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

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Introduction

Previous studies showed that the BOLD signal is related to change in blood oxygenation and flow. Distinguishing the contribution of these factors to the BOLD signal is very important for understanding the physiological meaning. However, it is hard to distinguish the contribution of these factors *in vivo*. The *in vitro* phantom study could be the best way to separately study these factors without any physiological limitation. The phantom experiment had two parts. i). to explore BOLD signal response to flow variation, blood oxygenation being constant. ii) to explore BOLD signal response to the change of blood oxygenation when the blood flow was constant.

Methodology

Fresh heparinized bovine blood was circulated in a phantom system (Fig 1). Twenty-two TEFLON tubes (inside diameter 1.19 mm) were used to build the microvessel model, which included 0º, 30º, 45º, 60º, and 90º flow directions related in the imaging plane. The tubes were bathed in stationary saline (Fig. 2a). 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 (Fig.2d,e). 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 (45º), thickness (1 mm), and matrix size (128×128). 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 phase encoding directions to examine angular effects. Image intensity data were analyzed on a voxel-by-voxel basis for regions within, between, and outside "vessels". Intra- and extra-vessel region (* mark Fig. 2a) was analyzed.

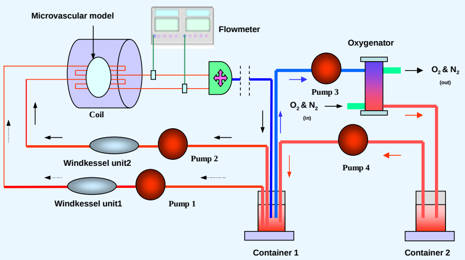

Figure 1. Diagram of the phantom system for *in vitro* experiment

Phantom system consisted of the microvessel model, pumps, Windkessel units, oxgenator. A Transonic® T201 2-channel blood flow meter was used to measure blood flow. An Instrumentation Laboratory® pH/Blood Gas Analyzer was used to measure blood oxygenation.

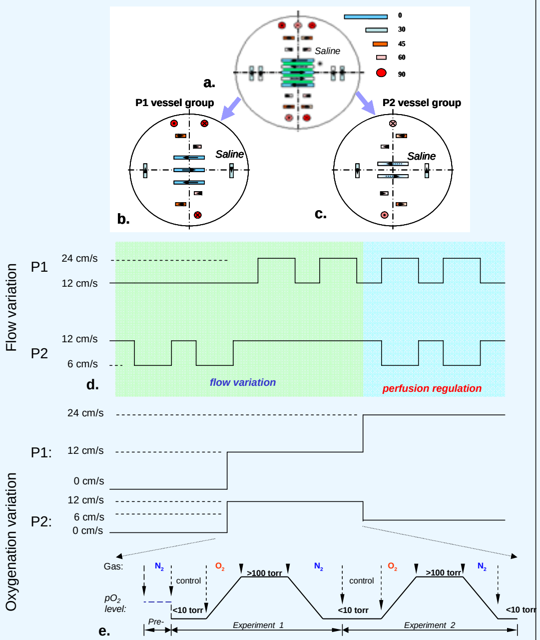

Figure 2. Diagram of flow and oxygenation variation experiment protocol

a) shows twenty-two "vessel" with different orientations,
b, c) show the vessels which were controlled by pump1 and pump2.
d) shows flow velocity set up.
e) shows the blood oxygenation. Each experiment has been repeated under the same flow velocity.

Results

[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 increased to 24 cm/s. Relative signal intensity outside the vessels change <1% (Fig. 3a,c). The relative signal intensity of all intra-vessel region showed a small enhancement if analyzing "perfusion regulation". When blood oxygenation was increased from <10 mmHg to > 100 mmHg, there was a massive signal enhancement (~500%) within vessels whatever the blood flow. Intriguingly, a significant signal decrease (~6%) was found in extra-vessel regions when the oxygenation was increased (Fig. 3b,d). 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 from intra- and extra-vessel region recovered to the baseline states. It showed that BOLD signal in intra- and extra-vessel regions response to oxygenation variation were much higher than that to flow variation (Fig. 4a,b).

Acknowledgements

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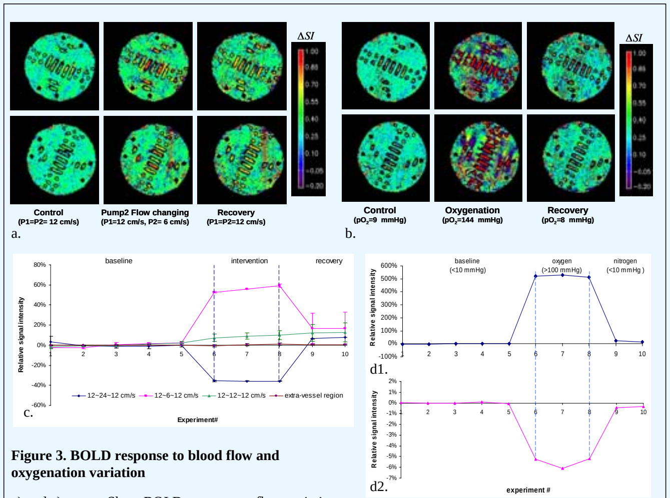

Figure 3. BOLD response to blood flow and oxygenation variation

a) and c) Show BOLD response to flow variation.
b), d1), and d2) show the BOLD response to oxygenation variation.
d1) and d2) show intra- and extra-vessel region response respectively.

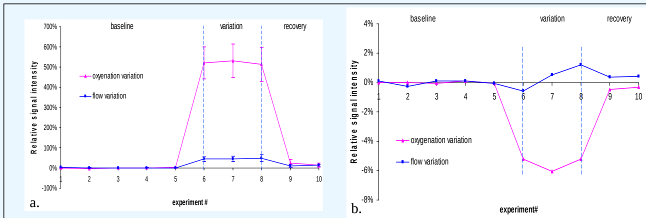

Figure 4. Comparison of intra- and extra-vessel regions response to flow and oxygenation variation

a) shows BOLD signal in intra-vessel region response to flow and oxygenation variation.
b) shows BOLD signal in extra-vessel region response to flow and oxygenation variation.

Discussion

The phantom study has been widely used in biomedical imaging research, since it is easy to regulate specific physiological properties. Our results show that the BOLD signal is sensitive to both blood flow and oxygenation, as recognized by others (FLOOD, Howe et al. 1999). The BOLD response to oxygenation variation was much higher than that to flow variation (Fig.4a). 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.

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