

# First indirect evidence that PSMA PET/CT surpasses conventional imaging in detecting occult prostate cancer spread

December 13 2021

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Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, [CC BY-SA 3.0](#)

Researchers at UCLA Jonsson Comprehensive Cancer Center led a large international study providing what is believed to be the first evidence (albeit indirect) that a recently approved imaging technique improves risk-stratification and long-term prognostic capabilities for patients with

high-risk prostate cancer whose conventional imaging showed only localized disease.

"Our findings also suggest that previously undetected, non-localized disease may be the primary driver of outcomes in this high-risk population," said Dr. Amar Kishan, chief of the Genitourinary Oncology Service for the Department of Radiation Oncology at the David Geffen School of Medicine at UCLA and the UCLA Jonsson Comprehensive Cancer Center. He is the senior author of an article in the Dec. 13 issue of *JAMA Network Open*.

Although early experience with PSMA PET/CT indicates it can detect low-volume, non-localized [prostate cancer](#) that is not seen with conventional imaging, direct, prospective evidence of its prognostic value is still several years away because clinical use of the technique has been available in the United States less than a year, said Kishan, associate professor and vice chair of clinical and translational research in the Department of Radiation Oncology at UCLA. But a tool created for this study may serve as a proxy for the new technology's long-term prognostic and clinical significance.

In a recently published study, UCLA researchers had developed a PSMA PET/CT-specific "nomogram," a tool that takes a variety of variables into account to predict the probability of finding non-localized disease using PSMA PET/CT in patients who appeared to have no regional lymph node involvement or distant metastasis based on conventional imaging at the time of diagnosis.

In this new study, the researchers—representing 15 centers in the U.S., Canada, Norway, Germany, and Spain—looked at the prognostic significance of the PSMA nomogram on long-term, clinically meaningful outcomes, then compared its prognostic capabilities with those of other, existing risk-stratification tools.

"The PSMA nomogram was designed to predict the positivity of PSMA PET/CT at initial diagnosis, without regard to eventual clinical outcomes, but interestingly, this PSMA PET/CT-based tool provided better risk discrimination than existing tools that were designed specifically to predict clinical outcomes. This may speak to the significance of using PSMA PET/CT findings as a marker of overall disease course, and our results contribute to a growing body of data supporting the clinical use of this technique in the initial evaluation and management of high-risk patients," said Dr. Michael Xiang, assistant clinical professor in the Department of Radiation Oncology at the David Geffen School of Medicine at UCLA. Xiang is the corresponding author and a co-first author of the paper, with Dr. Ting Martin Ma, resident physician in the Department of Radiation Oncology.

Among highlights and details:

- The study evaluated the prognostic significance of the PSMA nomogram (and, by proxy, PSMA PET/CT itself) on long-term, clinically meaningful endpoints, including distant metastasis, prostate [cancer](#)-specific mortality, and overall survival.
- The primary study included a cohort of 5,275 patients with high-risk or very high-risk prostate cancer, based on National Comprehensive Cancer Network criteria. The patients were treated at 15 centers between 1995 and 2018 using radiation or surgery.
- In statistical analyses, the PSMA nomogram was significantly prognostic of all clinical endpoints, regardless of treatment type.
- Findings were validated externally using two large registry-based cohorts: the Surveillance, Epidemiology, and End Results (SEER) Program database (23,989 patients), and the National Cancer Database (88,909 patients). Nomogram risk was significantly prognostic in age-related regression analyses.

Several of the *JAMA Network Open* article authors, including Kishan and Drs. Johannes Czernin, Jeremie Calais, Robert Reiter, Matthew Rettig, and Nicholas Nickols, are UCLA faculty and members of the UCLA Jonsson Comprehensive Cancer Center who helped lead the clinical trials for the use of PSMA PET imaging in the United States. Calais, co-senior principal investigator on this study, was senior author of a Sept. 16 article in *JAMA Oncology* on the diagnostic accuracy of PSMA PET technology for pelvic node metastasis detection. That study, a collaboration between UCLA and the University of California, San Francisco, led to U.S. Food and Drug Administration approval of the technology for this purpose.

"PSMA PET is now part of the National Comprehensive Cancer Network guidelines as a replacement of other front-line imaging tools. With [insurance coverage](#), this game-changer technology will ultimately become part of the routine staging of prostate cancer patients," said Calais, assistant professor and director of the Clinical Research Program of the Ahmanson Translational Theranostics Division of the Department of Molecular and Medical Pharmacology at UCLA. He is also a member of the UCLA Jonsson Comprehensive Cancer Center and the UCLA Institute of Urologic Oncology.

The FDA approved the first PSMA PET/CT imaging drug, Gallium 68 PSMA-11, in December 2020, with initial approval going to UCLA and UCSF. A second drug, Pylarify, was approved in May 2021. The [radioactive tracers](#) are limited to use in certain patients: those with suspected prostate cancer metastasis who are potentially curable by surgery or radiation therapy, and those with suspected prostate cancer recurrence, based on elevated prostate-specific antigen (PSA) levels.

Administered by IV injection, the drugs bind to prostate-specific membrane antigen (PSMA), a protein that is usually found in high levels in prostate cancer cells. The tracers can be imaged by positron emission

tomography (PET)/computed tomography (CT) to indicate the presence of cancer lesions.

**More information:** Performance of a Prostate-Specific Membrane Antigen Positron Emission Tomography/Computed Tomography–Derived Risk-Stratification Tool for High-risk and Very High-risk Prostate Cancer; *JAMA Network Open*. 2021;4(12):e2138550. [DOI: 10.1001/jamanetworkopen.2021.38550](https://doi.org/10.1001/jamanetworkopen.2021.38550) (Reprinted) December 13, 2021. [DOI: 10.1001/jamanetworkopen.2021.38550](https://doi.org/10.1001/jamanetworkopen.2021.38550)

Provided by University of California, Los Angeles

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