Dynamic ^{17}O-MRI at 3 Tesla for in vivo $CMRO_2$ Quantification

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Introduction

Malignant tumors predominately gain energy by high aerobic glycolysis (Warburg effect [1]). The metabolism of tumor cells in the brain can be monitored by assessing their cerebral metabolic rate of oxygen consumption ($CMRO_2$). Clinically, $CMRO_2$ is quantified with positron emission tomography (PET) using radioactively-labelled ^{15}O. Unfortunately, ^{15}O-PET is difficult to perform, because the procedure exposes the patient to ionizing radiation, and the short half-life of ^{15}O (about 2 ms) requires onsite isotope production with a cyclotron.

Another possibility to quantify $CMRO_2$ is direct ^{17}O-MRI at 7 or 9.4 Tesla [2, 3]. Unfortunately, high field MR systems are limited to a few academic institutions, and are not found in clinical routine. Recently, feasibility of cerebral and cardiac ^{17}O-MRI has been demonstrated at natural abundance at clinical field strength of 3 Tesla [4, 5]. In this work we show for the first time direct cerebral dynamic ^{17}O-MRI in a volunteers head at a field strength of 3 Tesla, which is commonly available in a clinical routine.

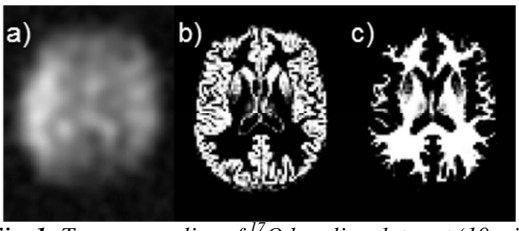

***Fig. 1**: Transverse slice of ^{17}O baseline data set (10 min) with 10 mm nominal resolution and SNR = 25; and segmented gray (b) and white matter (c) compartments used for $CMRO_2$ quantification.*

Materials and Methods

The ^{17}O-MRI measurements were performed at a clinical 3 Tesla MR system (Tim Trio, Siemens) using a custom-built Tx/Rx ^{17}O head coil [5] tuned to the ^{17}O resonance at f_0 = 16.7 MHz. For efficient administration of 70%-enriched ^{17}O gas (Nukem Isotopes, Germany) an MR-compatible re-breathing system was constructed consisting of a re-breathing mask and a demand oxygen delivery system (DODS, Oxytron3 Weinmann Hamburg, Germany) for gas supply. To demonstrate reproducibility of the gas administration and to optimize the spatial resolution, two ^{17}O inhalation experiments were performed in a healthy volunteer (male, age 49y) with a nominal isotropic resolution of 10 and 8 mm. In the experiments ^{17}O MR images were acquired during a baseline phase of 10 min under free breathing, an inhalation DODS-phase (4-5 min) when ^{17}O was administered, a re-breathing phase (5-8 min) with a closed rebreathing circuit, and a final wash-out phase (22-25 min), during which the volunteer was breathing room air. In total, 2.7 and 2.5 liter of enriched ^{17}O gas were delivered during the two measurements.

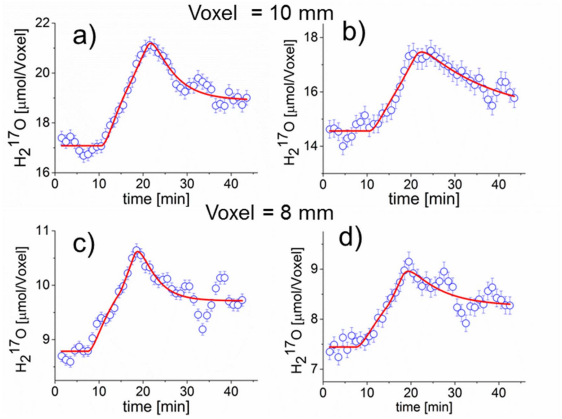

***Fig. 2**: Signal time courses for voxel sizes of 10 and 8 mm in gray (a, c) and white matter (b, d) are shown in absolute units of $H_2{}^{17}O$ [µmol/voxel] and fitted with a four phase metabolic model.*

A complete ^{17}O measurement consisted of 45 3D data sets of the brain with a temporal resolution of 1 min using an implemented density-adapted projection sequence (DAPR) [6]. Each data set in experiment 1/ 2 was acquired with the following imaging parameters: nominal resolution (10/ 8 mm)^3, TE = 0.52 ms, TR = 8/ 7 ms, T_{pulse} = 0.8 ms, BW = 150/ 175 Hz/px, T_{RO} = 6.7/ 5.7 ms, α = 69°, 1 average, 7500/ 8570 projections x 128 sample points per projection interpolated onto a 128³ matrix. The ^{17}O data were reconstructed based on Kaiser-Bessel regridding algorithm without using any filter (e.g. Hann window) [7]. To improve the SNR, view sharing was performed by adding 3 consecutive k-space data sets. Additionally, for co-registration and segmentation of brain compartments ^{1}H data were acquired (Fig.1) using a 3D MPRAGE sequence with the following parameters: TE = 2.86 ms, TR = 2300 ms, TI = 1100 ms, BW = 130 Hz/px, α = 12°, 1 average, FOV = (262 x 300) mm^2, SL = 1 mm, nominal resolution (0.6 x 0.6 x 1) mm^3, matrix: 448 x 512, T_{AQ} = 8:36 min. To obtain $CMRO_2$ values, gray matter (GM) and white matter (WM) regions were segmented, and a 4-phase model [3] was fitted to the signal-time curves using a non-linear least squares method (Fig. 2).

Results and Discussion

In both experiments an increase during and after ^{17}O administration of 20-24 % was seen both in GM and in WM. The $CMRO_2$ values for GM and WM are in a good agreement with literature values for 10 mm voxel size (Fig. 3), whereas the values for higher spatial resolution of 8 mm exceed literature values by 27-65%. In the 10 mm data sets an SNR of 12 was seen, and at 8 mm a lower SNR of 7 was observed, which might account for inaccuracies during $CMRO_2$ quantification due to the non-linear behavior of the magnitude signal at low SNR [9]. To overcome this limitation at higher spatial resolution, ^{1}H-constraint reconstruction could be applied.

In conclusion, two experiments were successfully performed at clinical field strength of 3 Tesla using a dedicated breathing system. These experiments are a first step to apply direct ^{17}O-MRI in tumor patients to investigate the oxygen turnover in oncology.

Tissue	$CMRO_2$ [µmol/g_{tissue}*min] 3 T, 10 mm	3 T, 8 mm	7 T, 9.4 mm	PET
Gray Matter	1.59±0.16	2.02±0.28	1.65±0.29	1.59±0.23
White Matter	0.71±0.07	1.07±0.15	0.83±0.14	0.65±0.10

***Fig. 3**: $CMRO_2$ values obtained with direct ^{17}O-MRI at 3 Tesla compared with literature values from 7 Tesla [3] and PET [8].*

References

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