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Novel methods for the detection of functional brain activity using 17O MRI

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Abstract

Detailed quantitative information about metabolic processes plays a crucial role in the potential cure and for treatment of many diseases such as Alzheimer's disease or brain tumours. In the last decades, radioactive tracers such as ^{15}O have been used to quantify $CMRO_2$ with PET imaging and this is regarded as the gold standard. However, such methods are complicated and expensive as a consequence of the short half-life (2 min) of ^{15}O and inherently include radiation exposure and invasive measurements such as blood probes to probe cerebral blood flow (CBF). Fick's principle of arteriovenous oxygen difference [1] connects $CMRO_2$ and CBF via the measure of oxygen extraction fraction (OEF).
The main goal of this work is to achieve non-invasive measures of OEF based on magnetic resonance imaging (MRI) to quantify $CMRO_2$ allowing straightforward and comfortable patient handling. MRI enables studies of large cohorts of healthy volunteers due to non-invasive measurements and a lack of radioactivity. This can be achieved first by quantitative relaxation time mapping of the transverse relaxation time (T_2) of venous blood only in proton (^{1}H) MRI or by a measurement following inhalation of ^{17}O gas and recording the signal curve of directly detected ^{17}O signal. Unfortunately, the most abundant isotope of oxygen (^{16}O) has a zero spin system, and cannot be detected with NMR experiments. In contrast, ^{17}O, a stable isotope with a half-integer spin (I=5/2), can be detected by MR. Fortuitously, however, in MRI it is only visible in the form of metabolically generated $H_2^{17}O$ and not as a gas. The low natural abundance of ^{17}O, of only 0.037% (of the oxygen atoms) and the low NMR sensitivity (2.9% that of ^{1}H) gives rise to the need for ultra-high-field MRI to reach a significant SNR per unit time.
Natural abundance images of a healthy male volunteer were acquired *in vivo* after having gained written consent within a clinical trial of a 9.4 T MRI system (Siemens AG, Erlangen, Germany) [2, 3]. These natural abundance images, which reflect the ^{17}O bound to protons as $H_2^{17}O$ and thus, the amount of water, are compared to ^{1}H-based quantitative water content imaging. For further studies, the voxelwise knowledge of the quantitative water content is necessary to quantify $CMRO_2$ based on the ^{17}O signal behaviour. To achieve that, methods which were originally used on 1.5 T scanners had to be adapted for the use at higher field strengths to overcome RF field inhomogeneities [4–11]. New correction methods were developed based on a well known correlation between tissue T_1 and proton density (PD) to estimate the receive bias field properly. These methods were tested for quantitative water content determination. Averaged results in grey (GM) and white matter (WM) respectively of 10 healthy volunteers are H_2O_{WM}=70.3±1.4 %, H_2O_{GM}=84.7±1.5 %,, $T_{1_{WM}}$=918±24 ms and $T_{1_{GM}}$=1509±14 ms.
Further, ^{1}H-based imaging methods called QUIXOTIC [12–14] and TRUST [15] appeared in the literature. These methods are based on changes of the proton transverse relaxation rate T_2 with different oxygen saturation levels. Quantitative values of venous blood T_2 were acquired using a so-called T2prep module or a multi-echo spin echo readout. While the first method suffers from long acquisition times the latter one from large echo-spacing of the spin echoes and stimulated echo effects. Both disadvantages were overcome using an adiabatic multi-shot multi-echo spin echo sequence, which does not suffer from stimulated echo effects and due to the multi-shot capabilities, the echo-spacing is reduced [16]. Mean values in GM of four healthy volunteers are found to be venous oxygenation Y_v=0.61±0.03, T_2=54±4 ms, $CMRO_2$=174±13 μmol/100g min and CBF=53±3 ml/100g min.