Non-invasive nodal staging in breast cancer with MRI Lymphography using gadofosveset; a pilot- study.

Published: 12-05-2011
Last updated: 27-04-2024

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

Summary

ID

NL-OMON36702

Source
ToetsingOnline

Brief title
Gadofosveset in breast cancer

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
Breast cancer, Lymph node metastases

Research involving
Human

Sponsors and support

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

Intervention

Keyword: (sentinel) lymph node, breast cancer, gadofosveset, MRI

Outcome measures

Primary outcome

The main study parameter will be the accuracy (sensitivity, specificity, NPV and PPV) of the MRL in predicting the involvement of metastases in the investigated lymph nodes. We will compare the results of the MRL with the pathological results of a negative SLNB or the ALND.

In cases with a positive MRL and negative SLNB, we will investigate if the MRL is really wrong, or that we probably found a case of a false negative SNLB procedure.

Secondary outcome

n.a.

Study description

Background summary

Lymph node status is one of the most important prognostic factors in breast cancer and is of particular value in choosing adjuvant therapy.
About 30% of breast cancer patients have histopathologically positive axillary lymph nodes.

Nowadays, all breast cancer patients undergo a mammography, breast ultrasound, histology, and a breast MRI. After the diagnosis breast cancer has been determined, the current nodal staging consists of an axillary ultrasound and possible cytologic or histologic punction followed by sentinel lymph node biopsy (SLNB) and/or an axillary lymph node dissection (ALND). After introduction of the MRL, first the accuracy has to be established. If MRL is equally accurate to the current nodal staging workup (most important is no false positive cases), skipping partly the SLNB and its histology might make this workup more efficient. So, accuracy will be researched by comparing the

current, invasive, nodal-staging with non-invasive MRL in relation to the golden standard, histological examination of the SLNB and/or ALND.

In addition, MRL might be able to detect extra-axillary lymph node metastases which could induce a change in treatment regimen for an unknown number of patients. Studies on a positive parasternal SLNB show a change in adjuvant treatment in 0.9% of the patients. Furthermore, it is known that the SLNB has a false negative rate of 9.8%. In this pilot study we will only investigate the axillary region with MRL. We know that a possible reason for a false negative SNLB is a low number of specimens removed during the SLNB procedure. MRL might be able to detect the nodes missed by SLNB.

Study objective

The aim of this pilot-study is to examine the accuracy of MRL compared to current nodal staging methods. We expect an acceptable accuracy of the MRL based on earlier studies with gadofosveset enhanced MRI in rectum cancer patients. A positive MRL could eventually replace the SLNB and the next step in the nodal staging of these patients should be an ALND. It is unlikely that the MRL can replace all SLNB*s considering the fact that it might not be able to detect nodal metastases smaller than 0.2mm. Detection of these metastases is crucial since they change adjuvant treatment regimen.

Study design

This pilot-study is designed as a single-center prospective cohort study. We plan to include 10 patients in this pilot-study. Patients will be recruited in the Maastricht Universitair Medisch Centrum (MUMC).
We expect a period needed to recruit of 5 months.

Beside the regular MRI with gadolinium contrast agent (Gadovist) patients will undergo an extra MRI with gadofosveset contrast agent at least 3 days later. With the MRI and coils used in this study we only investigate the axilla on the site of the breast cancer.

The accuracy of MRL will be determined on the basis of a node-to-node matching of imaged nodes to the definitive histopathology. The pathologic examination of the SNLB or ALND will be regarded as the golden standard for nodal involvement.

The pathologic examination will take place following the regular procedure. During microscopic examination each node will be recorded as benign, or isolated tumor cell (ITC) (pN0(i+)) (<= 0.2mm), or micrometastase (pN1mi) (0.2 <= 2.0mm) or macrometastase (pN1) (>2.0mm).
Overall nodal status will be reported following the regular procedure. With this result we can make the patient by patient analysis.

The results of the pathologic examinations will be compared to the results of the MRL. The MRL will be assessed by two radiologists, who will independently read all the images and they are blinded for earlier investigations. In the meantime they will receive feedback about the pathologic results, in order to make a learning curve possible.
Each lymph node visible on MRL will be scored as benign or malignant using a confidence level score (0= definitely benign, 1= probably benign, 2= possibly benign, 3= probably malignant, and 4= definitely malignant). Criteria for malignancy on gadofosveset-MRI will be low signal intensity and absence of a *relief* sign.
The diagnostic performance of gadofosveset-MRI will be analyzed on lesion by lesion basis and on patient by patient basis. In this way we can obtain precise validation of imaging findings with the underlying histopathology. The lesion by lesion results will be translated to a patient by patient validation in order to obtain a clinically more relevant assessment of the diagnostic performance on a patient basis.

Study burden and risks

The patient who participates in this study will undergo all regular investigations to come to a proper staging of the breast cancer. The current procedure on staging of breast cancer patients is extensive. The procedure includes in most cases a MRI scan of the breast. For this study we will perform an extra MRI with gadofosveset contrast agent of the breast and axilla a couple of days after the initial MRI scan. Further investigation needed for this study will not extra burdensome the patients, because all further procedures are already included in the regular treatment.

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

1. Patient with histopathologically confirmed invasive breast cancer about to undergo nodal staging.
2. Tumor must be a T2 according the TNM 6-classification.
3. Willing and able to undergo all study procedures
4. Has personally provided written informed consent.

Exclusion criteria

1. Age <18,
2. History of prior chemotherapy
3. History of prior radiotherapy of the surrounding areas of the axilla.
4. Pregnancy
5. Contra indications for MRI such as pacemaker, aneurysm clips or severe claustrophobia.
6. Allergy to any of the ingredients of Gadofosveset (Vasovist® /Ablavar®)
7. Being unable to give informed consent in person
8. Acute or chronic severe renal insufficiency (glomerular filtration rate <30 mL/min/1.73m2).
9. Acute renal insufficiency of any severity due to the hepato-renal syndrome or in the perioperative liver transplantation period.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-09-2011
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ablavar
Generic name:	Gadofosveset Trisodium
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	12-05-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-06-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-06-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	22-11-2011
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)
Approved WMO Date:	25-11-2011
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

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	EUCTR2011-000544-19-NL
CCMO	NL33426.068.11