Evaluation of a Clinical Prototype Near-InfraRed Fluorescence (NIRF) Imaging Device for Sentinel Lymph Node (SLN) Detection in Breast Cancer: a Technical Feasibility Study

Published: 29-05-2009
Last updated: 08-05-2024

Ergonomics and function of the imaging system - the NIRF imaging system should not interfere with the standard Sentinel Lymph Node mapping procedure and used safely by the surgeon while detection of ICG takes place. Duration: 1,5 hour clinical...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Observational non invasive

Summary

ID

NL-OMON31831

Source
ToetsingOnline

Brief title
Sentinel node detection with NIRF

Condition

- Breast neoplasms malignant and unspecified (incl nipple)
- Therapeutic procedures and supportive care NEC

Synonym
breast cancer, sentinel node procedure

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: BREAST CANCER, FLUORESCENCE IMAGING, INTRAOPERATIVE, SENTINEL NODE

Outcome measures

Primary outcome

Primary Objective:

• Ergonomics and function of the imaging system - the NIRF imaging system

should not interfere with the standard Sentinel Lymph Node mapping procedure

and used safely by the surgeon while detection of ICG takes place. Duration:

1,5 hour clinical procedure

Secondary outcome

Secondary Objective(s):

• The secondary endpoint of this feasibility study is the number and location

of detected sentinel lymph nodes compared to the standard detection of sentinel

lymph nodes with the use of patent blue and technetium-99 labelled colloid.

Study description

Background summary

Breast cancer is the most common form of cancer and second leading cause of death in women in Europe and the USA, with 450,000 new cases and 120.000 deaths yearly. Over the last thirty years, wide-spread mammographic screening, technological developments and raised physicians- and self-awareness have led to a rapid increase in the diagnosis of small, non-palpable breast cancer. Surgery of primary breast cancer is dependent on the resection of the primary tumor and identification of cancer spread to lymph nodes (LNs), both

independent prognostic factors for survival and recurrence of disease. The mapping of LNs and/or removal of suspicious LNs is a mainstay of minimally invasive cancer staging. For identification of tumor involvement in axillary lymph nodes (ALNs), the first-draining node, also denominated as the sentinel lymph node (SLN) is analyzed by histology. A cancer-free SLN indicates, with high certainty, absence of spread in the ALNs. Conversely, it is common practice that a positive SLN is followed by a lymphatic clearance without knowledge whether there is tumor involvement in the remaining LNs. Currently, the SLN is the only involved ALN in 57% of breast cancer patients with SLN metastases. Moreover, in case of an affected ALN, approximately 70% patients have non-metastatic remaining ALNs as determined after lymphatic clearance. Therefore, non-affected ALNs are often needlessly removed because the surgeons lack real-time information about the status of these LNs. In case of a SLN metastases of >2 mm , an additional axillary lymph node (ALN) dissection is performed during a secondary procedure, with 57% of the remaining axillary lymph nodes are negative by definitive histopathological examination . If a SLN contains a so-called micrometastases, (2mm - 0.2mm, ~25% of all SLN procedures), this number increases to 70-80% of ALNs negative for metastases. As such, the SLN procedure, although highly specific and sensitive, leads to substantial over-treatment in breast conserving therapy. In addition, this carries the risk of nerve injury, lymphedema, and decreased arm motion and seroma formation. Since breast sparing lumpectomy combined with radiotherapy is generally sufficient as a treatment for T1-T2 breast tumours in appropriately selected patients, breast conserving therapy (BCT) has become the standard treatment. BCT is considered to be less stressful compared to radical mastectomy and offers better cosmetic results and reduced wound infection risk. The most important disadvantage of BCT is the life-long risk for local recurrence of the primary tumour, in which case additional surgery is necessary. According to the Dutch guidelines for patients with palpable breast cancer stage I and II, diagnostics should be aimed at determination of the disease stage by staging of the locoregional process and if necessary axillary lymph node status and dissemination studies. In patients with palpable invasive breast cancer (stage I and II) the current guidelines advise preoperative imaging with endosonography, mammography or magnetic resonance imaging. In case of breast conserving treatment the aim of the procedures is to obtain optimal locoregional control with optimal cosmetic results. In this policy, the sentinel node (SLN) procedure is the current standard for staging of locoregional lymph node metastases in breast cancer patient with T1-2N0 status. Best results for detection of the SLN are obtained by injection of a radiocolloid and intraoperative injection of Patent Blue. New innovative imaging modalities like NIRF imaging intend to improve the detection of remaining axillary lymph nodes to be positive for tumor metastases simultaneously with the SLN. This may decrease the possibility of over-treatment in patients with T1-2N0 tumor status, and ultimately leading to decreased costs .

Study objective

Ergonomics and function of the imaging system - the NIRF imaging system should not interfere with the standard Sentinel Lymph Node mapping procedure and used safely by the surgeon while detection of ICG takes place. Duration: 1,5 hour clinical procedure.

Study design

Interventional study: a phase 0 technical feasibility study / non-randomized, open label, uncontrolled, single group assignment.
The study will be carried out in collaboration with the Technical University of Munich, Institute of Biological and Medical Imaging. The actual study will be carried out at the University Medical Center Groningen, Department of Surgery.

The study protocol is designed as follows:
1. Selection of patients with operable histology proven invasive breast cancer (T1-2cN0-1) are asked for participation and informed consent at the outpatient clinic for the proposed study if the apply to the inclusion criteria. Copies of the proposed study protocol are available at the outpatient clinic. Patients have at least 24 hours to decide whether they want to participate or not.
2. After approval and documented informed consent, a pregnancy test is performed and in case of a positive test the patient cannot be included. Next, the operative procedure is planned together with the NIRF imaging protocol. The pharmacist of the UMCG is informed of inclusion of the patient together with the planned date of operation for delivery of ICG.
3. at the day of admission (one day prior to surgery), the standard surgical procedure for lumpectomy, and the standard SLN procedure combined with ICG intratumoral injection in the operating room (OR) is again explained to the patient. The Department of Nuclear Medicine and Molecular Imaging at the UMCG will deliver the radioactive tracer for detection of the SLN.
4. at the day of surgery, the ICG compound will be delivered by the Hospital Pharmacy at the OR for intratumoral injection.
5. during anesthesia ICG will be injected with a dose of 0.5 mg (i.e. 1 ml of volume in a dose of 0.5 mg/ml).

Study burden and risks

The burden associated with participation consists of an additional injection of indocyanin green (ICG) intratumoral besides patent blue during anaesthesia for the detection of the SLN. Additionally, there is a chance of longer operative procedure by using a NIRF imaging camera (~30 minutes).
1. The possible most serious adverse event for injection of ICG is an allergic and anaphylactic reaction.
2. The possible effect of prolonged anesthesia because of testing the camera system and detection of the SLN is limited in itself because of a total time

of no longer than 2 hours.
3. There is no risk or burden of using the intraoperative imaging device, all necessary test for use of electrical devices in the OR are covered.
4. There is no risk of infection; the imaging device will be covered by special designed sterile drapes to prevent the risk of infection during a surgical procedure.

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

Women above the age of 21 who have biopsy-proven breast cancer, and who are undergoing sentinel lymph node mapping for staging and treatment of their disease.

Exclusion criteria

Pregnant women, significant renal (creatinine >, cardiac, or pulmonary disease (ASA III-IV), History of iodine allergy or anaphylactic reactions to insect bites or medication, presence or history of hyperthyroidism.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-09-2009
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ICG Pulsion ®
Generic name:	indocyanin green
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	29-05-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO

Date:	30-05-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2008-002370-34-NL
CCMO	NL23130.042.08