# Deriving Oxygen-Sensitive Contrast in Tissue from MRI: A Comparison between T2*-Weighted, T2-Prepared and SSFP Methods with an Ischemia Leg Cuff Model at 1.5T

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## Introduction

Assessment of changes in oxygen saturation in tissue is useful for interpreting physiological responses [1] and many pathological conditions, including cardiovascular [2] diseases. The conventional oxygen-weighted (BOLD) MR methods rely on $T_2$-prepared [3] or $T_2^*$-weighted [1-2] sequences. However, those techniques are time consuming, limited by poor oxygen sensitivity and poor image quality, particularly for cardiac imaging. Recently, oxygen-sensitive contrast with steady-state free precession (SSFP) has been proposed to detect microcirculatory oxygen changes [4]. The aim of this work is (1) to compare the oxygen-sensitive contrast derived from SSFP methods against $T_2$ preparation and gradient echo methods; (2) to demonstrate that the dependence of oxygen-sensitive contrast on $T_R$ and flip angle ($\alpha$) for SSFP imaging in order to validate previous theoretical findings [4] in an experimental ischemia leg cuff model [5].

## Methods

Experiments were performed on a Sonata 1.5T scanner (Siemens, Erlangen, Germany) using a flexible surface coil to image the mid calf of the lower leg of 6 healthy volunteers. Time and resolution matched SSFP, $T_2$-prepared with SSFP readout ($T_2$-prep) [6] and multi-gradient echo (mGRE) sequences were prescribed in each study with the following scan parameters: voxel size = $1.3\times1.3\times5.0$ mm$^3$, total scan time = 7 min; SSFP: $\alpha$ = 30°- 90° (increments of 30°), $T_R$ = 3.5 ms / 6.3 ms / 9.9 ms, $T_E = T_R / 2$; $T_2$-prep: $\alpha$ = 70°, $T_R$ = 3.1 ms; $T_2$-prep duration = 40 ms; mGRE: $\alpha$ = 15° and 6 echoes with $T_E$ = 2.19/5.42/8.65/11.9/15.6/19.9 ms. In order to induce temporary ischemia in the calf, a blood pressure cuff was placed on the thigh proximal to the knee and connected to the Hokanson E20 rapid cuff inflator (D.E.Hokanson Inc., Bellevue, WA) and the cuff was inflated to a pressure of 200-205 mmHg. Axial images of the mid calf were acquired during a 1 minute baseline period, followed by 3 minutes of imaging with the cuff inflated (ischemia), and then another 3 minutes of imaging with the cuff deflated (reactive hyperemia). Each volunteer was scanned 7 times: SSFP (5 times with different repetition times and flip angles), $T_2$ prepared SSFP (once) and mGRE (once) with a 5 minute break between each scan. From carefully chosen ROI's devoid of flow artefacts, signal intensity was measured and averaged from three regions of interest (ROI) within the muscle area: tibialis anterior, soleus and gastrocnemius (Fig. 1). To compare the oxygen sensitivity of the different sequences, oxygen contrast was computed as follows: oxygen contrast = $(S_{hyperemia} - S_{ischemia}) / \sigma_{noise}$ [Eq. 1], where $S_{hyperemia}$ and $S_{ischemia}$ are signal magnitudes during hyperemia (255-265s) and ischemia (215-235s), respectively and $\sigma_{noise}$ is the standard deviation of the background noise. The oxygen contrast in mGRE images was computed from the $T_E$ with the greatest signal difference between reactive hyperemia and ischemia.

## Results

A typical time series of the MR signal from the three different ROI's (Fig. 1) is shown in Fig. 2. Oxygen contrast measured with the three different sequences and the $T_R$ dependence of SSFP-based oxygen contrast is shown in Fig. 3. Fig. 4 shows the dependence of oxygen contrast on $\alpha$ at $T_R$ = 9.9 ms. Results show that increasing the $T_R$ and/or $\alpha$, increases SSFP-based oxygen contrast, consistent with theoretical prediction in whole blood [7]. Furthermore, the results also show that the difference in oxygen contrast between SSFP ($T_R$ = 6.3ms, $\alpha$ = 90°), $T_2$-prep and mGRE are statistically insignificant.

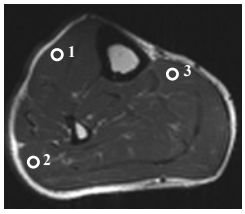


**Fig. 1:** Typical SSFP image ($T_R$ = 9.9 ms, flip angle = 90°) of a mid calf showing three regions of interest

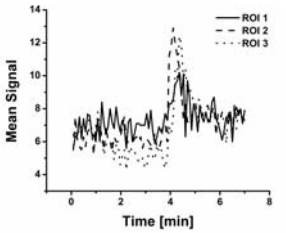


**Fig. 2**: Typical time course of the corresponding mean signal of the three ROI's drawn in Fig. 1. Note the oxygen contrast around 4min at hyperemia.

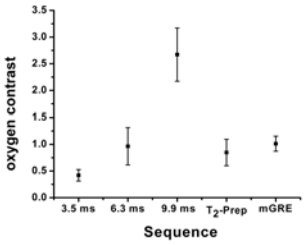


**Fig. 3:** Comparison of experimental oxygen contrast calculated with Eq. 1 for $T_2$-prep, mGRE and SSFP ($T_R$ = 3.5/6.3/9.9 ms). As $T_R$ increases, SSFP-based oxygen contrast increases. Also note that oxygen contrast between $T_2$-prep, mGRE and SSFP at $T_R$ = 9.9 ms and $\alpha$ = 90° is approximately the same.

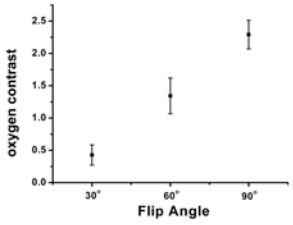


**Fig. 4**: Experimentally observed oxygen-sensitive contrast dependence on flip angle with SSFP imaging at $T_R$ = 9.9 ms. Note that oxygen contrast increases with increasing flip angle.

## Discussion and Conclusion

Our work compared oxygen contrast derived from SSFP method against previously explored $T_2$-prep and $T_2^*$-weighted methods in an experimental leg cuff model. Our results show that the oxygen-sensitive contrast with SSFP is strongly dependent on the repetition time and flip angle. Specifically, increasing $T_R$ and/or flip angle within the range studied can increase SSFP-based oxygen contrast. These results are particularly relevant for cardiac imaging aimed at detecting myocardial oxygen deficits. Since typical repetition times used in SSFP cardiac imaging are often on the order of 2.0 – 3.0 ms [8], we anticipate that conventional cardiac SSFP imaging will not be as sensitive as $T_2^*$-weighted or $T_2$-prep methods. We envision that longer repetition periods and high flip angles can substantially increase the SSFP-based oxygen sensitivity for cardiac BOLD work and will improve image quality due to acquisition in steady-state. However, given the blood volume in the leg is nearly 5 times less than in the heart, a similar study aimed at cardiac BOLD also needs to be done. In addition, it is also necessary to optimise the $T_R$ and flip angle against off-resonance and flow artefacts in the heart. More generally, we anticipate these results to be valid in any organ system where oxygen-sensitive contrast is sought as well.

**References [1]** Ogawa S et al. BioPhys J 1993;64(3):803-12; **[2]** Li D et al. MRM 1996;36 :16-20 ; **[3]** Brittain JH et al. MRM 1995;33(5):689-96; **[4]** Dharmakumar R et al. Proc 13th ISMRM. P. 2388 ; **[5]** Touissant JF et al. MRM 1996;35(1):62-69 ; **[6]** Fieno DS et al. Circulation 2004;110:1284 ; **[7]** Dharmakumar R et al. MRM 2005;53(3):574-583; **[8]** Carr J et al. Radiology 2001;219:270.