Automated deep learning framework: providing decision-making information for breast cancer management

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Breast cancer is the most common cancer among women worldwide,[1] and neoadjuvant chemotherapy (NAC) is considered the standard treatment for downstaging in most breast cancer patients.[2,3] However, the response rate to NAC varies among patients, and not all benefit from it.[4] This exposes patients who are not suitable for NAC to unnecessary drug side effects, affects prognosis and delays optimal timing for alternative treatments.

Axillary treatment has evolved from routine completion of axillary lymph node dissection (ALND) to sentinel lymph node biopsy (SLNB) for most breast cancer patients.[5] However, SLNB has a high false-negative rate, especially when fewer than three sentinel lymph nodes (SLNs) are removed. Invasive techniques such as dual tracing agents, removal of three or more SLNs, and the use of localization needles can improve the accuracy of SLNB, but these techniques may not be suitable for all patients. When all resected SLNs are negative, determining the optimal surgical strategy becomes challenging for surgeons. Therefore, predicting the efficacy of NAC and assessing axillary lymph node (ALN) status are two crucial aspects in the management of breast cancer patients.

Currently, traditional methods of analyzing medical imaging can provide information about tumor size and extent. However, the Response Evaluation Criteria in Solid Tumors (RECIST), based on tumor size and extent changes, are still insufficient in clinical practice to accurately predict NAC response.[6–8] Additionally, traditional methods such as biopsy, biomarkers, or medical imaging features cannot accurately assess ALN status. As recently reported in *eClinicalMedicine*, researchers have developed a fully automated and reusable deep learning (AutoRDL) framework based on pre-treatment ultrasound images to simultaneously predict both of these issues.[9] This study, including 2556 breast cancer patients from three hospitals, overcomes the barrier of traditional manual segmentation by establishing a tumor auto-detection segmentation model and extracting deep learning features to predict the pathological complete response (PCR) and axillary lymph node metastasis (ALNM). Furthermore, combining the image model with a clinical model further improves model performance. The performance of the model is further validated in two external validation sets. The deep learning framework holds promise in providing additional decision-making information for physicians managing breast cancer patients.

The integration of multiple tasks such as image super-resolution, tumor detection, ALNM status assessment, and NAC efficacy prediction into a single framework using artificial intelligence (AI) techniques such as deep learning represents the current trend in the application of AI in medical imaging research. The proposed AutoRDL framework in the article achieves outstanding performance across various tasks, providing a feasible, novel and valuable solution to address clinical problems. As scientific questions originate from clinical practice and serve clinical needs, there are some aspects that could be improved to design a research framework more closely aligned with clinical practice. For breast cancer patients undergoing NAC, pathological complete response (PCR) serves as an effective surrogate endpoint for predicting NAC prognosis. The article defines PCR as the absence of residual invasive tumor cells in both breast specimens and ipsilateral axillary lymph nodes (ypT0/is ypN0), indicating no residual invasive carcinoma in both the primary breast lesion and ALNs, thus overlooking the scenario where residual invasive carcinoma exists only in either the tumor or the axilla after NAC. Due to the heterogeneity and complexity of tumor cells, the response of breast tumors and ALNs to NAC may not be parallel. This evidence suggests that accurately identifying the post-NAC status of both breast lesions and ALNs is crucial for determining the optimal surgical strategy for the lesion and axilla. For breast cancer patients undergoing direct surgery, stratified prediction of ALN burden can further refine the current research framework.

Researchers utilized the gradient-weighted class activation mapping (Grad-CAM) method to visualize the model and explore its interpretability. This method reveals the regions that the model focuses on when making

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decisions, providing a relatively intuitive perspective for understanding the internal workings of the model. However, it's worth noting that these are typically considered post-hoc explanations, offering limited explanatory power and not fully revealing the complexity and multi-layered nature of the model's decision-making process. The "black box" problem of deep learning has always been a challenge, especially in the medical and health domains. Model interpretability not only relates to the transparency of scientific research but also directly affects the credibility of clinical decisions and the effectiveness of practical applications. Furthermore, in the foreseeable future, the primary goal of AI is not to replace humans but to assist them. Through model interpretability, doctors can better understand the model's decision-making process and may discover imaging features in medical images that were previously unnoticed. Ultimately, this might allow AI to become a doctor's assistant rather than a replacement, aiding doctors in improving the quality of medical decisions. In the future, it will be possible to conduct interpretability research using the latent space within deep learning models.

Contributors

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Declaration of interests

We declare no competing interests.

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