A pilot feasibility study of Dose dE-eScalaTion IN prostATe radIOtherapy with empty bladder usiNg the MRL - DESTINATION 1B(ladder)

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To develop a 5 fraction de-escalated dose SBRT protocol potentially capable of reducing side effects intended for prostate cancer patients with empty bladder

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

Summary

ID

NL-OMON57342

Source
ToetsingOnline

Brief title
DESTINATION 1B

Condition

- Reproductive neoplasms male malignant and unspecified

Synonym
prostate cancer, prostate carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Nederlands Kanker Instituut
Source(s) of monetary or material Support: Persoonlijk onderzoeksbudget van de

hoofdonderzoeker

Intervention

Keyword: MR-Linac, prostate, radiotherapy, toxicity

Outcome measures

Primary outcome

Technical feasibility of treating prostate cancer with toxicity-minimising radiotherapy on an MR-linac. Feasibility is defined as coverage of GTV boost D90% >42Gy on the post-treatment MRI.

Secondary outcome

• Physician reported GU and gastrointestinal (GI) toxicity (CTCAE grade) at baseline and the end of treatment then at 4 weeks and 3 months post-treatment.

• Late toxicity (CTCAE) at 1 and 2 years post-treatment

• Patient-reported outcome measures (PROMs) from the EPIC-26, IPSS, and IIEF-5 questionnaires.

Patients will be asked to complete PROMs at 4 weeks, 3 and 6 months, 1 and 2 years post treatment.

• PSA control and kinetics at 2 years post-treatment

Study description

Background summary

The prognosis of low and intermediate risk localized prostate cancer after surgery, radiotherapy or brachytherapy is excellent. Therefore, when choosing a treatment modality, the side effects are becoming increasingly important and research is focussed on a reduction in side effects.
To eradicate all tumour, external beam radiotherapy traditionally irradiates the tumour and the entire prostate to the full dose, including a safety margin

around the prostate. This means that a volume of healthy tissue is also irradiated, which causes the side effects of radiotherapy. Reducing the dose of healthy tissue that is irradiated leads to fewer side effects.
The side effects of external beam radiotherapy have been reduced due to continuous, iterative improvements in radiotherapy delivery technology. This has allowed us to harness the power of modern computing and discoveries in clinical physics, to create radiotherapy doses which conform very tightly to the edge of the prostate. This results in vastly less dose to the normal, healthy tissues around the cancer. The ultimate evolution of this progress is the MR-linac, a new radiotherapy machine which offers more precise dose delivery than ever before.
This study aims to investigate the benefit of MRI-guided adaptive SBRT, targeting dose where we know it is needed and reducing dose where the risk-benefit ratio suggests healthy tissue can be safely spared.

Up to now, to keep the dose to the bladder low and prevent side effects usually prostate radiotherapy is done with filled bladders. To limit anatomical changes and reduce the variation in bladder filling, in current clinical practice drinking protocols are applied, that instruct the patient to void the bladder and drink a fixed amount of liquid at a specified time prior to each treatment fraction. The effectiveness of such protocols is however quite disappointing , while the procedures cause considerable patient anxiety. Moreover, the filling of the bladder during the course of the fraction gives extra rise to intra-fraction motion, potentially reducing the accuracy of the treatment. With MRI-guided radiotherapy, especially with the DESTINATION treatment protocol, the dose to surrounding structures including the bladder is substantially reduced. This means that a filled bladder during treatment is probably no longer necessary.

Study objective

To develop a 5 fraction de-escalated dose SBRT protocol potentially capable of reducing side effects intended for prostate cancer patients with empty bladder

Study design

Single centre non-randomised feasibility study

Intervention

Radiotherapy

Study burden and risks

Although we do not expect it, more recurrences may occur after the DESTINATION treatment. In view of reported experiences in the literature, the probability

of this is very limited.
The additional burden for the patient is the 7 x completion of 3 questionnaires. The follow-up moments in the trial coincide with the regular follow-up moments.

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

1. Men aged >=18 years
2. Histological confirmation of prostate adenocarcinoma requiring radical radiotherapy
3. Gleason score 3+3, 3+4 or 4+3 (Grade groups 1, 2 or 3)
4. MRI stage T2 or less (as staged by AJCC TNM 2018)
5. MRI-visible tumour(s) of PIRADS v2 grade 3 or higher on T2 and

diffusion-weighted imaging and/or dynamic contrast-enhanced imaging with concordant pathology
6. Dominant lesion <50% of prostate on any axial slice and <50% total prostate volume
7. PSA <20 ng/ml prior to starting Androgen Deprivation Therapy (ADT).
8. Patients can be concurrently treated with ADT if this would be standard of care. LHRH analogues or Bicalutamide are permitted. ADT is not mandatory where this would usually be omitted.
9. WHO Performance status 0-2
10. Ability of the participant understand and the willingness to sign a written informed consent (IC) form.
11. Ability/willingness to comply with the patient reported outcome questionnaires schedule throughout the study.

Exclusion criteria

1. Contraindications to MRI (e.g. pacemaker, potentially mobile metal implant, claustrophobia)
2. IPSS 19 or higher
3. biopsies >=GG3 occult to MRI-defined lesion
4. Post-void residual >100 mls, where known
5. Prostate volume >90cc
6. Comorbidities which predispose to significant toxicity (e.g. inflammatory bowel disease) or preclude long term follow up
7. Unilateral or bilateral total hip replacement, or other pelvic metalwork which causes artefact on diffusion-weighted imaging
8. Previous pelvic radiotherapy
9. Patients needing >6 months of ADT due to disease parameters.
10. Previous invasive malignancy within the last 2 years excluding basal or squamous cell carcinomas of the skin, low risk non-muscle invasive bladder cancer (assuming cystoscopic follow up now negative) or small renal masses on surveillance.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2025
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO

Date:	27-02-2025
Application type:	First submission
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
Other	in progress
CCMO	NL87118.041.24