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Investigating the use of a novel imaging technique to identify early fibrotic lung disease

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Registration date 27/08/2024	**Overall study status** Ongoing	
Last Edited 27/08/2024	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims:
Investigating the use of a novel imaging technique to identify early fibrotic lung disease: The aim of this study is to determine which patients with mild lung abnormalities will go onto develop progressive lung scarring. By detecting lung scarring early on, treatment can be started promptly to reduce the development of symptoms and improve prognosis.

Diseases affecting the tissue of the lungs (called interstitial lung diseases or ILDs) can result in lung scarring or fibrosis. In some people, this scarring worsens over time and results in breathlessness, exercise limitation and reduced life expectancy. Frequently, these diseases are detected late when scarring is advanced. Treatment currently only slows down the disease but does not stop or reverse it. Therefore, it is important to try and identify the disease early and start treatment in a timely manner to reduce or delay the development of more severe disease.

Not uncommonly, early interstitial lung abnormalities (termed ILAs) are picked up incidentally on CT scans undertaken for other reasons. Because these abnormalities are mild, they do not generally cause symptoms and in some people, do not worsen over time or cause problems. In others, however, the ILAs will progress into an ILD. Currently, when the ILA is first seen on CT we are unable to determine who will develop disease. We therefore need to follow people up carefully over several years, which places a burden on both healthcare services and the patient, and can also result in significant anxiety for those concerned. Furthermore, there is no clear guidance on how often or for how long we should follow up these early lung abnormalities.

Hyperpolarised-Xenon MRI (HPX-MRI) is a novel imaging technique that can identify lung abnormalities that are not visible on chest x-ray or CT. HPX-MRI does not involve radiation and is safe and well tolerated. We wish to see whether this investigation, plus blood tests looking at specific proteins in the blood, can help us to tell the difference between minor lung abnormalities that will lead to disease from those that don’t. These tests may help us to better inform patients from the outset what their risk of developing disease is, and will also influence how we follow patients up. Most importantly, it will enable us to consider treatment early if there is evidence that the lung abnormalities are developing into disease.

In this project, we will undertake a HPX-MRI and blood tests soon after the ILAs are first picked up on a CT scan. We will then follow these up at regular clinic appointments for 3.5 - 4 years to see how many people have gone onto develop an ILD. We will do this by repeating CT scans of the lungs and breathing tests at different time points. We will then compare the HPX-MRI and blood markers to see whether abnormalities found at the start could be used to help predict those who went on to develop disease. This project will also help in developing a clinical pathway to ensure that monitoring and follow-up of patients with ILAs is more standardised.

Who can participate:
We require 50 study participants who have an ILA, between the ages of 50 and 85. We also require 10 healthy volunteers, who do not have any lung conditions, between the age of 50 and 85

What does the study involve for the participants?
All interventions are optional for the participant.
Xenon MRI: Participants will be asked to inhale hyperpolarised xenon gas (1L of gas per bag) to assess lung gas structure and function on 1 or 2 occasions.
Low dose research CT: one undertaken alongside baseline HPX-MRI and up to 3 repeat CT scans during the duration of the study if symptoms and signs have progressed
Blood sampling: 50ml blood sampling on up to 3 occasions over 3.5 - 4 years
Lung function tests

In addition to these, patients will also be asked questions about their health and symptom questionnaires involving:
Symptoms
MRCD score, KBILD questionnaire, 6MWD
Comorbidities
Risk factors, including drugs
Presence/absence of crackles
Presence/absence of clubbing
Clinical frailty score if >65

What are the possible benefits or risks of participating?
There are no immediate benefits to the participants, either personally or financially. The study might, however, improve our follow up and management of ILA in the future.
The risks are minimal. We are using a low dose CT scan, where the radiation dose is roughly the same as about 2 years of natural background radiation. Participants with ILA will have up to 4 of these scans over a 4 year period.
An MRI scan contains no radiation, and participants will be risk assessed prior to the scan to make sure it is safe for them. Normally, MRI scanning for research purposes would not be performed without further investigation if you have a heart pacemaker, mechanical heart valve, mechanical implant such as an aneurysm clip, hip replacement, or if you carry other pieces of metal that have accidentally entered your body. If a patient suffers with claustrophobia, we will not perform the MRI. The hyperpolarised xenon gas, when given in the small amounts (1 litre), is safe to breathe. It can lower the pitch of the participant’s voice for less than a minute. It can also make you feel giddy or light-headed for that duration, like breathing ‘laughing gas’. However, it does not have any lasting affects on the body after a few minutes. It can occasionally make someone feel transiently drowsy, nauseous or cause a headache.

Where is the study run from?
Oxford University Hospitals NHS Trust (UK)

When is the study starting and how long is it expected to run for?
March 2024 to June 2029

Who is funding the study?
Boehringer Ingelheim (UK)

Who is the main contact?
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Contact information

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
331994

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
17229, IRAS 331994

Study information

Scientific Title
Risk stratification of interstitial lung abnormalities using hyperpolarised xenon MRI and blood biomarkers

Acronym
FLIP

Study objectives
Hyperpolarised Xenon MRI will help identify progression of Interstitial Lung Abnormalities (ILA) into Interstitial Lung Disease (ILD) earlier than standard structural CT imaging by detecting functional abnormalities.
Interstitial Lung Abnormalities (ILAs) are incidental radiological abnormalities identified on chest Computed Tomography (CT) undertaken for other indications. Although these changes are considered too mild to cause symptoms, up to half will progress to interstitial lung disease (ILD). ILD commonly causes breathlessness, impaired exercise capacity and reduced life expectancy. The aim of this study is to investigate the use of hyper-polarised xenon MRI and blood biomarkers to determine whether it is possible to differentiate ILAs that represent early ILD from clinically insignificant lung abnormalities. Early detection of ILD will facilitate more timely initiation of treatment and potentially impact on disease trajectory and prognosis.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 14/03/2024, East of England - Cambridge East Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8000; CambridgeEast.REC@hra.nhs.uk), ref: 24/EE/0034

Study design
Pilot feasibility study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
The progression of interstitial lung abnormalities into interstitial lung disease

Interventions
We aim to recruit 50 study participants, between the ages of 50 and 85, with pre-existing ILA diagnosed within the last 2 years, and 10 healthy volunteers. Study participants will follow routine clinical pathway for monitoring of ILA's including a baseline CT chest. In addition to routine care, as part of the study, they will have a research Hyperpolarised Xenon MRI (HPX-MRI) after 3 months of consent and another at 24 months post consent. If needed, a repeat CT will also be performed if patient has progressive symptoms or signs of ILD. Control participants will have a baseline CT chest and one HPX-MRI at 3 months post consent. All subjects will also have blood biomarkers sampled at 3 months, 24 months, and 36-42 months post consent for routine bloods and biomarkers. At the baseline visit, 12 months, 24 months, and 36-42 months, study participants will be examined by a clinical research fellow, have their MRCD, KBILD, and frailty scored, have a 6 minute walk test and lung function tests.

Intervention Type
Other

Primary outcome(s)
To determine whether HPX-MRI abnormalities are detectable in ILAs outwith areas of abnormality visible on CT and to determine whether the presence of functional abnormalities detectable at baseline HPX-MRI correlate with radiological progression of ILAs and/or lung function decline a 1 litre breath hold low dose CT at baseline will be compared with a Hyperpolarised xenon MRI at baseline, and 4 years. Additional low dose CT scans will be taken if the patient shows evidence of progression via symptoms or lung function decline.

Key secondary outcome(s))
Measurement of selected serum biomarkers in ILAs to see if baseline levels correlate with risk of developing ILD, by analysing blood biomarkers at baseline, 2 years, and 3.5-4 years

Completion date
01/06/2029

Eligibility

Key inclusion criteria
1. Participant is willing and able to give informed consent for participation in the study.
2. Male or Female, aged over 18 and under 85 years of age
3. Investigators are of the opinion that the participant is able and willing to comply with the study requirements
3.1. Lung function tests that are normal or near normal – FVC and TLCO >70% predicted for age and gender
3.2. CT imaging fulfils criteria for ILA –
3.2.1. Incidental identification of non-dependent abnormalities on Chest CT, including ground glass or reticular abnormalities, lung distortion, traction bronchiectasis and honeycombing
3.2.2. Occupying up to 10% of the lung as agreed independently by two consultant thoracic radiologists

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
50 years

Upper age limit
85 years

Sex
All

Key exclusion criteria
1. Unable to provide informed consent
2. Contraindication to MRI e.g. shrapnel injury, heavily tattooed, severe claustrophobia
3. Any significant disease or disorder which, in the opinion of the investigator, might influence the interpretation of the clinical data e.g. Significant co-pathology (e.g. emphysema, poorly controlled asthma, heart failure, pulmonary thromboembolic disease, Covid-19 condition, pneumotoxic agents resulting in lung damage)
4. Clinical frailty score of 6 or above
5. Female participant who is pregnant, lactating or planning pregnancy.

Date of first enrolment
01/06/2024

Date of final enrolment
01/06/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Oxford University Hospitals
John Radcliffe Hospital
Headley Way
Headington
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Sponsor information

Organisation
Oxford University Hospitals NHS Trust

ROR
https://ror.org/03h2bh287

Funder(s)

Funder type
Industry

Funder Name
Boehringer Ingelheim

Alternative Name(s)
Boehringer Ingelheim Pharmaceuticals, Inc., Boehringer Ingelheim International GmbH, BI, BIPI

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

Stored on REDcap, the data will only be accessible and reviewed by the research team within Oxford University Hospitals. Consent has been sought from participants to be able to share anonymised data with colleagues outside of the organisation only if their analysis is required.

IPD sharing plan summary

Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes