Online Supplement for

Quantitative ^{18}F-FDG PET/CT to assess pulmonary inflammation in Chronic Obstructive Pulmonary Disease

Laurence Vass[1*] Marie Fisk[1], Joseph Cheriyan[1,2], Divya Mohan[3,8], Julia Forman[2], Adelola Oseni[4], Anand Devaraj[4], Kaisa M Mäki-Petäjä[1], Carmel M McEniery[1], Jonathan Fuld[5], Nicholas S Hopkinson[3], David A Lomas[6], John R Cockcroft[7], Ruth Tal-Singer[8],

Michael I Polkey[3], Ian B Wilkinson[1]

1- Division of Experimental Medicine and Immunotherapeutics, University of Cambridge

2- Cambridge Clinical Trials Unit, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

3- Department of Radiology, Royal Brompton & Harefield NHS Foundation Trust, London, UK

4- NIHR Respiratory Biomedical Research Unit, Royal Brompton & Harefield NHS Foundation Trust and Imperial College, London, UK

5- Division of Respiratory Medicine, University of Cambridge, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

6- UCL Respiratory, Division of Medicine, Rayne Building, University College London, UK

7- Department of Cardiology, Wales Heart Research Institute, Cardiff University, Cardiff, UK

8- Medical Innovation, Value Evidence and Outcomes, GSK RD, Collegeville, Pennsylvania, USA.

Joint first authors

Corresponding Author: Marie Fisk, Box 98, Level 3, ACCI Building, Cambridge University Hospitals NHS Foundation Trust, Hills Road, CB2 0QQ.Tel: +44 (0) 1223-336806. Fax: +44 (0) 1223-296006 . Email:mf503@medschl.cam.ac.uk.

Methods:

Acquisition

All subjects were scanned at two sites: Cambridge University Hospitals NHS Foundation Trust using a GE690 PET/CT scanner or at Invicro, Hammersmith using a Siemens Biograph TruePoint 6 PET-CT scanner with closely matched protocols. Participants were told to fast for 6 hours prior to the scan, a blood glucose test was performed and if > 11mmol participants were rescheduled. Prior to the PET scan participants underwent an CT Attenuation Correction (CT-AC) scan; this was acquired under normal breathing. ^{18}F-FDG was administered intravenously in the antecubital vein; the target administered activity was 240MBq. Venous blood samples were drawn from the contralateral arm at 12 time points for the POB correction (at 1, 2, 3, 4, 5, 7, 10 , 15, 20, 30, 45 and 60 minutes). PET data was acquired under list mode and binned into 23 frames (8x15s, 3x60s, 5x120s, 5x300s, 2x600s); histograms were reconstructed at either 2mm nominal slice thickness using DIFT (Siemens) or 3.27mm nominal slice thickness using 3D Fore FBP (GE). Corrections for attenuation, deadtime, decay and scatter were incorporated. The DICOM files were converted into a single 4D Nifti file for analysis.

Lung Image Analysis-further information

To determine the net trapping, or rate of FDG tracer uptake (defined by Ki), time activity curves (TACs) of the different lung regions of interest (whole lung, upper, middle and lower (each average of right and left) were obtained and transformed by Patlak graphical analysis. The rate of FDG uptake was quantified using the normalised Patlak graphical technique, nKi, as described previously [3], [10]; where Ki is divided by the intercept of the Patlak plot. The intercept represents the steady state partition coefficient of the tracer between tissue and

plasma within the region of interest. nKi values were averaged in anterior-posterior direction to limit any potential effect of gravity.

Results

Table S1

Comparison of nKi values across regional lung volumes within subject groups.

	Upper lung	Middle lung	Lower lung	P-value[+]
COPD	3.9 ± 1.3	3.6 ± 1.2	3.5 ± 1.4	0.107
α_1ATD-COPD	3.8 ± 1.1	4.2 ± 1.1	3.8 ± 1.7	0.699
Smokers	4.5 ± 1.3	4.3 ± 1.4	4.0 ± 1.3	0.685
Never-smokers	2.7 ± 0.8	2.7 ± 0.6	3.3 ± 1.4	0.264

Values are reported as $\times\ 10^{-3}$ ml/cm^3/min^{-1}. [+] overall comparison for upper, middle and lower lung within subject groups.

Figure S1 Comparison of nKi values across total pack years smoked quartiles within the

usual-COPD group
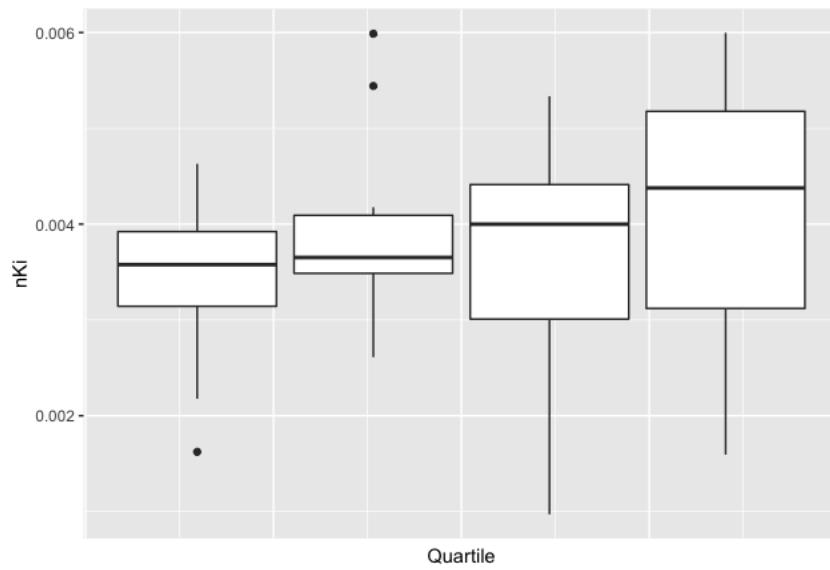
Box plots starting from left ≤ 25 years, 26-≤41years, 42-≤60 years, 61-≤110 years. No

statistical difference in nKi between quartiles (p>0.1).