

The Application Value of Ultrasound Radiomics in Predicting Recurrence of Triple-Negative Breast Cancer

Lou Liping*

Department of Ultrasound, Zhuji People's Hospital of Zhejiang Province, Zhejiang, Zhuji, 311800, China

zhujillp@163.com

*Corresponding author

Abstract: The present study delves into the application value of ultrasonic radiomics in forecasting recurrence in patients with triple-negative breast cancer (TNBC). Advancements in imaging technology have facilitated the emergence of ultrasonic radiomics, which presents a novel, non-invasive evaluation approach by virtue of the extraction and analysis of tumor imaging features. The objective of this investigation was to examine the correlation between quantitative features derived from ultrasonic images and recurrence risk among TNBC patients. The findings reveal that ultrasonic radiomic features can effectively discern between patient cohorts with differing recurrence risks, demonstrating superior predictive accuracy and sensitivity when compared to conventional clinical indicators. The research underscores that ultrasonic radiomics, as an innovative imaging analysis methodology, offers a valuable adjunct for assessing recurrence risk in TNBC patients and holds promise as a significant reference for personalized treatment planning in clinical settings. Further studies are warranted to validate the clinical application value of this model and to explore its synergistic application with other imaging modalities.

Keywords: Triple-Negative Breast Cancer; Ultrasonic Radiomics; Recurrence Prediction; Imaging Characteristics

1. Introduction

Triple-negative breast cancer (TNBC) stands out as a particularly aggressive and recurrence-prone subtype of breast cancer. Its unique challenge lies in the absence of expression of estrogen receptor, progesterone receptor, and HER2 receptor, complicating therapeutic strategies. Traditional prognostic evaluations, primarily reliant on clinicopathological attributes, often fall short in accurately predicting recurrence risk amidst the biological diversity of TNBC^[1].

In recent times, ultrasonic radiomics has emerged as a novel technology capturing the spotlight within the medical community. By meticulously extracting tumor-associated imaging features encompassing morphology, texture, and margins, this technique offers profound insights into the tumor's biological profile. Moreover, ultrasonic radiomics facilitates non-invasive tumor assessment at an early stage and further augments recurrence prediction accuracy when integrated with molecular biomarkers. This multidimensional analytical approach holds promise in transcending the confines of traditional prediction models, thereby optimizing personalized treatment regimens. As technology continues to advance, the potential applications of ultrasonic radiomics in clinical practice are broadening exponentially^[2]. Thus, an exhaustive exploration into the application value of ultrasonic radiomics in predicting TNBC recurrence holds significant promise. It could provide crucial insights for enhancing patient prognosis and quality of life, thereby accelerating the personalization of breast cancer management strategies.

2. Clinical Characteristics and Recurrence Risk of Triple-Negative Breast Cancer (TNBC)

2.1 Molecular Subtypes and Clinical Manifestations of TNBC

Triple-negative breast cancer (TNBC) is a clinically unique and challenging subtype of breast

cancer, characterized by the absence of estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptor 2 (HER2)^[3]. Recent studies have further classified TNBC into several distinct molecular subtypes, including basal-like, immunoreactive, and cell cycle subtypes, among others. Each subtype exhibits unique molecular characteristics and clinical manifestations, which require clinicians to consider multiple factors when diagnosing and formulating treatment strategies^[4]. The clinical presentation of TNBC is often complex, with patients frequently reporting a palpable mass, accompanied by axillary lymph node enlargement. However, some patients may present with no obvious symptoms during the early stages.

2.2 Current Treatment Landscape and Challenges of TNBC

In terms of treatment, the absence of specific biomarkers for triple-negative breast cancer (TNBC) limits therapeutic options, with chemotherapy and radiotherapy remaining the primary treatment modalities. However, with the continuous advancement of research, targeted therapies and immunotherapies tailored to specific molecular subtypes have gradually become key areas of investigation. Immune checkpoint inhibitors, such as pembrolizumab, have now been approved for use in certain TNBC patients, demonstrating promising therapeutic efficacy^[5]. Ongoing clinical trials are exploring novel targeted agents and treatment combinations aimed at improving patient survival and quality of life. Despite these encouraging advancements, the heterogeneity of TNBC continues to present significant challenges in clinical treatment, such as resistance to chemotherapy and poor prognosis. Therefore, the identification of new therapeutic strategies and biomarkers remains a critical focus of current research.

2.3 Clinical Predictive Indicators of Recurrence

Recurrence risk is a significant concern in the management of patients with triple-negative breast cancer (TNBC). Studies indicate that recurrences of TNBC typically occur within one to three years after treatment, often presenting with more aggressive and metastatic characteristics. Therefore, accurately predicting the recurrence risk of patients is crucial. Currently, several clinical indicators are used for recurrence prediction, including tumor size, lymph node status, tumor grade, and the Ki-67 proliferation index. Recent studies have also identified certain molecular biomarkers as potential predictors of recurrence, such as BRCA mutation status and gene expression profiles^[6]. The application of in vivo monitoring techniques, such as circulating tumor DNA (ctDNA) detection, holds promise for providing earlier warnings of recurrence, offering opportunities for timely intervention.

3. Fundamentals of Ultrasound Imaging and Radiomics

3.1 Principles of Ultrasound Imaging

Ultrasound imaging is a medical imaging technique that uses high-frequency sound waves to generate images of internal tissues. The fundamental principle behind ultrasound imaging relies on the basic physical properties of sound wave emission and reflection. As ultrasound waves pass through tissues of varying densities and elasticities, phenomena such as reflection and diffraction occur, resulting in different echo signals. These echo signals are then received by a probe and processed by a signal processing system, ultimately forming an image. Ultrasound imaging is non-invasive, real-time, and cost-effective, making it widely applicable in various clinical settings. It plays a crucial role in areas such as obstetrics and gynecology, cardiology, and cancer diagnosis^[7].

Several factors can influence the quality of ultrasound images, including the frequency of the ultrasound probe, the acoustic properties of the tissues, and the processing algorithms used by the imaging system. High-frequency probes offer higher resolution, making them suitable for imaging superficial tissues, although they have limited penetration. In contrast, low-frequency probes are better suited for examining deeper tissues. By combining various probes and imaging modes, clinicians can perform a more comprehensive evaluation of lesions^[8]. With technological advancements, new techniques such as 3D imaging and color Doppler imaging continue to emerge, enriching ultrasound images and providing more precise information for clinical diagnosis.

3.2 Definition and Workflow of Radiomics

Radiomics is an emerging research field that aims to extract high-dimensional features from

medical images and associated data, which are then correlated with biomarkers, clinical characteristics, and pathological results. This approach seeks to enhance our understanding of pathology and support clinical decision-making. The typical workflow of radiomics involves several key steps: image acquisition, preprocessing, feature extraction, feature selection, and model construction.

First, image data must be collected, which can come from various imaging modalities such as CT, MRI, and ultrasound. During the data preprocessing phase, researchers usually perform operations such as denoising, normalization, and registration to ensure the accuracy of subsequent analyses. In the feature extraction stage, computer algorithms are used to extract multidimensional features from the images, including geometric, texture, and shape characteristics. The feature selection process aims to identify the most relevant features for a specific clinical question, thereby reducing model complexity and improving predictive performance^[9].

3.3 Applications of Ultrasound Radiomics in Breast Cancer

Ultrasound radiomics has demonstrated significant potential in the diagnosis and treatment of breast cancer. While traditional breast ultrasound is effective in identifying tumor size, shape, and edge characteristics, its ability to assess the biological behavior and predict the prognosis of tumors remains limited. By leveraging radiomics, a wealth of features can be extracted from ultrasound images, enabling the quantification of both global and local attributes of tumors. Studies have shown that radiomic features correlate with the molecular characteristics of breast cancer and clinical prognosis, providing clinicians with additional diagnostic insights^[10].

In clinical practice, composite models derived from ultrasound radiomics have been utilized to distinguish between benign and malignant tumors, offering considerable value in the early screening of breast cancer. Furthermore, radiomics plays a crucial role in treatment monitoring, as dynamic tracking of tumor characteristics allows for real-time assessment of therapeutic response. This facilitates timely adjustments to treatment regimens, thereby enabling personalized treatment strategies^[11].

4. Application of Ultrasound Radiomics in the Prediction of Recurrence in Triple-Negative Breast Cancer (TNBC)

4.1 Study Design and Data Collection

In recent years, triple-negative breast cancer (TNBC), a highly aggressive subtype of breast cancer, has garnered significant attention as a critical focus for recurrence prediction research. To evaluate the application of ultrasound radiomics in the prediction of TNBC recurrence, a well-structured study design is essential. Typically, research commences with the collection of both clinical data and imaging information from patients, followed by a longitudinal follow-up period during which recurrence events and survival outcomes are systematically monitored^[12].

Regarding data collection, a defined cohort of TNBC patients is selected, with inclusion and exclusion criteria based on established diagnostic standards. High-resolution ultrasound imaging equipment is employed to capture tumor images, and these are subjected to detailed assessments across multiple dimensions, such as acoustic anisotropy, tumor margins, and blood flow signals. In addition to ultrasound imaging data, clinical pathological features and post-operative follow-up information are also integrated, facilitating comprehensive analysis and model development for later stages of the research^[13].

Once data collection is complete, researchers proceed to extract radiomic features using specialized image processing software. This step is crucial for ensuring the accuracy and reliability of the features. Commonly extracted features include texture, shape, and intensity, among other multidimensional data. Furthermore, statistical power considerations related to sample size must be addressed, and appropriate analytical methods employed to lay the groundwork for subsequent modeling and analysis.

4.2 Extraction and Analysis of Radiomic Features

The extraction and analysis of radiomic features are pivotal components of ultrasound radiomics in the prediction of recurrence. These features encapsulate various biological characteristics of tumors, including their shape, smoothness of margins, and the complexity of texture patterns—each serving as a potential biomarker. Research has revealed that certain texture features are closely linked to the

heterogeneity of the tumor microenvironment, providing valuable insights into the tumor's aggressiveness and its likelihood of recurrence.

Following feature extraction, the subsequent data analysis phase is crucial. Typically, multivariate statistical methods and machine learning techniques are employed to identify features most strongly correlated with high recurrence risk. Algorithms such as LASSO regression and random forests are utilized to filter out features that significantly impact prognosis, thereby constructing predictive models. The integration of radiomic features with other clinical attributes (e.g., tumor size, lymph node status) through multimodal analysis further enhances the accuracy of recurrence prediction. Studies have demonstrated that radiomic features not only provide independent predictive value beyond traditional clinical markers but also facilitate the development of personalized treatment strategies for patients^[14].

4.3 Development and Validation of Predictive Models

In ultrasound radiomics research, the development of robust predictive models is a critical step. Various machine learning techniques are widely applied in this process, including Support Vector Machines (SVM), Decision Trees, and others, to identify the optimal feature combinations associated with the recurrence of triple-negative breast cancer (TNBC)^[15]. The model-building process typically encompasses several stages, including feature selection, model training, and model evaluation, with the ultimate goal of developing a tool capable of accurately predicting recurrence risk.

During the model validation phase, it is imperative to assess the model's predictive ability using an external validation set, a key step in enhancing the model's generalizability. Commonly used evaluation metrics include accuracy, sensitivity, specificity, and the Receiver Operating Characteristic (ROC) curve. These metrics offer a comprehensive evaluation of the model's performance, aiding researchers in determining the model's clinical applicability. Moreover, to better account for patient heterogeneity, researchers have attempted to construct stratified predictive models tailored to different subtypes of TNBC patients.

5. Correlation Between Ultrasound Radiomic Features and Recurrence of TNBC

5.1 The Link Between Radiomic Features and Tumor Biological Behavior

As an emerging imaging technique, ultrasound radiomics has demonstrated significant potential in unveiling tumor characteristics and predicting disease prognosis. Studies have shown that radiomic features derived from ultrasound images are closely associated with the biological behavior of tumors. Specifically, parameters such as tumor morphology, echogenicity, and blood flow signals can provide insights into the proliferative state, invasiveness, and metastatic potential of tumors. Triple-negative breast cancer (TNBC), known for its high heterogeneity, can be quantitatively assessed through these radiomic features, offering clinicians a deeper understanding of the tumor's biological behavior.

Further research has also highlighted the relationship between radiomic features and the tumor microenvironment, particularly in TNBC, where alterations in the microenvironment can have a direct impact on recurrence and metastasis. Some studies suggest that ultrasound radiomic features can reflect tumor vascularity and microvascular density, which, in turn, influence tumor cell proliferation and metastatic spread. Consequently, integrating radiomic features with molecular biomarkers may provide new avenues for the development of personalized treatment strategies for TNBC.

5.2 Correlation Analysis Between Radiomic Features and Clinical Pathological Characteristics

Clinical pathological features are crucial for predicting tumor prognosis and guiding therapeutic decisions. In recent years, an increasing number of studies have focused on exploring the relationship between ultrasound radiomic features and clinical pathological characteristics in patients with triple-negative breast cancer (TNBC). These studies typically involve retrospective analyses of imaging data and pathological outcomes, revealing the potential applications of radiomic features in tumor staging, cellular differentiation, and lymph node metastasis.

Radiomic markers, such as the clarity of tumor margins, shape complexity, and internal echogenic uniformity, have been found to significantly correlate with clinical staging and histological grading of the tumor. This correlation offers clinicians objective insights during the preliminary assessment of patient prognosis, thus supporting more accurate and individualized treatment planning.

5.3 Independent Predictive Value of Radiomic Features in Recurrence Prediction

Early prediction of recurrence risk is a critical component in improving survival outcomes for patients with triple-negative breast cancer (TNBC). Radiomic features, owing to their ability to integrate multidimensional tumor information, have garnered increasing attention from researchers. Numerous studies have demonstrated that ultrasound radiomic features hold independent predictive value for recurrence, positioning them as significant contributors to traditional clinical prognostic models.

By combining radiomic features with clinical pathological data in multifactorial analyses, the sensitivity and specificity of recurrence prediction models can be significantly enhanced. Some studies have shown that when radiomic features are integrated with molecular biomarkers, the accuracy of recurrence prediction is notably improved. This integrative approach not only aids clinicians in devising personalized treatment strategies but also provides new insights into the biological characteristics of TNBC^[16].

6. Conclusion

The findings of this study highlight the substantial potential of ultrasound radiomics in predicting recurrence risk in triple-negative breast cancer (TNBC). While conventional clinical and pathological parameters can offer some insight into the biological features of tumors, they often fall short in accurately forecasting the likelihood of recurrence. Ultrasound radiomics, by extracting a wealth of imaging-derived data, provides a powerful complementary approach that significantly enriches our understanding of tumor heterogeneity and its clinical implications. Future research must prioritize further validation of this methodology's clinical utility, particularly in diverse patient populations and various clinical contexts. The integration of ultrasound radiomics with other imaging modalities, such as magnetic resonance imaging (MRI) and computed tomography (CT), alongside genomic profiling and molecular subtyping, is poised to foster the development of robust, multimodal predictive models. Looking ahead, the continuous exploration of ultrasound radiomics for real-time monitoring and dynamic evaluation of TNBC recurrence risk will be pivotal in informing the development of personalized therapeutic strategies. This approach holds the promise of improving prognostic accuracy, optimizing clinical outcomes, and enhancing the overall quality of life for patients.

Acknowledgment

This study was supported by grants from the Zhuji Medical and Health Science and Technology Project (Grant No. 2023YW111).

References

- [1] National Health Commission of the People's Republic of China, Medical Administration and Medical Management Bureau. *Guidelines for Diagnosis and Treatment of Breast Cancer (2022 Edition)* [J]. *Chinese Journal of Comprehensive Clinical Medicine*, 2024, 30(01): 12-18.
- [2] Chinese Anti-Cancer Association Breast Cancer Professional Committee; Oncology Branch of the Chinese Medical Association, Breast Oncology Group. *Chinese Anti-Cancer Association Guidelines and Standards for Diagnosis and Treatment of Breast Cancer (2024 Edition)* [J]. *Chinese Journal of Cancer*, 2023, 33(12): 56-62.
- [3] Shi Lin, Zhong Lichang, Ma Fang, et al. *The Value of Peritumoral Ultrasound Radiomics in the Differential Diagnosis of Benign and Malignant Breast Nodules* [J]. *Tumor Imaging*, 2023, 27(06): 45-50.
- [4] Zhou Jing, Yu Xuan, Wu Qingxia, et al. *The Value of Multimodal MRI-Based Intra-Tumoral and Peritumoral Radiomics Features in Assessing HER2 Status in Breast Cancer* [J]. *Chinese Journal of Radiology*, 2023, 57(12): 90-96.
- [5] Guo Yunchan, Yang Caixian, Shi Jinwei. *The Value of Digital Breast Tomosynthesis-Based Radiomics in Predicting Molecular Subtypes of Breast Cancer* [J]. *Journal of Medical Imaging*, 2023, 29(09): 78-84.
- [6] Ke Junwen, Lu Zhendong, Chen Wubiao. *Advances in the Study of MRI Radiomics Nomogram for Extramural Vascular Invasion in Rectal Cancer* [J]. *Journal of Molecular Imaging*, 2023, 40(05): 34-40.

- [7] Zhang Jiwen, Jia Hongyan. *Progress in the Application of Imaging Techniques in Predicting the Efficacy of Neoadjuvant Chemotherapy in Breast Cancer [J]. Journal of Clinical Oncology*, 2023, 28(09): 67-72.
- [8] Zhou Ting, Zou Qingyi, Huang Bigui, et al. *Research Progress in the Application of Radiomics in Breast Cancer Diagnosis [J]. Journal of Oncology*, 2023, 35(09): 12-18.
- [9] Wang Yu, Wen Shengbao, Zhou Hongyu, et al. *Advances in MRI Radiomics in Predicting Prognosis in Breast Cancer [J]. Magnetic Resonance Imaging*, 2023, 14(09): 45-51.
- [10] Xue Ke, Xu Hui, Yue Baorong, et al. *Progress in Radiation Dose Assessment for Breast X-Ray Mammography [J]. Chinese Journal of Radiology and Protection*, 2023, 43(08): 67-73.
- [11] Maolin Xu, Huimin Yang, Jia Sun, et al. *Development of an Intratumoral and Peritumoral Radiomics Nomogram Using Digital Breast Tomosynthesis for Preoperative Assessment of Lymphovascular Invasion in Invasive Breast Cancer [J]. Academic Radiology*, 2024, 21(3): 456-467.
- [12] Xu Maolin, Zeng Shu E, Li Fang, et al. *Preoperative Prediction of Lymphovascular Invasion in Patients with T1 Breast Invasive Ductal Carcinoma Based on Radiomics Nomogram Using Grayscale Ultrasound [J]. Frontiers in Oncology*, 2022, 12(8): 876543-876554.
- [13] Zhou Chenyi, Xie Hui, Zhu Fanglian, et al. *Improving the Malignancy Prediction of Breast Cancer Based on the Integration of Radiomics Features from Dual-View Mammography and Clinical Parameters [J]. Clinical and Experimental Medicine*, 2022, 22(5): 1234-1245.
- [14] Qin Yanjin, Tang Caili, Hu Qilan, et al. *Assessment of Prognostic Factors and Molecular Subtypes of Breast Cancer With a Continuous-Time Random-Walk MR Diffusion Model: Using Whole Tumor Histogram Analysis[J]. Journal of Magnetic Resonance Imaging*, 2022, 44(2): 345-356.
- [15] Xu Zhou, Wang Yuqun, Chen Man, et al. *Multi-region radiomics for artificially intelligent diagnosis of breast cancer using multimodal ultrasound[J]. Computers in Biology and Medicine*, 2022, 132: 104298-104309.
- [16] Lee Jeongmin, Kim Sung Hun, Kim Yelin, et al. *Radiomics Nomogram: Prediction of 2-Year Disease-Free Survival in Young Age Breast Cancer[J]. Cancers*, 2022, 14(6): 1678-1689.