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 infection. We hypothesised that selective ion-flow mass spectrometry (SIFT-MS) breath analysis might allow discrimination in 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 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.

Dimethyl disulphide was also significantly higher in CF + Pa (95.2 [41.3–211.2] vs. 35.5 [22.1–79.8], p < 0.01). When combined with 2-AA, area under ROC curve was 0.867.

Counter to our sputum results, there was no difference in HCN between CF + Pa and CF-Pa (8.1 [5.0–11.9] vs. 6.9 [4.4–11.0], n/s) or between all CF patients and healthy controls (7.8 [4.9–11.5] vs. 7.0 [4.6–11.5], n/s).

Our early in vitro data showed decreased butanol above Pa cultures, suggesting consumption. This was replicated in breath with lower levels in CF + Pa vs. CF-Pa (37.4 [24.3–87.6] vs. 91.7 [46.9–143.7], p < 0.05).

Of VOCs likely to be of host origin, isoprene was increased in CF vs. controls (108.0 [83.4–195.5] vs. 69.6 [46.9–89], p < 0.01) with no difference between CF + Pa vs. CF-Pa. Acetone was reduced in CF (269.9 [161.9–356.4] vs. 324.9 [236.7–598.9], p < 0.01).

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.

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 sputum sample or deep throat swab. Patients categorised as having P. aeruginosa infection were included in the analysis.

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 40.0 (46.7) and mean (SD) LCI 10.3 (3.0) lung volume turnovers. 49% had P. aeruginosa infection.

Forty-three children were recruited (24M), mean (SD) age 11.7 (3.4) years. Mean (SD) FEV1%pred 85.2 (16.6), mean (SD) FEF25–75%pred 66.0 (27.6) and mean (SD) LCI was 7.8 (1.8) lung volume turnovers. 16% had P. aeruginosa infection.

Compared to FEV1%pred and FEF25–75%pred, LCI had the greatest sensitivity and specificity to discriminate between CF patients with and without P. aeruginosa in both adults and children. Adult AUCROC (SE) for LCI = 0.82 (0.05), p < 0.0001, compared with FEV1%pred = 0.66 (0.07), p = 0.021 and FEF25–75%pred = 0.64 (0.07), p = 0.044 (Figure 1). Child AUCROC (SE) for LCI = 0.85 (0.10), p = 0.004, compared with FEV1%pred = 0.80 (0.12), p = 0.014 and FEF25–75%pred = 0.67 (0.13), p = 0.152.

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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FEASIBILITY OF CONDUCTING COMPLEX PHYSIOLOGICAL MEASUREMENTS IN LONDON PRIMARY SCHOOLS: THE SIZE & LUNG FUNCTION IN CHILDREN (SLIC) STUDY

Despite recognised ethnic differences in lung function, most reference ranges are based on White subjects. Ethnic minorities comprise 40% of the London population, which impacts on healthcare provision. Even when available, selection of appropriate equations is complicated by the increase in admixed populations and complexities of defining ‘ethnicity’. As part of the Wellcome Trust SLIC study (www.ucl.ac.uk/slic) to determine the extent to which body shape, size and composition contributes to ethnic differences in lung function, we examined the feasibility of conducting complex physiological measurements in a multi-ethnic population of London primary school children.

Methods 14 London schools participated in the study. Science workshops were presented one week prior to commencing assessments. Consent forms and information packs were distributed to all children. All children with parental consent were eligible and were categorised into 4 broad ethnic groups: White; Black; South-Asian (Indian subcontinent) and Other/mixed. Assessments were performed at school in 5–11 year-old children and included detailed anthropometry, 3D photonic scan for body shape; body composition; spirometry and saliva samples (cotinine and DNA analysis).

Results Parental consent for anthropology and spirometry was obtained in 54% of those approached. Amongst these, 88% and 96% provided specific consent for DNA samples and access to GP records respectively (Table 1). Assessments were performed in 2175 children (mean (SD)age: 8.22(1.63); 34%White; 29% Black; 25%South-Asian; 12%Other/mixed ethnicities), 1045 (48%) of whom had follow-up assessments a year later. Preliminary analysis indicates: 18% had chronic respiratory illness or acute symptoms at time of test. 12% children had a diagnosis of ‘asthma ever’, with 6% having current asthma (Table 1).

Summary Conducting a field study to undertake complex physiological measurements is feasible even in young children. However, the relatively high prevalence of chronic or acute respiratory disease at time of testing in this age group, combined with exclusions due to technically unsatisfactory spirometry means that results from ~30% of children may be excluded if analysis of results is to be based on a ‘healthy’ population. Such factors must be accounted for when designing respiratory field studies to ensure adequate sample size to reach definitive conclusions.

REFERENCE

INTERSTITIAL LUNG DISEASE: CLINICAL

INTERSTITIAL LUNG DISEASE MULTIDISCIPLINARY DISCUSSION: SIX YEARS OF DATA FROM A TERTIARY SERVICE

Introduction Accurate diagnosis in Interstitial Lung Disease (ILD) is vital in optimising patient management. An integrated approach involving a multidisciplinary team (MDT) of physicians, radiologists and pathologists is strongly advised in ATS/ERS guidelines. This has been shown to improve diagnostic confidence. Consensus diagnosis post multidisciplinary team discussion often differs from that reached by individual clinicians. Our centre, which provides a tertiary interstitial lung disease service in the North of England, implemented multidisciplinary discussion in 2005. Our patient cohort is larger than series previously presented at both national and international respiratory meetings. Literature search also did not identify any published data with either an equal or greater patient population.

Aims To review interstitial lung disease MDT outcomes and to determine if discussion resulted in a change of diagnosis and whether this impacted on subsequent patient management.

Methods Retrospective review of both patient clinical notes and MDT meeting minutes. Literature search also did not identify any published data with either an equal or greater patient population.

Abstract S10 Figure 1. Adult ROC curve

Abstract S11 Table 1. Consent, asthma status & spirometry success rates of study population

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<td>742</td>
<td>629</td>
<td>435</td>
<td>411</td>
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<tr>
<td>Total Tested</td>
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<td>629</td>
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<tr>
<td>Total Spirometry (%)</td>
<td>533 (71.8%)</td>
<td>435 (69.2%)</td>
<td>411 (76.1%)</td>
<td>195 (73.9%)</td>
</tr>
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</table>

Data presented as %.
Abbreviations: DNA: Deoxyribonucleic acid (for genetic ancestry); GP: General Practitioner; Current asthma: defined as those having symptoms and/or asthma medication over the past 12 months; based on data from healthy children and after exclusions from poor health and poor performance.