Sentinel Lymph Node Mapping in Breast Cancer Patients Through Fluorescent Imaging Using Indocyanine Green: The INFLUENCE Trial

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The detection rate of the ICG method to identify the SLN in breast cancer patients is not inferior to the standard 99mTc method.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	Breast therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON29593

Source
Nationaal Trial Register

Brief title
INFLUENCE trial

Condition

- Breast therapeutic procedures

Health condition

Breast cancer

Research involving
Human

Sponsors and support

Primary sponsor: St. Antonius Hospital
Source(s) of monetary or material Support: St. Antonius Innovatiefonds 2019: € 45.000,- (for the lease of the fluorescent camera and medicine)

Intervention

- Surigical procedure

Explanation

Outcome measures

Primary outcome

Identification rate of SLNs by the fluorescent signal of ICG and by 99mTc.

Secondary outcome

- Number of lymph nodes identified with ICG and standard 99mTc. - Percentage of patients in whom fluorescent SLNs were identified of the total patients with identified SLNs by the standard 99mTc. - Percentage of SLNs that is fluorescent, but not positive for 99mTc. - Percentage of SLNs that are not fluorescent but positive for 99mTc. - Pathology of SLN found by ICG and 99mTc including micro- and macro metastasis and isolated tumor cells (ITCs). - Percutaneous intraoperative visualization of the SLN and lymph drainage with the camera by ICG before skin incision: yes, weak, no; only lymph vessel, no both lymph vessel and node are not visible. - Detection time: average time between skin incision and SLN resection in minutes. - Complication rates from the SN procedure by ICG and 99mTc, including lymph edema, (wound)infection, (temporarily) skin discoloring, bleeding and a mild allergic reaction.* - Number of serious adverse events from ICG and 99mTc, including severe allergic reaction, death or other serious adverse events as described in chapter 9.

Study description

Background summary

Rationale: Identifying lymphatic metastases is an important prognostic factor in the survival rate of breast cancer and the presence of lymphatic metastases carries consequences for further treatment. The golden standard for obtaining the SLN in patients with breast cancer is radio guided surgery with radioisotope technetium (99mTc). However, the use of 99mTc may present adverse effects and logistical challenges. A promising alternative method is the use of fluorescence imaging using indocyanine green (ICG). It is non-ionizing, easy to apply, patient- and surgeon friendly, safe, easy to obtain and cost-effective. Objective: In this non-

inferiority study, we aim to identify the diagnostic value of indocyanine green (ICG) fluorescence imaging for SLN mapping versus the standard-of-care 99mTc in the SLN procedure for breast cancer patients. Study design: This is a single institution, single arm diagnostic efficacy trial identifying the diagnostic value of indocyanine green (ICG) fluorescence imaging for SLN mapping versus the standard-of-care radioisotope technetium (99mTc) in the SLN procedure for breast cancer. Study population: Women with breast cancer who are admitted to the St. Antonius Hospital. Inclusion criteria include clinically node-negative, invasive early T1 or T2 breast cancer conformed by biopsy, preoperative axillary ultrasound to confirm clinical node-negative status and indication for lumpectomy with SLN procedure. Intervention: All included patients will receive standard of care implying 99mTc injection the day before surgery. Consequently, 5 mg (2 ml) ICG will be injected periareolar after administration of general anaesthesia and before incision. The lymphatic vessels and sentinel lymph node will be visualized by fluorescent imaging usng the Fluobeam800 © camera. A surgically considered incision in the axilla is made while taking into account the marker of the ICG hotspots. Then the excised nodes are tested for 99mTc activity with the standard gamma detecting probe as control. Lastly, the axilla will be explored with the standard gamma-probe for residual lymph nodes, and by common sight and palpation as a control. Main study parameters/endpoints: Identification rate of SLNs by the fluorescent signal of ICG compared to the standard of care 99mTc.

Study objective

The detection rate of the ICG method to identify the SLN in breast cancer patients is not inferior to the standard 99mTc method.

Study design

Intraoperative, postoperative (pathology outcomes) and short term complications, and for complications such as lymph edema 6 months postoperatively.

Intervention

All included patients will receive standard of care implying 99mTc injection the day before surgery. Consequently, 5 mg (2 ml) ICG will be injected periareolar after administration of general anaesthesia and before incision. The lymphatic vessels and sentinel lymph node will be visualized by fluorescent imaging usng the Fluobeam800 © camera. A surgically considered incision in the axilla is made while taking into account the marker of the ICG hotspots. Then the excised nodes are tested for 99mTc activity with the standard gamma detecting probe as control. Lastly, the axilla will be explored with the standard gamma-probe for residual lymph nodes, and by common sight and palpation as a control.

Contacts

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Eligibility criteria

Age
Adults (18-64 years)
Adults (18-64 years)
Elderly (65 years and older)
Elderly (65 years and older)

Inclusion criteria

- Clinically node-negative, invasive early T1 or T2 breast cancer confirmed by biopsy. - Preoperative axillary ultrasound to confirm clinical node-negative status. - Indication for lumpectomy and SLN procedure. - Written informed consent according to ICH/GCP and national regulations.

Exclusion criteria

- Patients < 18 years old. - Mastectomy. - Known allergy for indocyanine green (ICG) or radioisotope technetium (99mTc) or intravenous contrast, iodine, shellfish. - Other concurrent or history of other solid tumor. - Hyperthyroidism or thyroid cancer. - T3 breast cancer confirmed by biopsy. - Palliative surgery for locally advanced breast cancer (cT4). - Pregnancy or breast feeding. - Psychological, familial, sociological or geographical factors that could potentially hamper compliance with the study protocol.

Study design

Design

Study phase: 4

Study type:	Interventional
Intervention model:	Single
Allocation:	Non controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-08-2020
Enrollment:	100
Type:	Actual

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion

Date:	17-02-2020
Application type:	First submission
Review commission:	Medical Research Ethics Committees United (MEC-U) Postbus 2500 3430 EM Nieuwegein 088 320 8784 info@mec-u.nl

Study registrations

Followed up by the following (possibly more current) registration

ID: 49864
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL8402
CCMO	NL71617.100.19
OMON	NL-OMON49864

Study results

Results posted: 31-07-2023

Actual enrolment: 102

Summary results

"Objective: The aim was to compare the (sentinel) lymph node detection rate of indocyanine green (ICG)-fluorescent imaging versus standard-of-care 99m Tc-nanocoilloid for sentinel lymph node (SLN)-mapping.

Background: The current gold standard for axillary staging in patients with breast cancer is sentinel lymph node biopsy (SLNB) using radio-guided surgery using radioisotope technetium (99m Tc), sometimes combined with blue dye. A promising alternative is fluorescent imaging using ICG.

Methods: In this noninferiority trial, we enrolled 102 consecutive patients with invasive early-stage, clinically node-negative breast cancer. Patients were planned for breast conserving surgery and SLNB between August 2020 and June 2021. The day or morning before surgery, patients were injected with 99m Tc-nanocolloid. In each patient, SLNB was first performed using ICG-fluorescent imaging, after which excised lymph nodes were tested with the gamma-probe for 99m Tc-uptake ex vivo, and the axilla was checked for residual 99m Tc-activity. The detection rate was defined as the proportion of patients in whom at least 1 (S)LN was detected with either tracer.

Results: In total, 103 SLNBs were analyzed. The detection rate of ICG-fluorescence was 96.1% [95% confidence interval (95% CI)=90.4%-98.9%] versus 86.4% (95% CI=78.3%-92.4%) for 99m Tc-nanocoilloid. The detection rate for pathological lymph nodes was 86.7% (95% CI=59.5%-98.3%) for both ICG and 99m Tc-nanocoilloid. A median of 2 lymph nodes were removed. ICG-fluorescent imaging did not increase detection time. No adverse events were observed.

Conclusions: ICG-fluorescence showed a higher (S)LN detection rate than 99m Tc-

nanocoilloid, and equal detection rate for pathological (S)LNs. ICG-fluorescence may be used as a safe and effective alternative to 99m Tc-nanocoilloid for SLNB in patients with early-stage breast cancer."

Adverse events
No ICG-related adverse events.