ISRCTN12223638 https://doi.org/10.1186/ISRCTN12223638

Study of the way unevenness in lung function changes with treatment in airways disease

Submission date
11/04/2019

Recruitment status
Recruiting

Registration date
10/05/2019

Overall study status
Completed

Last Edited
02/10/2023

Condition category
Respiratory

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
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 (or heterogeneity) of lung function. We believe that these new measurements of heterogeneity may provide important information about lung function that will be useful for the management of patients.

As such, an important aim of the study is to evaluate whether the measures of lung heterogeneity change in response to standard therapy and how they change in comparison to standard clinical markers of airways disease. Another important aim is to determine whether measurements of inhomogeneity can predict response to treatment.

What does the study involve?
In this observational study, we will undertake measurements of lung heterogeneity in up to 100 adult patients with airways diseases at baseline and at various time points along their standard clinical care pathways. The measurements are made during a 15-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 8-10 min and then 100% oxygen for the final 5 min. These tests will be undertaken at baseline, and before/after therapeutic interventions including inhaled salbutamol, inhaled and/or oral corticosteroids, and/or 'biological' antibody-based therapy. Each patient will be studied for no longer than two years in total.

Who can participate?
Adult patients with airways diseases looked after at Oxford University Hospitals can participate in the study.

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 so far have found the tests relatively easy to perform.

Where is the study run from?
The study is running at the University of Oxford and Oxford University Hospitals.

When is the study starting and how long is it expected to run for?
February 2017 to September 2023

Who is funding the study?
The overarching project and the development of the study gas analyser is being funded by the NIHR Oxford Biomedical Research Centre. The particular study of inhomogeneity in lung function before and after therapy is being funded by GlaxoSmithKline UK Limited.

Who is the main contact?
Professor Peter Robbins
peter.robbins@dpag.ox.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Peter Robbins

ORCID ID
http://orcid.org/0000-0002-4975-0609

Contact details
Department of Physiology, Anatomy & Genetics,
Sherrington Building,
University of Oxford,
Oxford
Oxford
United Kingdom
OX1 3PT
01865 272500
peter.robbins@dpag.ox.ac.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
PID12157

Study information

Scientific Title
How are non-invasive measures of lung inhomogeneity affected during treatment of airways disease?

Study objectives
We have developed a method for measuring unevenness of lung function (lung heterogeneity) that provides very sensitive markers of lung physiology. We hypothesise that these markers of lung heterogeneity will change in response to treatment in patients with airways diseases, and may predict therapeutic response.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/05/2017, the South Central Oxford A Research Ethics Committee (Bristol Research Ethics Committee Centre, Whitefriars, Level 3 Block B, Lewins Mead, Bristol, BS1 2NT; 0207 1048045; nrescommittee.southcentral-oxforda@nhs.net), ref: 17/SC/0172.

Study design
Observational longitudinal study

Primary study design
Observational

Secondary study design
Longitudinal study

Study setting(s)
Hospital

Study type(s)
Other

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

Health condition(s) or problem(s) studied
Airways disease

Interventions
Current interventions as of 07/12/2022:
This is an observational study in which indices of lung heterogeneity are measured in patients with airways disease. Patients will be studied at baseline and on further occasions over a two-year period, according to their clinical pathway. Measurements will be made before and after clinical interventions (performed as part of clinical care) that might include salbutamol, inhaled or systemic corticosteroids and/or biological therapies.

A “Lung Heterogeneity test” is undertaken which involves breathing on a mouthpiece with the nose occluded for up to 20 minutes. During the test the inspired gas varies from breathing normal air to breathing gas enriched with oxygen (up to 100%), carbon dioxide (up to 8%) and/or trace amounts of acetylene, methane or carbon monoxide (<1%). Up to 4 tests can be performed on a single visit, and these may be performed before and after intervention (e.g. salbutamol inhalation). 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 also undertake additional clinical diagnostic tests of airways function, e.g. spirometry testing, measurement of exhaled nitric oxide (FeNO), induced sputum analysis, blood tests (FBC) and asthma control questionnaire scores (ACQ5).

Participants will be followed up to two years, with multiple visits (as described above) alongside their clinical pathway. All patients give written informed consent.

Previous interventions:
This is an observational study in which indices of lung heterogeneity are measured in patients with airways disease. Patients will be studied at baseline and on further occasions over a two year period, according to their clinical pathway. Measurements will be made before and after clinical interventions (performed as part of clinical care) that might include salbutamol, inhaled or systemic corticosteroids and/or biological therapies.

Participants give written consent for the study. Each study visit coincides with a clinical visit (along the patient’s clinical pathway).

A “Lung Heterogeneity test” is undertaken which involves breathing on a mouthpiece with the nose occluded for up to 20 minutes. During the test the inspired gas varies from breathing normal air to breathing gas enriched with oxygen (up to 100%), carbon dioxide (up to 8%) and/or trace amounts of acetylene, methane or carbon monoxide (<1%). Up to 4 tests can be performed on a single visit, and these may be performed before and after intervention (e.g. salbutamol inhalation). 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 also undertake additional clinical diagnostic tests of airways function, e.g. spirometry testing, measurement of exhaled nitric oxide (FeNO), induced sputum analysis, blood tests (FBC) and asthma control questionnaire scores (ACQ5).

Participants will be followed up to two years, with multiple visits (as described above) along their clinical pathway.

Intervention Type
Other

Primary outcome measure
Change in lung heterogeneity indices following treatment (pre-treatment baseline, and then 1 week, 5 weeks and/or 3 months post-treatment, depending on the treatment given). The indices are measured during the lung heterogeneity test: σCL:VA (standard deviation of the compliance: volume distribution), σVD:VA (standard deviation of the deadspace:volume distribution) and VDtot/VAtot (ratio of total deadspace to total alveolar volume).

Secondary outcome measures
1. Correlation between baseline lung heterogeneity indices and other clinical markers of disease e.g. FeNO, blood eosinophil count, sputum eosinophil count, FEV1, FEV1/FVC ratio and ACQ5 score.
2. Correlation between changes in lung heteroegeneity indices and changes in other clinical markers of disease measured using FeNO, blood eosinophil count, sputum eosinophil count, FEV1, FEV1/FVC ratio and ACQ5 score before and after treatment (1 week, 5 weeks and 3 months).

Overall study start date
02/02/2017

Completion date
15/09/2023

Eligibility

Key inclusion criteria
1. Aged over 18 years
2. Diagnosis of airways disease

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
150

Total final enrolment
91

Key exclusion criteria
1. Inability to tolerate mouthpiece/nose-clip
2. Pregnancy

Date of first enrolment
25/06/2018

Date of final enrolment
01/10/2026

Locations

Countries of recruitment
England

United Kingdom

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

Study participating centre
Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital
Headington
Oxford
United Kingdom
OX3 9DU

Sponsor information

Organisation
University of Oxford

Sponsor details
Clinical Trials & Research Governance
Joint Research Office
Boundary Brook House
Headington
Oxford
England
United Kingdom
OX3 7GB
+44 1865 289885
ctrg@admin.ox.ac.uk

Sponsor type
University/education

Website

N/A

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Funder Name
NIHR Oxford Biomedical Research Centre

Results and Publications

Publication and dissemination plan
We intend to present the results of this study at academic conferences, and to submit reports of the study outcome for peer-reviewed publication in scientific journals.

Intention to publish date
01/03/2024

Individual participant data (IPD) sharing plan
Current IPD sharing statement as of 07/12/2022:
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.

Previous IPD sharing statement:
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Interim results article	Preliminary results in a small subset of patients and healthy volunteers under same ethics approval	10/03/2020	07/12/2022	Yes	No
HRA research summary			28/06/2023	No	No
Basic results		30/09/2023	02/10/2023	No	No