PSMA-PET/CT imaging in the EArly detection of Cancer of the Prostate with High Risk Features

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To assess whether PSMA-PET/CT imaging can be used as a tool to select men for prostate biopsy, or otherwise is able to reduce the number of bothersome biopsy cores in those with an increased risk of aggressive prostate cancer*

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Prostatic disorders (excl infections and inflammations)
Study type	Observational invasive

Summary

ID

NL-OMON50089

Source
ToetsingOnline

Brief title
PEACH trial

Condition

- Prostatic disorders (excl infections and inflammations)

Synonym
Malignancy of the prostate, Prostate Cancer

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: CCA grant

Intervention

Keyword: Detection, High Risk, Prostate cancer, PSMA

Outcome measures

Primary outcome

OUTCOME MEASURES. It is assessed:

1) the (reduced) number of prostate biopsy procedures in the

18F-PSMA-diagnostic pathway,

2) the (reduced) number of prostate biopsy cores taken,

3) the (increased) number of clinically significant (Gleason score 3 + 4 = 7, 4

+ 3 = 7,8-10) prostate cancers detected per prostate biopsy session,

4) the calculated (reduced) number of complicated urinary tract infections such

as urosepsis due to prostate biopsy.

Secondary outcome

ND

Study description

Background summary

PSMA-PET/CT imaging has gained wide attention as a superior staging modality in men with PCa. Its diagnostic value has been well established for recurrent PCa after initial curative treatment, and is currently investigated for its (metastatic) staging potential of newly diagnosed high-risk PCa [1,2,3]. This image modality has therefore altered diagnostic and treatment decisions, and may presumably alter clinical outcome as well.

As of present, bone scintigraphy and CT scan of the abdomen is still indicated as a staging tool for bone metastatic and/or regional lymph node metastases in men with PSA * 20 ng/mL according to the Dutch urological guidelines and the guidelines of the European Association of Urology (EAU).

The performance of PSMA-PET/CT imaging as a tool to select men with a suspicion of potentially aggressive PCa for targeted instead of systematic biopsy, and alternatively, to refrain from bothersome prostate biopsy in patients who may not need it, is a scientific area that has not been investigated.

Study objective

To assess whether PSMA-PET/CT imaging can be used as a tool to select men for prostate biopsy, or otherwise is able to reduce the number of bothersome biopsy cores in those with an increased risk of aggressive prostate cancer*

Study design

INTERVENTION.
In all men with PSA between 20 - 50 ng/mL, the 18F-PSMA driven diagnostic pathway is applied. First, all men will undergo PSMA-PET/CT imaging before diagnostic prostate biopsy. A *positive* for cancer 18F-PSMA-PET/CT will result in 2-4 (targeted) prostate biopsies directed towards PSMA-avide areas in the prostate. For ethical reasons, routine systematic prostate biopsies are taken in the same biopsy session. A *negative* for cancer PSMA-PET/CT will result in routine systematic prostate biopsies only. Ethically, it is not yet permissible to withhold men with a *negative* for cancer PSMA-PET/CT a systematic prostate biopsy.

IMAGING PROTOCOL 18F-PSMA-PET/CT
All studies will be performed on a Ingenuity Time of flight 64 slices PET-CT scanner (Philips Medical Systems, Best, the Netherlands) with an axial field per view of 18 cm. High-dose CT (HD-CT) will be collected using a beam current of 50 mAs at 120 keV. CT will be reconstructed using an image matrix size of 512 x 512 resulting in voxel sizes of 1.17 x 1.17 mm and a slice thickness of 5 and 2 mm, respectively. For PET, data will be reconstructed by means of a raw action ordered subset expectation maximization algorithm using default reconstruction parameters. Time of flight information will be used during reconstruction. Reconstructed images will have an image matrix size of 144 x 144, a voxel size of 4 x 4 mm and a slice thickness of both 5 and 2 mm.

All patients will undergo the standard 18F-PSMA image acquisition protocol at our institution. No extra preparation is needed. A good hydration is required, 1L of water within 1 hour prior to performing the scan. Patients will be asked to empty the urinary bladder before the scan. Two hours post-injection of a standard activity of 300 MBq 18F-PSMA, HD-CT will be performed, followed by a whole body PET from mid-thigh to the basis of the skull. The acquisition time will be 4 min per bed position. The total acquisition time for the whole body PET/CT will be, on average, 30 minutes.

IMAGE ANALYSIS

Data analysis will be conducted on the Department of Nuclear medicine of the Amsterdam UMC, location VUmc. Reconstructed images will be transferred to offline workstations. Data analysis will be performed using in-house developed software tools. Foci with increased PSMA expression will be drawn on the reconstructed PET images of the prostate. Similarly, suspected metastases (i.e., increased PSMA expression incompatible with physiological tracer uptake) will be drawn on the reconstructed whole-body PET images. Volumes of interest will be determined using standardized methods, and will then be utilized for calculating the standardized uptake value (SUV) measures corrected for body weight. A *positive* for cancer 18F-PSMA-PET/CT within the prostate gland is defined as intense uptake, exceeding the background of the normal prostate tissue. A *negative* for cancer 18F-PSMA-PET/CT is defined as no uptake within the prostate gland.

BIOPSY PROTOCOL
Prostate biopsy is routinely performed by transrectal ultrasound (TRUS). In this, an ultrasound image is obtained of the prostate and a puncture line is given in the transverse and sagittal plane (Figure 2). Unfortunately, most prostate cancers are iso-echoic and cannot be differentiated adequately from normal benign tissue.

Systematic prostate biopsies are therefore obtained from the peripheral zone of the prostate. All hospitals perorm transrectal biopsies. The OLVG, the AVL and the AMC hospital also perform transperineal prostate biopsies. Dependent on prostate size, 8, 10, or 12 biopsy cores are taken for transrectal prostate biopsy, that is 4, 5, or 6 on each side respectively. For transperineal biopsy this amounts to 20-22 cores over the whole prostate.

Targeted prostate biopsies are taken *cognitively*. This technique has been adopted from mpMRI directed and targeted biopsies in patients with an indication for prostate biopsy. In this, the images on mpMRI are translated cognitively into TRUS images, so that mpMRI suspicious lesions can be targeted. Cognitive targeted biopsies have not been found inferior to mpMRI driven biopsies, i.e. in which patients are situated in an MRI scanner and in whom biopsies are performed MRI guided. PSMA driven targeted prostate biopsies are performed in a similar manner to mpMRI targeted biopsies.

In those with PSMA-PET avide lesions, 2-4 additional (targeted) biopsies are obtained by directing the puncture needle towards the area of interest. Pathological analysis is performed on the prostate biopsy cores routinely in which special attention is given to the location and the side of the prostate of individual biopsy cores as well as on the identification of individual targeted biopsy cores.

Study burden and risks

Potential issues of concern

* PSMA-PET/CT is associated with an additional radiation exposure of 8 mSv.
* Targeted extra biopsies will be performed in patients with PSMA avide lesions on PSMA PET/CT scan

Previous exposure of human beings with the test product(s) and/or products with a similar biological mechanism

* Previous men that had a PSMA-PET/CT scan did not have immediate negative consequences because of a single radiation exposure
* Allergies to the nuclear tracer PSMA have not been reported as of yet.
* Previous men that underwent targeted biopsies along routine systematic prostate biopsies in studies with mpMRI did not experience an increased rate of complicated urinary tract infections or other complications such as hematuria

Analysis of potential effect

* The additional risk of risk can be calculated with the following validated link: http://www.xrayrisk.com/calculator/calculator.php

In this electronic risk calculation used by radiologists and nuclear physicists, the type of radiation examination, age, the number of exposures, and the average dose is filled in.

Then the total effective dose is calculated, and the additional cancer risk, compared to the baseline cancer risk.

For instance, a man of 65 years undergoing a PSMA-PET/CT will receive an extra radiation dose of 8 mSv.

The additional cancer risk for this man is 0,0267% (one in every 3734), against a baseline lifetime risk of 44.9%

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

Men * 45 years with no history of PCa and no prior prostate biopsies with suspected, potentially aggressive PCa due to an elevated PSA-level between 20 and 50 ng/mL are eligible.

Exclusion criteria

- Previous diagnosis of prostate cancer
- Previous prostate biopsy
- Previous PSMA PET/CT scan

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):	01-11-2019
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	28-06-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-06-2020
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
ISRCTN	ISRCTN
CCMO	NL68849.029.19