Application of MOBILE (Mapping of Oxygen By Imaging Lipids relaxation Enhancement) in stroke : preclinical and clinical studies.

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Target audience: MR scientists with interest in molecular imaging, neuroimaging and hypoxia imaging.

Purpose and objectives: There is a critical need for methods able to monitor dynamically and noninvasively brain oxygenation in clinical practice, to aid in the selection of patients who may still benefit from thrombolytic treatment beyond conventional time-based guidelines (1). Conventional MRI methods include DWI imaging (able to determine the extent of the ischemic lesion within the first hours) and T_1, T_2 measurements as well as FLAIR to follow the stroke area upon a few hours after the first event. Variations in T_1 and T_2* 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 (2), while T_1 is sensitive to dissolved oxygen which acts as a T_1-shortening paramagnetic contrast agent (3). However, this last technique lacks of sensitivity. The aim of the current work was to apply the MOBILE technique (for Mapping of Oxygen By Imaging Lipids relaxation Enhancement), 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 of oxygen in lipids than in water (4), in a stroke pre-clinical model (photothrombic mouse model) and clinical stroke patient at 11.7T and 3T respectively.

Material and Methods:

Stroke model & 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 (control area) and insulted (stroke area) hemispheres.

Preclinical MR experiments: experiments were performed with a 11.7T (Bruker, Biospec), and with a quadrature volume coil. 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 MOBILE experiment, the imaging frequency offset was determined thanks to a single pulse spectrum and applied in the same IR FISP protocol and water signal was spoiled using a $\pi/2$ hermite saturation pulse with a bandwidth of 5400Hz.ms.

Clinical protocol: MOBILE was implemented on a 3T clinical MRI (Philips) scanner in order to demonstrate (i) its capability to follow oxygen variations after a hyperoxic breathing challenge on volunteers (n=3) and (ii) its ability to point out a difference in oxygenation between insulted area (stroke) and intact area: assessing R_1 H_20, R_1 Lipids, and R_2* under air breathing.

Clinical MR experiments: MR imaging was performed at 3.0T (Achieva; Philips Medical System) using a transmit/receive head coil. T_1 measurement were realised with a Look Locker sequence (T1 TFE, T1 Turbo Field Echo sequence) applied during 24 seconds with TR/TE/NA/Flip angle/tfe= 3.467ms/1.45 ms/1/5°/10. 140 images with 20 mm of thickness and 80x80 pixels were obtained. For MOBILE measurements, the same sequence was used and a 90° SPIR pulse was added (Spectral saturation by Inversion recovery) to spoil water with a BW of 300Hz centered on the water peak. The acquisition lasted 4 minutes and 117 images with 20 mm of thickness and 80x80 pixels were obtained. 3 acquisitions of each (R_1 global, R_1 lipids and R_2*) were acquired during air breathing and hyperoxic challenge on healthy volunteers. The MOBILE sequence was also applied on one stroke patient.

Results: MOBILE is able to evidence a difference in basal oxygenation status in preclinical models (Fig.1.) and to follow the pO_2 variations induced by a hyperoxic challenge. 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.2). The translational application of MOBILE was also successful in following the oxygenation raise during 100% oxygen breathing on healthy volunteers (Fig. 3). In order to distinguish basal pO_2 in the stroke patient, R_1 of lipids, global R_1, and R_2* were measured in two ROIs encompassing normoxic and injured area, and we observed a higher drop in R_1 lipids than in global R_1 (Fig.4, Fig.5.).

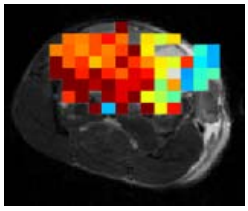

Fig.1. Typical map of R1 lipids on stroke model

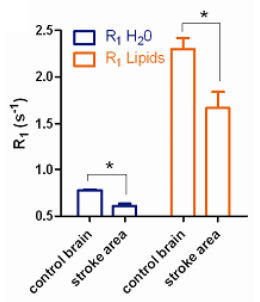

Fig.2. Differences in basal brain R_1 H_20 and R_1 Lipids

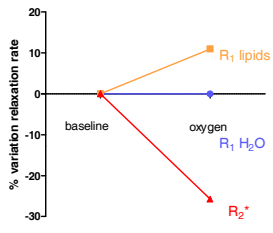

Fig.3 Relative change in relaxivity during carbogen breathing in volunteers

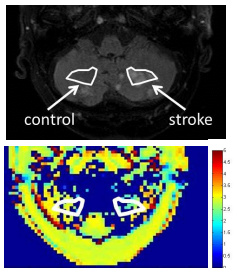

Fig.4. Anatomical brain image showing stroke area (a) and R_1 lipids map (b)

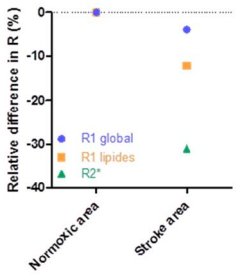

Fig.5. Typical pO_2 differences observed between safe brain and stroke area.

Conclusions: MOBILE was able to follow variations induced by a hyperoxic challenge in preclinical and clinical studies. In those two cases, MOBILE seems to be more sensitive than the two other conventional techniques. The lack of concordance between the 3 measurements in the translational application also suggest that MOBILE might be complementary to the R_2* measurements, more sensitive to the vascular oxygenation.

References:

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