

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

<b>Submission date</b> 02/12/2021	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 08/12/2021	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 03/10/2025	<b>Condition category</b> Cancer	<input type="checkbox"/> 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

Vasileios.Pitsinis@nhs.scot

## Contact information

### Type(s)

Scientific

### Contact name

Mr Vassilis Pitsinis

### Contact details

Breast Unit

Ninewells Hospital

Dundee

United Kingdom

DD1 9SY

+44 (0)1382 660111

Vasileios.Pitsinis@nhs.scot

# Additional identifiers

## Clinical Trials Information System (CTIS)

Nil known

## Integrated Research Application System (IRAS)

301478

## ClinicalTrials.gov (NCT)

Nil known

## Protocol serial number

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

## Study type(s)

Diagnostic

## 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(s)**

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

## **Key secondary outcome(s)**

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

## **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

## **Healthy volunteers allowed**

No

## **Age group**

Adult

**Lower age limit**

18 years

**Sex**

Female

**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**

United Kingdom

England

Scotland

**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

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

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?
<a href="#">Results article</a>		01/12/2024	03/10/2025	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Other unpublished results</a>		19/03/2024	11/04/2024	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Protocol file</a>	version 1	06/10/2021	16/08/2023	No	No