Biparametric versus Multiparametric MRI for Prostate Cancer Diagnosis: The PRIME Diagnostic Clinical Trial

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Key points

Question

Is biparametric MRI non-inferior to multiparametric MRI in the detection of clinically significant prostate cancer?

Findings

In this level-1, prospective, multicentre, within-patient, non-inferiority trial of 490 biopsy-naïve men, biparametric MRI was non-inferior to multiparametric MRI for detection of Gleason Grade Group 2 or higher prostate cancer (difference, -0.4%; 95% confidence interval, -1.2% to 0.4%; p=0.5).

Meaning

In men with suspected prostate cancer, providing image quality is adequate, an abbreviated biparametric MRI, with or without targeted biopsy, could become the new standard of care for prostate cancer diagnosis.

Abstract

Importance

Multiparametric MRI (mpMRI), with or without prostate biopsy, has become the standard of care for diagnosing clinically significant prostate cancer (csPCa). Resource capacity limits widespread adoption. Biparametric MRI (bpMRI) which omits the gadolinium contrast sequence, is a shorter and cheaper alternative offering time-saving capacity gains for health systems globally.

Objective

To assess whether bpMRI is non-inferior to mpMRI for csPCa diagnosis.

Design, setting and participants

A prospective, multicentre, within-patient, non-inferiority trial of biopsy-naïve men from 22 centres (12 countries) with clinical suspicion of prostate cancer (elevated prostate-specific antigen (PSA) and/or abnormal digital rectal examination (DRE)) from April 2022 to September 2023, with the last follow-up conducted on 03 December 2024.

Interventions

Participants underwent mpMRI, comprising T2-weighted (T2-WI), diffusion-weighted (DWI) and dynamic contrast-enhanced (DCE) sequences. Radiologists reported abbreviated bpMRI first (T2-WI and DWI), blinded to DCE. After unblinding, radiologists reported the full mpMRI. Patients underwent a targeted biopsy with or without systematic biopsy if either bpMRI or mpMRI was suggestive of csPCa.

Main outcomes and measures

The primary outcome was the proportion of men with csPCa. Secondary outcomes included the proportion of men with clinically insignificant cancer. The non-inferiority margin was 5%.

Results

555 men were recruited, of whom 490 were included for primary outcome analysis. Median (IQR) age was 65 (59-70) years and PSA was 5.6 (4.4-8.0) ng/mL. The proportion of patients with abnormal DRE was 12.7%. BpMRI was non-inferior to mpMRI, detecting csPCa in 143 of 490 men (29.2%), compared to 145 of 490 men (29.6%) (difference, -0.4%; 95% CI, -1.2% to 0.4%; p=0.5). BpMRI detected clinically insignificant cancer in 45 of 490 men (9.2%), compared to 47 of 490 men (9.6%) on mpMRI (difference, -0.4%; 95% CI, -1.2% to 0.4%). Central quality control demonstrated that 99% of scans were of adequate diagnostic quality.

Conclusion and relevance

In men with suspected prostate cancer, providing image quality is adequate, an abbreviated bpMRI, with or without targeted biopsy, could become the new standard of care for prostate cancer diagnosis. With approximately 4 million prostate MRIs performed globally annually, adopting bpMRI could substantially increase scanner throughput and reduce costs worldwide.

Trial registration

ClinicalTrials.gov Identifier NCT04571840

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Introduction

In the past five years, multiparametric MRI (mpMRI) with or without prostate biopsy has become an international standard of care for prostate cancer diagnosis[1–3]. A mpMRI consists of three sequences: T2-weighted, diffusion-weighted and dynamic contrast-enhanced (DCE) imaging. However widespread adoption is challenging due to resource issues and increased demand for prostate MRI[4,5].

One solution is to adopt a shorter, less resource-intensive scan without the DCE sequence[6,7], known as biparametric MRI (bpMRI). This reduces scan time from 30–40 minutes to 15–20 minutes, thus increasing scanning capacity[6,8,9]. Using contrast-medium for mpMRI necessitates a medical practitioner to be present in case of an allergic reaction, meaning that by avoiding a patient injection, bpMRI is less resource intensive in terms of staff and scanner time. Further, it is known that the contrast-medium used, gadolinium, deposits in the brain, bone, liver and skin[10,11]. In addition to the cost of the contrast-medium and its administration, gadolinium contamination of the environment has been observed[11].

Most studies comparing bpMRI to mpMRI are typically small, single-centre, unblinded retrospective, and without MRI quality assurance[7,12,13]. They typically use a scoring system[14] which already assumes that DCE has a limited role in cancer detection, limiting their ability to show a difference in cancer detection[15]. Further, biopsies were typically either not targeted to MRI-suspicious areas or done on basis of the full mpMRI information only, without considering what would have been done without the DCE. The only randomised trial comparing bpMRI to mpMRI showed

significant cancer detection in favour of mpMRI (24% vs. 33%) but without statistical significance due to being underpowered[16]. Genuine uncertainty remains as to whether DCE improves significant cancer detection. Contrast is also thought to play an important role in staging decisions and evaluating involvement of key anatomical structures around the prostate, thus influencing treatment eligibility options and treatment planning[17,18].

We designed the Prostate Imaging using MRI +/- contrast Enhancement (PRIME) trial, to overcome these limitations[15,19] and investigate whether bpMRI is non-inferior to mpMRI for the detection of clinically significant prostate cancer (csPCa).

Methods

Trial design

PRIME, NCT04571840, was a prospective, international, multicentre, within-patient, non-inferiority, level-1 evidence diagnostic yield study conducted in 22 centres in 12 countries (eTable 1, Supplement 3). A diagnostic yield study is one which evaluates and compares the proportion of men with a target condition detected by different diagnostic tests. Men who gave written informed consent were enrolled into the study and underwent mpMRI. The trial protocol has been published[19] and was approved by the ethical review board at each participating institution (Supplement 1). The trial was monitored by an independent Global Trial Steering Committee.

Participants

Participants were recruited in outpatient clinics and were eligible if they were referred with clinical suspicion of prostate cancer based on elevated PSA or abnormal digital rectal examination (Figure 1). Participants were required to have PSA ≤ 20ng/mL and no prior MRI or biopsy. Self-reported ethnicity data were collected on enrolment using predefined categories to characterise the ethnic composition of the study cohort (Table 1).

MRI and prostate biopsy

Patients underwent mpMRI using a 1.5 or 3.0T scanner with a pelvic phased-array coil, with or without an endorectal coil (eTable 2, Supplement 3). T2-weighted, diffusion-weighted and DCE sequences were acquired according to Prostate Imaging – Reporting and Data System version 2.1 (PI-RADSv2.1) guidelines[14]. Image quality for each scanner was optimised to be guideline compliant at each site[13].

A site radiologist first evaluated the bpMRI (T2-weighted and diffusion-weighted imaging), strictly blinded to DCE sequences (Figure 1). Successful blinding was confirmed for each case by an independent clinician or dedicated computer workflow. Suspicious areas on bpMRI were identified by the radiologist and assigned a score according to the Likert[20] and PI-RADSv2.1 scoring systems[14] on a scale from 1 to 5, with higher numbers indicating a greater likelihood of csPCa. Both scoring systems were defined as 1 (highly unlikely), 2 (unlikely), 3 (equivocal), 4 (likely) and 5 (highly likely) to contain csPCa. Radiologists were mandated to record the bpMRI based decision and biopsy-target recommendations before DCE was revealed. This allowed an unbiased assessment of bpMRI's standalone contribution to cancer detection.

After immediate unblinding to DCE, the radiologist re-evaluated all three sequences and generated a new mpMRI report. If a completely new suspicious region was identified that was absent on bpMRI, or if an existing bpMRI lesion appeared significantly larger on mpMRI, the newly revealed region (or non-overlapping portion of the enlarged lesion) was marked as a separate, DCE-specific target for biopsy.

Areas on either bpMRI or mpMRI suggestive of cancer, scoring 3 (equivocal for csPCa), 4 (likely for csPCa), or 5 (highly likely for csPCa) on either the Likert or PI-RADSv2.1 scores underwent targeted prostate biopsy. Systematic biopsies were taken on MRI-negative sides of the prostate.

If the MRI was not suggestive of csPCa, scoring 1 or 2 on both the Likert and PI-RADSv2.1 scales, bilateral systematic biopsies were undertaken if there was high clinical suspicion of prostate cancer, with a PSA density of ≥ 0.15ng/mL/mL; with a PSA density < 0.15ng/mL/mL, no prostate biopsy was taken.

MRI-targeted biopsy registration was performed by visual or software-assisted registration[21,22] via the transperineal or transrectal route, according to local expertise. Biopsy operators took 4 cores from each suspicious area on MRI. The full biopsy schema is in the protocol[19].

eTable 3 in Supplement 3 provides details regarding the experience of the clinicians in the trial.

Outcomes

The primary outcome was the proportion of men with csPCa, defined as the presence of a single biopsy core indicating disease of Gleason grade group (GGG) 2 or greater (the range for GGG is 1 to 5, with higher scores indicating a more aggressive form of prostate cancer). Secondary outcomes included the proportion of men with clinically insignificant cancer (GGG 1), test performance and the proportion

of patients in whom DCE made a difference to treatment eligibility or planning. The secondary outcomes are listed in eTable 4 in Supplement 3. Outcomes were reported according to the START[21] and STARD[23] guidelines (eTables 5 and 6 in Supplement 3).

Follow-up

Participants were followed until their treatment decision. Participants who underwent further diagnostic tests or treatment were followed until after these procedures. Patients with negative test results returned to standard of care PSA monitoring.

Multidisciplinary team meeting

Radiologists, oncologists and urologists involved in the delivery of radiotherapy, surgery, focal therapy or active surveillance for prostate cancer led a dedicated trial muti-disciplinary team meeting. Treatment eligibility options and detailed treatment planning by individual treatment modality were discussed for each participant based on their clinical information including patient-reported outcome measures, bpMRI images and prostate biopsy results, blinded to any DCE-information or DCE-specific biopsies[19]. The group was then unblinded to DCE images and DCE-specific biopsies and re-evaluated the participants' treatment options and planning.

Patient-reported outcome measures

Participants completed baseline International Index of Erectile Function-5 and International Prostate Symptom Score questionnaires[24,25] to ascertain erectile function and lower urinary tract symptoms.

Central quality control

Following completion of the trial, radiologists and pathologists at the coordinating centre, unaware of the results of the original reports, reviewed all the MRIs and 15% of the original pathological specimens, chosen at random from participants at each site. MRIs were evaluated using the PI-QUAL scoring system[26] on a scale from 1 to 5, with higher numbers indicating a higher quality scan.

Statistical analysis

The statistical analysis plan (Supplement 2) was prespecified and approved by the clinical trial group lead, statistician and chief investigator, prior to data analysis.

Using a non-inferiority margin of 5 percentage points and a one-sided alpha level of 2.5%, 400 men would provide 90% power to show non-inferiority of bpMRI to mpMRI, assuming an mpMRI underlying probability of detecting clinically significant cancer of 38%. This sample size was increased to 500 to allow for a 20% rate of dropout or exclusion after enrolment. A non-inferiority margin of 5 percentage points was chosen following a consensus meeting of clinicians and patients. This was determined to be the clinically acceptable trade-off between a small potential drop in cancer detection against the substantial practical, safety, and economic benefits of

bpMRI over mpMRI. Detailed justification of the sample size is provided in the protocol (Supplement 1).

For the primary outcome, the proportion of men with csPCa detected by bpMRI-targeted biopsy was defined as the number of men with csPCa identified on bpMRI-targeted biopsy divided by the number of men undergoing bpMRI. Similarly, the proportion of men with csPCa detected by mpMRI-targeted biopsy was defined as the number of men with csPCa identified on mpMRI-targeted biopsy divided by the number of men undergoing mpMRI. For the primary outcome, the Likert score was used to derive a suspicious MRI requiring MRI-targeted biopsy, planned sensitivity analyses were performed using the PI-RADS v2.1 scale. Detailed derivation of the status of each patient is given in the statistical analysis plan (Supplement 2). A p-value was obtained using a McNemar test.

A sensitivity analysis of the primary outcome was performed using a more stringent definition of csPCa of any core containing GGG 3 or greater.

For secondary outcomes, the results are reported as point estimates with 95% confidence intervals (CIs). The widths of the CIs were not adjusted for multiplicity, so the intervals should not be used for inference. Further analysis details are provided in eSection 3, Supplement 3.

Results

Trial population

From April 2022 through September 2023, 555 men were enrolled into the study from 22 centres in 12 countries. Of these, 490 men were eligible for the primary outcome analysis (Figure 1). Baseline characteristics of the population are given in Table 1.

MRI scans were carried out on 39 scanners, 435/490 (88.8%) on 3.0T scanners, reported by 30 radiologists (eTable 7 in Supplement 3). MRI identified 308/490 (62.9%) men with at least one suspicious area for biopsy. In those men, the median number of suspicious areas identified was 2 [IQR:1-2]. Of men undergoing targeted biopsy, 193/319 (60.5%) were via the transperineal route and 260/319 (81.5%) were carried out using software-assisted or fusion registration (eTables 8 and 9 in Supplement 3).

Outcomes

The proportion of scans scoring 3 or greater on the Likert scale leading to a biopsy indication was 273/490 (55.7%) for bpMRI and 280/490 (57.1%) for mpMRI (difference, 1.4 percentage points) (Table 2; eTable 10A in Supplement 3). DCE identified newly suspicious areas in 31 of 490 patients (6.3%). Of these 31 patients, 21 (67.7%) had a suspicious area not visible on bpMRI, and 10 (32.3%) had a

suspicious area that was significantly larger on mpMRI. Twenty-nine of 31 patients (93.5%) derived no additional csPCa detection from the DCE-specific biopsy.

BpMRI was non-inferior to mpMRI for detection of csPCa, detecting 143 of 490 men (29.2%), compared to 145 of 490 men (29.6%) for mpMRI (difference, -0.4 percentage points; 95% CI, -1.2 to 0.4; p=0.5). This result was consistent in the sensitivity analysis using GGG 3 or higher to define csPCa (difference, -0.4 percentage points; 95% CI -1.2 to 0.4) (eTable 11 in Supplement 3).

For clinically insignificant cancer detection, bpMRI detected 45 of 490 men (9.2%), compared to 47 of 490 men (9.6%) on mpMRI (difference, -0.4 percentage points; 95% CI -1.2 to 0.4). Biopsy outcomes and test performance characteristics are given in Tables 2 and 3.

Sensitivity, specificity, positive and negative predictive values were similar for bpMRI (98.0%, 61.6%, 53.1%, 98.6%, respectively) and mpMRI (99.3%, 60.1%, 52.5%, 99.5%, respectively (Table 3; eTable 12 in Supplement 3). There were no major differences in sensitivity (difference -1.4 percentage points, 95% CI, -3.9 to 1.2) or specificity (difference 1.5 percentage points, 95% CI, -1.2 to 4.2). Results were consistent when using the PI-RADSv2.1 scoring system instead of the Likert scoring system (eTable 10B, eTable 12 in Supplement 3).

Radiological T-staging decisions, likelihood of extracapsular extension, and involvement of the bladder neck, seminal vesicle, urethral sphincter and rectal wall were very similar between bpMRI and mpMRI (eTable 13-14 in Supplement 3).

After review at the post-trial multi-disciplinary team meeting with rotating clinician panels, DCE sequences or DCE-specific biopsies made a difference to treatment eligibility decisions in 21/488 (4.3%; 95% CI 2.7 to 6.5) of cases and treatment planning decisions, for example, in how surgery, radiotherapy or focal therapy were planned to be delivered, in 15/488 (3.1%; 95% CI 1.7 to 5.0) of cases (eTable 15 in Supplement 3).

Central review of image quality (eTable 16 in Supplement 3) revealed 482/488 (98.8%) of scans were of adequate diagnostic quality, scoring 3 or higher on the PI-QUALv1 scale. In those 143/488 (29.3%) without optimal diagnostic quality scans, scoring 4 or lower, 117/143 (81.8%) had an issue with the quality of the T2W or DWI sequences and 49/143 (34.3%) had an issue with the quality of the DCE sequence (eTable 17A, 17B in Supplement 3). Central quality review of biopsy specimens is outlined in eTable 18 in Supplement 3.

For both bpMRI and mpMRI with or without targeted biopsy, csPCa would have been missed by a targeted-only biopsy approach, and detected by systematic biopsy in 3/476 (0.6%, 95% CI 0.1 to 1.8) of patients (eTable 19A, 19B in Supplement 3), leading to a total csPCa prevalence in the cohort of 148/490 (30.2%; 95% CI 26.2 to 34.5).

Adverse events are described in eTable 20 in Supplement 3.

Discussion

The PRIME study demonstrates that a shorter and less resource-intensive bpMRI, detects as much clinically significant cancer as the full mpMRI, without increasing the diagnosis of clinically insignificant cancer. Despite earlier concerns that lack of contrast information would lead to more biopsy recommendations, we found no evidence of this, with biopsy rates being very similar between bpMRI and mpMRI. Although DCE sequences identified a small proportion of new suspicious areas on the mpMRI not seen on the bpMRI, the majority of these did not reveal significant cancer; overall, test performance characteristics were also very similar between both bpMRI and mpMRI.

With approximately four million prostate MRIs performed annually, these findings have critical global health implications[4], and saving a significant proportion of scanner time and staff time should increase access to imaging and represent a major opportunity cost saving. The significant benefits of a bpMRI approach include a shorter scan for the patient, improved scanner throughput for the healthcare system, avoiding the need for use of gadolinium contrast, elimination of cannulation and contrast-agent safety risks, avoiding the need for a physician to be present during scanning and reduced environmental toxicity[6,11,27].

DCE sequences have been thought to be particularly important in the local staging of prostate cancer and involvement of key anatomical structures around the prostate[17,18]. However, we found that bpMRI did not really differ from mpMRI in this evaluation. Further, the use of DCE sequences only changed treatment eligibility decisions or treatment planning decisions in a minority of cases.

Additional findings include that systematic biopsy on MRI-negative sides of the prostate identified only a very small proportion of men with significant cancer and could likely be omitted.

A previous randomised trial showed an approximate 9% increase in significant cancer detection in favour of mpMRI, which we did not observe here[16]. However, our findings are consistent with most published studies comparing bpMRI and mpMRI[7,12,15], although these studies had major limitations.

Strengths of PRIME include its design as an appropriately powered prospective multicentre study in many different health care settings and optimised DCE prior to commencing the study to give the best chance of demonstrating any possible added value of contrast[13]. We ensured strict blinding of radiologists who had to submit their bpMRI findings and biopsy plans from this before being shown the contrast sequences and performed biopsies based not just on what the mpMRI suggested but also what the bpMRI suggested. For the first time, we evaluated the added value of DCE in treatment decision eligibility and planning in a blinded multi-disciplinary team meeting. We also carried out our primary analysis using the Likert scoring system, which permits radiologists to weight DCE findings higher than with the PI-RADSv2.1 scoring scale thus realistically permitting a difference between a man being offered a biopsy or not. We permitted centres to use their local expertise with respect to radiologists, biopsy operators, biopsy access route and registration technique, which increases the generalisability of the results.

We considered a randomised design, but chose a within-patient trial design as it had a number of advantages[19]: first, our patient group and funding peer-reviewed panel preferred this trial design as if one of the techniques was inferior, patients in a randomised design would be denied the benefit of targeted biopsies from the other arm. Second, the within-patient design is a more efficient trial design requiring a sevenfold lower sample size with equivalent quality of evidence in a diagnostic study. Third, patients act as their own controls, therefore allowing us to draw conclusions regarding the value of DCE sequences on a per patient level. Fourth, it allows for the evaluation of the impact of contrast on staging decisions and treatment eligibility decisions at an individual patient level.

There are limitations. First, MRI quality was good in PRIME, as participating sites' protocols had been optimised prior to taking part[13]. Thus, we would advise centres to ensure that their scans are of good quality prior to considering adopting a bpMRI approach. Our pre-trial quality control which included both academic and non-academic centres globally suggests that providing an MRI scanner is less than 10 years old, it is very feasible to deliver optimal scan quality, compliant with international standards, with simple optimisation[13], regardless of whether the centre is academic or not, or whether they possess 1.5T or 3.0T scanners. We have demonstrated that this can be achieved without any cost requirements to upgrade equipment and with basic modifications to scanning protocols in line with international guidelines on minimal standards for MRI conduct[13], thus we believe this is achievable in most centres. Further, our approach to optimise scan quality pre-trial may have given results in favour of mpMRI detecting more cancer over bpMRI, as we found that in unoptimised scans amongst our trial network that DCE was the least

well-done sequence[13,22,26] whereas in PRIME our post-trial central evaluation demonstrated that DCE was of high quality. Of note, a suboptimal bpMRI scan was not likely to be compensated for by the DCE sequence as in most of these cases, the DCE was also suboptimal (eTable 17 in Supplement 3).

Second, it is important to consider the possibility of anchoring bias underestimating significant cancer detection by mpMRI, as radiologists could have been less likely to deviate from their report on the bpMRI when declaring their mpMRI findings as they had already seen the bpMRI. Conversely, as clinicians were aware of the hypothesis of the study, the standard of care was mpMRI prior to the trial and as the core group designing the study used DCE in their daily practice, the results were more likely to have been biased in favour of mpMRI detecting cancer. This is because radiologists knew that the purpose of the study was to see if areas of suspicion seen when DCE was revealed harboured significant cancer, thus they would have paid more attention to the DCE sequences than they might have in routine clinical practice and thus, may have been more likely to declare a DCE-specific lesion.

Third, our results reflect practice in centres with highly experienced radiologists and biopsy operators. It is therefore important to address the need for structured training and quality control in other centres. Widespread, successful implementation of bpMRI and targeted biopsy would be supported by educational programmes and a standardised approach to reporting, potentially including formal accreditation, to ensure diagnostic accuracy is maintained across diverse practice settings[28–31]. Such initiatives are important in aiding clinicians to interpret scans without the perceived safety net of contrast-enhanced sequences[32].

Fourth, whilst a shorter scan that avoids the use of contrast, requires fewer staff to deliver and has similar clinical outcomes, is likely to be cost-effective, a formal health economic analysis is planned and will be reported separately.

Finally, while the immediate focus must be on education and quality improvement[13,28–31], the development of artificial intelligence tools to support image interpretation could play a significant role in augmenting the future diagnostic pathway and should be a focus of future work[33–35].

Conclusion

In summary, in this international multicentre non-inferiority trial, we have demonstrated that amongst experienced radiologists and providing image quality is adequate, bpMRI performs very similarly to mpMRI for cancer detection, staging and treatment planning. We provide level-1evidence that bpMRI could be an alternative first-line diagnostic test to mpMRI for cancer diagnosis in men with suspected prostate cancer.

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Figure Legends

Figure 1. Flow of participants in the PRIME trial.

Radiologists first reported the biparametric MRI (T2-WI + DWI) blinded to DCE, with independent verification of blinding. They recorded bpMRI-based decisions and biopsy targets before DCE was revealed. After immediate unblinding to DCE, radiologists re-evaluated all sequences and generated an mpMRI report. Any new suspicious regions or significantly larger lesions on mpMRI compared to bpMRI were marked as separate, DCE-specific biopsy targets.

[a] Each MRI lesion is scored 1–5 representing the likelihood of clinically significant prostate cancer using both Likert and PI-RADSv2.1 scoring systems, with the highest score on either system determining the subsequent pathway. A score of 1 indicates clinically significant cancer is highly unlikely, 3 is equivocal and 5 indicates it is highly likely. In this trial, scores of 1-2 were considered 'non-suspicious,' and providing PSA Density ≤ 0.15, they were recommended to avoid biopsy. Scores of 3-5 were considered “suspicious” and recommended to undergo targeted ± systematic biopsy.

[b] Nine participants identified with no lesions on biparametric MRI and multiparametric MRI, but a PSA density ≥ 0.15 did not have systematic biopsy.

[c] Clinically significant prostate cancer (csPCa) was defined as the presence of any cancer with a Gleason Grade Group (GGG) of 2 or greater. The proportion of men diagnosed with csPCa was the primary outcome. The GGG system is the standard for grading prostate cancer aggressiveness, ranging from GGG 1 (least aggressive) to GGG 5 (most aggressive). Higher scores indicate a more aggressive tumour and a poorer prognosis.

Abbreviations: bpMRI, biparametric MRI; DCE, dynamic contrast-enhanced sequence; DWI, diffusion-weighted sequence; DRE, digital rectal examination; mpMRI, multiparametric MRI; PI-RADS, Prostate Imaging Reporting and Data System; PSA, prostate-specific antigen; PSAD, prostate-specific antigen density; T2-WI, T2-weighted sequence.

Figure 2. Difference in proportion of men with clinically significant prostate cancer between bpMRI and mpMRI, with non-inferiority margin and 95% CI.

The lower bound of the 95% confidence interval does not cross the non-inferiority margin, indicating that bpMRI-targeted biopsy is non-inferior to mpMRI-targeted biopsy.

Tables

Table 1. Baseline characteristics of participants

Characteristic	All participants (n = 490)
Age (years), median [IQR]	65 [59-70]
Ethnicity (self-reported), n (%)	
Asian	17 (3.5)
Black, African or Caribbean	20 (4.1)
Mixed or Multiple	2 (0.4)
Other[a]	14 (2.9)
White	437 (89.2)
Obesity (BMI > 30 kg/m²), n (%)	32 (6.5)
Medical history, n (%)	
Family history of prostate cancer	92 (18.8)
Any tumour within last 5 yrs	10 (2.0)
Myocardial infarction	12 (2.5)
Peripheral vascular disease	10 (2.0)
Cerebrovascular disease	10 (2.0)
Chronic pulmonary disease	15 (3.1)
Diabetes without organ damage	26 (5.3)
Diabetes with organ damage	2 (0.6)
On blood thinning medication	23 (4.7)
Abnormal DRE, n (%)	62 (12.7)
PSA (ng/mL), median [IQR]	5.6 [4.4-8.0]
WHO Performance Status[b], n (%)	
0: Fully active	469 (95.7)
1: Restricted in strenuous activity	20 (4.1)
2: Self-caring but unable to work	1 (0.2)

[a] The ‘Other’ category (n=14) includes men that self-reported their ethnicity as Arabic-Asian (n=1), Chinese (n=1), Hispanic (n=1), Inder (n=1), South Asian (n=1), Turkish (n=1), Not disclosed (n=8).

[b] WHO Performance Status: a scale to assess a patient’s functional ability, ranging from 0 (fully active) to 5 (dead). Higher scores indicate a greater degree of disability.

Abbreviations: DRE, Digital rectal examination; PSA, Prostate-specific antigen; WHO, World Health Organisation.

Table 2. Comparison of outcomes between biparametric and multiparametric MRI

Outcome	bpMRI (n=490) n (%; 95% CI)	mpMRI (n=490) n (%; 95% CI)	Difference[a] (% points; 95% CI)
Clinically significant cancer[b] (Primary outcome)	143 (29.2; 25.2 to 33.4)	145 (29.6; 25.6 to 33.9)	-0.4; (-1.2 to 0.4), p=0.5
Gleason Grade Group[c] 2	70 (14.3)	70 (14.3)	
Gleason Grade Group 3	39 (8.0)	40 (8.2)	
Gleason Grade Group 4	13 (2.7)	13 (2.7)	
Gleason Grade Group 5	21 (4.3)	22 (4.5)	
Clinically insignificant cancer (Gleason Grade Group 1) (Secondary outcome)	45 (9.2; 6.8 to 12.1)	47 (9.6; 7.1 to 12.6)	-0.4; (-1.2 to 0.4)
Proportion of patients with biopsy indication[d]	273 (55.7; 95% CI 51.2 to 60.2)	280 (57.1; 95% CI 52.6 to 61.6)	1.4, 95% CI -0.5 to 3.4
Proportion of patients with no biopsy indication[d]	217 (44.3)	210 (42.9)	1.4; (-3.4 to 0.5)
No cancer on biopsy (benign)	85 (17.3)	88 (18.0)	-0.7; (-2.2 to 1.4)

[a] Difference between rates are shown in percentage points.

[b] As per primary outcome definition of clinically significant cancer, which was defined as the presence of a single biopsy core indicating disease of Gleason Grade Group 2 or greater. It was assessed for non-inferiority of bpMRI compared to mpMRI with a pre-specified margin of 5 percentage points. Clinically insignificant cancer was therefore defined as the presence of disease only of Gleason Grade Group 1.

[c] The Gleason Grade Group (GGG) system classifies prostate cancer based on glandular architecture seen on histology from biopsy. It is derived from the sum of the two most common Gleason patterns (each scored 1-5), then mapped to a Grade Group from 1 to 5, where higher groups indicate more aggressive disease. Specifically: GGG 1 = Gleason ≤6 (3+3; clinically insignificant cancer), GGG 2 = Gleason 7 (3+4), GGG 3 = Gleason 7 (4+3), GGG 4 = Gleason 8 (4+4, 3+5 or 5+3), GGG 5 = Gleason 9-10 (4+5, 5+4, or 5+5).

[d] As indicated by a Likert score of 3 or greater.

Table 3. Test performance characteristics

Table 3A. Test performance characteristics of biparametric MRI

		Clinically significant prostate cancer, n (%)		
		Present	Absent	Total
bpMRI, n (%)	Positive	145	128	273
	Negative	3	205	208
	Total	148	333	481

Sensitivity: 145/148=98.0% (95% CI: 94.2, 99.6)
Specificity: 205/333=61.6% (95% CI: 56.1, 66.8)
Positive Predictive Value: 145/273=53.1% (95% CI: 47.0, 59.2)
Negative Predictive Value: 205/208=98.6% (95% CI: 95.8, 99.7)

Table 3B. Test performance characteristics of multiparametric MRI

		Clinically significant prostate cancer, n (%)		
		Present	Absent	Total
mpMRI, n (%)	Present	147	133	280
	Absent	1	200	201
	Total	148	333	481

Sensitivity: 147/148=99.3% (95% CI: 96.3, 100.0)
Specificity: 200/333=60.1% (95% CI: 54.6, 65.4)
Positive Predictive Value: 147/280=52.5% (95% CI: 46.5, 58.5)
Negative Predictive Value: 200/201=99.5% (95% CI: 97.3, 100.0)

Difference (95% CI) in sensitivity: 1.4 (95% CI: -1.2, 3.9)
Difference (95% CI) in specificity: 1.5 (95% CI: -1.2, 4.2)

Contingency tables (2x2) and corresponding test performance characteristics for the biparametric (bpMRI) and multiparametric (mpMRI) pathways. The tables cross-tabulate the MRI result (positive defined as a Likert score ≥3, or negative) against the final histological diagnosis of clinically significant prostate cancer being present or absent. Analyses for diagnostic performance were performed on n=481 out of 490 participant cohort, excluding 9 participants who did not undergo systematic biopsy as per protocol.