Indirect ^{17}O MRI using T1ρ at 11.7 T

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Introduction ^{17}O MRI provides quantitative cerebral metabolic rate of oxygen ($CMRO_2$) measurements through monitoring the dynamic changes of metabolically generated $H_2{}^{17}O$ from $^{17}O_2$ gas. In ^{17}O MRI, only the metabolized $H_2{}^{17}O$ is detectable (molecular $^{17}O_2$ is not detectable), which simplifies both $CMRO_2$ measurement and quantification compared to the multi-tracer PET approach. ^{17}O nuclide can be detected directly (1) or indirectly (2,3). Direct detection is simpler but is only feasible at ultra-high fields due to low ^{17}O gyromagnetic ratio and has limited spatial resolution. Indirect method, on the other hand, can be done at clinical field strengths and has high spatiotemporal resolution, but is less straightforward (4). Indirect detection can be achieved via T2-weighted MRI with ^{17}O decoupling or spin-lock T1ρ MRI.

In this study, we explored the feasibility of ^{17}O T1ρ MRI on rats at 11.7T with the long-term goals of cross validation with direct detection method and applications to animal models of neurological disease. We first investigated the feasibility of a novel $^{17}O_2$ delivery system which involves intravenous injection of a perfluorocarbon (PFC) blood substitute with dissolved $^{17}O_2$, instead of the, more common, $^{17}O_2$ gas inhalation. Moreover, in addition to measuring quantitative basal $CMRO_2$, we evaluated two modulations known to change $CMRO_2$: hypothermia and focal ischemic stroke. In the stroke model, diffusion- and perfusion-weighted MRI (DWI and PWI) were also acquired to delineate acute stroke lesion.

Methods Male Sprague–Dawley rats (225-250g, n=4) were anesthetized with 2% isoflurane in air during surgery and maintained with 1.2~1.5% during MRI. A femoral vein was catheterized. For the hypothermia study (n=1), ^{17}O MRI was measured at 37°C and 34°C. For the stroke study (n=3), permanent focal brain ischemia was induced by intraluminal middle cerebral artery occlusion (MCAO) at the right hemisphere. O_2 saturation, heart rate, respiration rate, and rectal temperature were monitored continuously and maintained within normal physiological ranges.

$^{17}O_2$ was dissolved in PFC using a system developed by Rockland Technimed LTD. Blood gas was measured to ensure full ^{17}O saturation (average = 841 mmHg). After 2 or 3 mins of baseline T1ρ-weighted MRI, 1~1.4 mL/kg of ^{17}O/PFC was injected and the scan continued for 8-10 mins. Typically, 2-5 injections were made on each animal.

MRI was performed on an 11.7T Bruker Biospec with a Tx/Rx quadrature coil. T1ρ-weighted MRI was acquired using fast spin echo, on-resonance spin lock at 125 Hz, TR/TE_{eff}=1000/25 ms, ETL=16, central encoding, and 1.2 partial Fourier acceleration. For T1ρ map, images were acquired with TR/TE_{eff}=2000/16.6 ms, ETL=8, 6 different spin lock times from 20-120 ms, and spin lock at 1250 Hz. For stroke study, DWI was acquired with conventional spin echo, TR/TE = 2000/15.8 ms, b = 0 and 3 directions of 1000 sec/mm^2, δ = 2.6 ms, and Δ = 7.46 ms. PWI was acquired with dynamic susceptibility contrast with intravenous Gd-DTPA administration once at 3 hrs after stroke onset. All images were obtained with FOV = 2.56x2.56 cm, matrix=64x64 on a single slice.

Data analysis was performed using codes written in Matlab. ^{17}O T1ρ data were converted to metabolic $H_2{}^{17}O$ concentration (2). T1ρ map was calculated pixel-by-pixel by fitting the signal to six spin lock durations. DWI and PWI were analyzed as described in (5).

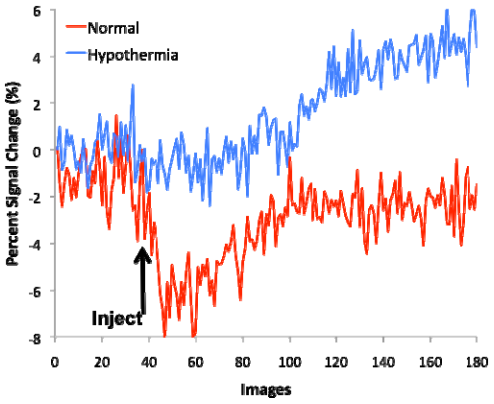

Figure 1. Normalized percent signal change of a representative subject under normal and hyopothermia.

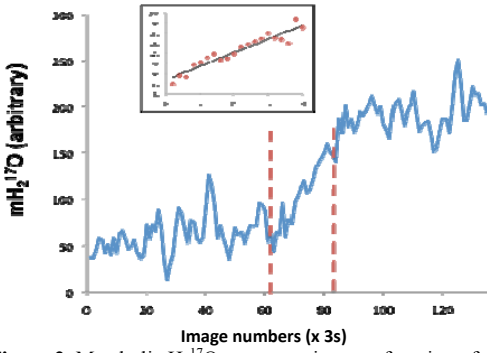

Figure 2. Metabolic $H_2{}^{17}O$ concentration as a function of image number. Injection was made at image #61. Inset: data of one min post-injection that are taken for $CMRO_2$ estimation (over image # 62-82).

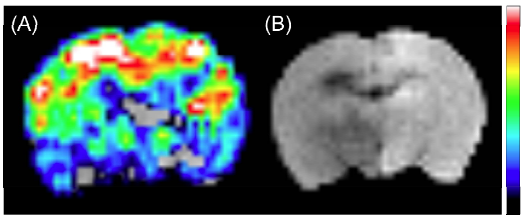

Figure 3. (A) $CMRO_2$ index map and the corresponding (B) DWI of a rat subjected to focal ischemia.

Results and Discussions **Figure 1** shows the T1ρ-weighted signal time courses for normal and hypothermic conditions. T1ρ-weighted signal decreased less significantly at 34°C than 37°C after ^{17}O/PFC injection, indicative of reduced $CMRO_2$. **Figure 2** shows the time course of metabolic $H_2{}^{17}O$ concentration from one animal under normothermia. Two repeated scans were averaged and data within 1 min post-injection (inset in figure 2) were used to calculate $CMRO_2$. The basal $CMRO_2$ was estimated to be 2.10 μmol/g/min (r^2 = 0.9), consistent with that reported by ^{17}O direct detection in rats ($CMRO_2$ = 2.19 μmol/g/min) (7). **Figure 3** shows the $CMRO_2$ map after 1 hr focal ischemia and the corresponding DWI depicting the hyperintense stroke lesion. PWI confirmed perfusion deficit (data not shown). $CMRO_2$ in the cortices were higher than the subcortical regions. $CMRO_2$ was slightly reduced in the ischemic lesion at this time point although DWI lesion was large, suggesting some tissue with DWI hyperintensity may be amendable to therapeutic interventions.

Conclusion This study demonstrates the feasibility of ^{17}O T1ρ indirect detection MRI to quantitatively image $CMRO_2$ with high spatiotemporal resolution. It is further demonstrated that the novel $^{17}O_2$ delivery system that involving injection of dissolved $^{17}O_2$ in PFC blood substitute is practical. ^{17}O T1ρ MRI reliably detects: *i)* absolute basal $CMRO_2$ that is consistent with published literature, *ii)* $CMRO_2$ reduction under hypothermia and, *iii)* $CMRO_2$ reduction in focal ischemic stroke. Future studies will improve in sensitivity and spatial resolution, evaluate the spatiotemporal progression of acute stroke, and cross validate with ^{17}O direct detection MRI. We anticipate ^{17}O T1ρ MRI with the practical PFC delivery system will enable many applications and can be readily applied to humans at clinical field strengths.

References 1. Zhu et al. PNAS. (2002). 2. Reddy et al. JMR Series B (1995). 3. Tailor et al. NI (2004). 4. Zhu et al. NMR Biomed. (2005). 5. Shen et al., JCBFM 23:1479 (2003).