Mapping of Oxygen By Imaging Lipids relaxation Enhancement (MOBILE): Application in a murine stroke model.

Julie Magat[1], Caroline Vandeputte[2], Uwe Himmelreich[2], Bénédicte F Jordan[1], and Bernard Gallez[1]

[1]*Biomedical Magnetic Resonance Group, Université Catholique de Louvain, Brussels, Belgium,* [2]*Biomedical Nuclear - Magnetic - Resonance Unit, Katholieke Universiteit Leuven, Leuven, Belgium*

Purpose and objectives:

Imaging brain tissue oxygenation shortly after an acute ischemic stroke may help to aid in the selection of patients who may still benefit from thrombolytic treatment beyond conventional time-based guidelines (1). There is indeed literature in support of using advanced neuroimaging to select patients for treatment beyond the 3-hour time window cutoff and explore potential applications and limitations of oxygenation/perfusion imaging in the treatment of acute ischemic stroke (2). There is a critical need for methods able to monitor dynamically and noninvasively brain oxygenation. Variations in T_1 (longitudinal relaxation rate) and T_2* (transversal relaxation rate) are potentially valuable magnetic resonance imaging (MRI) tools to quantify changes in tissue 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). The aim of the current work was to implement the MOBILE technique, a method developed 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), in a mouse stroke model. For that purpose, we assessed relative brain tissue oxygenation in the insulted brain hemisphere versus the intact hemisphere. Capacity of response of both hemispheres to an hyperoxic breathing challenge was also assessed, and the measurements were compared with T_1 H_20 and T_2*.

Material and Methods:

Protocol: We used the photothrombic stroke model with unilateral lesion in 10 mice in order to test the sensitivity of MOBILE to: (i) basal brain tissue oxygenation by comparing the intact and the insulted hemispheres and (ii) response to carbogen breathing in the intact (controle area) and insulted (stroke area) hemispheres. Photoillumination was performed for 5min after iv injection of the photosensitizer Rose Bengal in a tail vein.

MR experiments: 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/32x32, 4 segments. 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.

Results:

Our data show that MOBILE was able to identify differences in basal brain tissue oxygenation in comparison with R_1 H_2O and R_2* methods, as seen on matched typical maps of R_1 of water, R_1 of lipids (Fig.2&3), and R_2*. The method was also highly sensitive to normal brain tissue hyperoxygenation during the carbogen challenge, contrarily to the insulted area. Indeed, the relative change in R_1 of lipids was 4.5 times higher than the relative change in R_1 of water in response to carbogen breathing in the control area (n=10, Fig.4). The stroke area was not able to respond to carbogen breathing using MOBILE or BOLD MRI (not shown).

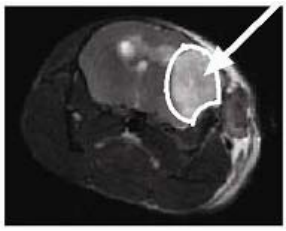

Fig.1 Anatomical brain image showing unilateral stroke lesion

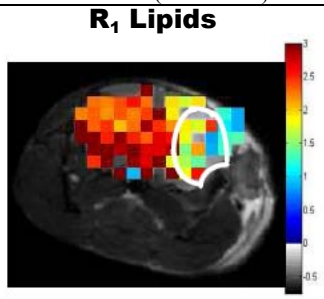

Fig.2 Typical R_1 Lipids map

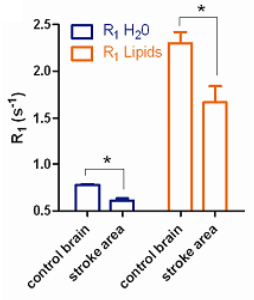

Fig.3 Differences in basal brain R_1 H_20 and R_1 Lipids

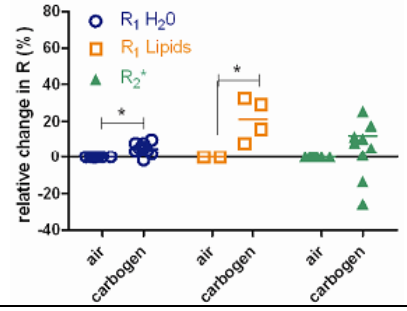

Fig.4 Relative change in relaxivity during carbogen breathing

Discussion

MOBILE was able to identify the relative difference in brain tissue oxygenation between both hemispheres with a higher sensitivity than R_1 H2O and R_2*. MOBILE also showed that the intact brain region was able to respond to an hyperoxic breathing challenge, whereas the stroke region was not responding. Knowing that R1 is mostly influenced by tissue oxygenation whereas R2* is more dependent on blood oxygenation, MOBILE could be a useful complementary tool to map brain tissue oxygenation early after an ischemic stroke event.

References:

(1) Asdaghi N, et al. Nat Rev Neurol. 7, 6-7 (2011), (2) Duffis EJ, et al, Neurosurg Focus. 30, E5 (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.