This included the removal of noise sources: 1) temporal drifts (3^{rd} order polynomials); 2) noise mostly related to the phase of respiration (Φnoise-regressor); 3) noise related to the phase of cardiac cycle (4 cardiac RETROICOR regressors); 4) signal fluctuations due to changes in the respiratory volume rate and 5) cardiac rate. For removal of noise source 2), Φnoise-regressor was compared to the use of 4 respiratory RETROICOR regressors. The % fMRI signal variance explained (VE, %) by sources 1)-5) was computed at the voxel level as the R^2 value adjusted for the degrees of freedom, multiplied by 100. The stimulus regressor was included as an additional 6) source of variance for the stimulus session only. VE was then averaged across voxels in the visual cortex. Slice-timing correction, motion correction, co-registration between different 4D-volumes was then applied to M and Φ data. M signal fluctuations were converted to % signal changes relative to their time average (ΔM/M, %). M and Φ activity maps ($p < 0.05$ Bonferroni corrected) during stimulation and at rest were obtained respectively by linear regression of each voxel signal with a stimulus regressor and with the average timeseries across voxels of the M task-activation map (after temporal low-pass filtering of rest-data at $f_C = 0.073$ Hz). The Φ signal fluctuation amplitude $<\Delta\Phi>$ was computed as the standard deviation over time of averaged Φ time-courses in common positive and negative Φ and M activity maps. The average change in fractional frequency shift ($<\Delta\omega/\omega_0>$, ppm) was computed from $<\Delta\Phi>$ according to: $<\Delta\omega/\omega_0> = <\Delta\Phi>/(2\pi\gamma_T B_0 TE)$, with $\gamma_T B_0 = 298$MHz.

Results: For each source, VE during visual stimulation in the visual cortex is shown in Fig. 1. Similar results (not shown) for noise sources 1-5) were found at rest. The VE by low-frequency drifts and Φnoise-regressor (~94% and ~20% in Φ and M data, respectively) was higher than the VE by drifts and the respiratory RETROICOR regressors ($p < 0.05$). In addition, when pre-processed with the Φnoise-regressor, Φ activation maps showed much more widespread activity than when pre-processed with the respiratory RETROICOR regressors (Fig. 2). The overlap of Φ and M maps (both positive and negative) was much larger when using the Φnoise-regressor and reached (35.9 ± 2.9) % and (37.3 ± 2.7) % during stimulation and rest respectively, compared to (4.9 ± 1.5) % and (5.0 ± 1.5) % for the RETROICOR regressors. Similar time-courses (Fig. 2C) were observed for Φ and M signals (average absolute correlation value ± s.e. across subjects was 0.52±0.02 and 0.42±0.01 during stimulation and rest, respectively, $p< 10^{-8}$) indicating the same BOLD origin of Φ and M signal changes. $<\Delta\omega/\omega_0>$ (average ± s.e. across subjects) was equal to (0.42 ± 0.03) ppb and (0.31 ± 0.03) ppb during stimulation and rest, respectively.

Discussion and Conclusions: Widespread BOLD-related Φ signal changes/frequency shifts could be detected at 7T by the use of optimized pre-processing to remove unwanted Φ signal fluctuations. The measured Φ signal changes do not seem to be confined to venous sinuses, and are attributed to susceptibility changes in pial and intracortical veins. BOLD Φ signal changes may therefore provide complementary information to BOLD M images and allow quantitative assessment of blood oxygenation.

References: [1] Menon, Magn Reson Med, 47:1-9, 2002. [2] Hahn, Neuroimage, 44:742-52, 2009. [3] Bianciardi, et al., Magn Reson Imag, 27:1019-29, 2009.

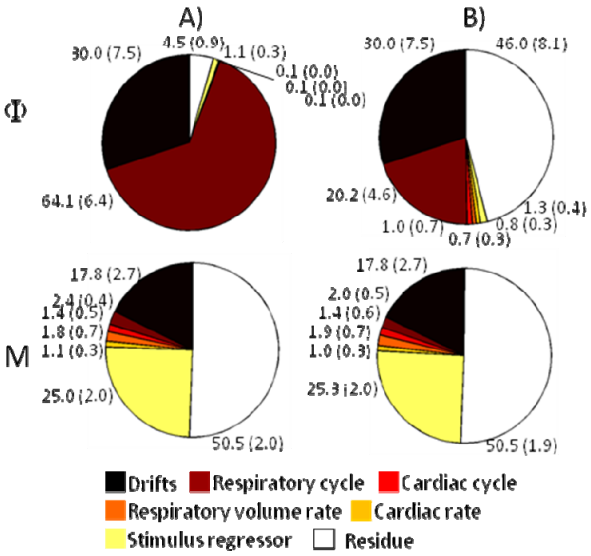

Fig. 1 Pie-charts showing VE of Φ and M fMRI data during visual stimulation relative to sources 1-6 of signal fluctuation (average (s.e.) values across subjects). A) & B) differ only for the regressor used to model source 2: A) Φnoise-regressor; B) respiratory RETROICOR regressors. The residue includes thermal noise, noise related to motion correction (processing step applied afterwards), and residual uncorrected signal fluctuations due to instrumental/physiologic noise, and to neuronal processes.

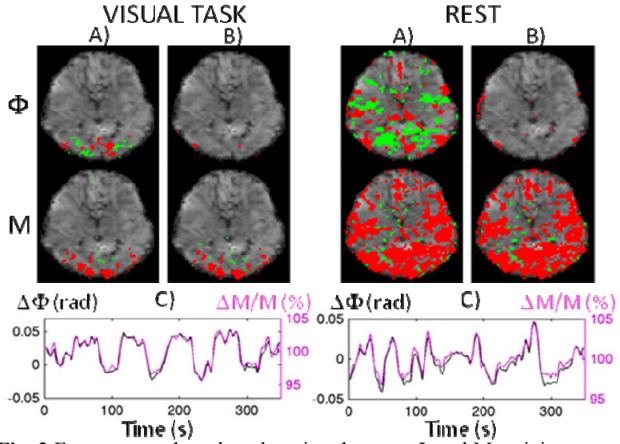

Fig. 2 For an example task and resting data-set: Φ and M activity maps (red/green = positive/negative) after physiologic noise correction including A) Φnoise-regressor, B) respiratory RETROICOR regressors; C) averaged Φ (black) and M (magenta) time-courses in common positive and negative Φ and M activity maps (before averaging across voxels, time-courses in negative activity maps were multiplied by -1).