adrenal disease. Despite being a nonfunctional agent, pentixafor targets the C-X-C motif chemokine receptor 4, which is overexpressed in various adrenal pathologies, thereby offering valuable diagnostic information.

Our findings demonstrated that ^{68}Ga-pentixafor PET/CT has higher diagnostic accuracy than adrenal CT and shows better concordance with surgical outcomes than does adrenal venous sampling. ^{68}Ga-pentixafor PET/CT offers a practical, noninvasive alternative for initial diagnostic work-up, particularly in patients for whom adrenal venous sampling is not feasible or fails.

We acknowledge that pentixafor has limitations as a nonfunctional agent, especially in quantifying hormone dysfunction or autonomy within the adrenal gland. However, its role in evaluating adrenal lesions, such as nodules or adrenocortical carcinoma, remains significant. The ability to identify C-X-C motif chemokine receptor 4 expression provides valuable diagnostic and potentially prognostic information, contributing to personalized patient management.

We agree that advancements in functional imaging agents such as FNP-59 hold potential for the future of adrenal imaging. However, ^{68}Ga-pentixafor has evidentially provided a practical, noninvasive alternative for initial diagnostic work-up for primary aldosteronism, particularly for differentiating subtypes in patients with adrenal micronodules. Further research and technologic advancements will continue to refine and enhance the imaging techniques, ultimately improving patient outcomes.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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Considerations Surrounding the Sentinel Lymph Node in Prostate Cancer and Unanswered Questions

TO THE EDITOR: We read with interest the article "The Diagnostic Value of the Sentinel Node Procedure to Detect Occult Lymph Node Metastases in PSMA PET/CT Node–Negative Prostate Cancer Patients" published by Duin et al. (*1*). We acknowledge that this multidisciplinary team has good expertise in the field of sentinel lymph nodes (SLNs) in prostate cancer, so we would like to provide a few comments.

First, the results reported are nothing new since evidence of the feasibility of SLN biopsies has been shown for many years (*2*), but we must admit that this technique has trouble finding its way to routine use. How could the authors explain such reluctance to routinely perform SLN biopsies in cases of prostate cancer?

Second, the comparison with negative findings in prostate-specific membrane antigen (PSMA) PET/CT is not that easy given the variable performance reported in the literature. Corfield et al. reported a sensitivity of detecting metastases in ^{68}Ga-PSMA-11 PET/CT ranging from 33% to 99% (*3*). Moreover, interpreting negative results is challenging. In their paper, Duin et al. reported macrometastases (with PSMA expression immunohistochemically) in 36% of their patients with negative PET/CT results, whereas Klingenberg et al. showed that pathologic nodes were missed in PET/CT in the cases of either micrometastases or metastases without PSMA expression (*4*).

Third, the authors suggest performing SLN biopsies in patients with negative PSMA PET/CT findings, which could appear conflicting with the findings reported by Kopp et al., highlighting the reliable negative predictive value compared with the poor positive predictive value (*5,6*). Should SLN biopsies then be performed in cases of positive PSMA PET/CT instead?

Fourth, we agree that SLN findings could modify the treatment choice. However, in the case of pathologic involvement, there is an upstaging that may lead to treatment escalation without evidence of benefits in oncologic outcomes. Besides, with negative findings, would it be safe to deescalate treatment even if the risk of nodal involvement is estimated to be high according to nomograms? As a matter of fact, Hötker et al. reported that Briganti 2019 nomogram performed better than ^{68}Ga-PSMA-11 PET/CT and multiparametric MRI to predict nodal metastases (*7*).

Lastly, the authors did not document SLNs in difficult-to-reach anatomic locations. But we strongly believe that such uncommon lymphatic drainage could explain some patterns of relapse (*8*), and the SLN technique thus appears to be relevant to enable an individualized and tailored treatment (*9*).

We are enthusiastic to see a multidisciplinary team emphasizing the benefits in using SLN testing for the staging of prostate cancer. Here, we emphasize some unanswered problems that would need to be addressed before implementing such a technique in our daily practice.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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REPLY: We thank the authors of the letter to the editor for their thoughtful comments on our article, "The Diagnostic Value of the Sentinel Node Procedure to Detect Occult Lymph Node Metastases in PSMA PET/CT Node–Negative Prostate Cancer Patients" (*1*). We appreciate the opportunity to clarify several key points.

First, translating the sentinel lymph node (SLN) procedure into routine clinical prostate cancer practice is challenging. SLN procedures require preoperative planning and collaboration with specialized nuclear medicine facilities. Although emerging evidence shows positive short to intermediate outcomes, long-term randomized controlled trial data are lacking.

Second, we agree that interpreting negative prostate-specific membrane antigen (PSMA) PET/CT findings is complicated by different scanning protocols and PSMA-targeting tracers. Both Klingenberg et al. (*2*) and Jilg et al. (*3*) showed that most lymph node metastases not detected on PSMA PET/CT had PSMA expression on immunohistochemistry, and the detection rate increased with larger lymph node metastases. These findings suggest that lymph node metastases on PSMA PET/CT rarely lack PSMA expression but are often missed because of low tumor volume.

Third, performing SLN biopsies in patients with negative PSMA PET/CT scans is supported by previous research (*4*) demonstrating that adding SLN biopsy to PSMA PET/CT for primary lymph node staging in intermediate- and high-risk prostate cancer patients yields 100% sensitivity. In higher-risk populations, the negative predictive value of PSMA PET/CT decreases while the positive predictive value increases (*5*). Therefore, minimizing the risk of missing lymph node metastases in high-risk populations justifies SLN biopsies even in patients with negative PSMA PET/CT scans. Moreover, macrometastases detected by PSMA PET/CT may result in false-negative SLN detection due to lymph blockage, making SLNs less reliable.

Fourth, regarding treatment escalation in node-positive patients, large retrospective studies show improved survival after whole-pelvis radiotherapy in clinically or pathologically node-positive patients (*6*). Recently, the randomized POP-RT trial showed that prophylactic whole-pelvis radiotherapy was associated with improved survival in high-risk patients (*7*). We hypothesize that a substantial subset of patients had undetected PSMA PET/CT nodal metastases, benefiting from nodal treatment intensification. Nevertheless, long-term randomized data supporting treatment escalation based on nodal status are needed.

Finally, SLNs in challenging locations were left in situ if multiple nodes were present on preoperative SPECT, as removing these nodes might increase surgical complications. Of 31 patients with SLNs left in situ, 10 were pN1 (32%) and 21 were pN0 (68%). Studying radiologic recurrence patterns in these patients could indicate false-negative cases due to unresected SLNs. As many of these patients are still receiving androgen-deprivation therapy, it is too early to report on these results.

We share your enthusiasm for SLN mapping in prostate cancer staging and appreciate your efforts to highlight important considerations. Building on retrospective evidence for SLN-directed radiotherapy, the ENTAIL trial, a randomized control trial to evaluate the oncologic value of SLN-based radiotherapy field tailoring, is currently awaiting approval from the Medical Ethics Committee of The Netherlands Cancer Institute.

DISCLOSURE

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