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	Recruiting
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional research previously applied in human subjects

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: St. Antonius Ziekenhuis

Source(s) of monetary or material Support: ZonMw

Intervention

- Surigical procedure

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

Explanation

N.a.

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 trail 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, and cost-effectiveness. 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 trial design across three phases: Phase I) pre-implementation (Tc99); Phase II) transition period (Tc99 and ICG); Phase III) post-implementation (ICG). Based on site readiness and in consultation with the participating centers, three clusters will be formed, each consisting of two or three hospitals. Clusters will transition to the next phase at fixed intervals of three months, 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 preoperative 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

Trial sites in the Netherlands

Diakonessenhuis Utrecht
Target size: 175

Ziekenhuisgroep Twente
Target size: 355

Alrijne Ziekenhuis
Target size: 290

Canisius Wilhelmina Ziekenhuis
Target size: 325

Spaarne Gasthuis
Target size: 355

Dijklander Ziekenhuis
Target size: 290

Noordwest Ziekenhuisgroep
Target size: 410

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Patients >= 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 biospy 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 phase:	N/A
Study type:	Interventional research previously applied in human subjects
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Other type of control
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-04-2025
Enrollment:	1760
Duration:	1 months (per patient)
Type:	Actual

Medical products/devices used

Product type:	N.a.
Registration:	No

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N.a.

Ethics review

Approved WMO Date:	06-11-2024
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-06-2025
Application type:	Amendment
Review commission:	MEC-U

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
Research portal	NL-005321