FES (16α-[18F]-fluoro-17β-estradiol)-PET: Towards a new standard for staging of clinical stage II/III and recurrent, estrogen receptor positive (ER+) breast cancer? Pilot study to compare [18F]FES-PET and [18F]FDG-PET.

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To determine whether [18F]FES PET/CT improves staging for women with clinical stage II/III or LRR, ER+ breast cancer as compared to standard [18F]FDG PET/CT.

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

Summary

ID

NL-OMON50317

Source
ToetsingOnline

Brief title
FORESIGHT

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
Breast cancer, mammary carcinoma.

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Cancer Center Amsterdam

Intervention

Keyword: [18F]FDG PET, [18F]FES PET, Breast cancer, Staging

Outcome measures

Primary outcome

1) Percentage of patients with a correctly changed treatment plan according to information obtained with [18F]FES PET/CT compared to [18F]FDG PET/CT at staging.

2) Percentage of metastatic lesions detected with [18F]FES PET/CT compared to [18F]FDG PET/CT at staging.

3) Percentage of missed metastases with [18F]FES PET/CT compared to [18F]FDG PET/CT (at staging and developed during follow-up).

4) Percentage of correct treatment plans as well as diagnostic confidence after 6 months of follow-up as determined by the adjudication committee based on the added information obtained with [18F]FES PET/CT compared to [18F]FDG PET/CT.

Secondary outcome

1) The relationship between the level of [18F]FES/[18F]FDG uptake in the primary tumor, lymph node and distant metastases and standard (size, location of lesion, histological subtype, grade, ER/PR/HER2 expression levels, Ki67%/mitotic index)/experimental clinicopathological parameters (intensity of ER staining, tumor cell and microvessel density, infiltration of lymphocytes,

amount of necrosis and stroma, expression of glucose

transporter-1 (GLUT1) of the primary tumor, lymph node and distant metastases).

2) Cut off value for [18F]FDG SUV (max and peak) below which [18F]FES PET/CT

adds information for staging.

3) Cut off value for grade and ER expression level below which or above which,

respectively, [18F]FES PET/CT adds information for staging.

Study description

Background summary

Accurate staging is of great importance in patients with clinically locally advanced primary breast cancer (LABC, stage III) or locoregional recurrent (LRR) breast cancer for making a correct treatment plan. According to current guidelines, staging is performed with positron emission tomography (PET) using the 2-[18F]fluoro-2-deoxy-D-glucose ([18F]FDG) PET tracer, combined with diagnostic computed tomography (CT). However, previous studies have shown that this technique (with the current PET tracer) might not be sufficient for accurate staging. Specifically in low grade, estrogen receptor positive (ER+) breast cancer metastases can be missed due to the low metabolic activity, leading to low uptake of [18F]FDG. Therefore, there is a clinical need to improve staging procedures. 16α-[18F]-fluoro-17β-estradiol ([18F]FES), an ER-targeted PET tracer, allows imaging of ER+ tumor lesions regardless of their metabolic activity. Patients with clinically LABC and LRR have a 25-50% risk of distant metastases. Correct identification of distant metastases allows adaptation of the treatment plan to avoid burdensome treatment with surgery, systemic and radiotherapy in order to maintain quality of life. In case of oligometastases, correct identification increases the likelihood for cure with local treatment. In the current study we will compare disease staging with [18F]FES- and [18F]FDG PET in patients with clinical stage II/III or LRR breast cancer.

Study objective

To determine whether [18F]FES PET/CT improves staging for women with clinical stage II/III or LRR, ER+ breast cancer as compared to standard [18F]FDG PET/CT.

Study design

In this multicenter observational study with invasive measurements, patients with clinically ER+ clinical stage II/III and LRR breast cancer will be included. All patients will undergo the current *standard* diagnostic procedures including a histological biopsy of the primary tumor, cytology of axillary lymph nodes and imaging procedures with mammography, ultrasound of breast and axilla, magnetic resonance imaging (MRI) breast and whole body [18F]FDG PET combined with diagnostic chest/abdominal CT. The histological and/or cytological biopsies will be performed before or more than 4 days after the [18F]FDG PET/CT scan to avoid biopsy related [18F]FDG uptake. The *experimental* imaging procedure with [18F]FES PET/CT will be performed within 21 days before or after the [18F]FDG PET/CT with at least a 24 h interval between both tracer administrations to allow for sufficient decay.
After evaluation of the obtained scans, an *experimental histological biopsy* of a lymph node metastasis will be obtained and clinically relevant [18F]FDG+ and/or [18F]FES+ lesions and/or suspicious lesions on CT will be biopsied according to standard clinical practice for pathological analyses. New (experimentally) identified and pathologically confirmed metastases will be included in the subsequent treatment plan. The standard follow-up will take place every 3 months for a time period of 24 months after diagnosis to detect potentially missed metastases. At 6 months of follow-up, the treatment plan will be evaluated by an independent committee (surgeon, medical oncologist and nuclear physician/radiologist). We expect to include the total number of patients (40 patients) in 18 months.

Study burden and risks

Patients will receive an intravenous cannula for tracer injection and blood sampling, causing potentially transient discomfort at the site of the cannula insertion. Tumor biopsy will be performed from an easy accessible lesion and the most frequent complications that can occur are discomfort, bleeding and (local) infection. The risk of complications from a tumor biopsy is considered low: 0.24-1.6% and 0.11-0.48% for major complications and mortality, respectively. Radiation exposure from a [18F]FES PET and [18F]FDG PET scan usually ranges between 4-11 mSv and 7-8 mSv, respectively. Radiation exposure from a diagnostic CT scan ranges between 8-14 mSv. The total radiation burden is considered justifiable when compared to the information that can be obtained from this study, in this patient group with breast cancer.
For the [18F]FES PET scan: patients will be asked to fast for 4 hours prior to the scan.
Imaging with [18F]FES PET may improve staging for patients with breast cancer as it may show tumor lesions that could not be identified with [18F]FDG PET, the current standard for staging. If this is the case, the initial treatment goal and intensity can be adjusted which can have beneficial effects for the patient.

Contacts

Public
Vrije Universiteit Medisch Centrum

De Boelelaan 1118
Amsterdam 1081 HV
NL
Scientific
Vrije Universiteit Medisch Centrum

De Boelelaan 1118
Amsterdam 1081 HV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Clinical stage II/III or locoregional recurrent breast cancer (all histological types) with ER+ and low grade according to Bloom Richardson criteria (grade 1-2)
- Females aged 18 years or older at screening
- Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0-2
- Candidates for treatment with curative intent (patients are also allowed for inclusion in the current study if they have undergone recent surgery (<6 weeks) for current breast cancer and require staging because of unexpected stage III disease)
- [18F]FDG PET/CT imaging should be performed for staging according to standard of care (in case [18F]FDG PET/CT imaging has already been performed, patients can be included <=21 days after this scan)

- Estimated glomerular filtration rate (eGFR) >=30 ml/min
- Written and signed informed consent

Exclusion criteria

- History with another cancer within the last 5 years, except non-melanoma skin cancer
- Undergoing treatment for current breast cancer such as (neo)adjuvant chemotherapy, hormonal therapy (only in case of Tamoxifen), radiotherapy or investigational drug therapy
- Pregnancy or lactating women
- Any medical, psychological or social condition that may interfere with the subject*s safety and participation in the study, will lead to exclusion from this study

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-12-2018
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	16&alfa;-[18F]fluoro-17β-estradiol
Generic name:	[18F]FES
Product type:	Medicine

Brand name:	2-[18F]fluoro-2-deoxy-D-glucose
Generic name:	[18F]FDG

Ethics review

Approved WMO Date:	03-10-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-10-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-01-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-08-2020
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2018-002013-35-NL
CCMO	NL66099.029.18