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Early detection of chronic obstructive pulmonary disease (COPD) using a novel technique for assessing lung unevenness (inhomogeneity)

Submission date
03/11/2023

Recruitment status
Recruiting

Registration date
17/01/2024

Overall study status
Ongoing

Last Edited
18/01/2024

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
Chronic obstructive pulmonary disease (COPD) affects 400 million people and is the 3rd leading cause of death worldwide. Patients suffer symptoms (cough/wheeze/breathlessness) that limit their quality of life. Approximately 70% of cases are caused by cigarette smoking. One reason for the poor outcomes is late diagnosis. The current tool used to diagnose COPD is a breathing test called spirometry. Results on spirometry only become abnormal when significant damage has already occurred and it cannot detect early or subtle changes in the small airways of the lung, which is where COPD starts.

Our research group at the University of Oxford has developed a new type of analyser that very accurately measures the flow of different gases breathed into and out of the lungs. We have also developed a mathematical approach to analysing these data that identifies unevenness (heterogeneity) in the lung and provides multiple new sensitive measures of lung function. In preliminary studies on small groups of people, we found that one of these measurements of heterogeneity show great promise as a sensitive marker of early problems in the small airways.

In this project, we want to understand more about the new measurements in people at increased risk for developing COPD, for example chronic smokers, and investigate whether our new test can be useful in detecting changes in lung function, earlier than is currently possible by the available breathing tests. To achieve this we will compare measurements of lung heterogeneity using our new test obtained in smokers (who have normal spirometry) and no diagnosis of airways disease with those obtained in non-smokers of the same age. Another aim is to compare our measures of lung heterogeneity with other lung function tests and to investigate their association with other disease markers (for example symptoms and airway inflammation).

Who can participate?
People between the ages of 25-60 years without a current diagnosis of respiratory disease can participate in the study. Both chronic smokers and non-smokers can participate.

What does the study involve?
The study involves a series of assessments of lung function, and a blood test. The lung heterogeneity measures are made using a 12-minute test during which the patient breathes normally through a mouthpiece, with their nose occluded by a nose clip. Each patient will breathe normal air for the first 7 min and then 100% oxygen for the final 5 min.

The other breathing tests that participants will be asked to perform are standard lung function tests such as forced spirometry, oscillometry and exhaled nitric oxide measurement. Participants will complete two questionnaires to allow us to assess their day-to-day lung health.

What are the possible benefits and risks of participating?
We do not expect participants in this research to benefit directly from their participation, but we hope that the results of the study will benefit patients in the future. We do not expect the gas mixtures breathed during this study to have any adverse health effects, and most patients studied with this technique so far have found the tests relatively easy to perform.

Where is the study run from?
University of Oxford and Oxford University Hospitals (UK)

When is the study starting and how long is it expected to run for?
May 2017 to December 2028

Who is funding the study?
This study is funded by 'Asthma + Lung UK', a charity working to improve lung health in the UK via research and campaigning.

Who is the main contact?
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Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Protocol serial number
DPG23\35

Study information

Scientific Title
A novel lung function Test foR Early dETection of chronic Obstructive Pulmonary disease (COPD)

Acronym
TREETOP

Study objectives
We have developed a novel non-invasive method for measuring unevenness (heterogeneity) in gas-exchange across the lung. This provides multiple, new and sensitive physiological measures of lung function (heterogeneity indices). We hypothesise that these new lung heterogeneity measures will detect changes in lung function in chronic smokers, who are at risk of developing COPD, earlier than currently possible by the available diagnostic tools.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 17/05/2017, South Central Oxford A Research Ethics Committee (Bristol Research Ethics Committee Centre, Whitefriars, Level 3 Block B, Lewins Mead, Bristol, BS1 2NT, United Kingdom; +44 207 1048045; nrescommittee.southcentral-oxforda@nhs.net), ref: 17/SC/0172

Primary study design
Observational

Study design
Observational cross-sectional cohort study

Study type(s)
Diagnostic, Other, Screening

Health condition(s) or problem(s) studied
Chronic obstructive pulmonary disease

Interventions
This is an observational study in which indices of lung heterogeneity are measured in people who smoke but do not have diagnosed airways disease.

A “Lung Heterogeneity test” is undertaken which involves breathing on a mouthpiece with the nose occluded for up to 15 minutes. During the test the inspired gas varies from breathing

normal air (for 7-10 minutes) to breathing gas enriched with oxygen (up to 100% for a further 5 minutes). The composition of inspired and expired gas is analysed continuously using a novel in-airway gas analyser, and collected data are subsequently analysed using a mathematical model of gas exchange.

Participants are also asked about their smoking, medical and drug history, as well as their symptoms using respiratory symptom questionnaires (COPD Assessment test, St George's Respiratory Questionnaire).

Participants also undertake additional clinical diagnostic tests of respiratory function, e.g. spirometry testing, measurement of exhaled nitric oxide (FeNO) and impulse oscillometry, and blood tests (e.g. FBC and CRP).

All participants give written informed consent.

Intervention Type
Other

Primary outcome(s)
Lung heterogeneity indices: σlnCL (standard deviation of alveolar compliance distribution across lung volume), σVD (standard deviation of deadspace distribution across lung volume), VD (total anatomical deadspace), and VD/FRC (ratio of total deadspace to functional residual capacity) measured using the novel technique at the Research Visit in chronic current smokers (tobacco smokers of >= 10 pack-years) with non-obstructive spirometry vs non-smoker healthy controls

Key secondary outcome(s)
1. Effect of participant pack years of smoking measured using smoking history data within questionnaires obtained at the Research Visit on the lung heterogeneity parameters.
2. Other potential markers of disease in smokers, e.g. markers of inflammation in blood (eosinophil count, CRP), exhaled nitric oxide and symptoms scores measured at the Research Visit and their correlation with the novel lung heterogeneity indices.
3. Other lung function measures: FEV1 % predicted , FEV1/FVC, FEF25-75%, measured with spirometry, and R5-R20, measured with impulse oscillometry at the Research Visit and their correlation with the novel heterogeneity indices.

Completion date
31/12/2028

Eligibility

Key inclusion criteria
1. Age 25-60 years
2. Current smokers with >10 pack years smoking history (Not applicable for the control group who are non-smokers)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
25 Years

Upper age limit
60 Years

Sex
All

Key exclusion criteria
1. Current diagnosis of respiratory disease
2. Pregnancy
3. Significant cardiovascular disease e.g. heart failure

Date of first enrolment
22/01/2024

Date of final enrolment
31/12/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Oxford
Department of Physiology, Anatomy and Genetics
Sherrington Building,
Sherrington Road
Oxford
United Kingdom
OX1 3PT

Study participating centre
Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital
Headley Way
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Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
Asthma and Lung UK

Alternative Name(s)
asthmalunguk, Asthma + Lung UK, Asthma UK

Funding Body Type
Private sector organisation

Funding Body Subtype
Research institutes and centers

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available routinely, but requests for data sharing can be made to the study team.

IPD sharing plan summary
Available on request