BOLD Phantom Investigations of the Relationship between Blood Oxygenation, Flow Variation and Intra- and Extra-vessel Signal Change

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<u>Introduction:</u> Deoxyhemoglobin ($dHbO_2$) is paramagnetic and can serve as an endogenous contrast agent causing signal loss in echo planar MR images. Interventions improving tumor vascular oxygenation, which convert $dHbO_2$ to HbO_2 are expected to produce signal gain. Increasingly, BOLD MRI is being applied to assess tumor physiological state and therapeutic response in patients and it is the basis of much fMRI. The BOLD signal is also related to blood flow and volume. In some cases unexpected signal decreases have been reported accompanying interventions that are often referred to as "steal phenomena". We have observed this in our animal and clinical BOLD studies prompting us to develop phantom investigations to examine possible causes.

<u>Methods:</u> Fresh heparinized bovine blood was circulated in a system comprising pumps, tubing, windkessel unit, and oxygenator. Twenty-two TEFLON tubes (inside diameter 1.19 mm) were used to build the phantom, which included 0 °, 30 °, 45 °, 60 °, and 90° flow directions related in the imaging plane (Fig. 1). The tubes were bathed in stationary saline (Fig. 1). The blood flow in the phantom "vessels" was separately controlled by two pumps providing flow rates of 0, 6, 12 to 24 cm/s and oxygen and nitrogen were used to adjust partial pressure of oxygen in the blood. PO_2 values ranged from <10 mmHg to >100 mmHg. MR experiments were performed at 4.7 T. A FLASH sequence was used with TR/TE (200/10 ms), FOV (50×50 mm), flip angle (45°), thickness (1 mm), and matrix size (128×128) giving 0.15 mm^3 voxels. There was no flow compensation applied. Following five baseline measurements the blood flow or oxygenation were changed through multiple cycles with final return to baseline state. Each experiment included swapping image read- and phase- encode directions to examine angular effects. Image intensity data were analyzed on a voxel-by-voxel basis for regions within, between, and outside "vessels".

<u>Results:</u> ^{1}H MRI showed a signal change within "vessels" when blood flow was altered with a gain of ~ 50% when flow was decreased from 12 to 6 cm/s and a loss of ~ 36% when was increased to 24 cm/s. Relative signal intensity outside the vessels changed <1%. When blood oxygenation was increased from <10 torr (hypoxic venous blood) to > 100 mmHg (arterial blood) there was a massive signal enhancement (~500%) within vessels whatever the blood flow. Intriguingly, a significant signal decrease (~6%) was found in regions close to, but outside vessels when the oxygenation was increased. This small change was observed whether blood was flowing or stopped. When blood oxygen partial pressure increased, this phenomenon was observed in all flow and non-flow states. When experimental conditions (flow or oxygenation) were changed back to the baseline, the signal recovered to the baseline states.

<u>Discussion:</u> The phantom study has been widely used in biomedical imaging research, since it is easy to regulate specific physiological properties. Our results show that that the BOLD signal is sensitive to both blood flow and oxygenation, as recognized by others (FLOOD, Howe *et al.* 1999). Using the sequence and parameters here, the enhancement effect was much greater accompanying oxygenation than blood flow. Perhaps most important is the observation of significant signal changes outside the "vessels". While it was 1/100th that observed within the vessels, in principle it could lead to specific interpretations with respect to tissue physiology. It may contribute to observations interpreted as the steal effect. It appears that as oxygenation increases, the change of magnetic susceptibility within vessels causes signal decrease in nearby extra-vessel regions. We believe these observations may be an important caveat in fMRI and BOLD investigations.

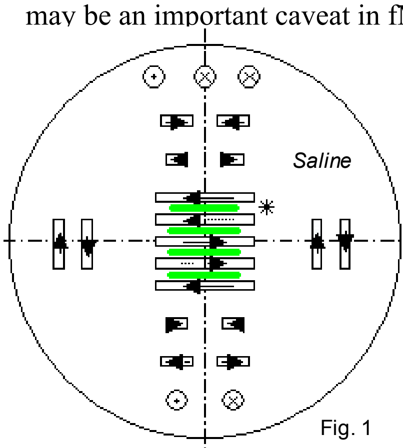

Fig. 1

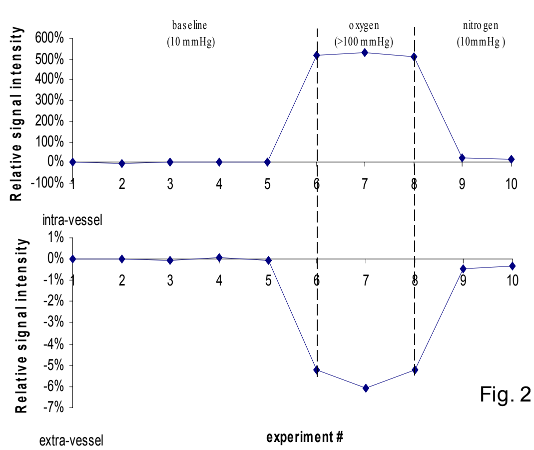

Fig. 2

Figure 2. Upper trace shows signal response in blood vessels accompanying variation in blood pO_2 from < 10 mmHg to > 100 mmHg. The gain approached 500%. Simultaneously, a signal loss ~ 6 % was found between the vessels (marked by * in Fig. 1).

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