^{17}O imaging for the evaluation of physiological function in the tumor bearing mice

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Introduction: The application of ^{17}O MRI method has been proposed in the measurements of regional cerebral blood flow and cerebral metabolic rate of oxygen consumption[1-3]. Since hypoxic tumor cells are resistant to the radiation, monitoring the tumor oxygenation and blood flow is important for the effective treatment. Irrespective of such expectation, low sensitivity and short T_2 of ^{17}O make the direct measurement difficult. In order to overcome these difficulties, proton-detected ^{17}O MRI[4], Chemical Shift Imaging[5], gradient echo and projection reconstruction[6] have been proposed. In this study, FISP was employed for $H_2{}^{17}O$ imaging at 7.0 T.

Methods: A water phantom (70 ml, natural abundance ^{17}O) was used for sequence comparison, FISP, Flash and FSE, and optimization. Saline of 0.5 ml containing 1 – 5% ^{17}O prepared from 10% ^{17}O water (Cambridge Isotope Laboratories, Inc) was i.v. injected to tumor bearing C3H/He mice (25 – 30 g). MRS/MRI was performed under ketamine and xylazine anesthesia on 7T/400mm/SS system (NIRS/KOBELCO/Bruker) with 50 mm $^{1}H/^{17}O$ Litz coil (Doty Scientific Inc.). ^{17}O images of mice were obtained by true FISP under the following parameters; TR/TE 6.54/3.28 ms, flip angle 60º, FOV 32×8 cm, matrix size 128×32, 100 or 15 mm slice thickness. After imaging experiment, organs were excised for ^{17}O spectral measurements.

Results: Estimated T_2* from FWHM of $H_2{}^{17}O$ in a phantom and a mouse were 6 and 2 ms, respectively. The S/N in the image of a water phantom by FISP was 1.6 times higher than that by Flash (TR/TE 10.1/5.2 ms and flip angle 75º) for the same data acquisition time, and the minimum TE was still too long for $H_2{}^{17}O$ by FSE. FISP ^{17}O-Image of a tumor bearing mouse with natural abundance $H_2{}^{17}O$ in 10 min is shown in Fig.1a. After the injection of 5% ^{17}O saline, the whole body signal intensities of both ^{17}O spectra and images were increased ca. 10 times higher than pre injection, which was sufficient for the visualization of the organ profile by ^{17}O images (Fig. 1b). Whole body image intensity was still more than 50% of maximum value 15 hours after the injection (Fig.1c). The signal intensities of tumor in i*n vivo* image and *ex vivo* spectrum at 15 h after injection were 6 and 4.5 times higher than those from non-^{17}O saline injected mouse, respectively.

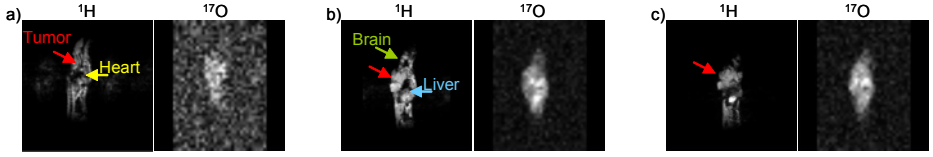

Fig.1. ^{17}O images (sagittal) of a tumor bearing mouse on the back at pre (a), 15 min (b) and 15 h (c) after 5% ^{17}O saline injection, without window functions.

Discussion: FISP was the best in imaging of ^{17}O water among FISP, Flash, and FSE. The low resonance frequency of ^{17}O, 40 MHz at 7 T, brought us the advantage of high sensitivity of FISP over the susceptibility problem. The distribution of $H_2{}^{17}O$ in mouse was successfully visualized by FISP in 10 min under a spatial resolution of 2.5 mm. The regional ^{17}O image intensities were in good agreement with the ^{17}O NMR spectral intensities of excised organs. The increases in intensity both in the images and spectra after ^{17}O saline injection were in proportional to the increase in the ^{17}O concentration in the extracellular fluid. The feature of ^{17}O signals observed here reports the physical state of water *in vivo*, which is to be studied further. Here, a feasibility of $H_2{}^{17}O$ mapping depicting water dynamics from blood flow to diffusion is shown. The extension of this technique to visualize the oxygen consumption in the brain and tumor using $^{17}O_2$ gas is promising.

Reference: (1) Zhu XH. et al, NMR in Biomed 18:83 (2005), (2) Ronen I.et al, PNAS 95:12934 (1998), (3) Arai T. et al, Brain Res 45:451 (1998), (4) Ronen I. et al. MRM 32:789 (1994), (5) Xhu XH. et al, MRM 45:543 (2001), (6) Fiat D. et al, Neurol Res 26:803 (2004)