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Functional magnetic resonance lung imaging using inhaled hyperpolarised 129Xenon

Submission date	Recruitment status	[ ] Prospectively registered
29/10/2015	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
17/11/2015	Completed	[X] Results
Last Edited	**Condition category**	[ ] Individual participant data
05/04/2023	Respiratory	

Plain English summary of protocol

Background and study aims
Chronic obstructive pulmonary disease (COPD) is a severe disease which affects the lungs. COPD is known as an obstructive lung disease, as over time the airways become narrowed or blocked. This disease cause shortness of breath which is worse when the sufferer exerts themselves. Currently, the main way to diagnose COPD is by using lung function tests (breathing tests to measure how much air they are breathing in and out), and CT scanning (a scan which uses X-rays and a computer to create detailed images of inside the body). However, lung function tests only show how well the lungs are working as a whole and CT scanning is risky as it exposes patients to potentially damaging radiation. MRI scanning is a type of scan which uses strong magnetic fields and radio waves to produce a detailed picture of the inside of the body. This type of procedure is less risky than a CT scan but is not able to produce as detailed a picture of the lungs. Xenon (129Xe) is an unreactive gas which is plentiful in the atmosphere. Studies have shown that when it is hyperpolarised (making it more negatively charged), it dissolves in the body's tissues and can show how well the blood and air are moving in the lungs on an MRI scan. The aim of this study is to find out if using hyperpolarised 129Xe and MRI scanning is a reliable way of testing lung function.

Who can participate?
Adults who are able to hold their breath for 10 seconds, and are either healthy or suffering from COPD.

What does the study involve?
Participants are divided into three groups: those suffering from COPD and healthy volunteers. At the start of the study, all participants attend a screening visit where they have their lungs and hearts tested to see if they are suitable to take part in the study. The patients who are able to take part then attend a second visit. At this visit, participants are asked to inhale (breathe in) 1 litre of non-polarised xenon (neutral). They then go into the MRI scanner and inhale 1 litre of hyperpolarised xenon while they are scanned. During this time, the amount of oxygen in the blood and their heart rate is measured. This process is repeated three times during the visit. Participants in the healthy volunteer group are invited to an optional follow-up session where

the scan is repeated (without the non-polarised xenon inhalation step). A selection of participants from each group is asked to attend several more visits in order to repeat the scan so the reliability of the results can be measured.

What are the possible benefits and risks of participating?
There is no direct benefit of taking part in the study. There are no notable risks of taking part, however there is a small risk that some participants may experience claustrophobia during MRI.

Where is the study run from?
Medical Imaging Unit, University of Nottingham Medical School (UK)

When is the study starting and how long is it expected to run for?
December 2013 to December 2021

Who is funding the study?
University of Nottingham (UK)

Who is the main contact?
Professor Ian Hall

Contact information

Type(s)
Scientific

Contact name
Prof Ian Hall

Contact details
Department of Respiratory Medicine (QMC)
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United Kingdom
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Additional identifiers

Clinical Trials Information System (CTIS)
2013-004336-30

Protocol serial number
13104

Study information

Scientific Title
Functional magnetic resonance lung imaging using inhaled hyperpolarised 129xenon in healthy volunteers and patients with chronic obstructive pulmonary disease

Study objectives
Current study hypothesis as of 22/12/2022:
This study aims to assess hyperpolarised 129Xe MRI as an imaging modality in healthy volunteers and patients with COPD and to compare the data to other markers of disease severity, namely lung function tests.

Previous study hypothesis:
This study aims to assess hyperpolarised 129Xe MRI as an imaging modality in patients with COPD and IPF and to compare the data to other markers of disease severity, namely lung function tests.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee East Midlands - Nottingham, 31/12/2013, ref: 13/EM/0401

Study design
Single-centre case-control study

Primary study design
Observational

Study type(s)
Diagnostic

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

Interventions
Current interventions as of 22/12/2022:
There are two groups of participants: healthy volunteers and patients with COPD.

Screening visit
At the screening visit, the trial procedure is explained to the potential participants, and informed consent is obtained. Thereafter, they will undergo a physical examination, lung function test, and ECG to ensure they are eligible to participate. If deemed eligible, they will be invited for the first study visit. The screening visit is expected to take up to 90 minutes.

First Study visit
At the first study visit, after monitoring vital signs, and MRI checklist, the participant will initially be given 1L non-polarised xenon to inhale in a clinical area to monitor for side effects. If side effect free, they will enter the MRI scanner, be asked to inhale up to 1L hyperpolarised xenon, and MR images are obtained. Oxygen saturation and heart rate will be monitored while the patient is in the scanner, and this will not last more than 20 minutes. After an observation period of 30 minutes, this process will be repeated up to 3 more times, with the participant monitored for at least 30 minutes after each scan. They will receive a phone call 24 hours afterwards to monitor their well-being. The study visit is expected to take up to 5-6 hours.

Second study visit
This is only applicable to healthy volunteers and is optional. The procedure is the same as the

first study visit but excludes the inhalation of non-polarised xenon. The study visit is expected to take up to 5-6 hours.

Follow-up study visit
After at least a week, where participants have consented to be contacted for follow-up studies, they may be contacted for follow-up scans to assess the repeatability of measurements. Participants will not be asked to attend more than 3 study visits in total. The study visit is expected to take up to 5-6 hours.

Previous interventions:
There are three groups of participants: healthy volunteers, patients with COPD and patients with IPF.

Screening visit
At the screening visit, the trial procedure is explained to the potential participants, and informed consent obtained. Thereafter, they will undergo physical examination, lung function test, and ECG to ensure they are eligible to participate. If deemed eligible, they will be invited for the first study visit. The screening visit is expected to take up to 90 minutes.

First Study visit
At the first study visit, after monitoring vital signs, and MRI check list, the participant will initlally be given 1L non-polarised xenon to inhale in a clinical area to monitor for side effects. If side effect free, they will enter the MRI scanner, asked to inhale up to 1L hyperpolarised xenon, and MR images are obtained. Oxygen saturations and heart rate will be monitored while the patient is in the scanner, and this wiil not last more than 20 minutes. After an observation period of 30 minutes, this process will be repeated up to 3 more times, with the participant monitored for at least 30 minutes after each scan. They will receive a phone call 24 hours afterwards to monitor wellbeing. The study visit is expected to take up to 5-6 hours.

Second study visit
This is only applicable to healthy volunteers, and is optional. The procedure is the same as the first study visit, but excludes the inhalation of non-polarised xenon. The study visit is expected to take up to 5-6 hours.

Follow up study visit
After at least a week, where participants have consented to being contacted for follow up studies, they may be contacted for follow up scans to assess repeatability of measurements. Participants will not be asked to attend more than 3 study visits in total. The study visit is expected to take up to 5-6 hours.

Intervention Type
Other

Primary outcome(s)
1. Pattern of spontaneously resolving ventilation defects measured using 129Xe MRI lung imaging completed over a 4-week period
2. Estimates of lung volumes measured using 129Xe MRI lung imaging completed over a 4-week period

Key secondary outcome(s))

1. Compare 129Xe MRI-obtained lung function parameters with matched clinical data e.g. (pulmonary function tests) over a 4-week period, allowing comparison with existing clinical diagnostic techniques and determining correlation with disease severity
2. Use the images obtained to set up standard sequencing protocols and define algorithms and inform power calculations for subsequent studies
3. Safety data measured using study records before and after 129Xe inhalation

Completion date
31/12/2021

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 22/12/2022:
General inclusion criteria:
1. Aged 18 years or over
2. Capacity to give informed consent
3. Normal blood pressure (systolic BP > 100 mmHg and diastolic BP > 70 mmHg)
4. Resting heart rate > 50 bpm
5. For women, negative urinary β-hCG at the screening and subsequent visits
6. Subject able to hold breath for 10 seconds
7. Subject able to fit into 129Xe chest coil used for MRI
8. Subject able to understand the requirements of the study and to cooperate with the study procedures

Healthy volunteer inclusion criteria:
No significant respiratory disease within the last year

COPD patient inclusion criteria:
1. Evidence of airflow obstruction (FEV/FVC <0.7) and FEV1 <80% predicted post bronchodilator
2. Minimum FVC 1.5L

Previous participant inclusion criteria:
General inclusion criteria:
1. Aged 18 years or over
2. Capacity to give informed consent
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Healthy volunteer inclusion criteria:
No significant respiratory disease within the last year

COPD patient inclusion criteria:
1. Evidence of airflow obstruction (FEV/FVC <0.7) and FEV1 <80% predicted post bronchodilator
2. Minimum FVC 1.5L

IPF patient inclusion criteria:
1. Diagnosis of IPF by high resolution CT scan
2. Full pulmonary function test performed within 12 months prior to imaging
3. Minimum FVC 1.5L

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
53

Key exclusion criteria
Healthy volunteer exclusion criteria:
1. Unsuitable for MRI scanning (e.g. have metal implants or pacemaker or contraindicated following questionnaire)
2. Acute respiratory illness within 30 days of MRI
3. Subject has received an IMP (not including hyperpolarized 129Xe) within 30 days of MRI and administration of 129Xe deemed inappropriate in context of other study
4. Subject deemed unlikely to comply with instructions during imaging
5. Do not meet the inclusion criteria above
6. Subject not deemed fit enough to tolerate procedure
7. Subject deemed unsuitable by clinical investigator for other reasons

COPD and IPD patient exclusion criteria:
1. Unsuitable for MRI scanning (e.g. have metal implants or pacemaker or contraindicated following questionnaire)
2. Acute respiratory illness within 30 days of MRI
3. Subject has received an IMP (not including hyperpolarized 129Xe) within 30 days of MRI and administration of 129Xe deemed inappropriate in context of other study
4. Subject deemed unlikely to comply with instructions during imaging
5. Do not meet the inclusion criteria above
6. Subject not deemed fit enough to tolerate procedure
7. Subject deemed unsuitable by clinical investigator for other reasons

Date of first enrolment
01/03/2015

Date of final enrolment
31/12/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Nottingham
University Park
Nottingham
United Kingdom
NG7 2RD

Sponsor information

Organisation
University of Nottingham

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
University/education

Funder Name
University of Nottingham

Alternative Name(s)
The University of Nottingham

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Not know at time of registration.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			05/04/2023	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes