Vaccine-Related Lymph Nodes

The Emerging Pitfalls of $^{18}$F-Fluorocholine and $^{68}$Ga-PSMA-11 PET/CT in the Era of COVID-19 Vaccination

Loïc Ah-Thiane, MD,* Ludovic Ferrer, PhD,*† Bruno Maucherat, MD, * Vincent Fleury, MD,* Maelle Le Thiec, MD,* Daniela Rusu, MD, PhD,* and Caroline Rousseau, MD, PhD*†

Purpose: Vaccination against coronavirus disease 2019 (COVID-19) is currently ongoing in France with the aim of covering most of its population, thanks to 4 authorized vaccines, the BNT162b2mRNA (Pfizer-BioNTech), mRNA-1273 (Moderna), ChAdOx1-S (AstraZeneca), and Ad26.COV2.S (Janssen) vaccines. The vaccination campaign started with patients older than 75 years or with severe comorbidities, then the adult population as a whole, and now covers teenagers. In this way, more than 74.7% of the population has received at least 1 dose of vaccine, and 66.3% are fully vaccinated, at the time of writing (October 2021).

Local and systemic reactions are described after COVID-19 vaccines, and a commonly reported adverse effect after administration in the deltoid muscle is an ipsilateral swollen or sensitive axillary lymph node (LN). Several cases were encountered rapidly in imaging departments, with visualization of axillary and supraclavicular LNs. This was noted during breast cancer screening in patients undergoing breast ultrasound or MRI, leading to recommendations to avoid PET/CT misinterpretation and incorrect patient treatment. For example, in a context of inflammation.

With the number of vaccine doses received ($P = 0.041$), with a short delay between vaccine and PET/CT realization ($P < 10^{-5}$), and with a higher prostate-specific antigen level for patients with PCa ($P = 0.032$), but not with age or vaccine type. The vaccine-related nodes appeared in 85% of the cases, in the 30 days after vaccine injection, were limited in size and uptake, and were most often limited to the axilla level 1 area.

Conclusions: Detecting positive LNs after COVID-19 vaccination is not an exclusive $^{18}$F-FDG PET/CT pattern but is common on $^{18}$F-fluorocholine and possible on $^{68}$Ga-PSMA-11 PET/CT. Confronting PET/CT findings with clinical data (such as date and site of injection) seems essential in the current pandemic context, just as it does for the radiopharmaceuticals used in PCa to avoid PET/CT misinterpretation and incorrect patient treatment.

Key Words: COVID-19, vaccination, $^{18}$F-fluorocholine, $^{68}$Ga-PSMA-11, PET/CT, pitfalls

Results: Of the 226 patients in our cohort study, 120 patients underwent an $^{18}$F-fluorocholine PET/CT, 79 a $^{68}$Ga-PSMA-11 PET/CT, 6 an $^{18}$F-DOPA PET/CT, and 21 a $^{68}$Ga-DOTATOC PET/CT. A total of 67.3% of patients (152/226) received BNT162b2mRNA (Pfizer-BioNTech), 26.5% (60/226) ChAdOx1-S (AstraZeneca), 4.9% (11/226) mRNA-1273 (Moderna), and 1.3% (152/226) received BNT162b2mRNA (Pfizer-BioNTech), 26.5% (60/226) ChAdOx1-S (AstraZeneca), 4.9% (11/226) mRNA-1273 (Moderna), and 1.3% (152/226) received Ad26.COV2.S (Janssen) vaccines.

None of our patients undergoing $^{18}$F-fluorocholine and $^{68}$Ga-PSMA-11, $^{18}$F-DOPA or $^{68}$Ga-DOTATOC PET/CT presented any vaccine-related lymphadenopathy. Vaccine-related LNs were statistically associated with the nature of the radiopharmaceutical ($P < 10^{-4}$), with the number of vaccine doses received ($P = 0.041$), with a short delay between vaccine and PET/CT realization ($P < 10^{-5}$), and with a higher prostate-specific antigen level for patients with PCa ($P = 0.032$), but not with age or vaccine type. The vaccine-related nodes appeared in 85% of the cases, in the 30 days after vaccine injection, were limited in size and uptake, and were most often limited to the axilla level 1 area.

Conclusions: Detecting positive LNs after COVID-19 vaccination is not an exclusive $^{18}$F-FDG PET/CT pattern but is common on $^{18}$F-fluorocholine and possible on $^{68}$Ga-PSMA-11 PET/CT. Confronting PET/CT findings with clinical data (such as date and site of injection) seems essential in the current pandemic context, just as it does for the radiopharmaceuticals used in PCa to avoid PET/CT misinterpretation and incorrect patient treatment. For $^{18}$F-FDOPA or $^{68}$Ga-DOTATOC PET/CT, this seems to have a lesser impact.

Key Words: COVID-19, vaccination, $^{18}$F-fluorocholine, $^{68}$Ga-PSMA-11, PET/CT, pitfalls

(Clin Nucl Med 2022;47: 575–582)
PATIENTS AND METHODS

Patient Recruitment

All consecutive patients undergoing a whole-body PET/CT between February and July 2021, for any indication and with a radiopharmaceutical different from \(^{18}\)F-FDG, were eligible for inclusion in the study if they had received at least 1 dose of COVID-19 vaccine before their PET/CT. Patients were excluded in case of missing data, a site of administration different from the deltoid muscle (eg, gluteal muscle), known malignant involvement of axillary and supraclavicular LNs, or if the second dose was not with the same vaccine as the first (eg, ChAdOx1-S [AstraZeneca] followed by BNT162b2mRNA [Pfizer-BioNTech]).

All patients were informed and gave their consent for access to their data, and none objected to these data being used for research purposes. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was examined and approved on July 6, 2021 by the local ethics committee of the institutional review board and registered under number 2021-114.

Data Collection

Our study consisted of analyzing a cohort of patients whose data were collected prospectively. All patients were interviewed about their vaccination status on the day of their PET/CT. The data collected for each patient included sex, age, oncological status, current oncologic treatment, number of doses of COVID-19 vaccine already received, date(s) of administration, side(s) of administration, type of vaccine, and tumor marker if relevant. Data collection also included the examination date, indication, and radiopharmaceutical administered.

PET/CT Analysis

All imaging was performed on a PET/CT Vision 450 (Siemens Erlangen, Germany). Images were acquired (3 minutes per step) 1 or 2 hours after injection, depending on the radiopharmaceuticals. Low-dose CT 3D acquisition without contrast product injection was performed considering the system’s voltage and current adaptation. Four hundred forty pixel-wide PET images were reconstructed using the TrueX algorithm (Siemens) and time-of-flight (4 iterations, 35 subsets) and Gaussian postfiltering (2-mm full-width at half-maximum). Finally, the images were sent to our picture archive and communication system.

All PET/CT images were interpreted by senior nuclear medicine physicians and reviewed by one of them. The number of axillary and supraclavicular LNs with a radiopharmaceutical uptake was recorded, as well as their location and size.

An LN was taken into consideration if its SUV\(_{\text{max}}\) was greater than mediastinum uptake and/or if the diameter of its smaller axis was greater than or equal to 10 mm.

Its location was determined as axilla level 1 (below the pectoralis minor), axilla level 2 (beside the pectoralis minor), or axilla level 3 (above pectoralis minor) according to the Berg classification.\(^{18}\) Its size was measured directly on the CT images from the PET/CT.

These positive LNs were considered vaccine-related if they were on the same side as the injection and if involvement with the primitive tumor was very unlikely. This likelihood was assessed on a clinical basis, depending on patient disease stage, on whether or not there was a progression, on the presence of other lymphatic areas involved, and knowing the natural spread of the cancer afflicting pelvic and retroperitoneal nodes in the first place for PCa for instance, and this translated in practice in the conclusion of our examination interpretation by the absence of needing complementary (imaging or pathological) examinations to explore these nodes. Cases of LNs related to proven or potential tumor involvement were excluded from the cohort study; those cases were mainly PCa with extended nodal involvement at diagnosis or PCa with nodal metastatic progression. Patients presenting positive vaccine-related axillary or supraclavicular LNs made up our case group, whereas patients without vaccine-related LNs served as a comparison group. The incidence on PET/CT of positive vaccine-related axillary and supraclavicular LNs was our primary finding.

Statistical Analysis

Categorical variables were reported as frequencies, and continuous variables as medians with the first and third quartiles (Q1–Q3 range).

As the number of PET/CT using \(^{18}\)F-FDOPA and \(^{68}\)Ga-DOTATOC as radiopharmaceuticals was small, those cases were not included in the statistical analysis. We thus decided to limit our statistical analysis to patients with PCa, which was the largest number of patients, for better comparability.

The \(\chi^2\) test was used to compare proportions between groups.

Logistic regression models were used to find a correlation between positive axillary and supraclavicular LNs and independent variables such as sex, age, oncological status, current oncologic treatment, number of doses of COVID-19 vaccine already received, date(s) of administration, side(s) of administration, type of vaccine, and prostate-specific antigen (PSA) level.

We considered as statistically significant a \(P\) value strictly less than 0.05.

RESULTS

Patient Characteristics

Of all the patients who had a PET/CT in our nuclear medicine department and who were screened with regard to our inclusion and exclusion criteria, 226 patients were included in our study cohort. The selection process is described in a flowchart (Fig. 1). Patients underwent PET/CT using \(^{18}\)F-FCH for 120 of them, \(^{68}\)Ga-PSMA-11 for 79 patients, \(^{18}\)F-FDOPA for 6, and \(^{68}\)Ga-DOTATOC for 21 patients.

With \(^{18}\)F-FCH, the indications were mainly biochemical recurrence of PCa in 82.5% (99/120) of patients, then initial assessment in 17.5% (21/120) of patients, and exploration of parathyroid nodules in 1.7% (2/120) of patients.

With \(^{68}\)Ga-PSMA-11, the indications were limited by the French Regulation Agency and limited to biochemical recurrence of PCa after noncontributive \(^{18}\)F-FCH PET/CT.

With \(^{18}\)F-FDOPA and \(^{68}\)Ga-DOTATOC, the indications were the initial assessment or follow-up of neuroendocrine tumors.

As described in Table 1, we observed a majority of patients with PCa, hence a high proportion of men (212/226), with only 14 women in our cohort. Patients’ ages ranged from 46 to 89 years. All patients were vaccinated with 1 of the 4 vaccines that received authorization in France. Most patients received the BNT162b2mRNA (Pfizer-BioNTech) vaccine, approximately one fourth received the ChAdOx1-S (AstraZeneca) vaccine, and very few received the mRNA-1273 (Moderna) or Ad26.COV2.S (Janssen) vaccines. A total of 54.9% (124/226) of patients had fully completed their vaccination schedule with 2 doses (or only 1 for the Janssen vaccine) before their PET/CT.

Positive Vaccine-Related Axillary or Supraclavicular LNs

In \(^{18}\)F-FCH PET/CT, 51/120 patients (42.5%) presented with positive vaccine-related LNs. For these patients, the time between...
the last dose of vaccine received and the PET/CT ranged from 1 to 86 days, with a median of 15 days, and approximately 85% of vaccine-related LNs cases were found to be in the 30 days after an injection.

Of the 61 patients who had received only the first dose of vaccine, 27 (44.3%) presented with vaccine-related LNs. Of the 59 fully vaccinated patients, 24 (40.7%) presented with vaccine-related LNs. Distribution of positive LNs according to the type of vaccine is shown in a chart (Fig. 2).

In $^{68}$Ga-PSMA-11 PET/CT, 10/79 patients (12.7%) presented with positive vaccine-related LNs. For these 10 patients, the time between the last dose of vaccine received and the PET/CT ranged from

### TABLE 1. Patient Characteristics

|                          | Total (n = 226) | Cases (n = 61) | Controls (n = 165) |
|--------------------------|----------------|---------------|--------------------|
| Median age in years (Q1–Q3) | 71 (67–76) | 72 (67.5–77) | 71 (65–75) |
| Male (frequency)         | 212 (93.8%) | 62 (98.4%) | 150 (92.0%) |
| Radiotracers (frequency) |                |               |                    |
| $^{18}$F-Fluorocholine   | 120 (53.1%) | 51 (83.6%) | 69 (41.8%) |
| $^{68}$Ga-PSMA-11        | 79 (35.0%) | 10 (16.4%) | 69 (41.8%) |
| $^{18}$F-FDOPA           | 6 (2.7%) | 0 (0%) | 6 (3.6%) |
| $^{68}$Ga-DOTATOC        | 21 (9.2%) | 0 (0%) | 21 (12.8%) |
| Vaccines (frequency)     |                |               |                    |
| BNT162b2mRNA (Pfizer-BioNTech) | 152 (67.3%) | 46 (75.4%) | 106 (64.2%) |
| ChAdOx1-S (AstraZeneca)  | 60 (26.5%) | 12 (19.7%) | 48 (29.1%) |
| mRNA-1273 (Moderna)      | 11 (4.9%) | 2 (3.3%) | 9 (5.5%) |
| Ad26.COV2.S (Janssen)    | 3 (1.3%) | 1 (1.6%) | 2 (1.2%) |
| Fully vaccinated (frequency) | 124 (54.9%) | 30 (49.2%) | 94 (57%) |
| Median interval between last dose and PET/CT in days (Q1–Q3) | 26 (14–51) | 15 (7–28) | 32 (18–60) |

Cases: patients with positive vaccine-related axillary or supraclavicular LNs. Controls: patients with no vaccine-related LNs.
of vaccine-related LNs in comparison with the other 3 vaccines (odds ratio, 1.64; \( P = 0.14; 95\% \) confidence interval, 0.83–3.24).

### Intensity, Number, Size, and Location of the Vaccine-Related LNs

Most of the LNs that we retained as vaccine-related LNs had an \( \text{SUV}_{\text{max}} \) that was greater than the mediastinum uptake, but the intensity uptake remained moderate and less intense than the liver level.

Patients presented between 1 and 12 positive LNs, with a median of 3 LNs. Positive LNs ranged from 4 mm to 15 mm on the small axis. Few patients (14/61) presented LNs of more than 10 mm on the small axis.

Most patients (43/61) presented positive LNs limited to axilla level 1 only. Fifteen of 61 patients (24.6\%) and 6/61 patients (9.8\%) nonetheless presented positive LNs located at axilla level 2 and axilla level 3, respectively.

In additional statistical analyses for exploratory purposes only, neither the number of positive LNs nor the size of the LNs were significantly associated with number of doses received, patient age, type of vaccine, or PSA level.

### DISCUSSION

In the context of the current pandemic and ongoing vaccination campaign, our study plays a part in emphasizing the influence of COVID-19 vaccines on PET/CT interpretation. To our knowledge,
this study is the largest cohort to include non-FDG PET/CT and showed several distinctive features. First, a notable highlight was finding that patients receiving 2 doses of vaccine presented vaccine-related LNs less frequently than patients receiving a single dose. This finding was unexpected because the clinical trials for vaccine authorizations had reported higher rates of local and systemic adverse effects after the second dose of the BNT162b2 mRNA (Pfizer-BioNTech) or mRNA-1273 (Moderna) vaccines, and contrasted with other articles in the literature related to COVID-19 vaccination and 18F-FDG PET/CT, where patients presented vaccine-related LNs more frequently after the second booster dose. One hypothesis could be the high age of the patients (median age, 71 years in our cohort due to the pathology, which affects the elderly, compared with 18F-FDG cohorts with a wider range of diseases with younger median ages). How can this be explained? This result could be consistent with the fact that elder

FIGURE 4. An 81-year-old man underwent an 18F-fluorocholine PET/CT for rising PSA after PCa radiotherapy. Multiple left axillary LNs (red circle) with higher uptakes than the mediastinum were observed. The man received the first and second doses of the BNT162b2 mRNA (Pfizer-BioNTech) vaccine, respectively, 24 and 3 days before undergoing this PET/CT.

FIGURE 5. A 74 year-old man underwent a 68Ga-PSMA-11 PET/CT for rising PSA after radical treatment. Two right axillary LNs (red arrows) with higher uptake than the mediastinum were detected. The man received the first and second doses of the ChAdOx1-S (AstraZeneca) vaccine, respectively, 80 and 19 days before undergoing this PET/CT.
patients present fewer immune responses after vaccine administration. Impaired antibody response and lesser efficacy after influenza vaccination has already been demonstrated in older adults,22 and this phenomenon can be called “immunosenescence.” It describes several hallmarks of immune aging, such as a decreased number of naive CD8+ T-lymphocytes.23 More recently, similar observations questioning a lesser immune response in older people with regard to COVID-19 vaccination have started to be reported.24,25 To corroborate this finding, collecting patients’ serological status and antibody titration after each dose of vaccine could be relevant in future studies.

Otherwise, observations in 18F-FCH PET/CT had similarities with those in 18F-FDG PET/CT, starting with comparable incidence (42.5%) of vaccine-related LNs. For example, we can cite 2 cohort studies that were conducted in Israel between December 2020 and February 2021, including almost a thousand of patients who had received at least 1 dose of a COVID-19 vaccine and who underwent 18F-FDG PET/CT,20,21 and in both studies, approximately 45% of the patients presented hypermetabolic lymphadenopathies that were associated with the vaccine. Such observations led to advise to check the vaccine injection site and dates of the doses before interpreting the examination but also to avoid the administration in a potential confounding site (eg, left deltoid muscle in case of an ipsilateral breast cancer).26 This is a reminder that 18F-FCH, such as 18F-FDG, is not specific for cancer cells. In fact, 18F-FCH is a marker of phospholipid biosynthesis for cell membrane renewal. Its uptake has already been described in both benign tumors and malignancies,26,29 as well as in inflammatory sites, which were by far the most frequent situations.30–32 This may be explained by an increased need for membrane synthesis in case of intense proliferation of immune cells, as generally observed in activated LNs,33,34 leading to an increased uptake of 18F-FCH.35,36

Our cohort managed to find some rare cases of vaccine-related LNs detected in 68Ga-PSMA-11 PET/CT. They were less expected due to the properties of 68Ga-PSMA-11, which has a transmembrane enzyme used for its high uptake in PCa, although there can be uptake in benign and malignant diseases, as well as in a context of inflammation.37 The detailed mechanisms concerning PSMA uptake have yet to be elucidated, but neovascularization seems to play a preponderant role.38 This leads us to think that in our cases the vaccination mimics a SARS-CoV-2 infection a minima and generates inflammation, which is fertile ground for neovascularization, thus explaining the uptake. This is further supported by some reported cases of lung injuries related to COVID-19 detected in 68Ga-PSMA-11 PET/CT39 and by the observation of increased plasma levels of vascular cell adhesion molecule and vascular endothelial growth factor on account of SARS-CoV-2 infection.40

Our study aimed to compare different COVID-19 vaccines. The incidence rate of vaccine-related LNs was higher but not statistically significant with the BNT162b2 mRNA (Pfizer-BioNTech) vaccine. This might be due to a lack of power in the test for showing a significant difference, due to a limited number of patients. It is now well described that the frequency and nature of adverse effects can vary depending on the type of vaccine,41 and one study showed a different frequency of vaccine-related LNs in 18F-FDG PET/CT after the mRNA-1273 (Moderna) vaccine compared with the BNT162b2 mRNA (Pfizer-BioNTech) vaccine.42

Our statistical analyses highlighted an association between LN positivity and a higher level of PSA in patients with recurrent PCa. We may then hypothesize that a higher level of PSA reflects
a more aggressive form of the disease, leading to more systemic inflammation and thus immunogenicity, explaining a higher propensity to react to vaccination, but the difference is quite slight, and these results need to be confirmed at a larger scale.

Furthermore, definitions of positive vaccine-related LNs are variable and arbitrarily chosen, thus limiting the comparability between the various publications. Some authors considered an LN as positive if the ratio between the SUVmax in the ipsilateral and contralateral reference sites was greater than or equal to 1.5, as described by Thomassen et al., whereas others classified LNs by uptake intensity. Our definition of positive vaccine-related LNs was a semiquantitative scale similar to the Deauville score as it was convenient for its high level of proof in hematological malignancies for example and for its good reproducibility, whereas quantitative SUVs can vary considerably depending on multiple parameters.

Although our study added some new information to our knowledge as far as the impact of COVID-19 vaccination is concerned, collecting more data concerning less studied populations would be welcome, as would a more precise description of the pathophysiologic mechanisms involved. This seems even more relevant given that the vaccination campaign is ongoing and will continue, with the recommendation for a third booster dose of the vaccine, freshly supported by the positive results for efficacy and tolerance in phase III trials.

Besides, we found no cases of vaccine-related LNs in 18F-FDOPA or 68Ga-DOTATOC PET/CT. First, the low number of patients for these 2 radiopharmaceuticals may explain the absence of vaccine-related nodes. We might also find an explanation through their respective targeting mechanisms. Imaging 18F-FDOPA uses the property of taking up amino acids, transforming them into biogenic amines by means of decarboxylation, and storing them in the vesicles of tumor cells. This targeting probably explains the absence of vaccine-related nodes. 68Ga-DOTATOC targets somatostatin receptors, which are overexpressed in activated macrophages and T-lymphocytes, and are used in inflammation-related diseases such as autoimmune mechanisms, but not in relation to infection of either viral or bacterial origin. It could be nonetheless noted that cases of vaccine-related axillary LNs were reported in the literature in 68Ga-DOTATATE PET/CT indicated for pulmonary and rectal neuroendocrine neoplasms.

Finally, our study has a number of limitations. It indeed a retrospective analysis, although our data were collected prospectively from consecutive patients. Definition of vaccine-related LNs as expressed in our methodology was based on clinical data, so identified LNs were not certain to be inflammatory due to the lack of pathologic examination, but were very likely to be. Cases of LNs suspicious for malignancy, for instance PCa with extended nodal involvement at diagnosis or PCa with nodal metastatic progression, were discussed for complementary examinations such as ultrasonography at 6 to 8 weeks or nodal biopsies and were not reported for our present study.

Most of the patients in our cohort were men of advanced age due to the pathology and could not reflect patients with other pathologies or younger in age. In addition, we had a small number of patients undergoing 18F-FDOPA and 68Ga-DOTATOC PET/CT, limiting our conclusions with regard to these patients. We also tried to compare 4 different vaccines, but in practice, few patients were vaccinated with the mRNA-1273 (Moderna) or Ad26.COV2.S (Janssen) vaccines, which also limits our conclusions.

CONCLUSIONS

Thanks to a cohort of more than 200 patients, including several radiopharmaceuticals and different types of vaccine, we show that detecting positive LNs after COVID-19 vaccination is not limited to 18F-FDG PET/CT, but is common in 18F-FCH PET/CT and is also possible in 68Ga-PSMA-11 PET/CT. The vaccine-related nodes were limited in size and intensity, and were often limited to axilla level 1 and were closely associated with the time between the dose of vaccine and the date of the PET/CT. Understanding these pitfalls, combined with particularities in vaccine data, such as vaccination date and vaccination side, seems essential regarding the current pandemic context and the recent vaccine recommendations in elderly patients, to avoid misinterpreting images and adopting incorrect patient therapeutic protocols.

ACKNOWLEDGMENTS

The authors would like to thank the patients in the study and the nuclear medicine technologists at the cancer center. We also thank the French National Agency for Research (Investissements d’Avenir), LabelxIRON and EquipexArronaxPlus for their moral support and assistance.

REFERENCES

1. Mathieu E, Ritchie H, Ortiz-Ospina E, et al. A global database of COVID-19 vaccinations. Nat Hum Behav. 2021;5:947–953.
2. Info coronavirus COVID-19 - Vaccins. Gouvernement.fr. Available at: https://www.gouvernement.fr/info-coronavirus/vaccins. Accessed August 20, 2021.
3. Coronavirus (COVID-19) Vaccinations—Statistics and Research. Our World in Data. Available at: https://ourworldindata.org/covid-vaccinations. Accessed October 10, 2021.
4. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med. 2020;383:2603–2615.
5. Reactions and Adverse Events of the Pfizer-BioNTech COVID-19 Vaccine | CDC. 2021. Available at: https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/reactogenicity.html. Accessed August 20, 2021.
6. Local Reactions, Systemic Reactions, Adverse Events, and Serious Adverse Events: Janssen COVID-19 Vaccine (J&J) | CDC. Available at: https://www.cdc.gov/vaccines/covid-19/info-by-product/janssen/reactogenicity.html. Accessed August 20, 2021.
7. Local Reactions, Systemic Reactions, Adverse Events and Serious Adverse Events: Moderna COVID-19 Vaccine | CDC. Available at: https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/reactogenicity.html. Accessed August 20, 2021.
8. Mehta N, Sales RM, Babagbemi K, et al. Unilateral axillary adenopathy in the setting of COVID-19 vaccine. Clin Imaging. 2021;75:12–15.
9. Edmonds CE, Zuckerman SP, Conant EF. Management of unilateral axillary lymphadenopathy detected by 18F-FDG PET/CT in a patient affected by melanoma. Eur J Nucl Med Mol Imaging. 2021;48:2657–2660.
10. McIntosh LJ, Bankier AA, Vijayaraghavan GR, et al. COVID-19 vaccination-related uptake on FDG PET/CT: an emerging dilemma and suggestions for management. AJR Am J Roentgenol. 2021;217:975–983.
11. Ahn RW, Mootz AR, Brewington CC, et al. Axillary lymphadenopathy after mRNA COVID-19 vaccination. Radiol Cardiothorac Imaging. 2021;3:e210008.
12. Özütemiz C, Krystosek LA, Church AL, et al. Lymphadenopathy associated with the administration of a COVID-19 mRNA vaccine. Clin Nucl Med. 2021;36:848–853.
13. Avner M, Orevi M, Caplan N, et al. COVID-19 vaccine as a cause for unilateral lymphadenopathy detected by 18F-FDG PET/CT in a patient affected by melanoma. Eur J Nucl Med Mol Imaging. 2021;48:2659–2660.
14. Auger AJ, Liang JK, Bankier AA, Vijayaraghavan GR, et al. COVID-19 vaccination-related uptake on FDG PET/CT: an emerging dilemma and suggestions for management. AJR Am J Roentgenol. 2021;217:975–983.
15. Coates EE, Costner PJ, Nason MC, et al. Lymph node activity after COVID-19 vaccination with licensed vaccines for human papillomaviruses. Clin Nucl Med. 2021;42:329–334.
16. Burger IA, Usman L, Hary TF, et al. Incidence and intensity of F-18 FDG uptake after vaccination with H1N1 vaccine. Clin Nucl Med. 2011;36:848–853.
17. Nawaw AA, Searle J, Singh R, et al. Oxford-AstraZeneca COVID-19 vaccination-induced lymphadenopathy in FDG PET/CT—not only an FDG finding. Eur J Nucl Med Mol Imaging. 2021;48:2657–2658.
18. Berg JW. The significance of axillary node levels in the study of breast carcinoma. Cancer. 1955;8:776–778.
19. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med. 2021;384:403–416.
20. Cohen D, Krauthammer SH, Wolf I, et al. Hypermetabolic lymphadenopathy following administration of BNT162b2 mRNA Covid-19 vaccine: incidence assessed by 18F-FDG PET/CT and relevance to study interpretation. *Eur J Nucl Med Mol Imaging*. 2021;48:1854–1863.

21. Eifèr M, Tau N, Alhoubani Y, et al. Covid-19 mRNA vaccination: age and immune status and its association with axillary lymph node PET/CT uptake. *J Nucl Med*. 2022;63:134–139.

22. Yao X, Hamilton RG, Weng N, et al. Frailty is associated with impairment of vaccine-induced antibody response and increase in post-vaccination influenza infection in community-dwelling older adults. *Vaccine*. 2021;29:5015–5021.

23. Pawelec G. Age and immunity: what is “immunosenescence”? *Exp Gerontol*. 2018;105:4–9.

24. Soiza RL, Scicluna C, Thomson EC. Efficacy and safety of COVID-19 vaccines in older people. *Age Ageing*. 2021;50:279–283.

25. Chen Y, Klein SL, Garibaldi BT, et al. Aging in COVID-19: vulnerability, immunity and intervention. *Ageing Res Rev*. 2021;65:101205.

26. Delgado Bolton RC, Calapaiqui Terán AK, Erba PA, et al. Medical imaging in times of pandemic: focus on the cornerstones of successful imaging. *Eur J Nucl Med Mol Imaging*. 2021;48:1724–1725.

27. Ahmad Saad FF, Zakaria MH, Appanna B. PET/CT analysis of 21 patients with breast cancer: physiological distribution of 18F-choline and diagnostic pitfalls. *J Int Med Res*. 2018;46:3138–3148.

28. Bebehsit M, Haroon A, Bomanji JB, et al. Fluorocholine PET/computed tomography uptake, benign findings, and pitfalls. *PET Clin*. 2014;9:299–306.

29. Goineau A, Colombié M, Garibaldi BT, et al. Aging in COVID-19: vulnerability, immunity and intervention. *Ageing Res Rev*. 2021;65:101205.

30. Schillaci O, Calabria F, Tavolozza M, et al. Fluorocholine PET/CT physiological distribution and pitfalls in image interpretation: experience in 80 patients with prostate cancer. *Nuc Med Commun*. 2010;31:39–45.

31. Calabria F, Chiaraavalloti A, Schillaci O. [18]F-choline PET/CT pitfalls in image interpretation: an update on 300 examined patients with prostate cancer. *Clin Nucl Med*. 2014;39:122–130.

32. Calabria F, Chiaraavalloti A, Ciccio C, et al. PET/CT with [18]F-choline: physiological whole bio-distribution in male and female subjects and diagnostic pitfalls on 1000 prostate cancer patients: [18]F-choline PET/CT bio-distribution and pitfalls. A southern Italian experience. *Nuc Med Biol*. 2017;51:40–54.

33. Shukla GS, Olson WC, Perez SC, et al. Vaccine-draining lymph nodes of cancer patients for generating anti-cancer antibodies. *J Transl Med*. 2017;15:180.

34. Shah S, Wagner T, Nathan M, et al. COVID-19 vaccine-related lymph node activation—patterns of uptake on PET/CT. *BJR Case Rep*. 2021;7:20210040.

35. Wyss MT, Weber B, Honer M, et al. [18]F-choline in experimental soft tissue infection assessed with autoradiography and high-resolution PET. *Eur J Nucl Med Mol Imaging*. 2004;31:312–316.

36. Snider SA, Margison KD, Ghorbani P, et al. Choline transport links macrophage phospholipid metabolism and inflammation. *J Biol Chem*. 2018;293:11606–11611.

37. de Galizza Barbosa F, Queiroz MA, Nunes RF, et al. Nonprostatic diseases on PSMA PET imaging: a spectrum of benign and malignant findings. *Cancer Imaging*. 2020;20:23.

38. Salas Fragomeni RA, Amir T, Sheikhhabaei S, et al. Imaging of nonprostate cancers using PSMA-targeted radiotracers: rationale, current state of the field, and a call to arms. *J Nucl Med*. 2018;59:871–877.

39. Karasah Erkek B, Ömür Ö, Özkök S, et al. COVID-19 lung findings detected by [68]Ga-PSMA PET/CT for staging purposes in patients with prostate cancer. *Clin Nucl Med*. 2022;47:e17–e19.

40. Kristensen MK, Ploving RR, Berg RM, et al. Cell adhesion molecules and vascular endothelial growth factor at the systemic and alveolar level in coronavirus disease 2019 acute respiratory distress syndrome. *J Infect Dis*. 2021;224:1101–1103.

41. Meo SA, Bukhari IA, Akram J, et al. COVID-19 vaccines: comparison of biological, pharmacological characteristics and adverse effects of Pfizer/BioNTech and Moderna vaccines. *Eur Rev Med Pharmacol Sci*. 2021;25:1663–1669.

42. Skowran S, Gennari AG, Dittli M, et al. [18]F-FDG uptake of axillary lymph nodes after COVID-19 vaccination in oncological PET/CT: frequency, intensity, and potential clinical impact. *Eur Radiol*. 2022;32:508–516.

43. Thomassen A, Berber Nielsen A, Gerke O, et al. Duration of [18]F-FDG avidity in lymph nodes after pandemic H1N1v and seasonal influenza vaccinations. *Eur J Nucl Med Mol Imaging*. 2011;38:894–898.

44. Barrington SF, Qian W, Somer EJ, et al. Concordance between four European centres of PET reporting criteria designed for use in multicentre trials in Hodgkin lymphoma. *Eur J Nucl Med Mol Imaging*. 2010;37:1824–1833.

45. Lim J, Broughan J, Crowley D, et al. COVID-19’s impact on primary care and related mitigation strategies: a scoping review. *Eur J Gen Pract*. 2021;27:166–175.

46. Alshammari AF, Al-Sulaiman AM. The journey of SARS-CoV-2 in human hosts: a review of immune responses, immunosuppression, and their consequences. *Vaccines*. 2021;12:1771–1794.

47. Bar-On YM, Goldberg Y, Mandel M, et al. Protection of BNT162b2 vaccine booster against Covid-19 in Israel. *N Engl J Med*. 2021;385:1393–1400.

48. Hoegerle S, Altehoefer C, Ghanem N, et al. Whole-body [18]F Dopa PET for detection of gastrointestinal carcinoid tumors. *Radiology*. 2001;220:374–380.

49. Velikan F. Prospective of [68]Ga radionuclide contribution to the development of imaging agents for infection and inflammation. *Contrast Med Mol Imaging*. 2018;2018:9713691.

50. Brophy J, Henkle G, Rohren EM. DOTATATE uptake in an axillary lymph node after COVID-19 vaccination. *Clin Nucl Med*. 2021;47:174–175.

51. Shah HJ, Halperten JI, Watane GV, et al. COVID lessons continue: postvaccination somatostatin receptor-positive axillary nodes on DOTATATE imaging. *Clin Nucl Med*. 2022;47:e56–e58.