HYPERPOLARISED 3He MRI IS SUPERIOR TO LUNG CLEARANCE INDEX IN DETECTION OF VENTILATION ABNORMALITIES IN YOUNG CHILDREN WITH MILD CF

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Introduction Hyperpolarised 3He MRI provides high resolution images of lung ventilation and is more sensitive than spirometry to early changes in lung ventilation in cystic fibrosis (CF). Lung clearance index (LCI) is a global measure of ventilation heterogeneity which is also sensitive to early changes in the lungs in CF before spirometry. The aim of this study was to investigate the capability of hyperpolarised 3He MRI and LCI to detect ventilation changes in children with mild CF.

Methods 4 CF patients (FEV1 78–110% predicted) and 4 healthy volunteers have been assessed so far. 3He ventilation images were acquired at breath-hold following inhalation of hyperpolarised 3He, with 2.7x2.7x10mm resolution and full lung coverage using a 1.5T MRI system. The percentage of lung ventilated (VV%) was calculated as 3He ventilated volume divided by total lung volume segmented from 1H MR images. LCI was measured using 0.2% SF6 and a modified Innocor gas analyser. LCI was performed sitting and repeated supine to mimic the position adopted for MRI scanning. Spirometry and plethysmography were also performed. Gas trapping was calculated as% difference in plethysmographic versus washout FRC.

Results Healthy volunteers had a mean (standard deviation) age of 8.8(1.5) years, FEV1% predicted = 97(10) and gas trapping = 4.4(9.1)%; LCI sitting was 6.9,7.3,6.6 and 6.9, LCI supine was 7.3,7.5,6.8 and 6.4. Healthy volunteers had homogeneous ventilation in 3He ventilation images e.g. Fig1(a), and VV% = 94.5(2.8). CF patients had an age of 11.8(2.9) years, FEV1% predicted = 95(13), and gas trapping = 8.7(11.0). LCI sitting was 7.7,6.6,6.6 and 9.1, LCI supine was 7.8,7.3,7.1 and 11.8. Ventilation abnormalities were observed using 3He MRI in all four CF patients scanned (Fig 1(b-e), with order

Abstract S7 Figure 1. Comparison of change in lung function z-scores between 3m, 1y and 2y in NBS CF infants and healthy controls. Legend: Data are expressed as mean (SD). Closed circles represent NBS CF infants; open circles represent healthy controls. Lung function outcomes were expressed as z-scores which adjusted for age and body size as appropriate. Dashed lines indicate limits of normality (+/-2 z-scores).
SIFT-MS ANALYSIS AS A NON-INVASIVE DETERMINANT OF PSEUDOMONAS AERUGINOSA INFECTION IN PATIENTS WITH CYSTIC FIBROSIS

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Background There is evidence that Pseudomonas aeruginosa (Pa) produces volatile organic compounds (VOCs) such as hydrogen cyanide (HCN) and 2-aminoacetophenone (2-AA). VOCs in exhaled breath are therefore proposed as potential biomarkers of Pa infection. We hypothesised that selective ion-flow mass spectrometry (SIFT-MS) breath analysis might allow discrimination of CF patients with (CF + Pa) and without Pa (CF-Pa).

Methods 79 adults (31 CF + Pa, 22 CF-Pa and 26 healthy controls) provided starved, single tidal exhalation breath samples. VOCs in exhaled breath are therefore proposed as potential biomarkers of Pa infection. We hypothesised that selective ion-flow mass spectrometry (SIFT-MS) breath analysis might allow discrimination of CF patients with (CF + Pa) and without Pa (CF-Pa).

Results 2-AA was significantly higher in CF + Pa than CF-Pa (37.4 [24.3–87.6] vs. 11.7 [4.9–115.5] nL, p < 0.01). However, there was significant overlap and median co-efficient of variation was 35.41%; clinical utility is therefore questionable.

Conclusions 2-AA is a potential biomarker of Pa infection but clinical applicability is uncertain. Dimethyl disulphide and butanol also show promise. Mouth-exhaled HCN assessed by SIFT-MS does not appear to fulfil its promise as a Pa biomarker. Other VOCs assessed were either similar between Pa groups or different between healthy controls and CF, but unable to differentiate between Pa status. This study provides proof-of-concept for the development of a non-invasive tool with which to screen for lower airway bacterial infection in CF though a clinically applicable test remains some way off.

Abstract S8 Figure 1. Ventilation images from (a) a healthy volunteer and (b-e) patients with mild CF.

S9 SIFT-MS ANALYSIS AS A NON-INVASIVE DETERMINANT OF PSEUDOMONAS AERUGINOSA INFECTION IN PATIENTS WITH CYSTIC FIBROSIS

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Methods 79 adults (31 CF + Pa, 22 CF-Pa and 26 healthy controls) provided starved, single tidal exhalation breath samples into Nalophan™ bags. Quantification of 15 VOCs was performed within two hours on SIFT-MS. All results are presented as (median parts-per-billion by volume [IQR]).

Results 2-AA was significantly higher in CF + Pa than CF-Pa (5.0 [3.4–7.1] vs. 1.3 [0.0–3.2], p < 0.01). However, there was significant overlap and median co-efficient of variation was 35.41%; clinical utility is therefore questionable.

Conclusions 2-AA is a potential biomarker of Pa infection but clinical applicability is uncertain. Dimethyl disulphide and butanol also show promise. Mouth-exhaled HCN assessed by SIFT-MS does not appear to fulfil its promise as a Pa biomarker. Other VOCs assessed were either similar between Pa groups or different between healthy controls and CF, but unable to differentiate between Pa status. This study provides proof-of-concept for the development of a non-invasive tool with which to screen for lower airway bacterial infection in CF though a clinically applicable test remains some way off.

S10 LUNG CLEARANCE INDEX (LCI) AND PSEUDOMONAL AERUGINOSA IN ADULTS AND CHILDREN WITH CYSTIC FIBROSIS (CF)

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Introduction LCI obtained from multiple breath washout (MBW) is a sensitive measure of ventilation inhomogeneity in CF. Persistent colonisation with P. aeruginosa is associated with a decline in LCI in children (Kraemer et al. 2006). Further research is required to investigate the relationship between airways infection and LCI in adults.

Objective To investigate the sensitivity of LCI to P. aeruginosa in adults and children compared with FEV1%pred and FEF25–75% pred.

Methods Stable CF patients from adult & paediatric Northern Ireland CF centres were recruited. LCI was derived from MBW, using 0.2% SF6, and a modified Innocor™ device. P. aeruginosa status was determined from routine diagnostic culture of a spu- tum sample or deep throat swab. Patients categorised as having P. aeruginosa infection met the criteria of the Leeds criteria definitions and ROC curve analysis. ROC curves were performed on the AUCROC to determine the test sensitivity and specificity.

Results Sixty-seven adults were recruited (39M), median (IQR) age 27 (16) years. Mean (SD) FEV1%pred 71.8 (20.3), median (IQR) FEF25–75% pred 240.7 (46.7) and mean (SD) LCI 10.3 (3.0) lung volume turnovers. 49% had P. aeruginosa infection.

Conclusion LCI is more sensitive and specific to the presence of P. aeruginosa airways infection across the age groups in CF compared with spirometry.

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