Determination of oxygen consumption in calf muscle through combined ASL perfusion and T2 oxymetry measurements at 3.0 T.

Nicolas Decorte[1], Ericky Caldas de Almeida Araujo[1], Alexandre Vignaud[2], and Pierre G. Carlier[1]
[1]*Institute of Myology, AIM and CEA, Paris, 75013, France,* [2]*Siemens Healthcare, Saint Denis, France*

Introduction: Functional NMR imaging, among its many variations, offers the possibility to measure non-invasively muscle perfusion by arterial spin labeling (ASL) and blood oxygenation via the T2 dependence on haemoglobin saturation (1, 2). In this study, we show that muscle ASL and T2 determination of arterial and venous blood may be combined to calculate muscle oxygen consumption non-invasively and with a temporal resolution compatible with physiological studies.

Materials and Methods: Arterial and venous T2 oxymetry was combined with ASL determination of perfusion in the protocol illustrated in Figure1. These measurements were performed on four healthy volunteers (three men and one woman aged from 25 to 44 years) in normoxic and hypoxic conditions (breathing gas with only 10%O_2) in order to assess the sensitivity of our measurements over a range of saturation values. In parallel 4.5mL blood samples were drawn and used to titrate T_2 measurements in blood versus %HbO2 *in vitro* (Gas Analyzer GDS Opti CCA, Roche, France).

T_2 mapping: T_2 mapping was obtained using a standard multiple spin echo sequence (TR: 2000 ms, TE: 10 ms, flip angle 180°, FOV: 180 mm, matrix: 256x256 mm, bandwidth: 444 Hz/Px, PF: 6/8, slice thickness: 10 mm). For *in vivo* T2 determination, the segment investigated was cuffed in order to avoid flow interferences. The T_2 map was positioned on the popliteal crease and ROIs were traced on the popliteal artery and vein (Figure 2). ***ASL measurement of skeletal muscle perfusion:*** perfusion was measured in the gastrocnemius muscle using a 2D TrueFISP sequence with SATIR preparation (3) (TR: 3.6 s, ASL Labeling: 2000 ms, matrix: 96x96, FOV: 200mm, slice thickness: 10 mm). ***Calculation of muscle VO_2:*** taking a haemoglobin oxyphoric capacity of 1.31 mL/g of O_2, the maximal HbO_2 transport capacity is: $\mathrm{Tart}_{O_2(\mathrm{Hb})} = [Hb] \times 100\% \times 1.31 mL/g \cong 200 mL/L$

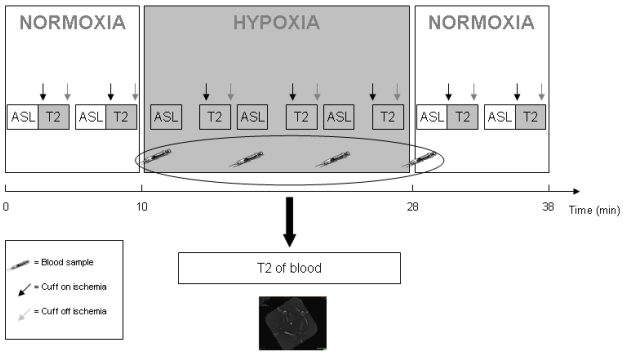

Figure 1. Hypoxic protocol with diagram of combined measurements

Considering the dissolved fraction of oxygen of 3.24 mL/L, gives the total capacity of O_2 transport in blood. By multiplying Tart O_2 with calf muscle perfusion (f) as measured by ASL, we obtained the oxygen supply to calf muscles. Tissue oxygen extraction was calculated from the differences in %HbO2 in the feeding artery and in the draining vein. The %HbO2 was derived from the T2 measurements *in vivo*, by interpolation of the sigmoid curve T_2 as a function of %HbO_2 determined *in vitro*, using either sigmoid (r^2=0.96) or Luz-Meiboom (4) (r^2=0.95) fits (Figure 3). Finally, by multiplying the arteriovenous differences in O_2 concentrations (TartO2 – TveiO2) with perfusion, we obtained muscle oxygen consumption: $\mathrm{VO}_{2muscle} = f \times \left(\mathrm{Tart}_{O_2(\mathrm{Hb})} - \mathrm{Tvei}_{O_2(\mathrm{Hb})}\right)$

Table 1. Individual values measured during the *in vivo* protocol. * Significantly different from normoxia (p<0.05).

	Perfusion (ml/min/100g)		VO2muscle (ml O2/min/100g)		Delta%HbO2 art vs.vein		Heart rate (bpm)	
Subjects	Normoxia	Hypoxia	Normoxia	Hypoxia	Normoxia	Hypoxia	Normoxia	Hypoxia
1	6.7	8.3	0.4	0.3	37.3	18.8	50	71
2	13.5	15.0	0.7	0.1	29.1	4.7	80	96
3	12.5	10.4	0.5	0.2	24.7	12.8	85	104
4	19.5	14.3	1.0	0.2	30.4	7.8	65	97
Mean	13.0	12.0	0.7	0.2 *	30.4	11.0 *	70	92 *
SD	5.2	3.2	0.3	0.1	5.3	6.1	16	14

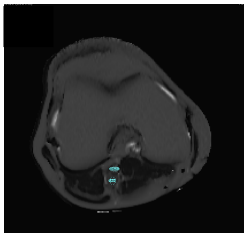

Figure 2. Axial T2 map

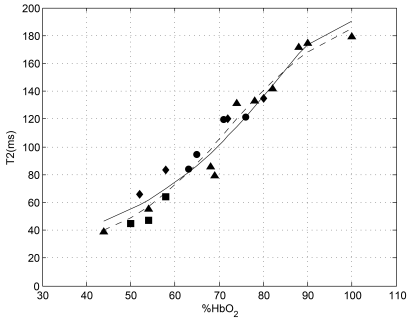

Figure 3. Relationship between T2 (ms) and %HbO_2 in each subject (different markers) with sigmoidal fit (- -) or Luz-Meiboom fit (—).

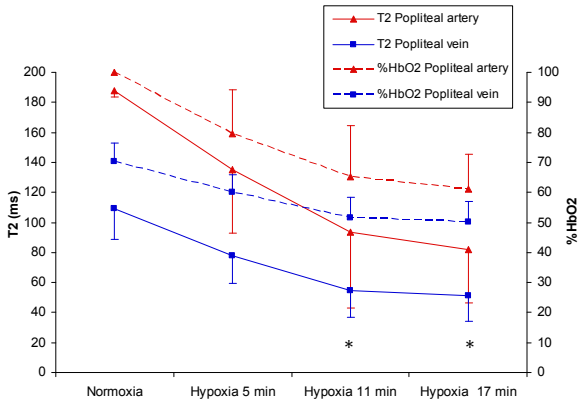

Figure 4. Measurements of T2 (ms) in artery (--) and vein (--) in two ambient oxygen availability conditions (normoxia vs. hypoxia 10% O_2). * Significantly different from normoxia with p<0.05.

Results: Figure 3 shows the in vitro calibration of blood T2 (in ms) against %HbO_2 The *in situ* %HbO_2 of arterial and venous blood in popliteal vessels of healthy subjects was calculated using this calibration curvein conditions of normoxia and hypoxia. Serial blood T2 determination *in vivo* was able to adequately monitor the expected changes in arterial and venous oxygenation during hypoxia. (Figure 4). The individual values obtained for each subject in normoxic vs. hypoxic conditions are reported in Table 1. Heart rate significantly increased in hypoxic condition (p=0.049), but there was no detectable effect on muscle perfusion. As expected, we observed a significant fall in arterial-venous delta%HbO_2 (p=0.038). Muscle VO_2 also decreased (p=0.025), presumably as a result of blunted local hemodynamic response in hypoxic peripheral muscle, owing to cardiac output redistribution towards essential organs.

Conclusion: These initial results are encouraging and confirm that muscle oxygen extraction and consumption can be determined using a combination of non-invasive NMR techniques, ASL and T2 oxymetry. It opens the way for multiple applications in muscle physiology and physiopathology.

1. Benaron DA, Benitz WE, Ariagno RL, Stevenson DK. Noninvasive methods for estimating in vivo oxygenation. Clin Pediatr (Phila) 1992; 31:258-273.
2. Wright GA, Hu BS, Macovski A. 1991 I.I. Rabi Award. Estimating oxygen saturation of blood in vivo with MR imaging at 1.5 T. J Magn Reson Imaging 1991; 1:275-283.
3. Raynaud JS, Duteil S, Vaughan JT, et al. Determination of skeletal muscle perfusion using arterial spin labeling NMRI: validation by comparison with venous occlusion plethysmography. Magn Reson Med 2001; 46:305-311.
4. Barth M, Moser E. Proton NMR relaxation times of human blood samples at 1.5 T and implications for functional MRI. Cell Mol Biol (Noisy-le-grand) 1997; 43:783-791.