[18F}-gelabeld FDHT in PET/CT voor detectie en stagering van ossale metastases in hormoon naïeve prostaatkanker.

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Primary Objective: the primary objective of this study is to determine the feasibility of [18F]FDHT PET/CT for in vivo evaluation of bone metastases in prostate cancer. Active locations will be compared with those seen on conventional imaging (bone...

Ethische beoordeling	Goedgekeurd WMO
Status	Werving gestopt
Type aandoening	Metastasen
Onderzoekstype	Observationeel onderzoek, met invasieve metingen

Samenvatting

ID

NL-OMON39807

Bron
ToetsingOnline

Verkorte titel
[18F]FDHT PET/CT in hormoon naïeve prostaatkanker

Aandoening

- Metastasen
- Prostaataandoeningen (excl. infecties en ontstekingen)

Synoniemen aandoening
prostaatkanker, uitzaaiing

Betreft onderzoek met
Mensen

Ondersteuning

Primaire sponsor: Universitair Medisch Centrum Groningen

Overige ondersteuning: Ministerie van OC&W,Astellas Pharma,Astellas Pharma;Dionex Benelux;IQ Therapeutics;NovioGendix Research;Philips Electronics Nederland,Dionex Benelux,IQ Therapeutic ,NovioGendix Research,Philips Electronics Nederland

Onderzoeksproduct en/of interventie

Trefwoord: FDHT, hormoon naïef, metastases, prostaatkanker

Uitkomstmaten

Primaire uitkomstmaten

First phase endpoint is the first [18F]FDHT PET. Lesions seen on this scan

will be compared with those seen of bone scintigraphy, MRI and/or CT. SUV will

be used to quantify uptake of [18F]FDHT PET in the lesions.

Second phase endpoint is the second [18F]FDHT PET. Again, SUV in the lesions

will be calculated and compared - reduction in both number of lesions, and

uptake per lesion- with those seen on the first scan.

Secundaire uitkomstmaten

Prostate Specific Antigen, Gleason Sum Score in relation to SUV differences

between the first and the second [18F]FDHT PET

Toelichting onderzoek

Achtergrond van het onderzoek

Bone scintigraphy, CT, [18F]FDG and [11C] and [F18]-choline PET and magnetic resonance imaging (MRI) are imaging modalities used to determine the extent of prostate cancer both in the primary tumor and in metastases. During therapy, some of these imaging tests can also be used to monitor progression or regression of disease.

For detecting lymph node metastasis, the sensitivity for CT and MRI is 42 en 39 percent respectively, with a specificity of 82 percent.1
Using PET with [18F]-labelled FDG as a radiotracer, cellular metabolism can be visualised and localised, when combining the PET with CT. Cancer in general has

a high metabolism, thereby leading to increased uptake of FDG. However, there is also an increased physiological FDG uptake in inflamed tissue PET scanning itself is relative insensitive for detecting regional lymph node metastasis in prostate cancer, which probably reflects low metabolic activity within prostate cancer cells.. In organ confined disease, FDG PET has only a sensitivity of 4 percent.2 In metastasised disease, FDG-PET resulted in an overall sensitivity of 65%.3 Looking at osseous lesions, FDG PET tends to indentify only those lesions with an aggressive prostate cancer in it, which causes high osteoclastic activity, which in turn has a higher uptake for FDG. This is not the case is slowly progressive bone disease.4 One study showed a sensitivity of 34% for bone metastasis in patients with PSA recurrence.5 [11C] and [18F]-choline PET are mostly useful for restaging prostate cancer; to localize lesions that are unrecognised clinically or on conventional imaging techniques.6,7
Altogether CT, MRI, and FDG PET have a fairly low sensitivity for detecting prostate cancer, and bone scintigraphy is the *gold standard* used to detect osseous lesions, however with low specificity.

Patients with metastasized prostate cancer are treated with androgen deprivation therapy, since androgens are the driving force behind disease progression. When patients are treated with androgen deprivation therapy, the cancer usually goes into regression. After 2-3 years, the cancer progresses again despite an androgen free environment. Studies have shown that androgen receptor expression is very low in these tumours, and that the cancer starts growing via alternative pathways.

In this pilot study, we study PET/CT scans in patients with hormone naive prostate cancer, using a targeted radiotracer: [18F]Fluoro-Dihydrotestosterone ([18F]FDHT). Several imaging studies have been published about this new tracer that show promising results. Dihydrotestosteron (DHT) is the most active metabolite of testosterone with a high intracellular uptake in prostate cancer cells. We try to evaluate the feasibility of [18F]FDHT as a radiotracer in subjects who did not received androgen deprivation therapy yet. Secondly we want to investigate differences in uptake in lesions after start of androgen deprivation therapy by performing a second [18F]FDHT PET three months after start of ADT. We hypothesize that after start of androgen deprivation therapy, the AR will be upregulated and therefore the standardized uptake value in the lesions will increase.
[18F]FDHT PET could be used to assess the extent of prostate cancer to monitor therapy response and to identify patients that have low androgen receptor expression, who are prone to respond worse to androgen deprivation therapy. For the latter, other therapeutic regiments could be initiated earlier.

Doel van het onderzoek

Primary Objective: the primary objective of this study is to determine the feasibility of [18F]FDHT PET/CT for in vivo evaluation of bone metastases in

prostate cancer. Active locations will be compared with those seen on conventional imaging (bone scintigraphy, CT and/or MRI)

Secondary Objective(s): the secondary objective is to determine differences in uptake in lesions using [18F]FDHT PET/CT three months after start of androgen deprivation therapy.

Onderzoeksopzet

This pilot study compromises two phases:
• the first phase is to assess [18F]FDHT PET/CT as a marker for detecting advanced hormone naive prostate cancer lesions, compared to all lesions seen on bone scintigraphy, CT and/or MRI
• The second phase is to determine differences in uptake in lesions using [18F]FDHT PET/CT three months after start of androgen deprivation therapy and it's relation with Gleason Sum Score and initial PSA.

Candidates for this study imaging study are subjects with metastasized prostate cancer,
• confirmed by positive bone scan, suspicious lesions >=2 in bone.
• who have not been treated with androgen deprivation therapy yet.
• Who do not require require immediate start of androgen deprivation therapy because of imminent pathological fractures or spinal cord lesion

For the first phase, one [18F]FDHT PET/CT will be performed to get a baseline scan after informed consent has been given by the patient. After this scan, patients will start androgen deprivation therapy as is standard in these patients. They will be treated with LHRH analogues or via surgical castration, that do not interfere with the occupancy of the androgen receptor. Patients will not receive anti-androgens, because these cause a competitive antagonism on androgen receptor level, which could interfere with binding of the [18F]FDHT.

During the second phase, subjects will be scanned a second time, 3 months after start of androgen deprivation therapy, in order to monitor occupancy of the androgen receptor, which is indicative of potential treatment efficacy..
The subjects will be gathered by urologists or urology residents via the University Medical Centre Groningen. Referring hospitals will also be informed in order to gather a sufficient sample size within 12 months.

To obtain informed consent, patients will receive a brochure containing information about this study, investigational procedures, possible side effects and the logistics concerning the scanning, in addition to the information the patient already has received on the outpatient department from a urologist.

For the first scan subjects will get an indwelling venous catheter for administration of [18F]FDHT PET/CT. Subjects will also be given a urinary

catheter. The main reason for this is that a bladder filled with [18F]FDHT and its metabolites could compromise the imaging in the pelvic area , which is why the bladder has to be empty during scanning.
Although [18F]FDHT has been studied in clinical pilot studies before without reporting of side effects, we will monitor adverse reactions in this protocol as we have used a new synthesis protocol for the tracer.
To identify adverse reactions to the infusion (e.g. anafylaxia) as early as possible, patients will be monitored via pulse oximetry and blood pressure measuring at certain points (before scanning, 10 minutes after administration [18F] FDHT, and after scanning).

Patients will receive a total dose of 200 MBq of [18F]FDHT. After the administration, patients have to wait for one hour. After that the patients will be placed in the PET/CT camera (Biopgraph mCT, Siemens Medical Systems, Knoxville, Tennessee, U.S.A.). After scanning, the patient will be observed shortly either at the radiology department or urology department, to see whether any side-effects occur. When no adverse reaction occurs, the indwelling intravenous catheter will be removed, and so will be the urinary catheter. When the patient is able to micturate, he can return home.

The procedure for the second scan is the same as the first scan.

The PET scans results will be reported by a nuclear medicine physician. All suspected lesions will be noted, both in lymph nodes and in bone. Using the SUV, uptake in lesions will be calculated by the principal investigator of this study.

Then, the PET scans will be compared to bone scintigraphy, CT and/or MRI. The locations of the lesions will be compared to evaluate the similarity between [18F]FDHT PET/CT and the other imaging studies.

For the second phase the images of the second [18F]FDHT PET/CT will be compared with the initial [18F]FDHT PET/CT. Again, the SUV will be calculated lesion by lesion for the second scan. After that, SUV*s in the first and second scan will be compared in order to determine whether androgen deprivation therapy was effective for the individual subjects. Statistical analysis will be performed using SPSS Statistics version 21.

Inschatting van belasting en risico

The burden of this study outweighs the possible benefits of the study in all prostate cancer patients. This study could lead to improved imaging resulting in a more patient specific treatment plan, or possibly treating with curative intent, in those otherwise treated palliative (and vice versa). Another possible results of a new tracer could be to monitor therapy response in patients, in order to see in an earlier stage who is responding to treatment

and who is not. This way, non-responders can quit therapy and its side effects.

Contactpersonen

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Locaties

Landen waar het onderzoek wordt uitgevoerd

Netherlands

Deelname eisen

Leeftijd
Volwassenen (18-64 jaar)
65 jaar en ouder

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Mannen, vijftig jaar of ouder, met gemetastaseerd prostaatkanker, bevestigd door positieve botscan met twee of meer verdachte laesie, die nog niet behandeld zijn met androgeen deprivatie therapie. Tevens mogen zijn geen andere maligniteit hebben en moet er informed consent zijn.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

• actieve kanker naast de prostaatkanker
• geen papieren informed consent
• eerdere androgeen deprivatie therapie
• jonger dan 50 jaar
• dreigende pathologische fracturen of ruggenmerglaesie ten gevolgd van metastases waarvoor directe start van androgeen deprivatie therapie nodig is

Onderzoeksopzet

Opzet

Type: Observationeel onderzoek, met invasieve metingen

Blindering:	Open / niet geblindeerd
Controle:	Geen controle groep
Doel:	Diagnostiek

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	13-06-2014
Aantal proefpersonen:	20
Type:	Werkelijke startdatum

In onderzoek gebruikte producten en hulpmiddelen

Soort:	Geneesmiddel
Merknaam:	[18F]FDHT
Generieke naam:	16beta-[18F]fluoro-5alfa-dihydrotestosteron

Ethische beoordeling

Goedgekeurd WMO

Datum:	19-06-2013

Soort:	Eerste indiening
Toetsingscommissie:	METC Universitair Medisch Centrum Groningen (Groningen)
Goedgekeurd WMO Datum:	11-02-2014
Soort:	Eerste indiening
Toetsingscommissie:	METC Universitair Medisch Centrum Groningen (Groningen)
Goedgekeurd WMO Datum:	08-08-2014
Soort:	Amendement
Toetsingscommissie:	METC Universitair Medisch Centrum Groningen (Groningen)
Goedgekeurd WMO Datum:	13-04-2015
Soort:	Amendement
Toetsingscommissie:	METC Universitair Medisch Centrum Groningen (Groningen)

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
EudraCT	EUCTR2013-002415-10-NL
CCMO	NL42254.042.13