

PROSTATE CANCER: IMAGING IN PROSTATE CANCER

NEW DEVELOPMENTS FOR BETTER IMAGING

10 QUESTIONS TO ASK YOUR DOCTOR ABOUT IMAGING IN PROSTATE CANCER

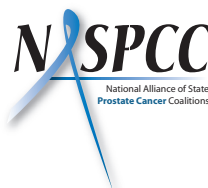
- 1. What is “Imaging” in prostate cancer?**
Imaging is a visual representation of part of the body using radiographic techniques to diagnose a disease, see extent of disease, or monitor progression. Examples are Ultrasound (prostate biopsy); MRI and multi-parametric MRI (mpMRI) (prostate biopsy, cancer detection and/or follow-up); PET/CT with FDG or choline or fluciclovine or PSMA.
- 2. What is the difference between ultrasound-guided biopsy and MRI-targeted biopsy?**
Prostate biopsy can be done with ultrasound guidance or with MRI guidance, or both (fusion biopsy). Multi-parametric MRI (mpMRI) is the most widely used imaging technique for locating and staging the tumor in the prostate, and provides more detailed images than ultrasound.
- 3. What is the difference between Conventional Imaging and Molecular Imaging?**
Conventional imaging such as x-rays, mpMRI, CT and ultrasound, offers pictures of physical structure, while molecular imaging shows activity within the body at the cellular level. Molecular imaging includes nuclear medicine, in which radioactive materials (“tracers”) are injected into the body and can be detected to help diagnose disease. Molecular Imaging is more sensitive and can reveal disease not normally seen with conventional imaging.
- 4. What is PSMA?**
Prostate-Specific Membrane Antigen (PSMA) is a protein molecule found on the surface of most prostate cancer cells. Since PSMA is highly expressed in prostate cancer, especially aggressive disease, it is a specific target for molecular imaging and therapy.
- 5. What are the newer agents in molecular imaging?**
New FDA-approved tracers for molecular imaging targeting PSMA (PSMA-PET/CT) include **gallium 68 PSMA-11** and **fluorine 18 DCFPyL** (Piflufolastat - Pylarify); both are used for suspected metastasis prior to planned surgery/radiation, and for suspected biochemical recurrence based upon rising PSA levels. PSMA PET/CT provides high specificity for preoperative nodal staging for men with unfavorable intermediate and high-risk disease.
- 6. Are there studies that support the use of the new agents in molecular imaging?**
Yes, various clinical trials have shown the superiority of molecular imaging over conventional imaging. Patients benefit to the extent that sites of disease can be accurately identified and characterized.
- 7. Does the use of newer molecular imaging agents change management?**
Recently a study of PSMA-11 at UCSF and UCLA showed that the use of molecular imaging changed the course of management in over half of the enrolled prostate cancer patients. The CONDOR study with Pylarify had a similar result.
- 8. What is the role of PSMA in small volume oligometastatic disease or more widespread metastatic disease?**
PSMA PET/CT can identify even very small sites of oligometastatic disease, allowing for better planning for focal radiation therapy and improved outcomes. With more widespread metastatic disease, PSMA PET/CT can identify extent of disease and PSMA expression, allowing for PSMA-targeted therapy with a radionuclide such as lutetium-177 (theranostics).
- 9. What are the limitations of these types of molecular agents?**
Even if more sensitive and specific than conventional imaging, PSMA PET/CT molecular imaging is still not perfect and undetected microscopic lesions can still exist.
- 10. What is “theranostics”?**
The term refers to the combined use of one radioactive drug to image prostate cancer, plus a second radioactive drug to deliver treatment to the cancer and to metastatic sites, by using the same molecular target: PSMA. “You see the target, you treat the target.”

CAVEAT: For patients at initial staging or with a biochemical recurrence, the timing of PSMA PET/CT Imaging can be critical.

Knowledge is Power!

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National Alliance of State Prostate Cancer Coalitions



PROSTATE CANCER: IMAGING IN PROSTATE CANCER FOR PHYSICIANS

The More Sensitive
and Specific
the Imaging,
the Better the Care

PLEASE REVIEW THE PATIENTS' QUESTIONS AND ANSWERS ON THE REVERSE SIDE

1. Conventional imaging such as contrast-enhanced CT or mpMRI, displays anatomical structures. PET Molecular imaging allows visualizing biological processes at the cellular level of activity within the body, providing more sensitive and specific imaging of even very small disease sites, allowing a more targeted approach to therapy.
 2. Biopsies are performed with either ultrasound, MRI guidance, or both. MRI- targeted biopsy increases the detection of clinically significant prostate cancer while limiting the detection of clinically insignificant disease (**PROMIS Trial**). "mpMRI in conjunction with ultrasound fusion biopsy detects more clinically significant disease while missing lower volume and clinically indolent disease."
www.auanet.org/guidelines/guidelines/mri-of-the-prostate-sop
 3. With conventional imaging, the cancer is often not visible until it has grown or is widespread. But PET molecular imaging, based on the biologic processes of the prostate cancer cell, ie. increased metabolism or overexpression of cell surface proteins, can deliver images of lesions as small as 2-4 millimeters.
 4. PSMA is prostate-specific membrane antigen, a glycoprotein found on the surface of most prostate cancer cells, especially in aggressive disease. PSMA is a natural target that can be used for molecular imaging **and** treatment. PSMA PET/CT is a molecular imaging study in which a radioactive tracer binds to the extra-cellular part of PSMA on the outside of the prostate cancer cell and emits small amounts of radiation, allowing visualization of even very small amounts of disease. Ideally this imaging should be done before initiation of a new therapy.
 5. New FDA-approved tracers for molecular imaging (PSMA-PET/CT) include **gallium 68 PSMA-11** (December, 2020) and **fluorine 18 DCFPyL** (Piflufolostat - Pylarify) (May, 2021); both are used for suspected metastasis prior to planned surgery/radiation, and for suspected biochemical recurrence based upon rising PSA levels. PSMA PET/CT provides high specificity for preoperative nodal staging for men with unfavorable intermediate and high-risk disease. **Fluciclovine (Axumin)** (May, 2016) is an older molecular imaging agent detecting increased amino-acid metabolism only approved for suspected recurrence.
 6. Definitive clinical trials demonstrating the superiority of molecular imaging include **NCT0336847** and **NCT02940262** (for gallium-68 PSMA-11); and **OSPREY** and **CONDOR**, (for Pylarify).
 7. A UCSF/UCLA study of patients with biochemically recurrent prostate cancer showed that gallium-68 PSMA-11 PET/CT identified sites of recurrence leading to management changes in more than half of the patients, especially those with a PSA of 0.5 to less than 2. *J Nucl Med.* 2020; 61: 1793-1799. The CONDOR Study with 18F-DCFpyL-PET/CT showed a similar change in intended management.
 8. In true oligometastatic disease, visualizing very small sites of disease allows for better treatment planning with metastasis-directed focal therapy (EBRT) and potential improvement in outcomes. In widespread metastatic disease, PSMA PET may be used for therapy response assessment, and being able to visualize disease extent and confirm PSMA expression may lead to treatment with targeted radionuclides, such as lutetium-177 (theranostics).
 9. Even if more sensitive and specific than conventional imaging, PSMA PET/CT molecular imaging is still not perfect and undetected microscopic lesions can still exist. Other limitations include the possibility of false positives and the need to have consistent, reliable interpretations with well-trained readers. In small cell/neuroendocrine disease, PSMA may not be a suitable target since in a small percent very little PSMA is expressed. Use of anti-androgens can alter the amount of PSMA expression, and PSMA expression can occur in other tumors.
 10. Theranostics is using paired compounds for both imaging and therapy with the same molecular target. Example: gallium-68 PSMA-11 for imaging plus Lutetium-177 PSMA-617 for therapy. See PROSTATEPEDIA June 2021 Issue on Imaging: <https://online.flippingbook.com/view/49474542/> Another example: imaging (gallium-68 PSMA-11) plus antibodies or targeted car-T cells, or any imageable biomarker. See **VISION** and **Thera-P** Trials.
- CAVEAT: For patients with castration-naïve disease (initial staging or with biochemical recurrence), the timing of ADT and the PSMA PET/CT is critical. Ideally imaging should be done prior to therapy, since once it is initiated, it may make the lesions less detectable.**

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