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REVIEW

Deep Learning and Radiomics in Triple-Negative Breast Cancer: Predicting Long-Term Prognosis and Clinical Outcomes

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Abstract: Triple-negative breast cancer (TNBC) is a unique breast cancer subtype characterized by the lack of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) expression in tumor cells. TNBC represents about 15% to 20% of all breast cancers and is aggressive and highly malignant. Currently, TNBC diagnosis primarily depends on pathological examination, while treatment efficacy is assessed through imaging, biomarker detection, pathological evaluation, and clinical symptom improvement. Among these, biomarker detection and pathological assessments are invasive, time-intensive procedures that may be difficult for patients with severe comorbidities and high complication risks. Thus, there is an urgent need for new, supportive tools in TNBC diagnosis and treatment. Deep learning and radiomics techniques represent advanced machine learning methodologies and are also emerging outcomes in the medical-engineering field in recent years. They are extensions of conventional imaging diagnostic methods and have demonstrated tremendous potential in image segmentation, reconstruction, recognition, and classification. These techniques hold certain application prospects for the diagnosis of TNBC, assessment of treatment response, and long-term prognosis prediction. This article reviews recent progress in the application of deep learning, ultrasound, MRI, and radiomics for TNBC diagnosis and treatment, based on research from both domestic and international scholars.

Keywords: deep learning, MRI, radiomics, triple negative breast cancer, ultrasound

Breast cancer is among the most prevalent cancers affecting women worldwide, posing a significant threat to women's health. According to the World Health Organization (WHO), it is the most frequently diagnosed cancer globally and ranks fifth in cancer-related mortality.[1] Triple-negative breast cancer (TNBC) represents a distinct subtype, accounting for about 10 to 20% of all breast cancer cases.[2] TNBC is defined by the absence of ER, PR, and HER2 expression in tumor cells, making these patients unresponsive to hormone therapy and HER2-targeted treatments.[3] Consequently, chemotherapy remains the primary treatment option.[4] Numerous studies have indicated that TNBC generally carries a higher recurrence rate and poorer prognosis compared to other breast cancer subtypes.[5–7] Furthermore, TNBC often occurs in younger women and is associated with a higher prevalence of BRCA1 gene mutations.[8] Some researchers suggest that this may partly explain the higher incidence of TNBC in certain populations, such as Ashkenazi Jews.[9,10]

With the rapid advancement of artificial intelligence (AI), interest is surging in its medical applications to aid clinical decision-making. AI-driven techniques like deep learning and radiomics, which combine medical imaging with digital analysis, are increasingly being utilized to extract disease-specific information that is difficult to assess visually. In recent years, these methods have become significant research focal points.[11] In this context, quantitative analysis of multimodal,

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multidimensional data is essential for evaluating the spatiotemporal characteristics of various tissues, organs, and their surrounding microenvironments.[12] This article reviews recent research in deep learning and radiomics, focusing on their applications in the differential diagnosis of TNBC, assessing neoadjuvant chemotherapy (NAC) efficacy, and predicting long-term prognosis post-NAC. The objective is to examine the clinical potential and future applications of these technologies.

The literature retrieval strategy employed in this study extensively covered multiple authoritative databases, including PubMed, Web of Science, and China National Knowledge Infrastructure (CNKI), to ensure the comprehensiveness and diversity of the retrieval results. During the retrieval process, we meticulously selected a series of keywords that could be used independently or in combination to maximize the capture of relevant information. These keywords encompassed "ultrasound", "MRI", "radiomics", "deep learning", "triple-negative breast cancer/breast cancer", and "neoadjuvant chemotherapy." Our retrieval focused on literature published between 2016 and 2023, reflecting the latest advancements and research findings in this field in recent years.

Overview of Deep Learning and Radiomics

Radiomics involves extracting numerous features from medical imaging data to quantify tumor heterogeneity using advanced image processing and analysis techniques.[13] These features include tumor shape characteristics, first-order statistical properties, and texture features, all of which are not discernible through conventional imaging observation. Radiomics enhances accuracy in disease detection, diagnosis, classification, and prognostic evaluation.[14] By analyzing radiological images of tumors and surrounding tissues, it reveals subtle biological processes that provide insight into tumor behavior and treatment response.[15] The radiomics workflow typically includes the following steps:[16] ① Image Acquisition: High-quality medical images are obtained using modalities such as CT, MRI, and PET. ② Image Preprocessing: This stage involves standardizing images, reducing noise, and applying corrections to improve analysis quality. ③ Region of Interest (ROI) Selection and Segmentation: This step requires precisely delineating the area for analysis, usually focusing on the tumor region. ④ Feature Extraction: Quantitative features are extracted from the ROIs, capturing details of shape, intensity, and texture. ⑤ Feature Analysis: Statistical and machine learning techniques are applied to these features, facilitating disease characterization and aiding in predictions of treatment effectiveness and patient prognosis.

Deep Learning (DL) is a subset of machine learning that employs a multi-layer architecture of artificial neural networks, mimicking the information processing capabilities of the human brain.[17] This enables the model to make predictions and decisions by learning intricate patterns and features from extensive datasets. DL not only improves the accuracy and efficiency of feature extraction but also reveals potential image features that may be overlooked during conventional observation. With technological advancements, deep learning has become a pivotal force in advancing medical imaging, providing robust support for accurate diagnoses and personalized tumor treatments.[18,19]

In this framework, deep learning acquires features by conducting end-to-end training on coarse regions containing the targets.[20,21] Upon completing the training, depth features can either be integrated with semantic features for radiomics analysis or used directly for model predictions. In medical applications, convolutional neural network architectures—such as ResNet, GoogLeNet, and DenseNet—are frequently employed for tasks involving image and video processing. Over the past decade, deep learning has accelerated the development and integration of artificial intelligence technologies in healthcare. However, challenges persist, including the demand for substantial data and computational resources, along with concerns regarding model interpretability and transparency that necessitate urgent attention.[22]

Application and Comparison of Deep Learning and Radiomics in the Diagnosis and Treatment of TNBC

Recent research has established that deep learning and radiomics hold significant promise in predicting the biological characteristics of TNBC.[23] These methodologies aid clinicians in accurately identifying the tumor type and stage, choosing the most suitable treatment options, monitoring treatment effectiveness, evaluating patient survival probabilities, and delivering more personalized treatment recommendations. Given that ultrasound is the most widely utilized method for breast examination and MRI provides the highest resolution imaging in clinical settings, this article reviews the implementation of artificial intelligence technologies in these two imaging modalities.

Application of Deep Learning and Radiomics in the Diagnosis of TNBC

The current application of deep learning and radiomics in diagnosing and classifying TNBC has showed significant diagnostic efficacy.[24–37] For detailed information, refer to Table 1. In a study by Sha et al, involving 1223 patients, the diagnostic value of MRI radiomics for TNBC was evaluated, revealing a combined sensitivity of 0.72 and specificity of 0.91, with an area under the curve (AUC) of 0.88. Ma et al (2021) explored the use of quantitative features extracted from dynamic contrast-enhanced MRI (DCE-MRI) images of three-dimensional tumor volumes to differentiate TNBC from non-TNBC.[24,25] The findings indicated that a radiomics model based on 15 features achieved optimal performance,

Table 1 Deep Learning and Radiomics in the Diagnosis and Management of TNBC

Clinical Events	Test methods	Accuracy	Sensitivity	Specificity	AUC/C-index	Author (Publication Time)
Diagnosis of TNBC	MRI, Radiomics	—	0.72	0.91	0.88	Sha YS et al, 2022[24]
Identify TNBC from NTNBC	DCE-MRI, Radiomics	—	—	—	AUC was 0.741 for cross-validation and 0.867 for independent testing cohorts	Mingming Ma et al, 2021[25]
Molecular typing of breast cancer	Conventional ultrasound combined with contrast-enhanced ultrasound	0.854	—	—	—	Gong X et al, 2023[26]
Identify TNBC from NTNBC	Ultrasound deep learning (Resnet50)	0.889	0.875	0.9	0.9	Ye, H et al, 2021[27]
Diagnosis of TNBC	MRI deep learning	—	—	—	0.944	Yin HL et al, 2023[28]
Predicting pCR status after NAC in patients with TNBC	DWI + DCE-MRI, deep learning	—	—	—	The AUC was 0.97 ± 0.04 in the training group and 0.82 ± 0.10 in the internal validation group, while it was 0.86 ± 0.03 in the independent validation group and 0.83 ± 0.02 in the prospective blinded trial group	Zhou Z et al, 2023[29]
Predicting pCR status after NAC in advanced breast cancer	Ultrasound, deep learning Radiomics	—	—	—	AUC=0.94(95% CI:0.91–0.97)	Jiang M et al, 2021[31]
Predicting response to NAC therapy in patients with TNBC	MRI, Radiomics	—	—	—	AUC = 0.78 and 0.72 in training and testing cohorts	Hwang KP et al, 2023[30]
Predicting recurrence within 3 years after NAC in patients with TNBC	MRI, Radiomics	—	—	—	The radiomics model, which integrated MRI features obtained before and after neoadjuvant chemotherapy (NAC), achieved an AUC of 0.963 in the test group and 0.933 in the validation group	Mingming Ma et al, 2022[34]

(*Continued*)

Table 1 (Continued).

Clinical Events	Test methods	Accuracy	Sensitivity	Specificity	AUC/C-index	Author (Publication Time)
Predicting the likelihood of long-term recurrence and metastasis following neoadjuvant therapy in TNBC	DCE-MRI, Radiomics	87.5% in training group and 82.9% in validation group	—	—	AUC (0.917 for training group and 0.859 for validation group)	Xia B et al, 2021[36]
Predicting disease-free survival in triple-negative breast cancer	Ultrasound, Radiomics	—	—	—	The C-index of the model was 0.75 (95% CI = 0.72 to 0.78) in the training set and 0.73 (95% CI = 0.71 to 0.75) in the validation set	Yu F et al, 2021[37]

with AUCs of 0.741 during cross-validation and 0.867 in an independent test cohort. Gong et al combined conventional ultrasound with contrast-enhanced ultrasound radiomics to predict breast cancer molecular subtypes, showing that the accuracy of the combined ultrasound model surpassed that of the conventional model (85.4% vs 81.3%, $p < 0.01$).[26] These results highlight the substantial potential of MRI and ultrasound radiomics in the differential diagnosis and classification of TNBC.

Ye et al conducted a retrospective analysis of 934 ultrasound images of breast malignant tumors, which included 110 cases of TNBC and 824 cases of non-triple-negative breast cancer (NTNBC).[27] They employed a ResNet50 deep convolutional neural network for the analysis, resulting in an AUC of 0.900 for differentiating TNBC from NTNBC. The model showed an accuracy of 88.89%, with a sensitivity of 87.5% and specificity of 90.00%. Yin et al assessed the effectiveness of a deep learning model using multiparametric MRI to enhance radiologists' accuracy in the differential diagnosis of TNBC.[28] Their results showed that the deep learning approach performed exceptionally well in the validation group, achieving an AUC of 0.944. With the integration of artificial intelligence, the diagnostic AUC improved from 0.833 to 0.885 and from 0.823 to 0.876 for the two primary radiologists, respectively. For the two senior radiologists, the AUC increased from 0.901 and 0.950 to 0.925 and 0.975, respectively. These findings suggest that imaging combined with deep learning offers an automated and improved diagnostic process, making them promising noninvasive clinical tools for diagnosing TNBC. The incorporation of deep learning and radiomics techniques can substantially enhance diagnostic efficiency, potentially leading to earlier and more accurate detection and classification of TNBC.

To thoroughly evaluate the effectiveness of deep learning in ultrasound and MRI, alongside the application of radiomics in diagnosing TNBC, it is clear that the efficacy of deep learning and radiomics in MRI applications generally exceeds that of ultrasound diagnostics. Nevertheless, variations in study populations and the diagnostic criteria utilized across different research efforts highlight the need for further standardization in comparative analyses of the diagnostic efficacy of these two methodologies.

Deep Learning and Radiomics in TNBC Therapy Evaluation

Accurate evaluation of the impact of NAC for breast cancer is essential for determining appropriate surgical approaches and guiding the extent of breast cancer resection. Currently, the assessment of treatment efficacy in TNBC predominantly relies on biomarker detection, imaging studies, and clinical observations. Numerous studies suggest that deep learning and imaging-omics techniques play a significant role in optimizing treatment options and monitoring efficacy in TNBC patients. Zhou et al explored the effectiveness of applying deep learning to DCE-MRI and diffusion-weighted imaging (DWI) to predict pathological complete response (pCR) status in patients with TNBC.[29] Their study utilized images from 130 patients with TNBC to develop the models, achieving impressive results with an AUC of 0.97 ± 0.04 in the training group and 0.82 ± 0.10 in the internal validation group. In an independent validation cohort of 32 cases, the model maintained a robust AUC of 0.86 ± 0.03. Additionally, in another prospective blinded trial involving 48 patients, the model yielded an AUC of 0.83 ± 0.02. These findings indicate that multiparametric MRI-based deep learning can accurately predict pCR or non-pCR in patients with TNBC at an early stage. Hwang et al examined the utility of a radiomics model based on quantitative atlases derived from MRI to predict the response to NAC in patients with TNBC.[30] The multivariate radiomics model developed during mid-treatment achieved AUC values of 0.78 in the training cohort and 0.72 in the testing cohort. Although these results indicated moderate predictive power, they suggest that MRI-based radiological features obtained during mid-treatment may be valuable in identifying early responders to NAC in patients with TNBC.

Recently, numerous studies have employed multimodal methods to construct predictive models for pCR status in patients with TNBC. Jiang et al developed and validated a deep learning radiomic nomogram (DLRN) that utilized ultrasound and clinical data to assess pCR status in patients with locally advanced breast cancer following NAC.[31] The findings indicated that the DLRN accurately predicted pCR status, achieving an AUC of 0.94 in the validation cohort, with a 95% confidence interval (CI) of 0.91 to 0.97. Furthermore, the model's calibration was proven to be effective.

Hacking et al and Jimenez et al incorporated MRI radiomics alongside pathological sections and tumor-infiltrating lymphocyte (TIL) levels to predict pCR after neoadjuvant systemic therapy.[32,33] Their studies exhibited promising results for the clinical application of these approaches in accurately assessing treatment response.

In summary, deep learning and radiomics enable the automatic extraction of a wide range of quantitative features from medical images in a non-invasive manner, enhancing the evaluation of treatment efficacy in TNBC. The integration of fusion models, which incorporate multi-learning fusion or various machine learning techniques, can further refine the prediction of patients with TNBC responses to NAC. This approach helps tailor treatment decisions by identifying patients who may not benefit from standard care, enabling the implementation of more appropriate treatment regimens and ultimately improving treatment effectiveness and patient survival.

Application of Deep Learning and Radiomics in Predicting the Long-Term Prognosis of TNBC

In recent years, some researchers have begun to explore the application value of radiomics in predicting the long-term prognosis of TNBC, conducting preliminary investigations in this area. Ma et al (2022) developed a radiomics prediction model for systemic recurrence after NAC in TNBC based on automated segmented MRI.[34] The findings indicated that the AUC for the clinical model was 0.747 in the training set and 0.737 in the validation group for predicting systemic recurrence. In contrast, the AUCs for the radiomics model, which incorporated MRI features before NAC, after NAC, and both before and after NAC, were significantly higher, achieving values of 0.879, 0.91, and 0.963 in the training set, and 0.814, 0.802, and 0.933 in the validation set, respectively. These results show that the radiomics model based on a combination of MRI features before and after NAC is effective in predicting whether patients with TNBC will experience systemic recurrence within three years after treatment. This model could aid in the non-invasive identification of high-risk patients with TNBC at the risk of relapse after NAC, thus enhancing follow-up and treatment strategies and ultimately improving their prognosis.

Jiang et al focused on predicting TNBC prognosis by extracting imaging features related to peri-tumoral heterogeneity using DCE-MRI.[35] This model successfully predicted recurrence-free survival (P = 0.01) and overall survival (P = 0.004) in patients with TNBC. Bingqing also utilized radiomics features extracted from DCE-MRI prior to treatment, incorporating time-domain characteristics to construct a radiomics model aimed at predicting long-term recurrence and metastasis risk following neoadjuvant therapy.[36] The optimal model achieved an AUC of 0.917 in the training group and 0.859 in the validation group, with accuracy rates of 87.5% in the training group and 82.9% in the validation group. This study concluded that the DCE-MRI machine learning radiomics model, enhanced with time-domain characteristics, is valuable for predicting the long-term prognosis of patients with TNBC undergoing NAC.

While there are few radiomics studies in the field of ultrasound, Yu et al conducted a multicenter application study utilizing ultrasound radiomics features to predict disease-free survival (DFS) in TNBC.[37] This study identified ten significant radiomics characteristics to construct omics signatures, which were found to be independent risk factors for predicting DFS in both the training and validation sets ($p < 0.05$). The resulting clinic-radiomics model, which included axillary lymph node stage, Ki-67 index, and radiomics signatures, achieved a concordance index (C-index) of 0.75 (95% CI: 0.72 to 0.78) in the training set and 0.73 (95% CI: 0.71 to 0.75) in the validation set, showing moderate predictive efficacy.

After a thorough review of the existing domestic and international literature, we observed a limited number of studies focusing on the application of deep learning in predicting long-term prognosis for TNBC. This scarcity may be attributed to the complex and heterogeneous biological characteristics of TNBC, which complicate the extraction of imaging features that are closely linked to long-term outcomes. Despite significant advancements in deep learning for medical imaging analysis, its application in prognostic predictions for specific cancers remains largely exploratory. To enhance the validity and reliability of these models, more comprehensive clinical data and long-term follow-up studies are essential. Therefore, the current lack of research not only highlights the existing challenges in this domain but also suggests potential avenues for future investigations.

Comparative Analysis of Diagnostic and Predictive Efficacy of Deep Learning and Radiomics

There is currently no consensus on whether deep learning or radiomics demonstrates superior diagnostic or predictive power. The predictive accuracy of these two approaches is influenced by various factors, including individual patient differences, the type and volume of available data, and the methodologies used for model training. In certain contexts, models that utilize high-precision radiomic features and undergo iterative dimensionality reduction may provide better interpretability and performance.

In recent years, multimodal strategies that combine radiomics with deep learning have shown promise in enhancing predictive accuracy. The DLRN capitalizes on the strengths of both methods, improving the accuracy of prognostic predictions through the synergistic integration of automatically extracted features and radiomic characteristics derived from deep learning.[38,39]

Comparative Analysis of the Diagnostic and Predictive Efficacy of Deep Learning and Radiomics in HER-2 Positive Vs HER-2 Negative Breast Cancer

As another subtype of breast cancer with poor prognosis, HER-2 positive breast cancer is characterized by over-expression or amplification of the HER-2 receptor on the surface of tumor cells. Compared to other subtypes such as ER+/PR+/HER-2- and ER+/PR-/HER-2-, HER-2 positive breast cancer exhibits a higher risk of recurrence and metastasis. Therefore, imaging-assisted diagnosis and monitoring are particularly important in the management of this type of cancer. Existing studies have used deep learning algorithms to analyze breast MRI images to differentiate between HER-2 positive and HER-2 negative breast cancer. The results show that deep learning models achieve an accuracy rate of about 80% in identifying HER-2 positive breast cancer.[40,41] A literature search from 2019 to 2024 reveals that there are still very few studies on the evaluation of the efficacy of neoadjuvant chemotherapy for HER-2 positive breast cancer using deep learning and radiomics. Kim SY's team[42] developed a CNN deep learning model based on post-NAC dynamic contrast-enhanced MRI and clinical data to identify pathological complete remission in HER2 positive and triple-negative breast cancer. The study shows that the model established after cropping lesion images has certain diagnostic potential, but further optimization and external validation are needed to improve accuracy. It is evident that machine learning techniques have significant application potential not only in the clinical diagnosis and treatment of TNBC but also in the diagnosis and prognostic evaluation of other breast cancer subtypes. However, further development and exploration are still required.

Conclusion

Deep learning and radiomics are rapidly advancing in the research on diagnosis and treatment of triple-negative breast cancer (TNBC), demonstrating immense potential, particularly in playing a crucial role in assessing tumor heterogeneity. These advanced technologies can provide more comprehensive and detailed tumor information, effectively compensating for the limitations of traditional biopsy sampling. By deeply analyzing the relationship between radiomic features and tumor biological behavior, and developing more sophisticated machine learning algorithms, researchers can more accurately detect and analyze tumor heterogeneity, providing robust support for clinical diagnosis and treatment decisions. However, there remains a notable lack of research focused on predicting long-term prognosis. Meanwhile, deep learning and radiomics also face the following challenges in the diagnosis and treatment of TNBC.

Key challenges include the application of fusion methods, such as the DLRN, in diagnosing and treating TNBC. Additionally, there is a pressing need for the comprehensive acquisition and analysis of multimodal imaging data, particularly the integration of ultrasound and MRI using artificial intelligence. Furthermore, challenges related to artificial intelligence data acquisition and processing, the lack of interpretability of algorithms, and the limitations of clinical applications remain significant hurdles.

To address these challenges, it is essential to promote interdisciplinary collaboration, integrate multimodal data, and drive technological advancements. Such concerted efforts can systematically tackle the obstacles currently faced, unlocking the full potential of deep learning and radiomics and enabling their transformative impact on the precision diagnosis and treatment of TNBC.

Abbreviations

MRI, Magnetic Resonance Imaging; US, Ultrasound; TNBC, Triple-Negative Breast Cancer; ER, Estrogen Receptor; PR, Progesterone Receptor; HER-2, Human Epidermal Growth Factor-2; NTNBC, Non-Triple-Negative Breast Cancer; NAC, Neoadjuvant Chemotherapy; ROI, Region Of Interest; CNN, Convolutional Neural Network; ROC, Receiver Operating Characteristic; AUC, Area Under The Curve; DCA, Decision Curve Analysis; DLRN, Deep Learning Radiomics Nomogram; pCR, Pathological Complete Remission; npCR, Non-Pathological Complete Remission; DL, Deep Learning; AI, Artificial Intelligence.

Data Sharing Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethics Approval and Consent to Participate

The study is a literature review and does not require ethics.

Consent for Publication

Not applicable

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Disclosure

The authors declare that they have no competing interests.

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