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Commentary

Deep decision support for lymph node metastatic risk evaluation

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Due to the post-operative complications of axillary lymph node dissection (ALND), it is often reserved for breast cancer patients with sentinel lymph node (SLN) metastases [1]. Even with this conservative approach, 60–73% of patients undergoing ALND do not have lymph node metastases beyond the SLNs, raising substantial concerns of overtreatment [2]. To avoid unnecessary treatments with no clear survival benefit, various prediction models have been proposed to characterize individual patients' risks of non-sentinel lymph node (NLSN) metastasis [3]. However, reliable methods for identifying SLN positive patients with low risk of NSLN metastasis have remained elusive. Given the recent progress of deep learning in a wide range of diagnostic tasks and the availability of electronic health records (EHRs) [4–6], deep artificial neural networks may be well-suited for detecting lymph node metastases in breast cancer patients [7].

In this issue of EBioMedicine, Guo et al. designed deep learning models based on the DenseNet architecture to determine patients' SLN and NSLN metastasis status using axillary ultrasonography (AUS) images [7]. Prediction of SLN metastasis using a combined deep learning model and AUS report achieved an area under the receiver operating characteristic curve (AUC) of 0.848 (95% CI: 0.811–0.886) with a sensitivity of 0.984 (95% CI: 0.966–1) in the test set. This performance exceeded that of the deep learning model alone, the AUS report alone, clinical features, and a combined deep learning model incorporating clinical features. The model for NSLN metastasis prediction also achieved decent performance in the test set, with an AUC of 0.812 (95% CI: 0.740–0.884), a sensitivity of 0.984 (95% CI: 0.956–0.999), and a specificity of 0.393 (95% CI: 0.325–0.464). Taken together, Guo et al. demonstrated an increased ability to identify patients with low NSLN metastatic risk while minimizing the false-negative rate of NSLN evaluation.

This retrospective study effectively leverages the real-world data collected at two hospitals to develop machine learning-based diagnostic models. The authors of the study trained their models using the AUS and EHR data from one hospital and successfully validated the models in another, which demonstrated the robustness of their approaches. The observation that combining AUS images with reports has better performance in identifying SLN status than images alone or reports alone suggested the synergy between the data-driven models and experts' annotations. Although the specificity of the NSLN metastasis detection model has ample room for improvement, they showed the potential of deep learning radiomics for providing decision support to clinicians facing challenging diagnostic tasks.

To maximize the impact of the reported works, future studies can address a few issues that currently limit the clinical utility of the developed models. For example, study participants whose SLND shows no SLN metastases may not receive ALND, in accordance with the clinical guideline. Nonetheless, a seminal randomized controlled trial showed that the false-negative rate of SLN diagnoses based on SLND is close to 10% [8], making it difficult to ascertain the true performance of the reported models. In addition, missing data is a common issue in real-world data analyses. Like many other studies, the authors excluded patients with incomplete clinical, pathology, or ultrasonography data of axillary lymph nodes from their study cohorts before building machine learning models. This approach simplifies the model training process since their deep neural networks will not encounter any instances with missing information. However, this approach also assumes that all missing data are missing completely at random (MCAR) and can be safely omitted without adjustment. Due to the fact that the unavailability of clinical, pathology, and radiology data often results from the lack of clinical indications for the examinations, issues in adherence, or referral of patients due to medical or personal reasons, the MCAR assumption rarely holds. Furthermore, the data acquisition and model training protocols described in this study precluded ultrasonography images with breast tumors invisible to the human eyes or large tumors. It is uncertain how deep learning models would behave when encountering these exceptions without human assistance [9]. Lastly, the two hospitals participating in this study are affiliated with the same institute and reside in the same city. As such, the study population is relatively homogeneous, and the generalizability of the reported models to other populations and clinical settings is currently unknown [10].

In summary, the reported deep learning-based approaches have the potential for enhancing ultrasonography diagnoses of SLN and NSLN metastases in breast cancer patients. Future prospective studies

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are needed to validate the real-world performance of the developed models and assess their clinical utility in diverse populations.

Authorship Contribution Statement

E. M.: Literature search, Writing - original draft, Writing - review & editing. K.-H. Y.: Literature search, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

E. M. has no conflicts of interest to declare. K.-H. Y. is an inventor of a quantitative pathology analytical system (U.S. Patent 16/179,101, assigned to President and Fellows of Harvard College).

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