Hyperpolarized ^{129}Xe Lung MRI with trueFISP on Spontaneous Breathing Mice by Means of Continuous Delivery of Xe Gas Polarized under Low Pressure

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Introduction: The hyperpolarized (HP) noble gas MRI on mice is expected as an extremely valuable modality in studies of drug discovery because of the easy access to genetically engineered species as well as various disease models. In these studies, a non-invasive protocol that allows a long-term and repeated measurements on the same individual may be required, which will be realized by the use of spontaneously breathing protocols without using any tracheotomy or intubation. Although ventilation imaging using HP ^{3}He on spontaneous breathing animals was reported [1], it is more challenging for mice because of small lung tidal volume and high respiratory rates. Inherent advantage of HP ^{129}Xe such as high solubility in tissue and large chemical shift distribution as well as easier accessibility encourage extended study with HP ^{129}Xe. In the present study, HP ^{129}Xe trueFISP images are examined on spontaneous breathing mice using the low-pressure and continuous-flow type ^{129}Xe polarizer toward the development of a fully non-invasive method for lung functional imaging.

Methods: All MR measurements were performed with a Varian Unity INOVA 400WB high-resolution NMR spectrometer equipped with a 9.4-T vertical magnet (Oxford Instruments) and a imaging probe tunable to Larmor frequencies of ^{129}Xe (110.6 MHz) and ^{1}H (399.6 MHz) (Doty Scientific, Inc.). Male ddY mice were anesthetized and then attached a home-built mouth mask. To investigate the efficiency of our novel home-built ^{129}Xe polarizer [2] for in vivo study, gas-phase ^{129}Xe spectra and images were acquired from mouse lung under the two polarizing conditions. First, Xe gas was polarized at a pressure of 1 atm, which was routinely used for in vivo study in our group, and second, it was polarized at 0.15 atm. Mixed gas of 70%Xe(natural abundance)+30%N_2 was polarized and continuously delivered to the mouse after mixed with O_2. ^{129}Xe polarization was approximately 10% for 0.15 atm and 5% for 1 atm. Spoiled gradient echo (SPGR) pulse sequence was used for the comparison of two images acquired using HP ^{129}Xe polarized under two pressures (α=30°, TR/TE=300/1.5 ms, matrix=32×32 (zero filled to 64×64), FOV=50×50 mm^2, coronal slice of 10 mm thickness, NEX=16). Respiratory phase images were acquired using a trueFISP pulse sequence which was programmed in-house (α=40°, TR/TE=3.2/1.6 ms, matrix=64×32 (zero filled to 128×64), FOV=80×25.6 mm^2, ETL=32, coronal slice of 10 mm thickness, NEX=1). The k-space data were acquired with a centric phase encoding steps. By using these sequence parameters, one image can be acquired in 0.1 sec, which is sufficient for imaging certain respiratory phase even for mice. A series of images were acquired every 6 sec so that the depolarized ^{129}Xe magnetization was fully recovered by ventilation, and maximum and minimum intensity images were selected as inspiratory and expiratory images, respectively, from 20 images successively obtained.

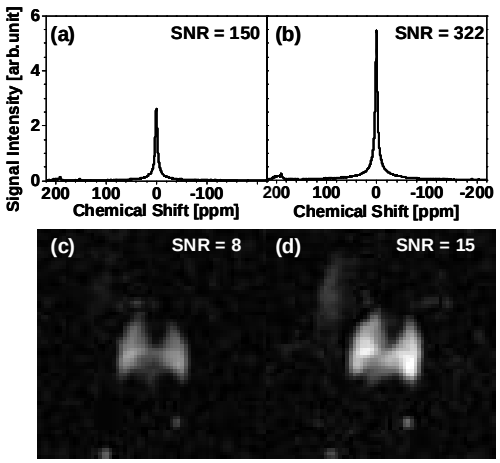

Figure 1. HP ^{129}Xe spectra (a, b) and gas-phase SPGR images (c, d) obtained from mouse lung. ^{129}Xe was polarized at a pressure of 1 atm (a, c) and 0.15 atm (b, d).

Results and Discussion: SNR of the spectrum and image acquired using HP ^{129}Xe polarized at 0.15 atm was 2 times that acquired at 1 atm, as is shown in Fig.1. By using the ^{129}Xe polarizer and the trueFISP pulse sequence, ^{129}Xe lung images at maximum inspiratory and expiratory phases were successfully obtained from spontaneously breathing mice (Fig. 2). In these images, distribution of the Xe gas in the lung and the signal intensity was observed in each phase. Hitherto HP noble gas imaging on spontaneously breathing animals have been reported with HP ^{3}He images wherein the animals breathed HP ^{3}He gas enclosed in a reservoir and radial k-space sampling and sliding window technique were used. On this contrary, the HP ^{129}Xe ventilation images obtained here from continuously delivered HP ^{129}Xe gas using trueFISP sequence will be better suited for further quantitative analysis since HP gas is supplied constantly at definite polarization devoid of cumbersome data treatment coming from polarization decrease in the HP gas reservoir. With the aid of the fast imaging sequence of trueFISP, temporal resolution has been extremely improved in the resulting images. Observation of images at a definite respiratory phase will be realized by navigating the signal acquisition by ECG or self-navigation technique.

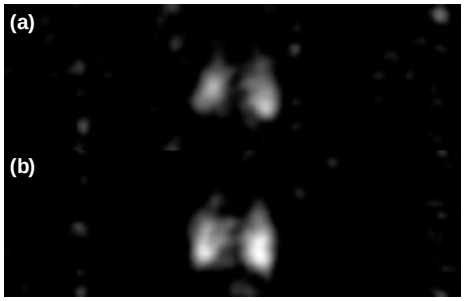

Figure 2. Gas-phase HP ^{129}Xe lung images of maximum expiratory (a) and inspiratory (b) phase obtained from spontaneous breathing mice with trueFISP.

Conclusion: A fast imaging of HP ^{129}X was realized with spontaneously breathing mice using a low-pressure ^{129}Xe polarizer and trueFISP sequence. This method will be used for lung functional analysis under high temporal resolution without any depolarization effect in reservoir bag, making data analysis easier than usually encountered.

References:

[1] V. Stupar, et al., NMR Biomed 2007;20:104. [2] H. Imai, et al., Concepts Magn Reson B 2008;33B:192.