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Commentary

Expanding applications of MRI-based radiomics in HER2-positive breast cancer

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Although contrast-enhanced breast magnetic resonance imaging (MRI) shows superior performance to ultrasound and mammography in evaluating response after neoadjuvant chemotherapy, early prediction of response prior to the initiation of treatment has been found to be less accurate. Evaluating response earlier, even before the initiation of treatment, could expand the clinical applications by allowing avoidance of ineffective treatment. Although earlier studies have reported several semantic features on multiparametric pretreatment MRI to be associated with pathologic complete response (pCR), such differences were noted only in certain subtypes (e.g., triple-negative breast cancer) and were based on relatively small study populations [1, 2]. However, radiomics has opened a new stage in MRI-based pretreatment prediction of pCR during the last five years. Radiomics is the process of extracting higher-dimensional data from digital medical images, which is motivated by the concept that quantitative image analysis can reveal information reflecting underlying pathophysiology. Pretreatment MRI-based radiomic models have shown promising results, with reported AUC results ranging from approximately 0.47 to 0.99 [3]. Yet, most studies have put all breast cancer subtypes together, and poorer performance has been reported in certain subtypes such as HER2-positive breast cancer [4]. This indicates the need for developing specific radiomic models, or at least the need for incorporating subtype information into model development.

The article by Bitencourt et al. published this month in EBioMedicine, is in line with the recent progress in radiomics research in breast cancer patients by focusing on developing a specific radiomic model for HER2-positive breast cancer [5]. Bitencourt and colleagues report the performance of a machine learning model incorporating clinical MRI-based parameters and radiomic MRI features for predicting pCR in HER2 overexpressing breast cancer. Its performance is comparable with those from meta-analyses of response based on post-treatment MRI, which have shown pooled sensitivity for residual disease of 63–88% and pooled specificity of 54–91% [6]. In addition, the authors have further expanded possible applications for radiomics in this subgroup, by developing and investigating the performance of a machine learning model in assessing HER2 expression level. The model showed encouraging results, with a sensitivity of 99.3%, specificity of 81.3% and a diagnostic accuracy of 97.4% in assessing HER2-expression levels (IHC 3+ vs. IHC <3+ but HER2 amplification detected by FISH). Considering that trastuxumab and pertuzumab target the HER2 receptor on the cell surface, it is reasonable to hypothesize that pCR is associated with HER2 IHC expression level, which has been supported by other studies [7, 8]. This work is another step in exploring the potential of imaging as a noninvasive tool for providing information on tumor biology and patient outcome.

It is noteworthy that higher levels of HER2 protein overexpression and pCR were associated with MRI-based radiomic features reflecting heterogeneity, whereas HER2 intratumor heterogeneity has been associated with incomplete response. This implies that radiomic heterogeneity cannot be considered to directly represent heterogeneity at a genetic or molecular level. Radiomic features likely reflect the influence of multiple factors, and can be used as biomarker itself to predict outcome. This has been shown in previous studies, where imaging features were strongly predictive of recurrence-free survival even after accounting for pCR [9].

However, radiomics research has its caveats. Despite the large amount of published research in the past few years, there is currently no wide-spread clinical application or widely used model in real clinical practice. To date, the majority of studies have been retrospective, single-institution studies using various equipment, imaging protocols and pre-or post-processing steps. Although multiple studies have showed the potential of radiomics, reproducibility and generalizability remain as unsolved issues. Although the authors developed the model using MRI studies performed by various institutions, which would be more favorable in building a generalizable model, the study lacks a separate test set for validation. Larger studies for both internal and external validation are needed to validate such preliminary results. In addition, utilizing multiparametric MRI including diffusion-weighted imaging and T2-weighted imaging could further improve performance and maximize the advantages of MRI, which has been shown in previous studies [4]. Incorporating radiomic features from peritumoral tissue regions could also improve the performance in predicting pCR and in distinguishing HER2-positive tumor

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biological factors [10]. The potential of MRI-based radiomics as a noninvasive biomarker in tumor imaging is unlimited, but on the contrary, its actual application to clinical practice is still largely limited by the lack of standardization and external validation.

In conclusion, the study by Bitencourt and colleagues contributes to further building and expanding applications of machine learning models using MRI-based radiomics, and shows its potential to assess HER2 expression level and pCR after neoadjuvant chemotherapy in HER2-positive breast cancer. Although validation by further larger studies are needed, studies like this one are paving the way towards establishing MRI-based radiomic models as a noninvasive biomarker in breast cancer.

Declaration of Competing Interest

The author has no conflicts of interest to disclose

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