Blood-Oxygen Level Dependent (BOLD) MRI of Healthy Human Liver

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Introduction: BOLD (blood oxygen level dependent) contrast is well known as the basis behind brain fMRI. For brain fMRI the O_2 demand changes with activation. In non-brain tissues we have shown that changing O_2 supply (e.g. by breathing 100% O_2) also leads to modulation of BOLD contrast and the signal change is related to blood volume and perfusion **[1]**. BOLD modulation has previously been demonstrated in liver following certain challenges **[2]**, including intake of a standardized meal **[3]**. Therefore, we proposed the liver may exhibit different hyperoxia-modulated BOLD signal behaviors when comparing fasted to postprandial states.

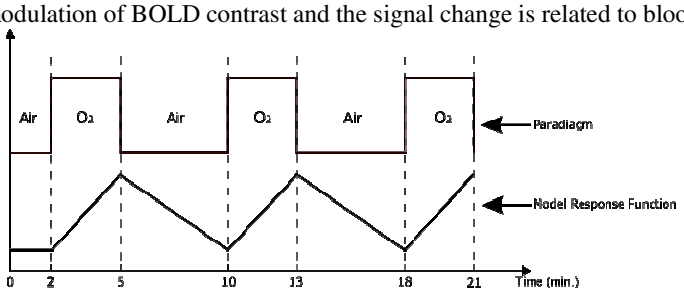

Fig. 1 Cross-correlation analysis using a model function

Methods: In a study approved by our local institutional IRB, healthy fasted human subjects (n=12) were scanned using a GE Signa HDX 3T short-bore MR scanner (GE Healthcare, Milwaukee, WI, USA) and 8-channel torso phased array coil. Subjects were fitted with the standard GE MRI respiratory bellows, placed over the abdominal area with greatest peak-to-peak respiratory motion. Respiratory motion/position was digitized every 4 ms and recorded using an MRIx data acquisition computer (Thulborn Associates, Chicago, IL, USA). Following localization of the hepatic portal bifurcation, a sagittal multiphase T2*-weighted GRE EPI sequence was employed (α=90°, 1 NEX, TE=35ms, TR=1000ms, 24cm FOV, 64×64 matrix, and 8mm thick, 1248 phases, 12 discarded acquisitions, total time=21minutes) before and 15 minutes following a controlled meal (235mL of Ensure Plus, Ross Prod. Div., Abbott Labs, Saint-Laurent, Que., Canada). A sagittal acquisition was chosen to minimize through-plane liver motion and allow free breathing during the scan **[4]**. To modulate liver BOLD contrast, 100% O_2 (15L/min) was cycled with medical air (21% O_2) in three cycles during each BOLD scan (**Fig. 1**). Image post-processing first involved motion correction, based on the correlation coefficient template matching algorithm **[5]**. This was followed by reduction in respiratory noise through a band-stop digital filter, written in Matlab, tailored to individual respiratory fluctuations. The motion-compensated BOLD image sets were finally analyzed using a pixel-wise cross-correlation with a *sawtooth* model function (**Fig. 1**) using the following equation:

$$cc = \frac{\sum_{i=1}^{n}(f_i-\mu_f)(r_i-\mu_r)}{\left[\sum_{i=1}^{n}(f_i-\mu_f)^2\right]^{1/2}\left[\sum_{i=1}^{n}(r_i-\mu_r)^2\right]^{1/2}}$$

where f_i **(*i*=1…n)** and r_i denote the measured pixel time-course and model-function time series, respectively. The calculated correlation coefficient (***cc***) scaled between -1 and 1 (0, uncorrelated). Any pixel time-course with ***cc*** greater than a threshold of 0.35 was considered an "activated" spot and assigned a color code which was superimposed on a T1-weighted image. Correlation analysis was done using AFNI (http://afni.nimh.nih.gov/). The activated pixels were counted and normalized to the total liver pixel number within the motion-compensated region.

Results: Two liver 'types' were observed: 8 subjects showed clear positive (+Ve) enhancement with hyperoxia cycling (44.62±21.11% significant activation) while 2 enhanced strongly negatively (-Ve) (23.39±14.88% significant). Repeat scans on different days gave consistent responses (i.e. either –Ve or +Ve). No matter if the response was –Ve or +Ve, both liver types showed diminished significant enhancement in the postprandial state (**Fig. 2**). This decrease was most significant (P<0.036, paired t-test) in +Ve livers (diminished to 13.41±12.61%).

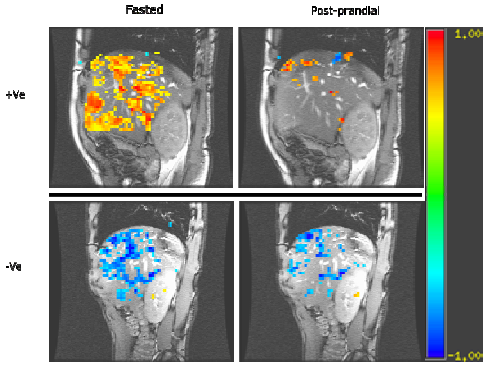

Fig. 2 Hyperoxia-induced +Ve/–Ve enhancement and attenuated effect of the meal

Discussion: The blocked design and sawtooth model function appeared feasible to reveal functional-active regions in liver parenchyma. The postprandial decrease in activated voxels could have been due to the elevated state of metabolism and thus O_2 extraction (+Ve livers). But, 100% O_2 was hypothesized to increase liver BOLD signal due to elevated blood oxyHb, providing everything else remains constant. However, negative enhancement with hyperoxia indicated that other BOLD related factors might also change, for example blood flow. Previous work showed blood flow from gut to the liver via the hepatic portal vein increased following a meal **[6]**. In our study diminished enhancement following a meal provided evidence that a meal may alter the proportions of arterial and portal venous blood, and the influence of arterial blood on BOLD signal change under hyperoxic conditions can be accordingly lowered. The significant diminution occurred in +Ve livers may indicate a pronounced alteration in blood supply. In addition, more subjects appeared to be +Ve's and the resting-state BOLD signal was usually lower in –Ve livers. It is therefore proposed that the concept of "activation percentage" may be a more reliable parameter for function investigation of +Ve livers rather than –Ve livers. Further work is required to verify the utility of this approach.

References: [1] Noseworthy *et al.* (2003) *Sem. MSK Radiol.* 7:307. **[2]** Foley *et al.* (2003) *Magn. Reson. Med.* 50:976; **[3]** Fan *et al.* (2006) ISMRM *abs.*14:3249; **[4]** Noseworthy *et al.* (2006) *Comput Asst. Tomog.* In Press; **[5]** Sussman *et al.* (2003) *IEEE Trans Med. Img.* 22:206; **[6]** Li et al. (1997) *Radiology* 204:71.