Translational implementation of non-invasive Magnetic Resonance brain oxygen mapping in acute (72 hours) ischemic stroke patients

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Target audience: Researchers interested in non-invasive brain oxygen mapping in a clinical setting

Purpose: Endogenous oxygen-dependent sources of contrast in MRI include variations of T_2* and T_1 values within tissue[1]. T_1 discloses sensitivity to dissolved oxygen, which acts as a T_1- shortening paramagnetic contrast agent[2]. Analysis of proton T_1 relaxation induced by paramagnetic molecular oxygen has previously shown capability to monitor changes in tissue oxygenation, the technique being therefore also referred to as '*oxygen-enhanced MRI*'[3-5]. Up to now, only relaxation of water and lipids protons has been investigated with the obvious prominence of signal from water, and therefore referred as to water proton relaxation or '*global*' R_1. We previously demonstrated the benefit of measuring selectively the spin-lattice (T_1) relaxation of lipids after suppressing water signal to increase the sensitivity of the method because of higher solubility of oxygen within lipids than water. The *'MOBILE'* (**M**apping of **O**xygen **b**y **I**maging **L**ipid **E**nhancement) pulse sequence was developed in the purpose of detecting changes in tissue oxygenation in preclinical models including ischemic ones[6]. We hereby investigated in a translational "proof of concept" way whether MOBILE should enable detection of brain oxygen deprivation in the clinical setting of acute (72 hours) ischemic stroke patients.

Methods:

Patient recruitment: 18 patients presenting an acute (72 hours) ischemic stroke were recruited after informed consent (study cleared by local EC). Because of motion artifacts, only 9 insulted areas have been included in the analysis. 12 volunteers were also recruited for the study to obtain a normative database of basal R_1 ($1/T_1$), values in healthy brain tissue. Parametric maps of global R_1, lipids R_1 and R_2* were generated for each patient and each healthy volunteer.

Clinical MR experiments: MOBILE was implemented on a clinical 3.0T MRI system (Achieva; Philips Medical System, Best, the Netherlands). Images were acquired using a transmit/receive head coil. Global T_1 measurement were realised with a Look Locker sequence (T1 TFE, T1 Turbo Field Echo sequence) applied during 10 seconds with TR/TE/flip angle/TFE/NSA= 3.467ms/1.45 ms/5°/10/1 to acquire one 20 mm thickness slice covering a FOV of 230x180 mm with a matrix size of 80² resulting in a voxel size of 3.91x5.08x20 mm. For MOBILE measurements, the same sequence was used with the addition of a 90° SPIR pre-pulse (Spectral saturation by Inversion recovery) to spoil water with a BW of 300Hz centered on the water peak. 38 images averaged 30 times with similar metrics than previous acquisition were obtained for total acquisition time of 4 min.

Results: Analysis was performed on manually delineated regions of interest (ROIs) contouring the infarcted area ('*Stroke*') and the contralateral mirror area in unaffected brain tissue ('*Control*') for each patient, as shown on the overlay of MOBILE map on anatomical FLAIR image (Fig.1). Pooled results on Figure 2 demonstrate that global R_1 (Fig.2a), lipids R_1 (Fig.2b), and R_2* highlight statistically significant differences between infarcts and unaffected mirror-ROIs in patients (with p=0.0269, p<0.0001, p=0.0195 respectively). Moreover, we found no significant difference between unaffected mirror-ROIs and healthy brain tissue in volunteers (p=0.2511, p=0.1099, p=0.1757 respectively). Pooled data histogram analysis demonstrated a 0.154 s^{-1} gap separated medians of infarcts versus mirror-ROIs for global R_1 (p< 0.027) and a 0.408 s^{-1} one for lipids R_1 resulting in drastically improved p-value at < 0.0001.

Figure 1

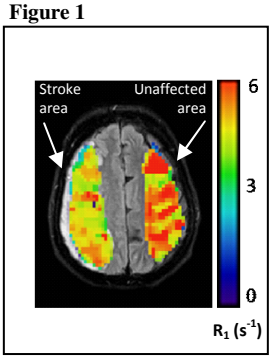


Figure 2

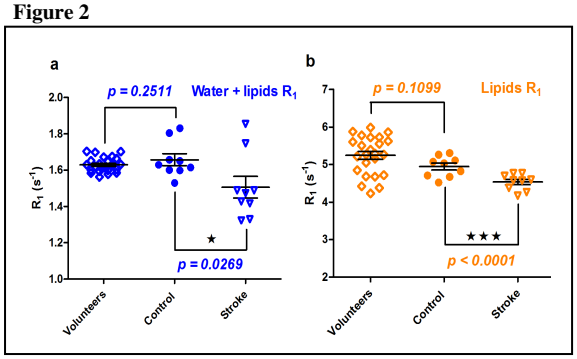
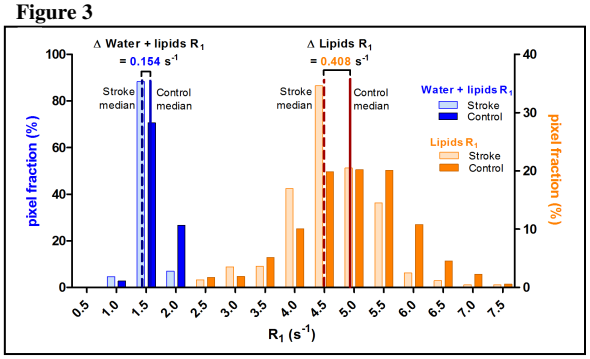


Figure 3



Discussion: The MOBILE sequence allows fast and noninvasive measurements of tissue pO_2 by exploiting the paramagnetic properties of molecular oxygen used as endogenous contrast agent. We targeted a patients' group presenting with early (72 hours) acute ischemic stroke since oxygen deprivation within brain tissue appeared as a paradigmatic condition in the purpose of quantifying tissue oxygenation in a clinical setting. Our hereby reported data demonstrated the feasibility and coherence of the results of such approach of brain pO_2 mapping through analysis of tissue T_1. By selectively recording relaxation enhancement of lipids instead of '*global*' T_1 measurement, the sensitivity is dramatically increased. A decrease in R_2* was also observed as expected, since a vasogenic edema appears in the second phase of the stroke process increasing T_2* independently from blood oxygenation effects resulting in a decrease in R_2*. To ensure reliability of measurements, we compared parametric values within contralateral unaffected brain tissue of patients to those recorded in healthy brain tissue of volunteers. We found very close correlation between baseline values in healthy volunteers and mirror-ROIs in unaffected brain tissue of stroke patients thereby suggesting the robustness of the MOBILE technique.

Conclusion: Feasibility in a clinical setting of *in vivo* pO_2 mapping within brain tissue of acute (72 hours) ischemic stroke patients by calculating and mapping the relaxation effect of molecular O_2 on water and lipid protons was demonstrated. Selective analysis of lipids relaxation enhancement by using the MOBILE technique significantly added in the purpose. The *in vivo* MOBILE approach for tissue pO_2 measurements using noninvasive and innocuous method repeatedly applicable on routine clinical MR imagers opens wide investigational fields in clinical practice.

References: **1.** Pacheco-Torres J, et al. *NMR Biomed.* 2011; 24**:**1–16 **2**. Matsumoto K, et al. *Magn Reson Med.* 2006; 56:240-6 **3**.O'Connor JP, et al. *Magn Reson Med.* 2007;58:490-6 **4.** O'Connor JP, et al. *Int J Radiat Oncol Biol Phys.* 2009;75:1209-1215 **5.** Burrell JS *J Magn Reson Imaging*. 2013;38: 429-34 **6.**Jordan BF, et al. *Magn Reson Med.* 2013; 70:732–744