In-Vivo Hyperpolarized 3He Lung Imaging in Mice Using x-Centric fGRE Sequence and Custom-Designed FlexiVent Ventilator

A. V. Ouriadov[1], R. Kennan[2], D. Slipetz[3], G. Santyr[1,4], D. Williams[3], B. K. Rutt[1,4], R. Hargreaves[3], and B. T. Chen[2,3]

[1]Imaging, Robarts Research Institute, London, ON, Canada, [2]Imaging, Merck Co., Rahway, NJ, United States, [3]Pharmacology, Merck Frosst Ltd., Kirkland, QC, Canada, [4]Medical Biophysics, University of Western Ontario, London, ON, Canada

INTRODUCTION

Hyperpolarized (HP) ^{3}He MR lung imaging in the live mouse is of great interest due to the increasing need for novel biomarkers with which to develop new therapies for respiratory diseases. Due to the size of the mouse, the requirements for high image resolution and animal preparations to establish a stable physiological condition and HP ^{3}He gas delivery are very challenging to meet (1). To achieve sufficient SNR for high image resolution, a pulse sequence with a very short echo time (TE) is preferred (very short ^{3}He T2*). Although the fast gradient-recalled echo (fGRE) sequence can provide the required short TE, it has not been widely used for high resolution HP ^{3}He lung imaging in mice. It was suggested that the frequency encoding (x) gradient could cause ^{3}He signal loss in the larger airways due to diffusion as image resolution increases (2, 3). To investigate the gradient-induced diffusion effect, the conventional fGRE sequence was modified for x-centric acquisition (Fig. 1) and variable flip angle (VFA) scheme. A custom-designed MR compatible flexiVent ventilator (Scireq, Montreal, QC, Canada) was built to link the imaging data with traditional spirometric measurement, in addition to provide mechanical ventilation and HP ^{3}He gas delivery.

METHODS

The animal protocol was approved by the Animal Use Subcommittee of the University Council on Animal Care at the University of Western Ontario and the animal care committee at Merck Frosst. HP ^{3}He MR imaging was performed on a GE clinical scanner (3T, Excite 12.0) which was converted using a home-made insert gradient coil (maximum gradient at 50 G/cm, 17 cm in diameter) to allow high resolution imaging for mice. A quadrature birdcage RF coil for mice (97.32 MHz, 3 cm in diameter and 6 cm in length, Morris Instruments, Ottawa, ON) was used for ^{3}He imaging. ^{3}He gas was polarized overnight (~35%) using an optical polarizer (Helispin, GE). The ^{3}He imaging (FOV = 2 cm, BW = 62.5 kHz) was performed in a phantom of a 10 ml syringe of 2 ml pure HP ^{3}He at 1 atm and in mice (20-30g) supported by the custom-built flexiVent ventilator. 2D-projection images of the phantom were acquired for matrix sizes of 64, 128, 256, 384, and 512 using the partial echo (62.5% of Kx) fGRE sequence and the x-centric fGRE sequence. To complete the scan within the short breath-hold (1 s) in mice using the x-centric scheme, only a fraction of phase-encoding lines (62.5% of Ky) was collected to compensate for the increased acquisition in Kx (full echo). Mouse images were acquired for matrix sizes of 64, 128, and 256.

RESULTS

Our phantom data demonstrate significant ^{3}He signal loss at high image resolution using conventional fGRE, not observed with the x-centric technique. To identify the source of the signal loss, the SNR values obtained from the phantom data were normalized with the respective first applied flip angle and respective pixel size. The normalized results from conventional and x-centric schemes were scaled using the respective 64x64 (312 µm) data (Fig. 2). The predicted signal strength at equivalent pixel sizes was calculated based on $S_{normalized} = \exp(-b \cdot D)$, where the b value is determined based on the applied x-gradient duration and amplitude and D is the diffusion coefficient of pure ^{3}He (2 cm^2/s). As compared to the conventional fGRE data in Fig. 2, the scaled normalized SNR of the phantom images using x-centric fGRE does not decrease significantly as image resolution increases. These results are consistent with the predicted signal data based on the calculated b values, suggesting that significant diffusion attenuation can be induced by the x-gradient using the conventional fGRE sequence. The custom-built flexiVent provides a reliable and repeatable lung functional measurement in mice as designed. The ^{3}He images were successfully acquired using the flexiVent as shown in Fig. 3. The proposed x-centric scheme recovered the lost signal in the major airway (shown by the arrow in Fig. 3).

CONCLUSIONS

We successfully acquired high-resolution HP ^{3}He lung images in mice using the x-centric fGRE sequence to minimize diffusion attenuation. Unlike the projection reconstruction approaches requiring oversampling, the proposed x-centric fGRE sequence together with the fractional Ky scheme is much efficient. This advantage allows completion of the scan (1 s) within a single breath for high-resolution true density-weighted HP ^{3}He lung imaging in mice. In addition, the custom-built flexiVent ventilator provides critical lung function data for image analysis and interpretation. The application of this described HP ^{3}He mouse lung imaging platform to investigate methacholine-provoked airway constriction using ovalbumin-sensitized mice will be presented separately.

REFERENCES

1. Chen et al. MRM 53(1):69-75, 2005
2. Dugas et al. MRM 52(6):1310-1317, 2004
3. Driehuys et al. MRM 58(5), 893–900 2007

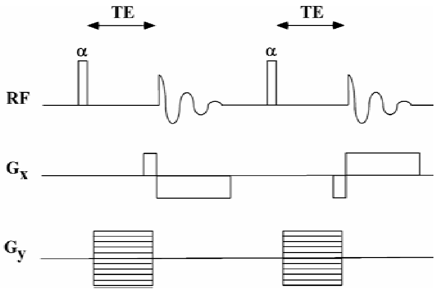

Figure 1 Modified fGRE using x-centric acquisition schemes to minimize signal loss due to diffusion is illustrated.

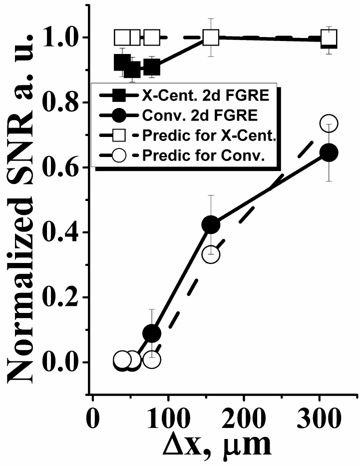

Figure 2 Scaled normalized SNR in the phantom images of respective resolutions acquired using conventional and x-centric fGRE sequences were shown. These data are consistent with the predicted data based on the calculated b values.

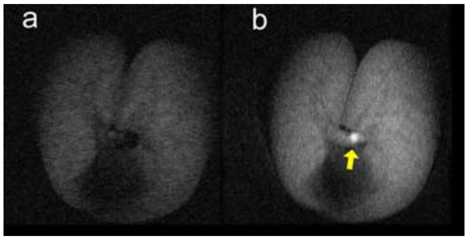

Figure 3 Mouse lung images (256x256, FOV = 2 cm, and BW = 62.5 kHz) using a) conventional (b=2.29 s/cm^2) and b) x-centric (b=0.04 s/cm^2) schemes. These data were acquired within a one-second breath-hold.

ACKNOWLEDGEMENTS

This work is supported by Merck Frosst Canada. The Helispin polarizer was made available by Merck and GEHC. The authors are grateful to Laura Gee for animal preparations.