

TO THE EDITOR: Since the large-scale deployment of coronavirus disease 2019 vaccination, several publications have mentioned many false-positive findings on PET examinations, mainly with ^{18}F -FDG but also with other radiopharmaceuticals (1). For instance, Notohamiprodjo et al. recently reported that the prevalence of vaccine-associated lymphadenopathy (VAL) on ^{18}F -rhPSMA-7.3 PET/CT was high, at 45% (2), but some points of the study deserve comment.

First, the authors stated that “increased ipsilateral axillary uptake of [prostate-specific membrane antigen (PSMA)] ligand is common” but omitted to mention some contradictory results in the literature. In fact, we prospectively constituted a cohort in which 120 and 79 patients underwent ^{18}F -fluorocholine or ^{68}Ga -PSMA-11 PET/CT, respectively, and we reported a 42.5% incidence of VAL for ^{18}F -fluorocholine PET/CT (which was comparable to the findings with ^{18}F -FDG) but only a 12% incidence for ^{68}Ga -PSMA-11 PET/CT (3). This difference cannot be due entirely to variable definitions of VAL between studies but may be explained by differences in the studied populations or in the radiopharmaceutical itself (4).

Second, the authors did not provide a documented hypothesis explaining the false-positive cases. A possible explanation comes from PSMA uptake in the context of neoangiogenesis (5). We hypothesized that coronavirus disease 2019 vaccination could induce production of vascular cell adhesion molecules and vascular endothelial growth factor, as observed during severe acute respiratory syndrome coronavirus 2 infection (6), leading to neovascularity and therefore PSMA uptake.

Third, as mentioned by the authors, “separate analysis among those vaccines was not performed.” Nevertheless, differences between vaccines could be expected since a metaanalysis found VAL more frequently after the Moderna vaccine than after the Pfizer-BioNTech vaccine (7), whereas a comparative study reported higher metabolic activity in the lymph nodes after Pfizer-BioNTech than after AstraZeneca (8).

Last, the authors do not suggest a clear management plan for these lymph nodes in clinical practice. Should they be closely monitored for development or regression by physical examination or by imaging? Should they be systematically analyzed by a pathologist? Some researchers are exploring ways to address this issue. For instance, radiomics could help differentiate VAL from malignant lymphadenopathies (9). Besides, innovative radiopharmaceuticals are under development and capable of overcoming postvaccination pitfalls, such as use of the ^{68}Ga -fibroblast-activation protein inhibitor, which showed no fixation in postvaccination axillary nodes, to replace ^{18}F -FDG (10).

In conclusion, the study provides valuable information about false-positive cases on PET imaging due to vaccination—a recurrent issue that needs to be addressed, even if some results can be challenged by other existing findings, notably in our work published previously. However, this study has the merit of reminding the imaging interpreter and the prescriber that PSMA ligand is not specific to prostate cancer and not even to the prostatic gland.

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REPLY: We are grateful for the commentary on our paper (1) by Ah-Thiane et al. and appreciate the reference to their publication on prostate-specific membrane antigen (PSMA) radioligand uptake by axillary lymph nodes after vaccination. We submitted the final version of our manuscript to *The Journal of Nuclear Medicine* on February 17, 2022, and their study was published in July 2022 (2). Therefore, we were unfortunately unable to discuss the study by Ah-Thiane et al.

It is interesting that Ah-Thiane et al. reported a substantially lower incidence of PSMA-positive axillary lymph nodes with ^{68}Ga -PSMA-11 (12%) than we found for ^{18}F -rhPSMA 7.3 (45%). This large difference may indeed point to differences in the studied population or of the radiopharmaceutical itself, but confirmation will require future studies.

We also thank Ah-Thiane et al. for pointing out that PSMA expression during angiogenesis may contribute to PSMA expression after vaccination. We had discussed that PSMA expression is not specific to the prostate and that PSMA RNA is found in many tissues, including lymph nodes (3,4). At the moment, there are, to our knowledge, no data to allow for definitive statements on what precisely causes PSMA radioligand uptake after vaccination.