Evaluation of a high-resolution dedicated hanging breast PET guided biopsy device for breast cancer diagnosis.

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The primary objective of the present study is to assess the feasibility and safety of a newly developed PET-guided breast biopsy system in breast cancer patients.

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

Summary

ID

NL-OMON42670

Source
ToetsingOnline

Brief title
MAMMOCARE

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breast cancer, breast malignancy

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Europese Unie,Oncovision

Intervention

Keyword: Biopsy, Breast, PET

Outcome measures

Primary outcome

Main study parameters

The main objective of the present study is to assess the feasibility and safety of 18F-FDG-guided biopsies using a high-resolution dedicated breast PET scanner (MAMMOCARE) in breast cancer patients.

1. Compare the F18-FDG uptake on the dedicated breast PET images with the conventional PET/CT images.

2. Analyse whether the biopsies of each patient contain enough tumor material for gene-expression and molecular subtyping analysis.

3. Check on the mammogram if the biopsy location (hydro-marker) corresponds with the location of the breast tumor.

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Secondary outcome

Secundary study parameters

1. Obtaining information about the duration of the 18F-FDG-guided biopsy

procedures

Outcome measure: The biopsy procedure starts when the patient lays on the MAMMOCARE bed and the first image acquisition starts. The biopsy procedure ends when the patient is allowed to stand up after the breast biopsies are taken.
The procedure time is expressed in minutes.

2. Comparison of the gene-expression and molecular subtyping between the breast biopsies taken from the tumour region with the highest 18F-FDG uptake and the tumour border.

Outcome measure: Comparing ER, PR, HER2, MIB-1 (Ki67), and AR status.

3. Measuring the radiation exposure for the physician during the biopsy procedure.

Outcome measure: Dosimetry (µSv) of pocket dosimeter and ring dosimeter.

Study description

Background summary

Biopsy of breast lesions is increasingly being performed with a variety of anatomical imaging techniques. Primary tumour 2-[F-18]-fluoro-2-deoxy-D-glucose (18F-FDG) uptake in breast cancer is significantly higher in tumours with prognostically unfavourable characteristics. An important aspect of improved tumour visualisation using functional imaging, e.g. positron emission tomography (PET) imaging, could be the evaluation of heterogeneity in 18F-FDG

uptake. The assessment of intratumoural 18F-FDG uptake may enable tumour sampling from the area with the highest 18F-FDG uptake (i.e. highly proliferative area). This might be particularly interesting in patients treated with neo-adjuvant chemotherapy, in whom pre-treatment biopsies are used for determination of the chemotherapeutic regimen. Uptake of 18F-FDG can also be helpful in the detection of radiographic occult lesions or discriminating a benign process such as scar from malignancy. A consortium of investigators, participating in the European Project MAMMOCARE, has developed a prototype breast biopsy device that is incorporated in a dedicated high-resolution PET breast scanner. This study will investigate the safety and accuracy of this new PET-guided biopsy device.

Study objective

The primary objective of the present study is to assess the feasibility and safety of a newly developed PET-guided breast biopsy system in breast cancer patients.

Study design

This is a prospective observational feasibility study.

Standard clinical protocol:
Patients will be prepared following a 6-h fasting period on the day of the conventional 18F-FDG PET/CT scan. A PET/CT (Philips Gemini Time-of-flight, Eindhoven, The Netherlands) will be used. The patient will be administered between 180-240 MBq 18F-FDG intravenously, according to standard protocol. PET/CT will be acquired at approximately 50 minutes after administration of 18F-FDG. First, a PET/CT of the thorax will be performed with the patient in prone position with hanging breasts. Subsequently, a whole body PET/CT will be performed with the patients in supine position.

18F-FDG PET-guided biopsy protocol:
After the conventional PET/CT scans, patients with demonstrated 18F-FDG-avid breast lesions will be transferred from the Nuclear Medicine department to the MAMMOCARE intervention room at the sixth floor (room number 6B.21). In here, 18F-PET-guided biopsies will performed by the Radiologist and Nuclear physician based on the following protocol (Figure 1):

Three biopsies, which is standard clinical practise at the NKI-AVL, of the primary breast tumour are performed. Two biopsies are taken from the area with the highest 18F-FDG uptake and one biopsy is taken from the tumour border using a commercial 9-gauge vacuum-assisted needle (Eviva, Hologic, IN, USA).

As safety check, a hydromarker will be inserted to indicate the biopsy location. Mammograms can visualise if the biopsy location (hydromarker)

correspond to the location of the tumour. Furthermore, the hydromarker is needed as orientation point to insert the 125I-marker.

Finally, a dose calibrator will be used to measure the presence and quantity of 18F-FDG in the breast biopsy specimens.

Radioactive 125I-seed placement:
A radioactive 125I-seed (similar to those used in brachytherapy of the prostate) will be placed, under ultrasound guidance, in the breast near the hydromarker in order to mark the location of the primary tumour. 125I has a half-life time of 60 days and is a 27 keV source of gamma radiation. This radioactive 125I marker can be visualised using ultrasound, X-ray and CT. Intra-operatively it can be detected with a gamma probe. This method enables surgical localisation of the primary tumour after neo-adjuvant chemotherapy because of the long half-life time of the radioactive 125I marker. This is part of the standard clinical workflow in these patients.

Mammography:
Directly after 125I-seed placement, all patients undergo mammograms in three different orientations (MLO, ML, CC) in order to locate the 125I-seed in vivo. This is part of the standard clinical workflow in these patients.

Histopathology examination of breast biopsies:
Primary tumour characterisation is determined by assessing the ER, PR, HER2, MIB-1 (Ki67), and AR status of the breast biopsies. The pathologist will evaluate the breast biopsies within 48 hours to check whether enough tumour tissue is obtained for standard gene-expression and molecular subtyping analysis. An additional ultrasound-guided breast biopsy is planned as back-up in case the PET-guided breast biopsies do not contain enough tumour tissue for pathological analysis. This additional ultrasound-guided breast biopsy procedure is planned a few days after the PET-guided biopsy. This additional biopsy procedure is cancelled when pathological analysis shows that enough tumour tissue is obtained.

Study burden and risks

Burden and risks associated with participation:

-Participation in this study does not involve a significant risk for the patient or personnel, but the patients do need to stay 2 hours longer in the hospital after their PET/CT scan.

-Additional radiation:
Patients receive an additional mammogram in one direction, which cause an additional radiation exposure of 0.3 mSv. This is within the normal reach of diagnostic procedures and no side effects or risks are expected.

The involved staff receives additional radiation exposure, because they have to stay near the patient during the biopsy procedure. A worst case scenario of radiation exposure is calculated (ANNEX 1 in study protocol: Berekening uitwendige stralingsbelasting medewerkers).
The additional total body radiation exposure after 20 patients is 0.9 mSv, and the radiation exposure of the hand is 1.6 mSv.
In reality, the radiation dosage to the personnel is limited by using proper lead shielding and distance during the biopsy procedure, while the personnel is not handling the biopsy needle.

-Biopsy needles:
The biopsy needles are thicker than the biopsy needles used in case of ultrasound-guided breast biopsies. 9-gauge needles are used instead of 14-gauge needles. These thicker needles can cause a higher risk for hematomas. These thicker needles are the same needles which are used in the NKI-AVL for stereotactic biopsies. Therefore, the Radiologist has experience using these needles and knows that these biopsy needles are safe to use.

-There is a low risk that the targeted biopsy region does not contain tumour cells, which means that the patients have to come back for a second biopsy. This risk is minimized by including breast cancer patients who have a relatively large tumour (stage II or III), which should make it relatively easy to perform a biopsy of the tumour

Benefit with participation

-The PET/CT scan for these patients will be scheduled within 1 week time instead of 2 weeks.

- Biopsies will be taken of the area with the highest 18F-FDG uptake. The benefits associated with this are still unknown. It is expected that this area of the tumour has the highest proliferation, and therefore, this tumour tissue is potentially ideal for the gene-expression and molecular subtyping analysis in order to determine the neo-adjuvant chemotherapy treatment. Histopathological analysis of breast biopsies taken from the breast tumour area with the highest proliferation may potentially lead to a more adequate personalised 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

-Women
-Age >18 years
-Patients who are referred to the AVL for neo-adjuvant chemotherapy treatment
-Histological confirmed breast cancer (stage II/III)
-Breast tumour >= 2cm

Exclusion criteria

- 18F-FDG non-avid primary tumour (SUVmax < 2.5) on conventional hanging breast PET/CT
- Breast tumour SUVmax lower than two times the SUVmax of surrounding normal breast tissue on conventional hanging breast PET/CT
- Primary tumours located within 2.5 cm distance from the chest wall (selection based on earlier performed mammography, hanging breast MRI or PET/CT).
- Active infection (breast or systemic) requiring antibiotics.
- Breast implant in affected breast
- Blood sugar level more than 10 mg/ml at time of 18F-FDG injection
- Anticoagulants usage with International Normalized Ratio (INR) > 2 on the day of biopsy

- Pregnancy

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	08-06-2015
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Generic name:	PET-guided biopsy system (MAMMOCARE)
Registration:	No

Ethics review

Approved WMO

Date:	07-08-2015
Application type:	First submission
Review commission:	METC NedMec

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	NL53479.031.15