Why do we need better omics in the breast cancer care?

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Axillary lymph node (ALN) status is both an important prognostic factor for breast cancer survival and a key factor in therapeutic decision making. For both locally advanced and certain subsets of early-stage breast cancer, chemotherapy is given prior to surgery and the pre- and post-chemotherapy ALN evaluation is vital to assess efficacy of treatment to determine the next steps in treatment. Since ALN metastasis (ALNM) strongly affects the risk of recurrence and treatment for breast cancer, an accurate assessment of ALNM that would help optimize therapy leading to better patient outcomes. Currently, two strategies are employed to predict and identify ALNM, imaging evaluation and clinicopathologic features (clinical staging, histology, molecular subtype). In [1], Y.Yu et al challenges the existing ALN assessment procedures and proposes a multi-omics signature comprising of clinicopathologic characteristics, molecular subtypes and radiomic features derived from ALN and tumor regions to train a machine learning (ML) to predict ALNM.

The clinical impact of this work from the machine learning perspective is two-fold; firstly, the radiomic features enable objective and non-invasive assessment of ALN. This is important since the diagnostic performance of manual methods to determine ALN status from auxiliary imaging or from clinicopathologic data comprising tumor grade, histological tumor size, lymphovascular invasion, proliferative index, and hormone receptor status is poor due to low sensitivity and specificity. A more accurate tool such as the proposed radiomics-based signature would help guide surgical decision making with surgeons selecting to do sentinel lymph node biopsy versus auxiliary dissection for women with a low-risk of having ALN and thus reducing surgical morbidity. Notably, the radiomics-based predictions are made objective through utilization of feature libraries comprising "handcrafted" software algorithms to compute feature values directly from expert-delineated two- or three-dimensional MRI image segments [2]. Robustness of these features is ascertained by testing the radiomics feature-based model on independent cohorts [1]. Although this was shown in another work, radiomics features extracted from tumor segments generated by different observers are independent of inter-observer manual segmentation variability [3].

Secondly, the radiomics-based signature enables the implementation of a personalized approach to individual risk assessment. This is possible since radiomic features are quantifiable data that represent those architectural and molecular tissue cues which are otherwise hidden to the radiologist eye. This idea is in line with a previous study which demonstrated that the expression of radiomics features can correlate with the level of tumor-infiltrating lymphocytes [4]. Furthermore, quantitative MRI radiomics can additionally predict both molecular classifications of breast cancer subtypes [5] and likelihood of response to targeted therapy [6]. The work by [1], Y.Yu et al. is a step forward because in their retrospective, multicenter and multicohort study, the ML predicted the ALN status, molecular subtype, proliferation index, clinical T stage, and disease-free survival with higher accuracy than conventional, state-of-the-art methods alone. Moreover, the model which learned only ALN and tumoral radiomics features was superior in predicting ALNM both to models based on clinicopathologic features (Table S6) and two radiologists evaluating ultrasound or MRI scans (Table S7, S8). Interestingly, select features in the combined ALN-tumor radiomics signature were differentially expressed in MRIs acquired between and after neoadjuvant chemotherapy, suggesting that the signature has the ability to reflect chemo-induced changes in the tumor.

Using key radiomic variables, feature panels to predict the ALN status, disease-free survival or other clinical outcomes can be developed. Such radiomics-based signatures could be incorporated into existing algorithms that utilize clinicopathologic and molecular features to enhance both the sensitivity and specificity and allow for the implementation of a much more refined and accurate approach to individual risk assessment. Going forward, multiomics-based nomograms could help guide clinical-decision making, surgical interventions and therapeutic regimens for breast cancer patients.

The next logical step in prognostic tool development would involve the automation of ALN segmentation in MRIs by artificial intelligence. The benefit would be a “hands-free” and more integrated way of feature extraction for ML and clinical use. Likewise, deep learning techniques can be substituted in lieu of “handcrafted” features to self-learn unique outcome-related characteristics of the tumor, ALN and surrounding tissues from images. Similar techniques have been explored in mammography [7,8] or DCIS recurrence
prediction from histology slides [9]. Yet, a significant effort is needed in order to collect and publicize MRI image data and concurrent metadata to explore the full range of MRI sequence data, which could identify novel factors to predict the ALNM and survival rates. The efforts by Y.Yu et al. [1] provide evidence that undertaking such efforts is worthy. This, and other efforts that follow, will further develop the concept of the virtual biopsy and through the incorporation of delta radiomics approaches help realize the promise of improved diagnosis and personalized therapeutics for breast cancer [10].

Declaration of Competing Interest

The authors declare no conflicts of interests.

Contributors

The authors drafted, edited, revised and approved the final version of the manuscript. Both authors contributed equally to this work.

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