

SPECT-CT imaging of $\alpha v \beta 3$ integrin reveals increased activity in patients with fibrotic interstitial lung disease compared to healthy controls

G. Dixon^{1, 2, 3, 4}, D. Little⁴, S. Cade⁴, J. Barnett⁹, D. Burch⁹, J. C. Rodrigues⁴, K. Tsaneva-Atanasova^{6,7,8}, S. L. Barratt^{1,11}, C. J. Scotton^{3,10}, M. A. Gibbons^{2,3,10}

1. Bristol Interstitial Lung Disease Service, North Bristol NHS Trust, Bristol, UK, 2. Exeter-South West Peninsula ILD Network, Royal Devon University Healthcare, Exeter, UK, 3. Department of Clinical & Biomedical Sciences, University of Exeter, Exeter, UK, 4. Royal United Hospitals Bath NHS Foundation Trust, Bath, UK, 5. Department of Health, University of Bath, Bath, United Kingdom, 6. Department of Mathematics and Statistics, Faculty of Environment, Science and Economy, University of Exeter, UK, 7. EPSRC Hub for Quantitative Modelling in Healthcare, University of Exeter, Exeter, UK, 8. Living Systems Institute, University of Exeter, UK, 9. Serac Healthcare Ltd, UK, 10. NIHR Exeter Biomedical Research Centre, University of Exeter, 11. NIHR Bristol Biomedical Research Centre, University of Bristol

Background

$\alpha v \beta 3$ integrins are transmembrane cell adhesion molecules involved in tissue fibrosis and are upregulated in vascular endothelial cells during angiogenesis [1]. Imaging $\alpha v \beta 3$ may demonstrate active inflammation in patients with fibrotic ILD.

Aims

We aimed to investigate the use of SPECT-CT imaging of $\alpha v \beta 3$ expression in patients with idiopathic pulmonary fibrosis (IPF), fibrotic hypersensitivity pneumonitis (fHP) and age- and sex-matched healthy controls (HCs).

Methods

HCs, IPF and fHP patients (n=5 each) were recruited to prospective observational study (PREDICT-ILD). Diagnoses were made by specialist ILD-MDT.

Participants received 740 MBq 99mTc-Maraciclalide IV (a novel molecular imaging agent) and underwent 20-minute baseline SPECT-CT scans 2 hours post injection.

Fused images were reviewed by nuclear medicine and thoracic radiologists and classified according to distribution/intensity of standardised uptake values (SUV) and radiological pattern.

Lung SUVmax was compared to lung SUVmin to provide a target-to-background ratio (TBR) and mean whole lung SUV was calculated.

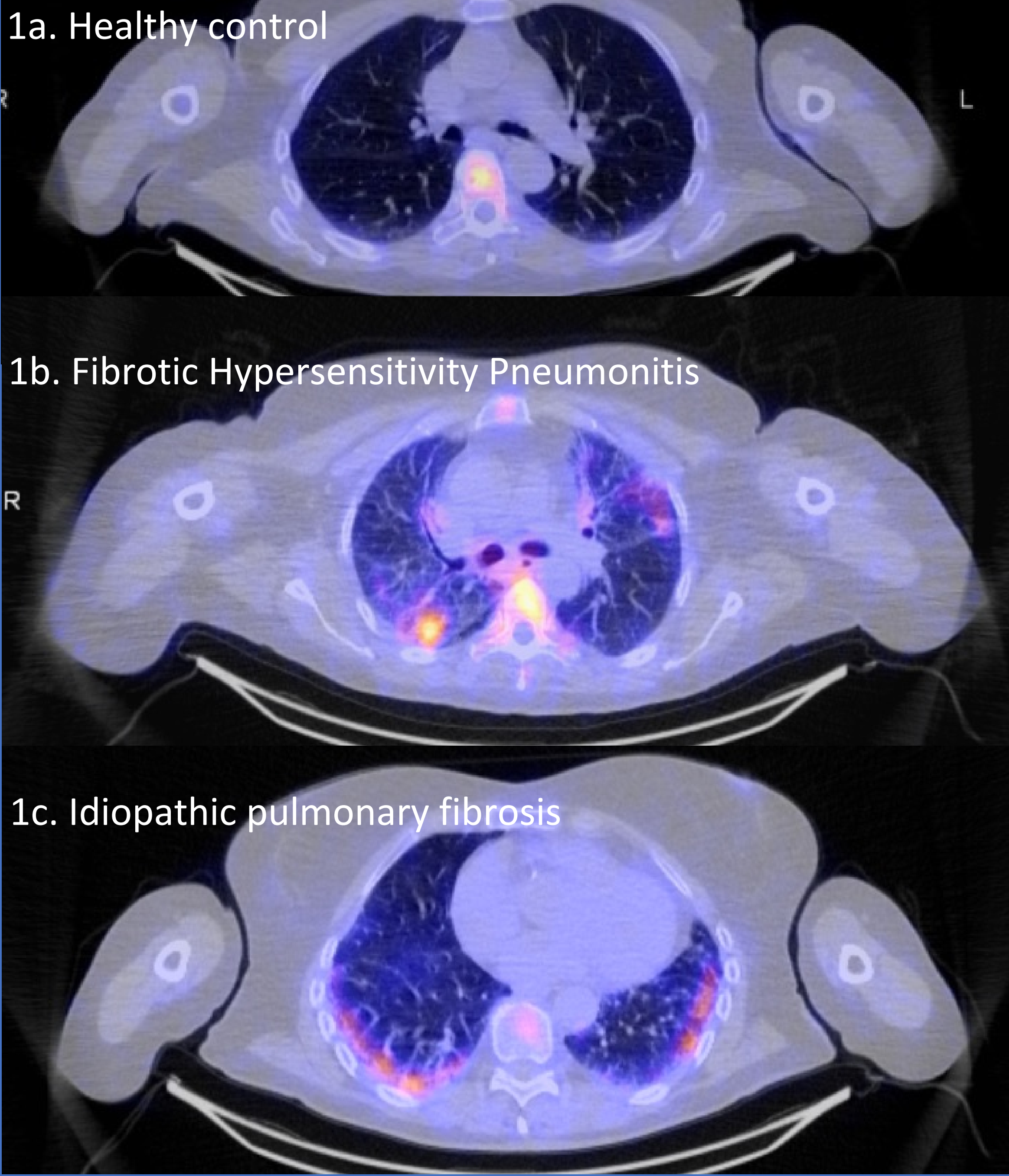
The study was funded by Serac Healthcare Ltd, EPSRC Hub for Quantitative Modelling in Healthcare, University of Exeter and Wellcome Trust GW4-CAT PhD Fellowship.

Results

Table 1. Demographics and lung function of 15 study participants.

	IPF	fHP	HCs
Age (median +/- IQR)	75 (12)	70 (9)	75 (6)
Gender M:F	4:1	2:3	3:2
Ever smokers	1/5	1/5	3/5
FVC % predicted (mean +/- 95% CI)	87.0 (72.2-101.8)	70.9 (54.5-87.4)	n/a
TLCO % predicted (mean +/- 95% CI)	52.0 (36.0-68.0)	52.1 (42.3-61.8)	n/a

Figure 1. Fused CT and $\alpha v \beta 3$ SPECT-CT series for 3 participants.



Results

$\alpha v \beta 3$ SPECT MeanSUV and target to background ratio is higher in patients with fHP vs healthy controls

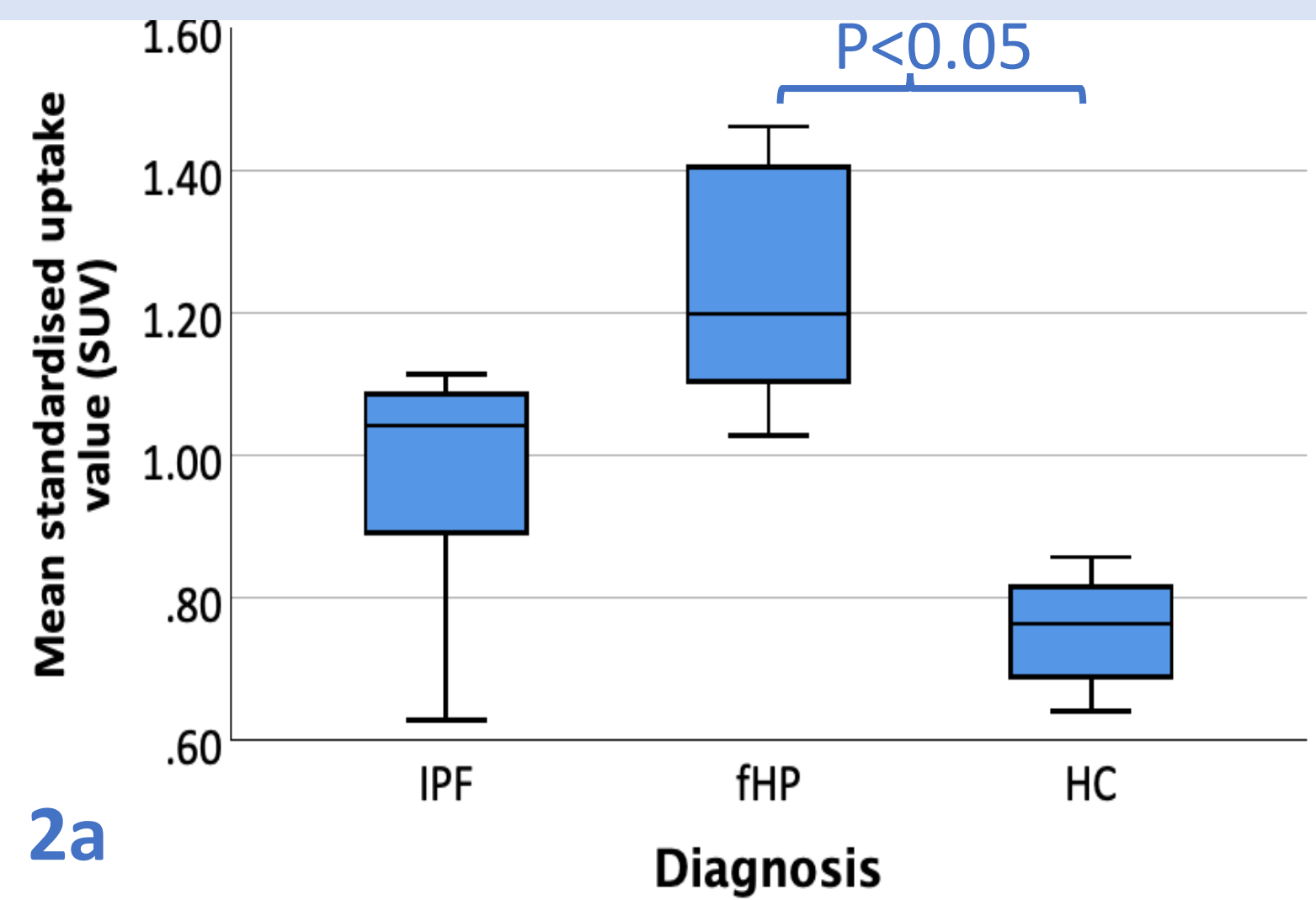


Figure 2a. Mean SUV between patients with idiopathic pulmonary fibrosis (IPF), fibrotic hypersensitivity pneumonitis (fHP) and healthy controls (HC).

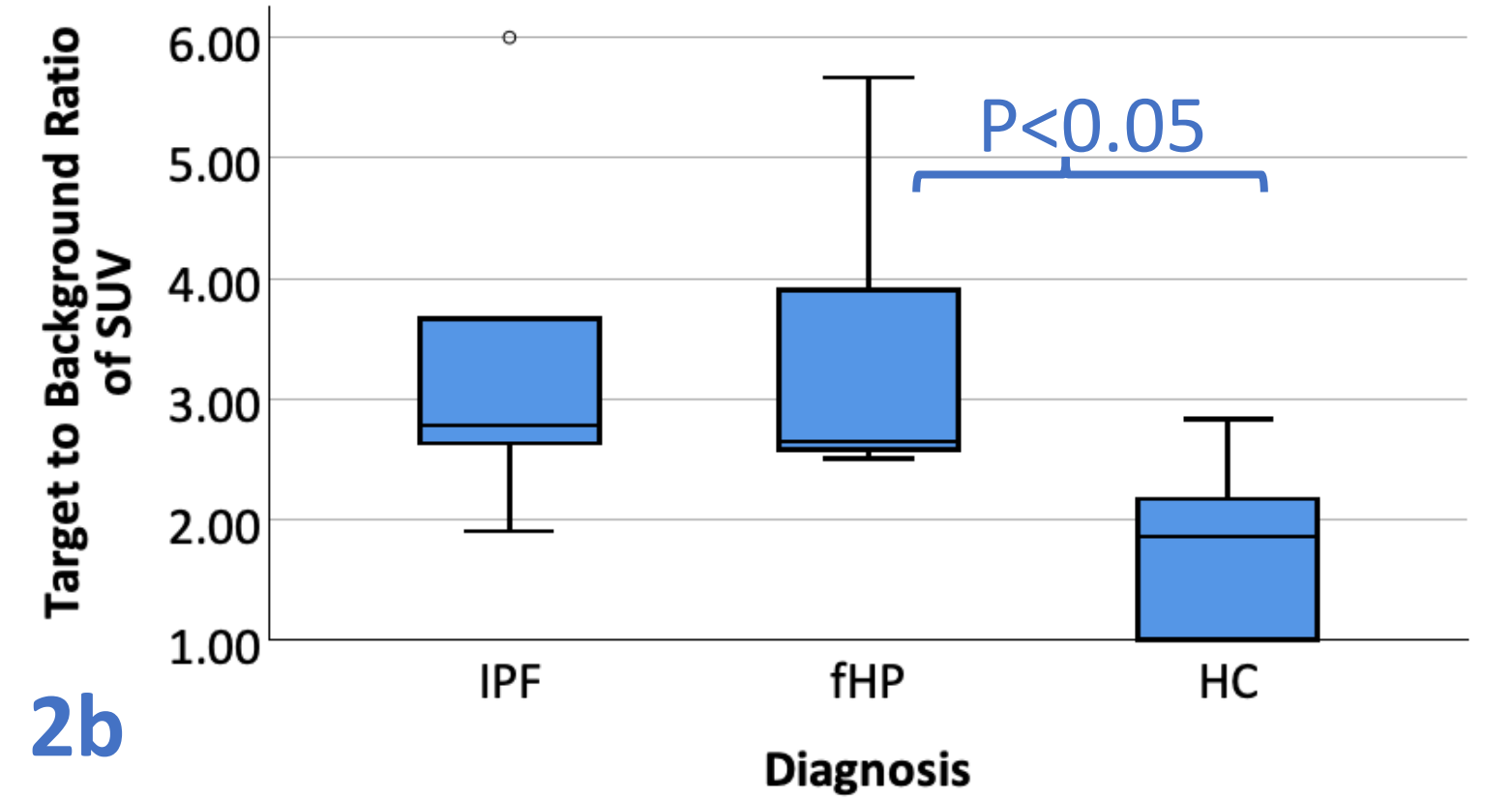


Figure 2b Mean Target to background ratio between patients with IPF, fHP and HCs

Table 1. Mean SUV, SUV skew, SUV kurtosis and Target to Background Ratio of 5 patients with IPF, fHP and HCs.

	IPF	fHP	HCs
Mean SUV (std)	0.95 (0.2)	1.24 (0.19)	0.75 (0.09)
Mean SUV Skew (std)	1.08 (0.34)	0.81 (0.31)	1.74 (0.15)
Mean SUV Kurtosis (std)	-0.17 (0.97)	-0.69 (0.73)	1.66 (0.53)
Mean Target to background ratio (std)	3.4 (1.6)	3.4 (1.4)	1.7 (0.8)

Conclusions

- Visualisation of inflammation in people with fibrotic-ILD is feasible.
- Whole lung SUVmax was greatest in those with fHP suggesting a role for $\alpha v \beta 3$ integrin activation in the pathogenesis of the disease.
- Low skew and negative kurtosis in fHP patients suggests a more heterogenous distribution of uptake in these patients compared to HCs