

Application Progress of Ultrasound Radiomics in the Evaluation and Prediction of Neoadjuvant Chemotherapy for Breast Cancer

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Abstract: Breast cancer is a malignant tumor with the highest incidence in women. In recent years, the incidence of breast cancer has shown an increasing trend, especially in younger patients, which seriously threatens the life and health of women. In order to improve the treatment effect of breast cancer, neoadjuvant chemotherapy has become a reliable strategy to cooperate with surgical treatment and improve the prognosis of advanced breast cancer, which is conducive to quickly and accurately curbing the growth of cancer cells, controlling the patients' condition, reducing their pain, and improving the cure rate of breast cancer patients. This paper analyzes the development history of ultrasound radiomics, explores its application in the evaluation and prediction of neoadjuvant chemotherapy for breast cancer, and clarifies the research results of multimodal ultrasound radiomics in the analysis of high-order characteristics of breast cancer tumors and the evaluation of tumor heterogeneity, so as to provide references for the clinical treatment of breast cancer.

Keywords: Ultrasound radiomics; Breast cancer; Neoadjuvant chemotherapy; Ultrasonography

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1. Introduction

The etiology of breast cancer is complex, including signaling pathways, cell turnover, and gene mutations, which will cause damage to the patient's immune system and blood circulation. Once the patient's cells are aging and the immune function is mutated, the tumor cells will grow rapidly, leading to the rapid deterioration of the patient's condition. Multimodal molecular imaging can accurately detect the specific molecular conditions of breast cancer cells and tissues, accurately feedback the dynamic characteristics of cancer cells at the molecular level *in vivo*, and provide accurate data for clinical diagnosis and treatment of breast cancer. Neoadjuvant chemotherapy is the current standard treatment for locally advanced breast cancer, which can effectively improve the survival rate of advanced breast cancer and control the spread of cancer cells in time. For patients who need downstaging breast-conserving surgery, MRI and ultrasound omics can be arranged to detect the functional information such as cancer cell diffusion, metabolism, and hypoxia in time, which can

be used to observe the overall morphology of the tumor non-invasively and quantitatively. This can measure the tumor development process and treatment response, provide accurate data for clinical treatment of breast cancer, and improve the survival rate of breast cancer patients.

2. Overview of neoadjuvant chemotherapy

Neoadjuvant chemotherapy (NAC) refers to a treatment where patients who do not have metastasis after receiving the first chemotherapy receive comprehensive chemotherapy in the stage of preparation for local treatment. At the same time, this treatment method can analyze the differences in molecular subtypes of breast cancer, screen out patients with poor treatment effects, and carry out local treatment for these patients to reduce the pain caused by chemotherapy^[1]. With the development of medical imaging technology, targeted drugs, and other new technologies, the treatment of breast cancer is gradually diversified. In order to help patients with advanced breast cancer control their disease, NAC combined with surgery is often used in clinical treatment, which effectively improves the survival rate of patients. In 2019, the Chinese expert consensus on neoadjuvant therapy of breast cancer pointed out that MRI imaging technology, X-ray, and other ultrasound imaging technologies can provide more accurate data for NAC treatment, help doctors accurately understand the patient's condition, and formulate a more reasonable NAC treatment plan^[2,3].

3. Overview of multimodality ultrasound radiomics

Radiomics is a new medical imaging concept based on the development of ultrasound images, which is an auxiliary method based on quantitative features. Lambin *et al.* analyzed radiomics in 2012^[4], and believed that radiomics is based on an automatic algorithm to obtain a large amount of relevant graph data from the region of interest, and then extract the relevant information of lesions through rigorous statistical algorithm and data mining technology, so as to provide accurate data for clinical diagnosis. They believe that ultrasound radiomics includes MR-ultrasound imaging, contrast-enhanced imaging, and other technologies, which can meet the needs of medical imaging examinations of different types of diseases. The image clarity is higher, and the image information such as organ morphology, edge, shadow, and echo area can be clearly displayed, providing effective information for clinical diagnosis^[4]. Ultrasound radiomics is more abundant than conventional ultrasound image modalities. It can use imaging technology and contrast technology to analyze tumors and accurately determine the stage of tumor development. It can also extract multimodal tumor indicators to reflect the molecular typing of tumors and provide references for subsequent treatment and prognosis evaluation^[4]. Liu *et al.* analyzed that MR radiomics has been widely used in the neoadjuvant treatment of breast cancer. The transformation process of ultrasound radiomics includes image data collection, ROI segmentation, feature extraction, statistical analysis, and modeling, which requires high operational ability of ultrasound imaging technicians^[5].

4. Biological basis of ultrasound radiomics in neoadjuvant chemotherapy of breast cancer

With the proposal of the concept of precision medicine, ultrasound radiomics has been widely used in the diagnosis and treatment of breast cancer. Ma *et al.* believed that ultrasound radiomics is more accurate than traditional immunohistochemical detection, which can detect the location of the lesion non-invasively, show the dynamic changes of the tumor at the cellular and molecular levels, and accurately evaluate the molecular

classification of tumor cells ^[6]. Ultrasound radiomics can provide accurate information for subsequent neoadjuvant therapy and prognosis evaluation of breast cancer. Jain believed that the cause of breast cancer is complex and it is a highly heterogeneous cancer ^[7]. Clinically, the molecular classification and lesion location of breast cancer are judged by different biological markers. Ultrasound radiomics technology is used to perform a non-invasive examination of breast tumors to obtain accurate information such as tumor location and molecular classification and to provide data for doctors to evaluate the histological evaluation, clinical staging, and targeted drug selection of breast cancer ^[7]. Valdora and Houssami believed that ultrasound radiomics is more accurate than chemical methods in the diagnosis of breast cancer subtypes, which can capture the characteristics of tumors at the genetic and cellular levels, diagnose tumor-related heterogeneity and molecular typing, which is beneficial to distinguish benign and malignant breast tumors as early as possible and reduce unnecessary biopsies ^[8].

5. Clinical application of ultrasound radiomics in neoadjuvant chemotherapy for breast cancer

With the development of virtual reality, artificial intelligence, and big data technology, ultrasound imaging technology is also developing. Ultrasound imaging is becoming clearer and clearer, which can provide more accurate data for the diagnosis and treatment of breast cancer. Li *et al.* analyzed the ultrasound image characteristics of breast masses, clarified the shape, edge shape, size of the masses, internal and posterior echo characteristics of the breast masses, and used statistical principles to analyze the clinical data to construct the ultrasound image model of breast masses, which was convenient for more accurate diagnosis of breast masses ^[9]. The probability of breast cancer was evaluated according to the information on the mass, and further examination and treatment were arranged for patients with abnormal ultrasound images ^[9]. Zha *et al.* analyzed the radiomics model of preoperative lymphatic vascular invasion in patients with invasive breast cancer, focusing on the analysis of breast ultrasound images of these patients, and using statistical correlation techniques to analyze the image information, the edge, shape, and echo area of breast masses, which is helpful to determine the classification of breast tumors, the location of lesions, and the spread of cancer cells ^[10]. They believed that ultrasound imaging can improve the accuracy of clinical diagnosis of breast cancer, help patients find the disease in time, improve the survival rate of breast cancer patients, and provide references for subsequent chemotherapy and neoadjuvant therapy ^[10]. Filiz *et al.* analyzed the application of ultrasound radiomics in predicting molecular subtypes and histological grades of breast cancer and clarified the basic information such as tumor molecular characteristics, tumor morphological characteristics, echo area, and edge position of molecular subtypes of breast cancer ^[11]. They believed that ultrasound radiomics could clearly show the characteristics of breast tumor morphology, margin, molecular typing, and heterogeneity. It provides references for the subsequent histological grading and chemotherapy of breast cancer. At the same time, they proposed that compared with Luminal B subtype breast cancer, Luminal A subtype breast cancer showed the characteristics of unclear boundaries and irregular edge on ultrasound images, and triple-negative breast cancer had limitations. These ultrasound characteristics can be used as clinical judgment criteria ^[11]. Cui *et al.* studied the relationship between ultrasound manifestations and molecular indicators of breast cancer and concluded that Ki-67 lesions are related to posterior acoustic enhancement, showing a positive correlation, and the disease can be judged according to breast echo enhancement; and Ki-67 and p53 breast cancer are related to tumor echo. These ultrasound findings can be used as the basis for the prediction of neoadjuvant therapy for breast cancer ^[12].

To evaluate the clinical efficacy of NAC in breast cancer using ultrasound radiomics, Braman believed that neoadjuvant therapy is widely used in the treatment of patients with advanced tumors ^[13]. Pre-chemotherapy

can reduce the volume of tumors, lay a good foundation for subsequent surgery, greatly reduce the possibility of breast cancer metastasis, control the development of patients' disease, and thus improve the cure rate of breast cancer. He believed that patients with locally advanced breast cancer should receive neoadjuvant chemotherapy promptly to kill the cancer cells in the breast as soon as possible, avoid the further spread of cancer cells, lay a good foundation for subsequent treatment, and also minimize patients' pain^[13]. Zhao *et al.* analyzed the application of contrast-enhanced ultrasound and elastography in neoadjuvant chemotherapy for breast cancer^[14]. They believed that ultrasound radiomics is the most commonly used technique in the evaluation of NAC treatment for breast cancer, and it is the most accurate case examination method, which can accurately analyze the volume, margin, and tissue infiltration of breast cancer. It is a non-invasive examination, which can relieve patients' pain and facilitate the attending doctor to flexibly adjust the clinical treatment plan^[14]. Yang and Wang analyzed the application of contrast-enhanced ultrasound and ultrasound elastography in the neoadjuvant treatment of breast cancer^[15]. According to the information from contrast-enhanced ultrasound and imaging, the hardness and micro blood supply of breast tumors can be obtained. In clinical practice, these two technologies can be combined with conventional ultrasound to analyze the volume, shape, and margin of breast tumors. According to the clear contrast-enhanced ultrasound and imaging technology, the patient's condition can be judged, and the targeted treatment plan can be formulated to further improve the clinical treatment effect of breast cancer NAC^[15]. Sun *et al.* evaluated the pathologic complete response (pCR) of breast cancer after neoadjuvant chemotherapy based on the results of ultrasound examination and believed that the detection accuracy of Luminal B subtype breast cancer was relatively high, which could more accurately determine the molecular typing of breast cancer, whether the cancer cells spread, and tumor volume, and more accurately detect the molecular typing of breast cancer cells^[16]. Therefore, the accuracy of pCR evaluation can be as high as 89.6%. They believed that the etiology of breast cancer is complex, and the molecular classification of tumors is also more complex, which brings a great challenge to clinical diagnosis and treatment. Ultrasound radiomics can detect the morphology, margin, volume, tissue composition, and molecular classification of breast tumors, and provide reference data for clinical judgment of breast cancer classification and chemotherapy effect^[16]. Lee *et al.* analyzed the ultrasound images of patients with advanced breast cancer after NAC treatment and found that the ultrasound images of breast tumors in many patients after treatment showed patchy hypoechoic areas without obvious blood flow signals, which could help the treating physician to determine whether the lesions had necrosis, liquefaction, or fibrosis^[17]. These results demonstrate the advantages of ultrasound radiomics in the treatment of neoadjuvant chemotherapy for breast cancer, which is worthy of further promotion in clinical practice. They believed that contrast-enhanced ultrasound (CEUS) and shear-wave elastography (SWE) are new imaging techniques that are widely used in the current ultrasound imaging combination, which can identify the nature of breast tumor lesions, intuitively present the hardness and micro blood perfusion information of tumor lesions, and provide reliable reference data for judging whether cancer cells are metastatic and breast cancer recurrence^[17].

6. Application of ultrasound radiomics combined with machine learning in NAC of breast cancer

With the rapid development of artificial intelligence technology, machine learning is gradually integrated into the field of medical ultrasound imaging, which effectively improves the clarity and accuracy of ultrasound images and provides effective technical support for clinical diagnosis and treatment. Virkkunen *et al.* analyzed the principles and characteristics of machine learning technology, clarified its application path in ultrasound radiomics, developed a new imaging technology combining ultrasound radiomics with machine learning, and explored the application of this imaging technology in NAC treatment in breast cancer^[18]. They believed that medical imaging

operators could use machine learning to automate the operation of relevant equipment, detect the patient's lesions, and obtain relevant image information. However, there are few studies on the application of ultrasound radiomics combined with machine learning in the non-invasive detection of breast cancer. Jiang *et al.* developed a deep learning-based radiomics nomogram to examine breast cancer patients before NAC treatment, evaluate patients' preoperative pCR, diagnose the type and condition of breast cancer patients in time, and further improve the survival rate and prolong the survival of breast cancer patients^[19]. Mishra *et al.* believed that ultrasound radiomics could be used to determine the malignant degree of breast cancer^[20]. With the help of machine learning, a data system can be established to collect ultrasound imaging reports of patients with different types of breast cancer, intelligently analyze the ultrasound imaging characteristics of patients with different types of breast cancer, and compare the ultrasound images of newly admitted patients with images in the database, to find malignant breast cancer patients in time and arrange them for treatment, so as to improve their survival rate. They also proposed the use of machine learning technology to establish a pipeline model, using computer technology to establish a model, analyze, and filter the sampling data, and establish a model based on breast ultrasound image data, so that clinicians can make diagnoses according to breast tumor morphology, texture, and invasive tissue classification, and further improve the treatment effect of NAC in breast cancer^[20].

7. Conclusion

In summary, the research on the application of ultrasound radiomics in the treatment of NAC of breast cancer has gradually increased, and the integration of ultrasound imaging technology and deep machine learning has gradually begun to be explored and has gradually become a hot topic in ultrasound medical research. In order to improve the accuracy of clinical diagnosis and treatment effect of breast cancer, hospitals should actively introduce ultrasound radiomics, carry out monitoring of MRI influence and contrast-enhanced ultrasound, and examine patients' breasts by non-invasive detection, determine the heterogeneity, molecular typing, morphology, and margin of breast tumors, and provide accurate data for subsequent NAC treatment, and arrange chemotherapy regimens reasonably, to further improve the survival rate of breast cancer patients.

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Disclosure statement

The authors declare no conflict of interest.

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