

**Background** We have previously demonstrated that individuals with bronchiectasis have a higher prevalence of cardiovascular disease compared to the general population.<sup>1</sup> It is unclear if this is due higher prevalence of cardiovascular risk factors amongst people with bronchiectasis or through other mechanisms.

**Methods** We conducted a cross-sectional study using electronic primary care data from the Clinical Practice Research Database (CPRD-GOLD) to estimate the prevalence of cardiovascular risk factors (smoking habit, diabetes, hypertension, hyperlipidaemia, family history of cardiovascular disease) and medication commonly prescribed to manage cardiovascular disease amongst people with and without bronchiectasis. Logistic regression was used to generate odds ratios for each risk factor or cardiovascular drug, adjusting for age and sex.

**Results** Approximately 3.9 million individuals were included in our study, 10,942 (0.3%) of which had a record of bronchiectasis. Individuals with bronchiectasis were predominantly female (60.4%) and the median age at time of diagnosis was 56.2 (Interquartile range: 40.6–67.5) years. The prevalence of hypertension, diabetes and hypercholesterolaemia was slightly lower in individuals with bronchiectasis. We also found that people with bronchiectasis were less likely to have prescriptions for beta blockers, angiotensin converting enzyme inhibitors or angiotensin II receptor blockers, anti-platelets and lipid lowering drugs (see Table 1).

**Conclusions** Patients with bronchiectasis have a lower prevalence of cardiovascular risk factors compared to the general population. This raises the possibility that other factors associated with bronchiectasis could be contributing to the increase risk in cardiovascular disease.

## REFERENCE

- 1 Navaratnam V, Millett E, Hurst JR, Thomas S, Smeeth L, Hubbard R, Brown JS, Quint JK. The association between bronchiectasis and cardiovascular disease: A population based study. *American Journal of Respiratory and Critical Care Medicine* 2014; 189:A3618

## COPD investigations

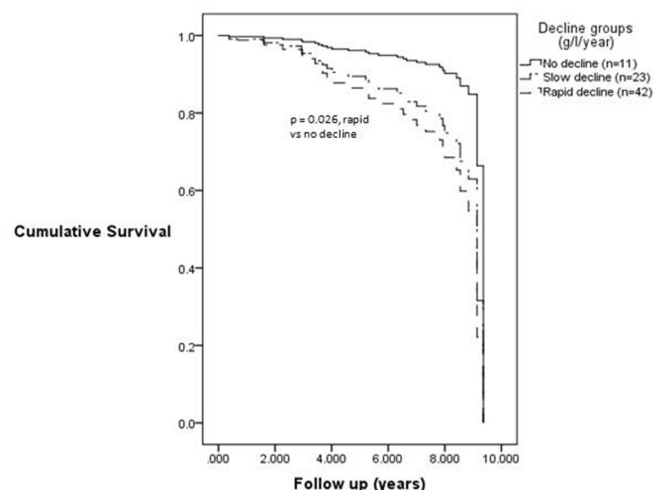
### S18 RATE OF DECLINE IN LUNG DENSITY MAY PREDICT LONG-TERM OUTCOME IN PATIENTS WITH ALPHA 1 ANTITRYPSIN DEFICIENCY (AATD)

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10.1136/thoraxjnl-2014-206260.24

**Introduction and objectives** Alpha-1-Antitrypsin Deficiency (A1ATD) is a genetically determined anti-proteinase deficiency which predisposes to emphysema.<sup>1</sup> Factors predicting mortality in untreated A1ATD patients include poor FEV1, gas transfer and low lung density.<sup>1</sup> Indeed the latter has been shown to be the most sensitive measure of progression and hence has become the primary outcome in recent studies of augmentation therapy.<sup>2</sup> We hypothesised that patients with the most rapid decline in lung density would be those most at risk of death and most in need of transplantation as the only viable rescue option.

**Methods** Augmentation naïve patients with 2 quantitative CT scans were selected from the UK A1ATD registry. The annual decline in lung density was determined using the difference between the 2 scans and patients were divided into those with no decline, a slow decline (0–2 g/l/year) or a rapid decline (> 2). Subsequent death or lung transplant was noted.



**Abstract S18 Figure 1** Cox regression analysis

A univariate analysis was undertaken dividing the population into 2 groups: Alive without transplant and dead. Median baseline density was significantly higher in the living than the dead group (55.40 g/l and 39.80 g/l respectively;  $p = 0.002$ ) and thus was included in a multivariate analysis, seeking association with subsequent death in a Cox regression analysis.

**Results** 77 patients were identified with sufficient data for analysis. 27 had died and 1 was transplanted and excluded from further analysis.

Slow decline in densitometry showed a trend to lower survival compared to no decline ( $p = 0.065$ ) but rapid decline was significantly associated with death ( $p = 0.026$ ; Figure).

**Conclusions** Decline in lung density may be a suitable surrogate measure for survival in AATD, and as augmentation therapy slows the decline in lung density<sup>2</sup> could identify a group more likely to benefit from augmentation in the shorter term.

## REFERENCES

- 1 Dawkins P, et al. Mortality in alpha-1-antitrypsin deficiency in the UK. *Respir Med*. 2009 Oct;103(10):1540–7
- 2 Stockley RA, et al. Therapeutic efficacy of alpha-1 antitrypsin augmentation therapy on the loss of lung tissue: an integrated analysis of 2 randomised clinical trials using computed tomography densitometry. *Respir Res*. 2010;11:136

### S19 IMAGING DERIVED REGIONAL LUNG FUNCTION USING HYPERPOLARISED XENON MRI (Xe-MRI) AND QUANTITATIVE COMPUTED TOMOGRAPHY (QCT) IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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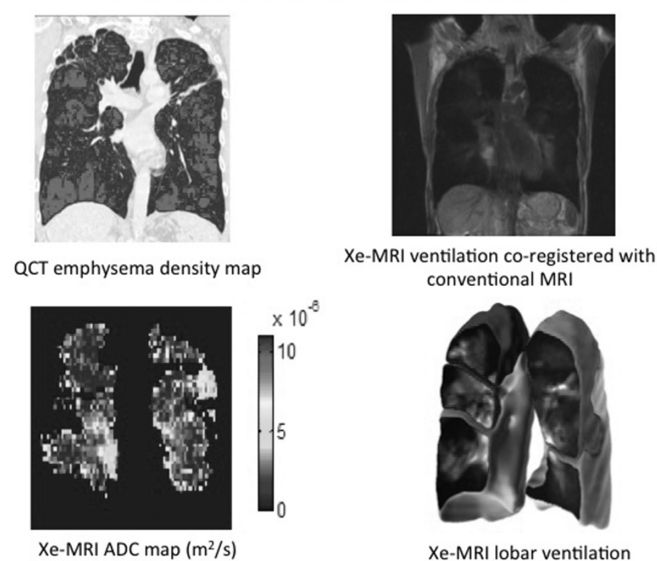
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**Introduction and objectives** To derive quantitative regional imaging lung function parameters using hyperpolarised xenon MRI (Xe-MRI) and computed tomography (QCT), and compare these to pulmonary function tests (PFTs) in subjects with chronic pulmonary obstructive disease (COPD).

**Methods** Twenty patients with COPD (stage II – IV GOLD criteria classification) underwent Xe-MRI at 1.5T, QCT, and PFTs.

Whole lung and lobar percentage ventilated volumes were obtained using automated segmentation of multi-slice Xe-MRI ventilation images acquired at a breath hold of FRC + 1L using in-house software. Average whole lung apparent diffusion coefficients (ADCs) were calculated from multi-slice Xe-MRI

## Xe-MRI and QCT from a subject with COPD



Abstract S19 Figure 1

diffusion-weighted images ( $b=20.855 \text{ sec/cm}^2$ ). Percentage predicted PFT results were established for each participant.

Whole lung and lobar QCT-derived metrics for emphysema and bronchial wall thickness were calculated from percentage of lung tissue with density of  $<950 \text{ HU}$  and  $\text{Pi10}$  (the square root of wall area for an airway with lumen perimeter of  $10 \text{ mm}$ ), respectively.

Pearson's correlation coefficients were used to evaluate the relationship between whole lung and lobar imaging measures and PFTs.

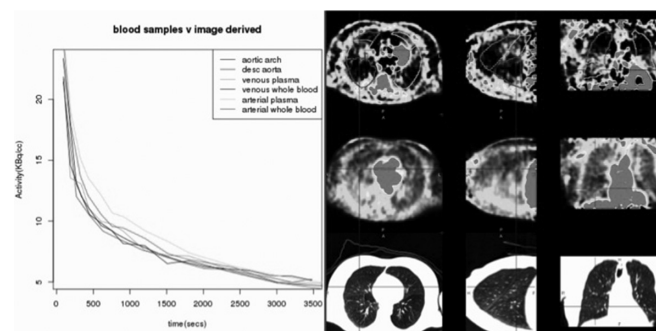
**Results** Xe-MRI whole lung average ADC showed significant correlation with: whole lung QCT percentage emphysema ( $r = 0.79$ ,  $p = 0.001$ ), whole lung  $\text{Pi10}$  ( $r = 0.68$ ,  $p < 0.05$ ), percentage predicted functional residual capacity (FRC) ( $r = 0.635$ ,  $p < 0.05$ ) and demonstrated significant negative correlation with percentage predicted TLCO ( $r = -0.81$ ,  $p < 0.001$ ). Whole lung QCT percentage emphysema showed a similar significant negative correlation with percentage predicted TLCO ( $r = -0.80$ ,  $p < 0.001$ ). Xe-MRI lobar percentage ventilated volume showed significant correlation with lobar QCT percentage emphysema ( $r = -0.51$ ,  $p < 0.001$ ). The QCT-derived metrics, percentage emphysema and  $\text{Pi10}$  demonstrated significant correlation on a whole lung ( $r = 0.75$ ,  $p < 0.015$ ) and lobar basis ( $r = 0.29$ ,  $p < 0.015$ ).

**Conclusion** This study demonstrates excellent correlation between Xe-MRI, QCT-derived metrics and PFTs in COPD. New quantitative whole lung and lobar functional imaging parameters have been derived that may be of value when assessing patients with COPD for regional treatment and in trialling new therapies. Although further investigation is required, this may represent the first integrated regional lung imaging technique linked to pulmonary functional outcomes.

## S20 18F-FLUORODEOXYGLUCOSE (18FDG) PET PULMONARY IMAGING: COMPARATIVE METHODOLOGY IN COPD PATIENTS

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10.1136/thoraxjnl-2014-206260.26



**Abstract S20 Figure 1** Shows an example of time activity curves from arterial, venous and image derived techniques (on left) and (on right) a Patlak image from venous plasma slope (1st row), intercept (2nd row) and CT (3rd row)

**Introduction** <sup>18</sup>FDG PET/CT imaging may be a useful tool to study COPD and lung inflammation; however the optimal protocol for this imaging biomarker has yet to be established.

**Method** We aimed to develop a combined <sup>18</sup>FDG-PET/CT imaging protocol optimised to quantify lung inflammation. Six patients with moderate-to-severe COPD underwent dynamic <sup>18</sup>FDG-PET imaging combined with blood sampling (both arterial and venous over 60 min) to determine the localised plasma activity time curve. High resolution CT (HRCT) was utilised to segmentate the lung and determine areas of emphysema. 3 sets of comparative input functions were analysed (arterial, venous and image derived arterial input functions). <sup>18</sup>FDG kinetics was fitted using the Patlak method.

**Results** Similar results were obtained using time activity curves from all three input functions. The arterial input was always found to be slightly higher than the others (Figure 1). Patlak analysis of the time-activity curves for each of the CT derived lung lobes allowed generation of images of slope (influx constant  $K_i$ ) and intercept (initial volume of distribution) (Figure 1). The acquisition of HRCT co-registered to FDG-PET allows more accurate demarcation and quantification of FDG in emphysematous areas of the lung. Attempt to improve the signal by excluding voxels without COPD tissue ( $-935$  to  $-300 \text{ HU}$ ) has been undertaken as well. The reproducibility of this technique is currently being studied where 20 patients are being scanned twice 4 weeks apart and compared to a baseline scan from 5 healthy controls.

**Conclusion** <sup>18</sup>FDG PET/CT imaging has the potential to be a non-invasive biomarker of lung inflammation in COPD.

## S21 CULTURE INDEPENDENT IDENTIFICATION OF BACTERIAL COMMUNITIES IN THE RESPIRATORY TRACT OF PATIENTS WITH COPD, HEALTHY NON-SMOKERS AND HEALTHY SMOKERS

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10.1136/thoraxjnl-2014-206260.27

**Introduction and aims** The role bacteria play in the development and progression of Chronic Obstructive Pulmonary Disease (COPD) is unclear. We used culture-independent methods to describe differences and/or similarities in microbial communities