

Implementation of fluorescent imaging using indocyanine green to identify sentinel lymph nodes during surgery for breast cancer.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON57101

Source

ToetsingOnline

Brief title

INFINITE trial

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym

Breast cancer, breast carcinoma

Research involving

Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis

Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Breast cancer, ICG, Implementation, Sentinel lymph node

Outcome measures

Primary outcome

Study endpoints are categorized into actual and anticipated implementation outcomes, client outcomes, and service outcomes. The primary endpoint is adoption, an actual implementation outcome, evaluated by the proportion of SLN procedures conducted with ICG only, Tc99 only, or both during Phase III, compared to the total SLN procedures in this phase using screening logs and hospital records.

Secondary outcome

All other outcomes are secondary. Fidelity, another actual implementation outcome, is measured through an intraoperative survey. Anticipated implementation outcomes such as appropriateness, feasibility, and acceptability are evaluated via a healthcare provider survey during Phase III. Client outcomes evaluate patient satisfaction through a survey sent to patients following their SLN procedure. Service outcomes encompass effectiveness, safety, cost-effectiveness, and the impact on necessary personnel, evaluated using perioperative data and hospital administration data.

Study description

Background summary

Breast cancer affects one in seven women. Detecting lymph node metastases via the sentinel lymph node (SLN) procedure is crucial for prognosis and treatment. The gold standard is a radio-guided surgery using radioactive technetium (Tc99), requiring preoperative injection and lymphoscintigraphy. However, the use of Tc99 poses significant burdens on patients, as it requires additional hospital visits or travel to different hospital due to the limited availability of nuclear medicine facilities. Tc99 also creates logistical challenges and lacks sustainability. A recently proven, equally effective and safe alternative method is peroperative real-time fluorescence imaging using Indocyanine Green (ICG). ICG offers many advantages over Tc99 to patients, health care providers, and society. Yet, the use of ICG for the SLN procedure remains limited, as hospitals face challenges due to uncertainty in transitioning and limited familiarity with recent findings. Implementation guidance is imperative for effective adoption, to avert (further) practice variation and to ensure patients benefit from this evidence-based alternative method.

Study objective

The INFINITE trial aims to successfully implement ICG-fluorescence for identifying the SLN by: 1) guiding the implementation process using the Effective Implementation of Change model developed by Grol and Wensing; 2) identifying and understanding the factors influencing implementation outcomes (i.e., barriers and facilitators), through the use of CFIR (Consolidated Framework for Implementation Research) determinants framework; 3) evaluating the outcomes of implementation efforts using a mixed methods approach and following the outcomes framework proposed by Proctor et al. 4) creating conditions for nationwide implementation. Secondary aims to guide implementation and create conditions for nationwide implementation (the proposed implementation program) include: 1) develop a uniform medical protocol for the use of ICG for the SLN procedure; 2) develop an implementation guide that aligns with current practice 3) develop educational materials for surgeons, modules for the curriculum of surgical residents (CASH), patient information materials and organizing interactive meetings (workshops) for surgical health care providers and their teams; 4) further substantiating the effectiveness, safety, cost-effectiveness and impact on necessary FTE*s of personnel. 5) disseminate and engage, increasing support and create a sense of urgency for ICG implementation by organizing informational sessions during annual conferences of the scientific associations; 6) Facilitate the scaling up of the implementation of the ICG for the SLN procedure to all hospitals in the Netherlands by incorporating ICG into the SLN guidelines.

Study design

ICG will be implemented in seven strategically chosen Dutch hospitals during the INFINITE trial. These hospitals have been selected to represent different areas, settings and sizes, ensuring broad applicability and support for

subsequent nationwide implementation.

The INFINITE trial is a multicenter hybrid effectiveness implementation study that employs a stepped-wedge cluster randomized trial design across three phases: Phase I) pre-implementation (Tc99); Phase II) transition period (Tc99 and ICG); Phase III) post-implementation (ICG).

Clusters will transition to the next phase at fixed intervals of three months when the randomization order dictates, creating an iterative learning cycle.

This approach allows for regular evaluations of the implementation strategies, process and products (protocol, implementation guide, educational materials and patient information). Process evaluations will inform adjustments using the ERIC-CFIR matching tool, ensuring swift integration of lessons learned to enhance implementation in the next cluster.

Intervention

Phase I (pre-implementation): SLN procedure with the standard of care using Tc99, which implies Tc99 injection and lymphoscintigraphy the day or the morning before surgery, followed by radio-guided surgery with a gamma-detection probe.

Phase II (transition period): SLN procedure using ICG and controlled by Tc99. Patients receive Tc99 injection and lymphoscintigraphy before surgery, with the surgeon blinded for imaging results. During surgery, after administration of general anesthesia and before axillary incision, 5mg (2 ml) ICG will be injected periareolar. The SLN procedure is performed with fluorescent imaging of ICG using a fluorescence camera. After excision of the SLN(*s), the standard gamma detecting probe is used to test the excised nodes and the axilla for Tc99 activity as control. The axilla will also be explored by common sight and palpation.

Phase III (post-implementation): SLN procedure using ICG as single tracer. 5 mg (2 ml) ICG will be injected periareolar after administration of general anesthesia and before axillary incision. The sentinel lymph node will be visualized by fluorescent imaging using a fluorescence camera and excised.

Study burden and risks

Consenting patients will not experience any extra burden from ICG-fluorescence. ICG will be administered under general anesthesia, so patients will not experience extra discomfort, neither do they need extra site visits or additional proceedings. ICG is safe to use: it is nonionizing and knows little to no complications and adverse events. Considering a cut-off of 2 additional nodes, the preferable topographic location of these nodes and the clinical experience with additional lymph node sampling, we expect no increase in risk of surgical morbidity. Patients might benefit from the intervention as ICG can increase the identification rate and the lack of a pre-operative visit to the

Nuclear Medicine department for technetium injection. Filling out the questionnaire regarding patient satisfaction of the SLN-procedure which will take up about 10 to 15 minutes only. Thus, both risks and burden are negligible.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

- Patients \geq 18 years old.
- DCIS or invasive breast cancer, confirmed by biopsy
- Clinically node-negative (cN0), confirmed by preoperative axillary ultrasound
- Indication for breast cancer surgery with sentinel lymph node biopsy via axillar incision

- Written informed consent according to ICH/GCP and national regulations.

Exclusion criteria

- Combined MARI procedure
- Known allergy for Indocyanine Green (ICG), intravenous contrast or iodine
- History of axillary lymph node dissection
- Hyperthyroidism or thyroid cancer
- Pregnancy or breast-feeding
- Psychological, familial, sociological or geographical factors that could potentially hamper compliance with the study protocol

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL	
Recruitment status:	Pending
Start date (anticipated):	01-12-2024
Enrollment:	2490
Type:	Anticipated

Medical products/devices used

Registration:	No
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Ethics review

Approved WMO
Date: 06-11-2024
Application type: First submission
Review commission: MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
CCMO	NL87551.100.24