Seeing the Unseen: Regional Lung Function Assessment in PCD and non-PCD Bronchiectasis using a Novel XV Scanner

Frohlich M[1,2], Strachan R[2], Hillenbrand C[3], Thomas P[4,5], Yates D[6,7], Sivam S[8,9], Eikelis N[10], Hardaker K[9,11], McBride J[1,2], Coward E[1,2], Plush L[2], Morgan L[9,11], Jaffe A[1,2]

[1]Discipline of Paediatrics and Child Health, School of Clinical Medicine, Faculty of Medicine and Health, UNSW Sydney, NSW, Australia. [2]Department of Respiratory Medicine, Sydney Children's Hospital, NSW, Australia, [3] Research Imaging NSW, Division of Research & Enterprise, UNSW Sydney, NSW, Australia. [4] Department of Respiratory Medicine, Prince of Wales Hospital, Sydney, NSW, Australia. [5] Prince of Wales Clinical School, Faculty of Medicine, UNSW Sydney, NSW, Australia. [6]School of Clinical Medicine, Faculty of Medicine and Health, UNSW Sydney. [7]Holdsworth House, Darlinghurst, Sydney, NSW, Australia. [8]Department of Respiratory and Sleep Medicine, Royal Prince Alfred Hospital, Sydney, Australia. [9]Faculty of Medicine and Health, University of Sydney, Sydney, Australia. [10]4DMedical, Melbourne, Victoria, Australia.[11] Department of Respiratory Medicine, Concord Hospital, Sydney, NSW, Australia.

Introduction/Aim: Early and accurate detection of lung disease in patients with bronchiectasis enables timely interventions that may slow disease progression. X-ray Velocimetry (XV) analysis is a novel technique to quantify regional lung ventilation using information captured by X-ray fluoroscopy. The utility of this technology to sensitively measure regional lung ventilation has been established in animal[1 2] and human trials.[3 4] The XV scanner is a new, non-invasive, quick and purpose-built device to capture images for XV analysis. This study aims to assess the feasibility of the XV scanner for assessment of lung function in patients with bronchiectasis due to Primary Ciliary Dyskinesia (PCD) and other causes.

Methods: Participants ≥ 18 years old with PCD and non-PCD bronchiectasis are being recruited from four sites across Sydney, Australia. Participants attend a single site, Research Imaging NSW, for their study visit. Each participant performs multiple breath nitrogen washout (MBNW) via tidal breathing and spirometry according to American Thoracic Society and European Respiratory Society standards. An XV scan is then performed, with cinefluorographic images across four synchronised angles captured during one breath cycle while the participant is seated in the XV scanner. The acquired images are combined with recent CT chest images of the participant, and XV analysis is performed to generate XV metrics and regional ventilation maps.

Results: Ten participants with bronchiectasis (6 PCD and 4 non-PCD bronchiectasis) have been recruited to this study. Demographics and baseline characteristics are shown in Table 1.

Metric	PCD (n=6)	Non-PCD bronchiectasis (n=4)	Total group (n=10)
Age, years	31 (24-50)	55 (37-60)	43 (24-57)
FEV_1 % predicted	45 (39-55)	49 (35-69)	45 (39-56)
FEV_1 z-score	-4.1 (-3.7 - -4.9)	-3.8 (-2.1 - -4.8)	-4.1 (-3.1 – -4.9)
FVC % predicted	72 (59-91)	76 (67-93)	73 (62-91)
FVC z-score	-2.1 (-0.7 - -3.5)	-1.7 (-0.5 - -2.6)	-2.0 (-0.7 - -3.2)
FEV_1/FVC %	53 (52-60)	57 (43-60)	55 (52-60)
FEV_1/FVC z-score	-3.5 (-3.1 - -3.6)	-3.1 (-2.6 - -4.1)	-3.3 (-2.9 - -3.6)

$LCI_{2.5}$	14 (12-16), n=5	19.5, n=1	15 (13-16)
TV, mL	483 (354-521)	520 (410-723)	483 (397-617)
VDP %	14 (13-17)	12 (10-18)	14 (10-17)
Total VH %	49 (44-52)	44.7 (40-55)	48 (43-52)
LVR %	18 (16-32)	30 (5-55)	18 (8-44)

Table 1 Summary of patient demographics and baseline characteristics. Data presented as median (IQR). LCI, lung clearance index; TV, tidal volume; total VH, total ventilation heterogeneity; VDP, ventilation defect percentage; LVR, low ventilation region.

All participants were able to complete acceptable and reproducible spirometry and the XV scan. One participant was unable to complete acceptable and reproducible MBNW. Three participants did not attempt MBNW due to infection control precautions at the study site.

Ventilation defect percentage (VDP) significantly correlated with FEV_1 z-score ($R^2 = 0.47$, p=0.029) but not FEV_1/FVC z-score or $LCI_{2.5}$. There was no correlation between ventilation heterogeneity (VH) or low ventilation regions (LVR) and FEV_1 z-score, FEV_1/FVC z-score or $LCI_{2.5}$ (Figure 1).

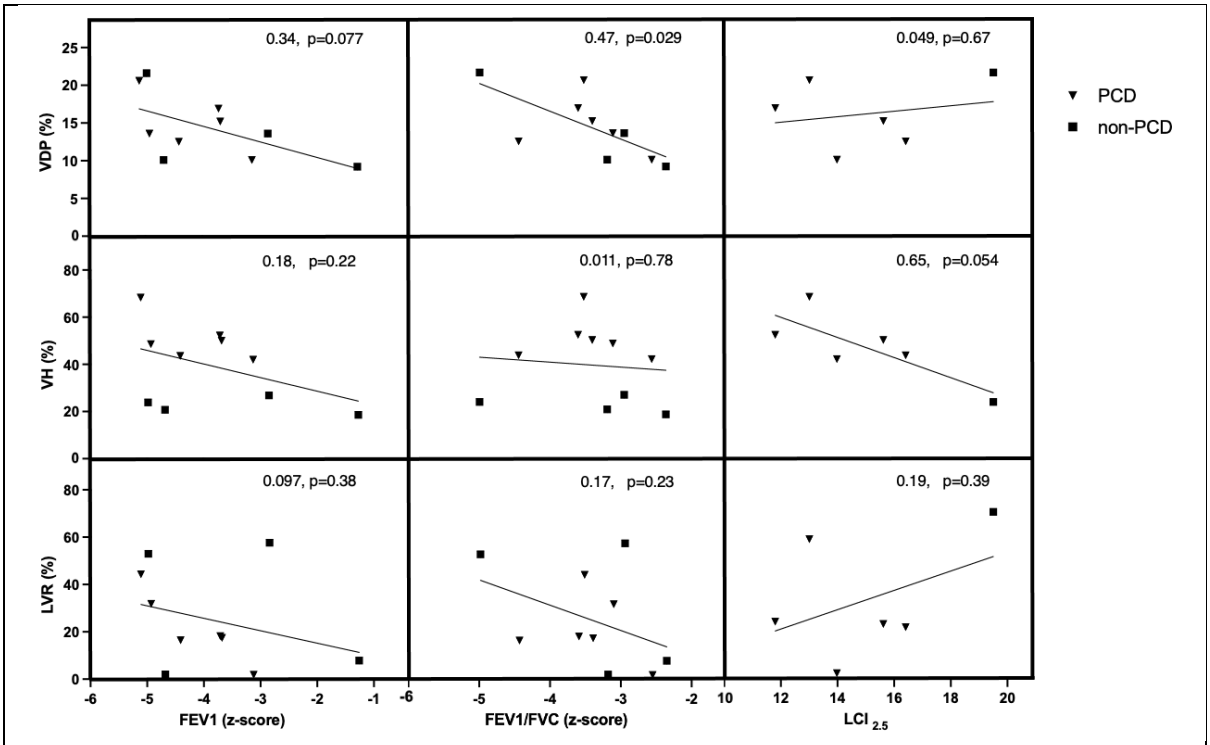

Figure 1 Scatterplots and linear regression (lines) of XV-derived ventilation metrics (VDP, VH and LVR) compared with spirometry (FEV_1 and FEV_1/FVC z-score) and MBNW ($LCI_{2.5}$) derived metrics. R-squared values derived from Pearson's correlation coefficient and *p*-values are reported for each plot. VDP, ventilation defect percentage; VH, ventilation heterogeneity; LVR, low ventilation region.

XV derived ventilation maps revealed the location of areas of lower than average ventilation in each participant (Figure 2).

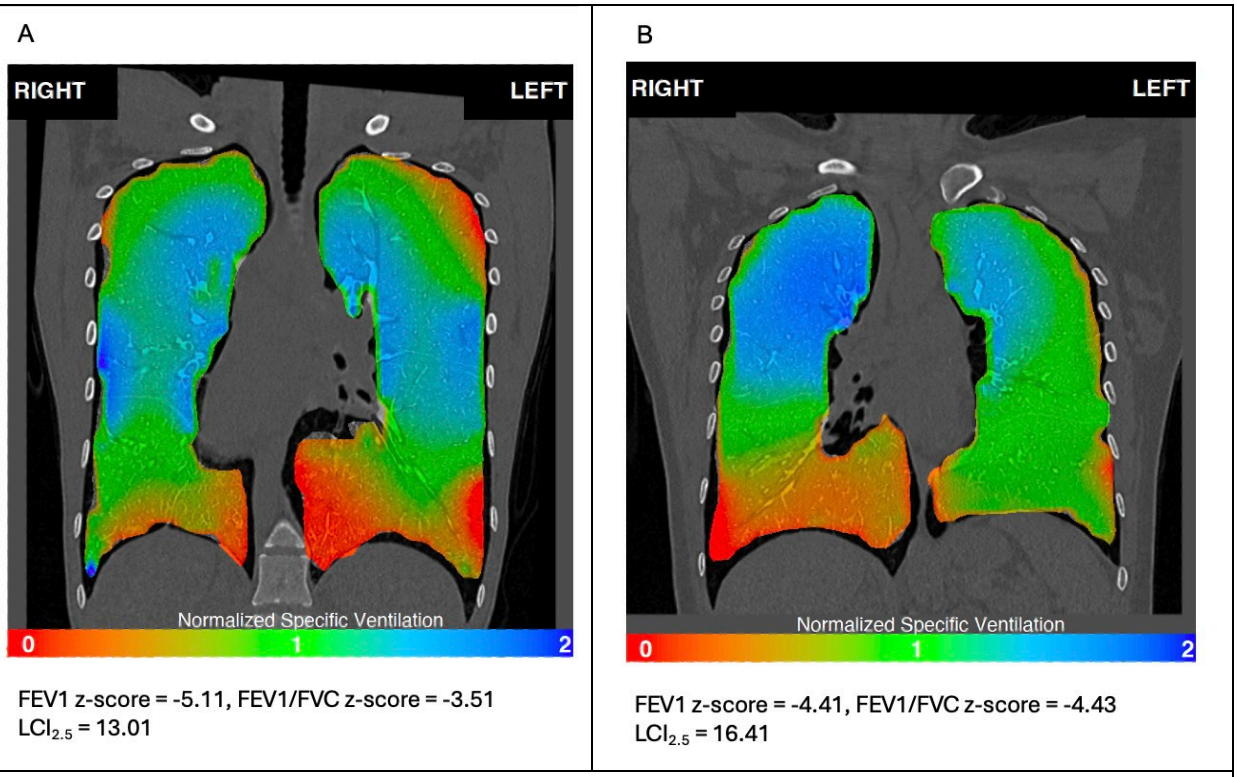

Figure 2 XV maps showing regional lung ventilation. Normalized specific ventilation reflects the specific ventilation throughout each participant's lungs normalized to their mean. Green represents areas of average ventilation, blue represents areas of higher than average ventilation, and red represents areas of lower than average ventilation. A) XV ventilation map of Case 1 with PCD, showing areas of lower than average ventilation in the left lower lobe, left upper lobe and right lower lobe. B) XV ventilation map of Case 2 with non-PCD bronchiectasis, showing areas of lower than average ventilation in the right lower lobe.

Conclusion: This study demonstrates the feasibility of using the XV scanner to assess regional lung function in adults with bronchiectasis. XV analysis of the images captured using the XV scanner provides detailed regional ventilation maps that highlight areas of ventilation heterogeneity not captured by global lung function tests. These early findings support the potential utility of the XV scanner as a sensitive, non-invasive tool for evaluating regional lung ventilation in bronchiectasis. Recruitment for this study is ongoing to further investigate these findings in a larger cohort.

Grant Support/acknowledgements: Funding for this research has been provided from the Australian Government's Medical Research Future Fund (MRFF) Grant RFRHPSI000013. The authors acknowledge Suily Liao, Simon Pilgrim and Nicholas Tranter (Research Imaging NSW) for their technical assistance with performing the XV scans. This project is supported by Research Imaging NSW and grants received by Dr Megan Frohlich from the Rotary Club of Sydney Cove and the National Health and Medical Research Council (NHMRC).

References:

1. Reyne N, Smith R, Cmielewski P, et al. Functional Lung Imaging Identifies Peripheral Ventilation Changes in β-ENaC Mice. *Respirology* 2025 doi: 10.1111/resp.70009 [published Online First: 2025/02/25]
2. Werdiger F, Donnelley M, Dubsky S, et al. Quantification of muco-obstructive lung disease variability in mice via laboratory X-ray velocimetry. *Sci Rep* 2020;10(1):10859. doi: 10.1038/s41598-020-67633-y [published Online First: 2020/07/04]
3. Kirkness JP, Dusting J, Eikelis N, et al. Association of x-ray velocimetry (XV) ventilation analysis compared to spirometry. *Front Med Technol* 2023;5:1148310. doi: 10.3389/fmedt.2023.1148310 [published Online First: 2023/07/13]
4. Karmali D, Afanador-Castiblanco S, Otvos T, et al. Regional lung volume changes with noninvasive positive pressure ventilation in healthy adults. *J Appl Physiol (1985)* 2025;138(3):731-38. doi: 10.1152/japplphysiol.00676.2024 [published Online First: 2025/02/13]