November 2026
As seen in *Applied Radiology*

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Addition of ^{68}Ga-PSMA-11 PET/CT to MRI in the Prostate Cancer Diagnostic Pathway: Addressing an Unmet Need

Munir Ghesani[1], Joseph Osborne[2], Paul Yonover[3], J Travis Mendel[4], Sanoj Punnen[5]

The addition of prostate-specific membrane antigen (PSMA) PET/CT with ^{68}Ga-PSMA-11 to multiparametric MRI (mpMRI) has the potential to improve the diagnostic pathway for suspected prostate cancer by enhancing risk stratification, identifying clinically significant disease that MRI alone may miss, and reducing unnecessary biopsies in appropriately selected patients.

Unmet Need in the Current Diagnostic Pathway

mpMRI has improved the diagnostic pathway for suspected prostate cancer and is now widely used before biopsy. However, important gaps remain. MRI may miss clinically significant lesions, biopsy can cause patient anxiety and post-procedural complications, and negative or inconclusive biopsy results may still leave diagnostic uncertainty. There remains a need for improved patient stratification, particularly in men with persistent clinical suspicion despite negative, non-suspicious, or equivocal MRI findings.

More than 1 million prostate biopsies are performed annually, and a substantial proportion are negative or detect clinically insignificant disease.[1] Although mpMRI has improved detection of clinically significant prostate cancer and reduced unnecessary biopsies, its negative predictive value may decline in higher-risk populations.[2] Men with negative or indeterminate MRI findings may still harbor clinically significant disease, and variability in MRI quality, reader expertise, and reference standards can limit reproducibility outside expert centers. ^{68}Ga-PSMA-11 PET/CT has therefore emerged as a promising complementary modality in the pre-biopsy setting.[3-5]

Evidence Supporting ^{68}Ga-PSMA-11 PET/CT as a Complementary Modality

Evidence from systematic reviews, multimodality trials, and the PRIMARY and PRIMARY2 trials supports the role of ^{68}Ga-PSMA-11 PET/CT as a complementary modality to mpMRI in the pre-biopsy diagnostic pathway.[6] Together, PRIMARY and PRIMARY2 evaluated ^{68}Ga-PSMA-11 PET/CT in combination with MRI and used the PRIMARY score as a standardized framework for ^{68}Ga-PSMA-11 PET interpretation. These data suggest that adding ^{68}Ga-PSMA-11 PET/CT to MRI may improve detection of clinically significant prostate cancer, identify lesions missed by mpMRI, and support more risk-adapted biopsy decisions. However, prospective validation remains important to define optimal patient selection, cost-effectiveness, and the clinical significance of ^{68}Ga-PSMA-11-positive lesions, particularly when MRI findings are negative or equivocal.

PRIMARY and PRIMARY2: Foundation for a ^{68}Ga-PSMA-11-Guided Strategy

The PRIMARY study evaluated ^{68}Ga-PSMA-11 PET/CT in biopsy-naïve men with suspected prostate cancer and demonstrated that combining ^{68}Ga-PSMA-11 PET/CT with mpMRI improved sensitivity and negative predictive value for clinically significant prostate cancer compared with mpMRI alone.[6]

The PRIMARY score was developed from this evidence base as a five-point

Affiliation: [1]Chief Medical Officer, United Theranostics; Former President, Society of Nuclear Medicine and Molecular Imaging; Former System Chief of Nuclear Medicine, Mount Sinai Health; Associate Professor of Radiology, Icahn School of Medicine at Mount Sinai. [2]Chief of Molecular Imaging and Therapeutics and Professor of Radiology, Weill Cornell Medicine. [3]Chief Data Officer and Director of Clinical Navigation, UroPartners, Chicago; Clinical Assistant Professor of Urology, University of Illinois Chicago. [4]Medical Director, Rio Grande Cancer Specialists. [5]Sanoj Punnen, MD MAS MBA, Pap Corps Champions for Cancer Research Endowed Chair in Solid Tumor Research, Professor and Vice Chair of Research, Desai Sethi Urology Institute, Co-lead for Cancer Control Research Program and Assistant Director of Clinical Research, Sylvester Comprehensive Cancer Center, Miller School of Medicine, University of Miami.
Disclosures: All authors received financial support from Telix Pharmaceuticals for authoring this article.
Munir Ghesani: Reports financial relationships with Siemens Healthineers, Telix Pharmaceuticals, Lantheus, ITM, Serac Life Sciences, Novartis, Blue Earth, Bayer, Cardinal, Genoplex, and Nusano. **Joseph Osborne:** Serves as an advisor to Telix Pharmaceuticals and Siemens Healthineers. **Paul Yonover:** Reports consulting and speaking relationships with Telix Pharmaceuticals and Veracyte, and consulting, speaking, and scientific advisory board relationships with GOPath. **J Travis Mendel:** Serves on the advisory board of Bayer; is a consultant and device trainer for Bioprotect; serves as a consultant to GE; and reports consulting and clinical trial principal investigator relationships with Telix Pharmaceuticals and Novartis. **Sanoj Punnen:** Serves as an advisor to Telix Pharmaceuticals.

framework to standardize intraprostatic ^{68}Ga-PSMA-11 PET interpretation and improve risk stratification for clinically significant disease.[6,7]

PRIMARY2 extended this approach in a randomized Phase 3 setting, evaluating ^{68}Ga-PSMA-11 PET/CT in men with non-suspicious or equivocal mpMRI findings and persistent clinical risk. In the ^{68}Ga-PSMA-11 PET arm, men with negative scans avoided biopsy, while those with positive scans underwent targeted biopsy.[8]

PRIMARY2 showed that an imaging-first strategy avoided biopsy in nearly half of men without compromising detection of clinically significant prostate cancer and substantially reduced detection of clinically insignificant disease.[8] This work provides a seminal evidence base for BiPASS, which extends the same ^{68}Ga-PSMA-11 and PRIMARY score approach into a registration-enabling program.

BiPASS: Translating Evidence into a Registration-Enabling Program

Building on PRIMARY and PRIMARY2, Telix Pharmaceutical's registration-enabling Phase 3 BiPASS trial is designed to evaluate ^{68}Ga-PSMA-11 PET/CT combined with MRI in men with suspected prostate cancer in the pre-biopsy setting. BiPASS incorporates the PRIMARY score as a core component of its imaging assessment methodology and is intended to support a standardized ^{68}Ga-PSMA-11 PET/MRI-informed diagnostic pathway.

The trial is titled: "A Single-Arm, Multicenter, Prospective, Open-Label, Longitudinal Phase 3 Study of Prostate-Specific Membrane Antigen (^{68}Ga-PSMA-11) Positron Emission Tomography (PET) Combined With Magnetic Resonance Imaging (MRI) Compared With Standard of Care (SOC) for the Detection of Prostate Cancer."

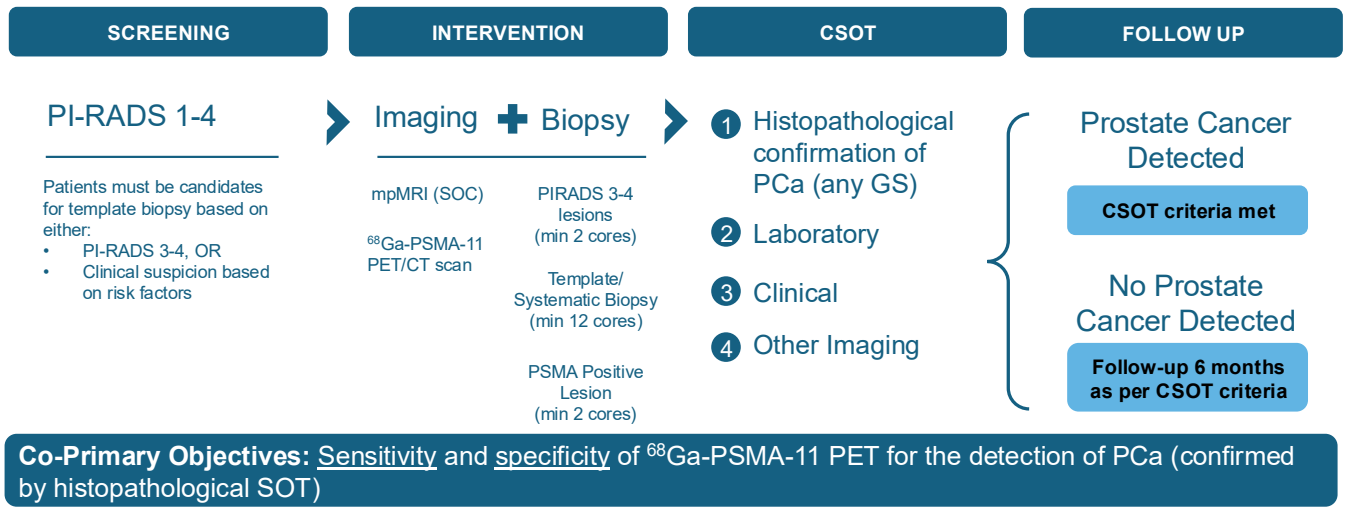
Key design elements include eligibility for men with PI-RADS 1–4 findings, exclusion of PI-RADS 5 disease, PET/CT plus biopsy assessment, template or systematic biopsy with at least 12 cores, targeted cores from MRI- and ^{68}Ga-PSMA-11-positive lesions, and 6-month follow-up using a composite standard of truth.

Within this registration-enabling framework, the use of ^{68}Ga-PSMA-11 is not simply a tracer selection but a key design feature that preserves continuity with the PRIMARY and PRIMARY2 evidence base. Because BiPASS is intended to evaluate whether ^{68}Ga-PSMA-11 PET combined with MRI can safely support biopsy deferral or more targeted biopsy in men with suspected prostate cancer, the imaging agent must maximize interpretive confidence and minimize avoidable sources of uncertainty. This is particularly important given published experience with certain ^{18}F-labeled ^{68}Ga-PSMA-11 agents, where higher rates of benign or indeterminate bone lesion (IBL) uptake have been reported and may increase the risk of false-positive interpretation.[9-11] False-positive interpretation of IBL detection can negatively impact treatment decisions and outcomes. By using the same ^{68}Ga-PSMA-11 platform and PRIMARY score framework evaluated in the foundational studies, BiPASS strengthens the clinical and regulatory rationale for testing a standardized, reproducible ^{68}Ga-PSMA-11 PET/MRI-informed pathway that can improve patient stratification, reduce unnecessary biopsies, and support broader adoption across academic and community practice settings.

Potential Clinical Impact

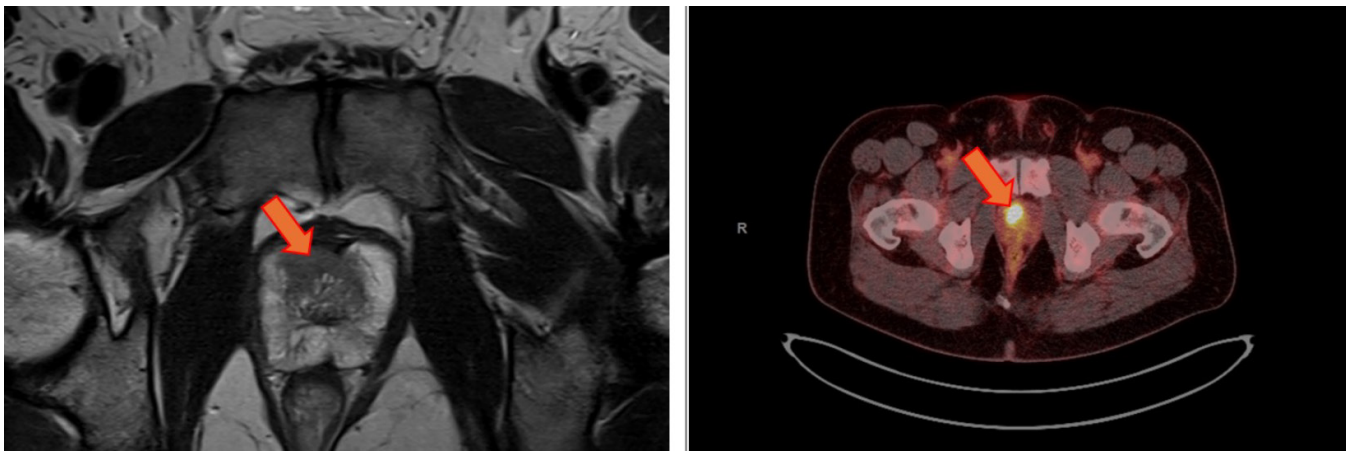
BiPASS could reshape the prostate cancer diagnostic pathway by positioning MRI and ^{68}Ga-PSMA-11 PET/CT as complementary tools. ^{68}Ga-PSMA-11 PET may identify lesions missed by MRI, including challenging anterior or MRI-occult lesions, while MRI may detect lesions that are PMSA-negative.[12]

BiPASS Trial Design



This study sponsored by Telix Pharmaceuticals. NCT07052214
CSOT, composite standard of truth; GS, Gleason Score

Case Study: 56-Year-Old Male with MRI (Left) and ^{68}Ga-PSMA-11 PET (Right)



Courtesy of Sanoj Punnen, MD

56-year-old male with elevated PSA came in for evaluation of a PSA that had increased from 2-3.5 over the year. An MRI showed a lesion in the right anterior peripheral zone. A biopsy was scheduled but ^{68}Ga-PSMA-11 was also requested by the patient and found an area of avidity in the right apex.

Biopsy showed a Gleason 8 high grade cancer in 2/2 cores from the target and Gleason 6 in 1/12 cores from the template biopsy.

Together, these modalities could support more precise biopsy targeting and reduce reliance on routine systematic sampling in appropriately selected patients.

The near-term clinical opportunity is a smarter biopsy strategy: using combined MRI and ^{68}Ga-PSMA-11 PET information to guide when biopsy is necessary, where biopsy should be targeted, and when biopsy may be safely deferred. This approach may improve patient experience, reduce unnecessary procedures, and provide more actionable anatomic and molecular information for treatment planning.

Clinical Adoption and Standardization Considerations

For BiPASS to translate from evidence generation into routine clinical practice, adoption will depend not only on diagnostic performance but also on whether the pathway can be implemented consistently across care settings. Academic centers may adopt earlier, particularly where ^{68}Ga-PSMA-11 PET infrastructure and multidisciplinary expertise are already established; however, broader community uptake will require clear reimbursement pathways, payer confidence, and eventual guideline incorporation, particularly within NCCN recommendations. Standardized ^{68}Ga-PSMA-11 PET interpretation, structured reporting templates, and reader training will be essential to ensure reproducibility across sites and to give clinicians confidence that biopsy deferral or more targeted biopsy decisions can be applied safely. In this context, the PRIMARY score provides a practical framework analogous to PI-RADS for MRI, supporting risk stratification and a common language for ^{68}Ga-PSMA-11-informed biopsy decision-making. The strongest adoption rationale is in men with persistent clinical suspicion and negative, non-suspicious, or equivocal MRI findings, where BiPASS could support a standardized, evidence-based shift from routine biopsy toward smarter, risk-adapted biopsy triage.

Evidence Thresholds for Clinical Confidence

Clinical adoption will require evidence that the pathway can safely support biopsy deferral without missing clinically significant cancer. A high negative predictive value will be essential, because missed clinically significant disease remains the central concern. Additional confidence may come from evidence of improved lesion localization, stronger alignment with pathology, and clinically meaningful impact on treatment planning, including radiation planning, focal boost strategies, nodal clinical target volume decisions, and salvage planning.

Discussion

Key risks and limitations include the possibility of missed clinically significant cancer if biopsy is deferred based on negative imaging; false-positive ^{68}Ga-PSMA-11-avid benign findings such as prostatitis, benign prostatic hyperplasia

nodules, or ganglia; uncertainty regarding the biology of ^{68}Ga-PSMA-11-positive, MRI-negative lesions; limited long-term oncologic outcomes for imaging-deferred cohorts; cost-effectiveness compared with mpMRI plus targeted biopsy; and operational constraints related to ^{68}Ga supply and PET capacity. Importantly, many of these risks are readily mitigated through protocol-defined eligibility criteria, standardized PRIMARY score interpretation, structured reporting, reader training, multidisciplinary review of discordant MRI and ^{68}Ga-PSMA-11 PET findings, and safety follow-up for patients in whom biopsy is deferred.

Medico-legal, reimbursement, and access concerns can be addressed through clear clinical algorithms, documented shared decision-making, payer evidence packages, phased implementation at experienced centers, and incorporation into clinical guidelines, which can strengthen payer confidence and support more consistent reimbursement as interpretation standards and operational workflows are established.

Standardized interpretation, structured reporting, and reader training will be necessary to reduce variability and ensure consistent performance in clinical practice.

From the community's urology perspective, BiPASS may shift biopsy practice from pattern-based sampling toward more targeted discovery of clinically significant disease. Combining ^{68}Ga-PSMA-11 PET with MRI could help avoid unnecessary biopsies while more precisely guiding biopsy in those who need them.

Balanced Interpretation

Overall, the evidence supports ^{68}Ga-PSMA-11 PET/CT as a promising complement to mpMRI rather than a replacement for careful clinical judgment. The most compelling near-term use case is selective biopsy avoidance or biopsy refinement in men with persistent suspicion of prostate cancer and negative, non-suspicious, or equivocal mpMRI findings. However, implementation should be guided by prospective validation, standardized interpretation, and confirmation that detected lesions represent clinically meaningful disease.

Conclusion

The addition of ^{68}Ga-PSMA-11 PET/CT to MRI has the potential to improve the prostate cancer diagnostic pathway by enhancing lesion detection, refining patient stratification, and reducing unnecessary biopsies in appropriately selected patients. PRIMARY and PRIMARY2 provide a strong evidentiary rationale, and BiPASS is positioned to test whether this approach can support broader clinical adoption in the pre-biopsy setting. Successful implementation will require prospective validation, standardized interpretation, reimbursement and access pathways, and evidence that detected lesions are clinically meaningful.

References

1) Vickers A, Cronin A, Roobol M, et al. Reducing unnecessary biopsy during prostate cancer screening using a four-kallikrein panel: an independent replication. *J Clin Oncol.* May 20 2010;28(15):2493-8. doi:10.1200/JCO.2009.24.1968

2) Ahmed HU, El-Shater Bosaily A, Brown LC, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. *Lancet.* Feb 25 2017;389(10071):815-822. doi:10.1016/S0140-6736(16)32401-1

3) Wagner T, Emberton M, Caglic I, et al. PSMA PET: the answer to MRI-occult prostate cancer... or another mirage? *Eur Radiol.* Sep 2026;36(9):7063-7072. doi:10.1007/s00330-026-12596-3

4) Regmi SK, Sathianathen N, Stout TE, Konety BR. MRI/PET Imaging in elevated PSA and localized prostate cancer: a narrative review. *Transl Androl Urol.* Jul 2021;10(7):3117-3129. doi:10.21037/tau-21-374

5) Cereser L, Evangelista L, Giannarini G, Girometti R. Prostate MRI and PSMA-PET in the Primary Diagnosis of Prostate Cancer. *Diagnostics (Basel).* Aug 17 2023;13(16)doi:10.3390/diagnostics13162697

6) Emmett L, Buteau J, Papa N, et al. The Additive Diagnostic Value of Prostate-specific Membrane Antigen Positron Emission Tomography Computed Tomography to Multiparametric Magnetic Resonance Imaging Triage in the Diagnosis of Prostate Cancer (PRIMARY): A Prospective Multicentre Study. *Eur Urol.* Dec 2021;80(6):682-689. doi:10.1016/j.eururo.2021.08.002

7) Emmett L, Papa N, Buteau J, et al. The PRIMARY Score: using intraprostatic (68)Ga-PSMA PET/CT patterns to optimize prostate cancer diagnosis. *J Nucl Med.* Nov 2022;63(11):1644-1650. doi:10.2967/jnumed.121.263448

8) Buteau JP, Moon D, Fahey MT, et al. Effect of [(68)Ga]Ga-PSMA-11 PET-CT in the diagnosis of prostate cancer in men with equivocal or clinically high-risk non-suspicious findings on multiparametric MRI (PRIMARY2): a multicentre, non-inferiority, phase 3, randomised controlled trial. *Lancet Oncol.* Jul 2026;27(7):839-848. doi:10.1016/S1470-2045(26)00120-8

9) Kroenke M, Mirzoyan L, Horn T, et al. Matched-pair comparison of (68)Ga-PSMA-11 and (18)F-rhPSMA-7 PET/CT in patients with primary and biochemical recurrence of prostate cancer: frequency of non-tumor-related Uptake and tumor positivity. *J Nucl Med.* Aug 1 2021;62(8):1082-1088. doi:10.2967/jnumed.120.251447

10) Rauscher I, Kronke M, Konig M, et al. Matched-pair comparison of (68)Ga-PSMA-11 PET/CT and (18)F-PSMA-1007 PET/CT: frequency of pitfalls and detection efficacy in biochemical recurrence after radical prostatectomy. *J Nucl Med.* Jan 2020;61(1):51-57. doi:10.2967/jnumed.119.229187

11) Seifert R, Telli T, Opitz M, et al. Unspecific (18)F-PSMA-1007 bone uptake evaluated through PSMA-11 PET, bone scanning, and MRI triple validation in patients with biochemical recurrence of prostate cancer. *J Nucl Med.* May 2023;64(5):738-743. doi:10.2967/jnumed.118.215434

12) Grefve J, Strandberg SN, Jonsson J, et al. Local staging of de novo prostate cancer using mpMRI, PSMA-PET and PSMA-PET/mpMRI - a comparative study. *EJNMMI Res.* Nov 17 2025;15(1):135. doi:10.1186/s13550-025-01334-3