

A way to avoid unnecessary sentinel node biopsies in patients with ductal cancer in situ

Submission date 06/11/2016	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 15/11/2016	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 07/03/2019	Condition category Cancer	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Ductal cancer in situ is a type of breast cancer in which the malignant cells are located in the milk ducts but have not yet breached and invaded to the surrounding tissues. It accounts for about 10% cases of breast cancers and is mostly detected by mammography (breast x-ray) as it does not typically form a palpable lump. As it is confined to the milk ducts, it cannot spread further to the lymph nodes or distant organs. Therefore, a biopsy (tissue sample) to assess the nodes in the axilla (armpit) is not considered mandatory. However, about 20 to 30% of cases with a diagnosis of DCIS before surgery are then found to have an invasive cancer in the surgical specimen. These patients have to undergo an axillary biopsy (sentinel node biopsy or SNB), in which the first node to which the lymph from the breast is drained (the sentinel node) is found and removed. The node is traditionally identified by injecting a radioactive substance (radioisotope) and blue dye into the breast and following the lymph vessels all the way to the sentinel node. Until now, there is no 100% accurate method to predict which patients with DCIS will be found to have invasive breast cancer after surgery. Current practice suggests that an SNB should be considered either in patients who are planned for a mastectomy (breast removal), since the SNB will not be as feasible after that, or to patients with certain aggressive symptoms, since they are most likely to have an undiagnosed invasive cancer. However, in that way, DCIS patients undergo unnecessary biopsies, resulting in side effects such as arm and shoulder pain, constricted range of motion and swelling (lymphedema), longer operative times and increased costs. Superparamagnetic Iron Oxide (SPIO) nanoparticles are a new tracer where the principle of magnetism is used to detect the sentinel node. The aim of this study is to find out whether using SPIO as a tracer avoids unnecessary SNBs in patients with DCIS.

Who can participate?

Patients with DCIS undergoing breast-conserving surgery or mastectomy

What does the study involve?

SPIO are injected at the first operation and the sentinel node is not removed. If invasive cancer is found, then the patient is taken to theatre for an SNB. If this is the case, all three methods (SPIO, isotope and blue dye) are used for the detection of the sentinel node. The aim is to see how

many patients are spared unnecessary procedures and the possible impact of that in breast cancer service units. Additionally, the feasibility of sentinel node detection in the second operation is also investigated.

What are the possible benefits and risks of participating?

The benefits of taking part in the study are that an unnecessary operation in the axilla with arm and shoulder restriction, pain, numbness and swelling can be avoided. Potential drawbacks include the very rare case (<1%) of missing an invasive cancer in the specimen that might have spread to the node. However, recent data from the USA have shown that patients with DCIS who did not undergo any form of axillary surgical evaluation had comparable survival to those who underwent axillary surgery. No financial compensation will be involved for participating in the study.

Where is the study run from?

1. Uppsala University Hospital (Sweden)
2. Västmanland County Hospital (Sweden)
3. Norrlands University Hospital (Sweden)
4. Gothenburg University Hospital (Sweden)
5. Kalmar County Hospital (Sweden)

When is the study starting and how long is it expected to run for?

April 2015 to December 2021

Who is funding the study?

Uppsala University (Sweden)

Who is the main contact?

Dr Andreas Karakatsanis
andreas.karakatsanis@surgsci.uu.se

Contact information

Type(s)

Scientific

Contact name

Dr Andreas Karakatsanis

ORCID ID

<https://orcid.org/0000-0003-3622-3575>

Contact details

Akademiska Sjukhusvägen ing 70

Uppsala

Sweden

751 85

+46 (0)765 864 826

andreas.karakatsanis@surgsci.uu.se

Additional identifiers

Protocol serial number

SentiNot

Study information

Scientific Title

The use of superparamagnetic iron oxide particles as a tracer to avoid unnecessary sentinel node biopsies in patients with a preoperative diagnosis of ductal cancer in situ

Acronym

SENTInel node biopsy in ductal cancer in situ; how to NOT do it (SENTINOT)

Study objectives

In Sweden, approximately 800 patients with DCIS are diagnosed each year. More than 50% of these patients undergo a sentinel node biopsy (SNB). As an in situ cancer by definition has not metastasized these SNBs are basically unnecessary. The preoperative investigation (mammography and core needle biopsy) can often signal which cases are DCIS. However, in some 15-20% of the cases, an invasive tumour component is diagnosed at the final histopathological examination of the specimen after surgery. Performing a SNB at a second operation has been considered less reliable as the lymph drainage is affected by the previous surgery and it has been considered impossible after a mastectomy since the location of the primary tumour cannot be established, and the lymphatic drainage is distorted. Also, if a SNB is performed and the patient develops a local recurrence the possibility to successfully perform a second SNB is decreased. The aim of this study, therefore, is to find a way to avoid unnecessary SNBs in patients with ductal carcinoma in situ (DCIS).

Ethics approval required

Old ethics approval format

Ethics approval(s)

Uppsala University Ethics Committee, 13/04/2015, ref: 2014:073

Study design

Prospective single-arm observation cohort

Primary study design

Observational

Study type(s)

Diagnostic

Health condition(s) or problem(s) studied

Ductal Cancer in Situ (DCIS)

Interventions

Sienna+ (2ml + NaCl 3ml) will be injected in association with the primary breast surgery on patients with a preoperative diagnosis of DCIS. The Sienna+ is injected close to the tumour, subcutaneously. The sentinel node (SN) is uploaded with Sienna+ but is not removed. The counts by SentiMag is measured transcutaneously at the end of the procedure.

The patient is scheduled for a visit to the breast unit within 2 weeks after surgery. If there is an invasive tumour component on the final histopathological examination, a sentinel node biopsy (SNB) will be performed at a second operation within 1-2 weeks. A preoperative injection of radioisotope will be made to maximize the chance to detect the SN.

This SNB will start with a registration of the magnetic- and isotope signal in the axilla, and the incision will be placed in relation to the signal. If no activity is measured, an injection of 1 ml Patent Blue Dye will be made in the area of the breast where the tumour was located. After a sufficient waiting time, 5-10 minutes, a small incision will be made in the lower part of the axilla, and careful dissection will be made to identify lymphatic vessels and lymph nodes. After a mastectomy, the lateral part of the earlier incision is used. If no SN is found, an axillary clearance or sampling will follow, according to the surgeon's decision. The SN will be sent for frozen section in order to avoid a third operation if SN metastases are present.

Intervention Type

Procedure/Surgery

Primary outcome(s)

Number of SNB procedures spared, defined as those cases of patients with a definite postoperative diagnosis of pure DCIS in whom no SNB will be performed

Key secondary outcome(s)

SNB detection rate in a second operation, defined as the number of successful SNBs for each patient and for each method (SPIO, isotope and blue dye) divided by the total amount of SNBs performed

Completion date

30/08/2021

Eligibility

Key inclusion criteria

1. Patients with a preoperative diagnosis of DCIS grade 3 any size or, DCIS grade 2 larger than 20 mm on mammography and planned for breast conserving surgery (BCS)
2. Patients with a preoperative diagnosis of DCIS, any grade and any size, planned for mastectomy

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Sex

All

Key exclusion criteria

1. Patients undergoing a direct reconstruction with autologous tissue
2. Intolerance/hypersensitivity to iron or dextran compounds or Sienna+
3. Patients with an iron overload disease
4. Patients with pacemakers or other implantable devices in the chest-wall, or prosthesis in the shoulder
5. Patient deprived of liberty or under guardianship
6. Pregnant or lactating patients

Date of first enrolment

01/05/2015

Date of final enrolment

30/12/2020

Locations

Countries of recruitment

Sweden

Study participating centre

Uppsala University Hospital

Uppsala

Sweden

751 85

Study participating centre

Västmanland County Hospital

Sweden

721 89

Study participating centre

Norrlands University Hospital

Umeå

Sweden

901 85

Study participating centre

Gothenburg University Hospital

Sweden

413 45

Study participating centre
Kalmar County Hospital
Sweden
391 85

Sponsor information

Organisation
Uppsala University

ROR
<https://ror.org/048a87296>

Funder(s)

Funder type
University/education

Funder Name
Uppsala Universitet

Alternative Name(s)
upsalauni, Uppsala Universitet, Sweden, Uppsala University, UU

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Sweden

Results and Publications

Individual participant data (IPD) sharing plan

The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	11/04/2019		Yes	No