HYPEROXIC BOLD CONTRAST IN PATIENTS WITH UNILATERAL ARTERIAL STENO-OCCLUSIVE DISEASE—COMPARISON WITH ^{15}O POSITRON EMISSION TOMOGRAPHY

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Target audience: Neuroradiologists, Neurologists, Neurosurgeons

Background and Purpose: Cerebral blood flow (CBF), cerebral metabolic rate of oxygen ($CMRO_2$), oxygen extraction fraction (OEF), and cerebral blood volume (CBV) can be measured with positron emission tomography (PET) with ^{15}O-labeled water, O_2 and CO. ^{15}O PET has been used clinically to see the misery perfusion: decreased CBF but relatively maintained $CMRO_2$. Recently, the blood oxygenation level-dependent (BOLD) contrast with hyperoxia (oxygen challenge) has been shown to possibly delineate the ischemic penumbra, corresponding to the region of misery perfusion. [1] We aimed to validate the ability of BOLD contrast imaging with mild oxygen challenge to estimate severity of ischemia in patient with arterial steno-occlusive disease. The BOLD contrast with hyperoxia was compared with the quantities obtained by ^{15}O PET, which is the gold standard for measuring CBF, $CMRO_2$ and OEF.

Theory: A small fractional change in the BOLD signal between a baseline state and an "activated" state is expressed as:
$\Delta BOLD = TE\ \kappa [dHb]_0^{\beta}\ CBV_0\ (1-(CBV/CBV_0)([dHb]/[dHb_0])^{\beta})$, where the suffix 0 indicates values for the baseline state; TE, the echo time; κ, a constant; [dHb], the concentration of deoxyhemoglobin in venous blood; β, assumed to be 1.5. [2] To compare ΔBOLD with PET data, we can calculate $[dHb]_0^{\beta}\ CBV_0$ using PET data. [dHb] = [Hb] (1- Sv), where [Hb] is the concentration of hemoglobin and Sv denotes the venous oxygen saturation, which can be calculated from the values of [Hb], arterial partial pressure of oxygen (PaO_2), and $CMRO_2$/CBF.

Methods: *Data acquisition*- We recruited 15 patients (13 men, 2 women; mean age, 64.5 years; range, 47-77 years) with unilateral chronic steno-occlusive disease of the internal carotid (IC) or middle cerebral artery. They were referred to our institute for evaluation of the state of cerebral hemodynamics and metabolism and gave informed consent to this study. Patients with history of recent cerebral infarction were excluded. Our institutional review board approved the study. After scanned on a 3T Siemens Verio system with a 32-channel head receive coil, ^{15}O PET study (acquisition of CBF [resting and CO_2 challenge to obtain cerebrovascular reactivity (CVR)], $CMRO_2$, OEF, and CBV) was performed on the next day. In MRI, an MPRAGE image was acquired with an 1 mm^3 resolution for registration of MRI data with PET data. Q2TIPS sequence [3] was performed with TR/TE, 3000/19 ms; TI_1, 700 ms; TI_2, 2200-2400 ms; a field of view, 25.6-cm; an imaging matrix, 64×64; 5 slices with a thickness of 8 mm (4 mm slice gap). The study consisted of three blocks of mild, moderate, and mild hyperoxia. To avoid for patients to perceive the change in gas deliveries, we adopted a mild hyperoxia as a baseline condition. During the mild (or moderate) hyperoxia, nearly 35% (or 50%) O_2, generated by mixture of room air and medical 100% O_2, was supplied with a facemask for routine clinical use. A nasal cannula was used to monitor partial pressures of end-tidal O_2 and CO_2, which were regarded as PaO_2 and $PaCO_2$, respectively. A series of 22 pairs of tag and control Q2TIPS images were obtained in each of the mildly hyperoxic blocks; 45 pairs of images were obtained in the moderately hyperoxic block. The time between the blocks was about 2 minutes.

Data analysis- All images were transferred to a personal computer and registration was performed with rigid-body transformation. The images were smoothed with a Gaussian kernel (full-width half-maximum of 10 mm). The successive tag and control Q2TIPS images were subtracted to produce a raw CBF map and added to produce a BOLD map [4]. A ΔBOLD map was generated from the BOLD map averaged across the baseline blocks and that averaged in the hyperoxic block. $[dHb_{air}]^{\beta}\ CBV_{air}$ maps were generated by combining clinically obtained [Hb] and PET data of $CMRO_2$/CBF on the assumption of PaO_2 of 100 mmHg at the PET study (breathing room air). The averaged difference between the lesional and contralateral sides (hemispheres) of the brain (LC difference) in ΔBOLD was compared with that in $[dHb_{air}]^{\beta}CBV_{air}$ by linear regression analysis.

Results: Mean PaO_2 was 173 mmHg in the mild hyperoxia and 294 mmHg in the moderate. Mean [Hb], 14.2 g/dL; mean CBF/CBF_0, 1.02. Fig. 1 shows images of a patient with left IC stenosis. Fig. 2 shows a significant correlation between LC difference in ΔBOLD and that in $[dHb_{air}]^{\beta}CBV_{air}$.

Discussion: Increased CBV and increased [dHb] both reflect the misery perfusion. Therefore, the product of these values may be a good indicator to see the degree of ischemia. Fig. 3 shows that CVR is associated similarly or more strongly with ΔBOLD compared with OEF acquired by PET.

Conclusion: Hyperoxic BOLD contrast imaging may be useful to estimate the severity of ischemia in chronic arterial steno-occlusive disease.

References: 1. Dani KA, et al. *Ann Neurol*. 2010;68:37-47. 2. Blockley NP, et al. *NMR Biomed.* 2012;doi:10.1002/nbm.2847. 3. Luh W-M, et al. *Magn Reson Med.* 1999;41:1246-54. 4. Wong EC, et al. *NMR Biomed.* 1997;10:237-49.

Fig. 1. Images of a patient with left IC stenosis. Color images are maps produced form PET data.

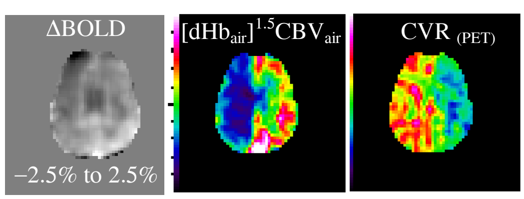

Fig. 3. a. CVR (PET) vs ΔBOLD. b. CVR (PET) vs OEF (PET).

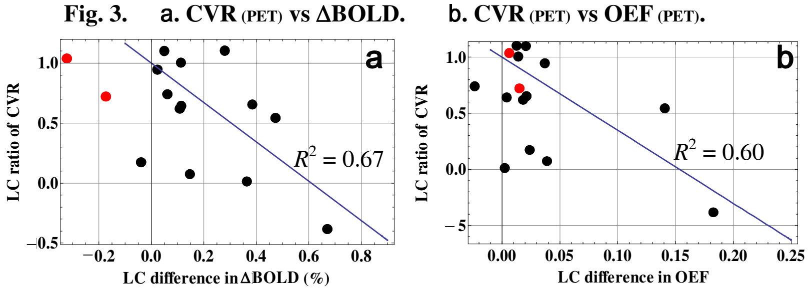

Fig. 2. ΔBOLD vs PET. The solid line shows a regression line excluding red points (patients with large infarct lesions).