Mapping of Oxygen By Imaging Lipids relaxation Enhancement (MOBILE): Application to Changes in Liver Oxygenation

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Purpose:

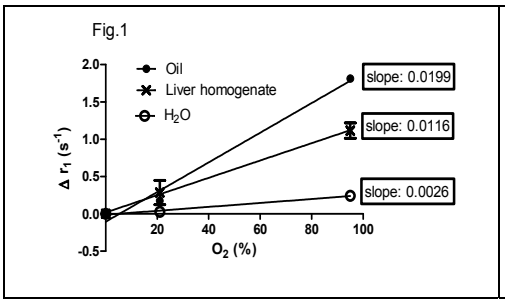
There is a critical need for methods able to monitor dynamically and noninvasively tissue oxygenation in humans with a large panel of applications to study ischemic diseases. Many current methods are either highly invasive, non-quantitative, or lack spatial resolution. T_1 and T_2* are potentially valuable tool to monitor tissue oxygenation, and their variations may reflect changes in tissue oxygenation. T_2* is sensitive to the relative Hb/HbO2 ratio in vessels, while T1 change is sensitive to dissolved oxygen which is paramagnetic and acts as a T1-shortening contrast agent. Recently, changes in tissue oxygen concentrations have been shown to produce proportional changes in MRI longitudinal relaxation rate R_1 of water (1). This technique, although non invasive and quantitative, still lacks a good sensitivity. In the present study, we propose to exploit the higher solubility property of oxygen in lipids than in water (2) to monitor the changes in R_1 of the lipid peak and translate it into pO_2 values. For this purpose, we developed a sequence that is able to map variations in oxygenation based on a rapid measurement of the relaxation properties of the tissue lipids. We called this technique *MOBILE* for Mapping of Oxygen By Imaging Lipids relaxation Enhancement. We first measured in vitro the relaxation properties of water and lipid components in pure aqueous or oil phases, and tissue homogenates equilibrated in different oxygen environments. We also monitored the evolution of the R_1 of lipids in vivo in the liver of mice before and during a carbogen breathing challenge.

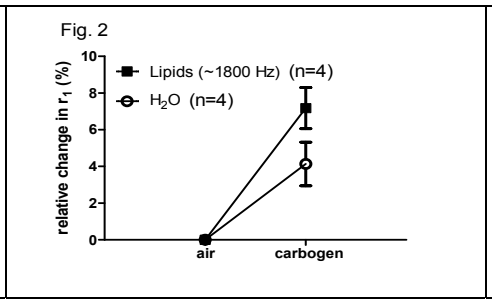
Material and methods:

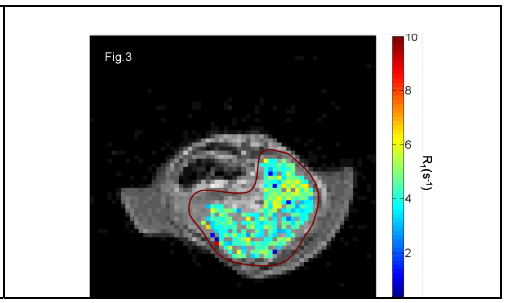
MR experiments: Experiments were performed with a 11.7T (Bruker, Biospec) system equipped with a quadrature volume coil (inner diameter of 40 mm and length of 100mm). A segmented IR FISP (Inversion-Recovery Fast Imaging with Steady state Precession) sequence (SSFP FID mode) was used to acquire parametric 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 total proton experiment (essentially reflecting the water peak), a series of 100 images were acquired between 30 and 11910 ms (TR=120 ms between segments) with a slice thickness of 1mm in order to sample the inversion recovery curve. For the lipids experiment, we first evaluated with a single pulse sequence the difference in Hertz between water and lipid peaks in the spectrum. These offsets were then used as an imaging frequency offset in the same IR FISP protocol. We added a $\pi/2$ hermite saturation pulse with a bandwidth of 5400Hz.ms to spoil the water signal. A series of 40 images between 30 and 3930ms (TR=100ms between segments) were acquired with a slice thickness of 3 mm. Then, images were treated using a home made program written in Matlab to determine the T_1 relaxation regions of interest.
Samples and animals: Calibration curves (R_1 as a function of % oxygen) were established in water, oil, and liver homogenates. For the proof-of-concept, lipid-rich tissues (liver in ob/ob male mice, n=4) were studied in mice anesthetized using isoflurane. Respiratory triggering was employed to acquire images during the expiration cycle to avoid motion artifacts. Three measurements were acquired during air breathing. Then, breathing gas was switched to carbogen breathing, and three measurements of R1 were acquired 10, 25, and 40 minutes during carbogen breathing.

Results:

The ΔR1 (expressed as % change of the value recorded at 0% oxygen) is presented in Fig.1. The higher solubility of oxygen led to a four to five times higher sensitivity when considering the evolution of R_1 of lipids as a function of oxygenation, compared to the $R_1$of water. The relative changes in R_1 before and after carbogen challenge are presented in Fig.2. Again, we observed a higher sensitivity of R_1 measured in lipids compared to the R1 of water after the carbogen breathing challenge that resulted in an increased tissue oxygenation. A typical lipid T1 map overlaid on an anatomical image of an ob/ob mouse liver is presented on Fig.3.







Conclusions:

The measurement of R_1 in lipids offers an increased sensitivity when monitoring the changes in tissue oxygenation compared to previously described techniques that measure the variations of R_1 in the water component.

References:

(1) O'Connor et al, Magn Reson Med 2009, 61, 75-83. (2) Bennett et al, Invest Radiol 1987, 22, 502-507.