Article:
Marshall, H., Collier, G.J., Johns, C.S. et al. (4 more authors) (2018) Imaging collateral ventilation in patients with advanced chronic obstructive pulmonary disease: relative sensitivity of 3 He and 129Xe MRI. Journal of Magnetic Resonance Imaging. ISSN 1053-1807

https://doi.org/10.1002/jmri.26273

Imaging collateral ventilation in patients with advanced chronic obstructive pulmonary disease – relative sensitivity of ^{3}He and ^{129}Xe MRI

[1]Helen Marshall PhD, [1]Guilhem J Collier PhD, [1]Christopher S Johns MD, PhD, [1]Ho-Fung Chan PhD, [1]Graham Norquay PhD, [2]Rod A Lawson MD, PhD, [1]Jim M Wild PhD

[1] Academic Unit of Radiology, University of Sheffield, Sheffield, UK

[2] Department of Respiratory Medicine, Sheffield Teaching Hospitals NHS Trust, Sheffield, UK

Corresponding author: Helen Marshall

University of Sheffield

C Floor, Royal Hallamshire Hospital

Sheffield, S10 2JF, U.K.

Tel: +44 (0) 114 215 9145

Fax: +44 (0) 114 271 1714

Email: h.marshall@sheffield.ac.uk

Grant support: This work was funded by the Medical Research Council (MR/M008894/1) and the National Institute of Health Research (NIHR-RP-R3-12-027). The views expressed in this publication are those of the authors and not necessarily those of the National Health Service, the National Institute for Health Research or the Department of Health.

Running title: Imaging collateral ventilation in COPD

Keywords: Hyperpolarized gas MRI, collateral ventilation, COPD

Endoscopic lung volume reduction (ELVR) can improve lung function, exercise capacity and quality of life of patients with severe chronic obstructive pulmonary disease (COPD). The assessment of collateral ventilation is key to the success of ELVR, as collateral ventilation from adjacent lung regions prevents collapse of the target lung segment (1).

The gold standard assessment of collateral ventilation is gas catheter bronchoscopy, but this is an invasive procedure requiring sedation (1). Assessment of lobar fissure integrity with anatomical computed tomography (CT) can assist in patient selection (1,2), but functional measurements of gas movement within the lungs have direct relevance.

Long-range diffusion measurements using hyperpolarized ^{3}He MRI are sensitive to the effects of collateral ventilation (3). Direct imaging of collateral and delayed ventilation has been demonstrated with time-resolved hyperpolarized ^{3}He MR imaging during breath-hold (4). However, ^{3}He has become increasingly scarce and expensive (5), motivating a shift towards ^{129}Xe MRI for most applications in the lungs (6). The aim of this work was to compare ^{3}He and ^{129}Xe time-resolved imaging for the detection of delayed and collateral ventilation in patients with severe COPD.

MATERIALS AND METHODS

Three patients with advanced COPD under consideration for ELVR were scanned using a 1.5T whole body MRI system (GE HDx, Milwaukee, WI) equipped for hyperpolarized gas imaging. This retrospective analysis was conducted with approval of the research governance and ethics board with a waiver of informed consent. Patients 1 and 2 were 64-year-old females, patient 3 was a 52-year-old male. Patients were positioned supine in a transmit-receive quadrature vest coil (Clinical MR Solutions, Brookfield, WI) tuned to the appropriate resonance frequency of ^{3}He or ^{129}Xe. Dynamic time-series ventilation images were acquired during breath-hold using a 3D coronal balanced steady state free precession sequence with full lung coverage (FOV=40-48cm, slice number=22-24), in-plane matrix 64x32, 10mm slice thickness and Cartesian centric phase encoding.

100mL hyperpolarized ^{3}He (~25% polarization (GE Healthcare, Amersham, UK)) and 900ml N_2 was inhaled from functional residual capacity (FRC). MR sequence parameters: θ=8.5º, TE=0.5ms, TR=1.6ms, BW=167kHz, scan duration=21s, and six dynamic volumes acquired at 0, 4, 7, 11, 15 and 19 seconds.

350mL hyperpolarized ^{129}Xe (129-enriched (86%), ~30% polarization) and 650ml N_2 was inhaled from FRC. MR sequence parameters: θ=6.5º, TE=1.4ms, TR=4.5ms, BW=16kHz, scan duration=23s, and six dynamic volumes acquired at 0, 4, 8, 12, 16 and 20 seconds.

To quantify dynamic changes in global lung ventilation, whole lung ventilated volume (VV) was calculated for each time point using automated spatial fuzzy C-means segmentation, a methodology which is robust to noise (7).

The free diffusion coefficient (D) and one-dimensional mean free diffusion path length ($z_{rms}=\sqrt{(2D\Delta t)}$) after time Δt (8) were estimated for ^{3}He and ^{129}Xe within the lungs. A volume of 6.6L of air, corresponding to the average FRC of the three patients, was used to estimate the experimental in situ gas mixture required for the calculation of D.

Volumetric unenhanced thoracic CT images and pulmonary function test results were also reviewed.

RESULTS

Centrilobular emphysema and hyperinflation were evident on the CT images of all patients. Patients 1, 2 and 3 had forced expiratory volume in one second of 28.5, 24.7 and 27.4 percent predicted, and residual volume of 272.1, 291.5 and 223.3 percent predicted, respectively. Patient 1 lost breath-hold after 13s of ^{3}He data acquisition and after 20s of ^{129}Xe data acquisition, patients 2 and 3 performed both breath-holds successfully.

^{3}He and ^{129}Xe images of gas distribution within the lungs at the first time-point and a later time-point during breath-hold for each of the three patients. Arrows highlight initially non-ventilated lung regions where signal increased over time in the ^{3}He images, but not in the ^{129}Xe images. Some evidence of delayed ventilation was observed with ^{129}Xe but only within lung regions which were ventilated at t=0s with ^{3}He. (Figures 1-3)

Whole lung ventilated volume increased over time for both gases, but the ratio VV_{3He}/VV_{129Xe} was greater at the end of the breath-holds than at t=0s. VV_{3He}/VV_{129Xe} increased from 1.10 to 1.19 for patient 1, from 1.37 to 1.54 for patient 2, and from 1.25 to 1.31 for patient 3.

The ratio of ^{129}Xe diffusivity to ^{3}He diffusivity within the hyperinflated lungs of a patient with a FRC of 6.6L is 0.15 for the estimated experimental gas mixtures ($D_{(129Xe\text{-}air,lungs)}$ = 0.13cm^{2}s^{-1}, $D_{(3He\text{-}air,lungs)}$ = 0.87cm^{2}s^{-1}). This was associated with a mean free diffusion path length of 2.0cm for ^{129}Xe and 5.1cm for ^{3}He on the time-course of the time-resolved experiment (Δt=15s).

DISCUSSION

The visualization of delayed and collateral ventilation with ^{3}He but not with ^{129}Xe, and the increased VV_{3He}/VV_{129Xe} ratio at the end of the breath-holds compared to t=0s, are likely due to the large difference in diffusivity between the gas mixtures used.

The observation of reduced ventilated volume in ^{129}Xe images when compared to ^{3}He images acquired from the same patients with COPD has been reported before for single time-point ventilation imaging (9). The diffusion coefficient of ^{129}Xe diluted in air ($0.14cm^2s^{-1}$) (8) is closer to that of air alone ($0.22cm^2s^{-1}$) (10) than ^{3}He diluted in air ($0.86cm^2s^{-1}$) (8). However, the higher diffusivity of ^{3}He highlights delayed ventilation which would take place on a longer time-scale for pure air rather than the ^{3}He-air mixture used for imaging; for example, it would take 60s for pure air to travel the same mean free diffusion path length as the ^{3}He-air mixture within the lungs would travel in 15 seconds. Even if it were feasible to image ^{3}He and ^{129}Xe at the same mean free diffusion path length, other inherent differences between the two gases, such as increased density and viscosity of ^{129}Xe compared to ^{3}He, may affect the relative sensitivity of ^{3}He and ^{129}Xe MRI.

In conclusion, although the number of patients studied was small, all showed instances where delayed and collateral ventilation were detected with ^{3}He MRI but not observed using ^{129}Xe MRI, indicating a limitation of time-resolved ^{129}Xe MRI for this emergent application.

ACKNOWLEDGEMENTS

Thanks to David Capener and Jody Bray for patient scanning, Jenny Rodgers and Leanne Armstrong for patient scheduling, and Oliver Rodgers for polariser operation.

REFERENCES

1. Slebos DJ, Shah PL, Herth FJ, Valipour A. Endobronchial Valves for Endoscopic Lung Volume Reduction: Best Practice Recommendations from Expert Panel on Endoscopic Lung Volume Reduction. Respiration 2017;93(2):138-150.
2. Koster TD, van Rikxoort EM, Huebner RH, et al. Predicting Lung Volume Reduction after Endobronchial Valve Therapy Is Maximized Using a Combination of Diagnostic Tools. Respiration 2016;92(3):150-157.
3. Woods JC, Yablonskiy DA, Choong CK, et al. Long-range diffusion of hyperpolarized 3He in explanted normal and emphysematous human lungs via magnetization tagging. J Appl Physiol (1985) 2005;99(5):1992-1997.
4. Marshall H, Deppe MH, Parra-Robles J, et al. Direct visualisation of collateral ventilation in COPD with hyperpolarised gas MRI. Thorax 2012;67(7):613-617.
5. Shea DA, Morgan D. The helium-3 shortage: supply, demand, and options for congress. Congressional Research Service, Library of Congress, Technical Report: R41419:7-5700; 2010.
6. Stewart NJ, Chan HF, Hughes PJC, et al. Comparison of (3) He and (129) Xe MRI for evaluation of lung microstructure and ventilation at 1.5T. J Magn Reson Imaging 2018.
7. Hughes PJC, Horn FC, Collier GJ, Biancardi A, Marshall H, Wild JM. Spatial fuzzy c-means thresholding for semiautomated calculation of percentage lung

ventilated volume from hyperpolarized gas and (1) H MRI. J Magn Reson Imaging 2017.

8. Chen XJ, Moller HE, Chawla MS, et al. Spatially resolved measurements of hyperpolarized gas properties in the lung in vivo. Part I: diffusion coefficient. Magn Reson Med 1999;42(4):721-728.

9. Kirby M, Svenningsen S, Owrangi A, et al. Hyperpolarized 3He and 129Xe MR imaging in healthy volunteers and patients with chronic obstructive pulmonary disease. Radiology 2012;265(2):600-610.

10. E.L. C. Diffusion: Mass Transfer in Fluid Systems. New York: Cambridge University Press: 1997.

FIGURE CAPTIONS

Figure 1

^{3}He images (top) and ^{129}Xe images (bottom) acquired from patient 1 during breath-hold; (a, d) at the start of the imaging sequence, t=0s, and (b, e) after 11 seconds, both shown with the same signal range. (c, f) show maps of signal increase from t=0s to t=11s. White arrows highlight a region of lung where ^{3}He signal increased over time, but ^{129}Xe signal did not. The coronal unenhanced thoracic CT (g) showed moderate centrilobular emphysema and hyperinflation, and an intact left oblique fissure. Mean signal to noise ratio (SNR) over the whole lung ventilated volume for that time-point is displayed for a, b, d and e.

Figure 2

^{3}He images (top) and ^{129}Xe images (bottom) acquired from patient 2 during breath-hold; (a, d) at the start of the imaging sequence, t=0s, (b, e) after 15 seconds, both shown with the same signal range. (c, f) show maps of signal increase from t=0s to t=15s. White arrows highlight regions of lung where ^{3}He signal increased over time, but ^{129}Xe signal did not. (g) CT showed severe centrilobular emphysema and severe hyperinflation, and all fissures appeared intact. Mean SNR over the whole lung ventilated volume for that time-point is displayed for a, b, d and e.

Figure 3

^{3}He images (top) and ^{129}Xe images (bottom) acquired from patient 3 during breath-hold; (a, d) at the start of the imaging sequence, t=0s, (b, e) after 15 seconds, both

shown with the same signal range. (c, f) show maps of signal increase from t=0s to t=15s. White arrows highlight regions of lung where ^{3}He signal increased over time, but ^{129}Xe signal did not. (g) CT showed severe centrilobular emphysema and hyperinflation, and all fissures appeared intact. Mean SNR over the whole lung ventilated volume for that time-point is displayed for a, b, d and e.