ISRCTN15235699 https://doi.org/10.1186/ISRCTN15235699

Imaging technologies for the detection of breathing infection in patients on breathing machines in the intensive care unit

Submission date
06/08/2025

Recruitment status
Recruiting

Registration date
21/08/2025

Overall study status
Ongoing

Last Edited
19/08/2025

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
This study will improve the way lungs are currently sampled to understand what is happening when patients on ventilators have suspected or confirmed lung infection. Often, changes seen on a patient's X-ray are not clear indications of whether a patient has an infection or what type of infection they have. Knowing this in the future will help doctors give the right treatment at the right time. During a routine bronchoscopy procedure, which is a procedure to examine the lungs in more detail, the research team will pass a very fine microscope into regions of the lungs and deliver small volumes of liquid imaging agents (called Smartprobes), which 'light up' when they come into contact with specific bacteria or immune cells. The study results will be compared with methods currently used by doctors that take longer to provide results. In the future, it is hoped that this technology can be used by health care organisations as a new method to diagnose and manage suspected lung infections.

Who can participate?
Anyone over the age of 18 years, already on a ventilator as part of their treatment, who has received abnormal results from a chest X-Ray due to suspected or confirmed infection in the lung. The patient also needs to be deemed healthy enough to undergo a bronchoscopy and able to consent to taking part or have someone consent on their behalf.

What does the study involve?:
After consent is taken, the research team will confirm the patient is eligible by looking at their medical records, and, if the patient is a woman of childbearing potential, a urine sample. During a bronchoscopy, a thin tube with a camera at the end, called a bronchoscope, is passed through the ventilator tube and moved into the airways. It helps to investigate, diagnose and treat certain conditions affecting the lungs. The bronchoscopy will be scheduled for as soon as possible after the screening visit and may be the same day. During the bronchoscopy, a small camera (imaging fibre) will be guided down the bronchoscope to image areas of the lungs. This imaging fibre will also be able to deliver small volumes of liquid SmartProbes to identify areas of infection and to sample areas deep in the lungs. These images will be captured on the imaging system. The clinical team may also need to obtain samples as part of clinical care (e.g. lung fluid

sample - BAL). Where possible, the research team will request any surplus quantities of these clinical samples. The research team would also like to take an additional blood sample (up to approximately 10 teaspoons), a very small amount of lung fluid from the deeper parts of your lung (less than 5 mL) and a swab from the patient's breathing tube before the procedure. A standard bronchoscopy procedure takes approximately 25-30 minutes to perform. The research procedure may lengthen the procedure by up to 25 minutes. Participants' medical notes may be reviewed, and routinely collected information relevant to the infection is documented up to 3 days before the bronchoscopy procedure.

What are the possible benefits and risks of participating?:
While there will be no direct benefit to participants, this study is testing new imaging technologies to see if they can help clinicians identify infection and inflammation in the lungs for the future benefit of patients. The information gained from this study will help us improve our understanding and treatment of lung infection and inform future development of the technologies and patient care.

The imaging system (KronoScan) and two of the three SmartProbes (BAC2 and NAP) have been used in a clinical study before, and no safety concerns have been seen to date. The imaging Fibre (EoT) and BAC3 (SmartProbe) have not previously been used in the clinical setting but have undergone extensive pre-clinical (lab) testing.

No adverse reactions to the SmartProbes that may be used in this study are anticipated - only a very small amount of the SmartProbe will be used (also known as a microdose); extensive testing has been conducted to demonstrate their safety for use in humans.

The risks of bronchoscopy are very low, with complications occurring in less than 1-2% of procedures. The main risk is air becoming trapped next to the lung (a pneumothorax), which may require a chest drain. This is extremely rare and will be managed by the clinical care team if it arises. In addition, to make sure that the bronchoscopy is safe, extra oxygen is given during the procedure. Sometimes the extra oxygen is required for 1-2 hours after the bronchoscopy. In a small number of patients, the extra oxygen is required for longer than that.

Participants will also have one additional chest X-Ray (CXR) than those who do not take part in the study. This procedure uses ionising radiation to form images of the body. Ionising radiation can cause cell damage that may, after many years, turn cancerous. Everyone is at risk of developing cancer during their lifetime. The normal risk is that this will happen to about 50% of people at some point in their lives. Taking part in this study will increase the chances of this happening to participants by 0.00001%.

Where is the study run from?:
This clinical investigation is a single-site study that will run from the Royal Infirmary of Edinburgh, UK

When is the study starting and how long is it expected to run for?:
April 2022 to December 2027

Who is funding the study?:
The Wellcome Trust, UK

Who is the main contact?:
Chief Investigator Prof Kev Dhaliwal at the University of Edinburgh, kev.dhaliwal@ed.ac.uk

Contact information

Type(s)
Principal investigator

Contact name
Dr Thomas Craven

ORCID ID
https://orcid.org/0000-0003-4984-5322

Contact details
Department of Critical Care
Royal Infirmary of Edinburgh
51 Little France Crescent
Edinburgh
United Kingdom
EH16 4SA
+44 (0)131 242 1186
thomas.craven@ed.ac.uk

Type(s)
Scientific

Contact name
Prof Kevin Dhaliwal

ORCID ID
https://orcid.org/0000-0002-3925-3174

Contact details
College of Medicine and Veterinary Medicine
Centre for Inflammation Research
Institute for Regeneration & Repair
University of Edinburgh
4-5 Little France Drive
Edinburgh BioQuarter
Edinburgh
United Kingdom
EH16 4UU
+44 (0)131 651 8294
kev.dhaliwal@ed.ac.uk

Type(s)
Public

Contact name
Mrs Jean Antonelli

Contact details

College of Medicine and Veterinary Medicine
Centre for Inflammation Research
Institute for Regeneration & Repair
University of Edinburgh
4-5 Little France Drive
Edinburgh BioQuarter
Edinburgh
United Kingdom
EH16 4UU
+44 (0)131 651 8294
jean.antonelli@ed.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
357508

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Sponsor Ref: AC24247, Funder Ref: 206035/Z/17/Z

Study information

Scientific Title
Optical Technologies for the Detection of Respiratory Infection in the Intensive Care Unit

Acronym
BAC2BAC (Study 1)

Study objectives
Determine the performance and safety of fibre-based endomicroscopy (KronoScan and Eyes on Target [EoT]) and intrapulmonary delivery of BACCOMBI for the characterisation of pulmonary infiltrates in mechanically ventilated participants.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 18/07/2025, Scotland A Research Ethics Committee (2nd Floor, Waverley Gate, 2-4 Waterloo Place, Edinburgh, EH1 3EG, United Kingdom; +44 (0)7814609032; Manx. Neill@nhslothian.scot.nhs.uk), ref: 25/SS/0051

Study design
Single-centre interventional cross-sectional cohort study

Primary study design
Interventional

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Characterisation of pulmonary infiltrates in medically ventilated participants in the Intensive Care Unit

Interventions
As this is a non-randomised, early-stage medical device investigation, a control/placebo group has not been included.

Non-clinical interventions:
a) Informed consent, taken once per participant by a member of the research team, taking an average of 30 minutes.
b) Review of clinical notes, taken eight times per participant by a qualified member of the research team, taking an average of 10 minutes.

Clinical Interventions:
a) Medical History: taken once per participant by a qualified member of the research team, taking an average of 10 minutes.
b) Pregnancy Test: taken once per participant if they are of childbearing potential, by a qualified member of the team, taking an average of 5 minutes.
c) Chest X-Ray: taken once per participant in the ICU by a qualified member of the research team, taking an average of 10 minutes.
d) Bronchoscopy with lavage - use of imaging technologies, and delivery of SmartProbes: taken once per participant by a medically qualified member of the research team, taking a maximum of 45 minutes.
e) Blood sampling: taken once per participant by a qualified member of the research team at bedside, taking an average of 5 minutes.
f) Nasopharyngeal sampling: taken once per participant by a qualified member of the research team by bedside, taking an average of 5 minutes.
g) Clinical observations: taken both pre- and post-bronchoscopy, eight times per participant by a qualified member of the research team, taking an average of 5 minutes.
h) Endotracheal aspirate sampling (from breathing tube): taken once per participant by a qualified member of the research team at bedside, taking an average of 5 minutes.
i) Check for Adverse Events: events that occur from the time of consent up until discharge from the study will be recorded at baseline, pre-bronch, during bronch, 15-30 mins post-bronch, 2 hours post-bronch, and 2-24 hours post-bronch
j) Check for any Device Deficiencies: assessed at time of bronchoscopy procedure
k) Constructed Reference Standard: data collected and assessed at all timepoints throughout participant's involvement in the investigation. Adjudication of data will occur after the participant has completed their involvement in the investigation.
l) Discharge/outcome data: taken 2 days post-bronchoscopy once per patient by a qualified member of the team using patient notes, taking an average of 10 minutes.

The imaging technology involved in the bronchoscopy intervention is two medical devices and three Clinical Investigation Agents (CIAs):
MEDICAL DEVICES:

- KronoScan - an imaging unit that utilises optical scanning for both florescence intensity and florescence lifetime imaging. This is a non-invasive medical device as it does not come in direct contact with the participant.
- Eyes on Target (EoT) - an imaging fibre that will be inserted down a compatible commercial bronchoscope and used to image and sample the internal microstructure of the lung. This is an invasive medical device.

CIAs/'SmartProbes':
- BAC2 - a modified cyclic antimicrobial peptide and specifically labels Gram-negative bacteria.
- BAC3 - a Gram-positive bacterial imaging agent based on the clinically utilized glycopeptide antibiotic vancomycin.
- NAP - designed to amplify fluorescent emission and ‘tag’ neutrophils in response processes in the pathway of neutrophil activation.
These three SmartProbes are collectively termed BACCOMBI.
BACCOMBI are not considered Investigational Medicinal Products (IMPs) for reasons detailed in the clinical protocol.

The devices and CIAs will be used during a clinically indicated or research-only bronchoscopy. The research part of the bronchoscopy procedure will be less than 25 minutes in duration. During the research procedure, KronoScan will be positioned at the bedside and connected to EoT using the proximal EoT SMA connector. EoT will be inserted down the working channel of the clinical bronchoscope into the segmental airways and extended through serial transbronchial passes into the alveolar sacs. Microdoses (<100 µg) of the sensitive and highly specific BACCOMBI will be delivered through the EoT delivery port. EoT is also capable of extracting small volumes of liquid instilled in the alveolar space. The distal tip of EoT may extend for up to 10 cm from the distal end of the clinical bronchoscope/navigation catheter to permit imaging, delivery of BACCOMBI, and sampling of fluid from the lung. The distal 10 cm of EoT will be the only part of the investigational devices in direct contact with the participant.

Intervention Type
Mixed

Primary outcome(s)
1. Safety of devices will be measured/assessed by:
1.1. The number of adverse events that occur assessed at all timepoints from baseline up to and including 24-48 hours post bronchoscopy
1.2. Vital signs (haemodynamic observations) assessed at baseline, pre-bronchoscopy, 2-24 hours post-bronchoscopy, and 24-48 hours post-bronchoscopy
1.3. Oxygenation levels assessed during the bronchoscopy procedure
1.4. Chest X-ray (CXR) - any CXR or CT scan done clinically up to 48 hours before the bronchoscopy, and then taken again as a research-only procedure 2 hours (±1 hour) post bronchoscopy
2. Device performance will be measured/assessed by:
2.1. Demonstrating delivery of BACCOMBI into the alveolar space assessed by live imaging viewed at the time of the bronchoscopy (if live imaging available) and/or from imaging data recorded during bronchoscopy that is later reviewed and analysed
2.2. Demonstrating the capability of Eyes on Target (EoT) to collect sufficient distal Alveolar Lavage (AL) samples for PCR or other analyses (≤100 µl), which is assessed by the volumes of samples collected and recorded during the bronchoscopy procedure

2.3. Demonstrating ability to visualise BACCOMBI in the alveolar space assessed by visualising the delivery of BACCOMBI at the time of the bronchoscopy (if live imaging available) and/or from imaging data recorded during bronchoscopy that is later reviewed and analysed

Key secondary outcome(s))
1. Quantification and characterisation of key inflammatory markers and inflammatory responses measured in BAL, AL, blood and ETA. This will be assessed after the samples are collected in either or both the NHS lab or the IRR research team labs
2. The range of micro-organisms characterised using nasopharyngeal swabs, BAL, ETA and/or AL assessed after samples are collected by the NHS lab
3. Antimicrobial susceptibility testing (AST) measured using up to two validated, quantitative molecular platforms in BAL assessed after samples are collected by NHS labs.
4. The performance of BACCOMBI (sensitivity, specificity, positive and negative predictive values) compared to three defined reference standards:
4.1. Constructed reference standard adjudicated by an expert clinical consensus panel for each participant using available clinical information. The adjudication will use all relevant data from microbiology, radiology, and clinical results collected at all timepoints of the study. The adjudication will occur after the participant's involvement has ended.
4.2. Semi-quantitative BAL culture (>104 colony-forming units/ml (cfu/ml) or equivalent). This will be assessed after the samples are collected by NHS labs.
4.3. Clinical Pulmonary Infection Score (CPIS) assessed at baseline.

Completion date
31/12/2027

Eligibility

Key inclusion criteria
1. Aged ≥18 years
2. Informed consent provided by the participant or by a personal legal representative
3. Participant is receiving invasive ventilation (mechanically ventilated)
4. Participant has an abnormal CXR with suspected pulmonary infection
5. Deemed suitable for bronchoscopy and study procedures by the attending consultant
6. Readily accessible target areas with bronchoscopy and fibre-based endoscopy
7. Participant meets the criteria as set out in the co-enrolment section of the protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Participant has a history of anaphylaxis and/or allergy to study SmartProbes (e.g. fluorescein)
2. Participant has a significant risk of bleeding (including any of the following: platelets at ≤50 x 109/L, therapeutic anticoagulation, APPTR >1.5, or INR >1.5)
3. Participant is a woman of childbearing potential and is pregnant and/or breastfeeding

Date of first enrolment
01/09/2025

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Royal Infirmary of Edinburgh at Little France
51 Little France Crescent
Old Dalkeith Road
Edinburgh
Lothian
United Kingdom
EH16 4SA

Sponsor information

Organisation
The University of Edinburgh & Lothian Health Board ACCORD

Funder(s)

Funder type
Research council

Funder Name
Wellcome Trust

Alternative Name(s)

Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1	27/05/2025	19/08/2025	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes