ISRCTN11171089 https://doi.org/10.1186/ISRCTN11171089

A study to find out the accuracy of short MRI and image-fusion biopsy for diagnosing prostate cancer

Submission date 30/06/2022	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 06/07/2022	**Overall study status** Ongoing	
Last Edited 07/04/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

The aim of this study is to improve the way prostate cancer is diagnosed by looking at two different types of MRI scans and two different types of prostate biopsy (tissue sample). A large study such as this is required to help the NHS decide how to diagnose prostate cancer in the future.

If a person is suspected of having prostate cancer, then they are referred by their GP. At the hospital clinic they will then have an MRI scan. If this scan shows that cancer might be present, then the doctor will usually suggest that the patient has a biopsy. There are two ways of doing a prostate MRI. One takes 30-40 minutes and requires a contrast injection called gadolinium (like a dye). This is called long MRI and is most commonly used in the NHS. Gadolinium is safe as it rarely causes any bad reaction but using it means that the scan takes more time. Another type of MRI takes 15-20 minutes and does not use the gadolinium contrast. This is called a short MRI. Many studies over the last 5 years have shown that the long and short MRIs are similar in their accuracy in diagnosing important prostate cancer. These studies have not been of high quality or large enough to change NHS practice.

Patients with suspicious areas on the MRI are usually advised to have a prostate biopsy. This involves taking tissue samples using a needle. The samples are then looked at under the microscope by a pathologist to see if cancer cells are present. There are two ways of doing a prostate biopsy. One is where the person doing the biopsy decides where to put the biopsy needle by looking at the MRI scans that were already taken on a computer screen. The needle is guided to the prostate using live ultrasound scans that are shown on a different screen near to the patient. The biopsy operator makes a judgement about where to place the biopsy needles. This is called visual registration. Tissue samples from other areas of the prostate that look normal on the MRI scans are also taken to ensure cancer is not missed. The other type of biopsy is called image fusion. During image fusion biopsy, the biopsy operator uses the MRI scans that were taken beforehand but laid on top of the live ultrasound images during the biopsy. This uses software and takes a few minutes longer to perform. Once the MRI images and ultrasound images are ‘fused’, the actual biopsies are taken as normal. Studies over the last 5 years have shown mixed results. Some have shown that image fusion biopsy is no better than visual registration biopsy, whilst a few have shown it might make a difference in improving cancer

detection. As a result, it is not known for certain which way is better. A large study is needed to show whether we need to do image fusion or not, in order for the NHS to decide whether or not to use it in all hospitals doing prostate biopsies.

Who can participate?
Patients with a prostate (either cis-male gender or trans-female gender with no prior androgen deprivation hormone use at all), aged 18 years or above, referred to hospital and advised to undergo a prostate MRI because of an abnormal digital rectal examination (regardless of PSA level) and/or an elevated PSA (within 6 months of screening visit): PSA 3.0 ng/ml or over for age 50-69 years, PSA 5.0 ng/ml or over for age 70 years and over, and if there is a family or ethnic risk for prostate cancer PSA 2.5 ng/ml or over for age 45-49 years

What does the study involve?
Participants will have an MRI scan of the prostate. This scan will either be a long MRI or a short MRI. The clinical team will then advise whether a biopsy is required. The biopsy is sometimes on the same day. There are no extra visits required for this study and the researchers will collect the information about the MRI and biopsy directly from the participants' health records.

What are the possible benefits and risks of participating?
The researchers do not expect any personal benefits for participants. However, patients who are randomised to have the short MRI would be in the scanner for a shorter period of time and would not have the gadolinium contrast injection. The researchers are confident that neither the short MRI nor the long MRI will risk the cancer getting significantly worse even if it were present but not seen by the scan.
There might be a small benefit in having image fusion targeted biopsy, but this is something the researchers are trying to find out. Studies have mainly shown similar cancer detection between visual registration and image fusion biopsy, but some small studies have shown a small advantage in using image fusion.
A biopsy might find unimportant cancers that might not cause any symptoms or problems in the participant's lifetime. Unimportant prostate cancers do not need to be treated as they do not shorten life. It is usually very safe to monitor unimportant prostate cancer using active surveillance.
With any tests for cancer there can be false negatives and false positives. No medical test is completely accurate. The researchers think these tests will pick up the majority of important prostate cancers. However, they may not pick up all cases of important prostate cancer (false negative). At the same time, the tests can sometimes be positive in patients who do not have important prostate cancer (false positive). These patients will be offered a prostate biopsy. Any type of prostate biopsy can sometimes cause side effects, such as discomfort, urine infection, difficulty passing urine, and blood in the urine, bowel movements or semen.
Third, some prostate cancers are unimportant because they will never cause symptoms or shorten life. They are harmless and do not require any treatment. Despite this, a few men are still worried and choose to have unnecessary treatment. This treatment can have side effects on sexual, urinary and bowel functions and have no effect on the length of a man's life.
On the other hand, important prostate cancers are those that do need to be treated. The researchers would like to find these as early as possible. Treatment options for these cancers will depend on other factors such as the PSA level, whether the cancer is contained to the prostate, how many areas of important cancer there are in the prostate and the grade of the cancer. The grade is reported by the pathologist to show how aggressive the cancer is. Most important prostate cancers contained in the prostate can be treated by surgery called prostatectomy, or radiotherapy using X-rays or focal therapy targeted to only areas of the prostate cancer using heat (HIFU) or freezing (cryotherapy).

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
February 2022 to January 2026

Who is funding the study?
Cancer Research UK

Who is the main contact?
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
303690

ClinicalTrials.gov number
NCT05574647

Secondary identifying numbers
CPMS 52871, IRAS 303690

Study information

Scientific Title
Imperial Prostate 7 - Prostate Assessment using Comparative Interventions – Fast MRI and Image-fusion for Cancer (IP7-PACIFIC)

Acronym
IP7-PACIFIC

Study objectives
To evaluate the role of biparametric MRI and image-fusion targeted biopsies for the detection of prostate cancer.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 16/06/2022, London Bromley Research Ethics Committee (Temple Quay House, 2 The Square, Temple Quay, Bristol, BS1 6PN, United Kingdom; +44 (0)207 104 8124; bromley.rec@hra.nhs.uk), ref: 22/LO/0366

Study design
Randomized; Interventional; Design type: Screening, Imaging

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

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

Interventions
IP7-PACIFIC incorporates two linked RCTs which will test whether bpMRI and image-fusion make a difference if used in clinical practice, across multiple centres, without the biases inherent in paired-cohort studies. The design provides economies of scale and scope compared to addressing these research gaps with two separate RCTs.

Since bpMRI is an abbreviated examination, clinicians and patients require reassurance that it is no worse than mpMRI. Therefore, the researchers plan a non-inferiority evaluation. This means they will determine whether mpMRI and bpMRI are similar in accuracy. The second randomisation will involve co-enrolment of a subgroup of the first randomised group i.e., patients referred for biopsy following a positive MRI (whether bpMRI or mpMRI). To justify the extra cost for the technology, the researchers would expect image-fusion to detect more clinically important cancers than visual estimation.

Participant flow through study:

Consent
Participants identified as eligible for the study will be sent the patient information after the clinical team has told them of the study. They will have the opportunity to discuss the study and the researchers will take consent remotely or face to face depending on patient preference and convenience.

There will be some optional consent points.

First, patients will also be asked to give optional consent for identifiable data to be linked with the national databases (ONS and HES database). The researchers will apply for subsequent funding from academic and charity funders to allow them to carry out the linkage work. The identifiable fields (NHS number) required for linkage will be encrypted using a one-way encryption algorithm. The researchers will ask patients if they are happy to give consent for their health status to be followed up over time. This will be done by linking their name and NHS number with records held by the NHS and maintained by the NHS Information Centre and NHS Central Register or any applicable NHS information system. This will allow the researchers to track what happens after the study finishes and observe if anyone gets cancer in future and about the type of cancer and treatment they have had. The researchers will also ask patients whether or not they give permission to be contacted by a member of the study research team within 10 years of signing their health status (including details of any other tests and treatment they have had since the study) and quality of life. If the patient decides to take part a member of the study research team may send this request to the patient's home address. The researchers would want to link individual trial information to national databases on cancer diagnosis, GP databases on healthcare and medication use and finally death registry to see if any of the men died from prostate cancer.

As prostate cancer is often a slow-growing disease which may not progress for many years the researchers will also ask patients if they are happy to keep personal data stored or accessed for 10 years on the NHSCR (National Health Service Care Register).

Second, in order to get an area-based estimate of deprivation, the participants' partial postcodes will be converted into an Index of Multiple Deprivation (IMD) score. The IMD is the established index of deprivation for England and Wales and has been adopted widely in studies across local and national government. Partial postcodes will be stored in the study database, only IMD rank, which is based on a detailed ward-level index of deprivation based on severe separate domains.

Study interventions
Participants who sign the informed consent form will be registered on the electronic case report form online and the software will generate a randomisation allocation for them for both randomisation 1 and randomisation 2. Randomisation 2 will only be relevant if participants are advised by their clinical team to have a biopsy based on their MRI and other clinical factors.

Participants will then fill in questionnaires for baseline genito-urinary and bowel function using validated questionnaires and overall health status; this will be online or via paper copies. The questionnaires will consist of the HADS score questionnaire, EPIC (urinary, erectile, bowel) questionnaires and EuroQoL (EQ-5D-5L).

Participants will then undergo either bpMRI or mpMRI according to their allocation. Blinding will not be possible. They will be asked again to fill in a questionnaire on their overall health status (EuroQoL [EQ-5D-5L]) after the MRI and before the biopsy. This will be online or via paper copies.

Once the MRI report is issued, the local clinical team will make a decision about advising a biopsy or not.

Participants advised to have a biopsy will undergo a visual estimation targeted biopsy or an image fusion targeted biopsy. Participants will then fill in questionnaires for baseline genito-urinary and rectal function and overall health status at 7-14 days and at day 35-90 of the biopsy; this will be online or via paper copies. Questionnaires will consist of HADS, EPIC and EQ-5D-5L

Participants who were given a biopsy will also be asked to report on their experience of prostate biopsy using the Patient Experience of TRUS Biopsy (PETB) 7-14 days after biopsy and 35-90 days after the biopsy.

Participants will also be asked to complete a questionnaire on their MRI-related side effects. They will be asked to complete this after their MRI but before the biopsy if they were given a biopsy.

Participants will receive either a paper or electronic request to report any side effects or complications of the MRI and/or biopsy to the study team at the same time as the questionnaires. This information will also be collected directly from health records. The results of the biopsy, if they underwent one, will be communicated by the local clinical team. This data and any treatment recommendations will be collected directly from case notes by the research team.

Intervention Type
Other

Primary outcome measure

Randomisation 1: bpMRI versus mpMRI
Proportion of clinically significant cancers, defined as any amount of Gleason ≥3+4 (ISUP Grade Group ≥2) on biopsy, detected in the randomised population of patients at risk. Timepoint: maximum 12 weeks following enrolment

Randomisation 2: Visual-registration targeting versus image-fusion targeting
Proportion of clinically significant cancers, defined as any amount of Gleason ≥3+4 (ISUP Grade Group ≥2) on biopsy, detected in the randomised population of patients biopsied for a suspicious MRI. Timepoint: maximum 12 weeks following enrolment

Secondary outcome measures

1. MRI and biopsy-related adverse events and serious adverse events measured using documentation at maximum 12 weeks following enrolment
2. The proportion of patients advised to undergo a needle biopsy and the proportion of patients undergoing a prostate biopsy after MRI. The researchers will document common reasons for patients who are advised to undergo a biopsy who decline and reasons for patients who are advised against a needle biopsy who still choose to have a biopsy. They shall record the number of patients with a non-suspicious bpMRI/mpMRI that are recommended for biopsy and the types of cancers subsequently detected. Timepoint: maximum 12 weeks following enrolment
3. The proportion of patients diagnosed with clinically insignificant prostates cancers, defined as any Gleason 3+3=6 on needle biopsy carried out after MRI. These will also be stratified by MRI score, presence of clinical risk factors and whether the biopsy was carried out on clinician recommendation or patient choice. Timepoint: maximum 12 weeks following enrolment
4. The proportion of patients diagnosed with clinically significant and clinically insignificant prostate cancers using other histological thresholds on prostate biopsy carried out after MRI. Similarly, as above, the researchers will also evaluate these proportions by MRI score at patient and lesion level (on a scale of 1 to 5) and by the presence or absence of clinical risk parameters. Timepoint: maximum 12 weeks following enrolment
5. The proportion of patients diagnosed with clinically significant and clinically insignificant prostate cancers using all histological thresholds on targeted biopsy using four targeted cores only compared to six targeted cores for the first targeted lesion. Timepoint: maximum 12 weeks following enrolment
6. Detection rates for each randomised group of known prognostic risk categories. These are D' Amico, National Comprehensive Cancer Network (NCCN) and Cambridge Prognostic Groups (CPG). Timepoint: maximum 12 weeks following enrolment
7. A comparison of the two MRI scoring systems, Likert and PIRADS (latest version as defined in MRI Reporting SOP), in terms of the proportion of patients biopsied and subsequently diagnosed with clinically significant and clinically insignificant prostate cancer, using each of the histological thresholds, on a prostate biopsy. This study would be an opportunity to conduct a robust comparison of the two reporting systems in a large sample and allow inclusion in meta-analyses with studies that used either one alone. Timepoint: maximum 12 weeks following enrolment
8. Characteristics of cancer in targeted versus systematic biopsies by MRI score, PSA, PSA density, age, ethnicity, family history and history of prior prostate biopsy with a multivariable evaluation to determine whether patients might avoid systematic sampling in the future. Timepoint: maximum 12 weeks following enrolment
9. External validation of the Imperial RAPID Risk Score (MRI+) and Imperial RAPID Risk Score (Systematic+) within each randomised group of the IP7-PACIFIC study, external validation at maximum 12 weeks following enrolment
10. Impact of prostate biopsy in each randomised group on patient-reported outcomes and

patient-reported experience measures using an updated version of the Prospective cohort study (Prostate Biopsy Effects: ProBE) questionnaire and the EQ-5D-5L health-related quality of life questionnaire, and stratified by type of biopsy (transrectal vs transperineal; for transperineal biopsy, limited systematic vs sectoral systematic). Timepoint maximum 12 weeks following enrolment
11. Analysis of biopsy rates and detection of cancer (by all histological thresholds) as well as patient-reported outcomes and experience measures in the randomised group will be conducted by centre using centre size. MRI scanner type (1.5 Tesla vs. 3.0 Tesla), type of biopsy route used (transrectal vs transperineal), number of systematic biopsies taken (limited systematic vs extended systematic biopsy), type of analgesia/anaesthetic (local anaesthetic, sedation or general anaesthetic) as additional stratification factors. Timepoint: maximum 12 weeks following enrolment

Overall study start date
01/02/2022

Completion date
31/01/2026

Eligibility

Key inclusion criteria
Summary: Patients with a prostate (either cis-male gender or trans-female gender with no prior androgen deprivation hormone use at all) referred to hospital urology departments by their GP due to a clinical suspicion of prostate cancer (elevated serum prostate specific antigen [PSA], abnormal feeling prostate on rectal examination). These patients are normally recommended to undergo a prostate MRI as part of standard care.

Randomisation 1: bpMRI versus mpMRI
Patients with elevated age-specific PSA or abnormal digital rectal examination of the prostate with PSA levels as determined by NICE guidance and local NHS Cancer Alliance or regional guidance. Recent UK consensus guidance [Prostate Cancer UK, 2016] from over 300 UK healthcare professionals and men affected by prostate cancer and endorsed by the British Association of Urological Nurses (BAUN), the British Association of Urological Surgeons (BAUS) and the Primary Care Urology Society (PCUS) also stipulates that patients with a family history (one or more first-degree male relatives) or ethnic risk group (those identifying as of Black-African/Black-Caribbean) should be further investigated with PSA ≥2.5 when aged 45-49 years. The researchers will approach these patients as well.

Randomisation 2: Visual registration targeting versus image fusion targeting
Suspicious finding on mpMRI or bpMRI from randomisation 1 requiring targeted biopsy (MRI categories 3, 4 or 5)

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 3600; UK Sample Size: 3600

Key exclusion criteria
Current participant exclusion criteria as of 07/04/2025:
Randomisation 1: bpMRI versus mpMRI
1. PSA >50 ng/ml. The rationale being that above this PSA level, rates of clinically important prostate cancers are quite high and a pre-biopsy MRI is likely to be of less utility.
2. Prostate biopsy within the previous 12 months from the date of screening. A prior biopsy can cause artefact changes which affect the quality of the images. These artefact changes can take 12 months to dissipate.
3. Prior prostate cancer diagnosis at any timepoint. Patients on active surveillance will have differing prior probabilities of clinically important cancer than those referred with a clinical suspicion and are therefore excluded.
4. Any absolute contraindication to MRI, gadolinium contrast or biopsy. Patients with one or two hip prostheses are excluded. These prostheses often cast a large imaging artefact over the prostate area on MRI, and radiologists prefer an mpMRI scan because the diffusion images can be particularly affected.
5. Contraindication to performing a biopsy guided by a transrectal ultrasound probe
6. Unable to give informed consent to the study

Randomisation 2: Visual registration targeting versus image fusion targeting
1. As above for randomisation 1
2. Patient refusal for biopsy

Previous participant exclusion criteria:
Randomisation 1: bpMRI versus mpMRI
1. PSA >50 ng/ml. The rationale being that above this PSA level, rates of clinically important PCa are quite high and a pre-biopsy MRI is likely to be of less utility.
2. Prostate MRI or prostate biopsy within the previous 24 months from the date of screening. A prior prostate MRI which is negative will add selection bias and a prior biopsy can cause artefact changes which affect the quality of the images. These artefact changes can take a number of months to dissipate and in some patients up to 9-12 months after the biopsy.
3. Prior prostate cancer diagnosis at any timepoint. Patients on active surveillance will have differing prior probabilities of clinically important cancer to those referred with a clinical suspicion and are therefore excluded.
4. Any absolute contraindication to MRI, gadolinium contrast or biopsy. Patients with one or two hip prostheses are excluded. These prostheses often cast a large imaging artefact over the prostate area on MRI and radiologists prefer a mpMRI scan because the diffusion images can be particularly affected.
5. Unable to give informed consent to the study

Randomisation 2: Visual registration targeting versus image fusion targeting
1. As above for randomisation 1
2. Patient refusal for biopsy

Date of first enrolment
01/10/2022

Date of final enrolment

30/11/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
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Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK; Grant Codes: PPRCPJT\100007

Alternative Name(s)
CR_UK, Cancer Research UK - London, CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
When the study is completed the results will be analysed and presented at international meetings before being published in a medical journal.

Intention to publish date
31/01/2027

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol file	version 3.0	18/12/2023	11/01/2024	No	No