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Vast improvements in oesophageal imaging

Submission date	Recruitment status	[ ] Prospectively registered
30/07/2019	Suspended	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
20/08/2019	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
23/04/2020	Cancer	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims

The study aims at improving the treatment pathway, and hopefully also the prognostic outcomes, of patients with, or at risk of developing, oesophageal cancer, by making a new imaging technique (X-Ray Phase Contrast Imaging, XPCI) available directly in the intervention room, to determine in real time whether biopsy samples, or tissues removed as part of a more invasive intervention, contain cancerous lesions and to what extent. At the moment, the standard way to determine whether human tissue is healthy or cancerous is histopathology. Histopathology is the study of changes in cells and tissues caused by disease. This has a turnaround time of several days if not weeks, which introduces a delay between an examination or an interventional procedure and the next therapeutic steps. During this time, some precancerous lesions can develop into cancer, and patients that could be treated with minimally invasive endoscopic treatment might end up requiring a larger operation. If XPCI can distinguish cancerous from healthy and precancerous lesions with high accuracy, clinicians would have rapid answers to key clinical questions, which would enable them to immediately determine the best course of action for the patient. Examples include use endoscopy to remove early stage cancers which, if not treated immediately, could later on require a major surgery (oesophagectomy), and ensuring that the entirety of the cancer has been removed hence reducing the need for more interventions.

Who can participate?

Patients over the age of 18 with either Barrett's Oesophagus, early stage oesophageal cancer, or locally advanced oesophageal cancer which has not metastasised (spread)

What does the study involve?

Although, as suggested by the name, XPCI involves the use of x-rays which are a form of ionizing radiation (i.e. radiation with a sufficient energy to detach electron from atoms, hence potentially causing biological damage), patients will not be subject to any exposure to ionizing radiation since only biopsies or resected tissue is x-rayed. During this study imaging is performed in a separate lab, while in future steps, should this project be successful, it would take place in the intervention room inside a fully shielded machine. This means that this research does not require any exposure to ionising radiation neither of patients nor of medical practitioners, neither now nor in the future.

What are the possible benefits and risks of participating?
Since this is an early stage study testing the potential of a new imaging technique, there would be no direct benefit if patients were to consent to take part in the study. Should the study be successful and lead to clinical adoption of the new technology, future patients with the same health condition may benefit. The only exception would be if a patient involved in the study for an early stage procedure (e.g. monitoring through biopsy collection) is subjected to the technology again at a later stage, after clinical adoption, for a subsequent procedure – however, this would be incidental and to some extent an “indirect” benefit.

Where is the study run from?
University College London Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
September 2018 to August 2023

Who is funding the study?
Engineering and Physical Sciences Research Council (UK)

Who is the main contact?
1. Dr Paul Wolfson
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
18/0089

Study information

Scientific Title
Improving the outcomes of oesophageal interventions through novel x-ray based imaging methods

Acronym
VIOLIN

Study objectives
This project aims at determining whether real-time, ultra-sensitive imaging can improve the outcomes for all stages of treatment of oesophageal cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/09/2018, London - Westminster Research Ethics Committee (4 Minshull Street, Manchester, M1 3DZ, UK; Tel: +44 (0)207 104 8012; Email: nrescommittee.london-westminster@nhs.net), REC ref: 18/LO/1382, IRAS: 244284

Study design
Single-centre observational clinical investigation or other study of a medical device (pre-clinical device development or performance testing)

Primary study design

Observational

Secondary study design

Study setting(s)
Hospital

Study type(s)
Diagnostic

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
Oesophageal cancer

Interventions
This project proposes to use a new imaging technique, called X-Ray Phase Contrast Imaging (XPCI), to improve the detection, staging, treatment and follow-up of oesophageal cancer. XPCI enables the achievement of significantly enhanced image contrast compared to standard X-ray imaging techniques, leading to detection of tissue features classically considered “x-ray invisible”. Moreover, research carried out at UCL demonstrated that XPCI is not limited to specialized and expensive research facilities, but that it can be implemented with commercially available X-ray tubes, i.e. it is compatible with a clinical environment.

In particular, this project aims at determining whether real-time, ultra-sensitive imaging can improve the outcomes for all stages of treatment of oesophageal cancer. These have been identified as streams 1-3 depending on the type of treatment, and different samples are involved in each stream: biopsies for stream 1, disk-shaped "endoscopic mucosal resections" (EMRs) for stream 2, and full oesophagus specimens for stream 3. In the various cases, the need is to determine whether the new imaging approach can differentiate between cancerous and pre-cancerous lesions (stream 1), determine tumour margins and penetration into the submucosa (stream 2), determine tumour margins, locate lymph nodes and determine their state of infiltration (stream 3). If successfully demonstrated, these achievements would have a very strong impact on the treatment of oesophageal cancers, potentially leading to more accurate surgical interventions and increased survival.

Following successful demonstration on oesophagus, proof-of-concept application to other diseases (for instance, colon biopsies) will be carried out towards the end of the project.

Intervention Type
Device

Phase
Not Applicable

Primary outcome measure
Stream 1 patients (biopsies): the number of samples accurately classified as healthy/pre-cancerous lesions, measured using X-Ray Phase Contrast Imaging (XPCI) at the baseline endoscopy

Stream 2 patients (endoscopic mucosal resection): the number of samples where the margins of the tumor are correctly identified (with tolerance of 2 mm), measured using X-Ray Phase Contrast Imaging (XPCI) at the baseline endoscopy
Stream 3 patients (oesophagectomy): the number of samples where the margins of the tumor are correctly identified (with tolerance of 2 mm), measured using X-Ray Phase Contrast Imaging (XPCI) at the baseline endoscopy

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
01/09/2018

Completion date
31/08/2023

Eligibility

Key inclusion criteria
1. Males and females over the age of 18 years
2. Ability to provide written, informed consent
3. For stream 1 (biopsies): patients with either suspected Barrett's Oesophagus presenting for endoscopy or patients with documented Barrett's Oesophagus presenting for follow-up endoscopy likely to require a biopsy
4. For stream 2 (endoscopic mucosal resections): patients with early stage oesophageal cancer
5. For stream 3 (oesophagectomy): patients with locally advanced oesophageal cancer which has not metastasised

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
370

Key exclusion criteria
1. Patients on anticoagulation undergoing high-risk procedures
2. Patients with esophageal varices that preclude biopsies
3. Patients with known eosinophilic esophagitis
4. Patients that are pregnant
5. Patients with a history of hemostasis disorders (Hemostasis disorders will include, but will not be limited to: patients with hemophilia or other congenitally acquired clotting factor

deficiencies, patients with cirrhosis with coagulopathy, patients known to have thrombocytopenia (<100,000 plt/ul) and individuals with von Willibrand's disease or other known platelet malfunction disorders)

Date of first enrolment
01/10/2018

Date of final enrolment
01/10/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University College London Hospitals NHS Foundation Trust
235 Euston Road
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Sponsor information

Organisation
University College London

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Sponsor type
University/education

Website
https://www.ucl.ac.uk/joint-research-office/

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Research council

Funder Name
Engineering and Physical Sciences Research Council

Alternative Name(s)
UKRI Engineering and Physical Sciences Research Council, Engineering and Physical Sciences Research Council - UKRI, Engineering & Physical Sciences Research Council, EPSRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a peer reviewed journal.

Intention to publish date
31/08/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Chief Investigator Prof Laurence Lovat (l.lovat@ucl.ac.uk).
Type of data: Deidentified patient imaging data
When the data will become available and for how long: With publication
By what access criteria data will be shared including with whom, for what types of analyses, and by what mechanism: With investigator support after approval of a proposal
Whether consent from participants was obtained: Patient consent was obtained

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No