# Letter to the Editor

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# The Optimal Timing of Imaging Examinations in Patients With Newly Diagnosed Breast Cancer in the COVID-19 Pandemic Era

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#### **Conflict of Interest**

The authors declare that they have no competing interests.

#### **Author Contributions**

Conceptualization: Chang JM; Supervision: Chang JM; Writing - original draft: Chang JM; Writing - review & editing: Chang JM, Ha SM.  See the letter "Ipsilateral Lymphadenopathy, COVID-19 Vaccination and Breast Cancer" in volume 25 on page 259.

We would like to thank Dr. Pathum Sookaromdee and colleague for their interest in our work [1]. We read their remarks with interest, and would like to provide a response to some points that Dr. Pathum Sookaromdee mentioned [2].

Our study was a retrospective study of patients with newly diagnosed breast cancer, who received concurrent coronavirus disease 2019 (COVID-19) vaccination in the ipsilateral arm, and underwent biopsy or surgery for axillary lymph nodes between April 2021 and September 2021. In our study population, the median interval between the most recent vaccination and imaging assessment was 26 days (range, 4–49 days) [1]. Previous reports have indicated that lymphadenopathy can develop as early as one day after the first dose, and is most likely to be seen within 14 days. However, the time to resolution of COVID-19 vaccine-associated lymphadenopathy varies, with persistent axillary lymphadenopathy observed up to 43 weeks post-vaccination [3]. In addition, patient and vaccine factors such as younger age, first dose, and mRNA vaccine type induce a higher incidence of axillary lymphadenopathy [4].

As Dr. Pathum Sookaromdee and colleague mentioned [2], the recommendation of avoiding imaging for the first 10 weeks after COVID-19 vaccination can be applied for healthy individuals without a high risk of metastatic lymphadenopathy since COVID-19 vaccine-associated lymphadenopathy spontaneously resolves with time, contrary to metastatic lymphadenopathy. The National Comprehensive Cancer Network recommends scheduling screening examinations before the first or 4–6 weeks after the second dose of the COVID-19 vaccine [5], and the European Society of Breast Imaging recommends imaging in cases of axillary lymphadenopathy at least 12 weeks from the second vaccine dose in patients without a history of breast cancer [6]. In the recent prospective investigation which evaluated temporal changes in COVID-19 vaccine-associated lymphadenopathy in healthy volunteers, persistent lymphadenopathy even after 12 weeks was observed in a significant number of women [7].

Since preoperative imaging examinations were not delayed after COVID-19 vaccination at our institution, the longest time interval between vaccination and imaging in our study was 49 days. This short time interval cannot provide conclusive differential points for lymphadenopathy, and additional analyses of the association between the characteristics of lymphadenopathy and the interval between vaccine doses in our study would not provide critical information for the differential diagnosis.

Delay in imaging examinations due to COVID-19 vaccination is not recommended for patients with newly diagnosed or suspected breast cancer [8]. If we delay imaging examinations for at least 12 weeks after the final vaccine dose, this stipulated time interval could provide some useful information for the differential diagnosis. However, delay in appropriate imaging examinations might lead to delayed axillary nodal staging and management, thereby resulting in an increased number of patients with advanced breast cancer after the COVID-19 pandemic [8].

In conclusion, our study did not satisfactorily present clinical or imaging variables for the diagnosis of COVID-19 vaccine-associated reactive lymphadenopathy to be distinguished from malignant lymphadenopathy. We believe that necessary imaging examinations at breast clinics should be performed without delay owing to vaccination, and to avoid this diagnostic dilemma, patients with newly diagnosed breast cancer should be educated and encouraged to receive vaccination in the contralateral arm or thigh, according to the recent guidelines [5,6]. Clinicians should be aware of the overlapping image features of reactive and malignant lymphadenopathy. Hence, they should interpret lymphadenopathy cautiously with due consideration to information related to COVID-19 vaccination and the overall nodal metastatic risk of individual patients.

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