Feasibility of MRI-guided focal salvage high-dose-rate brachytherapy for locally recurrent prostate cancer

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To assess toxicity of MRI guided focal salvage high-dose-rate brachytherapy as monotherapy in patients with locally recurrent prostate cancer. As secondary objectives, technical feasibility, quality of life and biochemical free survival (Phoenix...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON47701

Source
ToetsingOnline

Brief title
MRI-guided focal salvage HDR-BT for locally recurrent prostate cancer

Condition

- Reproductive neoplasms male malignant and unspecified
- Male genital tract therapeutic procedures

Synonym
prostate cancer, recurrent prostate carcinoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: high-dose-rate, MRI-guided, recurrent prostate cancer, salvage brachytherapy

Outcome measures

Primary outcome

Incidence of grade>=3 gastro-intestinal and/or urogenital toxicity after MRI guided focal salvage therapy for locally recurrent prostate cancer. Toxicity will be determined by the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 (National Cancer Institute).

Secondary outcome

- To determine the technical feasibility of MRI guided focal high-dose rate brachytherapy as salvage therapy for locally recurrent prostate cancer

- Quality of life

- Biochemical disease free survival (Phoenix criteria)

Study description

Background summary

Prostate cancer recurrence after primary treatment is common, despite improvements in primary curative treatment modalities. Various salvage treatment modalities, like radical prostatectomy, low-dose-rate brachytherapy, external beam radiotherapy, HIFU (high intensity focused ultrasound) and cryosurgery have been investigated. However, because of high failure and high toxicity rates, these treatment modalities remain unpopular. High failure rates can be reduced by excluding patients with a high risk for early distant metastasis. In these patients, salvage treatment will not be of benefit. High toxicity rates can be explained by the fact that salvage therapy is often performed on the entire prostate, which induces accumulation of a high irradiation dose on healthy tissues. To reduce the burden of a high radiation dose on healthy tissues, focal therapy is warranted. This can be achieved with MRI-guided focal salvage high-dose-rate brachytherapy. In the past, focal salvage treatment has not frequently been explored, since determination of

exact tumour location was not precise. Currently, our radiotherapy centre has a MRI high-dose-rate brachytherapy facility, allowing MRI guided catheter placement and treatment. With this facility, catheter placement can be done far more accurately, which makes focal treatment possible. Due to the steep dose fall-off, low radiation doses will be expected in the surrounding healthy tissues. Therefore, less toxicity to the organs at risk is expected. In earlier studies, salvage high-dose-rate brachytherpay has been shown to be feasible. Moreover, results regarding toxicity are promising. Therefore, we expect that MRI guided salvage treatment by using high-dose-rate brachytherapy will be of benefit in patients with recurrent prostate cancer.

Study objective

To assess toxicity of MRI guided focal salvage high-dose-rate brachytherapy as monotherapy in patients with locally recurrent prostate cancer. As secondary objectives, technical feasibility, quality of life and biochemical free survival (Phoenix criteria) will be determined.

Study design

Prospective development study, using MRI guidance to apply a single fraction of high dose rate brachytherapy as focal salvage monotherapy for treatment of locally recurrent prostate cancer. All patients with recurrent prostate cancer meeting the inclusion criteria, will be considered for inclusion.
Before treatment, a diagnostic MRI with contrast and a PSMA-PET scan will be made. During treatment, a MRI without contrast will be performed to visualize the brachytherapy catheters in relation to prostate anatomy. Six months after treatment, a third MRI will be performed to assess treatment response.
The time span for inclusion of patients in this study will be two years. Before treatment, toxicity of the primary treatment will be assessed. During the first 90 days after treatment, acute gastro-intestinal and genital-urinary toxicity will be monitored. Hereafter, late gastro-intestinal and genital-urinary toxicity will be assessed during a 10 year period. Toxicity and scoring of symptoms before and after treatment will be determined by using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 criteria and International Prostate Symptom Score (IPSS)questionnaire. Quality of life will also be measured before high-dose-rate brachytherapy treatment and during a 10 year period after treatment. The RAND-36, EORTC QLQ-PR-25, EORTC QLQ-C30 and IIEF-5 questionnaires will be used. For assessment of biochemical recurrence (Phoenix criteria), Prostate Specific Antigen (PSA) monitoring will be performed during each follow-up visit.
Follow-up consultations will be performed 4 weeks after treatment and thereafter every three months for the first year, every 6 months the second year and thereafter annually for up to ten years, according the Dutch prostate guideline.

Intervention

High-dose-rate brachytherapy will be performed for patients with recurrent prostate carcinoma. The treatment will include a single fraction of 19 Gy. Salvage high-dose-rate brachytherapy will be performed by insertion of catheters under ultrasound guidance. Before placement of the catheters, ultrasound images will be fused with the diagnostic MR. Delineation of the Gross Tumour Volume (GTV) will be performed by using the diagnostic MRI and the PSMA-PET scan. With the help of T2, Dynamic Contrast Enhanced (DCE) and Diffusion Weighted Imaging (DWI) sequences it is possible to make an accurate delineation of the GTV. The Clinical Target Volume) (CTV) will be defined as GTV with broader margins, to account for tumour extension. The Planning Target Volume (PTV) will have no extra margins. Based on these merged images, the catheters will be placed in the GTV. Consequently, the patient will be placed in the MRI and under MR guidance catheter displacement in the tumour will be adjusted for. Image datasets will be transferred to the treatment planning computer to create a simulation of dose distribution to GTV, CTV, prostate, urethra, rectum and bladder. The treatment will include a single fraction high-dose-rate treatment. After treatment, the catheters will be removed and the patient will be discharged from the hospital.

Study burden and risks

In order to keep toxicity to a minimum, strict dose constraints to the organs at risk will be applied. With state of the art planning procedures prior to focal salvage HDR-BT, a safe radiation dose to the CTV (clinical target volume) can be determined. If the dose to the organs at risk is exceeded, the dosage to the PTV will be decreased. To investigate quality of life, questionnaires will be used. The additional MRI scan during treatment of focal HDR brachytherapy will induce no additional health risks.
Because of the focal treatment, less toxicity of healthy tissues (bladder and rectum) is expected in comparison with current salvage treatment modalities. Furthermore, hormonal treatment in the future may be prevented or delayed by the use of MRI guided focal salvage HDR-BT. This will prevent hormone induced toxicity for the patient.
Focal salvage high-dose-rate brachytherapy treatment of prostate cancer has not frequently been implemented before. Therefore, long term effects after this treatment modality are unknown.

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

- Age >=18 years
- Biopsy proven local recurrence
- Biopsy proven recurrence at least 2 years after primary radiotherapy treatment (low-dose-rate brachytherapie or external beam radiation therapy)
- Limited and non-aggressive tumor presentation at time of salvage (Prostate Spedific Antigen (PSA) at time of salvage <10)
- Prostate Specific Antigen (PSA) doubling time more than 12 months
- Acceptable toxicity of primary radiation treatment (International Prostate Symptom Score (IPSS)<15)
- Tumour location technically feasible for brachytherapy
- Tumour on MRI and PSMA-PET scan within anatomical prostate borders (no extracapsular growth or metastasis)
- Karnofsky score >=70
- Written informed consent
- Fit for spinal anaesthesia

Exclusion criteria

- Distant metastasis
- Severe toxicity during primary radiation treatment (International Prostate Symptom Score (IPSS)>15)
- Patients who meet exclusion criteria for MRI following the protocol of the radiology department of the UMC Utrecht
- Anticoagulant administration continuously required, except for Ascal
- Discongruence between prostate biopsies and contrast MR imaging
- No prior prostate cancer treatment(s) (like a recent TURP (<6 months before focal salvage HDR treatment), HIFU, cryosurgery), except for radiotherapy

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-07-2013
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	16-04-2013
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	15-07-2014

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-08-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-11-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-11-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-11-2017
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-07-2019
Application type:	Amendment
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	NL42708.041.12