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Bronchial Thermoplasty Study: an observational study examining airway remodelling and repair in patients with severe persistent asthma treated with bronchial thermoplasty

Submission date
14/06/2013

Recruitment status
No longer recruiting

Registration date
16/07/2013

Overall study status
Completed

Last Edited
02/02/2018

Condition category
Respiratory

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Asthma is a common lung condition affecting 5-10% of adults in the UK. It is severe in about 10% of sufferers where patients have considerable symptoms despite appropriate treatment. Although we know quite a lot about asthma there is still a big gap in our basic knowledge of asthma especially with regards to the causes and mechanisms of the microscopic structural changes seen in the lungs of people suffering from asthma. Bronchial thermoplasty is a new treatment for patients with severe asthma. The technique uses radio waves that heat the lining of the lungs, destroying some of the muscle tissue that constricts (gets narrower) during an asthma attack. This has been proven to improve asthma control and asthma-related quality of life and has also been shown to reduce severe asthma exacerbations (when a patient has worsening of asthma symptoms) and also reduce hospital admissions. This study is investigating how the lung restores and repairs itself after thermoplasty, exploring the role of different cells in the process. We are hoping this will improve our understanding of the different changes seen in asthma and may help in developing new asthma treatments in the future.

Who can participate?
The study will recruit patients with asthma who are undergoing bronchial thermoplasty as part of their normal clinical care in various participating centres in the UK.

What does the study involve?
Each recruited participant will be involved in the study for about 6 months. Some of the visits and investigations would be undertaken as part of the standard clinical thermoplasty procedure that the participant has been scheduled for by the clinical team. Please see below for a visit by visit description.
Visit 1
The first visit will confirm if the patient wishes to take part and is suitable for the study, followed by a brief medical review and medical history. The participant will be asked to sign a consent form.

Visit 2
The participant will come into the research unit in the week before the scheduled clinical thermoplasty procedure to have some breathing tests, a sputum (phlegm and saliva) sample, a blood sample and some health questionnaires for research purposes. They will also undergo certain tests that are part of the normal pre-assessment visit as per normal clinical care. The participant will also be asked if you would be willing to have an Magnetic resonance imaging (MRI) scan that will involve a separate visit in the same week. The MRI scan is optional and the participant can opt out when signing the consent form. This visit will therefore take place over 3 separate days with the bronchial thermoplasty session being performed on the last day. During the participant thermoplasty procedure we would take samples from the lungs, this is also optional.
Visit 3 & 4
Visit 3 and 4 are the same. The participant comes into the research unit the week before the scheduled clinical thermoplasty procedure to have some breathing tests and a blood sample only. The participant will not have a repeat computerised tomography (CT) scan or MRI on these two visits. Therefore this visit will take place over 2 separate days with the bronchial thermoplasty session being performed on the last day.
Visit 5
This visit will involve two visits to the research unit. The first visit will involve breathing tests, CT scan, blood sample, sputum sample and health questionnaires. The second visit, if the participant wishes to do it, will be to have an MRI scan.
Visit 6
This visit will involve one visit to the research unit where the participant will have breathing tests, sputum sample and health questionnaires.
About the tests:
Blood Tests
A blood sample will be taken for safety measures as part of your pre-assessment visit. The research team will also take some blood for research and will look at cells that might be contributing to the healing process in asthma and will also look at the genetics specific to airways disease and not your personal genetics. In addition to the clinical care safety bloods the researchers will take a maximum of 50 ml per visit. This is equivalent to approximately 3 tablespoons.
Spirometry
This will involve breathing out as hard as possible several times, repeated once more after inhaling Ventolin (medicine used to treat/prevent asthma). The participant will most likely have had this test done before. This may cause some temporary light headedness and coughing.
Lung Function Testing
As part of the research the researchers would like to do further breathing tests on lung function. These tests involve breathing in safe gas mixtures and blowing tests to measure the irritation in your lungs. One breathing test is carried out sitting in a transparent glass booth. The breathing tests may cause some temporary light headedness and coughing.
Bronchial thermoplasty
The clinical team will have discussed with the participant about having bronchial thermoplasty as part of managing your asthma and will have talked through the procedure and associated risks. In summary, the participant will be having three sessions of thermoplasty at least 3 weeks apart. The first and second thermoplasty sessions will take place together with study visit 2 and 3, and will be treating both lower lobes of the lung sequentially i.e. one at visit 2 and the other at visit 3. The third thermoplasty session will take place together with study visit 4 and will be treating both upper lobes.
Bronchial biopsies and brushings (optional)
The research team will take samples (biopsies and brushings) from the breathing passages (bronchus airways) after the participant has had their routine thermoplasty sessions. This will be

performed using a thin flexible tube that will already have been used for your thermoplasty procedure and allows instruments to be introduced for taking samples. The tube is much thinner than the breathing passages and does not limit your ability to breathe. Once in the correct position, the doctor performing the procedure will take the samples that are needed. Cells from the lining of the breathing passages are collected by gently rubbing a soft brush against the side of the breathing passages. Small samples of the walls of the breathing passages are collected using forceps. Biopsies and brushings will only be taken from areas of the lungs that have not undergone thermoplasty during the same session or from areas of the lungs that have been treated 3 or more weeks ago, therefore these will be healed areas of the lungs. The biopsies and brushings will take an additional 5-10 minutes to your thermoplasty procedure.
In addition to the risks of the thermoplasty procedure, which will have been discussed with the participant by the treating doctor, by undertaking the additional biopsies and brushings there is a slightly increased risk of bleeding from the nose or on coughing.
MRI scan (optional)
An MRI scan uses a powerful magnet and a computer to produce detailed images of any part of the body. In this case we will be looking particularly at the lungs. An MRI scan does not involve X-rays but this technique does involve inhaling two types of gases, Helium and Xenon. The participant will be asked to lie on the scan table and breathe a small quantity of the gas. This is completely harmless. The participant will then be moved slowly into the scanner, which is shaped like a tube. The participant will also be asked to hold your breath for about 20 seconds a few times and the operator will explain this to you. The scan itself will take about 60 minutes and the participant will be monitored throughout the procedure.
At one point during the scan a small amount of contrast agent (similar to a dye) will be injected through a small plastic tube (the same as what is used to give a drip) into a vein in the arm. This is so that the scans are clear. The small needle to insert the dye into your arm will feel like a sharp scratch.
CT scan
A CT scan is a type of X-ray examination that gives much more information than a normal X-ray. It produces detailed images of the lungs, breathing passages and blood vessels. The scanner itself is shaped like a large donut and is not enclosed.
Low radiation dose CT scans will be performed for the purpose of this study. On average in the UK the annual background is 2.5 mSv; however, in Cornwall this is higher at 7.5 mSv per year. For each scan the participant will be exposed to less than 4 mSv; however, the total exposure of scans cannot exceed 10 mSv.
The CT scan will expose the participant to radiation. The dose of radiation will be higher than would normally be exposed to, and this may cause a very small increase in the risk of developing cancer. The risk of dying from cancer in the UK is 25%. If the participant were to have 10 mSv extra of radiation, then this risk goes up to 25.05%.
Sputum Test
Sputum sample would be obtained from the participant. This will enable the researchers to see how many inflammation-causing cells the airways contain. If the participant is unable to produce a spontaneous sample they will be asked to breathe in a mist of salty water and cough up any secretions at any time during the procedure. This may cause some chest tightness, wheezing and /or cough. These are all readily reversed by inhaling a bronchodilator (salbutamol inhaler).
Questionnaires
These health questionnaires will ask the participant about their condition, symptoms and how the condition affects their daily life. They should only take around 5 to 10 minutes to complete.

What are the possible benefits and risks of participating?
There is no direct benefit to taking part in the study. The information we get from this study may help in developing novel asthma treatments in the future. The participant will receive travel and car parking expenses for attending the research and it will be possible to arrange transport for

them. Refreshments will be provided such as tea and coffee.
The risks associated with the investigations undertaken as part of this study have been described in the about the tests section.

Where is the study run from?
This is a multicentre study with different UK centers participating.

When is the study starting and how long is it expected to run for?
The study started in June 2013 and the end date is Jan 2016. Each recruited participant will be involved in the study for approximately 6 months.

Who is funding the study?
The study is being funded by the Wellcome Trust and by AirPROM (an EU consortium consisting of academics and pharmaceutical partners). The study is also supported by the National Institute for Health Research Leicester Respiratory Biomedical Research Unit.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
14006

Study information

Scientific Title

An observational study examining airway remodelling and repair in patients with severe persistent asthma treated with bronchial thermoplasty: an imaging and immunopathological study

Study objectives
This observational study is looking to investigate the effects of an asthma treatment called Bronchial Thermoplasty.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee: East Midlands Leicester, 26/02/2013, ref: 13/EM/0068

Study design
Observational clinical laboratory study

Primary study design
Observational

Secondary study design
Other

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Topic: Respiratory; Subtopic: Respiratory (all Subtopics); Disease: Respiratory

Interventions
3He, 129Xe and 1H MRI imaging, Functional lung MRI with hyperpolarised (HP) gas MRI (Helium-3 and Xenon-129 MRI) and 1H perfusion MRI before and after thermoplasty to explore the relation between changes in lung ventilation heterogeneity and regional lung function, measured by lung MRI, and changes in immunopathology

Bronchial biopsies, Bronchial biopsies for histopathological and immunopathological examination and bronchial brushings for epithelial and transcriptomic analysis at baseline from the lobes that are not undergoning thermoplasty at the first bronchoscopy, then both treated and untreated areas at the second bronchoscopy and treated areas only at the third bronchoscopy.

Computed Tomography, Inspiratory and expiratory scans will be obtained at visit 2 and 5. Expiratory scans allow quantitative analysis of air trapping and emphysema, while inspiratory scans allow the quantification of bronchial wall thickening.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Changes in immunopathological features following thermoplasty; Timepoint(s): Before thermoplasty, 3 weeks post thermoplasty and 6 weeks post thermoplasty

Secondary outcome measures
No secondary outcome measures

Overall study start date
04/03/2013

Completion date
29/01/2016

Eligibility

Key inclusion criteria
1. Written informed consent must be obtained before any assessment is performed
2. Males and females of any race who are over the age of 18 years at the time informed the consent is obtained
3. Physician diagnosis of asthma, as per Global Initiative for Asthma (GINA) guidelines and currently prescribed inhaled corticosteroid (ICS) or inhaled corticosteroid-long-acting beta agonist (ICS-LABA) therapy GINA step 3 to step 5 asthma therapies
4. Patients assigned by the clinical team to receive bronchial thermoplasty as part of their asthma treatment plan

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
UK Sample Size: 20

Key exclusion criteria
1. Patients who are considered unsuitable for inclusion by the assessing physician due to serious co-morbidities such as cancer, emphysema or significant bronchiectasis

2. Recent (within 4 weeks of visit 1) or current lower respiratory tract infection
3. A positive hepatitis B surface antigen or hepatitis C virus antibody, as determined by medical history and/or subjects verbal report
4. A positive human immunodeficiency virus test or is taking anti-retroviral medications, as determined by medical history and/or subjects verbal report
Additional exclusion criteria for patients who have agreed to take part in the MR Imaging part of the study
4.1. Patients with a contra-indication to MRI scanning: i.e. patients who are non MRI compatible (ferro-magnetic metallic implants, pacemakers) as per the MRI questionnaire
4.2. Patients with potential adverse reactions to Gd-DTPA intravascular MRI contrast agent

Date of first enrolment
04/03/2013

Date of final enrolment
29/01/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Glenfield Hospital
Leicester
United Kingdom
LE3 9QP

Sponsor information

Organisation
University of Leicester (UK)

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Sponsor type
University/education

Website
http://www.le.ac.uk/

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Charity

Funder Name
Airway Disease Predicting Outcomes through Patient Specific Computational Modelling (AirPROM) (an EU consortium consisting of academics and pharmaceutical partners)

Funder Name
Wellcome Trust Grant Codes: 082265/Z/07/A

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
HRA research summary			28/06/2023	No	No