



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Journal of Radiology Nursing

journal homepage: www.sciencedirect.com/journal/journal-of-radiology-nursing

Axillary Lymphadenopathy Associated With COVID-19 Vaccination: Updates and Recommendations

Sandra L. Schwaner, MSN, RN, ACNP-BC *

Retired from University of Virginia Health System, Charlottesville, Virginia

A B S T R A C T

Keywords:

COVID-19 vaccination
 Coronavirus
 Breast cancer
 Lymphadenopathy
 Reactive lymphadenopathy
 Biopsy
 Recommendations
 Nursing care
 Patient education
 Screening mammogram

Lymphadenopathy (LAD) associated with vaccination has been documented as complicating the evaluation of metastatic malignancy. In the past this was a limited finding, primarily documented in association with smallpox and H1N1 vaccination. The advent of the novel mRNA vaccine for COVID-19 in December of 2021, and subsequent large scale vaccination effort, has resulted in a marked increase in the identification of LAD associated with vaccination. Because axillary LAD is a concerning sign of metastatic disease in breast cancer, identifying the difference between benign inflammatory reaction and concerning LAD and avoiding unnecessary additional imaging and biopsy is an essential skill. This article describes the current literature, recommendations for follow-up, and interventions to improve diagnostics.

© 2022 Association for Radiologic & Imaging Nursing. Published by Elsevier Inc. All rights reserved.

Background

Breast cancer will affect 1 in 8 women and 1 in 833 men in their lifetime ([Breast Cancer Statistics](https://www.breastcancer.org/symptoms/understand_bc/statistics),) https://www.breastcancer.org/symptoms/understand_bc/statistics. Mortality can be reduced 13% to 15% when mammography is used for early detection ([Løberg, 2015](#)). The Centers for Disease Control, (CDC) recommends that women aged between 50 and 75 years undergo routine mammogram every 1 to 2 years (CDC) <https://www.cdc.gov/cancer/breast/pdf/breast-cancer-screening-guidelines>. The Society for Breast Imaging and the American College of Radiology issued updated guidelines in 2021 ([Monticciolo et al., 2021](#)) that recommend a risk assessment by the age of 30 years, and annual mammograms beginning at the age of 40 years, especially if there is a strong family history of malignancy. They also recommend continuing mammograms for life, even after the age of 75 years. If breast cancer is diagnosed, follow-up imaging recommendations are based on the type of cancer and treatment ([Bychokovsky and Lin, 2017](#)). Annual mammogram is recommended of both affected and contralateral breast in cases where lumpectomy has been performed, contralateral breast only in setting of mastectomy

([Bychokovsky and Lin, 2017](#), [Løberg, 2015](#), [Lisler, Chaput, Sussman, and Ozekwelu, 2016](#)).

In patients being evaluated for or followed after a diagnosis of breast cancer, presence of axillary lymphadenopathy (LAD) is a strong prognostic indicator ([Jatoi, Hilsenbeck, Clark, and Osborne, 1999](#), [Mohseni, et al., 2014](#)). Morphologic characteristics of lymph nodes associated with metastasis include cortical thickness > 3 mm, loss of fatty hilum, and lobulation or asymmetry within the node ([Choi, Ko, Han, J, and Kang S, 2009](#), [Nguyen, et al., 2021](#)). Lymphadenopathy (LAD) associated with vaccination has been documented as complicating the evaluation of metastatic malignancy ([Bychokovsky & Lin, 2017](#); [Choi et al., 2009](#); [Mohseni et al., 2014](#)). In the past this was a limited finding, primarily documented in association with smallpox and H1N1 vaccination ([Fry et al., 2021](#); [Mingos et al., 2016](#); [Panagoitidis et al., 2010](#)).

Patients who exhibit unilateral LAD either undergo biopsy of lymph tissue immediately or return within 4 weeks for re-evaluation, if there is a thought that LAD may be reactive in nature. Imaging is not necessarily performed if there is no history of malignancy, no other symptoms, and the morphologic composition of the lymph node is consistent with reactive LAD. Biopsy is performed in the setting of persistent LAD, known malignancy, and/or concerning morphologic findings on ultrasound. Follow-up imaging is generally with ultrasound; computed tomography (CT) and magnetic resonance imaging are not recommended for specific evaluation of axillary LAD ([Bychokovsky and Lin, 2017](#), [CDC, Choi, Ko, Han, J, and Kang S, 2009](#), [Lisler, Chaput, Sussman, and Ozekwelu, 2016](#)).

Conflicts of Interest: The author(s) have no relevant disclosures. There was no grant funding or financial support for this manuscript.

* Corresponding author: Sandra L. Schwaner, MSN, RN, ACNP-BC, Retired from University of Virginia Health System, Charlottesville, Virginia 22901.

E-mail address: sandyschwaner@gmail.com.

<https://doi.org/10.1016/j.jradnu.2022.08.006>

1546-0843/\$36.00/© 2022 Association for Radiologic & Imaging Nursing. Published by Elsevier Inc. All rights reserved.

Current issues

As per information compiled by the CDC (Anonymous, 2022A), the Moderna vaccine developed for COVID-19 was associated with an 11.6% incidence of axillary swelling and/or tenderness after the first dose, increasing to 16% after the second dose. However, only 0.3% of cases presented with swelling equal to or more than 100 mm (10 cm). LAD was reported within 3–4 days of vaccination and lasted 1–2 days, per reports. The information compiled on the Pfizer-BioNTech vaccine, a similar M-RNA vaccine developed concurrently, did not include axillary swelling or LAD (Anonymous, 2022B).

Both vaccines received emergency approval for distribution in December 2021 and large-scale vaccination was undertaken. Shortly thereafter, radiologists began to note a dramatic increase in the amount of LAD observed on imaging that was being conducted to follow or screen for malignancy (Faermann, et al., 2021, Lam & Flanagan, 2022). As many journals were publishing online and making their articles freely accessible under emergency guidelines, the cases were rapidly identified (Tu, Gierada, & Joe, 2021, Kesharvarz, Yazdanpanah, Rafiee, & Mizandari, 2021). Kesharvarz et al., in a published review of these cases in April 2021, identified LAD as developing between 5 and 12 days after vaccination and lasting for 4–6 weeks in most circumstances, although some patients continued with LAD up to 12 weeks following vaccination. Most of these cases demonstrated radiologic findings of cortical thickening and preserved hilar fat, both of which are consistent with reactive LAD.

The Radiologic Society of North America, European Society of Breast Imaging, Society of Breast Imaging, and the American College of Radiology all released guidelines regarding imaging of axillary LAD in the setting of COVID-19 vaccination during the spring and summer of 2021 (Becker, et al., 2021, Schiaffino, et al., 2021, Lehman, et al., 2021). General recommendations included reporting the date, site, and laterality of vaccine to the radiology team (Society of Breast Imaging, 2021); obtaining imaging prior to vaccination if possible (Becker, et al., 2021); and requesting that the vaccine be administered on the contralateral side to any area of known concern if possible (Becker, et al., 2021). Imaging should of course be accompanied by clinical evaluation and vaccine-associated LAD moved from very low on the differential list to near the top. Opinion was varied on whether there should be a 4-week or 6-week interval before re-evaluation or biopsy. In patients with no history or symptoms, following clinical signs was most often recommended; in patients with symptoms or a positive history, biopsy or repeat imaging was recommended (Becker, et al., 2021, Schiaffino, et al., 2021, Society of Breast Imaging, 2021). In almost all cases, the maximum recommended interval before reassessment was 6 weeks.

Garreffa et al. published a literature review in November 2021, evaluating 15 full-text articles covering 2,057 patients, 737 of whom had LAD, primarily identified on Positron Emission Tomography-Computed Tomography which was being conducted for staging or follow-up of previously identified malignancy (Garreffa,

et al., 2021). In December, the American Journal of Radiology released an online article by Nugyen, et. al. (Nguyen, et al., 2021) which reviewed the cases of 94 women who had imaging findings of LAD evaluated with axillary ultrasound. Of the 94 women, 32 underwent biopsy.

The 94 patients in this retrospective study were re-evaluated between 12 and 15 weeks after their second dose of vaccine. Specific criteria for recommending biopsy were not addressed but generally are performed in cases of persistent LAD on follow-up. Nguyen found that women who received a biopsy recommendation were evaluated at a shorter interval (12.9 weeks) than those who did not receive a recommendation to biopsy (15.9 weeks). However, evaluation of those who did undergo biopsy indicated a 50/50 split between those evaluated less than 13 weeks after vaccine and those evaluated more than 13 weeks after their second dose of vaccine. Of those who were biopsied, 3 patients were diagnosed with malignant axillary adenopathy. All 3 fell into the group of those evaluated more than 13 weeks after vaccine. Their lymph nodes all shared characteristics of cortical thickness of 5 mm or more, loss of the fatty hilum, and focal cortical lobulation.

As of the writing of this article, the guidelines of the major organizations remain unchanged. However, increased attention to vaccine status, morphology of unilateral LAD, and careful history and physical exam has become even more important in the evaluation of potential metastasis.

Impact on radiology nursing

Experts agree that more data are warranted (Rochman, personal communication, 1/14/2022). However, all agree that follow-up imaging for patients with breast cancer should remain on schedule. Persons with concerns or symptoms should not hesitate to seek evaluation. It is recommended that, if possible, imaging occur prior to vaccination or booster dose. Waiting for 4 to 6 weeks after vaccine to image is acceptable (Becker, et al., 2021, Schiaffino, et al., 2021). However, symptomatic patients should not delay imaging on the basis of vaccination status (Becker, et al., 2021, Schiaffino, et al., 2021) (See Tables 1 and 2)

Radiologists need to include clinical findings and morphologic characteristics of LAD, including whether adenopathy is unilateral or bilateral, ipsilateral or contralateral to vaccine site, presence of cortical thickening > 3 mm, presence or absence of hilar fatty tissue, and whether the cortex is uniform or presents with a focal bulge or extracapsular extension (Becker, et al., 2021, Choi, Ko, Han, J, and Kang S, 2009, Faermann, et al., 2021, Lehman, et al., 2021, Özütemiz, et al., 2021). All sources emphasize that decision-making should be based on clinical evaluation, and one should not hesitate to proceed with tissue sampling if there is adequate concern. However, reactive LAD rises to the top of the differential list.

Radiology nurses and technologists need to consistently ask patients whether they have had a recent COVID vaccine or booster, and if so, record both the date and the arm in which the vaccine was administered. Communicate the information from nurse to

Table 1

Key points to consider

Key points

An increase in both symptomatic and asymptomatic axillary lymphadenopathy has been noted on imaging since the initiation of COVID-19 vaccination.

This can complicate the diagnostic process for diagnosing and following up on breast cancer cases.

Multiple organizations have developed guidelines for follow-up in this setting.

The nurse can alleviate anxiety by informing patients of this inflammatory reaction and assuring them of its probable resolution.

Patients who have a family or personal history of breast cancer or who remain symptomatic with LAD should be reimaged and undergo tissue sampling (biopsy) if concerning LAD persists.

The timing of this follow-up is currently 6 weeks, and may be extended, as data are showing that inflammatory LAD is persisting as long as 12 to 15 weeks after vaccine.

Table 2
Nursing interventions

Nursing interventions:
Document:
<ul style="list-style-type: none"> • Date of vaccination and any boosters. • Arm in which vaccine was administered. • Any symptoms (swelling, tenderness, and redness) experienced. • Family or patient history of breast cancer.
Communicate:
<ul style="list-style-type: none"> • Vaccine information to radiology team. • Likelihood of LAD being observed to patients having imaging > 6 weeks after vaccination (this may occur on mammogram, ultrasound, nuclear medicine imaging, Positron Emission Tomography-Computed Tomography, or magnetic resonance imaging).
Staff Education:
<ul style="list-style-type: none"> • Other nurses and care providers need to know about updated imaging guidelines in the setting of pandemic vaccination.
Patient Education
<ul style="list-style-type: none"> • Obtain needed imaging prior to vaccination if possible, or four to 6 weeks after vaccination, if not. • Request vaccine to be administered to the contralateral arm of a side of concern. This is true for breast patients and those with lung or other solid tumors. • Encourage patients to seek medical guidance for symptomatic lymphadenopathy regardless of vaccination status so that they can be followed clinically. • Assure patients that lymphadenopathy related to vaccination is not unusual and will resolve with time.

technologist, to reading radiologist, so the information can be used in evaluating the images. Ask about symptomatology, including duration and severity of any swelling or tenderness.

Patients who call questioning if they should follow through with a screening mammogram should be encouraged to do so (Anonymous, 2022C). It is recommended to wait 4 to 6 weeks after second vaccine or booster if they are otherwise asymptomatic and not at high risk or obtain imaging prior to vaccination, if possible. Do not delay vaccination. Both vaccination and imaging are important to maintaining health (Anonymous, 2022C).

Recommend to breast cancer patients that they have both vaccines and booster on the arm contralateral to the breast of concern. Do not delay follow-up examinations or scheduled biopsies, but make care providers aware of time and location of last vaccine. This recommendation also applies to people with other solid tumors, such as lung cancer, lymphoma, or melanoma tumors, where LAD is a diagnostic indicator being evaluated (González-Gómez & Lizarazo, 2021, Tu, Gierada, & Joe, 2021). Questions regarding whether someone should receive the vaccine while undergoing chemotherapy should be directed to the oncologist in charge of their care.

With regards to follow-up of identified LAD on imaging, there continues to be debate about the length of time before follow-up ultrasound and/or biopsy. Garreffa et al. (Garreffa, et al., 2021) evaluated 15 different studies of patients with LAD after COVID-19 vaccination. They found an incidence ranging from 14.5% to as high as 53%, much more than that in the CDC report. The University of Virginia is re-evaluating patients with LAD in 3 months (12 weeks) with ultrasound, proceeding with biopsy if LAD persists (Rochman, personal communication 1/14/22). Other organizations are following a similar protocol (Nicholson, personal communication 2/7/22), encouraging a return to routine screening, and evaluating positive cases of LAD 3 to 4 months later for resolution. While there has been an uptick in negative biopsies, there continue to be positive findings at this time period, making the decision to delay evaluation further a difficult one.

An interesting area for future research will be the immune response triggered by the COVID vaccine, identifying characteristics of patients who respond strongly. This may help predict reactive LAD, simplifying this issue in the future.

Nurses are often the initial contact of patients, both in the radiology setting and in the community. We can provide clear explanations and assure people that the radiologic community is closely evaluating the situation and making changes as indicated. As we all long for the end to the pandemic, we will continue providing the best care possible to all patients, using evidence-based practice.

Acknowledgments

Many thanks to Carrie Rochman, MD, Associate Professor of Radiology at the University of Virginia and Brandi Nicholson, MD, Fellow of the Society for Breast Imaging, and Radiologist with Augusta Health Radiology for their time and expertise on this topic.

References

- Becker, A., Perez-Johnston, r., Chikarmane, S., Chen, M., Homs, M., ... Vargas, A. (2021). Multidisciplinary Recommendations regarding post-vaccine adenopathy and radiologic imaging: Radiology scientific expert panel. *Radiology*, 300(2), E323-E327.
- Breast Cancer Statistics. Retrieved from: https://www.breastcancer.org/symptoms/understand_bc/statistics. Accessed February 22, 2022
- Bychokovsky, B., & Lin, N. (2017). Imaging in the evaluation and follow-up of early and advanced breast cancer: When, why, and how often? *The Breast*, 31, 318-324.
- CDC Breast Cancer Screening Guidelines. Retrieved from: <https://www.cdc.gov/cancer/breast/pdf/breast-cancer-screening-guidelines>.
- Choi, Y., Ko, E., Han, B., J, S., & Kang S, H.S. (2009). High-resolution ultrasonographic features of axillary lymph node metastasis in patients with breast cancer. *The Breast*, 18, 119-122.
- Faermann, R., Nissan, N., Halshtok-Neiman, O., Shalmon, A., Gotlieb, M., Yagil, Y., ... Sklair-Levy, M. (2021). COVID-19 Vaccination induced lymphadenopathy in a specialized breast imaging clinic in Israel: analysis of 163 cases. *Academic Radiology*, 28(9), 1191-1197.
- Fry, S., Couch, R., Tacket, C., Chickarmane, S., Chen, M., Homs, M., ... Vargas, H. (2021). Multidisciplinary Recommendations Regarding Post-Vaccine Adenopathy and Radiologic Imaging: Radiology Scientific Expert Panel. *Radiology*, 300(2), 323-327.
- Garreffa, E., Hamad, A., O'Sullivan, C., Hazim, A., York, J., Puri, S., ... Goetz, M. (2021). Regional lymphadenopathy following COVID-19 vaccination: Literature review and considerations for patient management in breast cancer care. *European Journal of Cancer*, 159, 38-51.
- González-Gómez, S., & Lizarazo, D. (2021). FDG PET/CT scan after vaccination in times of pandemic. *Radiology*, 299, E286.
- Retrieved from: <https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/reactogenicity.html>. Accessed February 3, 2022.
- Retrieved from: <https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/reactogenicity.html>. Accessed February 3, 2022.
- Retrieved from: <https://www.sbi-online.org/Portals/1/End-the-Confusion-Materials/recommendations-for-women-taking-covid-vaccine.pdf>. Accessed January 24, 2022.
- Jatoi, I., Hilsenbeck, S., Clark, G., & Osborne, C. (1999). Significance of axillary lymph node metastasis in primary breast cancer. *Journal of Clinical Oncology*, 17(8), 2334-2340.
- Kesharvarz, P., Yazdanpanah, F., Rafiee, F., & Mizandari, M. (2021). Lymphadenopathy following COVID-19 vaccination: Imaging findings review. *Academic Radiology*, 28(8), 1058-1071.
- Lam, D., & Flanagan, M. (2022). Axillary Lymphadenopathy After COVID-19 Vaccination in a Woman With Breast Cancer. *JAMA*, 327(2), 175-176.
- Lehman, C., D'Alessandro, H., Mendoza, D., Succi, M., Kambadakone, A., & Lamb, L. (2021). Unilateral lymphadenopathy after COVID-19 vaccination: a practical management plan for radiologists across specialties. *Journal of the American College of Radiology*, 18(6), 843-852.

- Lisler, J., Chaput, G., Sussman, J., & Ozekwelu, E. (2016). Follow-up after treatment for breast cancer: Practical guide to survivorship care for family physicians. *Canadian Family Physician*, 62, 805-811.
- Løberg, M., Lousdal, M.L., Bretthauer, M., & Kalager, M. (2015). Benefits and harms of mammography screening. *Breast cancer research*, 16(1). <https://doi.org/10.1186/s13058-015-0525-z>.
- Mingos, M., Howard, S., Giacalone, N., Kozone, D., & Jacene, H. (2016). Systemic Immune Response to Vaccination on FDG-PET/CT. *Nucl Med Mol Imaging*, 50, 358-361.
- Mohseni, S., Shojaiefard, A., Khorgami, Z., Alinejad, S., Ghorbani, A., & Ghafouri, A. (2014). Peripheral lymphadenopathy: approach and diagnostic tools. *Iranian Journal of Medical Sciences*, 39(2S), 158-170.
- Monticciolo, D., MD, Malak, S., MD, MPH, Friedewald, S., MD, Eby, P., MD, Newell, M.E., MD, Moy, L., MD, & Smetherman, D., MD (2021). Breast cancer screening recommendations inclusive of all woman at average risk: update from the ACR and Society of Breast Imaging. *Journal of the American College of Radiology*, 18, 1280-1288. <https://doi.org/10.1016/j.jacr.2021.04.21>.
- Nguyen, D., Ambinder, E., Myere, K., Mullen, L., Panigrahi, B., & Oluyemi, E. (2021). Covid-19 vaccine-related axillary adenopathy on breast imaging: Follow-up recommendations and histopathologic findings. *American Journal of Roentology*, 218, 997-998.
- Özütemiz, C., Krystosek, L., Church, A., Chauhan, A., Ellermann, J., Domingo-Musibay, E., & Steinberger, D. (2021). Lymphadenopathy in COVID-19 vaccine recipients: diagnostic dilemma in oncologic patients. *Radiology*, 300(1), E290-E294.
- Panagiotidis, E., Exarhos, D., Housianakou, I., Bournazos, A., & Datsiris, I. (2010). FDG uptake in axillary lymph nodes after vaccination against pandemic (H1N1). *Eur Radiol*, 20, 1251-1253.
- Schiaffino, S., Pinker, K., Magni, V., Cozzi, A., Athanasiou, A., Baltzer, P., ... Sardanelli, F. (2021). Axillary lymphadenopathy at the thime of COVID-19 vaccination: ten recommendations from the European Society of Breast Imaging (EUSOBI). *Insights Imaging*, 12, 119.
- Society of Breast Imaging. (2021). *SBI Recommendations for the management of axillary adenopathy in patients with recent COVID-19 vaccination*. (S. o. Imaging, Ed.).
- Tu, W., Gierada, D., & Joe, B. (2021). COVID-19 vaccination-related lymphadenopathy: What to be aware of. *Radiology: Imaging Cancer*, 3, e210038.