Clinical Investigation Plan:

DynaSSaur: Dynamic Chest X-ray with Simultaneous Spirometry

Principal investigator: David Green

Sponsor: Liverpool Heart and Chest Hospital

IRAS reference number: 322890

IRSCTN reference number: pending

Sponsor number: NA

Protocol version number: 4.1

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Signature page

The undersigned confirm that the following protocol has been agreed and accepted and that the Principal Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the Health Research Authority (HRA) and Ionising Radiation (Medical Exposure) Regulations 2017 (IR(ME)R) regulations, the Ionising Radiation Regulations 1999 (IRR99), any subsequent amendments of the study regulations, GCP guidelines, and other regulatory requirements as amended. I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation. I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay, that an honest, accurate and transparent account of the study will be given, and that any discrepancies from the study as planned in this protocol will be explained.

Principal investigator

Signature 

Date 30/06/2023

On behalf of the sponsor

Signature ……

Date ……

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Summary of Protocol versions

V1 30/01/2023- Original protocol version

V2 30/03/2023- Updated to reflect feedback from R&I committee meeting

V3 30/06/2023- Updated to reflect patient group information

V4 11/09/2023- Updated to reflect research and ethics committee conditions

V4.1 20/09/2023- Updated to reflect research and ethics committee conditions with tracked changes

List of Abbreviations

ARTP	Association for Respiratory Technology and Physiology
CF	Cystic fibrosis
COPD	Chronic obstructive pulmonary disease
CT	Computed Tomography
CXR	Chest x-ray
DAP	Dose area product
DCR	Dynamic chest x-ray
EED	Estimated effective dose
EPR	Electronic Patient Records
ERS	European Respiratory Society
ESD	Entrance surface dose (sometimes expressed as Entrance Skin Dose)
FEV1	Forced expiratory volume in 1 second
FDA	Food and Drug Administration
FPD	Flat-panel detector
FRC	Functional residual capacity
FSD	Focus-to-skin distance
FVCEx	Forced vital capacity
GCP	Good Clinical Practice
Gy	Gray
HRA	Health Research Authority
IR(ME)R	Ionising Radiation (Medical Exposure) Regulations
IRAS	Integrated Research Application System
IRS	Integrated Radiological Services, Ltd.
LHCH	Liverpool Heart and Chest Hospital
mA	Milliamperes
MHRA	Medicine and Healthcare products Regulatory Agency

mSv	Millisievert
NHS	National Health Service
NSR	Non-significant risk
PA	Posterior-anterior
PEF	Peak expiratory flow
RCCP	Registration Council for Clinical Physiologists
RV	Residual volume
SID	Source Image Distance
SR	Significant risk

Overview and Rationale

Dynamic Chest x-ray:

Dynamic Chest x-ray (DCR) is a new imaging technique that allows us to visualise the thorax and diaphragm in motion throughout the respiratory cycle by recording a series of x-ray images over a 10-20 second interval.

Radiation doses are lower than compared to those used in fluoroscopic or computer tomography (CT) imaging and therefore more comparable to simple chest x-ray (CXR).

Patient factors associated with respiratory disease may mean dynamic chest x-ray is better tolerated than conventional pulmonary function techniques such as spirometry and is also quick to perform.

The temporal component of the imaging opens up possibilities for clinical utilisation beyond imaging techniques that we already have available; for example, the direct visualisation of the chest and lung field in motion may provide clinically relevant information.

Computer analysis and image processing software available can facilitate the acquisition of quantitate data from the dynamic x-ray images. This information includes evaluation of Diaphragmatic motion; it is possible to measure diaphragmatic motion in terms of speed and distance throughout the respiratory cycle. Furthermore, analysis of DCR images by computer software one can automatically detect lung field area (projected lung area). The size of this projected lung area can be tracked over time through the entire series of images.

Spirometry:

The assessment of pulmonary function is essential for diagnosis and ongoing monitoring of most respiratory conditions. Spirometry – full inhalation and exhalation provides us with a forced expiratory volume of air in 1 second (FEV1) and a forced vital capacity (FVC) value as well as information in the form of flow volume loop and volume time graphs. Spirometry has a fundamental role in diagnosis and monitoring respiratory conditions such as asthma, chronic obstructive pulmonary disease (COPD), Cystic Fibrosis (CF) and pulmonary fibrosis. spirometry is the gold standard yet not all people can perform spirometry. DCR has the potential to measure dynamic movements of the respiratory fields, providing quantitate assessment of some aspects of lung function.

Cystic Fibrosis

CF is an autosomal recessive multisystem disorder that arises in a defect in in the cystic fibrosis transmembrane conductance regulator protein (CFTR). Dysregulation of ion transport by the defective CFTR protein leads to build up of thick secretion and pro inflammatory response. These thick secretions provide a favourable environment for chronic microbial colonisation by pathogens

such as *Pseudmonoas aeruginosa* which manifest as drive chronic infection, inflammation, acute infective exacerbations and progressive decline in lung function over time.

Cf is managed through a multi-disciplinary team (MDT) approach that requires careful monitoring of patients and the clinically relevant markers of their condition. The most prognostically important measurement of lung function is FEV1.

Cystic fibrosis Transmembrane (CFTR) modulators are a relatively new development in management of people with cystic fibrosis (pwCF) and represent a paradigm shift; this therapy directly affects the malfunctioning protein responsible for CF as opposed to conventional management options which seek to treat the consequences of the condition. This in combination with the current model of CF care is resulting in improved life expectancy and quality of life for many pwCF.

An important part of preserving pwCF's health is a once yearly review process called annual review; this a nationally recognised process although there may be some regional variation in practice. Annual review is a detailed assessment of every aspect of the patient's condition including a face-to-face review. At Liverpool Heart and Chest Hospital (LHCH) routine clinical care currently includes a dynamic chest x-ray and spirometry as part of this process

Previous Work with DCR in relation to pulmonary Function

Prior work has established that some DCR metrics correlate with some measures of lung function. For example, projected lung area has been demonstrated to correlate with total lung capacity. Furthermore, diaphragm motion has been shown to correlate with vital capacity and FEV1 in non – CF healthy volunteers.

Further work conducted in our large adult CF centre at LHCH has demonstrated significant improvement in changes in diaphragm movement and change in projected lung area in those treated for exacerbations of cystic fibrosis. In a smaller study here at LHCH in a CF cohort DCR metrics have also been shown to correlate with measures of lung volume. This work also demonstrated that the DCR procedure was well tolerated by the CF population and the procedure acquisition time proportional to a standard posteroanterior (PA) x-ray.

DCR as an assessment of pulmonary function

DCR provides an assessment of structures involved in respiration over time period and therefore could provide us with alternative insights into respiratory function. It may be possible that relating DCR to conventional lung function testing allows it to be used as a surrogate tool to measure some of these parameters used to assessment pulmonary function. Alternatively, it may provide different parameters of lung function which don't directly correlate with conventional testing, but in of themselves are clinically relevant.

In order to further evaluate the utility of DCR as a tool for assessment of baseline respiratory physiology, it is important to be able to compare it with real time conventional pulmonary function tests such as spirometry. Previous studies have compared sequential lung function testing to dynamic x-ray images; even if attempting a maximal effort there will be significant variability in 2 separate manoeuvres (i.e when sequentially performing a dynamic x-ray and then contiguously a spirometry). Currently there have been no studies which compare a dynamic chest x-ray with a simultaneous lung function study such as spirometry.

This study will therefore address this issue using performing simultaneous spirometry and DCR. Therefore one key aim of the study would be to establish how DCR compares with spirometry in a healthy population of individuals.

We would seek to also perform the DCR with simultaneous spirometry in a cohort of CF patients. DCR and spirometry are already performed as part of the annual review process. As highlighted DCR is generally well tolerated by pwCF. Spirometry can be physically or psychologically more challenging for pwCF. By performing simultaneous spirometry and DCR it would allow for a comparison with the healthy control group. This would provide the second aim of the Study to understand how we can relate DCR to pwCF's Spirometry.

Finally, as mentioned above DCR has become part of our annual review process in LHCH since 2019. The annual review process seeks to capture the clinically relevant information needed to assess the overall health of pwCF. By further analysing these DCR films with the other metrics of annual review process we may better understand how DCR relates to lung health over time. For example, are there any features of DCR which will predict future outcomes for pwCf. This study will therefore explore the relationship between longitudinal changes in DCR and key clinical measures of CF.

Aims:

1. Measure lung function via spirometry with simultaneous DCR in healthy controls
2. Measure lung function via spirometry with simultaneous DCR in pwCF
3. Investigate the relationship between spirometry and DCR in healthy controls, CF, and compare these two cohorts.
4. Investigate the relationship between DCR imaging and key clinical markers of CF recorded in the annual review process.

Null hypothesis: there is no relationship between parameters recorded by DCR and that of conventional spirometry in healthy individuals

Null hypothesis: there is no relationship between variables recorded by dynamic chest x-ray and that calculated by spirometry in people with CF.

Alternative hypothesis: We can correlate the findings on DCR with that of recorded spirometry findings.

Alternative hypothesis: there is a correlation between dynamic chest x-ray and that calculated by Spirometry in people with CF

Funding

This Study has received no specific resources from any funding agency either public or commercial.

Konica Minolta have provided a grant in kind with the dynamic x-ray machine, workstation and imaging software and technical support. Konica Minolta does not have any input in the clinical acquisition of data from relevant patient group.

Method and analysis

Study Setting

Single centre study based at Liverpool Heart and Chest Hospital. From a practical perspective the best place for the study given:

1. Dynamic x-ray machine is novel and located on site here
2. Tertiary centre for adult cystic fibrosis.

Part A : Real-time paired DCR and Spirometry in Healthy control Group

Aim: Explore relationship between the Dynamic CXR imaging and simultaneous spirometry in a healthy population with no known underlying lung condition.

Study design: The study involves the recruitment of healthy volunteers from general population. We would aim to recruit n=100 participants. The key investigations are Dynamic chest x-ray and paired spirometry as outlined below. Individuals will be recruited through a poster campaign successful in previous studies

Part B: Real-time paired DCR and spirometry in a CF subgroup.

Aim: Explore relationship between the Dynamic CXR imaging and simultaneous spirometry in a CF population

Study Design: This aspect of the study involves recruitment pwCF to perform DCR with paired spirometry, aiming to recruit n= 100 people. The above format would be repeated with paired spirometry and DCR in CF subgroup of LHCH patients. CF patients at LHCH attend a once yearly review process called annual review. The current format already includes a dynamic chest x-ray and spirometry as part of this Process (although not simultaneous). Through CF data base co-ordinator, a letter will be provided to all pwCF if interested.

This would allow for a Direct comparison of spirometry with DCR data. Furthermore, it therefore also allows for a comparison of Comparison with the control group. The structure of how these investigations are performed is outlined below.

Part C:

Retrospective Review of longitudinal DCR data with regards to clinical markers of CF status

Aim: To see how changes in key quantitative markers from DCR imaging relate to key CF clinical parameters

Study design: pwCF consenting for part B of the study will also be consented for using their current imaging as part of a longitudinal review of DCR imaging. Analyses will include an evaluation of the relationship between baseline DCR quantitative measurements and key clinical CF parameters that are recorded as part of their ongoing monitoring and care.

Schedule of Events

Below is highlighted a timetable for the schedule of events.

Table 1 – Schedule of Events for Healthy Volunteers

Contact	Purpose	Event	Duration
1	Indirect Contact	Individual contacts study team following poster campaign	N/A
1	Initial Direct contact	Provided with patient information sheet and consent information	20 minutes
2	Consent	Informed Consent taken	20 minutes
3	Attendance for imaging	Dynamic chest radiograph acquired with spirometry Completion of questionnaire	30 minutes

Table 2 – Schedule of Events for people with CF

Contact	Purpose	Event	Duration
1	Indirect Contact	Contacted via letter, patient information sheet enclosed	N/A
1	Initial Direct contact	Ensure provided with patient information sheet and consent information	20 minutes
2	Consent	Informed Consent taken	20 minutes
3	Attendance for imaging	Dynamic chest radiograph acquired with spirometry Completion of questionnaire	30 minutes

Once recruited the individual will attend for radiology department for the acquisition of the imaging and spirometry.

Dynamic chest X-ray procedure with paired spirometry

This study involves performing 2 simultaneous investigations – Dynamic x-ray and Spirometry, outlined below. For both parts of the Study A and B the process will be the same.

Spirometry:

Spirometry will be performed using validated and accredited spirometers that are used in clinical practice. The Study would utilise Geratherm® Spirostik™ spirometers (which can be Bluetooth or not) and documented using Geratherm® Blue Cherry™ software.

Subjects will perform spirometry in upright seated position which chest resting forward on the flat panel of the chest x-ray machine. The Spirometry instructions are given by a pulmonary physiologist who call out instructions. Spirometry requires a a deep inspiration followed by a maximal expiration into a hand held tube device. All pulmonary physiologists conducting the research at LHCH are accredited with the association for respiratory technology and physiology practioners(ARTP) and with the registration council for clinical physiologists (RCCP). The first 2 attempts will be spirometry only (as opposed to DCR). This is inline American Thoracic Society/European Respiratory Society repeatability and acceptability criteria (see below) and will allow a comparison with third spirometry attempt. The two non-DCR manoeuvres will facilitate volunteer comfort with the technique and allow for further coaching if required before the DCR image is captured. The third 'live' attempt will be recorded in conjunction with a DCR. The investigator tells the radiographer when to start recording the x-ray and breathing instructions are called out as per conventional Spirometry instructions.

All Spirometry will be reviewed by LHCH pulmonary physiologists and be entered on a clinical master datasheet. The following are the key Data points which will be recorded for the spirometry attempt with DCR (absolute and percentage predicted values):

- FEV1
- FVC
- FEV-1/FVC ratio

Table 3: ATS/ERS Repeatability and Acceptability Criteria

Spirometry	
Spirometry Within-Manoeuvre Criteria	**Spirometry Between-Manoeuvre Criteria**
3x Acceptable flow volume loops performed free from significant artefact including; *Cough during first second of exhalation, Glottis closure that influences the measurement* *Early termination or cut-off, Not maximal effort, Leak, Obstructed mouthpiece* *Duration ≥ 6s or until a plateau in the volume-time curve or if the subject cannot or should not continue to exhale*	*The two largest values of FEV1 must be within 0.150L of each other* *The two largest values of FVC must be within 0.150L of each other*

Dynamic Chest X-ray

Dynamic chest x-rays are performed in the x-ray room in Liverpool heart and chest Hospital. This is simultaneous with spirometry so will occur in the same place.

A physical anatomical marker (left/right) is manually added to the detector. Density is set to -2 on the control panel, and the dynamic study function selected. The tube filter is set at 1.0mm Al, 0.1mmCu (copper and aluminium). The SID (distance to detector) is set to 200cm. A 180cm focal distance grid (40L per cm, ratio 12:1, and 17 by 17 inch / 42.18cm x 42.18cm) is used. Exposure factors are set at tube voltage 100kVP, tube current 80mA, exposure duration 4.0ms. Collimation (the adjustment of the x-ray field size to the minimum needed to capture the required images for a specific patient) is performed as per a standard chest x-ray, usually around 40cm by 30cm. The patient is positioned in a posterior-anterior position.

The frame rate for those participants undergoing routine clinical imaging will be set at 15 frames per second (fps), the standard frame rate used clinically.

Breathing instructions are called out as per Spirometry instructions. The image capture is stopped once the breathing the spirometry action is complete (this can be completed in around 10s or 150 frames), or if the 220 frame limit is reached, whichever comes first. If the spirometry is suboptimal the procedure cannot be repeated.

Once the image capture/spirometry is complete, exposure factors are recorded by the operator, including the total number of frames and total duration in seconds.

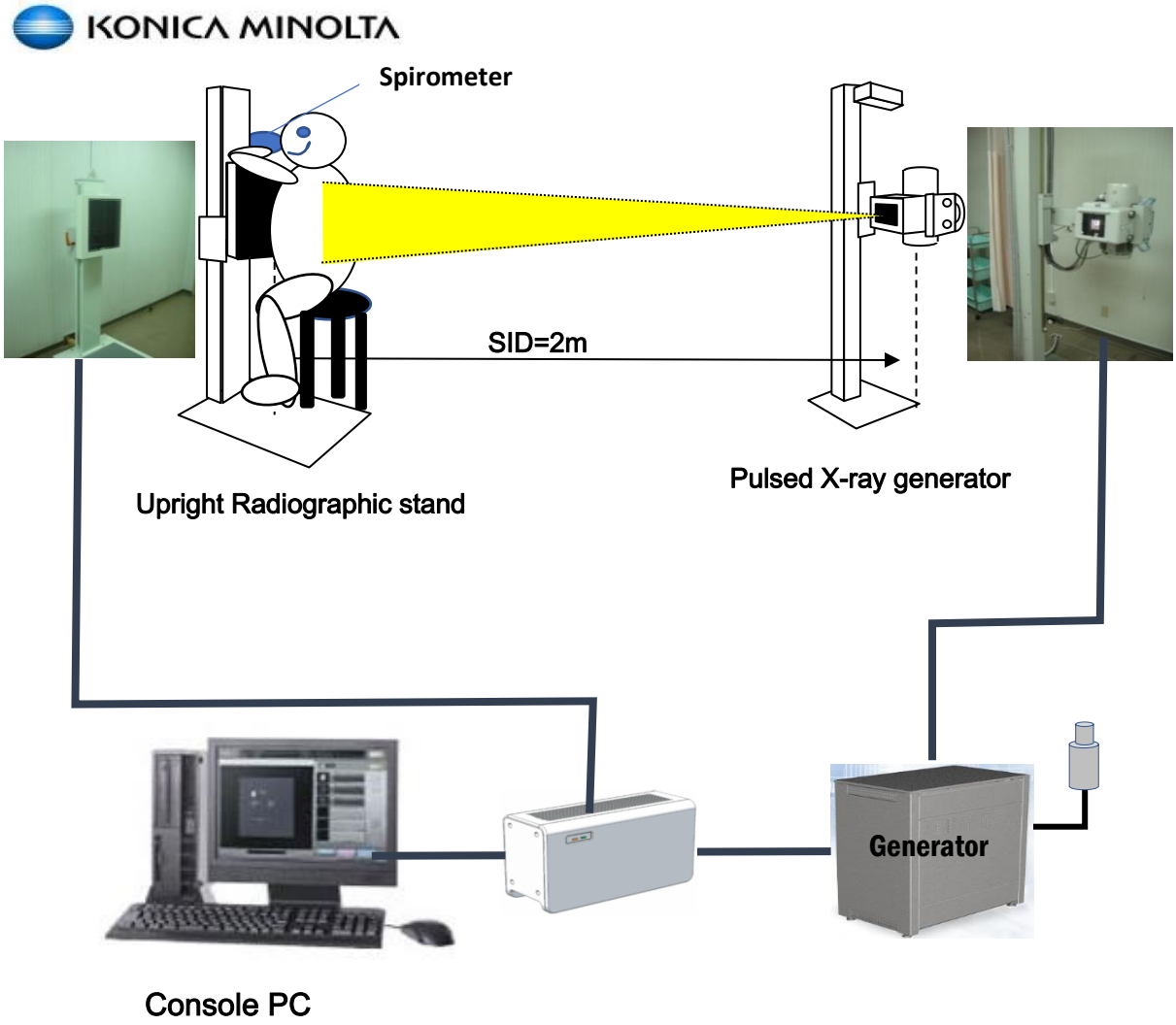
The images captured are transferred to the local PACS server as well as an NHS server. Images are then downloaded from the NHS server onto a secure workstation for analysis in the research department. Images are anonymised to comply with data protection policies. Images are then processed using Konica Minolta DI-X1 software and re-uploaded to the server.

The images acquired by the DCR are processed using the Di-X1 machine using the computer algorithms. Further updates to the machine may allow further analysis. Key quantitative measures derived from the D1-X1 analysis of the DCR currently include:

1. Diaphragmatic excursion – maximal inspiratory and expiratory in mm
2. Peak diaphragm velocity
3. Peak diaphragm velocity at inspiration / expiration
4. Peak distance from apex to diaphragm
5. Lung field area during range of maximal inspiration / expiration – as calculated by Konica Minolta software. Reviewed individually to ensure algorthim accurately detecting lung field area.

The Figure below demonstrates the room set up. The study volunteer attends room 2 where our DCR machine in LHCH is placed. The individual sits on a stool facing the FPD. The Radiographer , researcher and any pulmonary physiologist are by the control station. The volunteer holds the spirometer to their mouth. When instructions for Spirometry are given the Radiographer presses the button to record the DCR. The complete spirometry attempt is completed, and the x-ray ceased when the full motion completed. The DCR machine will stop after 220 frames the exposure will not continue if the full spirometry is not completed.

Figure 1- Room Setup



Unexpected findings on imaging or spirometry

Any unexpected or concerning findings that are observed either on dynamic chest radiograph or spirometry will be acted upon as soon as possible by a member of the investigating team. In the case of people with CF these findings will be communicated to the responsible physician caring for the individual, as well as to the individual themselves, as appropriate. For the healthy control group action will be governed by the nature of the abnormality and will facilitate communication with primary care physician; again, all actions and information will be communicated to the individual as appropriate.

Sample and Recruitment

This study is exploratory work and is ultimately hypothesis generating and as such no formal statistical power calculation has been carried out. Target recruitment numbers are therefore based on pragmatic assessment of the ability to recruit and measure successfully.

Recruitment Part A: The study involves the recruitment of healthy volunteers from general population. We would aim to recruit n=100 participants. Recruitment will be made through internal advertisement at LHCH hospital trust, University of Liverpool and Liverpool John Moore University

Recruitment Part B: People for part B of the study will be recruited through annual review process at CF clinic. As part of this process all people will undergo DCR and spirometry. They will be exposed to no further radiation, but it will mean that they have to perform an extra spirometry procedures. Individuals participating in part B will consent to using their investigation in part of the longitudinal review.

The Liverpool Heart and chest hospital has approximately 350 people with CF, however only 302 are present in the area (as opposed to being based in other areas which means they don't come to clinic). Transplanted individuals will be excluded (totalling 7) as well as pregnant individuals (currently 15). There is approximately 20% exacerbation rate and approximately 30% do not attend any given appointment. This would give us a projected population of just over 150 individuals to recruit from (please see Figure 2 below)**.**

It is important to note that this is a conservative estimate pwCF who have a current exacerbation or who DNA appointment may return for their annual review study at a later date (however this may not be within the study recruitment period)

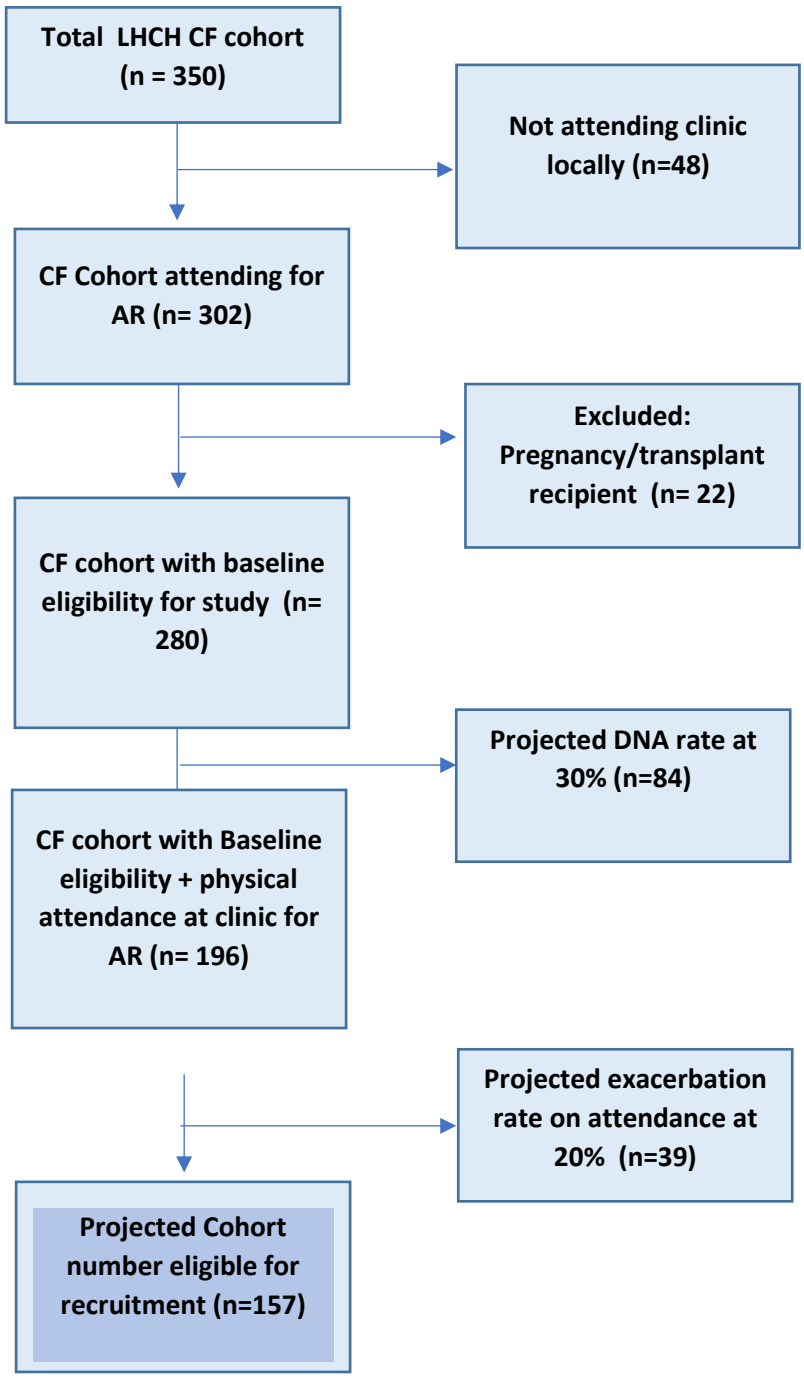
Consent

Informed consent will be obtained prior to the participant undergoing enrolment in the study. A patient information sheet will be provided prior to taking informed consent.

The opportunity to ask questions will be given. Capacity will be assessed in order to determine that informed consent can be given.

Participation will be voluntary, and consent can be withdrawn at any time.

Figure 2 - CF cohort selection flow chart



Participation enrolment criteria:

Part A: Real-time paired DCR and Spirometry in Healthy control Group

Inclusion criteria:

- Age: ≥ 17 years old and ≤ 50 years old

and

- No underlying respiratory illness (chronic or acute)

and

- Able to provide informed consent

Exclusion criteria

General exclusion criteria:

Any of:

- Potentially pregnant or lactating
- Inability to provide informed consent
- Unable or unwilling to sit to perform DCR/Spirometry in the radiology department
- Unable or unwilling to follow Spirometry breathing instructions (e.g., holding breath or taking a deep breath)
- Unable to perform reproducible spirometry and/or full pulmonary function studies within ATS-ERS criteria
- Significant radiation exposure within the last year (for example, numerous CT scans of chest)
- Involved, either currently or recently, in other studies involved non-routine exposure to sources of ionising radiation
- Any serious or active medical or psychiatric illness, which in the opinion of the investigators, would interfere with subject treatment, assessment, or compliance with the protocol
- Inability to complete spirometry performance in 20 seconds.
- Current Chest infection

Spirometry exclusion criteria

Any of:

- Unstable cardiovascular status, recent MI or PE (within 6 weeks)
- Haemoptysis of unknown aetiology (within 6 weeks)
- Pneumothorax (present, or occurring within 6 weeks)
- Within 24 hours of bronchoscopy
- Thoracic, abdominal or cerebral aneurysm
- Recent eye surgery or increased intraocular pressure
- Recent thoracic or abdominal surgery
- Acute nausea, vomiting or diarrhoea
- Pregnancy
- Undergoing treatment for TB

- **Part B: Real-time paired DCR and spirometry in a CF subgroup**

Inclusion criteria:

- Age: ≥ 17 years old ≤ 50

  and
- Attending the adult CF Unit at LHCH

  and
- Confirmed CF diagnosis (positive sweat test in childhood and by genotyping)

  and
- Able to provide informed consent

Exclusion criteria

General exclusion criteria, same as Group A (see above) plus:

- Recipient of Lung transplant
- Current exacerbation

Spirometry exclusion criteria (same as for Group A, see above)

Statistical analysis

Statistical analysis will be carried using the R software package, produced and supported by the R Foundation for Statistical Computing, under the GNU GPL v2 public license.

All data will be collated electronically and stored on a secure server in line with data protection.

Two-sided P-values of <0.05 will be considered as statistically significant. Confidence intervals will be presented where appropriate and feasible.

Comparison of the data will be primarily between dynamic chest x-ray results and spirometry data. Depending on the distribution of the dataset, paired t-tests or the relevant non-parametric equivalent will be used to analyse within groups. Categorical data will be presented as frequency and percentage. Continuous data will be presented as number of observations, mean, standard deviation, median and interquartile range as appropriate.

Proposed timetable of events

- **December 2022 –** Start of Protocol write up**.**
- **January 2023 –** research proposal submission to local research committee
- **March 2023-** Sure group review and revisions to protocol and study literature
- **July 2023 -**Iras application
- **September 2023 to September 2024 -** Data collection is projected to take around 365 days, aiming for completion end of July 2023. This allows for the recruitment of 2 'healthy volunteers' and 2 people with CF a week.
- **September to October 2024**- Data analysis
- **October/November/December 2024**- write up of research results +/- publication

Figure 3 – Gannt Chart of Projected Timetable December 2022 – December 2024

Task	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D
Protocol Write up																									
R&I committee meeting LHCH																									
Sure Group review																									
Iras Application																									
Study period																									
Data analysis																									
Results write up																									

Safety

Ionising Radiation

This study requires exposure to ionising radiation.

We are exposed to radiation in our daily lives and our annual average radiation exposure in the UK is 2.7mSv

An example of typical radiation doses from clinical investigations are included below.

Table 4 - Effective Doses for Common Radiological Examinations

Projection	Estimated effective dose (mSv)
Chest PA	0.014
Chest lateral	0.038
Coronary angiogram	3.9
CT chest	6.6
High resolution CT chest (HRCT)	1.2

The estimated effective dose in mSv as a consequence of a dynamic chest x-ray are determined by the settings of the machine. The settings used for the dynamic -xray machine in the LHCH environment are:

tube filter is set at 1.0mm Al, 0.1mmCu (copper and aluminium).

The SID (distance to detector) is set to 200cm. A 180cm focal distance grid (40L per cm, ratio 12:1, and 17 by 17 inch / 42.18cm x 42.18cm) is used.

Exposure factors are set at tube voltage 100kVP, tube current 80mA, exposure duration 4.0ms. Collimation (the adjustment of the x-ray field size to the minimum needed to capture the required images for a specific patient) is performed as per a standard chest x-ray, usually around 40cm by 30cm.

The patient is positioned in a posterior-anterior position.

The frame rate for those participants undergoing routine clinical imaging will be set at 15 frames per second (fps), the standard frame rate used clinically.

From a previous study ‘SPUDDS’ which utilised the dynamic chest X-ray in the same configuration the medical Physics Expert has calculated the procedural dose for the dynamic cxr at 15 fps for up to 20s to be 0.24 mSv.

Ionising radiation can cause cancer which manifests itself after many years or decades. Having a DCR at the above settings is approximately equivalent to 4 weeks background radiation. The risk of developing cancer as a consequence of taking part in this study is 0.0012% for one DCR. The natural life time risk of developing cancer is 50%. For people with CF there is no extra exposure to radiation

as this is part of routine clinical care. However, for the 'healthy volunteers' this is additional radiation exposure. This risk will be reflected in our patient information leaflet and consent process.

X-ray machine Safety

The Konica Minolta X-Ray imaging device to be used in the proposed study at Liverpool Heart and Chest Hospital is not an implanted device, nor a device that will support or sustain human life. Furthermore, imaging data from the device will not be used for diagnosing, curing, or otherwise altering patient management in any way. Usage of the device as proposed in this clinical protocol will not present a serious risk to the health, safety, or welfare of the subject.

In order to assure safety, a risk assessment of the Konica Minolta X-Ray system was performed by Integrated Radiological Services (IRS), Ltd. to identify potential hazards that could cause an injury to the patient, user, or service personnel and to provide a plan that eliminates or reduces the possibility of a hazard. This was conducted in April 2018 at LHCH, by IRS, Ltd., and updated in June 2021 by IRS, Ltd. Following software and firmware updates to the DCR system. The risk assessment includes the following classes of hazards: radiation safety, electrical safety, mechanical hazards, and electromagnetic compatibility. Testing has been performed to ensure compliance with applicable safety standards such as IEC 60601-1, IEC 60601-1-2, IEC 60601-1-3, IEC 60601-2-28, and IEC 60601-2-45.

In all areas of assessment, the Konica Minolta X-ray system was found to comply with applicable safety standards and, when used in accordance with the protocol and operating instructions, it is considered a non-significant risk, and possesses no known health hazards to patients, users or service personnel, outside of the inherent risks of ionizing radiation. Information on the ionizing radiation dose can be found in the previous section. The full report is available and can be provided by the investigating team.

Lung function testing safety

Spirometry will be carried out in line with ETS/ARS guidelines. Standard exclusion criteria will be applied (see exclusion criteria). All pulmonary physiologists conducting the research at LHCH are qualified ARTP practitioners and are RCCP registered.

Reporting of adverse events

Although there are no obviously identifiable adverse events foreseeable from the use of the dynamic chest x-ray machine, any adverse events will be recorded by any of the trial investigatory team and reported to the principal investigator, as well as by the Trust's Datix adverse clinical event recording system if these occur during a patient hospital attendance/inpatient stay. The principal investigator will notify the Research Ethics Committee of any significant adverse events.

Patient and public involvement

The study literature (Participant Information Sheet, consent documentation, questionnaire) will be discussed with the LHCH local patient involvement group (SURE group).

Data Management

Any patient-identifiable information will be removed from any published or presented data. For recording of patient information, patients will be assigned a unique patient identifying number, which will be used instead of their name in data analysis.

Data gathered will include dynamic CXR images sequences, Spirometry and some clinical data. These will be transcribed to a Microsoft Excel© database, stored securely within hospital facilities and in accordance with the Data Protection Act 2018.

All images will be stored and backed up via the local PACS system, and the unprocessed sequence data on a secure LHCH server. The PACS data and unprocessed sequence data will be accessed from two secure, devoted workstations within the hospital, although data will not be stored locally on the workstations. Any extrapolated or patient-specific data will be stored in accordance with the Data Protection Act 2018. No patient identifiable information will be stored outside of hospital servers.

Konica Minolta has provided the workstations and software necessary for image interpretation, although no patient identifiable information or images will be stored on third-party devices. Data interpretation will be carried out on local machines, then re-uploaded to the secure server, with local data being deleted concurrently. Support for the software package will be provided by Konica Minolta, and any adjustments or updates to the software will be provided by Konica Minolta.

Protocol and Registration

This study has received the following approvals:

LHCH Research and Innovation Committee meeting 23/01/2023

Sure group approval 16/06/2023

Competing interests

None of the contributors to this protocol declare any competing interests.

Sponsorship

This study will be sponsored by LHCH. Konica Minolta, Inc. have provided the dynamic x-ray machine, workstation and analytics software for use under a Loan Agreement.