

^{17}O T_1/T_2^* tissue-relaxation rates with anatomical contrast in the rat brain at 16.4 TH. M. Wiesner¹, D. Z. Balla¹, R. Pohmann¹, W. Chen², K. Ugurbil², and K. Uludag¹¹High-Field Magnetic Resonance Center, Max Planck Institute for Biological Cybernetics, Tübingen, Germany, ²Radiology, Center for Magnetic Resonance Research, University of Minnesota Medical School, Minneapolis, MN, United States

Introduction The measurement of cerebral metabolic rate of oxygen (CMRO₂) via direct NMR detection of the stable oxygen isotope ^{17}O is a promising tool to study neuroenergetics, brain activity and pathology [1]. Due to the low natural abundance of H_2^{17}O (0.037%) and fast relaxation rates of the ^{17}O nucleus [2-4], sequences with short acquisition delays and optimized acquisition parameters are crucial for ^{17}O imaging of metabolically produced cerebral water. It has been demonstrated that signal-to-noise ratio (SNR) of ^{17}O NMR increases almost quadratically with B_0 due to its field-independent quadrupolar relaxation properties [2, 3]. Thus, in comparison to studies at lower field strengths, the increased SNR available for MRS imaging (MRSI) at 16.4 T allows enhanced spatial resolution. Therefore, the aim of this study was the tissue-specific determination of ^{17}O relaxation times and the anatomical imaging of ^{17}O contrast in the rat brain.

Methods A 3-D chemical shift imaging sequence was chosen to minimize acquisition delays (here: 456 μs) for in-vitro & in-vivo ^{17}O MRSI [5]. All acquisitions were performed on a 16.4 Tesla magnet (Magnex/Varian Inc.) with a 26 cm bore diameter, maximal gradient-strength 1 T/m (Resonance Research Inc.) interfaced to an Avance III - Paravision 5.0 (Bruker BioSpin) console. Samples were excited by custom-built silver wire surface-coils (diameter 1 & 2 cm) tuned at $\omega_0=94.63$ MHz with a 50- μs RF hard pulse adjusted to a nominal flip angle of 90° for each sample and the inversion pulse was achieved by doubling the 90° pulse width. Spectral bandwidth was 9369 Hz (~ 100 ppm) throughout all scans.

Samples In-vitro: 25 g water-phantom with enriched 10% H_2^{17}O in a glass cylinder. Ex-vivo: 1 male Wistar rat (550 g).

In-vivo study 4 self-breathing isoflurane anesthetized male Wistar rats (470 \pm 50 g) with head fixated in a stereotaxic frame were studied. Exhaled gases were continuously monitored and body temperature was maintained at rectally measured 37 \pm 0.3 $^\circ\text{C}$ with an electric heat blanket. T_1 and T_2^* methodologies were validated on the enriched H_2^{17}O phantom in terms of distance from the coil and flip-angles.

Parameters for ^{17}O T_1 measurements (ex-vivo/in-vivo at natural abundance H_2^{17}O concentration): An 8-step inversion recovery method (TI 1.5 - 50 ms) with repetition times $\text{TR}>5T_1$ was used. Other parameters are: FOV 3.5 \times 3.5 \times 2.5 cm^3 ; matrix 15 \times 15 \times 7; TR 65 ms, spectral acquisition points 94; total acquired FIDs 51200 (max. 339 averages in the center of k-space) with an overall duration of 55 min per 3D ^{17}O MRSI volume.

Parameters for ^{17}O T_2^* measurements (ex-vivo/in-vivo): FOV 3.62 \times 3.62 \times 2.5 cm^3 ; matrix 51 \times 51 \times 7 (voxel-volume: 1.8 μl); TR 5.08 ms with an acquisition duration of 3.91 ms with 37 spectral points; total acquired FIDs 409600 (max. 205 averages in the center of k-space) with an overall duration of 34 min per 3D ^{17}O MRSI volume. Additional FLASH images, although at lower SNR due to longer acquisition delays, were used for qualitative verification of T_2^* -contrast and tissue separation obtained by 3D-CSI.

Data were reconstructed and further processed using MATLAB (Matworks): 1. Zero-filling and line-broadening were used for anatomical visualization of muscle, cortex and deeper (sub-cortical) brain tissue in images of the spectral integral (Fig. 1a). 2. Relaxometry was performed on raw-data: T_1 estimation was based on fitting of spectral peak intensity at different inversion times according to a mono-exponential function. Estimation of T_2^* was based on the decay rate of FIDs transformed into image space (Figs. 1b and 1c). All voxels selected for relaxometry were masked to have at least a spectral SNR > 12 and were less than 1 cm distant from the coil (Fig. 1c).

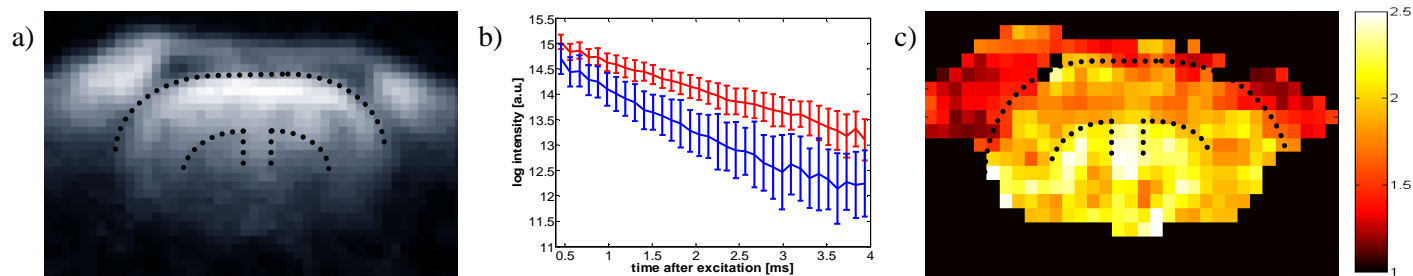
Results

Figure 1 (a) In-vivo CSI of natural abundance H_2^{17}O in a coronal slice of a rat head with inner brain-structures (highlighted by dotted lines for outlining cortical and deep sub-cortical brain regions). (b) log-scaled decays (in image-space) of muscle (blue) and brain tissue (red) of an in-vivo rat. (c) T_2^* map of the same slice as in (a) with structures of distinct T_2^* relaxation (scale in ms).

Phantom	T_1 : 6.24 \pm 0.37 (ms)	T_2^* : 2.24 \pm 0.09 (ms)	
Ex-vivo rat	T_1 : 4.09 \pm 0.05 (226 μl brain tissue)	T_2^* muscle tissue: 2.31 \pm 0.47 (86 μl)	T_2^* cortex: 2.48 \pm 0.51 (118 μl)
In-vivo rats	T_1 : 6.87 \pm 0.46 (155 μl brain tissue)	T_2^* muscle tissue: 1.50 \pm 0.20 (442 μl)	T_2^* cortex: 2.02 \pm 0.24 (597 μl)

Relaxation rates in ms (mean \pm std) and volume of selected voxels in brackets. Signal decay was mono-exponential.

Conclusions We have shown, for the first time, natural abundance ^{17}O brain images with anatomical contrast at 16.4 T. Significant difference in T_2^* of muscle tissue in comparison to cortex tissue was determined (Fig. 1b and Table). Fast T_2^* relaxation rate of muscle tissue might be beneficial for reducing partial-volume contaminations if read-out and TR is optimized for cortex H_2^{17}O . Furthermore, intra-cortical differences in intensity and T_2^* -relaxation were observed (e.g. cortex vs. deep sub-cortical areas in Figs. 1a and 1c), but their assignment needs ^1H -MRI anatomical overlay. The T_1/T_2^* values determined can be used to tune sequence parameters (e.g. Ernst angle, read-out duration, TR) to maximize SNR per unit time [6, 7], as required in functional CMRO₂ measurements by short inhalations of $^{17}\text{O}_2$ gas [1].

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References: [1] Zhu et. al. PNAS (2002), [2] Thelwall et. al. Proc. ISMRM (2003), [3] Zhu et. al. MRM (2001), [4] de Graaf et. al. JMR (2008), [5] Brown et. al. PNAS (1982), [6] Ernst et. al. Rev. Sci. Inst. (1966), [7] Pohmann et. al. JMR (1997).