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Bronchoscopic lung volume reduction for patients with emphysema

Submission date 07/11/2011	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 29/02/2012	**Overall study status** Completed	
Last Edited 20/10/2017	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Chronic obstructive pulmonary disease (COPD) is a common lung condition usually caused by smoking. The lungs become baggy and full of holes. Patients are unable to breathe out fully. This 'gas trapping' causes breathlessness, exercise limitation and poor quality of life and although tablets and inhalers provide some benefit many people are still very limited by their disease. A different approach is to use a fibreoptic camera (bronchoscope) to place valves into the airways of the lung to prevent air from entering the most over-inflated part. If the most damaged area of lung can be made to collapse this way it makes more space for the remaining healthier lung to function. Unfortunately, in many patients lung destruction breaks down the barriers (fissures) between the target lobe and adjacent lung, which allows to 'get round behind' the valves so that the lung does not collapse.

Who can participate?
Adult emphysema patients with intact interlobar fissures on their CT scan, the pattern that is most likely to respond.

What does the study involve?
Participants will be randomly allocated into one of two groups. One group will have valves placed to occlude the worst affected lobe of their lungs and the other group will have a bronchoscopy performed but no valves placed. This 'sham' bronchoscopy is acceptable to patients and has been used safely in other trials. Response to treatment will be assessed 90 days after the procedure. The primary outcome will be improvement in lung function but we will also look at changes in exercise capacity and health-related quality of life.

What are the possible benefits and risks of participating?
There is about a 1 in 20 risk of the lung that we have targeted collapsing. This is called a pneumothorax. This may cause chest pain and an increase in breathlessness but sometimes just shows up on a chest x-ray. If this does happen it may resolve spontaneously or we may need to insert a tube into your chest to let the air escape which could require you to spend a few days in hospital.

Where is the study run from?
The study is being run from the National Institute for Health Research (NIHR) Respiratory Biomedical Research Unit at Royal Brompton and Harefield NHS Foundation Trust and Imperial College, London (UK).

When is the study starting and how long is it expected to run for?
The study will start in March 2012 and run for 2 years.

Who is funding the study?
This research grant has been awarded by the Efficacy and Mechanism Evaluation (EME) programme, which is funded by the Medical Research Council (MRC) and managed by the NIHR.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
11647

Study information

Scientific Title
Bronchoscopic Lung Volume Reduction with endobronchial valves for patients with Heterogeneous emphysema and intact Interlobar FIssures

Acronym
BeLieVeR-HIFI

Study objectives
Studies have to date demonstrated modest overall group benefits with the placement of endobronchial valves in Chronic obstructive pulmonary disease (COPD). We hypothesise that it is possible to identify a group of COPD patients prospectively with heterogeneous emphysema and intact interlobar fissures in whom lobar occlusion can be achieved and hence lung volume

reduction, both to a significant degree and consistently. The study will therefore address the following questions, with outcomes assessed at 3 months post procedure.

1. Does endobronchial valve placement in this subgroup of COPD patients lead to a significant improvement in airflow obstruction (FEV1) compared to controls?
2. Will endobronchial valve placement in this group lead to significant improvement in lung volumes; residual volume (RV), total lung capacity (TLC), functional residual capacity (FRC) measured by body plethysmography compared to controls?
3. Will endobronchial valve placement in this group lead to significant improvement in exercise capacity (endurance time at 70% of maximum workload) and dynamic hyperinflation measured during endurance cycle ergometry as isotime end expiratory lung volume?
4. Will endobronchial valve placement lead to an improvement in walking distance assessed using the 6 minute walk test.
5. Will endobronchial valve placement in this group lead to significant improvement in health related quality of life?
6. Will the benefit seen in this group be of a magnitude likely to be sufficient to justify the cost of the procedure and complications that occur?

Ethics approval required
Old ethics approval format

Ethics approval(s)
London Bentham Research Ethics Committee, 02/12/2011, ref: 11/10/1608

Primary study design
Interventional

Study design
Double-blind randomised controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
COPD - heterogeneous emphysema

Interventions
Patients in the active treatment arm would have Zephyr (Pulmonx, California) valves placed bronchoscopically to occlude all segmental bronchi of the target lobe. The one way valves are placed via a delivery system passed through the working channel of a standard bronchoscope. They are silicone mounted on a nitinol frame and allow air and secretions to leave the target lobe. Procedures will be performed with sedation and local anaesthetic and would take less than 30 minutes.

The control group will have a similar bronchoscopy but without valve placement to blind them to treatment allocation. The use of sham bronchoscopy has been acceptable to patients, regulators and ethics committees in previous studies in this field and has been performed safely.

During the procedure (in both control and active treatment patients) collateral ventilation will be measured using a pressure catheter system to see how this relates to CT fissure integrity. We have not used this as one of our selection criteria as we are testing a CT based prediction system

but the additional data from the measurement of collateral ventilation may be of use in further developing targeting strategy

Patients will stay for 4 hours post procedure and have a chest x-ray performed before they go home to exclude pneumothorax; the x-ray will be reviewed by the treating physician.

Intervention Type
Procedure/Surgery

Primary outcome(s)
The percentage change in post-bronchodilator FEV1 measured 90 days post procedure.

Key secondary outcome(s)
Exercise Secondary endpoints will be change in endurance time on cycle ergometry at 70% baseline peak workload with a metabolic measurement cart to allow measurement of dynamic hyperinflation. The endurance exercise tests will be performed immediately after the lung function testing. Patients will perform inspiratory capacity (IC) manoeuvres each minute through the test. The IC value is subtracted from TLC to calculate end expiratory lung volume (EELV). Changes in EELV at isotime will be compared. Isotime refers to the last 30 second period completed in the shorter of the two exercise tests. Patients will perform an initial incremental test with 5-10 watt increments to establish the workload for the endurance test. This will be performed on a separate day from the first endurance cycle or with at least a two hour gap to ensure recovery.

A 6 minute walk test will also be performed at last one hour after the cycle test to allow time to recover according to ATS guidelines. Patients will have practised this on a previous occasion to reduce learning effects. The 6MWT has been chosen as this walking test is in the process of becoming accredited as an outcome measure by the FDA.

CT scanning: Changes in CT lung volume (total and lobar) will also be assessed as explanatory variables for improvement in exercise capacity and lung function.

Health status: The COPD assessment (CAT) score will be used to evaluate quality of life - this symptom score has been shown to be responsive both to exacerbations and to pulmonary rehabilitation. The SGRQ will be used alongside this as well as the EQ-5D to allow QALYs to be estimated.

Completion date
31/01/2014

Eligibility

Key inclusion criteria
1. Adult patients with stable severe COPD (GOLD stage III or IV with FEV1<50%pred)
2. Medical Research Council (MRC) dyspnoea score between 3 and 5
3. Total lung capacity (TLC)>100%predicted, residual volume (RV)>150% predicted
4. Six minute walk distance of <450m
5. Patients will be on optimum medical therapy including inhaled corticosteroids and long acting beta 2 agonist and anti-cholinergic agents unless they are intolerant or decline to use them
6. CT thorax must demonstrate heterogeneous emphysema with a defined target lobe with lung destruction and intact adjacent interlobar fissures. Scans will be reviewed by 2 radiologists

independently and a third will adjudicate on any disagreements. Radiologists will have to agree that the worst affected lobe of the lung has an emphysema score of >2 (according to the NETT study scoring system), that it is at least 1 point higher than ipsilateral lobes and that it has intact fissures visible on at least one projection

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Significant co morbidity which limits their exercise capacity or prognosis
2. Significant daily sputum production
3. Hypoxia (i.e. PO2<6.5Pa)

Date of first enrolment
01/02/2012

Date of final enrolment
31/01/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Brompton Hospital
London
United Kingdom
SW3 6NP

Sponsor information

Organisation
Imperial College London (UK)

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Government

Funder Name
National Institute of Health Research [NIHR] & Medical Research Council [MRC] (UK) - EME
Award ref: 10/90/10

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	12/09/2015		Yes	No
Results article	results	01/03/2017		Yes	No