Estimation of functional changes in blood oxygenation level in large veins from BOLD frequency shift and susceptibility maps

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Purpose: Blood fractional oxygen saturation is an indicator of oxygen delivery and metabolism, and may provide information about tissue function and viability. Current methods employed to estimate changes in the blood fractional oxygen saturation rely on the use of sophisticated fMRI sequences and modeling [1]. We aimed at estimating the functional change in blood fractional oxygen saturation in large veins during task performance by means of fMRI gradient echo echo-planar imaging (GE-EPI) of the signal phase (Φ).

Methods: Two subjects (1m/1f, age 19/24years) participated in the IRB-approved study (data-set1). GE-EPI SENSE-rate3 BOLD-fMRI was performed at 7T (GE-Medical-Systems) using 32 receive-only coil elements and parameters: echo-time (TE) = 31.5 ms, repetition time (TR) = 2.3 s, flip angle = 65°, number of slices (axial oblique) = 4, voxel-size = 2.5x2.5x2.5 mm^3, number of scans: 158. A high-resolution GRE image was also acquired (TE = 16 ms, voxel size = 0.41x0.41x0.41 mm^3, TR = 1.2s, flip angle = 70°). The task employed was visual fixation on a central dot during presentation of a visual stimulus (B/W checkerboard, flickering at 7.5Hz, block-design: 34.5 s OFF/34.5 s ON cycle). For each time-point and voxel, the Φ fMRI images were pre-processed as follows: subtraction of the first Φ time-point; removal of temporal wraps and of linear drift over time. For each slice and time point, the background spatial low-frequency Φ variation mostly related to the phase of respiration cycle was modeled by polynomial spatial fitting (model order 4), and employed as physiological noise regressor (Φnoise-regressor) for both magnitude (M) and Φ fMRI data. Physiological and instrumental noise correction was applied on both M and pre-processed Φ fMRI images on a slice-by-slice basis. This included the removal of: temporal drifts (3^{rd} order polynomials), noise mostly related to the phase of respiration (Φnoise-regressor) and cardiac cycle (four cardiac RETROICOR regressors [2]), and signal fluctuations due to changes in the respiratory volume rate [3] and cardiac rate [4]. Slice-timing correction, motion correction, co-registration between different 4D-volumes was applied to M and Φ data. M signal fluctuations were converted to % signal changes relative to their time average ($\Delta M/M$, %). Fractional frequency shift maps ($\Delta\omega/\omega_0$, ppm) were computed from Φ signal changes according to: $\Delta\omega/\omega_0 = -\Delta\Phi/(2\pi\gamma_T B_0 TE)$, with $\gamma_T B_0$ = 298MHz. $\Delta M/M$ and $\Delta\omega/\omega_0$ task activation maps were obtained by linear regression of each voxel signal with a stimulus regressor (statistical threshold: $p < 0.05$ Bonferroni corrected). A voxel in the sagittal sinus (approximately parallel to the external magnetic field) was identified (blue arrow, Fig. 1B) by inspection of the high-resolution GRE image. The average signal change in $\Delta M/M$ ($<\Delta M/M>$) and $\Delta\omega/\omega_0$ ($<\Delta\omega/\omega_0>$) during stimulation (ON periods) with respect to baseline (OFF stimulation periods) was calculated. Assuming a vessel parallel to the static magnetic field (B_0) and no partial volume effects, the average change in fractional oxygenation during stimulation with respect to rest ($<\Delta Y>$) was calculated as follows: $<\Delta Y> = -3/2 <\Delta\omega/\omega_0>/(\Delta\chi_{oxy\text{-}deoxy}Hct)$, with $\Delta\chi_{oxy\text{-}deoxy}$ = 0.18ppm, Hct=0.4. To overcome frequency shifts dependence on vessel orientation we computed susceptibility changes on a second data-set (1 subject, f, 23 years) with extended data coverage on the z-direction (same GE-EPI parameters as in data-set1 except for the number of slices = 40, orientation coronal). After applying the same processing as for data-set1, susceptibility values $\Delta\chi$ were computed from $\Delta\omega/\omega_0$ by means of Fourier-based computation by masked de-convolution filter ([5], alpha = 0.3) and the average signal change in $\Delta\chi$ ($<\Delta\chi>$) during stimulation with respect to baseline was calculated in the sagittal sinus; $<\Delta Y>$ was computed from $<\Delta\chi>$ according to: $<\Delta Y> = -<\Delta\chi>/(\Delta\chi_{oxy\text{-}deoxy}Hct)$.

Results: The optimized pre-processing (in particular the removal of the Φnoise-regressor) allowed the calculation of good quality $\Delta\omega/\omega_0$ activation maps for both subjects of data-set1 (Fig. 1). The strong anti-correlation (r-value = -0.7 for both subjects) between the $\Delta\omega/\omega_0$ and $\Delta M/M$ time-courses in the sagittal sinus (Fig. 2) confirms the BOLD origin of $\Delta\omega/\omega_0$ signal fluctuations. $<\Delta M/M>$ was = 10.5% and 11.0% in subject 1 and 2, respectively; $<\Delta\omega/\omega_0>$ was = -2.4 and -2.6ppb, yielding a $<\Delta Y>$ of 0.048 and 0.054, respectively in subject 1 and 2. From the second data-set, widespread susceptibility maps were obtained (Fig. 3). $<\Delta\chi>$ and $<\Delta Y>$ in the sagittal sinus were respectively -4.3 ppb and 0.060.

Discussion and conclusions: We have demonstrated the feasibility of measuring changes in blood fractional oxygen saturation in large vessels during visual stimulation from BOLD frequency shift and susceptibility maps obtained by conventional GE-EPI techniques. The obtained change in blood fractional oxygen saturation of 0.05-0.06 is close to that expected for large vessels during activation (0.07-0.1, [6]). The estimate of $<\Delta Y>$ from $<\Delta\omega/\omega_0>$ is robust (< 4% error) provided small estimation errors (< 10^o) in the vessel orientation. Computation of susceptibility changes instead overcomes the orientation dependence and local effects of $<\Delta\omega/\omega_0>$.

References: [1] He and Yablonskiy, Magn Reson Med, 57:115-26, 2007. [2] Glover et al., Magn Reson Med, 44:162-7, 2000. [3] Birn et al., Neuroimage, 31:1536-48, 2006. [4] Shmueli et al., Neuroimage 38:306-20, 2007. [5] Wharton et al., Magn Reson Med, 63:1292-304, 2010. [6] Uludag et al., Neuroimage 48:150-65, 2009.

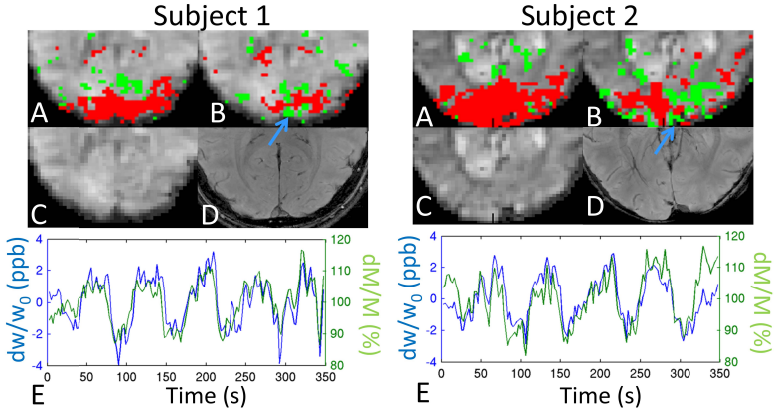

Fig. 1 For each subject of data-set1: A) dM/M, and B) dw/w_0 activation maps (red/green = positive/ negative correlation with stimulus regressor, $p < 0.05$ Bonferroni corrected) overlaid on a magnitude EPI image; C) magnitude EPI image; D) high-resolution GRE image; E) dw/w_0 and dM/M time-courses in the sagittal sinus (the sign of dw/w_0 was inverted for display purposes).

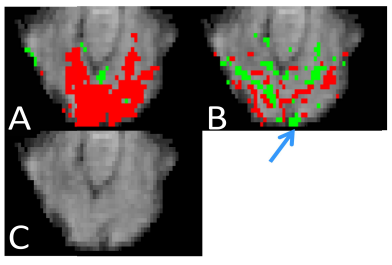

Fig. 2 For data-set2: A) dM/M, and B) d*X* activation maps (red/green = positive/negative correlation with stimulus regressor, $p < 0.05$ Bonferroni corrected) overlaid on a magnitude EPI image; C) magnitude EPI image.