Mapping of Oxygen By Imaging Lipids relaxation Enhancement (MOBILE): Application to monitor peripheral ischemia in a mouse model.

Julie Magat[1], Patrice D Cani[2], Nathalie Delzenne[2], Bernard Gallez[1], and Bénédicte F Jordan[1]

[1]*Biomedical Magnetic Resonance Group, Université Catholique de Louvain, Brussels, Belgium,* [2]*Metabolism and nutrition Group, Université Catholique de Louvain, Brussels, Belgium*

Purpose and objectives:

Peripheral vascular disease is responsible for the increased risk of lower limb amputation observed in diabetic patients and/or in patients presenting systemic atherosclerosis (1). Today a significantly better outcome is expected for these patients, based on improved technical options in peripheral revascularization (2). For that purpose, techniques able to assess quantitative peripheral pO_2 are mandatory to verify the efficacy of therapeutic approaches aimed to salvage limbs in diabetic patients with critical limb ischemia. Variations in T_1 and T_2* are potentially valuable MRI tools to changes in tumor oxygenation. T_2* is sensitive to the relative Hb/HbO2 ratio in vessels (3), while T_1 change is sensitive to dissolved oxygen which acts as a T_1-shortening paramagnetic contrast agent (4). We recently developed a method able to map variations in oxygenation based on the changes in the relaxation properties of the tissue lipids by exploiting the higher solubility property of oxygen in lipids than in water (5). The aim of the current work was to apply the MOBILE technique in order to map peripheral tissue oxygenation in a mouse model of peripheral ischemia. The capacity of response to an hyperoxic breathing challenge was assessed in the control and ligated leg, and R_1 Lipids (MOBILE), R_1H_2O, and R_2* were systematically compared.

Material and Methods:

Peripheral ischemia model: Femoral vein ligation was performed on C3H female mice (n=3) 2 hours before imaging. The femoral artery and vein were exposed and ligated with three sutures, one above and two after the origin of the natural collateral on the left hindlimb leg of the mouse.

MR protocol: Experiments were performed with a 11.7T (Bruker, Biospec), and with a quadrature volume coil (inner diameter of 40 mm and length of 100mm). A segmented IR FISP (Inversion-Recovery Fast Imaging with Steady state Precession) sequence (SSFP FID mode) was used to acquire parametric images of T_1 relaxation time. The acquisition parameters were TR/TE/FA/BW/matrix = 4 ms/1.2ms/5°/100kHz/64x64, 4 segments, and a total acquisition time of 1min20s. For the lipids experiment, we first evaluated the difference in Hertz between water and lipid peaks on a single pulse spectrum. These offsets were then used as an imaging frequency offset in the same IR FISP protocol and water signal was spoiled using a $\pi/2$ hermite saturation pulse with a bandwidth of 5400Hz.ms. Images were treated using Matlab to determine the T_1 relaxation (in ms) in regions of interest. For T_2* measurements, a Multi Gradient Echop (MGE) sequence is performed with 8 echoes (between 3.5 ms and 31.5ms and echo spacing equal to 4 ms) with a total acquisition time of 4min 48s. A 256x256 pixels matrix is obtained with TR/flip angle/slice thickness=1500ms/30°/1mm.

Mice were anesthetized using isoflurane and respiratory triggering was employed to avoid motion artifacts.

Results:

Our data show that R_1 lipids (MOBILE) is more sensitive than R_1 H_2O and R_2* to evidence (i) differences in basal tissue oxygenation (control vs ischemic leg) (Fig. 1) and (ii) relative changes in response to carbogen breathing (Fig.2). Significant changes in mean values were observed in the control leg in response to carbogen breathing for ΔR_1 Lipids (7.4 +/- 2.0 %, $p<0.05$), whereas no significant changes were observed for ΔR_1 H_20 (1.3 +/- 0.8 %) or Δ R_2* (9.6 +/- 3.8 %) ($p<0.05$). A factor of 5.7 is therefore achieved between ΔR_1 Lipids and ΔR_1 H_20. As expected, a lack of response to carbogen breathing was observed in the ischemic leg. Typical maps of changes in R_1 H_2O (Fig.3), R_1 Lipids (Fig.4), and R_2* (Fig.5) of the same leg are shown.

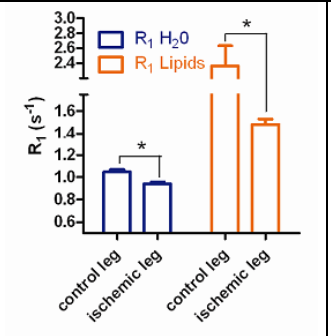

Fig.1 Basal tissue relaxation rates in control and ischemic legs

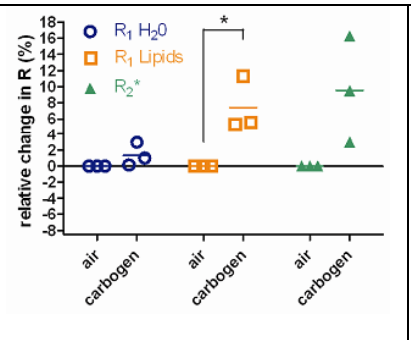

Fig.2 Relative change in relaxation rates during carbogen breathing

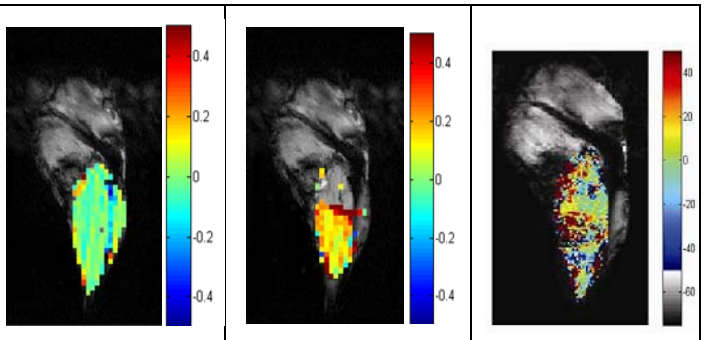

Fig.3, 4, 5 Maps of change in R_1 H_2O, R_1 Lipids, and R_2* during carbogen breathing

Discussion:

MOBILE (R_1 Lipids) was successfully applied in order to map peripheral tissue oxygenation in a peripheral ischemia model. The technique was able to identify basal differences in tissue oxygenation while comparing the ligated leg and the control leg, with a higher sensitivity than R_1 H_2O. Sensitivity to induced changes in tissue oxygenation via an hyperoxic breathing challenge was also higher with R_1 Lipids than R_1 H_2O.

References:

(1) Mohler ER 3rd. *Nat Clin Pract Cardiovasc Med.* **4**,151-62 (2007), (2) Weinberg MD, Lau JF, Rosenfield K, Olin JW. *Nat Rev Cardiol.* **8**, 429-41 (2011), (3) Baudelet et al, *Magn Reson Med* 2002, 48, 980-986 (4) O'Connor et al, *Int J Radiat Oncol Biol Phys* 2009, 75, 1209-1215 (5) Magat J. et al, *Proc. Intl. Soc. Mag. Reson. Med.* 19 (2011) 553.