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Is using a single tracer to identify lymph nodes during breast cancer surgery as good as using two tracers?

Submission date
02/12/2021

Recruitment status
No longer recruiting

Registration date
08/12/2021

Overall study status
Completed

Last Edited
11/04/2024

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The most common form of breast cancer can spread to lymph nodes in the armpit. The nearest lymph nodes to the tumour, which are the ones most likely to contain cancerous cells, are called sentinel lymph nodes (SLN). Women usually have two SLNs although this varies from person to person. At the time of surgery to remove a breast tumour, the surgeon will also remove the SLNs. To help the surgeons identify the SLNs, they usually inject two tracers that will show which are the sentinel lymph nodes. These are a fluorescent dye (Indocyanine Green [ICG]) and either a blue dye (Patent Blue dye) into the breast or a radioactive tracer given into the blood system at an appointment prior to the surgery (standard care).
More than half of newly diagnosed breast cancer patients will undergo routine SLN biopsy (where a sample of the lymph node tissue is taken for further testing in a laboratory) annually in the UK (at least 25,000 cases). Blue dye is becoming less popular as a tracer due to potential allergic reactions and staining of skin and breast tissues. In about a third of women this staining of the skin can last for 12 months and about 1 in 12 women still have staining after 3 years. Drawbacks of the radioactive tracer include availability, cost, patient inconvenience/discomfort, radiation exposure/disposal and mandatory licensing. Fluorescence tracing using ICG is sensitive and allows the surgeon to see which nodes to remove during surgery rather than in an image taken before surgery. It is possible that using fluorescence tracer would be just as accurate as the previous methods, but could avoid using blue dye and reduce the cost if the radioactive tracer could be replaced. The aim of this study is to compare ICG combined with a standard tracer versus ICG alone for SLN detection in early breast cancer.

Who can participate?
Women aged over 18 years undergoing surgery for breast cancer that has spread into tissues surrounding the breast

What does the study involve?
Participants at Ninewells Hospital will be randomly allocated to receive either ICG plus Patent

Blue Dye (standard care) or ICG alone (intervention). Participants at Addenbrooke's Hospital will be randomly allocated to receive either ICG plus radioisotope (standard care) or ICG alone (intervention).

What are the possible benefits and risks of participating?
Ninewells Hospital participants - randomisation to the fluorescent dye as a single tracer will mean there will not be any staining from the blue dye.
Addenbrooke's Hospital participants - randomisation to the fluorescent dye as a single tracer will mean there will be no exposure to radioactive material or the need for an extra visit to the hospital to get it.
The procedures being tested in this trial are currently used in standard care. The fluorescent dye can be easily seen by the doctor during surgery. The doctors carrying out this trial believe that they will be able to see all SLNs with only one tracer and it is very unlikely that they will miss any SLNs. Taking part in this trial is very unlikely put participants at any more risk than having routine standard care.
However, there is a very small risk that the fluorescent dye will not show the SLNs (this can also happen if both tracers are used). If this happens the doctor may remove more lymph nodes than he would normally do to make sure the SLNs are removed. Removing more nodes may slightly increase the risk of having seroma or lymphoedema. Seroma is a build-up of clear body fluid where tissue has been removed during surgery and lymphoedema is the swelling of tissues caused by a build-up of lymph fluid.

Where is the study run from?
Ninewells Hospital (UK)

When is the study starting and how long is it expected to run for?
May 2021 to March 2023

Who is funding the study?
Association of Breast Surgery (UK)

Who is the main contact?
Mr Vassilis Pitsinis
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
301478

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 51005, IRAS 301478

Study information

Scientific Title
A prospective randomised study comparing indocyanine green (ICG) fluorescence combined with a standard tracer versus ICG alone for sentinel lymph node (SLN) detection in early breast cancer

Acronym
INFLUENCE

Study objectives
It is hypothesized that fluorescence mapping can provide at least equivalent sentinel lymph node (SLN) detection rates but offers the opportunity for avoiding blue dye and could eventually lead to improved cost-effectiveness if the radioisotope is eventually abandoned for routine SLN biopsy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 21/10/2021, North West – Greater Manchester East Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street Manchester M1 3DZ, UK; +44 (0)207 104 8009; gmeast.rec@hra.nhs.uk), REC ref: 21/NW/0328

Study design
Randomized; Interventional; Design type: Diagnosis, Other

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Identification of sentinel lymph nodes during breast cancer surgery

Interventions
Participants will be identified from the breast cancer services at each site. Once consented, participants will be randomised using sealed opaque envelopes to receive either standard care or intervention to allow visualisation of the SLNs:
Tayside - either ICG plus Patent Blue Dye (standard care) or ICG alone (intervention)
Cambridge - ICG plus radioisotope (standard care) or ICG alone (intervention).

Participants will be assessed 2 weeks and 3 months following surgery for adverse skin reactions and the presence of staining.

The sensitivity of ICG fluorescence imaging alone for SLN detection compared to a combination of ICG and standard tracer will be confirmed by the percentage of patients with successful identification of the SLN using ICG alone or combined with a standard tracer, stratified by cohort.

Intervention Type
Procedure/Surgery

Primary outcome measure
Successful identification of the sentinel lymph node using a physical examination on Day 1

Secondary outcome measures
1. Tumour deposits in at least one node measured using a pathology evaluation on Day 1
2. Seroma formation measured using a physical examination at 2 weeks and 3 months
3. Cutaneous staining measured using a physical examination at 2 weeks and 3 months
4. Other adverse reactions to tracers measured using a physical examination at 2 weeks and 3 months

Overall study start date
01/05/2021

Completion date
31/03/2023

Eligibility

Key inclusion criteria
1. Female
2. Aged over 18 years
3. Biopsy-proven invasive breast cancer
4. Tumour(s) measuring <5 cm in radiological size

5. No record of clinical or sonographic evidence of abnormal axillary lymph nodes
6. Planned SLN biopsy to be carried out as per local standard care using ICG plus radioactive tracer (Cambridge only) or ICG plus Patent Blue Dye (Tayside only)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
Planned Sample Size: 100; UK Sample Size: 100

Key exclusion criteria
1. Neoadjuvant chemotherapy
2. Prior ipsilateral axillary surgery or breast excision biopsy
3. Pregnant or breastfeeding

Date of first enrolment
20/01/2022

Date of final enrolment
09/01/2023

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Ninewells Hospital
Dundee
United Kingdom
DD1 9SY

Study participating centre

Addenbrooke's Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Sponsor information

Organisation
NHS Tayside

Sponsor details
Level 3 Residency block
Ninewells Hospital
Dundee
Scotland
United Kingdom
DD1 9SY
+44 (0)1382383297
tascgovernance@dundee.ac.uk

Sponsor type
Hospital/treatment centre

Website
http://www.nhstayside.scot.nhs.uk/index.htm

ROR
https://ror.org/000ywep40

Funder(s)

Funder type
Charity

Funder Name
Association of Breast Surgery

Alternative Name(s)
British Association of Surgical Oncology, ABS, BASO

Funding Body Type
Government organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Results and Publications

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

Intention to publish date
31/03/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to the patients have not consented for this.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol file	version 1	06/10/2021	16/08/2023	No	No
Other unpublished results		19/03/2024	11/04/2024	No	No