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Study of fewer, larger doses of radiotherapy for men with localised prostate cancer

Submission date 18/02/2021	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 26/02/2021	**Overall study status** Ongoing	
Last Edited 29/04/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

There are several approaches suitable for the treatment of prostate cancer including surveillance (no active treatment) in some cases, and active treatment approaches involving brachytherapy, surgery and external radiotherapy. Advancements in radiotherapy technology mean that doctors can reduce the number of treatments and this study is looking at how fewer treatments can be used to cure localised prostate cancer. The aim of this study is to investigate whether stereotactic body radiotherapy (precise X-ray treatment, called SBRT for short) is best given in five treatments (also called fractions) over 10 days or in two treatments over 8 days. SBRT is stereotactic body radiotherapy, a very precise targeted method of giving radiotherapy. The researchers expect that the chance of being cured with either five or two treatments is likely to be similar, and also similar to the standard 20 treatments, although they can't know this for sure until they have completed further study. They want to find out if the new, shorter treatment (two doses of radiotherapy) has a similar level of side effects as the five-dose treatment and is suitable for further study. They do not know if the side effects will be different, and they don't know which treatment results in the best chance of cancer cure with the fewest side effects.

Who can participate?

Men aged 18 and over who have been diagnosed with prostate cancer and for whom a team of prostate cancer specialists feel would be suitable for the treatment.

What does the study involve?

Everyone who agrees to take part in this study will be allocated to one of two groups of patients. Half of the patients will receive five SBRT treatments over 10 days and half of the patients will receive two SBRT treatments over 8 days. All treatment within this study will be delivered on a new, state of the art, radiotherapy machine called an MR-linac (Magnetic Resonance Linear Accelerator). It puts together an MRI scanner with a radiotherapy treatment machine called a Linear Accelerator. The use of the MR-linac means there is no extra radiation dose given when taking images (unlike CT scans or X-ray). It also enables doctors to adapt or 'tweak' the radiotherapy plan each day if needed to more precisely target the prostate. Patients

will be reviewed in clinic or by telephone at the end of radiotherapy treatment and then at 2, 4, 8 and 12 weeks after the end of treatment. After this the patients will be assessed in clinic or by telephone 6, 12 and 24 months later and then annually until 5 years following treatment.

What are the possible benefits and risks of participating?
Participants may potentially benefit from SBRT treatment which delivers a high dose of radiation to the prostate with relative sparing of surrounding healthy tissue. There is also a potential benefit from the MR-linac's ability to see the prostate and re-calculate the radiotherapy dose on a daily basis. This includes changing the radiotherapy plan if any anatomy has changed (for example the rectum [back passage] is full and this has moved or 'squashed' the prostate into a different shape).
All treatments may cause side effects. The risks and side effects of standard radiotherapy are well known but SBRT is not usually standard of care in the UK at the present time and therefore there may be some side effects which are more or less common than those experienced after or during standard radiotherapy. Recent results suggest that patients treated with prostate SBRT (five fractions) have similar short-term (up to 3 months) side effects compared to those receiving standard prostate radiotherapy over 20 or 39 treatments. The researchers are not yet sure that the long-term side effects of five and two fractions will also be the same as larger numbers of treatments, but they think they will be similar.
Radiotherapy treatment can cause side effects because the healthy tissues in the pelvis (mostly the bladder and bowel) are exposed to the radiation. Radiotherapy can occasionally cause people to feel more tired than normal. Most men experience some side effects but nearly all of these are temporary. For example, after standard radiotherapy, at 2 years after treatment around 1 in 20 (5%) of patients have ongoing side effects which they class as "moderate"; in total around 1 in 8 (12%) may be affected at some point. Around 1% of men will have severe side effects from radiotherapy at 2 years after treatment. The two-fraction treatment is new and so side effects in this study may be more common, or different, to the usual standard treatment.

Where is the study run from?
The Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) working in partnership with The Royal Marsden Hospital (UK)

When is the study starting and how long is it expected to run for?
December 2019 to April 2028

Who is funding the study?
The Jon Moulton Charity Trust (Guernsey)

Who is the main contact?
1. Dr Alison Tree, Alison.Tree@icr.ac.uk
2. Stephanie Burnett, hermes@icr.ac.uk

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-stereotactic-body-radiotherapy-for-prostate-cancer-hermes

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
285291

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 46537, IRAS 285291

Study information

Scientific Title
The HERMES trial: Hypofractionated Expedited Radiotherapy for Men with localisEd proState cancer.

A phase II randomised study of ultrahypofractionated stereotactic body radiotherapy in men with localised prostate cancer

Acronym
HERMES

Study objectives
To investigate how hypofractionated expedited radiotherapy can be used to cure localised prostate cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/01/2021, London – Chelsea Research Ethics Committee (Research Ethics Committee (REC) London Centre, Skipton House, 80 London Road, London, SE1 6LH, UK; +44 (0) 207 104 8029; chelsea.rec@hra.nhs.uk), REC ref: 20/LO/1162

Study design
Randomized; Interventional; Design type: Treatment, Radiotherapy

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Prostate cancer

Interventions
HERMES is a single-centre, randomized phase II trial which recruits men with intermediate or lower high risk localised prostate cancer to one of two radiotherapy prescriptions; men either receive five-fraction stereotactic body radiotherapy (SBRT) over 10 days or two-fraction SBRT over 8 days.

Adult patients with newly diagnosed intermediate or lower high risk localised prostate cancer planned for radiotherapy with curative intent will be approached to participate in HERMES.

Study procedures:
All study-related activities will be performed after the investigator has obtained informed consent from the patient. Complete medical history, demography- including age and ethnicity, concurrent illness and concomitant medications will be collected. Physical examination, WHO performance status, and local blood tests for PSA and testosterone, and a research MRI will be performed. Patient eligibility will be determined based on study inclusion/exclusion criteria and the patient will be randomised on to the study to obtain a study-specific patient number.

Once on study, in order to plan radiotherapy treatment, the patient will require two separate scans; a radiotherapy CT (computerised tomography) and an MRI (Magnetic Resonance Imaging)

planning scan. The radiotherapy CT is part of standard of care. The MRI scans are standard for SBRT patients but are additional compared to the preparation of patients receiving conventional 20 treatment radiotherapy.

During treatment, the patient will have MRI scans every day before and during radiotherapy treatment. The treatment takes around 45 minutes per day (maximum 60 minutes).

As part of this study, patients are asked to have some additional research MRI scans. These scans may be done either during or after treatment whilst on the MR-linac or may be done on a different day. This will help design and plan treatments with the MR-linac in the future and will help us learn more about how prostate cancer is killed by radiation, but these extra research scans will not influence the treatment received.

Once the treatment is finished, the patient can go home and is not expected to feel unwell. Patients will be assessed and followed up as part of the study after radiotherapy, at weeks 2, 4, 8 and 12, month 6 and yearly thereafter to assess side effects and to complete quality of life forms. Additional research MRI scans will be performed at week 2 and week 12 after radiotherapy.

Intervention Type
Procedure/Surgery

Primary outcome(s)
The proportion of patients with CTCAE Grade 2+ genitourinary (GU) toxicity at any point from the start of radiotherapy to 12 weeks post-treatment

Key secondary outcome(s))
Secondary outcome measures:
1. Physician-reported CTCAE GU and GI toxicity reported during treatment and at 12 weeks post-treatment will be summarised according to grade and treatment received using descriptive statistics at each timepoint
2. Physician-reported CTCAE Genitourinary (GU) and Gastrointestinal (GI) late toxicity: late toxicity (CTCAE) at 1, 2 and 5 years post-treatment will be summarised according to grade and treatment received at each timepoint
3. Quality of life patient-reported outcomes: combined data from the IPSS (International Prostate Symptom Score), EPIC-26 (Expanded Prostate Index Composite-26), EQ-5D (EuroQol-5D) and IIEF-5 (International Index of Erectile Function) QOL instruments will be summarised. Changes from baseline will be assessed within treatment groups, and multiple regression models (e.g. ANCOVA, ordinal logistic regression or longitudinal models) will investigate patient and clinical factors that may be associated with change in patient-reported outcomes. Change from baseline measured at 12 weeks, 1, 2 and 5 years post-treatment
4. Time to event: PSA (Prostate-Specific Antigen) control and biochemical failure/progression measured at 2 and 5 years

Exploratory outcome measure:
Bi-parametric MRI prostate imaging parameters during treatment: descriptive statistics will be used to report and analyse the change in ADC (apparent diffusion coefficient) between baseline and 4 weeks and between baseline and 12 weeks

Completion date
30/04/2028

Eligibility

Key inclusion criteria
All participants will be recruited at The Royal Marsden Hospital in the UK. Eligible men will be identified in oncology clinics and discussed at Multi-Disciplinary Team (MDT) meetings at The Royal Marsden.
1. Men aged ≥18 years
2. Histological confirmation of prostate adenocarcinoma requiring radical radiotherapy
3. Gleason score 3+4 or 4+3 (Grade groups 2 or 3)
4. MRI stage T3a or less (as staged by AJCC TNM 2018)
5. PSA < 25 ng/ml prior to starting ADT
6. Patients will be concurrently treated with androgen deprivation therapy for at least 6 months, as per standard of care. Men who need longer courses of ADT (maximum 12 months) will be considered on a case-by-case basis, and bicalutamide monotherapy is accepted as an alternative to LHRH analogues if required
7. WHO Performance status 0-2
8. Ability of the participant understand and the willingness to sign a written informed consent form
9. Ability/willingness to comply with the patient-reported outcome questionnaires schedule throughout the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Male

Key exclusion criteria
1. Contraindications to MRI (e.g. pacemaker, potentially mobile metal implant, claustrophobia)
2. IPSS 13 or higher
3. Post-void residual > 100 ml
4. Prostate volume > 80cc
5. Comorbidities which predispose to significant toxicity (e.g. inflammatory bowel disease) or preclude long term follow up
6. Unilateral or bilateral total hip replacement, or other pelvic metalwork which causes artefact on diffusion-weighted imaging
7. Previous pelvic radiotherapy
8. Patients needing 2-3 years of ADT due to disease parameters
9. Previous invasive malignancy within the last 2 years except 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.

10. Patients will all be concurrently treated with Androgen deprivation therapy for at least 6 months, as per standard of care. Men who need longer courses of ADT may be considered on a case by case basis, and bicalutamide monotherapy is accepted as an alternative to LHRH analogues if required. Men who do not need/are not able to have hormone therapy are also included

Date of first enrolment
01/04/2020

Date of final enrolment
30/09/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Royal Marsden NHS Foundation Trust
Fulham Road
London
United Kingdom
SW3 6JJ

Sponsor information

Organisation
Institute of Cancer Research

ROR
https://ror.org/043jzw605

Funder(s)

Funder type
Charity

Funder Name
The Jon Moulton Charity Trust (Guernsey)

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be available on request from the HERMES trial team via hermes@icr.ac.uk via completion of a data access request form after such time that the primary analysis publication and any other key analyses have been completed. Optional advanced consent/authorisation for the possible future sharing of information collected about patients will be obtained at trial entry.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes