MagSNOLL: Magnetic Sentinel Node and Occult Lesion Localisation: A feasibility study using magnetic nano particles for sentinel node biopsy and localization of occult breast cancers.

Published: 09-10-2014
Last updated: 15-05-2024

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

Summary

ID

NL-OMON44817

Source
ToetsingOnline

Brief title
MagSNOLL Multicentre study

Condition

- Breast neoplasms malignant and unspecified (incl nipple)
- Breast disorders
- Breast therapeutic procedures

Synonym
1) Sentinel Lymph Node metastases and Occult lesion localisation in breast cancer patients.
2) Cancer in Sentinel Lymph nodes

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Twente
Source(s) of monetary or material Support: Technology Strategy Board CR&D - Biomedical Catalyst: Feasibility Award

Intervention

Keyword: Occult Lesion Localisation, SentiMag, Sentinel Lymph Node Biopsy, Sienna+

Outcome measures

Primary outcome

Primary endpoint: 1) Successful localisation (Confirmation that *peak* SentiMag

TM readings correspond to centre of the excised lesion on specimen radiograph).

Secondary outcome

Secondary endpoints: 1) Margin involvement 2) re-operation rates 3) SLNB

success rates (magnetic technique +/- blue dye and standard technique) 4)

Volume of specimen 5) Weight of specimen 6) Operative time 7) Complications 8)

Radiological localisation time 9) Patient recorded outcome measures. 10) Cost

11) Accuracy of MRI for the localization of SLNs.

Study description

Background summary

The MagSNOLL Multicentre Trial is a continuation of two earlier conducted studies (SentiMAG and MelaMAG Trial). The initial clinical pilot study was conducted by Chief Investigator, Mr. Michael Douek, at University College Hospital. Ten patients with newly diagnosed breast cancer scheduled for sentinel node biopsy were recruited prior to surgery. These patients received a radioisotope injection and underwent lymphoscintigraphy a day prior to surgery. On the morning of surgery, they received a subcutaneous injection and underwent

lymphoscintigraphy a day prior to surgery. On the morning of surgery, they received a subcutaneous injection of a SPIO tracer (Endorem, Guerbet, Paris) in the MRI Department. Dynamic axillary MRI before and after injection of the SPIO identified lymphatic tracts and sentinel nodes in 5/6 patients (1 scan failed for technical reasons).
Under general anesthetic, patients routinely received an intradermal injection of patent blue dye (Guerbet, Paris). The sentinel nodes were localized using both a gamma-probe and magnetometer prototype 1. Skin localization with magnetometer prototype 1 ands the gamma probe were identical. A total of 19 sentinel nodes were resected from 9 patients. Intra-operative localization using the combined technique was successful in detecting 19/19 (100%) nodes and using magnetometer prototype 1 alone in 19/19 (100%). Once found by the surgeon, most sentinel nodes were easily identified as black from SPIO deposition.

Following the initial pilot study, several challenges were identified, including interference from large metal objects, the shape of the probe and the stability of the magnetic field. These were rectified and a second prototype was developed (prototype II). The Chief Investigator relocated to Guy's Hospital and a further 43 patients were recruited into an extended phase I/II trial. The overall ex-vivo SentiMAG Multicentre trial SLN detection rate was 86% (37/43 patients) and was higher in patients who received SPIO more than one hour prior to surgery (93%, 14/15 patients). Data on the laboratory performance of the CE-marked SentiMAG was performed successfully on the 6th Decembre 2010.

Study objective

The principal objective of the study is to determine if the performance of the new technique (magnetic tracer and magnetometer) is equivalent to the performance of the standard technique (patent blue dye and radioisotope, wire localization).

The primary objective of the MRI is to localize the SLN, the secondary objective of the MRI subprotocol is to determine if MRI can be used as an non-invasive method for identification of metastasis in lymph nodes.

Study design

The MagSNOLL Multicentre Trial is a phase II paired equivalence trial. The study will be coordinated from Kings's College Londen (Guy's Hospital) by the Chief Investigator Mr. Michael Douek. The trial aimed to recruit 160 patients. Patients will receive a radioisotope injection and a intra tumoral Sienna+ injection. In cetres that also participate in the MRI sub protocol, patients will undergo a pre-operative MRI after the injection of Sienna+. At the Medisch Spectrum Twente pre-operative MRI scans will be performed depending on the availability of the MRI scanning slots.

Intra-operatively, patients will receive an intradermal injection of patent blue (Guerbet, Paris). The occult lesion and all sentinel nodes detected intra operatively using the the SentiMAG will be excised and sent separately to the pathology department. Then the standard technique, the gamma probe, is used to see whether there is activity remained behind. This tissue will be removed and sent to the pathology department separately. The removed breast tissue will be checked for the presence of the hydrophilic clip marker, at the radiology department.

All lymph nodes will be assessed histologically and the nodal status will be related back to the SLNB detection rate with each technique.
Patients will be followed post-operatively (7-14 days after surgery) to assess if staining occurs or for any other adverse event. If staining is present, photographs will be taken. Further follow-up is at 3 months and at 1 year. Patients will be followed up for a total of 5 years, in accordance with current local policies.

Intervention

The Medisch Spectrum Twente and the ZGT will participate the standard protocol and the MRI sub protocol. As part of the MRI subprotocol, patients will undergo an MRI scan prior tho the scheduled operation. The scan will take roughly 30 minutes and involves lying down in a tubular scanner. After the intra-tumoral injection of 0,5ml Sienna+ several scans are performed. The scan may need to be repeated if the contrast is not yet visible at 2 or 24 hours after the initial scan, but further injections will not be required.

The operation will be performed as already planned by the surgeon. In addition to the normal patent blue and radioactive injection, an additional injection of Sienna+ and placing an hydrophilic clip marker is administered. During surgery, the sentinel nodes and occult lesion will be detected with the SentiMAG magnetometer. All excised nodes will be sent seperately to the pathology department.

Study burden and risks

As already mentioned in Section E9 of this form, there is a chance of developing skin discoloration (tattoo) after injection of Sienna+. However, this is a prevalent problem with the use of blue dye and not with the use of a magnetic tracer. In previous SentiMAG studies, we used a magnetic dye that is similar to Sienna+, called Endorem. Injection of Endorem resulted in minimal skin discoloration in only 6 of 51 patients.

Another potential risk might be the chance of developing adverse reactions to Sienna+. However, when similar materials to Sienna+ have been injected intravenously in significantly higher doses, less than 1% of the patients

exhibited adverse reactions, subcutaneous injection and the majority of the dose is intended to be surgically removed (with the cancer tissue and nodes) leaving only a small interstitial residue.

Sienna+ has been reviewed and tested as specified in EN 10993-1-2009 based on specified site of injection and showed no serious reaction after injection.

The great advantage of this method is the detection of the lymph nodes and the tumor without the use of radio-active substances. This is not only a benefit for the patients regarding the radiation, but has also logistical and administrative benefits for the hospital.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1) Patients (male or female) with histologically proven breast cancer visible on ultrasound and suitable for SLNB.
2) Patients available for follow-up for at least 12 months

Exclusion criteria

1) Intolerance / hypersensitivity to iron or dextran compounds or Sienna+.
2) Patients who cannot/ do not receive radioisotope for SLNB.
3) Patients with an iron overload disease
4) Patients with pacemakers or other implantable devices in the chest-wall.;Exclusion criteria MRI subprotocol:
1) Metallic splinters in the eye
2) Ferromagnetic haemostatic clips in the central nervous system.
3) Claustrophobia.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-11-2014
Enrollment:	60
Type:	Actual

Medical products/devices used

Generic name:	Sienna+ and SentiMAG

Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	09-10-2014
Application type:	First submission
Review commission:	METC Twente (Enschede)
Approved WMO Date:	17-11-2014
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	27-09-2016
Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	08-12-2017
Application type:	Amendment
Review commission:	METC Twente (Enschede)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 26455
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
Other	18397

Register	ID
CCMO	NL48593.044.14
OMON	NL-OMON26455