Prostate Imaging using MRI ± contrast Enhancement (PRIME) Frequently Asked Questions

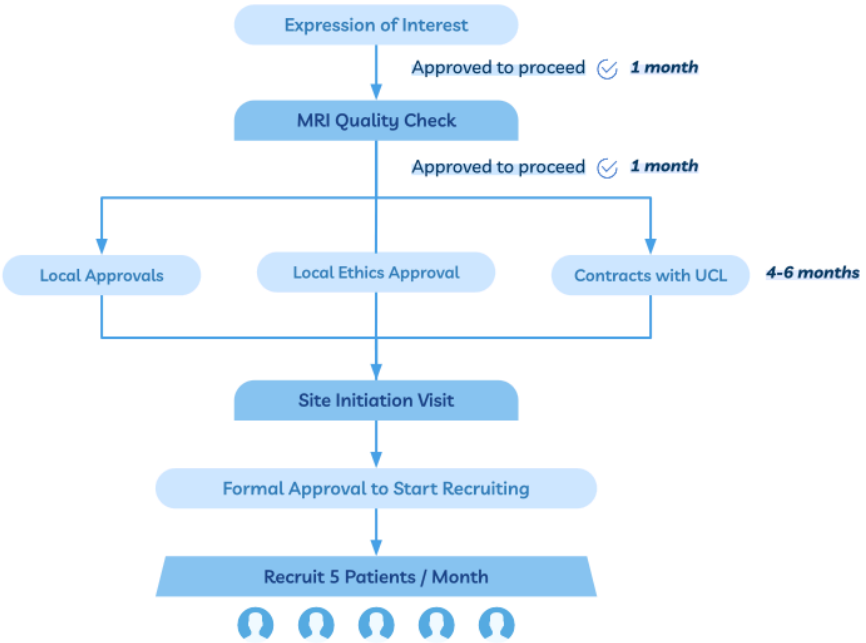
A study assessing whether bi-parametric MRI is non-inferior to multi-parametric MRI in the diagnosis of clinically significant prostate cancer

Contents

Sites under setup

What is the approval process to take part in PRIME?

1. Sites are invited to submit an expression of interest. Following approval of data regarding the site's detection rates of prostate cancer, sites are invited to take part in the MRI Quality Control stage.
2. As part of the MRI Quality Control stage, sites are reviewed based on biopsy score results, protocols of their MRI machines, and DICOM image quality of their scans.
3. On approved for MRI Quality Control, sites will be invited to being obtaining local approvals, local ethics approvals and to organise contracts with UCL.
4. Sites will then undergo a site initiation visit, followed by final approval to being recruiting patients to the study.



How many sites will take part in PRIME?

We aim to have 25 sites involved in PRIME.

How many sites have been approved to take part?

Over 50 sites have expressed an interest to take part in PRIME. From that, around 20 sites have completed the MRI eligibility, quality control stage. Once approved for MRI eligibility, sites begin the contract process, however, we do not expect that all sites will complete this step. The 25 sites taking part will be on a first come first served basis. If the full 25 sites have completed the setup process, it is possible that we may no longer consider further sites to participate in the study. If this seems like it is likely to happen at any stage, we will immediately give investigators who have started the process notification at the earliest possible time.

How many patients is each site expected to recruit, is there an upper limit, and over what time period?

Every site will have a target to recruit 30 patients. Once this is met, we will decide whether to continue or limit recruiting. This target may be altered depending on overall site recruitment in progress (I.e. it could be less than 30 patients per site). Authorship will be based around the number of patients each site recruits. We want this study to be generalisable and therefore we want to recruit from multiple centres, therefore we may be flexible in altering the number of patients recruited in each centre. We would not expect any single site to recruit over 50 patients over a two-year period.

Is there any per patient funding allocated?

There is allocation for per patient funding. The final amount is due to be confirmed, but we estimate that this will be around €1000-€1500 in total for 30 patients.

Why are both LIKERT and PIRADS v2.1 being used to report MRIs?

A major limitation of studies investigating the role of contrast is that they typically rely on the PIRADS scoring system only. Normally, a threshold of a score of 3 or above is used to trigger a biopsy. As PIRADS already assumes that contrast has a minimal role and doesn't change a 2 to a 3, it would technically not be possible that a study only using PIRADS would show any added value of significant cancer detection by the use of the contrast sequence. To truly evaluate the contrast sequence a scoring system, like Likert, that assumes that it is possible that contrast has a role needs to be used to differentiate between a 2 and a 3. Therefore, we ask you to score Likert first, then PIRADS since that will be an international standard that may be used and allows results across centres to be more comparable.

This paper (https://pubmed.ncbi.nlm.nih.gov/31627804/) provides a summary on the similarities and differences between Likert and PIRADS v2.1 scoring.

We will provide a guide on the differences between the two for the study, and our radiologists will be happy to provide training.

Can patients with negative MRI and PSA density <0.15 be included?

The trial protocol is for them not to be biopsied. If the local protocol is to biopsy every patient with a negative MRI and low PSAD then please let us know in advance as we need to make a decision as to whether we would permit your centre being involved in the study. These would technically count as protocol deviations.

There is however a technicality where you would not biopsy the patient immediately, but have a management decision appointment after results of the MRI. After this appointment technically the patient leaves the study and the urologist can thereafter do what they want. If they plan to take a biopsy, we collect the results of the biopsy as the last data entry point (i.e. no more patient visits but just a pathology data collection for them) - this caters for some patients for whom their treating clinician would like to perform biopsy. However, we ideally do not want this technicality to be used on every patient that falls into this category.

Why do we need to collect functional questionnaires such as IPSS and IIEF scores?

We are doing a virtual central multi-disciplinary team meeting which requires hypothetical treatment eligibility decisions to be made when blinded and then unblinded to contrast information. Knowing some key baseline information collected in a validated and internationally accepted way allows these decisions to be made in a more informed way, particularly when dealing with patients from different centres and countries.

How do I edit the list of trial personnel at my centre?

Following MRI Quality Control approval, your centre will have been sent the PRIME Study Site Contact and Policy REDCap form as part of your LIP email (https://redcap.link/PRIMEStudySCD). The form requires you to list the details of the personal at your centre that will be involved in the PRIME Study. At the minimum, it asks for each individual, their title, full name, job title, email address, telephone, mobile phone and start date.

Once the form is completed, you will be presented with the following page. It is **strongly recommended** that you:

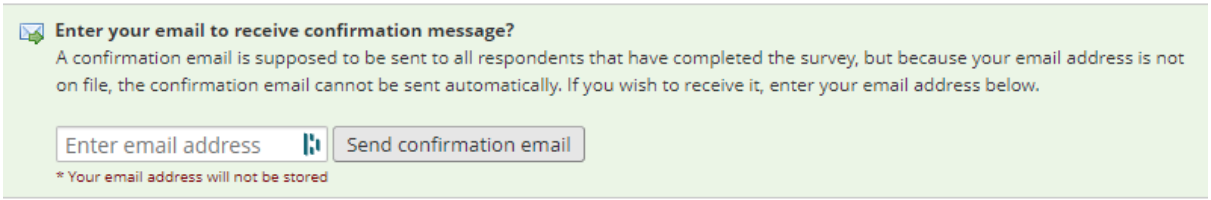
1. Enter your email address to receive a .pdf copy of your responses for your own records.
2. Make a note of the return code. As you may be required to update this document throughout the duration of the PRIME Study, this return code will enable you to make edits to the form. This return code is specific to your own form.

Close survey

Thank you for completing the Site Contact and Policy Document. Do not close this page.

Please:

- Enter your email address below to receive a confirmation message and a .pdf copy of your responses. **This is strongly recommended**.
- Make a note of your return code in case you need to make amendments to your details in the future. **This is strongly recommended**. This code can be shared with other colleagues if they will help with providing further details regarding the MRI protocols for each scanner.



If you have forgotten your return code or are unable to access the form to make edits, please contact us and we will be able to assist you.

<u>If you require to add an additional trial personal</u>

1. Please access the site contact and policy document at this address: https://redcap.slms.ucl.ac.uk/surveys/index.php?s=UkDBVoDaD7P5ARJb&__return=1
2. Please enter your unique return code.
3. Navigate to the relevant section of the form (i.e. number of radiologists) and increase to the relevant number of individuals.
4. Enter the individuals' information.
5. Navigate to the "Site update" section of the form. Please enter the date of the amendments, provide a short summary of the changes made to the form, and provide a signature to verify these amendments.
6. Click submit.
7. Enter your email address to receive a .pdf of your updated form and make a note of your return code.

<u>If you require to remove a trial personal</u>

1. Please access the site contact and policy document at this address: https://redcap.slms.ucl.ac.uk/surveys/index.php?s=UkDBVoDaD7P5ARJb&__return=1
2. Please enter your unique return code.

3. Navigate to the relevant section of the form (i.e. number of radiologists) and navigate to the relevant individual.
4. Please enter the end date for this individual. This should be the date the individual has stopped working on the PRIME Study.
5. Navigate to the "Site update" section of the form. Please enter the date of the amendments, provide a short summary of the changes made to the form, and provide a signature to verify these amendments.
6. Click submit.
7. Enter your email address to receive a .pdf of your updated form and make a note of your return code.

Describe the investigator's international research experience

The Chiefinvestigator, Dr Veeru Kasivisvanathan has 10 years of research experience in international research. He has led the practice changing PRECISION study (NCT02380027), a randomised trial in prostate cancer diagnosis across 23 centres in 11 countries around the world. This was published in the New England Journal of Medicine and led to the first major change in the way that we diagnose prostate cancer for 30 years. Dr Kasivisvanathan also ran the IDENTIFY study (NCT03548688), a prospective observational study in 11,000 patients in more than 100 centres around the world.

Describe the investigator's experience with this locality and study population

The Chief investigator, Dr Veeru Kasivisvanathan has 10 years of research experience in prostate cancer. Specifically, he has an expertise in prostate cancer diagnosis studies using the same study population, having led the practice changing PRECISION study (NCT02380027), a randomised trial in prostate cancer diagnosis which was published in the New England Journal of Medicine and led to the first major change in the way that we diagnose prostate cancer for 30 years.

Specific to Canada

Dr Kasivisvanathan has run international studies in Canada before; the PRECISION trial included patient recruitment at Jewish General Hospital, Montreal, Canada and collaboration with Sunnybrook Health Sciences Centre, Toronto, Canada.

Specific to UK

Dr Kasivisvanathan has an active study portfolio of over 9 studies including UK patients in clinical trials and observational studies.

Describe any current social, economic, and political considerations regarding the locality where the research will be conducted, that may impact the research

I am unaware of any social, economic, and political considerations regarding the locality where the research will be conducted.

Specific to Canada

Dr Ghai may be able to answer further if the question specifically refers to Canada.

Potential documents you may require to complete the contracts process

1. Budget template

The budget is in the site agreement, at Schedule 3 – Study Support Arrangements – Section A Financial Agreements. At the moment, there is only provision in there for recruitment costs.

2. Clinical trial agreement

The site agreement should be in the Local Information Pack (LIP). The site agreement is also known in the UK as the 'mNCA', so it may be called that in the LIP.

3. CMS approval

UCL does hold insurance for clinical trials and covers claims up to £15,000,000.

UCL, as Sponsor of the PRIME study, is *prima facie* accountable and liable to participants who are injured as a result of participating in this study, or to their Personal Representatives in the event of death of a participant as a result of participating in this study. In the event that such harm suffered by the participant is as a result of the study's design, rather than the negligent acts or omissions by the Site, then UCL will remain liable to the participant and UCL holds appropriate Clinical Trials insurance cover to the value of £15,000,000 per claim. If, on the other hand, the harm suffered by the participant is as a result of the Site's failure to correctly follow the study Protocol and/or some other negligent act or omission by the Site, then notwithstanding UCL's responsibility as the Sponsor or the study, UCL shall seek to recover from the Site any losses it incurs as a result of such acts or omissions by the Site, in accordance with the site agreement between UCL as Sponsor and the Site in question.

As the UK is no longer part of the European Union, does PRIME have a European legal representative?

The following is a response provided by UCL as the sponsor for PRIME:

"If the study is a non-CTIMP study and UCL is the data controller with European sites processing data on UCL's behalf, UCL Research Ltd need to be a legal representative in the EU. Assigning additional representatives in the EU does not require an amendment to be notified in the UK. Similarly, no amendment is required in the UK to establish any arrangements solely in relation to the study's management and conduct outside the UK that do not affect the approved UK study. Sponsorship of the

relevant study will remain with UCL. UCL's insurance will cover UCL Research Limited and the activities that it will carry out in the EU. There are no extra processes for insurance that need to be taken by researchers for trials that have EU sites."

After Site Initiation Visit / Data Collection / eCRF

How will you facilitate the blinding process?

There are two methods in which you may implement this blinding process. During the meeting, we will also discuss this. Please find briefly some information on this:

- The first method is using the MIM software. All sites taking part in PRIME will be given access to this. The integrated workflow will only reveal the bpMRI sequences first. Once the bpMRI report is submitted, MIM will automatically unblind the DCE sequence, and then the radiologist can report the mpMRI scans.
    - The MIM workflow access is currently being sorted out for you.
- The second method is for an independent person to confirm that the radiologist did not view the DCE sequence when reporting the bpMRI sequence, and then to unblind and report the mpMRI sequence.

My patient did not have a DRE before MRI?

If the participant did not have a Digital Rectal Exam (DRE) at the time the baseline information is being collected. Please remind the biopsy operator to complete a DRE before the biopsy. In addition, the DRE could be performed by a clinician at any time before the biopsy during another visit. If the patient is not going on to have a biopsy, data from the primary care referral may be used instead.

My patient does not know his family history of prostate cancer?

If the participant does not remember or does not know if they have any family history of prostate cancer, please select 'no'.

What is the difference between cores 'taken' at Visit 3 Biopsy and cores 'taken' at Biopsy Pathology?

The number of cores taken at biopsy should follow the biopsy instructions in the protocol. The biopsy operator should document the number of cores taken in the operation note. This should be transferred to the Visit 3 → Biopsy → Biopsy Details. This information will be used to assess compliance of the protocol.

The number of cores taken at biopsy **may not be the same** as the number of cores taken / reported at biopsy pathology. This is because cores may fragment after being taken at biopsy. This information will be used to assess other outcomes, for example, proportion of positive cores.

For patients

I am interested in the PRIME Study, how do I take part?

The PRIME Study is about to start recruitment and will be recruiting from various hospital around the UK and internationally. The only way patients can participate in the study is if they are being investigated for prostate cancer after being referred from their GP. Once patients are referred to a hospital for further investigations such as an MRI scan, they may then be approached to participate if they meet the participation criteria. If you think you may have prostate cancer, please consult your GP urgently. If you have been referred by your GP to a hospital for further investigations, please speak to the Urology team there to ask if they are recruiting for the PRIME study and if you would be eligible to participate.

If you are interested to follow the trial progress, you can do so by checking this page periodically: https://www.ucl.ac.uk/surgery/research/department-targeted-intervention/urology/prime-trial-infor

mation. Once the study has started recruitment, you will be able to check this page to see which hospitals are currently recruiting patients.