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A Study on the accuracy and development of best practices using fluorescence for precision surgery in colorectal cancer

Submission date
29/05/2017

Recruitment status
No longer recruiting

Registration date
08/09/2017

Overall study status
Completed

Last Edited
18/10/2017

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
Surgery for colon cancer is still variable because we don't know exactly how much surrounding tissue to remove along with the main primary cancer. Recurrence risk (i.e. risk of the cancer coming back or spreading elsewhere) could be lowered if we can remove this important nearby tissue with greater precision. Although some surgeons have suggested performing a bigger operation to remove more of the surrounding tissue, a bigger operation potentially has complications and it may be unnecessary for certain patients. By using a specialised dye at the time of surgery we may be able to better define exactly how much surrounding tissue needs to be removed in each patient thus reducing that specific patient's individual risk of recurrence. If we remove the cancer and precisely the right amount of tissue nearby that might also contain cancer cells, this could reduce the chances of spread to other sites such as the liver. If successful, this technique will allow each operation to be tailored to each patient. A patient who doesn't need a bigger radical operation would be spared such 'over-treatment', Conversely, a patient who does actually need a bigger operation to minimise the chance of residual cancer cells being left behind would gain benefit from having a bigger operation upfront to avoid potential 'under-treatment'. The aim of this study is to examine the validity of using indocyanine green (ICG) fluorsecence imagining has the ability to guide proper cancer resections (tumour removal) in colorectal cancer.

Who can participate?
Adults aged 18 and older who are scheduled to have a colorectal resection.

What does the study involve?
Participants are identified from the colorectal cancer multidisciplinary team meeting who are suitable for surgery. Their treatment plans remain the same. During the operation, participants are injects a dye next to the cancer and then use a special camera to highlight all the potential tissue nearby that might have some cancer cells within it. This allows the surgeon to remove the main primary cancer and precisely the right amount of surrounding tissue. The normal treatment for colorectal cancer is to remove the cancerous part of the bowel. In addition surrounding normal bowel is also removed. This is to ensure that the cancer is removed completely. Once the

bowel has been removed for your tummy we would then take some tissue samples from the specimen that is analysed to see how well this method works at removing the cancer cells.

What are the possible benefits and risks of participating?
There are no direct benefits or risks with participating.

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

When is the study starting and how long is it expected to run for?
February 2017 to April 2018

Who is funding the study?
University College London Hospitals NHS Foundation Trust (UK)

Who is the main contact?
Mr Heman Joshi

Contact information

Type(s)
Scientific

Contact name
Mr Manish Chand

Contact details
University College London Hospitals
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
357/1

Study information

Scientific Title
Study of ICG Fluorescence imaging in colorectal cancer patients undergoing a minimally invasive surgical resection

Acronym
FLICC II

Study objectives
The aims of this study is to determine the validity for Indocyanine green (ICG) fluorsecence imagining in intraoperative localisation of tumours, determining dissection planes, demonstrating lymphatic drainage, and sentinel node mapping in colorectal cancer, to determine the accuracy for ICG fluorescence imaging to demonstrate lymphatic drainage and sentinel node mapping in colorectal cancer and to establish if ICG fluorescence imaging has the ability to guide proper oncologic resections in colorectal cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration.

Study design
Observational case series

Primary study design
Observational

Secondary study design
Case series

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Colorectal Cancer

Interventions
Participants with a colorectal cancer presenting for surgical management are included in this study. Patients who are scheduled for a minimally invasive (robotic assisted laparoscopic or laparoscopic) colorectal resection are evaluated at baseline to determine if they meet the inclusion/exclusion criteria of the protocol.

A colonoscope is used for direct intraluminal visualization of the primary tumor. After the primary tumor is localised with the colonoscope, ICG is injected into the into the submucosa of the bowel by the tumor- 1mL aliquots in a concentration of 5mg/10mL at 4 points within 1-2cm of the mass.

Intraoperative imaging using a specialized laparoscope with near infrared (NIR) function is used for lymphangiography. The ICG dye binds to circulating proteins and is visualised as it is excited by fluorescent light in the NIR spectrum from a specialized laparoscope intra-operatively. Localisation of positive lymph nodes can be detected laparoscopically. The mesentery containing the lymph nodes draining the tumor will then be examined in real-time with the laparoscope.

All cases are recorded, and both real-time and retrospective evaluation is performed to assess tumor localization, lymph node drainage, and sentinel node identification. After resection, the pathologic specimen is evaluated for the lymph node yield, resection margins, and sentinel lymph node evaluation. The tagged lymph node(s) are excised and separately processed to further examination as sentinel lymph nodes (SLN). For nodal analysis, lymph nodes up to 10mm in diameter are bivalved, and nodes larger than 10mm are grossly sectioned in slices up to 2 mm and processed to paraffin blocks for hematoxylin and eosin staining. If none of the lymph nodes revealed metastases, stepwise sections of 250µm distance will be performed on the nodes until sampled completely.

At each level, at least 2 serial sections are cut at 5µm thickness and one of them separated for immunohistochemical staining. If no tumor cells are found by hematoxylin and eosin staining, at least 4 serial sections per lymph node are stained by immunohistochemistry (pan-cytokeratin antibody MNF116 visualized with streptavidin-AP, DAKO, Germany). Uncertain findings after hematoxylin and eosin staining are clarified by immunohistochemistry. To exclude false-positive results by staining of perifollicular reticulum cells or plasma cells, CK-positive cells will only considered as tumor cells if they reveal unequivocal cytomorphological criteria of a tumor cell on double staining with hemalaun. This approach enables the pathologist to identify tumor deposits up to a diameter of 0.25 mm with a probability of 100%, tumor deposits up to a diameter of 0.1 mm with a probability of 50%.

Intervention Type
Procedure/Surgery

Primary outcome measure
1. Accuracy of ICG fluorescent lymphangiography to create a sentinel lymph node map in colorectal cancer is measured during pathological analysis
2. Time to lymphatic drainage and sentinel node visualization with ICG … is measured using a fixed time from injection of ICG molecule
3. Accuracy of ICG fluorescent lymphangiography for determining appropriate resection margins in colon cancer cases is to be determined from this study.

Secondary outcome measures
Cost benefit is measured using a financial analysis at the end of the study.

Overall study start date
01/02/2017

Completion date
01/04/2018

Eligibility

Key inclusion criteria

1. Benign or malignant colorectal disease that are being scheduled for a minimally invasive colorectal resection
2. 18 years of age and older
3. Either gender
4. Are able to have the procedure must be performed through a laparoscopic or robotic approach
5. Have a planned resection with hand sewn or stapled anastomosis
6. The colorectal procedure must be the primary procedure for the episode of care, and patients must participate in all follow-up appointments
7. Willing and able to give informed consent for participation in the study, adhere to protocol requirements and agree to participate in the study program

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
50

Key exclusion criteria
1. Subjects who undergo conversion to the open approach are excluded from the analysis, but conversion from robotic or single port to hand assisted or multi-port laparoscopic are included, with documentation
2. Pregnant or nursing
3. Another condition or general disability or infirmity that in the opinion of the investigator precludes further participation in the study.
4. Under 18 years of age
5. Incomplete medical records
6. Renal dysfunction with creatinine > 110 mg/dL
7. Known allergy or history of adverse reaction to ICG, iodine or iodine dyes
8. Intra-operative incidental finding of Stage IV cancer

Date of first enrolment
01/04/2017

Date of final enrolment
01/12/2018

Locations

Countries of recruitment
United Kingdom

Study participating centre
University College London Hospitals
NW1 2BU

Sponsor information

Organisation
University College London Hospitals

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235 Euston Road
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/042fqyp44

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
University College London Hospitals NHS Foundation Trust

Alternative Name(s)
University College London Hospitals, UCLH

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Plans to publish in a high impact peer reviewed journal and present interim data at international conferences in our field.

Intention to publish date
01/04/2019

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Heman Joshi heman.joshi@nhs.net

IPD sharing plan summary
Available on request