Oxygen-Sensitive Contrast in Blood for Steady-State Free Precession Imaging

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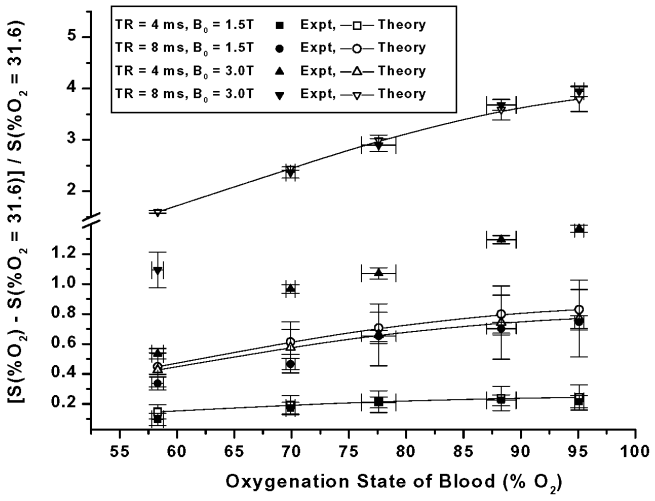
Introduction Blood is a magnetically inhomogeneous medium with the magnetic susceptibility of red blood cells (RBC) strongly dependent on the percent blood oxygen saturation level ($\%O_2$) (1). Previously, this idea has been exploited to quantify $\%O_2$ *in vivo* with spin-echo sequences (1,2). However, the scan times associated with these techniques are on the order of tens of seconds to minutes which limit their diagnostic usefulness 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 signal-to-noise ratio (SNR) (3). Recently, the possibility of SSFP-based oxygen contrast has been reported (4). However, previously explored mechanisms (5) based on bulk frequency shifts ($\Delta\omega_{Bulk}$) cannot explain this contrast. This paper shows that the dominant mechanism for SSFP sensitivity to $\%O_2$ arises from the motion of spins through local field inhomogeneities in and around deoxygenated RBCs. Further, the extensive parameter space of SSFP is explored with the intent of optimizing it for robust oxygen-based contrast at 1.5T and 3.0T. In addition, an analytical model capable of reporting quantitative measures of $\%O_2$ in real-time is put forward.

Theory and Simulations Blood can be considered as a two-pool system (plasma and RBCs) with a relative frequency shift ($\Delta\omega_{RBC}$) determined by $\%O_2$; thus, a two-pool model including exchange was used to characterize the SSFP signal behaviour in whole blood. This analysis was performed by solving the modified Bloch equations as in (6) but also considering longitudinal magnetization. In this context, the influence of the parameter set Ψ = {number of pulses needed to reach steady state (N), echo time (TE), $\Delta\omega_{Bulk}$, flip-angle (α), and typical RF phase-cycling patterns} on SSFP signal in the absence of the oxygen effect (ie. $\Delta\omega_{RBC} = 0$) was studied. In the regime where SSFP signals are relatively insensitive to these parameters, the influence of oxygen effect was studied by modulating $\Delta\omega_{Blood}$ corresponding to changes in $\%O_2$. In addition, to understand how this contrast behaviour is affected by adjustable parameters TR, field strength (B_0), α, and the uncontrollable parameter, exchange time (τ_{ex}), a further study was conducted with a reasonable set of parameter values. The first part of the study showed that when N>1000 the signals converged to steady state. The dependence of SSFP signal behaviour when $\Delta\omega_{RBC} = 0$ on other parameters (TE, $\Delta\omega_{Bulk}$, α, RF-cycling patterns) resembled the results previously reported with one-pool systems. Flip angle showed relative insensitivity to changes in $\Delta\omega_{Bulk}$ for α between 30^o-60^o with RF-phase-cycling. Increasing TR (4 ms to 8ms), B_0 (1.5T to 3.0T), and α (within 30^o-60^o) can increase oxygen-sensitive SSFP contrast. In addition, it was found that when the exchange times between pools (plasma, RBC) are on the order of TR, contrast is optimized for TRs larger than approximately 4ms.

Experimental Methods and Results To validate the theoretical predictions of SSFP signal behaviour in the absence of oxygen effect and then to verify contrast manipulation possibilities explored theoretically, experiments were performed on GE Signa systems operating at 1.5 T and 3.0 T on blood samples collected from healthy human volunteers. The oxygen level of the blood samples was adjusted by agitating the blood in the presence of nitrogen gas and the oxygen saturation level was measured before and after the MR scans with an oximeter. Scanning procedure involved applying a 2D balanced-SSFP sequence (128 x 128 matrix, 24 cm FOV, axial slices of thickness = 10 mm, head-coil). During the experiment, the blood samples were repeatedly mixed to avoid blood settling and their temperature was maintained at 36 +/- 2 ^oC with a hot water bath. This experiment was performed 3 times. On each occasion, measurements were repeated 5 times; signals collected were used to compute means and standard deviations over a given region of interest. Validation of the first part of the theoretical study looking at the dependence of the parameter set Ψ on SSFP signal when $\Delta\omega_{RBC} = 0$ was performed on fully oxygenated blood samples ($\%O_2$ = 97.1 +/- 0.4) by varying the desired parameter under study while keeping all others constant. To experimentally study the SSFP signal dependence on $\%O_2$ and also to optimize contrast, 6 blood samples were oxygenated to various levels between 31.5+/-0.9 and 95.1+/-0.4. During this set of experiments, Ψ = {N = 1000, $\alpha = 60^o$, TE = TR/2, RF phase-cycling}. Steady-state signals were measured for each blood sample at B_0 = 1.5T and 3.0T at TR = 4 and 8 ms. The study of the dependence of SSFP signal stability on Ψ when $\Delta\omega_{RBC} \sim 0$ confirmed the theoretical predictions. The experimental validation of the theoretical predictions regarding oxygen-sensitive SSFP signal contrast, defined here as the magnitude of the difference between SSFP signal (S) at variable $\%O_2$ and signal at $\%O_2$ = 31.6 normalized by signal at $\%O_2$ = 31.6, is shown in the figure below. The theoretical points were computed by modulating the frequency difference between the two pools to account for changes in $\%O_2$ and taking into account the variability of τ_{ex} in the literature (3.1-5.7 ms) (6). The theoretical results are connected with a spline fit. Results show that increasing TR and/or B_0 can strongly affect the oxygen-sensitive contrast in a manner consistent with theory, within the limits of experimental error, physical constants used, and the limitations of the two-pool model.



SSFP-based MR Oximetry When the Luz-Meiboom approximation (7), a previously used model in spin-echo-based oximetry, is applied to the SSFP signal equation (with $\Delta\omega_{Bulk} = 0$) (8), it leads to an oxygen-sensitive signal equation with similar adjustable parameters as discussed in (2). When this equation was fitted to the experimentally observed results in figure, the results showed strong correlation. The fitted parameters also compared favourably with those that had been reported with spin-echo techniques (9). However, the expected scaling of these parameters with doubling of field strength was not observed at the low TR.

Discussion Acquiring MR images in real-time that can show qualitative, spatially dependent oxygen contrast can be useful for quick assessment of suspected oxygen impairment. In addition, if one is able to acquire quantitative, fast oxygen maps *in vivo*, the diagnostic utility of MR-based oximetry could be improved. This paper serves to explain how SSFP-based oxygen contrast may be generated, the primary mechanism that explains this contrast, and how one may be able to obtain fast quantitative maps of blood oxygenation state. We envision that with an optimized pulse sequence, the oxygen-sensitive SSFP technique could be instrumental in improving the interpretation of physiology and potentially in extending the current diagnostic capabilities of MR oximetry.

References

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