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Potential Causes of False-Negative Interpretations in ^{68}Ga -PSMA PET/CT for the Detection of Local and Recurrent Prostate Cancer

An Underexposed Issue

Derya Yakar, MD, PhD, Walter Noordzij, MD, PhD, and Thomas C. Kwee, MD, PhD

Abstract: ^{68}Ga -PSMA PET/CT has emerged as a highly promising diagnostic method for the evaluation of prostate cancer. Although it is increasingly recognized that its specificity is imperfect, data on false-negatives in the prostate have been underreported. We present 3 cases with false-negatives for local (recurrent) prostate cancer on ^{68}Ga -PSMA PET/CT, using multiparametric MRI and histopathology as reference standard. Metal artifact of prostate gold markers placed for external beam radiation therapy, low level of PSMA uptake, and bladder spillover are potential causes of misinterpretation. Awareness of these diagnostic pitfalls may improve ^{68}Ga -PSMA PET/CT interpretation.

Key Words: ^{68}Ga -PSMA PET/CT, false-negative, multiparametric MRI, prostate cancer

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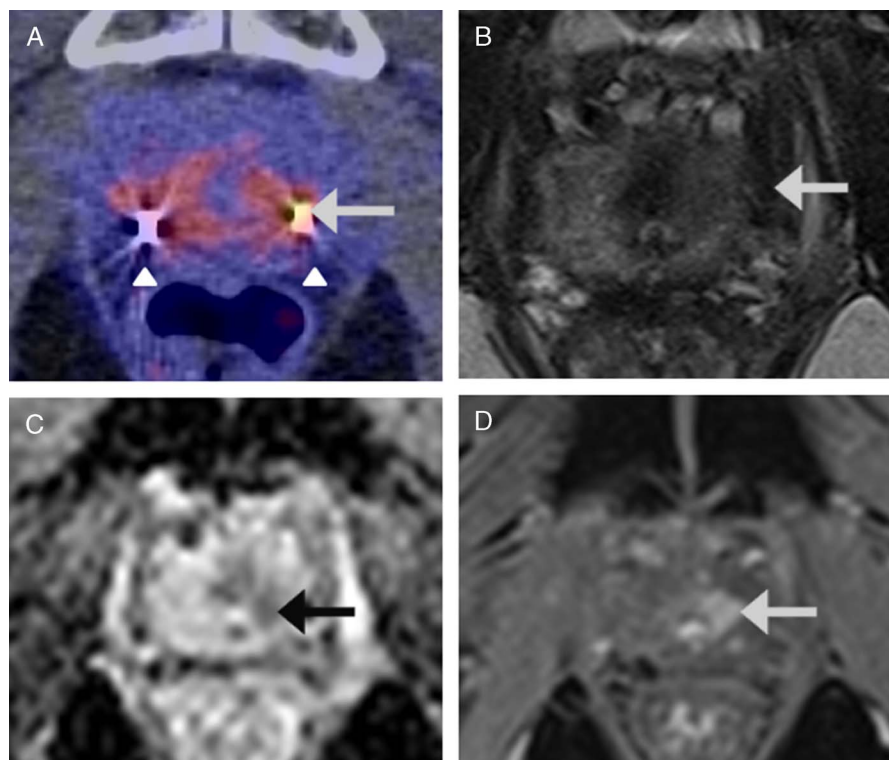


FIGURE 1. A 53-year-old patient with biochemical recurrence (prostate-specific antigen [PSA] 9.1 ng/mL) after external beam radiation therapy (EBRT). Axial ^{68}Ga -PSMA PET/CT (A) shows the gold markers placed for EBRT (arrowheads) and focally increased uptake (arrow). The latter was prospectively interpreted to be due to metal artifacts.¹ There were no signs of metastatic disease. Multiparametric MRI (mpMRI) performed 6 days later showed a local recurrence in the left peripheral zone on axial T2-weighted (B, arrow), apparent diffusion coefficient map (C, arrow), and contrast-enhanced (D, arrow) images. Targeted MRI transrectal ultrasound (TRUS) fusion biopsy confirmed recurrent disease (Gleason 4 + 3). In post-EBRT patients, recurrent disease may be confused for metal artifacts on ^{68}Ga -PSMA PET/CT (and vice versa). A helpful hint to avoid this pitfall and to suggest recurrent disease instead of a true metal artifact is the absence of “artificial” uptake around other gold markers.

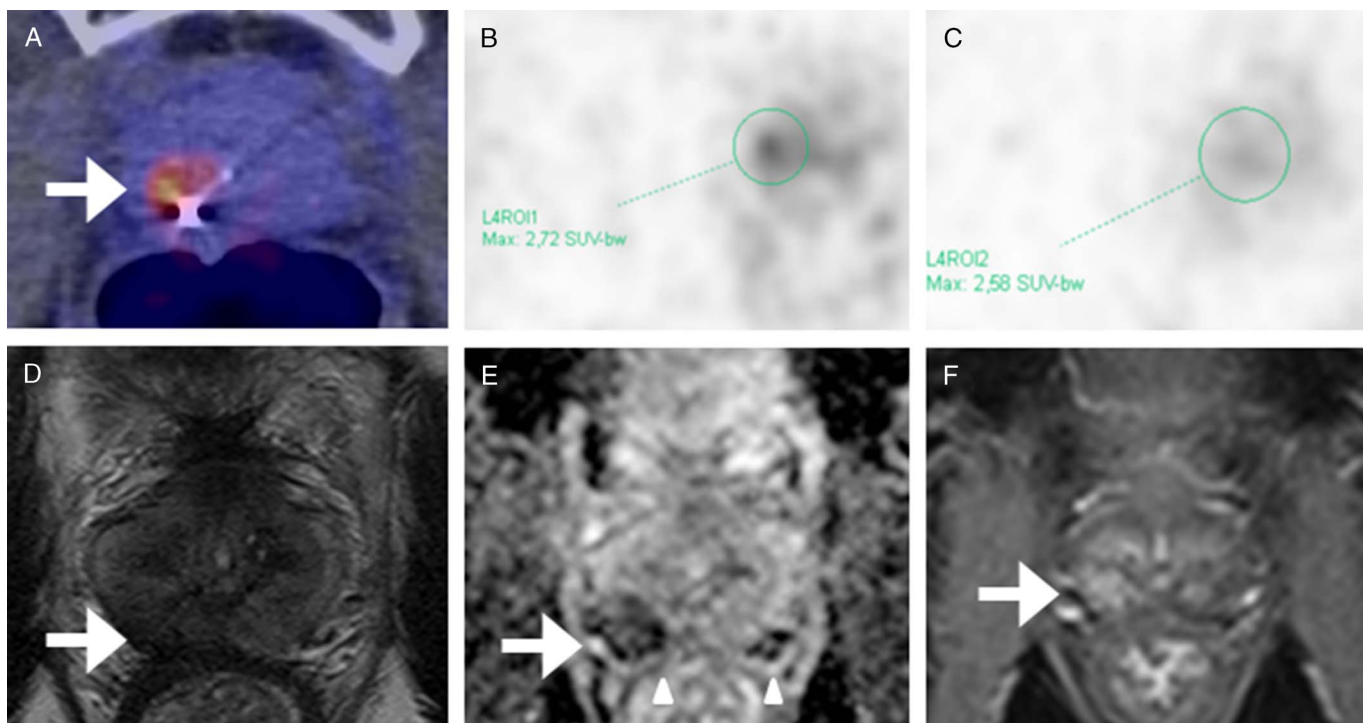


FIGURE 2. A 77-year-old man with biochemical recurrence (PSA 3.0 ng/mL) after EBRT. On axial ^{68}Ga -PSMA PET/CT (A), focal uptake was seen (arrow); however, its SUVmax of 2.72 (B) was hardly different (approximately 5%) from background noise with an SUVmax of 2.58 (C). Therefore, it was prospectively called negative for local recurrence. ^{68}Ga -PSMA PET/CT suggested only 1 suspicious lymph node in the right obturator area (not shown). Multiparametric MRI (performed 6 days later) showed a local recurrence in the right peripheral zone on T2-weighted (D, arrow), apparent diffusion coefficient map (E, arrow), and contrast-enhanced (F, arrow) images. Targeted MRI-TRUS fusion biopsy confirmed recurrent disease (Gleason 4 + 3). In this case, a lesion with only slight focal PSMA uptake, which was interpreted as benign, turned out to be malignant. Overlap of SUV values between malignant and benign prostate disease on ^{68}Ga -PSMA PET²⁻⁶ should be taken into account, and additional mpMRI should be performed.

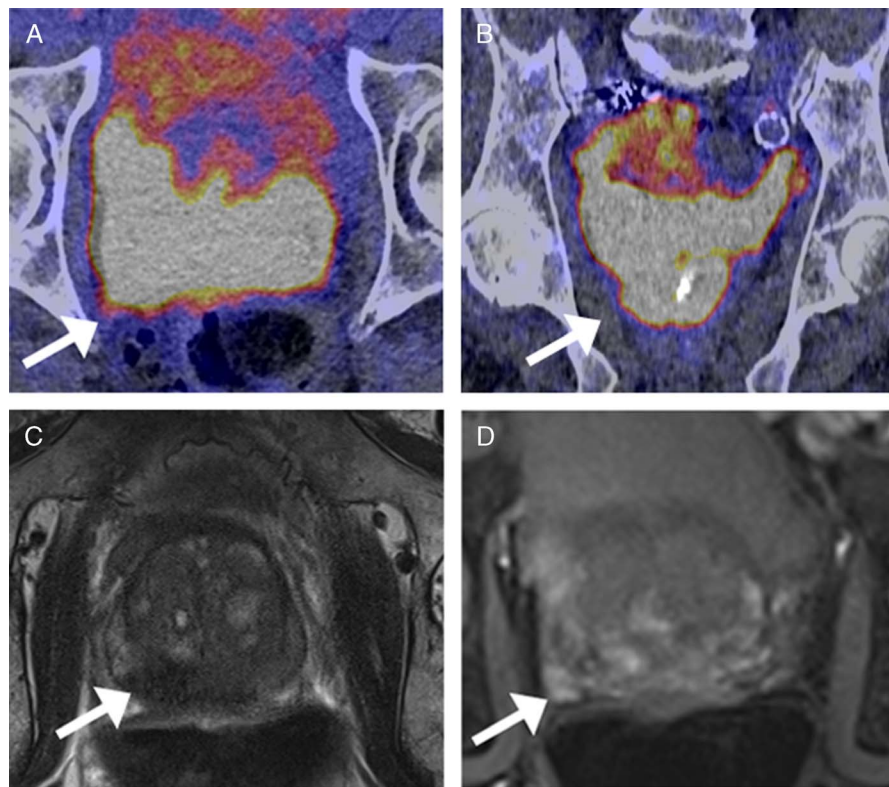


FIGURE 3. A 73-year-old man with PSA 12 ng/mL and prostate cancer diagnosed by systematic TRUS biopsy (Gleason score 5 + 4 in both sides). On axial and coronal ^{68}Ga -PSMA PET/CT (A, B), the prostate was prospectively read as negative for cancer, and the high activity in the pelvis was interpreted as spillover from the bladder (arrows). Multiparametric MRI (performed 3 days later) revealed multiple areas suggestive of prostate cancer, of which the largest lesion is shown on T2-weighted (C, arrow) and contrast-enhanced (D, arrow) images. Furthermore, numerous suspicious lymph nodes and bone lesions were seen (not shown). Spillover from the bladder is a well-known phenomenon in ^{18}F -FDG-PET,⁷ but also appears to be an issue in ^{68}Ga -PSMA PET.⁸ Despite the fact that PET/CT scanning was done after administration of furosemide and bladder emptying in this patient, bladder spillover could not be prevented. Even though it did not have any impact on patient management in this case, bladder spillover can be a source of clinically relevant false-negatives on ^{68}Ga -PSMA PET/CT in other patients. Particular caution and additional mpMRI should be warranted in patients with considerable bladder spillover and who do not have any signs of extraprostatic disease on ^{68}Ga -PSMA PET/CT.