Detecting Microcirculatory Oxygen Saturation Changes with 2D-Balanced Steady-State Free Precession Imaging

R. Dharmakumar[1], X. Qi[1], J. Hong[1], G. A. Wright[1]

[1]Dept Medical Biophysics, Sunnybrook & Women's College HSC, University of Toronto, Toronto, ON, Canada

Introduction Blood is a magnetically inhomogeneous medium with the magnetic susceptibility of red blood cells (RBC) strongly dependent on the oxygen state of blood (1). Previously, this idea has been exploited to quantify intravascular oxygen state in both *in vitro* and *in vivo* studies with gradient-echo and spin-echo sequences (1,2). These methods have also been extended to detect regional oxygen consumption in different organ systems (3,4). However, the scan times associated with these techniques are on the order of tens of seconds to minutes or are limited by poor signal-to-noise ratio (SNR) restricting the diagnostic usefulness of this technique particularly for some cardiac applications. Over the past decade steady-state free precession (SSFP) imaging has gained recognition for its ability to provide fast scans with high SNR (5). Recently, the possibility of intravascular SSFP-based oxygen contrast has been reported (6). In this paper, we explore the possibility of detecting microcirculatory oxygen changes with the SSFP technique. We hypothesize that exchange of spins between extravascular and intravascular spaces leads to the establishment of SSFP signals that are dependent on the oxygen saturation of the blood in the microcirculation. We tested our hypothesis with theoretical and experimental animal models as described below.

Theory: Methods and Results Microcirculations of kidney cortex and skeletal muscle were modeled as two-pool systems that are composed of an extravascular and intravascular space. This model accounted for relaxation constants, spin-residence times, blood hematocrit, field strength (B_0), and relative blood volume. This analysis was performed by solving the modified Bloch equations similar to (7) but also considering longitudinal magnetization. It has been previously shown that SSFP signals are strongly dependent on the number of pulses to reach steady state, echo time, flip angle, phase-cycling pattern, and T_R (8). Simulations showed that, to minimize the sensitivity to static off-resonance and to maximize the oxygen effect, the optimum parameter set needs to be such that the flip angle (α) = 60°, $T_E = T_R/2$, T_R = 8 ms, number of pulses to get to steady state = 1000, and the RF is phase cycled between $+\alpha$ and $-\alpha$. Following similar arguments as (2), it has also been demonstrated that T_2 of whole blood (T_{2b}) may be estimated from $1/T_{2b} = 1/T_{2o} + K(1-\%O_2/100)^2$, where $\%O_2$ is the blood oxygen saturation and T_{2o} and K are parameters that depend on T_R, α, and B_0 (6). Using this information, placing a frequency shift between the intravascular and extravascular pool that varied linearly with field strength and blood oxygen state, and adjusting the fraction of magnetization between the pools, the dependence of oxygen contrast on field strength and relative blood volume were modeled. The simulations were performed assuming a normoxic state with $\%O_2$ = 88% and hypoxic state with $\%O_2$ = 63% at B_0 = 1.5T and 3.0T and assuming a relative blood volume of 2% in muscle and 22% in the cortex. From the resulting signals, oxygen-sensitive contrast values were computed, where *Oxygen Contrast = [Normoxic Signal – Hypoxic Signal]/[Normoxic Signal* x $\Delta\%O_2$*]*, with $\Delta\%O_2$ = 25%. The study showed that oxygen sensitive contrast may be observed in SSFP images and that this contrast is strongly dependent on field strength and moderately dependent on blood volume as shown in Table 1.

Experiments: Methods and Results In order to validate the theoretical predictions of SSFP signal behaviour, experimental studies were performed in 6 healthy New Zealand white rabbits. Temporary systemic arterial hypoxia was induced in the rabbits by varying the partial pressure of O_2 of breathing gases such that $\%O_2$ was varied from ~ 88% at normoxic state to ~ 65% at hypoxic state. Heart rate and $\%O_2$ were monitored with a pulsed oximeter. Once the desired $\%O_2$ was reached, $\%O_2$ was held relatively constant (+/- 4%). Subsequently, 2D-balanced SSFP was prescribed on one slice containing the dorsal muscle and the cortex of the kidney of the rabbit. The scan parameters were: flip angle = 60°, acquisition matrix = 256 x 256, T_R = 8 ms, T_E = 4 ms, number of pulses to reach steady-state = 1000, field of view = 22cm, and slice thickness = 10 mm. This experiment was repeated 5 times on each animal at two different field strengths (1.5T and 3.0T). The results showed the presence of oxygen sensitive contrast in both tissue types (Table 1). In particular, we observed approximately 65% mean signal change between the normoxic and hypoxic states in the kidney cortex at 3.0T. The contrast showed a strong dependence on field strength as predicted from the theoretical calculations. The mean contrast values also showed dependence on relative blood volume. However, there was a discrepancy between the theoretical and experimentally derived contrast values in the relative dependence on blood volume. The experimental results also showed a greater variability in contrast for muscle than for kidney cortex.

Table 1: Theoretically and experimentally derived oxygen contrast in microcirculations of the rabbit at 1.5T and 3.0T

Field Strength/ Tissue	Theoretical Oxygen Contrast	Experimental Oxygen Contrast
1.5T Muscle	0.36	0.23 +/- 0.13
1.5T Kidney Cortex	0.48	0.72 +/- 0.16
3.0T Muscle	1.67	1.18 +/- 0.72
3.0T Kidney Cortex	1.85	2.60 +/- 0.45

Discussion & Conclusion Our work explored the possibility of observing oxygen-sensitive contrast in microcirculation with 2D-balanced SSFP sequence. The hypothesis that oxygen sensitive contrast may be obtained with this method was tested with theoretical and experimental models. Theory and experiment confirmed that it is possible to observe oxygen sensitive contrast in microcirculation. The theoretical prediction of B_0 dependence on oxygen-sensitive contrast was consistent the experimental results. However, there was a discrepancy between experimentally observed mean contrast and that predicted by the theoretical model. These discrepancies may be linked to the inherent limitations of the theoretical model where the following are not accounted for: (1) field variations in the extravascular space; (2) vasodilation/compensatory mechanisms that are activated in response to global hypoxia; and (3) variations in simulation parameter values from actual values.

References

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