HYPo-fractionated Radiotherapy of Lymph Node Metastases guided by NanO-MRI in Prostate Cancer Patients: A Pilot Study (HYPNO-study)

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To evaluate the feasibility and efficacy of MR-guided stereotactic body radiotherapy (SBRT) to nano-MRI detected regional lymph node metastases in patients with biochemical recurrent prostate cancer after radical prostatectomy.

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

Summary

ID

NL-OMON50988

Source
ToetsingOnline

Brief title
HYPNO-trial

Condition

- Reproductive neoplasms male malignant and unspecified
- Prostatic disorders (excl infections and inflammations)

Synonym
prostate carcinoma; prostate cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Lymph node metastasis, Nano-MRI guidance, Prostate cancer, Stereotactic adiotherapy

Outcome measures

Primary outcome

The primary endpoints of the study are 1-year PSA-relapse free survival as

parameter for disease control and technical feasibility.

Secondary outcome

Secondary endpoints include acute and late treatment related toxicity and

radiologic response.

Study description

Background summary

In patients with biochemical recurrent prostate cancer after radical prostatectomy early local salvage radiotherapy to the prostatic fossa offers a second option for treatment with curative intent. However, in a substantial number of patients a secondary biochemical recurrence occurs due to metastatic disease, e.g. in regional lymph nodes or as distant metastases.
Recent developments in imaging of recurrent prostate cancer patients, such as PSMA-PET/CT, enable earlier detection of a local and regional/distant recurrence, thereby identifying patients who may benefit of local treatment and those in which unnecessary local radiotherapy can be omitted. Although patients with regional metastases have historically been regarded as incurable, high-precision, high-dose-per-fraction radiotherapy techniques have shown to be able to eradicate oligo-metastatic disease, thereby leading to a prolonged progression-free survival and delay of systemic therapy or, in a subgroup of patients, potentially cure. Several reports have mentioned the safety and tolerability of this so-called stereotactic body radiotherapy (SBRT) to pelvic lymph nodes. The introduction of dedicated treatment machines integrating

MR-imaging with linear accelerators (MR-linac) are expected to improve SBRT accuracy even more by daily adaptive treatment planning based on online imaging with high soft tissue contrast.
Nano-MRI has shown to be able to detect lymph node metastases down to a size of 2 mm, which may be well below the resolution of PSMA-PET/CT. Using the ability of nano-MRI to detect such small lymph node metastases, lymphatic prostate cancer recurrences could be detected at a very early stage making an early local SBRT of the recurrent lymph nodes possible. The high-spatial resolution of nano-MRI when used in combination with MR-Linac can enable very precise, individually tailored SBRT options for oligometastatic lymph node spread in prostate cancer patients. Also, implementation of nano-MRI may improve the stratification of patients for local or regional therapy, thereby preventing overtreatment of the prostatic fossa and undertreatment of small pathologic lymph nodes.

Study objective

To evaluate the feasibility and efficacy of MR-guided stereotactic body radiotherapy (SBRT) to nano-MRI detected regional lymph node metastases in patients with biochemical recurrent prostate cancer after radical prostatectomy.

Study design

Single-arm, single-center prospective feasibility study, phase IIA according to the R-IDEAL framework.

Intervention

Participating patients will undergo nano-MRI imaging, including the infusion of the ferumoxtran-10 contrast agent.

Patients who are eligible for stereotactic radiotherapy will be treated 5 x on the MR-linac with an overall treatment time of 2 weeks (approximately 1 hour per treatment). This replaces the 'standard' radiation treatment of the prostatic fossa consisting of 26 fractions with an overall treatment time of 6.5 weeks (approximately 10 minutes per treatment).

Study burden and risks

Investigation and treatment:

Eight hospital visits in 5 weeks (approximately 1 hour per visit).
These visits consist of:

1) MRI of the prostatic fossa, followed by infusion of nano-contrast agent.

2) one day later nano-MRI for lymph node imaging.
3) one week later planning CT for preparation of the radiation treatment (standard of care).
4) two weeks later start of radiation treatment: a total of 5 treatments (one hour each). This replaces the standard radation treatment of the prostatic fossa, consisting of 26 fractions (10 minutes each) with an overall treatment time of 6.5 weeks.

Follow-up

Follow-up is mostly comparable to regular follow-up.
Following treatment the first follow-up visit will take place 6 weeks after treatment and every 3 months until 1 year after treatment. Thereafter, follow-up will be once every 6 months until 5 years after treatment. At every follow-up PSA will be measured.
At 3, 12 and 24 months after treatment an extra nano-MRI will be performed preceded by infusion of the contrast agent one day earlier. This will take 6 extra visits of approximately one hour each.

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

- Biochemical recurrent prostate adenocarcinoma after radical prostatectomy.
- PSA level >= 0.2 ng/ml
- No macroscopic disease on PSMA-PET/CT
- No local recurrence on MRI.
- <= 4 foci harbouring regional lymph node metastases (up to 6 nodes in total) on nano-MRI (below aortic bifurcation).

Exclusion criteria

- If any of the abovementioned does not apply.
- Concurrent or previous androgen deprivation therapy.
- Previous pelvic radiotherapy.
- Active inflammatory bowel disease (Crohn*s disease or ulcerative colitis).
- Contraindication for MR-imaging according to local Radiology protocol or unable to undergo MR-linac treatment (e.g. due to claustrophobia or body circumference).
- Ferro-magnetic objects in the pelvis or hip causing disturbing susceptibility artifacts (at the discretions of the radiologist).
- Inability to give informed consent.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-10-2022
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ferumoxtran-10 Lyophilisate
Generic name:	Ferrotran Lyophilisate

Ethics review

Approved WMO Date:	10-08-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-09-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-06-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2021-003779-32-NL
CCMO	NL77171.091.21