Cerebrovascular reactivity-based calibration of presurgical motor activation maps to improve detectability of the BOLD signal in patients with perirolandic brain tumors

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Introduction: Reduced or impaired cerebrovascular reactivity (CVR) in patients with brain tumors and other cerebral diseases can generate false negative or spuriously decreased BOLD fMRI activation during performance of presurgical mapping of motor and language cortex in patients who are potentially candidates for lesion resection. This phenomenon, referred to as neurovascular uncoupling (NVU) has been documented in the literature as cases of discordance between the results of presurgical BOLD fMRI and intraoperative cortical stimulation or clinical functional status[1]. No gold standard imaging technique is yet available to detect NVU; however, recent studies have shown that CVR mapping using a breath hold (BH) task can detect the potential for NVU in both patients with low grade and high grade gliomas[2, 3]. In the past a model has been proposed to calculate activation maps in a group of normal volunteers calibrated by the mean group BH CVR. In this study we applied a new calibration technique to individual patient motor activation maps calibrated by BH CVR at a single subject level in five patients with perirolandic low grade gliomas.

Materials and Methods: Five patients with perirolandic low grade gliomas referred for presurgical motor mapping with BOLD fMRI were included in this pilot study, approved by the Institutional Review Board. Images were acquired on a 3T Siemens Trio scanner. Structural imaging included a 2D T2 FLAIR (TR=9000 ms, TE=115 ms, TI=2500 ms, voxel size 1.0x1.0x3.0 mm^3) sequence. A T2* GRE single shot EPI BOLD sequence (TR=2000 ms, TE=30 ms, voxel size 3.75x3.75x4.0 mm^3) was used for functional imaging. Patients performed a battery of tasks (3 minutes long with 30 second blocks of rest alternating with 30 second epochs of motion) to map the motor cortex including a bilateral self-paced finger tapping task, a vertical tongue movement task and a bilateral foot flexion and extension task. They performed also a 4 minute long BH task (40 seconds normal breathing alternating with 16 seconds of BH repeated 4 times) for CVR mapping. Standard activation maps, expressed as T-value maps for the motor tasks and BOLD percentage signal change (PSC) maps for the BH task, were created using GLM analysis. A ROI ipsilateral to the lesion ("ipsilesional,"IL), including the lesion and surrounding cortex up to two gyri away from the lesion margins, and a contralateral ROI (CL) including equivalent normal tissue were drawn. Subsequently for each patient BH CVR calibrated maps were generated for the task, whose expected ipsilesional activation was reduced or absent due to reduced CVR, using the following algorithm voxel wise in the ROIs:

$$t_{calib} = t_{meas}\left(1 - x + x\frac{\overline{S_{BH\_CL}^{average}}}{S_{BH}}\right) \qquad x = \begin{cases} 1 & \text{elsewhere} \\ 0 & \text{if } t_{meas} < t_{thr} \text{ AND } S_{BH} > 0.5 * S_{BHmean\_IL} \end{cases}$$

where t_{calib} represents the BH CVR calibrated t-value, t_{meas} the standard t-value $\overline{S_{BH\_CL}^{average}}$ is the average BH PSC in the CL ROI, S_{BH} is the PSC after BH, t_{thr} is the threshold used in generating the standard t-value activation maps and S_{BHmean_IL} is the average BH PSC in the IL ROI. To assess the effect of BH CVR calibration on activation, contrast maps were created by subtracting standard T-maps from calibrated T-maps. The difference in activation was considered statistically significant at $p<0.05$ level.

Results: Figure 1 shows an example of standard thresholded t-map, the BH CVR-calibrated map and contrast map in one patient who performed a finger tapping task. In Table 1 the average CVR in the IL and CL ROI and the number of voxels where the t-value difference before and after calibration was significant in the IL ROI are reported. In all cases reduced CVR was present in the IL ROI and after BH CVR normalization in the IL ROI the increase of activation was statistically significant.

Discussion and Conclusions: In this preliminary study we demonstrate the feasibility of minimization of false negative motor task-based activation through normalization of t-value activation maps accounting for ipsilesional decreases in regional CVR.

References: 1)Ulmer *et al*. AJNR 2003; 24:213. 2) Pillai and Zacà. TCRT 2012; 11:361. 3) Zacà and Pillai ISMRM 2012.

Table 1: Number of voxels in the IL ROI where difference of activation was statistically significant ($p<0.05$) before and after calibration and average CVR (BOLD PSC) in the IL and CL ROI

			Number of voxels IL ROI	CVR measurement (BOLD BH PSC)	
	Task	Threshold	Diff p<0.05	IL ROI	CL ROI
Case 1	Finger Tapping	9.5	35	0.562	0.9889
Case 2	Finger Tapping	4.5	45	0.0322	0.1672
Case 3	Finger Tappng	4.5	29	0.7669	1.0094
Case 4	Foot Motor	8.5	54	0.3853	0.6002
Case 5	Tongue Motor	3.5	13	0.0347	0.1663

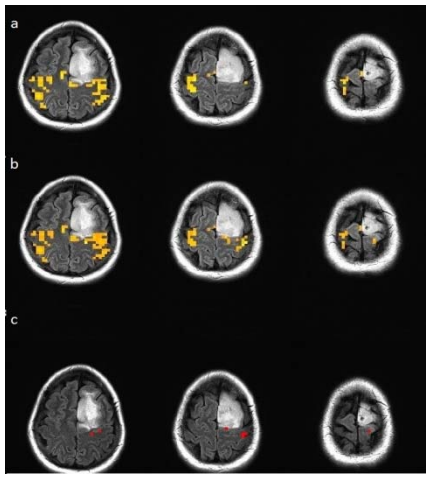

Figure 1: The top row shows a standard BOLD activation map (t<9.5) obtained during performance of a bilateral finger tapping task by a patient. The middle row corresponds to the breath holding calibrated map and the last row shows voxelwise statistically significant differences in t-value between the pre and postcalibrated maps at the $p<0.05$ level