Feasibility of Human Lung Ventilation MR Imaging using Naturally-Abundant Xenon with Optimized 3D SSFP

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Target Audience: Hyperpolarized gas MRI community; respiratory clinicians and physiologists.

Introduction & Purpose: To date, magnetic resonance (MR) imaging of lung ventilation with hyperpolarized (HP) noble gases (^{3}He and ^{129}Xe) has typically been performed with spoiled gradient echo (SPGR) pulse sequences and has required ~ 300 - 400 mL doses of ^{3}He or ~ 500 mL - 1 L [1] doses of isotopically-enriched xenon (ENXe, 86% ^{129}Xe) gas for diagnostic quality images. Larger doses of ENXe have been necessary due to historically lower nuclear polarizations of ^{129}Xe and the 3-fold lower gyromagnetic ratio when compared to ^{3}He. These gases are not cheap (~ 850 USD / L of ^{3}He and ~ 170 USD / L of ENXe). Naturally-abundant xenon (NAXe, 26% ^{129}Xe) may present an economically-attractive alternative (~ 30 USD / L), but has not been demonstrated to date in humans due to signal-to-noise ratio (SNR) limitations. Recent advances in gas polarization technology [2, 3] have enabled polarizations of ^{129}Xe to equal and surpass those achieved routinely for ^{3}He in volumes sufficient for human lung MRI. In addition, optimized steady-state free precession (SSFP) imaging strategies can provide SNR benefits over SPGR for HP gases [4]. The aim of this work was to demonstrate the possibility and potential of HP NAXe gas for high-quality routine clinical imaging of pulmonary ventilation by optimization of 3D SSFP sequences for maximal SNR, via numerical simulations and experimental measurements of MR signal dynamics.

Methods: MR ventilation imaging was performed at 1.5 T (GE HDx) on one healthy smoker (HS) and two healthy never-smokers (HN1, 2), and at 3 T (Philips Achieva) on one subject (HN1). ^{129}Xe gas was polarized to ~ 50% using an in-house spin-exchange optical pumping polarizer [5, 6], comprising a diode laser with integrated volume holographic grating [3] coupled to an optical train by a solid fibre. A 3D SSFP sequence was optimized for image SNR by: a) in-vivo measurement of ^{129}Xe k-space filters and b) numerical simulation of the Bloch equations (see [4]), for different imaging bandwidths and flip angles, considering the effective T_2 due to diffusional dephasing of ^{129}Xe MR signal from the action of imaging gradients. Volunteers inhaled 1 L of NAXe and maintained breath-hold during a 3D SSFP acquisition with sequence parameters (at 1.5 T): field-of-view (FOV), 40 cm; 4.2 x 4.2 x 10 mm^3 voxel (96 x 96 in-plane, 20-24 anterior-posterior "slices"); flip angle, 10°; echo/repetition time, TE/TR = 2.1/6.4 ms; receiver bandwidth, ± 8 kHz; total breath-hold, 11 - 15 sec. At 3 T, the parameters were: voxel = 4.2 x 4.2 x 8 mm^3; flip angle, 12°; TE/TR = 1.5/4.7 ms; bandwidth, ± 8.5 kHz; breath-hold, 8 sec. To assess NAXe image quality, 3D SSFP MR imaging was repeated at 1.5 T using 400 mL of ENXe and 200 mL of ^{3}He, each balanced to 1 L with N_2 gas. For ^{3}He (polarized to ~ 25%), the TE/TR and bandwidth were 0.6/1.9 ms and ± 83.3 kHz, respectively.

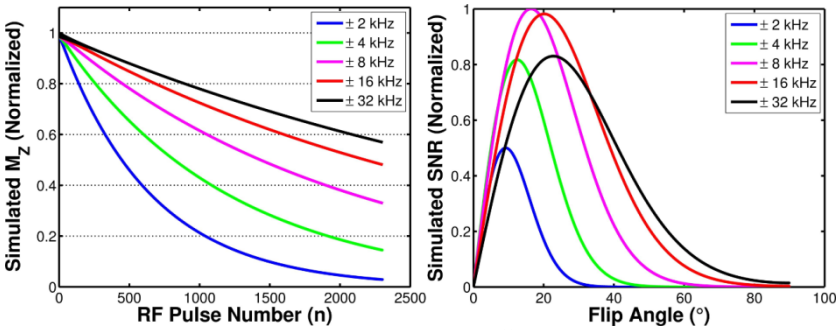

Figure 1: Left – simulated k-space filtering during a ^{129}Xe SSFP imaging experiment as a function of imaging bandwidth. Right – corresponding SSFP image SNR versus imaging bandwidth and flip angle. In both cases, the voxel size was 4.2 x 4.2 x 10 mm^3.

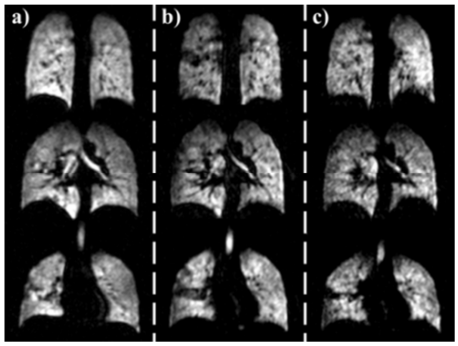

Figure 2: Comparative coronal MR image slices from a healthy smoker after inhalation of a) 200 mL HP ^{3}He, b) 400 mL ENXe and c) 1 L NAXe, obtained at 1.5 T with an optimized 3D SSFP sequence.

Results & Discussion: Simulated and measured k-space filters highlighted that decreasing image bandwidth (increasing read gradient "b value") caused more rapid decay of ^{129}Xe MR signal due to increased diffusional dephasing (simulations, Figure 1, left). ^{129}Xe 3D SSFP image SNR was found to be relatively robust to flip angle variations; this is a practical advantage for routine clinical imaging using patient friendly flexible RF coils of variable transmit field homogeneity. An optimum imaging bandwidth of between ± 8 and ± 16 kHz was predicted for maximal SNR (Figure 1, right). All acquired NAXe lung MR images were of diagnostic quality, with mean SNRs of 25 – 40 for voxel sizes of 4.2 x 4.2 x 8/10 mm^3. The high SNR permitted identification of minor ventilation defects in the lungs of the healthy smoker, similar to that expected in early stage lung disease. NAXe images were of comparable SNR to those obtained with modest doses of ENXe and ^{3}He (Figure 2), with no loss in diagnostic information. A > 30% improvement in mean SNR was measured at 3 T compared with 1.5 T, consistent with recent findings for SPGR sequences [7]. An example 3D SSFP NAXe dataset acquired at 3 T is shown in Figure 3. In future work, it may be feasible to acquire same-breath structural (^{1}H) and functional (NAXe) scans of the lung, by reducing the breath-hold of ventilation scans with NAXe, e.g. via compressed sensing [8]. Furthermore, additional technological developments are needed to facilitate polarization of ^{129}Xe in large "batches" for on-demand gas delivery [2] and hence to expedite routine repeated clinical scanning procedures.

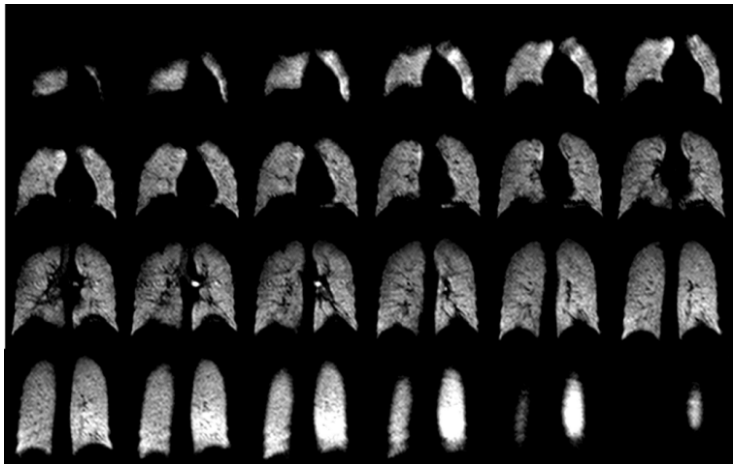

Figure 3: 3D SSFP volumetric MRI data-set of a healthy never-smoker subject (HN1), acquired using 1 L of naturally-abundant xenon gas at 3 T.

Conclusions: In conclusion, with optimization of MR pulse sequences and advances in polarization technology we have demonstrated diagnostic-quality pulmonary ventilation imaging with inexpensive naturally-abundant xenon gas.

References: [1] B. Driehuys et al., Rad. 2012;262(1):279-89. [2] P. Nikolaou et al., PNAS. 2013;110(35):14150-5. [3] N. Whiting et al., Journ Appl Phys B. 2012;106(4):775-88. [4] J. M. Wild et al., JMR. 2006;183(1):13-24. [5] G. Norquay et al., Journ Appl Phys. 2013;113(4):044908-9. [6] G. Norquay et al., In: Proc PING14: Hyperpolarised Noble Gases, Les Houches, 2014. [7] X. Xu et al., MRM. 2012;68(6):1900-4. [8] S. Ajraoui et al., MRM. 2010;63(4):1059-69.