

# Both oxygen supply and phosphocreatine recovery rate show proximo-distal gradients along the human tibialis anterior after exercise

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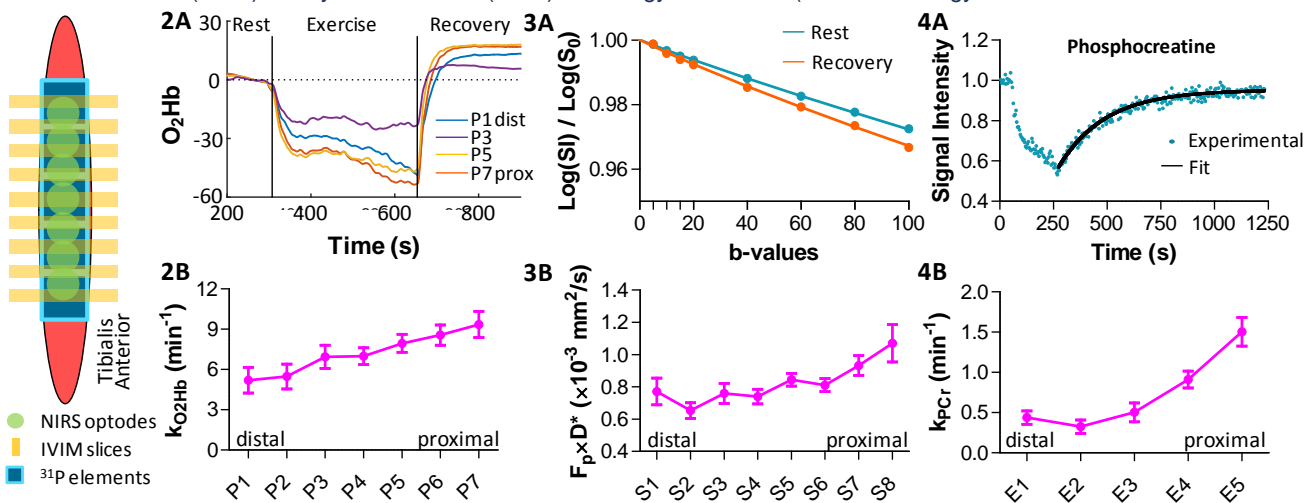
**Introduction:** The phosphocreatine (PCr) recovery rate ( $k_{PCr}$ ) of muscles after exercise, reflecting their oxidative capacity<sup>1</sup>, varies between subjects and muscles<sup>2,3</sup>. Recently, we demonstrated that  $k_{PCr}$  also varied substantially within a single muscle, i.e. in the tibialis anterior (TA)<sup>4</sup>. As  $k_{PCr}$  depends on muscles' capacity to utilize O<sub>2</sub> for ATP production and O<sub>2</sub> supply, we wondered if O<sub>2</sub> supply also varied spatially within the TA. Therefore, we applied near infra-red spectroscopy (NIRS) to study the temporary imbalance of O<sub>2</sub> supply and utilization, intravoxel incoherent motion imaging (IVIM) for muscle perfusion and <sup>31</sup>P-MRS during and after isometric exercise of the TA.

**Methods:** In two sessions twelve healthy male volunteers (age: 26±3y) performed isometric dorsiflexion of the right ankle until exhaustion at 30% of their maximum voluntary contraction. During the first session, oxyhemoglobin (O<sub>2</sub>Hb) changes were measured with NIRS (OxyMon, Artinis) simultaneously at seven positions along the TA during rest, exercise, and recovery (Fig1). The rate of O<sub>2</sub>Hb recovery was fitted by:  $O_2Hb(t) = O_2Hb_0 + \Delta O_2Hb(1 - e^{-k_{O_2Hb} \times t})$ . During the second session, measurements were performed in a 3T MR system (Prismafit, Siemens). We acquired nine transverse diffusion-weighted (DW) slices (Fig1; SE-EPI; SPAIR; TR/TE=2000/40ms; voxel size = 2.75x2.75x10mm<sup>3</sup>; gap=11.3mm; acquisition time=1min18s; b=0,5,10,15,20,40,60,80,100,150,200,400,600s/mm<sup>2</sup>). The signal decay on these DW images was fitted with a bi-exponential model<sup>5,6</sup>  $S_b = S_0 \left( (1 - F_p)e^{-b \times D} + F_p e^{-b \times D^*} \right)$ . From this the blood flow related parameter  $F_p \times D^*$  during rest and recovery was determined. Second, we collected <sup>31</sup>P-MR spectra (pulse-acquire; FA=48°; TR=2060ms; NA=2; 1 spectrum/coil element; NOE) using a home-built ladder-shaped <sup>31</sup>P-phased array coil containing five coil elements positioned on the TA for reception (Fig1; signal localization through the coil element sensitivity profiles). The  $k_{PCr}$  was fitted by:  $PCr(t) = PCr_0 + \Delta PCr(1 - e^{-k_{PCr} \times t})$ . Linear mixed models were used to assess the linear dependence of  $k_{O_2Hb}$ ,  $F_p \times D^*$ , and  $k_{PCr}$  along the length of the TA.

**Results:** The  $k_{O_2Hb}$ ,  $F_p \times D^*$ ,  $k_{PCr}$  all showed significant linear relationships with optode position (p=0.01), slice position (p=0.031) and coil element (p<0.01), respectively (Fig 2,3 and 4). All three outcome measures were higher proximally than distally.

**Discussion and Conclusion:** We observed higher post-exercise perfusion and faster phosphocreatine and oxyhemoglobin recovery proximally than distally in the TA. This indicates that also O<sub>2</sub> supply recovers faster proximally than distally.

**References:** <sup>1</sup>Kemp(2015) Acta Physiol (Oxf). <sup>2</sup>Larsen(2009) J Appl Physiol. <sup>3</sup>Fleischman(2010) J Clin Endocrinol Metab. <sup>4</sup>Boss(2018) J. Physiol. <sup>5</sup>Le Bihan(1988) Radiology. <sup>6</sup>Federau(2012). Radiology



**Figure 1:** Optode, slice and coil element positioning along the TA

**Figure 2: NIRS results.** A) Typical O<sub>2</sub>Hb signal during rest, exercise and recovery at four positions. B)  $k_{O_2Hb}$  along the TA.

**Figure 3: IVIM results.** A) Typical signal decay curve of the DW signal in the TA during rest and recovery. B)  $F_p \times D^*$  along the TA.

**Figure 4: <sup>31</sup>P-MRS results.** A) Typical phosphocreatine signal during rest, exercise and recovery. B)  $k_{PCr}$  along the TA.

