



RESEARCH

INFORMATION

PET-MRI to Improve Staging and Personalise Treatment for Prostate Cancer: PRISTINE Study



AIMS

- Prostate cancer is the most commonly diagnosed cancer in men in Scotland. When a man is diagnosed, doctors have to work out how far the cancer has spread before they can recommend the right treatment. One of the most important questions is whether cancer cells have reached the lymph nodes in the pelvis — small glands that drain fluid from the area, and a common first place for prostate cancer to spread to. The answer changes what treatment is offered, and how extensive an operation needs to be.
- At present that question is answered using several separate tests on different days: an MRI scan of the prostate, a bone scan, and finally the removal of the pelvic lymph nodes during surgery so that they can be examined under a microscope. This is slow and costly, and the scans are known to be unreliable at finding cancer in lymph nodes — largely because they judge whether a node looks abnormally large, rather than whether it actually contains cancer.
- PET/MRI combines two types of scan in a single machine and a single appointment. The MRI part shows the body's structure in fine detail, while the PET part uses a small, safe injection of a radioactive tracer to show where cancer cells are active. The tracer used in this study targets PSMA (prostate-specific membrane antigen), a protein found in large amounts on prostate



cancer cells but on very few normal cells — so cancer should show up because of what it is, rather than simply because of how big it looks. Because it is all done in one visit — so-called “one-stop imaging” — it could also be quicker for patients and cheaper for the NHS than the current run of separate tests. Throughout this report, “PSMA PET/MRI” means this one combined scan.

- This project set out to test whether one-stop PSMA PET/MRI is accurate and efficient enough to improve on the current staging pathway for men with higher-risk prostate cancer. We compared what the scan predicted against what was actually found when the prostate and the pelvic lymph nodes were removed at surgery and examined in the laboratory — the most reliable answer available, and the proper yardstick for judging any scan. If the scan proved reliable, men could get a faster, single-visit answer, and some might safely be spared unnecessary lymph node surgery.



KEY FINDINGS

- 37 men agreed to take part; 32 went on to have surgery and had complete laboratory results available for analysis. Their average age was 65.7 years. Their average PSA (prostate-specific antigen — a blood test that rises when prostate cancer is active) was 24.5 ng/mL. A normal PSA is below about 4 ng/mL, so this is markedly raised, confirming that everyone in the study had significant, higher-risk cancer.
- PSMA PET/MRI made little difference to judging how far the cancer had grown within and just around the prostate itself, compared with a standard MRI. Where the scan did show cancer growing into the seminal vesicles (two small glands that sit next to the prostate), it was always right — but it missed more than four in ten of the cases that the laboratory later confirmed.
- The laboratory found cancer in the pelvic lymph nodes in 14 of the 32 men (43.8%). PSMA PET/MRI had correctly identified only 3 of those 14. Every man the scan flagged did turn out to have cancer in his lymph nodes, so a positive scan can be trusted — but 11 men who did have cancer in their lymph nodes were given the all-clear by the scan. The deposits it missed were tiny: about 4 mm across on average, less than half a centimetre.



- The key message is about what a clear scan does not tell you. A negative PSMA PET/MRI cannot rule out cancer in the pelvic lymph nodes and should not on its own be used as a reason to leave those lymph nodes in place at surgery.



WHAT DID THE STUDY INVOLVE?

This was a single-centre study based in Edinburgh. Participants were recruited before their treatment and followed forwards in time — what researchers call a prospective cohort study. Men were invited to take part if they had a new diagnosis of prostate cancer that was at higher risk of having spread, had already completed their standard NHS staging scans, had chosen to have surgery, were fit enough for an operation, and could safely have an MRI.

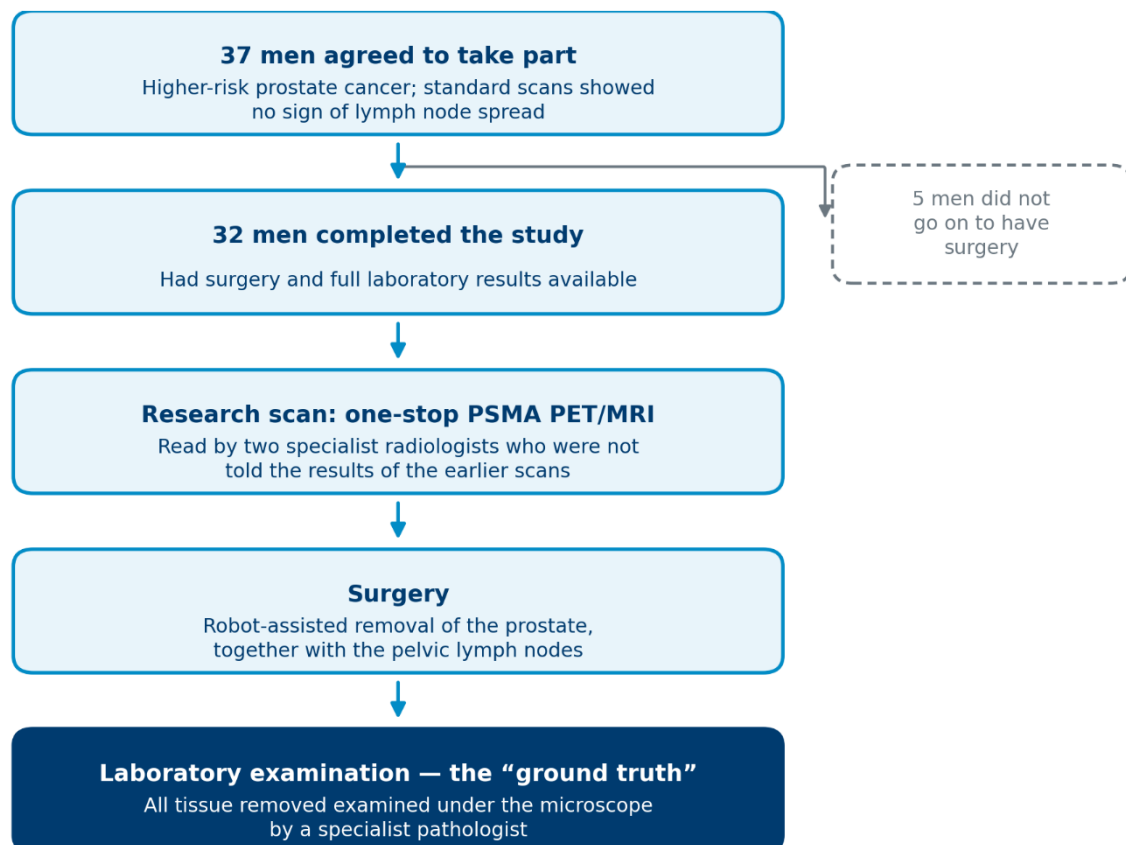
37 men agreed to take part. Five did not go on to have surgery as planned, leaving 32 men with complete results. Their average age was 65.7 years, and their average PSA was 24.5 ng/mL — well above the normal level of about 4 ng/mL. Fuller details of the group are given in Table 1 in the next section.

Everyone had already had the scans normally used in the NHS: a detailed MRI of the prostate and a bone scan. The reason for testing PSMA PET/MRI on top of these is that a standard MRI judges a lymph node mainly by its size and shape — and a normal-looking node can still contain cancer. PSMA PET/MRI was expected to do better, because the PSMA tracer sticks to a protein carried by prostate cancer cells, so cancer should light up even inside a node that looks perfectly normal. Doing the PET and the MRI together also means one appointment instead of several.

Each man then had a PSMA PET/MRI scan shortly before his operation. The scans were read by two specialist radiologists who were not told the results of the earlier scans, so that their reading could not be influenced by what had gone before. The men then had robot-assisted radical prostatectomy — keyhole surgery to remove the prostate — along with removal of the pelvic lymph nodes. Everything taken out was examined under the microscope by a specialist pathologist. Because this looks directly at the tissue, it gives the most reliable answer available about whether the cancer had spread, and it is the yardstick — the “ground truth” — against which we measured the scan.



This design is what makes the study useful. Most previous work has compared one type of scan against another, which can only ever show which scan finds more — not which scan is right. Very few studies have checked PSMA PET/MRI against tissue removed at surgery, and fewer still have done so in precisely the group of men in whom the scan would actually be used to make a decision: those whose standard scans have already come back clear. By doing exactly that, this study shows how far the scan can be relied upon in real practice. Figure 1 sets out how the study worked.



The scan's prediction was compared with what was actually found

Figure 1: How the study worked, from recruitment through to laboratory examination of the tissue removed at surgery.



WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

Demographic summary		
Age - years (average)		65.7 ± 6.5
PSA - ng/ml (average)		24.5 ± 21.4
T Stage – count (%)	T2	14 (43.8%)
	T3a	10 (31.2%)
	T3b	8 (25.0%)
Gleason grade - count (%)	3 + 4	13 (40.6%)
	4 + 3	11 (34.4%)
	3 + 5	3 (9.4%)
	4 + 4	2 (6.3%)
	4 + 5	3 (9.4%)

Table 1: Demographic summary of participants in the PRISTINE study

- We recruited 37 men in total. Of these, 32 remained in the study, went on to have surgery as planned, and had final laboratory reports available for evaluation.
- Prostate cancer staging uses two systems: TNM staging and the Gleason score. TNM staging describes the T stage (the size of the tumour, and whether it has grown beyond the prostate gland), the N stage (whether it has spread to nearby lymph nodes) and the M stage (whether it has spread to distant parts of the body — known as metastatic disease). The higher the T, N and M stage, the more advanced the cancer. In this report: T2 means the cancer is still contained within the prostate; T3a means it has grown just beyond the outer edge of the prostate; T3b means it has grown into the seminal vesicles; N0 means no lymph node spread has been found; and N1 means it has. Staging also uses the Gleason score, which describes how aggressive the cancer cells look under the microscope — the higher the Gleason score, the more aggressive the cancer.
- On the standard MRI, just under half the men were staged T2 (43.8%) and a quarter T3b (25%). Adding PSMA PET/MRI changed this very little: two men moved from T2 to T3b because the scan showed cancer in the seminal vesicles, taking the proportion staged T2 down to 37.5% and the proportion staged T3b up to 31.2%. This is not a surprise — improving T staging is not what the scan is mainly for. When the tissue itself was examined after surgery, far more cancer had grown beyond the prostate than any scan had suggested (T2 6.3%, T3a 46.9%, T3b 46.9%). This is





expected too: a microscope can pick up tiny amounts of cancer at the very edge of the prostate that are simply too small for any scan to show.

- The lymph nodes are the real issue. Whether cancer has reached the pelvic lymph nodes shapes the operation itself — in particular, whether the surgeon should carry out an extended lymph node dissection, removing a wider area of lymph nodes. At present that decision rests on a risk calculator rather than on any scan. A scan that could answer the question reliably would let surgery be tailored to the individual: more extensive where the nodes are involved, and less extensive — with fewer side effects — where they are not. This is the main reason there is interest in PSMA PET/MRI.
- The scan did find some cancer that the standard MRI had missed — but it missed far more than it found. The standard MRI had identified lymph node spread in only 1 man (3.1%). PSMA PET/MRI picked out 2 more, bringing the total to 3 men (9.4%) before surgery, and all 3 were confirmed correct in the laboratory: the scan never raised a false alarm. However, the laboratory went on to find cancer in the lymph nodes of a further 11 men whose PSMA PET/MRI had been clear. In total, 14 of the 32 men (43.8%) had cancer in their pelvic lymph nodes, and the scan had spotted only 3 of them.
- Put in the terms that matter to a patient: when PSMA PET/MRI reported no lymph node spread, it was right only about 62% of the time (its negative predictive value, 62.1%). Close to four in every ten men given the all-clear by the scan did in fact have cancer in their lymph nodes. This directly challenges the claim that PSMA PET/MRI can be used to decide against removing the lymph nodes at surgery. The full performance figures are given in Tables 2 and 3 below.
- Tables 2 and 3 use the standard measures of how well a test performs. In plain English: sensitivity is the proportion of men who really did have spread that the scan managed to pick up; specificity is the proportion of men who really did not have spread that the scan correctly cleared; positive predictive value is how often the scan is right when it says spread is present; negative predictive value is how often it is right when it says there is none; and accuracy is the proportion of all men the scan classified correctly. For a scan meant to reassure doctors that lymph node surgery can safely be avoided, the negative predictive value is the figure that matters most — and it is the one our study found wanting.





N1 staging	Value	95% CI
Sensitivity	21.4%	4.66% - 50.8%
Specificity	100%	81.5% - 100%
Positive Predictive Value	100%	29.2% - 100%
Negative Predictive Value	62.1%	55.5% - 68.3%
Accuracy	65.6%	46.8% - 81.4%

Table 2: Performance metrics for PSMA PET/MRI for diagnosing N1 disease compared to ground truth histopathology reports.

T3b staging	Value	95% CI
Sensitivity	57.1%	28.86% - 82.34%
Specificity	100%	81.5% - 100%
Positive Predictive Value	100%	63.06% - 100.00%
Negative Predictive Value	75%	62.1% - 84.6%
Accuracy	81.3%	63.6% - 92.8%

Table 3: Performance metrics for PSMA PET/MRI for diagnosing seminal vesicle invasion compared to ground truth histopathology reports.

- No participant showed any sign of the cancer having spread to distant parts of the body (metastatic disease) at the outset, which is what our entry criteria were designed to ensure, and neither PSMA PET/MRI nor the laboratory found any distant spread afterwards. To be clear, this applies only to distant spread: as described above, both PSMA PET/MRI and the laboratory examination did change some men's T stage and N stage.
- Because so many affected lymph nodes were missed, we went back and measured how large those missed cancer deposits actually were. On average they were just 4 mm across — less than half a centimetre. An earlier study found that the deposits PSMA PET/MRI does successfully detect average around 8 mm (Grubmüller et al., 2018). The likeliest explanation for our results is therefore a simple one: in these men, most of the cancer in the lymph nodes was simply too small for the scan to see. Cancer that is present but invisible on scans is sometimes described as “occult” disease.



WHAT IMPACT COULD THE FINDINGS HAVE?

Before this study, there was very little prospective evidence from men who went on to have surgery and whose lymph nodes were then examined in detail in the laboratory. This study provides direct, tissue-verified evidence that, in men who look lymph node negative on standard scans, any cancer remaining in the lymph nodes is often simply too small for PSMA PET/MRI to detect. It therefore clarifies an important limitation of using PSMA PET/MRI to “rule out” pelvic lymph node disease in this setting.

Is it better than a standard MRI? Partly — but not in the way that would matter most. PSMA PET/MRI found lymph node spread in 2 men that the standard MRI had missed, and it never wrongly flagged a man who did not have spread. So, when it is positive, it can be believed and acted upon. But when it is negative it offers little more reassurance than a standard MRI, because both miss the small deposits of cancer that make up most of the disease in this group of men.

- **For patients:** a clear PSMA PET/MRI should not be taken to mean that the cancer has definitely not spread to the pelvic lymph nodes. It should not, by itself, be a reason to leave the lymph nodes in place during surgery, or to leave them out of radiotherapy planning. Decisions about treating the lymph nodes should continue to be made in the usual way.
- **For clinical practice:** a positive PSMA PET/MRI is trustworthy and can be acted upon with confidence. A negative one is not, and surgeons and oncologists should continue to rely on established risk calculators — not on a clear scan — when deciding whether an extended lymph node dissection is needed.
- **For policy and the NHS in Scotland:** PSMA PET/MRI is an expensive test, and PET/MRI scanners are scarce. Our findings suggest that adding it routinely after standard staging is unlikely, on its own, to improve lymph node decisions for men like those in this study and would be hard to justify on cost grounds without clearer evidence that it improves patients' outcomes. Prostate cancer is now the most commonly diagnosed cancer in Scotland, so establishing where a costly new test does not help is valuable in itself: it protects men from false reassurance, and it allows NHS resources to be directed where they will do more good.



HOW WILL THE OUTCOMES BE DISSEMINATED?

Findings from this study have so far been presented at one local and one international meeting: the NHS Lothian R&D Conference 2025 (poster presentation) and the Société Internationale d'Urologie 2025 congress (poster presentation). Both presented interim findings; the study has since closed to recruitment.

Academic dissemination and timescale: we plan to present the final results at a major international imaging meeting — the Radiological Society of North America or the European Congress of Radiology — and to submit the full findings to a peer-reviewed journal. The results have already been presented at the SUI conference and later this year we aim to present. We are also preparing a manuscript for submission to the high impact Journal of Nuclear Medicine.

Dissemination to patients and the public: we will send a plain-English summary of the results to everyone who took part in the study. We will also work with prostate cancer charities — such as Prostate Scotland and Prostate Cancer UK — and with NHS Lothian's communications team to make the findings accessible to patients and the wider public.

Patient and public involvement: we previously gave a lecture to the Lothian Prostate support group about our study, and we hope to be invited back to deliver the results of the study. We also plan on working with prostate cancer UK to publish and disseminate the results.

Next steps: The central question raised by this study is whether PSMA PET/MRI can be made sensitive enough to detect the very small lymph node deposits it currently misses. Answering it will require a larger, multi-centre study, and would benefit from newer PSMA tracers and higher-resolution PET detectors.



CONCLUSION

The study achieved its main aim: to test one-stop PSMA PET/MRI against the gold standard of laboratory examination of tissue removed at surgery.



The result is a clear, two-sided message. When PSMA PET/MRI showed cancer in the pelvic lymph nodes, it was always right — including in two men whose standard MRI had shown nothing. A positive scan can therefore be trusted and acted upon. But when the scan was clear, that told us very little: it missed 11 of the 14 men who did in fact have cancer in their lymph nodes, because those deposits were mostly only around 4 mm across. A negative PSMA PET/MRI cannot be used to rule out lymph node spread and cannot justify leaving the pelvic lymph nodes alone at surgery.

These findings sit alongside international work on PSMA PET, which has reported that the scan detects somewhere between roughly 30% and 69% of node-positive cases. Our figure is lower, and we believe the reason is straightforward: our participants had already been cleared by standard scans, so only the smallest and hardest-to-see disease was left to find. Rather than contradicting earlier studies, our results show what happens at the limit of the technology — in exactly the group of men in whom a scan would be used to make a decision.

In its present form, therefore, the technique needs further development — above all, better sensitivity for small deposits — before it can be relied upon to rule out lymph node spread. Confirming this will require larger, multi-centre studies.

The take-home message: PSMA PET/MRI is worth believing when it finds something, but not when it finds nothing. It is not yet good enough to allow men with higher-risk prostate cancer safely to avoid having their pelvic lymph nodes removed and examined.



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