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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

Registration date
15/11/2016

Overall study status
Completed

Last Edited
07/03/2019

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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
http://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

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Secondary study design
Cohort study

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
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 transcutanously 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 measure
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

Secondary outcome measures
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

Overall study start date
01/04/2015

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

Age group
Adult

Sex
Both

Target number of participants
300

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

Sponsor details
Box 256
Uppsala
Sweden
751 05

Sponsor type
University/education

Website
uu.se

ROR
https://ror.org/048a87296

Funder(s)

Funder type
University/education

Funder Name
Uppsala Universitet

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

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
Sweden

Results and Publications

Publication and dissemination plan
A pre-planned interim analysis is planned until 30/06/2018.
For full trial results, planned publication in a high-impact peer reviewed journal is intended approximately on 30/04/2022.

Intention to publish date
30/04/2022

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