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Роль маммографии в радиомике рака молочной железы

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АННОТАЦИЯ

Маммография — в настоящее время единственный способ скрининга рака молочной железы (РМЖ). Хотя цифровая маммография служит основным и наиболее широкодоступным методом для выявления РМЖ, её эффективность в обнаружении и оценке внутриопухолевой гетерогенности опухоли ограничена. Пункционная биопсия не может отразить гистологической картины опухоли в целом из-за небольшого размера образца ткани или опухоли. По этой причине выбор подходящего лечения и определение прогноза становится затруднительным. В этом случае такой неинвазивный подход, как медицинская визуализация, даёт более полное представление об опухоли, перспективен при «виртуальной биопсии», а также в контроле прогрессирования заболевания и ответа на терапию.

Радиомика с помощью текстурного анализа позволяет взглянуть на снимок как на группу числовых характеристик, выйти за пределы привычного качественного зрительного восприятия интенсивностей и перейти к более глубокому анализу цифровых, пиксельных данных с целью повышения точности дифференциальной диагностики. Метод радиогеномики, являясь естественным продолжением радиомики, фокусируется на определении экспрессии генов исходя из лучевого фенотипа опухоли. В обзоре рассматриваются возможности применения маммографии в радиомике и радиогеномике РМЖ.

В статье представлен обзор литературы баз данных PubMed, Medline, Springer, eLibrary, а также найденных с помощью Google Scholar актуальных российских научных статей. Полученная релевантная информация объединена, структурирована и проанализирована с целью изучения роли маммографии в радиомике РМЖ.

Ключевые слова: рак молочной железы; маммография; радиомика; радиогеномика; искусственный интеллект.

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The role of mammography in breast cancer radiomics

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ABSTRACT

Mammography is still the only screening method for breast cancer. Although digital mammography is the most common and widely used method for detecting breast cancer, it is ineffective at detecting and assessing intratumoral heterogeneity. Due to the small size of the tissue sample or tumor, biopsies often fail to represent the entire tumor. For this reason, selecting a treatment and determining a patient's prognosis becomes difficult. In this case, medical imaging is a noninvasive approach that can provide a more comprehensive view of the entire tumor, act as a "virtual biopsy," and be useful for monitoring disease progression and response to therapy.

Radiomics with texture analysis allows you to look at an image as a group of numerical data, moving beyond the usual visual perception and into a deeper analysis of digital, pixel data to improve the accuracy of differential diagnosis. Radiogenomics is a natural extension of radiomics that focuses on determining gene expression based on radiologic tumor phenotype. The purpose of this review is to evaluate the role of mammography in breast cancer radiomics and radiogenomics.

The article presents a literature review of relevant Russian scientific articles found in databases such as PubMed, Medline, Springer, eLibrary, and Google Scholar. The information obtained was then pooled, structured, and analyzed to examine the role of mammography in breast cancer screening radiomics.

Keywords: breast cancer; mammography; radiomics; radiogenomics; artificial intelligence.

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乳房造影检查在乳腺癌放射学中的作用

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简评

乳房造影检查是目前筛查乳腺癌的唯一方法。尽管数字乳房x线照相术是检测乳腺癌的主要和最广泛可用的方法，但其在检测和评估肿瘤的肿瘤内异质性方面的有效性有限。由于组织样本或肿瘤体积小，穿刺活检不能反映整个肿瘤的组织学图片。由于这个原因，选择适当的治疗方法和确定预后变得复杂。在这种情况下，医学成像这样的非侵入性方法给出了肿瘤的更完整的画面，是有希望的»虚拟活检»，以及用于监测疾病的进展和对治疗的反应。

使用纹理分析的放射学允许您将图像视为一组数值特征，超越通常的定性视觉感知强度，并继续深入分析数字，像素数据，以提高差分诊断的准确性。放射基因组学方法是放射组学的自然延伸，侧重于根据肿瘤的放射表型确定基因的表达。该综述探讨了在乳腺癌的放射组学和放射基因组学中使用乳房造影照相术的可能性。

本文概述了PubMed，Medline，Springer，eLibrary数据库的文献，以及使用Google学术搜索找到的相关俄罗斯科学文章。将获得的相关信息组合，结构与分析，以研究乳房造影照相术在乳腺癌放射组学中的作用。

关键词：乳腺癌;乳房x光检查;放射学;放射基因组学;人工智能。

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BREAST CANCER: RELEVANCE AND CHARACTERISTICS

Breast cancer (BC) is a pressing issue in modern oncology since it ranks first in terms of prevalence among all malignant neoplasms in women [1]. In Russia, the incidence of BC was 89.8 cases per 100,000 female population in 2018 [1]; in 2019, 73,366 breast cancer cases were detected, with 27.7% of patients in stages III and IV [2].

BC is a heterogeneous disease, which means that tumor morphology and expression subtypes differ depending on the receptor status of BC [3, 4]. Further, the expression of the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) determines BC receptor status. The proliferation marker Ki-67 and the epidermal growth factor receptor are also immunochemically stained to determine the molecular subtype of BC [4].

The following are the five molecular subtypes of BC:

1) Luminal A [ER+, PR+ high (≥20%), HER2-, Ki-67 low (≤20%)]: estrogen-dependent low-aggressive tumors with no overexpression of HER2 protein receptors; characterized by high expression of the ER gene
2) Luminal B [ER+, PR+ low (≤20%), HER2-, Ki-67 high]: estrogen-dependent tumors with no overexpression of HER2 protein receptors
3) Luminal B [ER+, HER2+, any Ki-67 level, any PR]: estrogen-dependent aggressive tumors; expressed amplification of the HER2 oncogene; apparent expression of the ER gene
4) HER2 positive [ER- and PR-, any Ki-67, HER2+]: estrogen-independent aggressive tumors; expressed amplification of the HER2 oncogene
5) Triple negative (basal-like): estrogen-independent aggressive tumors with the worst survival rates (ER-, PR-, HER2-) [3–5]

Tumor biology is known to influence the selection of therapy as well as the outcome prognosis, with ER+ and PR+ patients having a longer relapse-free survival ability, while triple-negative BC (TNBC) (ER-, PR-, HER2-) has the most aggressive course and the worst survival rates [3, 6]. The use of biological markers to identify BC subtypes improves patient survival by allowing for more accurate disease diagnosis. For example, patients with ER and PR expression in their tumors should receive endocrine therapy, while patients with HER2 expression should receive anti-HER2 therapy [7].

Intratumoral heterogeneity is defined as the heterogeneity of the morphological structure and the variability in the expression of various markers by individual groups of cells within the same tumor [8, 9]. On the other hand, morphological intratumoral heterogeneity can be defined as diversity in different areas of the tumor, i.e., spatial heterogeneity, or as tumor progression in time, i.e., heterogeneity in time [8]. Due to such heterogeneity of neoplasms and the small size of the puncture tissue sample, the biopsy cannot reflect the histological presentation of the tumor as a whole. Therefore, choosing the appropriate treatment and determining the prognosis becomes difficult. When the tumor is small, biopsies can be difficult. In this case, a noninvasive approach such as medical imaging provides a more consistent view of the tumor and holds promise for "virtual biopsy," as well as monitoring disease progression and response to therapy [7, 10–12].

EARLY DIAGNOSTICS OF BREAST CANCER AND PREDICTION OF THE OUTCOME OF THERAPY

Cancer detection at an early stage is an effective method to reduce patient mortality [13]. Mammography is still the only method for screening and diagnosing BC [10]. Although digital mammography is the most commonly used method for early detection of BC, its efficiency in detecting findings is limited, and mammography has a lower sensitivity in patients with high mammary gland density (ACR-C and D) [14], since the pathological lesion can be overlapped by fibroglandular structures in the image [15, 16]. Despite the reduced sensitivity in one of the groups of patients, digital mammography currently has the best combination of sensitivity and specificity in diagnostics of BC, but these two indicators vary between 75%–90% and 80%–90%, respectively, depending on the country [15]. In their recent study, O. Demircioglu et al. [17] showed that the interpretation of low-quality images by radiologists with limited experience leads to overdiagnosis and unnecessary painful invasive procedures in roughly half of clinical cases [6, 15, 17].

Recent advances in artificial intelligence (AI) technologies used for image analysis hold promise for detecting tumors and reducing the burden on doctors, evaluating treatment, and monitoring disease progression [6]. However, in BC, the primary tasks of clinical practice and research are early detection of the disease prognosis and prediction of the response to therapy. From this point of view, other applications of AI are possible, such as using texture analysis to determine the cancer subtypes and predict treatment response [6, 18, 19].

The interpretation of images by a radiologist with an assessment of the tumor structure, its relationship to the surrounding tissues, special aspects of the location, and structure of microcalcifications are all part of the mammographic study analysis. To create truly personalized therapy, a quantitative (objective) assessment of the lesion is also required [6].

Intratumoral heterogeneity is important for accurate diagnosis, clinical prognosis (response to treatment, survival rate, disease progression, etc.), and treatment of oncological diseases [20, 21]. Early detection of tumor resistance to therapy is critical for improving outcomes, allowing for timely treatment regimen changes [6].

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Thus, there is a need to improve the efficiency of detection, prediction of outcome, and response to treatment of BC. A unique set of techniques, combined in radiomics and radiogenomics, is gaining traction as a tool for maximizing the information that can be extracted from virtually any modality of digital medical imaging [15].

RADIOMICS AND RADIOGENOMICS

Radiation diagnostic images contain information that indicates pathophysiological processes, and this relationship can be identified using quantitative image analysis [22]. To put it another way, tumor characteristics at the cellular and genetic levels are reflected in the phenotypic patterns of the tumor, which can be manifested and detected in images [23].

Radiomics is a process that includes the stages of preparation and subsequent quantitative analysis of multidimensional data obtained from digital medical images (the "omic" suffix appears in the names of molecular biology fields that deal with large amounts of data [24]). Radiomics is defined as image analysis that uses specific algorithms to extract numerical characteristics of images in order to create classification models to improve medical decision-making support, as well as to determine the disease prognosis [25, 26] and treatment [27], which is especially significant for personalized therapy. In radiomics, one area of interest in an image is used to obtain a set (sometimes tens or hundreds) of numerical characteristics, each of which can hold a certain information and theoretical aspect (often referred to as a "radiomic sign"), which is not available in normal viewing of images [15]. Radiomics transforms medical imaging data into a dataset of order statistics by using automatic texture sign extraction algorithms for digital medical images [28]. In other words, radiomics with the use of texture analysis allows you to think of an image as a collection of numerical characteristics, go beyond the usual visual perception, and analyze multidimensional data.

Radiogenomics is a technology that connects a patient's genotype to an imaging phenotype. It should be noted that the term "radiogenomics" can also refer to genetic variability and its relationship with response to radiation therapy [29, 30], but it is more often used to assess the relationship between the image characteristics of a tumor or any other disease and its gene expression patterns and gene mutations [25, 26].

Radiogenomics is a method for determining gene expression in a tumor based on its radiation phenotype. This is important because tumors are heterogeneous, and radiomics data are extracted from the region of interest (tumor) as a whole rather than from a separate sample [22]. Radiogenomics also allows for the assessment of treatment response that is not solely based on the traditional measurement of tumor size over time [25]. The combination of radiomics and radiogenomics can detect gene abnormalities in images [6]. Radiomics and radiogenomics improve the accuracy of clinical diagnosis and have prognostic value by identifying relationships between various types of clinical data [22].

STAGES OF RADIOMICS

When considering radiomics as a process, several major stages can be distinguished, namely, image acquisition, highlighting the area of interest, extraction of radiomic signs from the area of interest (texture analysis of images), analysis of textural signs, and construction of various prediction and classification models using the obtained radiomic data with the option of including additional information (e.g., clinical, demographic, or genomic data; the presence of comorbid conditions) [22, 23, 31]. The stages of radiomics are depicted in Fig. 1, and their more detailed characteristics are discussed further below:

1. Determination of the clinical problem and ***acquisition of digital medical images***, excluding low-quality studies.

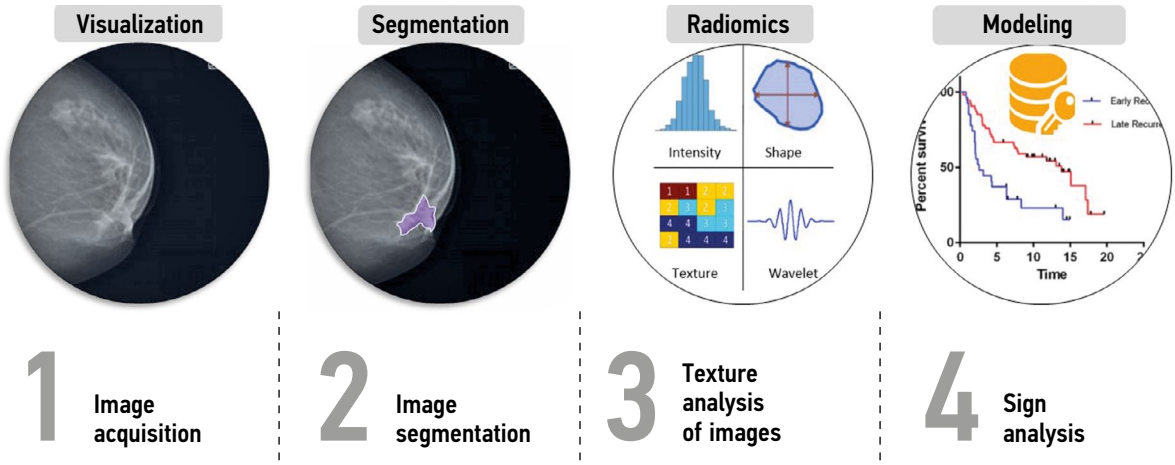

Fig. 1. The diagram illustrates the typical stages in radiomics. After obtaining medical images (1), they are manually or automatically segmented (2). Using special software or programming language modules, radiomic signs of the first and higher orders are extracted from segmented regions of interest (3). Next, the analysis and selection of the most significant textural signs obtained are carried out. Finally, based on the analyzed radiomic data, various clinical and diagnostic models of classification or prediction are constructed (4)

2. ***Segmentation of images*** to the main analyzed areas of interest [32], such as a malignant neoplasm, to assess intratumoral heterogeneity. Many tumors have indistinct boundaries, which complicates the reproducibility of their segmentation [33]. Although it is preferable to use semiautomatic or fully automatic selection of the area of interest using special software, in some cases, expert specification and manual selection are required [23, 34]. The selection process of the region of interest is not standardized, and the region of interest may contain the entire tumor or some of its parts [35, 36]. Manually determining the region of interest is time-consuming and variable due to differences in image interpretation by different radiologists [33], which ultimately affects the accuracy of the radiomic models constructed; however, modern deep learning technologies using big data are capable of mitigating this effect [37].

3. ***Extraction of a variety of radiomic signs*** from a segmented region of interest using mathematical operations involving numerical values of intensities and relative positions of pixels or voxels in images. The extracted quantitative signs are classified into two categories: morphological signs (volume and shape) and histogram signs (description of the intensity of gray tone levels) of the first, second, and higher orders [26, 34].

Morphological signs reflect the shape of the region of interest. For planar images, 2D signs of shape are relevant, such as the perimeter-to-surface ratio and roundness as a measure of the approximation of the shape of the region of interest to the shape of a circle. For example, a stellate tumor will have a higher surface-to-volume ratio than a round tumor [31].

First-order histogram signs [38] indicate the distribution of gray-level intensities for pixels in the region of interest. The most common signs (mean and median) in this category indicate the width of the range of intensities; entropy is a measure of irregularity in the distribution of intensities (higher values indicate a more heterogeneous region) [39]. However, first-order statistics do not account for the spatial arrangement of pixels.

Second-order histogram signs [38], also known as texture signs, indicate the spatial relationship between two adjacent pixels with the same or different brightness values. The most common technique for extracting texture signs is based on a gray-level co-occurrence matrix, which is a matrix whose rows and columns represent gray intensity-level values; the matrix cells indicate the number of times the corresponding gray values are in a certain relationship (angle and distance between the pixels analyzed). For example, signs obtained by using such a matrix include second-order entropy, which indicates heterogeneity; energy, which describes image homogeneity; and contrast range, which determines the local change in intensities [10]. In radiomics, texture analysis provides information on the measure of intratumoral heterogeneity [22, 40].

Figure 2 shows a comparison of the histogram signs of the first and second orders, as well as the formation of the adjacency matrix of the gray tone level, where Fig. 2 (*a*) presents two original images, Fig. 2 (*b*) histograms of the

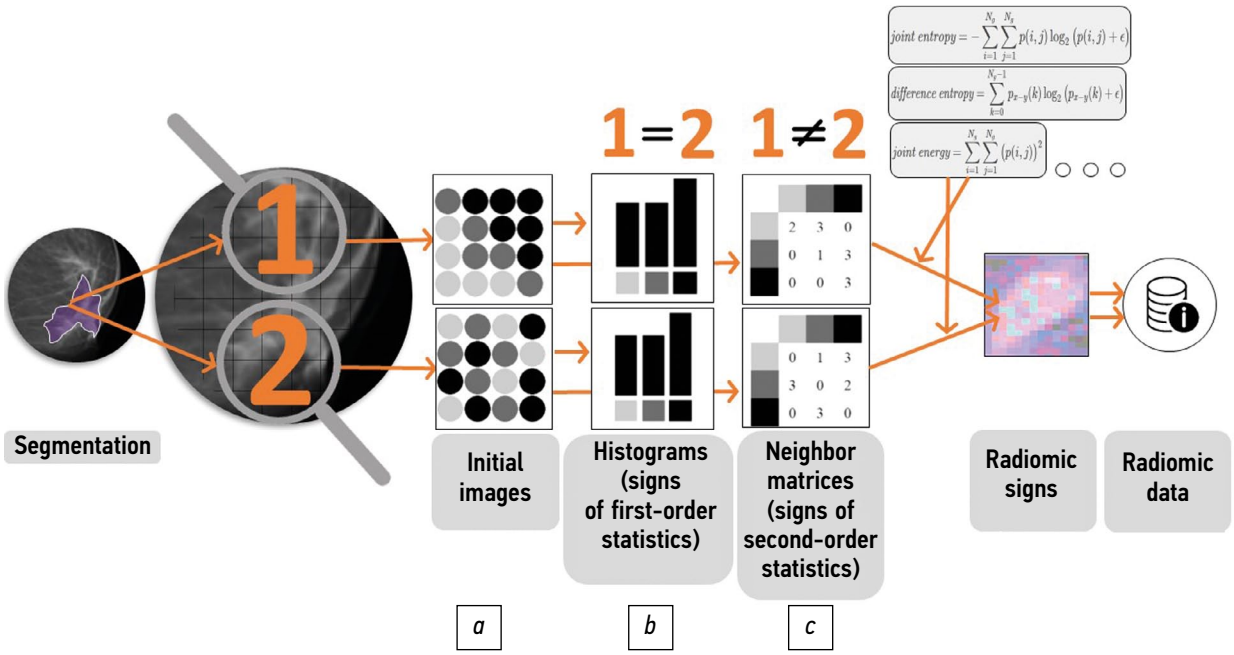

Fig. 2. Comparison of histogram signs of the first and second orders. The two different initial regions of interest of the segmented image (*a*) comprise an equal number of pixels in light gray, dark gray, and black shades. Brightness histograms based on the number of pixels of certain shades (histogram signs of the first order) are the same (*b*). These signs do not indicate the mutual arrangement of the pixels. Adjacency matrices (second-order histogram signs) reflect the heterogeneity of images (*c*). In the future, mathematical algorithms derived from the obtained histograms of intensities and adjacency matrices of the gray level will be used to calculate a variety of radiomic signs for analysis and modeling

first order, and Fig. 2 (*c*) grayscale adjacency matrices obtained for the original images. The row and column headings of these matrices contain the shade of gray numbers. Each cell of the table contains the number of horizontal pairs of pixels, in which pixels with the shade indicated in the header of the row and column of this cell are located relative to each other at an angle of 0º [41]. Subsequently, mathematical algorithms from the obtained histograms of intensities and adjacency matrices of the gray level are used to calculate a set of radiomics signs for analysis and modeling.

4. ***Analysis and modeling***: the radiomic signs obtained, depending on the question posed, can be analyzed in various ways, ranging from statistical models to machine learning methods.

Given the large amount of data extracted from the images, step 1 is selection or reduction of signs. Irreproducible signs should be excluded, since they most probably lead to false results of the models constructed [42, 43].

Step 2 is multivariate data analysis [31] and the construction of models classified into three main groups: predictive, explanatory, and descriptive [15]. Descriptive models are used to obtain a broad representation of each sign, summarizing its key characteristics. Thus, explanatory methods often used for biomedical data frequently focus on the ability of the model to establish a relationship between a sign and an outcome, such as the relationship between the texture characteristics of the gray-level coincidence matrix and the morphological type of BC within the region of interest. Further, machine learning methods are used to create predictive models, which analyze the probability of certain outcomes based on the input data obtained [15], such as a radiomic model for predicting the lack of response to neoadjuvant BC chemotherapy. Before using the models in clinical settings, the quality and reproducibility of the results of operation obtained should be assessed [31].

EXPERIENCE, POSSIBILITIES, AND PROSPECTS FOR USING MAMMOGRAPHY IN RADIOMICS AND RADIOGENOMICS OF BREAST CANCER

Recognition of a malignant neoplasm

The most difficult and crucial step in mammography is classifying mammogram findings as benign or malignant [44]. In their recent study, N. Mao et al. [45] demonstrated that using quantitative signs in conjunction with AI can provide greater diagnostic efficiency when using mammography compared to the efficiency of diagnostics performed by experienced radiologists [15].

The process of classifying microcalcifications as benign or malignant based on images is still a difficult task for radiologists [46]. When suspicious calcifications are detected, texture analysis of images can be performed in conjunction with AI methods, potentially reducing the number of unnecessary biopsies [47, 48].

Specific features of the mammary gland parenchyma may reflect biological risk factors for BC. H. Li et al. [49] showed that using textural signs extracted from mammograms of the affected and contralateral (with normal parenchyma) glands improves the accuracy of digital mammography in the diagnosis of BC. Studies reveal that radiomics with high sensitivity and specificity can distinguish between malignant and benign mammary gland neoplasms [50].

Definition of BC subtypes

Recent radiogenomics studies have confirmed the relationship between MR signs of BC imaging and molecular subtypes, namely, luminal A, luminal B, HER2, and TNBC [51]. Although mammography images provide less information than magnetic resonance imaging (MRI), several studies are currently underway to demonstrate the potential of mammography in radiomics and radiogenomics of BC. In their study, W. Ma et al. [10] demonstrated the possibility of predicting the molecular subtype of BC by extracting radiomic characteristics from mammographic images. The most significant signs were roundness, concavity, mean gray value, and correlation. The results revealed that luminal subtypes and TNBC have distinct textural signs, in contrast to other subtypes, which allow them to be quantitatively distinguished using radiomics.

In some BC patients, the use of neoadjuvant chemotherapy does not provide an effective therapeutic response, resulting in delayed surgery, poor prognosis, and increase in treatment costs. Moreover, the use of radiomics in conjunction with independent clinical risk factors (e.g., Ki-67 index, HER2 status) has been shown to improve the predictive model of nonresponse to neoadjuvant chemotherapy [52].

Early detection of a more aggressive subtype of BC, namely, TNBC, using medical imaging will allow clinicians to prescribe treatment prior to definitive biopsy confirmation [53]. In a study by H.X. Zhang et al. [53], TNBC had greater roundness and concavity compared to other subtypes; the area under the ROC curve (receiver operating characteristic curve; classic ROC curve, a graph of sensitivity versus specificity [54]) was used to assess the accuracy of these two signs in differentiating TNBC from other BC subtypes and was greater than 0.70 [53, 55]. In this study, the skewness coefficient (a histogram attribute reflecting the skewness of the distribution of values relative to the mean) of all subtypes was less than 0 (negative or left-sided skewness). Further, the asymmetry coefficient of TNBC was found to be lower than the coefficients of the other subtypes under study. Therefore, the above radiomic signs can be considered as potential markers of differences between TNBC and other subtypes of BC in the future [53].

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Predicting the development of BC and the possibility of personalized screening

Radiomics-based technologies can help advance personalized screening by developing tools for individual risk assessment and including them in decision-making support tools for mammographic screening, as well as individual screening intervals [56–58]. A higher density of mammary glands has been linked to an increased risk of BC development [59]. The term "density" refers to the degree of attenuation of X-ray radiation as it passes through the gland and reflects the distribution of fibroglandular tissue. However, the definition of density alone does not represent the entire complexity of the gland structure. Image-derived textural signs have been proposed as markers of changes in the parenchyma, indicating a link to the development of BC [57, 59]. In their study, D. Kontos et al. [59] (2019) identified radiomic phenotypes on mammograms that reflect the complexity of the parenchyma (in addition to density) and are independently associated with BC. In contrast to the conventional definition of density, textural signs indicated a subtler and more localized complexity of the parenchymal pattern. The density of the mammary glands differed between the phenotypes of low and medium complexity of the parenchyma but was similar for the other phenotypes. There are interesting data on the phenotype with the least complexity (parenchyma complexity) in women with high mammary gland density due to their greater homogeneity, whereas the phenotype with low and medium parenchyma complexity included a small number of high-density images [59].

Preoperative detection of axillary lymph node metastases

BC metastases are most commonly found in the axillary lymph nodes. Axillary lymph node status is an important factor in determining overall and relapse-free survival in BC patients [60]. An accurate preoperative determination of the status of the axillary lymph nodes can provide doctors with information that allows them to decide whether or not to perform lymphadenectomy and prescribe adjuvant therapy. Currently, the status is determined by biopsy of the sentinel lymph node, which can lead to complications, such as damage to blood vessels and nerves, as well as the development of lymphedema; and diagnostics using imaging methods has a low sensitivity [60]. J. Yang et al. [60] developed a model that includes radiomic signs extracted from mammograms, which can be used as a noninvasive method for determining metastases in the axillary lymph nodes prior to surgery when combined with additional clinical and pathological information.

LIMITATIONS ON THE APPLICATION OF RADIOMICS

Although radiomics and radiogenomics hold great promise for the advancement of personalized medicine, they must be validated on an independent dataset to confirm their diagnostic and predictive value. It will take time for these technologies to gain significant practical value in cancer research and even more time before they can be applied in clinical practice. These limitations are due to the fact that the available large amounts of data do not currently contain the full characteristics of patients [6]. The complexity of the reproducibility of radiomics results is associated with disadvantages at each stage, namely, different textural signs are obtained on different equipment and visualization protocols [61, 62]; the gold standard for manual tumor segmentation is time-consuming and operator-dependent [63]; semiautomatic and automatic segmentations, which reduce variability [64, 65], are not standardized; there is obvious repeatability between texture signs, necessitating the reduction of the size of the data [66, 67]; and there is no clear explanation of the relationship between the unit of radiomics (the basic unit of the texture) and human tissues. Furthermore, any "meaningful" research results obtained should be reviewed when the underlying theory is unclear and technical methods are not standardized [68].

PROSPECTS FOR USING MAGNETIC RESONANCE IMAGING IN BREAST CANCER RADIOMICS

Convincing evidence have been accumulated that MRI of the mammary glands is superior in diagnostic accuracy to traditional diagnostic methods such as mammography [69]. Aside from detecting more cases of duct carcinoma in situ, MRI of the mammary glands often changes the stage of the oncological process, which helps to optimize the treatment process.

It has been established that radiomic signs extracted from MR images of mammary glands indicate tumor heterogeneity and vascularization [70], as well as enable to differentiate duct carcinoma from a benign focus [71]. Existing radiomic models continue to lag behind expert mammologists in terms of area under the curve for differentiating benign from malignant lesions [72]. However, promising results in identifying suspicious (BI-RADS 4 and 5) lesions using diffusion-weighted imaging radiomics have been obtained [73].

Radiomics appears to be capable of assisting in clinical decision-making while avoiding potentially invasive interventions in the armpit. Two different studies have shown that the radiomic model can predict sentinel lymph node metastases [74, 75], which is extremely important in clinical practice.

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Another application of radiomics is associated with the Ki-67 proliferation index, which is used as a prognostic marker in BC [72]. Recent studies have investigated the possibility of predicting the expression of the Ki-67 proliferation marker using radiomics of a series of dynamic contrast enhancements [76–79].

CONCLUSION

One of the key concepts in radiomics is that ray diagnostic images contain data that can provide more information about the region of interest than previously believed. Mammography is the most effective method for early detection of BC. Mammographic images can be used for radiomic analysis, which can be used to identify malignant neoplasms, BC subtypes, disease progression, and response to treatment.

Radiomics-based technologies, such as in the field of mammography, may be incorporated into medical decision-making support tools in the future to determine strategies for individual screening, follow-up, and possibly preventive therapy. However, it should be noted that radiomics is still in its early stages of development, with much more research needed before clinical application.

Radiomics mammography provides important diagnostic and prognostic information about BC, which has the potential to reduce the need for invasive and often complicated procedures. Although radiomics-based techniques will not replace biopsy in the near future, pending support with new research, the integration of radiomics and radiogenomics into clinical practice will be one of the most important and promising tasks in achieving the goal of reducing BC mortality.

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