HMG-B1 than culture negative samples. Due to the confounding effect of infection, our analysis excluded 90 BAL samples with positive cultures. Concentrations of IL-1a were significantly higher in culture negative BAL from BOS patients (median 2.411, range [AJF1] 0.073–19.078 pg/ml) than from Non-BOS patients (median 1.424, range [AJF2] 1.159–17.41 pg/ml; p=0.001). No significant difference in HMG-B1 concentrations between the two groups was observed (BOS median 58.906, range 0–197.5; Non-BOS median 76.25, range 0–211.563 ng/ml; p=0.2378). Longitudinal measurements of IL-1a in BOS patients showed significantly higher levels 3 months before or after BOS diagnosis (median 3.935, range 1.122–13.544 pg/ml), compared to >3 months before BOS diagnosis (median 2.015, range 0.073–14.669 pg/ml; p=0.0153). There was no such difference in HMG-B1 concentrations (p=0.9164).

Conclusions An increase in the alarmin IL-1a, but not HMG-B1, is associated with BOS development. The cellular source of IL-1a requires further evaluation but may be a marker of airway epithelial injury and/or play a mechanistic role in BOS development *via* its secretion by other cell types.

S54 POLYMERS OF Z α1-ANTITRYPSIN ARE ASSOCIATED WITH PULMONARY INFECTION POST LUNG TRANSPLANTATION

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Z antitrypsin (Z-AT) polymerises in the liver and is associated with early onset emphysema. Polymers of Z-AT are not only inactivate as antiproteinases, but also act as a pro-inflammatory stimulus. We studied patients with emphysema post lung transplantation, with and without AT deficiency, to examine the relationship between polymers and the presence of infection and inflammation. Bronchoalveolar Lavage Fluid (BALF) was obtained at scheduled surveillance, and when clinically indicated to assess for infection, rejection and airway injury. BALF was assessed by ELISA and immunoblot using a monoclonal antibody to polymeric AT (ATZII). BALF cell pellets were lysed, and HLE activity was used as a measure of BALF neutrophil numbers. 16 patients post-transplant were evaluated, 6 Z-AT patients (15 samples); 9 infective tracheobronchitis, 3 airway stenosis, 1 reflux, 2 normal, and 10 M-AT patients (20 samples); 7 infective tracheobronchitis, 8 rejection, 5 normal. All samples apart from one in the Z-AT group contained polymers; median (IQR) 292 (430–40.2) ng/ml. In one patient BALF was initially negative for polymers, but subsequent samples were positive. Polymers were present in association bacterial infection, colonisation, airway injury and surveillance bronchoscopy of asymptomatic patients. Airway stenosis/inflammation and bacterial tracheobronchitis was associated with a higher amount of polymers (347.35 (SEM±57 ng/ml) than Z-AT with normal findings (142±101 ng/ml). Immunoblot confirmed the classical ladders of polymers in Z-AT group, but not in M-AT group. BALF of Z-AT group had a higher free HLE than M-AT; 139(226.5–102.75) ng/ml vs 74(105.25–46) ng/ml, respectively; p≤0.001. Free HLE in Z-AT was correlated with polymer concentrations in BALF; r^2=0.63. Total neutrophil numbers were higher in Z-AT compared with M-AT; OD405, 0.57±0.07 vs 0.37±0.04, respectively; p=0.033. BALF neutrophil numbers were significantly higher in the infected Z-AT (0.54±0.1) vs infected M-AT (0.31±0.1), p=0.026. We have shown that polymers of Z-AT are present in BALF of transplanted individuals. Furthermore, this was associated with excess neutrophils, and closely correlated with free HLE. The production of polymers results in further reduction of the anti-proteinase and anti-inflammatory protection in the lung and leads to neutrophil influx. This may to predispose Z-AT individuals to exaggerated lung destruction and a worse outcome after lung transplantation.

Clinical and mechanistic studies in thoracic malignancy

S55 COST-EFFECTIVENESS AND QUALITY OF LIFE RESULTS FROM THE ASTER STUDY: ENDOBRONCHIAL AND ENDOSCOPIC ULTRASOUND VS SURGICAL STAGING IN POTENTIALLY RESECTABLE LUNG CANCER

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Background We recently published clinical results of ASTER, a randomised controlled trial in which endosonography, a strategy of combined endoscopic (EUS) and endobronchial (EBUS) ultrasound (followed by surgical staging if these tests were negative for malignancy), had significantly higher sensitivity and negative predictive value than surgical staging alone for mediastinal staging in NSCLC. Here we present ASTER quality of life (QoL) and cost-effectiveness outcomes.

Methods EuroQoL EQ-5D questionnaire was performed at baseline, end of staging, 2 and 6 months post randomisation. The UK EQ-5D social tariff was applied to calculate utility values. Quality-adjusted survival was estimated using the area under the utility curve. Full resource use information was recorded for all patients and NHS 2008–2009 Reference Costs were applied. Total expected costs over 6 months were estimated by summing the resource use multiplied by its unit cost and taking the sample average for each group.

Results Of 241 randomised patients, 144 (60%) provided EQ-5D data at baseline; of these 139 (97%) were followed up at the end of staging, 132 (92%) at 2 months and 124 (86%) at 6 months. At the end of staging, those randomised to endosonography had significantly better QoL than those randomised to surgical staging (utility difference=0.11, 95%CI 0.02 to 0.19). At all other time points, there was little difference between the groups, so that quality adjusted survival over the 6 months was similar (4.1 vs 4.0 months respectively). Complete resource use data were available for 172/214 (71%) patients. Other than the number of thoracotomies performed (66% of patients in the surgical staging arm and 53% in the endosonography arm) resource use did not differ between the two groups. The endosonography group had a non-significant cost saving of £746 per patient compared to the surgical staging group.

Conclusions Given that (a) the sensitivity of endosonography was significantly higher than that of the surgical staging arm; (b) QoL post-staging was higher in the endosonography arm and (c) there is no difference in cost between the two strategies, mediastinal staging should commence with endosonography proceeding to surgical staging if there is no evidence of malignancy.

S56 EBUS-TBNA PREVENTS MEDIASTINOSCOPIES IN PATIENTS WITH ISOLATED MEDIASTINAL LYMPHADENOPATHY: A PROSPECTIVE CLINICAL TRIAL AND COST MINIMISATION ANALYSIS

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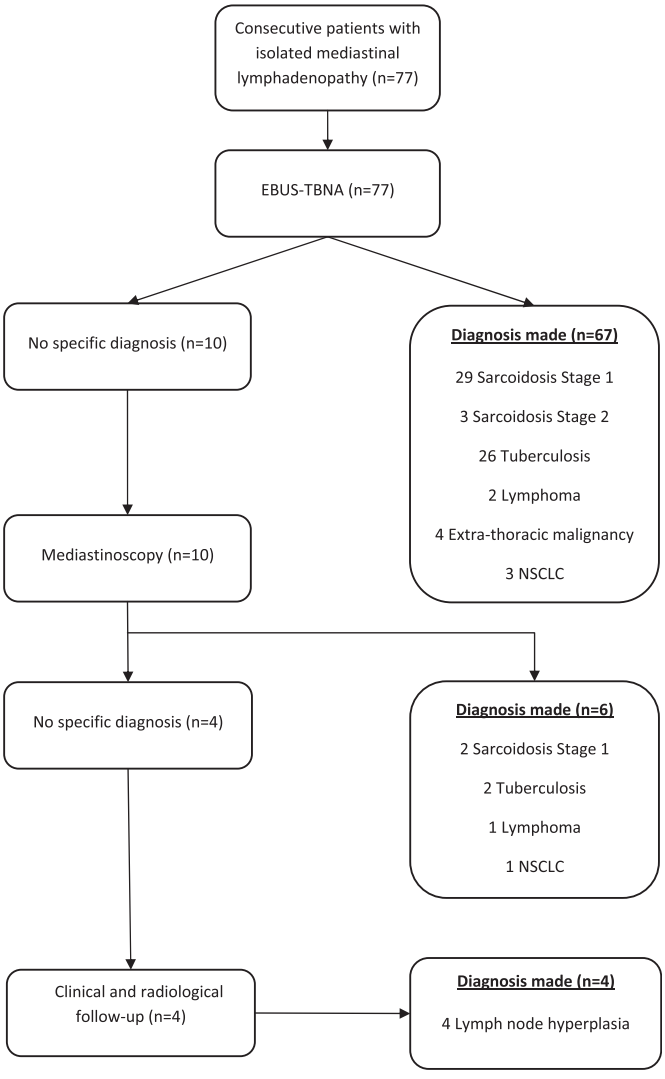
Introduction Isolated mediastinal lymphadenopathy (IML) is a common presentation to respiratory physicians and

mediastinoscopy is traditionally considered the gold-standard investigation when a pathological diagnosis is required. EBUS-TBNA is established as an alternative to mediastinoscopy in patients with lung cancer. However, the utility and healthcare costs of EBUS-TBNA in patients with IML is unknown.

Methods This prospective clinical trial recruited 77 consecutive patients with IML who were referred for mediastinoscopy from five centres between April 2009 and March 2011. All patients underwent EBUS-TBNA. If the results from EBUS-TBNA were not conclusive, patients underwent mediastinoscopy. The co-primary endpoints were the proportion of mediastinoscopies saved and NHS costs. The Bonferroni correction was applied to the type 1 error to account for multiple significance testing. Economic evaluation of the EBUS-TBNA strategy (where negative EBUS-TBNA is followed by mediastinoscopy) vs mediastinoscopy alone from an NHS perspective was carried out using a decision tree model and univariate threshold sensitivity analysis.

Results EBUS-TBNA prevented 87% of mediastinoscopies (97.5% CI 78 to 96%, p<0.001) but failed to provide a diagnosis in 10 patients, all of whom underwent mediastinoscopy (Abstract S56 figure 1). Mediastinoscopy provided a specific diagnosis in 6 cases while the remaining four patients had clinical and radiological follow-up of at least 6 months duration. The sensitivity and negative predictive value of EBUS-TBNA in patients with IML was 92% (95% CI 83 to 95) and 40% (95% CI 12% to 74%) respectively. No significant complications of EBUS-TBNA or mediastinoscopy were observed.



Abstract S56 Figure 1 Flowchart of patients in the REMEDY trial.

The patients included in the trial were similar to a historical control group of 68 patients with IML undergoing mediastinoscopy in 2008. The cost of the EBUS-TBNA strategy was £1871 per patient while a strategy of mediastinoscopy alone was £3268 per patient (p<0.001). Threshold sensitivity analysis demonstrated that the EBUS-TBNA strategy was less costly than mediastinoscopy if the cost per EBUS-TBNA procedure was <£2828.

Conclusions EBUS-TBNA is a safe, highly sensitive and cost-saving initial investigation in patients with IML being referred for mediastinoscopy. The low negative predictive value of EBUS-TBNA in this setting indicates that mediastinoscopy should be performed in cases of negative EBUS-TBNA.

Trial registration clinicaltrials.gov NCT00932854.

S57 GENE EXPRESSION PROFILING OF ENDOBRONCHIAL ULTRASOUND-DERIVED CYTOLOGICAL ASPIRATES FROM HILAR AND MEDIASTINAL LYMPH NODES IN NSCLC

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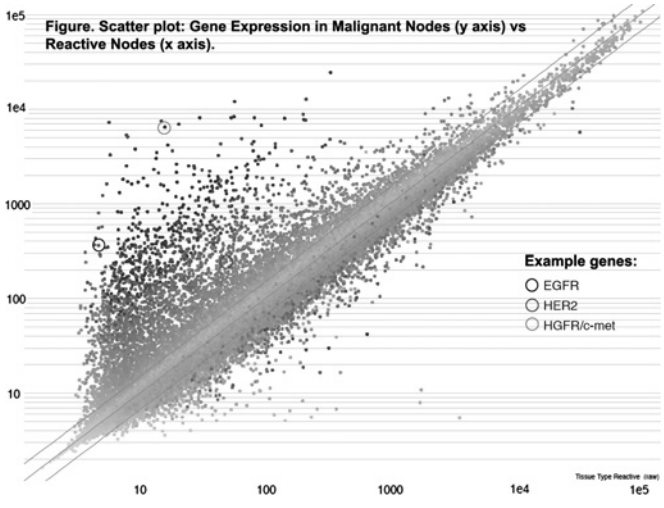
Introduction Endobronchial Ultrasound (EBUS) allows minimally-invasive hilar and mediastinal lymph node sampling and has an established role in the diagnosis and staging of lung cancer. Molecular biomarker development is becoming increasingly relevant in lung cancer management, however the suitability of EBUS-derived aspirates for detailed molecular analysis is not fully defined. Gene expression profiling (GEP), a powerful micro-array technology, which assesses genome-wide changes in gene expression, can generate individual-specific molecular signatures that can provide prognostic information and predict treatment responsiveness. Here we demonstrate the feasibility of using EBUS-derived cytological aspirates from benign and tumour infiltrated lymph nodes in patients with NSCLC for GEP.

Methods Cytological aspirates from six patients with known NSCLC that had been referred for EBUS to stage the mediastinum were selected for GEP. Three patient samples were infiltrated by NSCLC and three were benign. NSCLC-infiltrated and benign lymph nodes were compared for differences in gene expression.

Results RNA was available at a yield (median 17.5 μg, range 0.7–62.3 μg) and integrity (RIN Median 7.1, range 5.3–8.0) suitable for amplification and GEP. Reactive and malignant nodes were differentiated by principal component analysis and hierarchical



Abstract S57 Figure 1 Scatter plot: Gene expression in malignant nodes (y axis) vs reactive nodes (x axis).