Partial volume corrected $CMRO_2$ determination in a glioblastoma patient by ^{17}O MRI

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PURPOSE In healthy brain tissue virtually all metabolic energy is provided by oxidative metabolization of glucose. In tumor cells, however, this process is markedly shifted towards the anaerobic pathway even if sufficient oxygen is present ('Warburg effect'). Thus, the cerebral metabolic rate of oxygen consumption ($CMRO_2$) can provide valuable information on cell viability and tissue health. By ^{15}O PET studies, reduced $CMRO_2$ was found in brain tumors [1]. In recent years, MRI of the stable oxygen isotope ^{17}O has been shown to be able to assess cellular oxygen consumption noninvasively [2]. In this study, we performed an $^{17}O_2$-inhalation experiment on a histopathologically verified glioblastoma (WHO grade IV) patient. The $CMRO_2$ was quantitatively evaluated after partial volume correction (PVC) of the data.

METHODS Direct ^{17}O MRI was carried out on a 7 Tesla MR system (Magnetom 7T, Siemens AG, Healthcare Sector, Erlangen, Germany) with a custom-built single tuned birdcage head coil [3]. A 3D data set was acquired every 50 s with an isotropic nominal spatial resolution of 8.5 mm with a density-adapted projection reconstruction pulse sequence (TR/TE = 8.3/0.57 ms, T_{RO} = 5.6 ms, 6000 projections, $\theta = 60°$, T_{AQ} = 53 min) [4]. During $^{17}O_2$ inhalation (t_{start} = 10 min to t_{stop} = 19 min) a total of 4.7 ± 0.1 l of 70%-enriched ^{17}O gas (Rockland Technimed Ltd., Airmont, NY, USA) were delivered to the patient in small gas pulses (V = 40 ml/pulse) via a demand oxygen delivery system (Oxytron3, Weinmann, Hamburg, Germany) [3]. The 'geometric transfer matrix' algorithm [5] for PVC was adapted to the MRI methodology and applied to the ^{17}O data before $CMRO_2$ determination. Therefore, registration and segmentation of high resolution ^1H data was carried out on T_1-weighted images (FMRIB Software Library, FSL) delineating white matter (WM), gray matter (GM), cerebrospinal fluid (CSF), the necrotic part of the tumor (NE), contrast enhancing parts of the tumor (CE) and perifocal edema (PE). The point spread function of the radial sequence, needed for the GTM algorithm, was determined from simulations of the sampled k-space volume incorporating T_2^* relaxation [6]. A three-phase model was used to determine $CMRO_2$ [2]. Quantification of the $H_2{}^{17}O$ concentration was carried out using the baseline signal intensity before gas delivery as an internal reference. Water fractions of the compartments were set to $\lambda_{CSF} = 1$, $\lambda_{GM} = 0.83$, $\lambda_{WM} = 0.71$ [7] and $\lambda_{CE} = 0.71$, $\lambda_{NE} = 0.95$, $\lambda_{PE} = 0.90$ [8], respectively.

RESULTS AND DISCUSSION The relative signal increase after $^{17}O_2$ inhalation is shown in Figure 1 (w/o PVC). Values range from less than 2% increase in the center of the tumor up to more than 25% in the periphery of the brain. The region of minimal increase is in good agreement with the necrotic part of the tumor. The highest signal gain was found in the areas of the gyri with a high gray matter fraction which is in agreement with the higher oxygen consumption of gray matter compared to white matter. Signal time curves before and after PVC are shown in Figure 2. PVC leads to a shifting especially in the CSF signal for which a delayed increase is obtained. Also the GM signal is significantly increased (approx. 4%). As the enrichment fraction α depends on many physiological parameters in the case of pulsed $^{17}O_2$ delivery method (e.g. tidal volume), it was estimated in the range of 0.2 to 0.4. The $CMRO_2$ values are given in Table 1 in units of µmoles/g/min. In necrotic tumor areas (NE) as well as in CSF the model yields $CMRO_2 = 0$. This data is in accordance with ^{15}O PET results obtained in brain tumors where a consistent decrease is found in the lesions [1]. However, the $CMRO_2$ we obtained in GM is higher than the PET data by a factor of 2-3. This difference is in the range of the shift arising from the PVC. Because of the vicinity of the CSF compartment to the edge of the brain, errors in the intensity correction may occur that lead to an overestimation of the GM signal.

Tab.1: $CMRO_2$ [µmoles/g/min] obtained for different enrichment fractions α with a least-squares fit of the three-phase [2] model.

	GM	WM	CE	PE
α = 0.2	5.2	0.8	0.7	0.5
α = 0.3	3.5	0.5	0.5	0.4
α = 0.4	2.5	0.4	0.4	0.3

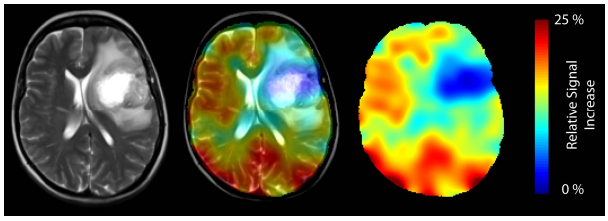

Fig.1: Mapping of relative signal increase after $^{17}O_2$ inhalation and corresponding anatomical reference. Signal change ranges from less than 2% in the necrotic part of the tumor to more than 20% in regions of high gray matter concentration.

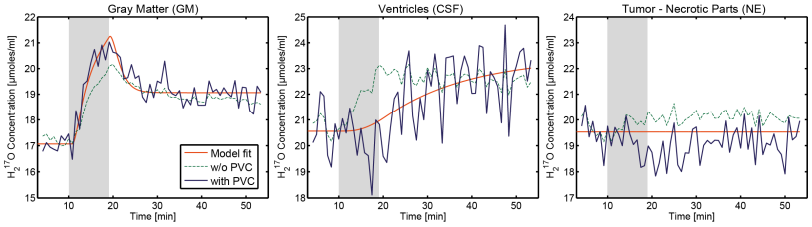

Fig.2: Signal time curves of GM, CSF and the necrotic tumor region. Intensities are given before and after PVC; additionally, the fit (α=0.3) of the three-phase model is displayed. The PVC leads to noise amplification especially in the case of CSF. After PVC no increase in CSF is found during $^{17}O_2$ delivery.

CONCLUSION In this work, we performed the first $^{17}O_2$-inhalation experiment on a tumor patient. A partial volume correction algorithm was applied and the $CMRO_2$ of brain and tumor compartments was determined. In agreement with PET results, we found decreased oxygen consumption in the tumor compared to normal brain matter.

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