Methods : As a part of an on-going collaboration between PneumaCare Ltd. and Queen Elizabeth (QE) Hospital (Birmingham, UK), 107 healthy adult subjects between ages of 18 to 69 were measured with SLP during 4 to 5 minutes of seated tidal breathing. Parameter means and standard deviations for males and females aged 18–39 and 40–69 were calculated and gender and age related comparisons were made (t-test).

Results Tables 1 summarises the normative values for males and females older and younger than 40 years. Three parameters showed age related differences and one parameter showed a gender related difference.

Conclusion Preliminary normal values for SLP derived tidal breathing parameters are reported. Some gender and age related differences are apparent. It is interesting that tPTEF/tE was significantly lower in the older participants, possibly a sign of natural airway obstruction associated with age.

REPEATABILITY OF STRUCTURED LIGHT PLETHYSMOGRAPHY (SLP) FOR MEASUREMENT OF RESPIRATORY RATE IN NORMAL SUBJECTS

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Introduction Structured Light Plethysmography (SLP) captures movements of a light grid projected onto the thoraco-abdominal (TA) wall to produce a waveform from which a primary derived output is Respiratory Rate (RR). Assessment of repeatability is essential for clinical use, however, physiological variability can confound results. RR agrees within ± 2 breaths per minute (brpm)[1] with Respiratory Inductance Plethysmography (RIP) measured simultaneously on one occasion. We propose that if measurements are repeatable, there would be no difference in agreement between devices over a series of sessions.

Aim This study assessed repeatability of the agreement between SLP and RIP.

Methods 14 subjects (7 male, 7 female) with no respiratory diagnosis underwent 5 minutes of simultaneous measurement with SLP and RIP during quiet breathing. This was repeated on 3 occasions over 2 days, by the same operator, at the same location and using the same devices. RR were calculated for thorax (THRR), abdomen (ABRR) and the entire thoraco-abdominal (TARR) signals for both devices. Agreement between the two devices was assessed using Bland-Altman plots with LOA set at < ± 2 breaths/min.

Results For TARR and THRR, all points were within 2 SD of the mean; for ABRR, 1 of 14 points was outside of 2 SD, but the LOA were within < ± 2 breaths/min. The mean differences between the two devices were 0.476, 0.605 and 0.524 breaths/min for TARR, THRR and ABRR, respectively.

Conclusion Agreement was observed between the two devices for each set of repeated measurements. We conclude that measurement of RR are repeatable.

REFERENCE

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CTAS – A CT SCORE TO QUANTIFY DISEASE ACTIVITY IN PULMONARY SARCOIDOSIS

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Introduction A major gap in the management of sarcoidosis is the lack of accessible and objective methods to measure disease activity. Since 90% of patients have pulmonary involvement, we explored if a disease activity score based on thoracic CT scan could address this clinical issue.

Methods High resolution CT scans from 100 consecutive sarcoidosis patients at a regional sarcoidosis service were scored for extent of CT abnormalities known to relate to granuloma or lymphocytic infiltration from published CT-pathological studies. These individual abnormality scores were then correlated against serum ACE, sIL-2R and change in forced vital capacity (FVC) to identify CT abnormalities that reflect contemporaneous disease activity. The sum of these scores, or **CT A**ctivity **S**core (CTAS) was then validated against FVC response to treatment.

Results and discussion CT extent scores for nodularity, ground-glass opacification, inter-lobular septal thickening and consolidation correlated significantly with at least one of the disease activity parameters and were used to form CTAS. CTAS was found to predict FVC response to treatment at one year and was highly reproducible between radiologists. An abbreviated CTAS (aCTAS), constructed from presence or absence of the four CT abnormalities also showed significant correlation with FVC response to treatment. CTAS and aCTAS also correlated with response to treatment in the fibrotic subgroup.

Conclusions CTAS provides a concept for an objective and reproducible CT scoring method to quantify disease activity in sarcoidosis. The score can potentially be used to stratify patients according to disease activity, determine response to treatment and establish if fibrotic sarcoidosis is active.

DEVELOPMENT OF 18F AND 68GA-LABELLED CYCLIC PEPTIDES FOR POSITRON EMISSION TOMOGRAPHY IMAGING OF αVβ6 IN IDIOPATHIC PULMONARY FIBROSIS

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Biomarkers, capable of identifying the stage and aggressiveness of idiopathic pulmonary fibrosis (IPF) at the time of diagnosis, would improve the accuracy of prognostication and facilitate targeting anti-fibrotic drug therapy to patients who are most likely to benefit. The integrin $\alpha_v\beta_6$ is highly expressed in injured lung epithelium and is a key activator of transforming growth factor β (TGF-β), which plays a crucial role in the initiation and maintenance of fibrosis. Positron emission tomography (PET) imaging tracers that permit visualisation of lung $\alpha_v\beta_6$ expression have potential as novel therapeutic and prognostic biomarkers in IPF.

Several $\alpha_v\beta_6$ integrin-binding cyclic peptides were synthesised using solid phase supported peptide synthesis and functionalised

via their N-terminus or side chain amino group with a 6-amino- or a 6-azidohexanoic acid spacer to provide a convenient attachment site for either 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) or an 2-ethynyl-6-[18F]-fluoropyridine prosthetic group for radiolabelling with ^{68}Ga or ^{18}F, respectively. The $\alpha_v\beta_6$-binding capability of these peptide derivatives was assessed by competitive binding enzyme-linked immunosorbent assay (ELISA) and flow cytometry. Peptide derivatives that displayed strong affinity for $\alpha_v\beta_6$ were taken forward to "hot" cell surface binding experiments to evaluate their selectivity for the target. Stability of radiolabelled peptides was measured in human serum.

Competitive binding ELISA experiments (Figure 1) and flow cytometry experiments, showed that cRGD1 and cRGD4 were able to inhibit the binding of $\alpha_v\beta_6$-specific 10D5 mAb to $\alpha_v\beta_6$ with IC_{50} values of 6.6 nM and 1.6 nM, respectively. Labelling cRGD1 and cRGD4 with fluorine and gallium resulted in IC_{50} values of 12.2 nM and 1.2 nM for ^{19}F-Pyr-cRGD1 and ^{68}Ga-DOTA-cRGD4, respectively. Serum stability studies of ^{68}Ga-DOTA-cRGD4 have shown that this tracer is >90% stable after 2 half-lives of ^{68}Ga (136 min).

Radiolabelled cyclic RGD peptides have showed favourable binding and stability characteristics to warrant their investigation by PET imaging *in vivo*. A xenograft murine model using $\alpha_v\beta_6^+$ and $\alpha_v\beta_6^-$ tumours is currently under development to validate tracer uptake and biodistribution *in vivo*.
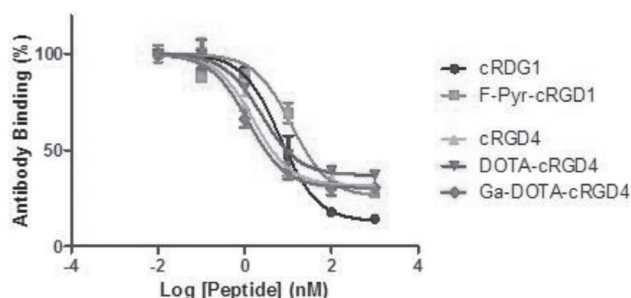
Abstract P40 Figure 1 $\alpha_v\beta_e$ competitive binding ELISA between labelled/non-labelled cyclic peptides and the $\alpha_v\beta_e$ –specific mAb (clone10D5)

| P41 | A PROSPECTIVE COHORT STUDY TO MEASURE IN-VIVO CHANGES IN LUNG GLUCOSE METABOLISM IN PATIENTS WITH SSCL-ILD USING FDG-PET |

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Background Systemic sclerosis (SScl) is a chronic inflammatory autoimmune rheumatic disease with a UK prevalence of 2–10 per 100,000. It is a heterogenous disease characterised by varying degrees of dermal and organ fibrosis. Interstitial lung disease (ILD) occurs in 60–80% of patients and ranges from mild, clinically trivial disease to extensive fibrosis that results in respiratory failure and premature death. Therapeutic options include cyclophosphamide, mycophenylate mofetil and rituximab. Clinical decisions are complex and decisions to treat or not have historically been based on radiology and lung function tests, neither of which (at a single time point) give a dynamic view of disease progression. Novel biomarkers are urgently needed to predict disease activity, progression and response to treatment in patients with SScl-ILD.

Aims To investigate the potential of 18Fluoro-deoxyglucose Positron Emission Tomography (FDG-PET)/CT to act as a prognostic and response biomarker in patients with SScl-ILD.

Methods 35 SScl-ILD patients were prospectively recruited for 18F-FDG-PET/CT. Patients were screened for lung involvement using clinical assessment, chest X-ray and pulmonary function testing (PFT). Those with confirmed SScl-ILD underwent combined high resolution CT scan (HRCT)/PET scanning. The imaging signal and clinical findings were correlated with the need for, and response to, therapy. Follow up was with clinical assessment, PFT and when a change in treatment was indicated, repeat imaging.

Results The overall maximum pulmonary uptake of 18F-FDG (SUVmax), the minimum pulmonary uptake or background-lung-activity (SUVmin) and target-to-background (SUVmax/SUVmin) ratio (TBR) were quantified using routine region-of-interest analysis. Kaplan-Meir analysis was used to identify associations with disease progression and response to treatment

Conclusions We have shown that high pulmonary uptake of 18F-FDG is associated with disease activity and progression in patients with SScl-ILD. These PET findings can be used to give additional information, supplemental to PFTs, which may then aid clinical treatment decisions.

| P42 | INCREASED FDG UPTAKE IN AREAS OF 'NORMAL' LUNG IN IDIOPATHIC PULMONARY FIBROSIS |

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Background Idiopathic pulmonary fibrosis (IPF) has a variable disease course and we lack biomarkers that accurately predict prognosis or treatment response. Positron Emission Tomography-Computed Tomography (PET-CT) provides structural and functional information about the lung. A study of 25 IPF patients reported increased 18[F]-FDG uptake in areas of normal lung compared to controls.[1] If confirmed, this raises the possibility that PET-CT can identify 'microscopic fibrosis' with prognostic implications. We assess 18[F]-FDG uptake in areas of lung with normal CT appearance in a second IPF cohort.

Methods PET-CT scans undertaken for cancer staging at an interstitial lung disease tertiary referral centre were reviewed. IPF patients and controls without lung disease were identified. 18[F]-FDG uptake was assessed using manual region of interest (ROI) placement in areas of lung with normal CT appearance in IPF patients and controls. ROI were placed away from the mediastinum and concomitant tumours. 18[F]-FDG uptake within ROI was expressed as maximum and mean standardised uptake values (SUV) normalised using body weight. Mean Hounsfield Units (HU) were evaluated to assess for subtle differences in radiodensity within ROI. Data are presented as mean ± SD. Unpaired, 2-tailed T-tests were used to compare between group differences with a P value < 0.05 considered significant.

Results Forty-five subjects were included in this study (15 IPF and 30 controls). Lung cancer was the most common concomitant malignancy in both groups.

There was no difference in mean HU within ROI between IPF and controls (−719 ± 79 HU in IPF and −723 ± 147 HU in