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Review paper

The role of magnetic resonance imaging (MRI) in breast cancer molecular subtypes

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Abstract

Breast cancer heterogeneity is crucial for treatment decision-making and prognosis prediction. Magnetic resonance imaging (MRI) is a key tool in breast imaging, providing a non-invasive assessment of morphological characteristics, cell density, hemodynamics, and vascular proliferation. Integrating MRI with advanced techniques such as radiomics, habitat imaging, and artificial intelligence enables a deeper understanding of tumor morphology and biological behavior through analysis of imaging features, thereby characterizing the heterogeneity inherent in breast cancer. This review explores MRI's role as an imaging biomarker for evaluating breast cancer molecular subtypes, aiming to support personalized treatment strategies and improve therapeutic outcomes.

Key words: breast cancer, heterogeneity, molecular subtype, magnetic resonance imaging, habitat imaging, radiomics.

Introduction

Breast cancer shows significant heterogeneity, driven by various genetic alterations in breast epithelial cells, leading to diverse disease manifestations in individual patients [1]. These differences are vital for choosing effective treatments and improving patient outcomes. Early detection and careful treatment selection are crucial for improving patient survival and quality of life.

Magnetic resonance imaging (MRI) not only provides anatomical details but also reveals the tumor microenvironment, including angiogenesis, cellular density, and perfusion patterns [2,3]. Advances in MRI technology have significantly improved its accuracy and expanded its applications in medical diagnosis and research. It is crucial for distinguishing between benign and malignant breast lesions and evaluating molecular subtypes. Radiomics is a non-invasive technique that links tumor physical state with radiological features by extracting quantitative tumor characteristics [4-7]. Habitat imaging further identifies unique tumor subregions with distinct imaging characteristics, each representing a microenvironment with shared genetic and phenotypic traits, thereby reflecting the intra-tumor heterogeneity [8-10]. In recent years, artificial intelligence (AI)-based methods have shown superior capability in capturing complex imaging patterns and predicting molecular subtypes with improved diagnostic performance.

A comprehensive understanding of breast cancer's intrinsic molecular subtypes is fundamental to addressing its heterogeneity. Evaluating these subtypes is not only of academic interest but also essential for guiding personalized treatment strategies and predicting disease progression. This review explores the potential of MRI as an imaging biomarker in distinguishing benign from malignant breast tumors and assessing molecular subtypes, aiming to facilitate individualized treatment approaches and improve clinical outcomes.

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Authors' contribution:

A Study design · **B** Data collection · **C** Statistical analysis · **D** Data interpretation · **E** Manuscript preparation · **F** Literature search · **G** Funds collection

Breast cancer heterogeneity

Breast cancer exhibits substantial diversity due to genetic mutations in mammary cells, resulting in variations in appearance, symptoms, and clinical outcomes [1]. Key factors such as tumor characteristics, hormone receptors, human epidermal growth factor receptor 2 (HER2) expression, and Ki-67 index, along with genetic analysis, classify breast cancer into distinct molecular subtypes: luminal A, luminal B, HER2-enriched, and basal-like/triple-negative breast cancer (TNBC) [11].

Inter-tumor heterogeneity, which varies among patients, significantly influences treatment decisions and clinical outcomes. Intra-tumor heterogeneity refers to the presence of diverse phenotypic and genetic tumor cell populations within a single tumor, affecting treatment response and resistance to chemotherapy and other systemic therapies. If the more biologically active regions of the tumor exhibit resistance, disease progression may occur, adversely impacting treatment efficacy and patient survival [12]. Both inter- and intra-tumor heterogeneity arise from intrinsic factors such as genetic, genomic, and epigenomic alterations, as well as cellular behaviors. Additionally, extrinsic factors, including microenvironmental influences such as hypoxia, vascularization, cancer-stromal interactions, and immune responses, further contribute to tumor heterogeneity [1,13].

Accurately assessing tumor heterogeneity over time is essential for personalized treatment strategies. This begins with evaluating molecular subtypes in newly diagnosed breast cancer patients through a comprehensive assessment encompassing pathology, molecular biology, imaging, and clinical characteristics. Although these approaches aid in subtype classification, they are not without challenges and limitations.

Molecular biology methods for distinguishing breast cancer subtypes

Gene expression profiling is the gold standard for identifying breast cancer molecular subtypes. This technique quantifies messenger RNA levels to elucidate gene expression patterns, providing insights into tumor cell biology, including growth, differentiation, invasion, and metastasis [14]. However, multi-gene testing faces several challenges – it requires fresh tissue samples, is time-consuming, and entails high costs, limiting its widespread clinical application [15].

Given these limitations, immunohistochemical analysis has become a widely used alternative for characterizing breast cancer subtypes. This method classifies tumors based on protein receptor expression, particularly estrogen receptor (ER), progesterone receptor (PR), HER2, and Ki-67 levels [16]. However, immunohistochemistry also presents challenges, including the need for invasive tissue sampling and potential sampling errors associated with core needle biopsy. Variability in receptor status reporting across laboratories and the risk of compromising tumor tissue integrity during specimen processing further complicate analysis. Additionally, the absence of standardized protocols and inter-observer variability among pathologists may further limit its reliability and reproducibility [12,17].

MRI for distinguishing breast cancer molecular subtypes

MRI offers superior soft tissue resolution and multiparametric imaging, making it a key tool in breast cancer diagnosis, staging, and treatment evaluation. Compared to other imaging modalities, MRI provides clearer visualization of breast anatomy and lesions, particularly in dense breast tissue and complex cases. It integrates morphological, functional, and metabolic information, aiding early detection, precise localization, and subtype classification.

In clinical practice, MRI stands out among imaging techniques by offering both anatomical and functional insights, including blood flow and metabolism, making it effective in assessing intra-tumoral and peritumoral regions [18]. Traditional MRI parameters, such as volume transfer constant, rate constant, and apparent diffusion coefficient (ADC), may not fully capture tumor heterogeneity.

Recent advances, including radiomics and habitat imaging, enhance MRI's ability to quantify tumor complexity. These techniques provide deeper insights into tumor structure and biology, improving molecular characterization, guiding personalized treatment, and aiding prognosis.

Dynamic contrast enhancement MRI

Angiogenesis, particularly neoangiogenesis, plays a key role in tumor growth, progression, and metastasis. Neoangiogenesis refers to the abnormal development of tumor-induced microvessels under the stimulation of pro-angiogenic factors such as vascular endothelial growth factor, ultimately giving rise to vessels with irregular structure and impaired function [19]. These abnormal blood vessels are closely related to tumor aggressiveness and result in characteristic enhancement patterns on imaging [2].

Dynamic contrast enhancement MRI (DCE-MRI) is significant in evaluating tumor neoangiogenesis, as it captures enhancement patterns that reflect the density, permeability, and architecture of newly formed microvessels. It allows for non-invasive and dynamic evaluation of tissue perfusion and vascularity in breast cancer, offering insights into lesion morphology, spatial distribution, and vascular behavior [20]. However, variability in imaging protocols, patient populations, and radiologist expertise affects its specificity and sensitivity. Continuous technological advancements are essential to improve diagnostic accuracy.

Semi-quantitative analysis

DCE-MRI aids breast cancer diagnosis by analyzing contrast kinetics and enhancement patterns. Time-intensity curves (TICs) – classified as wash-in, plateau, or wash-out – differentiate malignancies (rapid enhancement followed by contrast clearance, reflecting aggressive neoangiogenesis) [2,21] from benign tumors (gradual wash-in) [3,22]. Semi-quantitative parameters (peak time, signal ratio, area under the curve) derived from TICs further quantify these differences, driven by malignant hypercellularity and leaky vasculature [2,23].

Molecular subtypes exhibit distinct kinetics: HER2-enriched tumors show early rapid clearance due to hypervascularity, while luminal A (frequently associated with in situ lesions) and TNBC (with necrosis/fibrosis) often retain persistent enhancement [24-26]. High Ki-67 tumors favor plateau/wash-out curves [27]. Morphologically, TNBC presents as round/oval rim-enhancing masses, HER2-enriched as spherical, and luminal A/B as spiculated [28,29]. Combining kinetics with morphology improves subtyping, though semi-quantitative metrics lack permeability data and are scanner-dependent [30].

Quantitative analysis

Quantitative analysis uses pharmacokinetic modeling to track contrast agent exchange between plasma and the extracellular space, generating key parameters: transfer constant, rate constant, and extracellular extravascular space fraction. These assess tumor perfusion, neoangiogenesis, and vascular permeability [3,31]. The transfer constant reflects contrast diffusion into the tumor, the extracellular space fraction measures interstitial volume, and the rate constant describes contrast return to plasma [32].

Malignant tumors show higher perfusion, blood volume, and permeability, reducing extracellular space and increasing transfer and rate constants [33]. Benign tumors, with lower vascularity, exhibit slower contrast exchange. Despite high permeability, malignant tumors maintain a stable transfer-to-extracellular space ratio, explaining the debated link between extracellular space fraction and malignancy [34,35].

ER/PR expression negatively correlates with the transfer constant, as ER/PR-positive tumors grow slowly, with less neovascularization. Conversely, ER/PR-negative tumors have higher vascularity and contrast accumulation [35]. The transfer constant correlates with Ki-67 expression, indicating greater vascular differentiation, permeability, and aggressiveness [36].

HER2 status shows no significant impact on transfer constant or extracellular space fraction, likely due to variability in gene amplification [35]. However, HER2-positive tumors grow rapidly, potentially slowing contrast diffusion. TNBC exhibits higher transfer and rate constants, suggesting greater neoangiogenesis and hyperperfusion [37].

While DCE-MRI aids breast cancer assessment, its high sensitivity can lead to false positives and unnecessary biopsies. Advancements are needed to improve accuracy and reliability [38,39].

Ultrafast DCE-MRI

Ultrafast DCE-MRI is an advanced imaging technique that assesses tumor vascular distribution more rapidly than traditional DCE-MRI, significantly reducing scan time and improving efficiency [40]. It is particularly effective in detecting highly vascular lesions, especially in cases where conventional DCE-MRI is affected by background parenchymal enhancement [41]. Unlike traditional methods, ultrafast DCE-MRI does not rely on contrast agent clearance but instead analyzes the time-signal intensity curve to extract kinetic parameters such as maximum slope, enhancement time, and contrast agent arrival time, providing insights into ultra-early inflow dynamics [42].

Subcentimeter tumors and benign lesions often exhibit overlapping MRI kinetic and morphological features. However, ultrafast DCE-MRI excels in distinguishing malignant subcentimeter lesions classified as Breast Imaging Reporting and Data System 4-5, showing higher maximum slope values and shorter contrast agent arrival times compared to benign lesions [43]. Thus, ultrafast DCE-MRI is emerging as a powerful tool in distinguishing between benign and malignant subcentimeter breast tumors, potentially reducing the need for unnecessary biopsies.

The kinetic parameters of ultrafast DCE-MRI correlate closely with histopathological and molecular subtypes. Invasive breast cancer, compared to ductal carcinoma in situ, exhibits higher maximum slope and shorter contrast agent arrival time due to increased vascularity and faster blood flow [44]. More aggressive subtypes, such as TNBC and HER2-enriched tumors, demonstrate even shorter arrival times. Additionally, higher Ki-67 expression is associated with elevated maximum slope values, while tumors with poor prognostic factors tend to show shorter enhancement times and steeper slopes [45,46]. These findings provide valuable insights into breast cancer biology, aiding in diagnosis and classification.

Diffusion-weighted imaging

Diffusion-weighted imaging (DWI) assesses tumor cell density by measuring water molecule movement restriction in the extracellular space. Variations in cell density, extracellular space, and tissue microstructure influence diffusion-weighted signal intensity, providing insights into the tumor's biological characteristics [47].

In clinical practice, ADC values are used to assess water molecule diffusion, reflecting tumor cell and membrane integrity [48]. As cell density increases, extracellular volume decreases, restricting water diffusion and correlating inversely with tumor cell proliferation [38].

High Ki-67 expression indicates greater cell proliferation, leading to denser cell clusters and lower ADC values [48]. HER2-positive tumors show increased neoangiogenesis and blood flow due to vascular endothelial growth factor production, which may reduce diffusion restriction and result in higher ADC values compared to HER2-negative tumors [49]. However, some studies suggest no significant association between receptor status and ADC values [50].

Previous studies have reported overlapping ADC differences among breast cancer subtypes, likely due to variations in imaging techniques and the inclusion of diverse tissue areas in the analysis [51]. Additionally, determining the optimal threshold for ADC values is challenging due to variations in ADC thresholds [52]. Selecting the appropriate b-value is crucial for image quality and ADC accuracy. Higher *b*-values increase DWI specificity but may reduce the signal-to-noise ratio, affecting ADC values [53]. Given the inherent heterogeneity of breast cancer, whole-tumor ADC analysis is preferred over single-layer methods for better subtype differentiation [54].

Intravoxel incoherent motion imaging

Several studies have indicated that the ADC value, derived from a mono-exponential model based on Gaussian water diffusion, is associated with tissue cellularity. However, this model overlooks heterogeneous water diffusion in tissues, resulting in significant overlap of ADC values across different breast lesions [55]. In complex biological environments, water diffusion is influenced by blood microcirculation, leading to non-Gaussian distribution. Advanced diffusion models, such as intravoxel incoherent motion imaging (IVIM) and diffusion kurtosis imaging (DKI), offer a better description of water molecule diffusion in tumors by accounting for blood flow perfusion. IVIM employs a bi-exponential model with varying *b*-values to assess both tissue diffusivity and microvascular perfusion. Lower *b*-values capture tissue and capillary diffusion, while higher b-values provide insights into true water molecule diffusion [56]. IVIM generates three parameters – the true diffusion coefficient, the pseudo-diffusion coefficient, and the perfusion fraction – offering quantitative insights into tissue cellular and vascular conditions without the need for contrast agent injection [57].

Malignant tumors generally have higher cell density than benign lesions, which reduces the extracellular space available for water molecule diffusion, resulting in lower true diffusion coefficient values. On the other hand, malignant tumors often exhibit increased neovascularization, enhancing blood flow perfusion and raising the perfusion fraction [58]. However, distinguishing benign from malignant breast lesions based on the perfusion fraction and the pseudo-diffusion coefficient remains inconsistent. This may be due to the irregular blood flow in malignant lesions, caused by tortuous blood vessels and necrosis, leading to variations in the measurements [59].

HER2-positive tumors show higher perfusion fraction and pseudo-diffusion coefficient values than HER2-negative tumors, indicating increased neoangiogenesis and blood flow, which are consistent with their aggressive characteristics [60]. TNBC, known for its high proliferation and neoangiogenesis, also demonstrates elevated perfusion fraction and pseudo-diffusion coefficient values [61]. However, when TNBC presents with necrosis, central perfusion is reduced, leading to lower values [60]. High Ki-67 expression is associated with dense tissue and restricted water diffusion, suggesting that true diffusion coefficient values may serve as reliable indicators of cell density and proliferation [59]. Additionally, proliferation and neoangiogenesis correlate positively with Ki-67 expression, perfusion fraction, and pseudo-diffusion coefficient values [60]. Using IVIM to measure these parameters could help differentiate breast cancer subtypes.

Diffusion kurtosis imaging

DKI is an advanced diffusion model that reveals complex tissue microstructure through non-Gaussian diffusion patterns, offering a more accurate assessment of tissue complexity compared to conventional DWI. It highlights subtle variations in MRI signal attenuation, providing deeper insight into tissue diversity and water molecule interactions [62]. DKI highlights two key parameters: the mean diffusion coefficient and mean kurtosis coefficient. The mean diffusion coefficient reflects the extracellular space fraction and decreases with restricted diffusion, often due to higher cellularity, tissue disorganization, and reduced extracellular space [63]. The mean kurtosis coefficient measures signal deviation from the Gaussian distribution, indicating tissue complexity, with higher values suggesting increased cellular irregularities [64].

The heterogeneity of breast cancer results in a higher mean kurtosis coefficient and lower mean diffusion coefficient in malignant lesions compared to benign ones [65,66]. An increased mean kurtosis coefficient in malignant tumors indicates that the complex microstructure of heterogeneous breast cancer tissue causes more irregular water molecule diffusion and greater deviation from a Gaussian distribution. Additionally, the mean diffusion coefficient from the non-Gaussian model is higher than the ADC from the conventional mono-exponential model, suggesting that ADC may not fully capture tissue diffusion complexity. In contrast, the mean diffusion coefficient from DKI offers a more complete characterization [65]. These variations in kurtosis and diffusion coefficients help differentiate benign from malignant lesions.

Lesions with high Ki-67 expression, indicating increased cellular proliferation and density, show a positive correlation with the mean kurtosis coefficient and a negative correlation with the mean diffusion coefficient. These lesions typically have higher cellularity and greater necrosis,

restricting water diffusion and increasing tissue complexity [67,68]. Among subtypes, luminal A exhibits the lowest mean kurtosis coefficient, suggesting less intratumoral microperfusion and lower non-Gaussian diffusivity. Luminal B shows a relatively low mean diffusion coefficient, likely due to ER/PR positivity and high Ki-67 expression, which inhibit neoangiogenesis and increase cellularity, restricting water diffusion [69]. HER2 expression is linked to higher cell density and increased blood flow, affecting water molecule movement, though correlations with diffusion parameters are inconsistent due to tumor heterogeneity and measurement variations [67,69,70]. ER expression inhibits vascular generation, reducing blood perfusion and leading to lower mean diffusion coefficients [69].

However, DKI lacks standardized protocols for selecting *b*-values, requiring multiple high *b*-values ($b > 1000$ s/mm^2) to effectively capture diffusion kurtosis. This makes DKI more complex and time-consuming than traditional DWI.

Synthetic MRI

Synthetic MRI (SyMRI) is an advanced quantitative imaging technique that simultaneously measures T1, T2, and proton density in a single scan using a multi-dynamic multi-echo sequence. This technology reduces scan time and improves clinical utility compared to traditional MRI [71]. Tissue magnetic properties, influenced by cellular composition and microstructure, lead to changes in relaxation times. SyMRI can differentiate between benign and malignant breast lesions by capturing T1, T2, proton density, and ADC value changes associated with increased cell density in malignancies [71,72]. Combining SyMRI with DCE-MRI may enhance diagnostic accuracy [73]. Pre-enhancement T1 values differ significantly between benign and malignant masses, with malignant lesions showing higher values. Malignant lesions, with distinct microvascular architecture, exhibit rapid post-contrast signal enhancement. Analyzing T1 and T2 values, both pre- and post-contrast, along with relative changes (ΔT%), helps quantify lesion enhancement and aids in differentiation, as ΔT1% in malignant lesions is significantly higher than in benign ones [74].

TNBC and HER2-enriched breast cancers show increased cell density and elevated vascular endothelial growth factor, promoting angiogenesis. This may explain the higher T1, T2, and post-contrast T2 values observed in these cancers [75,76]. TNBC tumors often exhibit internal necrosis, leading to higher T2 values [75,77], while HER2-enriched cancers, with increased cellularity and angiogenesis, show higher PD values [75]. Elevated cell density may reduce tumor extracellular space and free water content. In contrast, ER-positive breast cancers have lower vascular endothelial growth factor levels and less neoangiogenesis, resulting in lower T1, T2, and pre-contrast T2 values [78]. These insights help inform breast cancer diagnosis and treatment.

MRI radiomics for distinguishing molecular subtypes of breast cancer

Radiomics, an emerging analytical technique, extracts quantitative data from image pixels using mathematical formulas to analyze pixel grayscale and spatial correlations in digital images [79]. It detects microscopic features in tissue, aiding in non-invasive diagnosis, prognosis, and treatment evaluation by characterizing tumors [4]. Unlike biopsies, which may suffer from sampling errors, radiomics captures the heterogeneity of the entire tumor [80]. Radiomics features can be classified into first-order, second-order, higher-order, and wavelet features, with first- and second-order features commonly used for breast cancer characterization.

First-order statistical features, often represented in histograms, summarize the distribution of pixel intensities within the regions of interest (ROI), condensing data into parameters such as mean, median, maximum, minimum, uniformity, entropy, skewness, and kurtosis. These features reveal tumor information that conventional radiological techniques might miss, aiding in the evaluation of tumor heterogeneity [4,81]. However, while histogram analysis helps evaluate molecular subtypes, it simplifies the grayscale intensity distribution and overlooks pixel spatial positioning [80,82].

Second-order statistical features, or "texture features," examine the relationships between adjacent pixel values within the ROI, assessing spatial positions and signal intensities. Texture analysis yielding various quantified parameters such as entropy, energy, angular second moment, inverse difference moment, and correlation are related to lesion heterogeneity, contributing to disease characterization, prognosis, and treatment response evaluation [83,84]. While texture analysis partially captures intra-tumoral heterogeneity, it assumes uniform mixing and does not account for phenotypic differences within regions [85]. Additionally, its lack of standardization and reliance on specialized software and complex post-processing present challenges for clinical implementation.

Radiomics, utilizing various quantitative features from MRI sequences, can develop non-invasive predictive models with high diagnostic accuracy for breast cancer [5-7]. For example, DCE-MRI radiomics features effectively differentiate between subtypes, such as luminal A versus luminal B, luminal B versus TNBC, and HER2-enriched versus other subtypes. Features reflecting lesion structure heterogeneity, such as co-occurrence matrices and geometric shapes, show robust predictive potential [86]. A study found that radiomic signatures derived from tumor segmentation on the ADC map outperformed other methods in identifying molecular subtypes of breast cancer [87]. TNBC, with lower cellularity and higher diffusion, exhibited higher histogram metrics for ADC, IVIM true diffusion coefficients, and DKI coefficients compared to non-TNBC [57].

The size and location of the ROI in breast lesions can influence ADC values and measurement reproducibility [88]. Therefore, first-order histogram analysis of ADC is less effective in predicting molecular subtypes. Many studies rely on ADC measurements from manually delineated ROIs from a single slice of a lesion, which may limit the ability to fully reflect tumor characteristics. Whole-volume radiomics analysis of ADC provides a more reliable approach for assessing heterogeneous breast lesions.

Habitat imaging for distinguishing molecular subtypes

As tumors grow, uncontrolled cell proliferation leads to the formation of unique microenvironments with distinct metabolism, vascular distribution, and cellular arrangement. These changes influence key biological processes such as cell proliferation, cell cycle regulation, and apoptosis, thereby affecting tumor initiation and progression [12]. Tumor cells form intratumoral subregions through interactions between the environment and cellular responses [89]. These subregions, sharing similar environmental conditions, contain cells with comparable genotypes and phenotypes, forming the "habitat" for specific tumor cell types [90]. MRI data, either from individual sequences or multiparametric alignment, can help cluster and partition these habitat subregions. These subregions may show subtle heterogeneity on MRI.

Conventional MRI quantifies the average parameters of the entire ROI using different sequence image data, without considering spatial information. In contrast, habitat imaging partitions and combines image voxels from these MRI sequences into parameterized habitat subregions. These subregions define the tumor microenvironment, reflecting the relative proliferation and reduction of cells and vessels [91]. These habitat subregions are dynamic, changing over time to reflect the tumor's continuous evolution [92]. This method provides a more precise assessment of the tumor's biological properties, revealing intra-tumoral heterogeneity beyond just size and location [93]. Quantifying the volume fraction of each habitat allows for an accurate evaluation of tumor components, making it a sensitive biomarker for monitoring tumor composition changes. Habitat imaging is currently applied in evaluating gliomas and breast cancer. It helps in diagnosing malignancies, assessing therapeutic efficacy, and predicting prognosis with precision [9,10,94,95].

Radiomic features derived from habitat subregions revealed a deeper level of tumor heterogeneity compared to the entire tumor [6]. Researchers segment lesion pixels into three habitat subregions – early, intermediate, and late enhancement – using DCE-MRI peak time values. Extracting radiomic features from these subregions distinguishes luminal from non-luminal breast cancer subtypes, with early enhancement showing the best performance [96]. HER2 2+ status correlates with angiogenesis, and predictive models based on early enhancement offer a sensitive, rapid, user-friendly, and cost-effective way to predict HER2 2+ status [97]. A recent study quantified the degree of kinetic heterogeneity (the proportions of tumor pixels with delayed washout, plateau, and persistent components within a tumor) of breast cancer based on delayed enhancement kinetics derived from computer-aided diagnosis. Compared to the luminal subtype, TNBC displayed heightened kinetic heterogeneity and ADC heterogeneity ($[ADC_{max} - ADC_{min}]/ADC_{mean}$), whereas HER2-enriched exhibited increased dynamic heterogeneity. Furthermore, multivariate analysis revealed significant associations between elevated dynamic heterogeneity and both TNBC and HER2-enriched tumors, while higher ADC heterogeneity was notably associated with the TNBC subtype [91]. Given the overexpression of vascular endothelial growth factor in TNBC and HER2-enriched breast cancer, newly formed blood vessels with irregular structure and abnormal function are generated. These vessels are more permeable than the normal vascular system, potentially leading to spatial heterogeneity.

Acquiring clinically relevant pharmacokinetic parameters typically requires long imaging times. To address this, a study devised hypervascular, hypovascular, and nonviable habitats by extracting semi-quantitative parameters from routine DCE-MRI and DWI sequences, eliminating the need for additional acquisitions [98]. The hypervascular cellular habitat, characterized by low ADC and a high wash-in/wash-out ratio, represents vascularized, cellular-rich tumor components with early contrast enhancement and delayed washout. The volume fraction of hypervascular cellular habitat effectively distinguishes TNBC from non-TNBC patients. In contrast, the nonviable habitat, with high ADC and a low wash-in/wash-out ratio, indicates reduced vascular and cellular distribution, typically reflecting inactive tumor areas. A higher proportion of nonviable habitat is seen in the TNBC group, likely due to a higher necrosis rate in TNBC.

AI in molecular subtyping

AI has rapidly emerged as a transformative tool in medical imaging, offering the ability to extract, integrate, and interpret vast amounts of complex data. Owing to its multiparametric nature, breast MRI provides an ideal dataset for AI-driven analysis. Imaging sequences and techniques such as DCE-MRI, DWI, and radiomics offer diverse information. Processed through machine learning or deep learning algorithms, these data can uncover subtle imaging features and patterns closely associated with tumor biology [99]. AI applications in breast imaging show substantial potential in precision medicine, facilitating objective assessment of tumor heterogeneity and improving non-invasive prediction of molecular subtypes.

Recent advances in deep learning have enabled fully automated classification of breast cancer molecular subtypes using DCE-MRI. A novel framework integrating 3D

ResUNet for lesion segmentation and an ensemble of 2D and 3D ResNet architectures for subtype prediction has demonstrated high accuracy across multiple datasets. Compared with traditional radiomics and earlier 2D/3D CNN models, the proposed method achieved superior performance, particularly for TNBC [100]. Another study highlights the effectiveness of AI-based multiparametric MRI, integrating DCE-MRI and non-mass enhancement DWI via deep neural networks, in classifying breast cancer molecular subtypes. Compared to single-modality approaches, multiparametric MRI significantly improved predictive performance. Global feature-level fusion of deep neural networks outputs enabled robust classification while minimizing overfitting. The findings underscore the value of combining complementary imaging information and deep learning to enhance noninvasive molecular profiling in breast cancer [101]. By extracting and interpreting complex intra- and peri-tumoral features, AI models reveal microenvironmental patterns not discernible through conventional analysis. Recent research demonstrates that AI-driven frameworks incorporating delayed-phase features significantly improve subtype classification accuracy, especially for aggressive phenotypes such as TNBC and HER2-enriched tumors [102]. These findings highlight the potential of AI-enhanced radiomics as a noninvasive, whole-tumor profiling strategy.

Although AI is unlikely to replace invasive tissue sampling, imaging biomarkers hold promise as complementary tools, offering a noninvasive means to extract predictive information from the entire tumor prior to treatment.

Summary and outlook

Clinical MRI applications face challenges, including data inconsistencies across field strengths and manufacturers, complex data interpretation, and the need for improved repeatability. Future research should prioritize increasing sample sizes, standardizing scanning protocols, and refining analysis methods. The integration of emerging technologies, particularly AI-driven analysis, enhances the synergy between radiomics, habitat imaging, and multiparametric MRI. This combination allows for more accurate feature extraction and better tumor assessment, providing deeper insights into tumor heterogeneity and its biological characteristics. Such advancements, driven by AI and emerging imaging technologies, are crucial for enhancing molecular subtype prediction and advancing precision oncology, leading to more personalized breast cancer diagnosis and treatment planning.

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References

1. Lüönd F, Tiede S, Christofori G. Breast cancer as an example of tumour heterogeneity and tumour cell plasticity during malignant progression. Br J Cancer 2021; 125: 164-175.
2. Xiao J, Rahbar H, Hippe DS, Rendi MH, Parker EU, Shekar N, et al. Dynamic contrast-enhanced breast MRI features correlate with invasive breast cancer angiogenesis. NPJ Breast Cancer 2021; 7: 42. DOI: 10.1038/s41523-021-00247-3.
3. Ao F, Yan Y, Zhang ZL, Li S, Li WJ, Chen GB. The value of dynamic contrast-enhanced magnetic resonance imaging combined with apparent diffusion coefficient in the differentiation of benign and malignant diseases of the breast. Acta Radiol 2021; 63: 891-900.
4. Mayerhoefer ME, Materka A, Langs G, Häggström I, Szczypiński P, Gibbs P, Cook G. Introduction to radiomics. J Nucl Med 2020; 61: 488-495.
5. Guo Y, Kong QC, Li LQ, Tang WJ, Zhang WL, Ning GY, et al. Whole volume apparent diffusion coefficient (ADC) histogram as a quantitative imaging biomarker to differentiate breast lesions: correlation with the Ki-67 proliferation index. Biomed Res Int 2021; 2021: 4970265. DOI: 10.1155/2021/4970265.
6. Parekh VS, Jacobs MA. Multiparametric radiomics methods for breast cancer tissue characterization using radiological imaging. Breast Cancer Res Treat 2020; 180: 407-421.
7. Fan W, Sun W, Xu MZ, Pan JJ, Man FY. Diagnosis of benign and malignant nodules with a radiomics model integrating features from nodules and mammary regions on DCE-MRI. Front Oncol 2024; 14: 1307907. DOI: 10.3389/fonc.2024.1307907.
8. Kim JY, Kim JJ, Hwangbo L, Lee JW, Lee NK, Nam KJ, et al. Diffusion-weighted MRI of estrogen receptor-positive, HER2-negative, node-negative breast cancer: association between intratumoral heterogeneity and recurrence risk. Eur Radiol 2020; 30: 66-76.
9. Tar PD, Thacker NA, Babur M, Lipowska-Bhalla G, Cheung S, Little RA, et al. Habitat imaging of tumors enables high confidence sub-regional assessment of response to therapy. Cancers (Basel) 2022; 14: 2159. DOI: 10.3390/cancers14092159.
10. Kazerouni AS, Hormuth DA 2nd, Davis T, Bloom MJ, Mounho S, Rahman G, et al. Quantifying tumor heterogeneity via MRI habitats to characterize microenvironmental alterations in HER2+ breast cancer. Cancers (Basel) 2022; 14: 1837. DOI: 10.3390/cancers-14071837.
11. Jeibouei S, Akbari M E, Kalbasi A, Aref AR, Ajoudanian M, Rezvani A, Zali H. Personalized medicine in breast cancer: pharmacogenomics approaches. Pharmacogenomics Pers Med 2019; 12: 59-73.
12. Ramón Y Cajal S, Sesé M, Capdevila C, Aasen T, De Mattos-Arruda L, Diaz-Cano SJ, et al. Clinical implications of intratumor

heterogeneity: challenges and opportunities. J Mol Med (Berl) 2020; 98: 161-177.
13. Vitale I, Shema E, Loi S, Galluzzi L. Intratumoral heterogeneity in cancer progression and response to immunotherapy. Nat Med 2021; 27: 212-224.
14. Tendl KA, Bago-Horvath Z. Molecular profiling in breast cancer – ready for clinical routine? memo – Magazine of European Medical Oncology 2020; 13: 445-449.
15. Hasan AM, Al-Waely NKN, Aljobouri HK, Jalab HA, Ibrahim RW, Meziane F. Molecular subtypes classification of breast cancer in DCE-MRI using deep features. Expert Systems with Applications 2024, 236: 121371. DOI: https://doi.org/10.1016/j.eswa.2023.121371.
16. Adani-Ifè A, Amégbor K, Doh K, Darré T. Breast cancer in togolese women: immunohistochemistry subtypes. BMC Womens Health 2020; 20: 261. DOI: 10.1186/s12905-020-01130-2.
17. Stevanovic L, Choschzick M, Moskovszky L, Varga Z. Variability of predictive markers (hormone receptors, Her2, Ki67) and intrinsic subtypes of breast cancer in four consecutive years 2015-2018. J Cancer Res Clin Oncol 2019; 145: 2983-2994.
18. He X, Wang Z, Zhou Y, Feng Y. The value, diagnostic efficacy and clinical significance of functional magnetic resonance imaging in evaluating the efficacy of neoadjuvant chemotherapy in patients with triple negative breast cancer. Front Oncol 2023; 13: 1132186. DOI: 10.3389/fonc.2023.1132186.
19. Fukumura D, Jain RK. Tumor microvasculature and microenvironment: targets for anti-angiogenesis and normalization. Microvasc Res 2007; 74: 72-84.
20. Leithner D, Wengert GJ, Helbich TH, Thakur S, Ochoa-Albiztegui RE, Morris EA, Pinker K. Clinical role of breast MRI now and going forward. Clin Radiol 2018; 73: 700-714.
21. Xue F, Meng Y, Jiang J. Diagnostic value of dynamic enhanced magnetic resonance imaging combined with serum CA15-3, CYFRA21-1, and TFF1 for breast cancer. J Healthc Eng 2022; 2022: 7984591. DOI: 10.1155/2022/7984591.
22. Karavas E, Ece B, Aydın S. Type 2 dynamic curves: a diagnostic dilemma. World J Radiol 2022; 14: 229-237.
23. Galati F, Rizzo V, Trimboli RM, Kripa E, Maroncelli R, Pediconi F. MRI as a biomarker for breast cancer diagnosis and prognosis. BJR Open 2022; 4: 20220002. DOI: 10.1259/bjro.20220002.
24. Seyfettin A, Dede I, Hakverdi S, Düzel Asıg B, Temiz M, Karazincir S. MR imaging properties of breast cancer molecular subtypes. Eur Rev Med Pharmacol Sci 2022; 26: 3840-3848.
25. Pinker K, Shitano F, Sala E, Do RK, Young RJ, Wibmer AG, et al. Background, current role, and potential applications of radiogenomics. J Magn Reson Imaging 2017; 47: 604-620.
26. Bergholtz H, Lien TG, Swanson DM, Frigessi A; Oslo Breast Cancer Research Consortium (OSBREAC); Daidone MG, Tost J, Wärnberg F, Sørlie T. Contrasting DCIS and invasive breast cancer by subtype suggests basal-like DCIS as distinct lesions. NPJ Breast Cancer 2020; 6: 26. DOI: 10.1038/s41523-020-0167-x.
27. Tuan Linh L, Minh Duc N, Tra My TT, Viet Bang L, Minh Pham T. Correlations between dynamic contrast-enhanced magnetic resonance imaging parameters and histopathologic factors in breast cancer. Clin Ter 2021; 172: 453-460.
28. Moffa G, Galati F, Collalunga E, Rizzo V, Kripa E, D'Amati G, Pediconi F. Can MRI biomarkers predict triple-negative breast cancer? Diagnostics (Basel) 2020; 10: 1090. DOI: 10.3390/diagnostics-10121090.
29. Du S, Gao S, Zhang L, Yang X, Qi X, Li S. Improved discrimination of molecular subtypes in invasive breast cancer: comparison of multiple quantitative parameters from breast MRI. Magn Reson Imaging 2021; 77: 148-158.
30. Huang Y, Zheng C, Zhang X, Cheng Z, Yang Z, Hao Y, Shen J. The usefulness of bayesian network in assessing the risk of triple-negative breast cancer. Acad Radiol 2020; 27: e282-e291. DOI: https://doi.org/10.1016/j.acra.2019.12.023.
31. Lai T, Chen X, Yang Z, Huang R, Liao Y, Chen X, Dai Z. Quantitative parameters of dynamic contrast-enhanced magnetic resonance imaging to predict lymphovascular invasion and survival outcome in breast cancer. Cancer Imaging 2022; 22: 61. DOI: 10.1186/s40644-022-00499-7.
32. Kazama T, Takahara T, Hashimoto J. Breast cancer subtypes and quantitative magnetic resonance imaging: a systemic review. Life (Basel) 2022; 12: 490. DOI: 10.3390/life12040490.
33. Shao Y, Bao X, Song C, Cui D. Application of dynamic enhanced magnetic resonance imaging in the diagnosis of hematological malignancies. J Healthc Eng 2021; 2021: 4623850. DOI: 10.1155/2021/4623850.
34. Li X, Fu P, Jiang M, Zhang J, Tan L, Ai T, Li X. The diagnostic performance of dynamic contrast-enhanced MRI and its correlation with subtypes of breast cancerJ]. Medicine (Baltimore) 2021; 100: e28109. DOI: 10.1097/MD.0000000000028109.
35. Cheng X, Chen C, Xia H, Zhang L, Xu M. 3.0 T magnetic resonance functional imaging quantitative parameters for differential diagnosis of benign and lesions of the breast. Cancer Biother Radiopharm 2021; 36: 448-455.
36. Setiawan K, Suryawisesa IB, Widiana IK, Sudarsa IW. Does a 40% cut-off point for ki-67 expression have a role in identifying the development of distant metastasis within 2 years in locally advanced triple negative breast cancer patients? Eur J Breast Health 2023; 19: 274-278.
37. Li A, Pan Y, Chen B, Huang R, Xia J, Jin Y, Zheng J. Evaluation of quantitative dynamic contrast-enhanced (DCE)-MRI parameters using a reference region model in invasive ductal carcinoma (IDC) patients. Int J Imaging Syst Technol 2021; 31: 215-222.
38. Tezcan S, Ozturk FU, Uslu N, Akcay EY. The role of combined diffusion-weighted imaging and dynamic contrast-enhanced MRI for differentiating malignant from benign breast lesions presenting washout curve. Can Assoc Radiol J 2021; 72: 460-469.
39. Ulas C, Das D, Thrippleton MJ, Valdés Hernández MDC, Armitage PA, Makin SD, et al. Convolutional neural networks for direct inference of pharmacokinetic parameters: application to stroke dynamic contrast-enhanced MRI. Front Neurol 2019, 9: 1147. DOI: 10.3389/fneur.2018.01147.
40. Kataoka M, Honda M, Ohashi A, Yamaguchi K, Mori N, Goto M, et al. Ultrafast dynamic contrast-enhanced MRI of the breast: how is it used? Magn Reson Med Sci 2022; 21: 83-94.
41. Honda M, Kataoka M, Iima M, Miyake KK, Ohashi A, Kishimoto AO, et al. Background parenchymal enhancement and its effect on lesion detectability in ultrafast dynamic contrast-enhanced MRI. Eur J Radiol 2020; 129: 108984. DOI: 10.1016/j.ejrad.2020.108984.
42. Honda M, Kataoka M, Onishi N, Iima M, Ohashi A, Kanao S, et al. New parameters of ultrafast dynamic contrast-enhanced

breast MRI using compressed sensing. J Magn Reson Imaging 2019; 51: 164-174.
43. Onishi N, Sadinski M, Gibbs P, Gallagher KM, Hughes MC, Ko ES, et al. Differentiation between subcentimeter carcinomas and benign lesions using kinetic parameters derived from ultrafast dynamic contrast-enhanced breast MRI. Eur Radiol 2019; 30: 756-766.
44. Onishi N, Sadinski M, Hughes MC, Ko ES, Gibbs P, Gallagher KM, et al. Ultrafast dynamic contrast-enhanced breast MRI may generate prognostic imaging markers of breast cancer. Breast Cancer Res 2020; 22: 58. DOI: 10.1186/s13058-020-01292-9.
45. Goto M, Sakai K, Yokota H, Kiba M, Yoshida M, Imai H, et al. Diagnostic performance of initial enhancement analysis using ultra-fast dynamic contrast-enhanced MRI for breast lesions. Eur Radiol 2018; 29: 1164-1174.
46. Yamaguchi K, Nakazono T, Egashira R, Fukui S, Baba K, Hamamoto T, Irie H. Maximum slope of ultrafast dynamic contrast-enhanced MRI of the breast: comparisons with prognostic factors of breast cancer. Jpn J Radiol 2020; 39: 246-253.
47. Zhang M, Horvat J V, Bernard-Davila B, Marino MA, Leithner D, Ochoa-Albiztegui RE, et al. Multiparametric MRI model with dynamic contrast-enhanced and diffusion-weighted imaging enables breast cancer diagnosis with high accuracy. J Magn Reson Imaging 2019; 49: 864-874.
48. Maric J, Boban J, Ivkovic-Kapicl T, Djilas D, Vucaj-Cirilovic V, Bogdanovic-Stojanovic D. Differentiation of breast lesions and distinguishing their histological subtypes using diffusion-weighted imaging and ADC values. Front Oncol 2020; 10: 332. DOI: 10.3389/fonc.2020.00332.
49. Goto M, Le Bihan D, Sakai K, Yamada K. The diffusion MRI signature index is highly correlated with immunohistochemical status and molecular subtype of invasive breast carcinoma. Eur Radiol 2022; 32: 4879-4888.
50. Rupa R, Thushara R, Swathigha S, Athira R, Meena N, Cherian MP. Diffusion weighted imaging in breast cancer – can it be a noninvasive predictor of nuclear grade? Indian J Radiol Imaging 2020; 30: 13-19.
51. Meyer H J, Wienke A, Surov A. Diffusion-weighted imaging of different breast cancer molecular subtypes: a systematic review and meta-analysis. Breast Care (Basel) 2022; 17: 47-54.
52. Billy CA, Darmiati S, Prihartono J. Diagnostic accuracy of diffusion weighted imaging compared to magnetic resonance spectroscopy in differentiation of benign and malignant breast lesions: a systematic review and meta-analysis. Eur J Radiol 2023; 168: 111124. DOI: 10.1016/j.ejrad.2023.111124.
53. Messina C, Bignone R, Bruno A, Bruno A, Bruno F, Calandri M, et al. Diffusion-weighted imaging in oncology: an update. Cancers (Basel) 2020; 12: 1493. DOI: 10.3390/cancers12061493.
54. Horvat JV, Bernard-Davila B, Helbich TH, Zhang M, Morris EA, Thakur SB, et al. Diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC) mapping as a quantitative imaging biomarker for prediction of immunohistochemical receptor status, proliferation rate, and molecular subtypes of breast cancer. J Magn Reson Imaging 2019; 50: 836-846.
55. Wang Y, Jin Y, Li M, Zhang J, Wang S, Zhang H, Song B, et al. Diagnostic performance of mono-exponential DWI versus diffusion kurtosis imaging in breast lesions: a meta-analysis. Medicine (Baltimore) 2022; 101: e31574. DOI: 10.1097/MD.0000000000031574.
56. Yao FF, Zhang Y. A review of quantitative diffusion-weighted MR imaging for breast cancer: towards noninvasive biomarker. Clin Imaging 2023; 98: 36-58.
57. Qin Y, Wu F, Hu Q, He L, Huo M, Tang C, et al. Histogram analysis of multi-model high-resolution diffusion-weighted MRI in breast cancer: correlations with molecular prognostic factors and subtypes. Front Oncol 2023; 13: 1139189. DOI: 10.3389/fonc.2023.1139189.
58. Liang J, Zeng S, Li Z, Kong Y, Meng T, Zhou C, et al. Intravoxel incoherent motion diffusion-weighted imaging for quantitative differentiation of breast tumors: a meta-analysis. Front Oncol 2020; 10: 585486. DOI: 10.3389/fonc.2020.585486.
59. Meng N, Wang X J, Sun J, Huang L, Wang Z, Wang KY, et al. Comparative study of amide proton transfer-weighted imaging and intravoxel incoherent motion imaging in breast cancer diagnosis and evaluation. J Magn Reson Imaging 2020; 52: 1175-1186.
60. Uslu H, Önal T, Tosun M, Arslan AS, Ciftci E, Utkan NZ. Intravoxel incoherent motion magnetic resonance imaging for breast cancer: a comparison with molecular subtypes and histological grades. Magn Reson Imaging 2021; 78: 35-41.
61. Ma Y, Shan D, Wei J, Chen A. Application of intravoxel incoherent motion diffusion-weighted imaging in differential diagnosis and molecular subtype analysis of breast cancer. Am J Transl Res 2021; 13: 3034-3043.
62. Honda M, Le Bihan D, Kataoka M, Iima M. Diffusion kurtosis imaging as a biomarker of breast cancer. BJR Open 2023; 5: 20220038. DOI: 10.1259/bjro.20220038.
63. Zhang J, Chen Y, Zhang E, Li N, Yuan H, Lang N. Use of monoexponential diffusion-weighted imaging and diffusion kurtosis imaging and dynamic contrast-enhanced-MRI for the differentiation of spinal tumors. Eur Spine J 2020; 29: 1112-1120.
64. Zhang J, Xing X, Wang Q, Chen Y, Yuan H, Lang N. Preliminary study of monoexponential, biexponential, and stretched-exponential models of diffusion-weighted MRI and diffusion kurtosis imaging on differential diagnosis of spinal metastases and chordoma. Eur Spine J 2022; 31: 3130-3138.
65. Zhou WP, Zan XY, Hu XY, Liu X, Sudarshan SKP, Yang SD, et al. Characterization of breast lesions using diffusion kurtosis model-based imaging: an initial experience. J Xray Sci Technol 2020; 28: 157-169.
66. Yang ZL, Li Y, Zhan CA, Hu YQ, Guo YH, Xia LM, Ai T. Evaluation of suspicious breast lesions with diffusion kurtosis MR imaging and connection with prognostic factors. Eur J Radiol 2021; 145: 110014. DOI: 10.1016/j.ejrad.2021.110014.
67. Meng N, Wang X, Sun J, Han D, Bai Y, Wei W, et al. A comparative study of the value of amide proton transfer-weighted imaging and diffusion kurtosis imaging in the diagnosis and evaluation of breast cancer. Eur Radiol 2020; 31: 1707-1717.
68. Huang Y, Lin Y, Hu W, Ma C, Lin W, Wang Z, et al. Diffusion curtosis at 3.0T as an in vivo imaging marker for breast cancer characterization: correlation with prognostic factors. J Magn Reson Imaging 2019; 49: 845-856.
69. Kang HS, Kim JY, Kim JJ, Kim S, Lee NK, Lee JW, et al. Diffusion kurtosis MR imaging of invasive breast cancer: correlations with

prognostic factors and molecular subtypes. J Magn Reson Imaging 2022; 56: 110-120.
70. You C, Li J, Zhi W, Chen Y, Yang W, Gu Y, Peng W, et al. The volumetric-tumour histogram-based analysis of intravoxel incoherent motion and non-Gaussian diffusion MRI: association with prognostic factors in HER2-positive breast cancer. J Transl Med 2019; 17: 182. DOI: 10.1186/s12967-019-1911-6.
71. Li X, Fan Z, Jiang H, Niu J, Bian W, Wang C, et al. Synthetic MRI in breast cancer: differentiating benign from malignant lesions and predicting immunohistochemical expression status. Sci Rep 2023; 13: 17978. DOI: 10.1038/s41598-023-45079-2.
72. Gao W, Zhang S, Guo J, Wei X, Li X, Diao Y, et al. Investigation of synthetic relaxometry and diffusion measures in the differentiation of benign and malignant breast lesions as compared to BI-RADS. J Magn Reson Imaging 2020; 53: 1118-1127.
73. Matsuda M, Tsuda T, Ebihara R, Toshimori W, Takeda S, Okada K, et al. Enhanced masses on contrast-enhanced breast: differentiation using a combination of dynamic contrast-enhanced MRI and quantitative evaluation with synthetic MRI. J Magn Reson Imaging 2020; 53: 381-391.
74. Sun SY, Ding Y, Li Z, Nie L, Liao C, Liu Y, et al. Multiparameter MRI model with DCE-MRI, DWI, and synthetic MRI improves the diagnostic performance of BI-RADS 4 lesions. Front Oncol 2021; 11: 699127. DOI: 10.3389/fonc.2021.699127.
75. Li Q, Xiao Q, Yang M, Chai Q, Huang Y, Wu PY, et al. Histogram analysis of quantitative parameters from synthetic MRI: correlations with prognostic factors and molecular subtypes in invasive ductal breast cancer. Eur J Radiol 2021; 139: 109697. DOI: 10.1016/j.ejrad.2021.109697.
76. Gao W, Yang Q, Li X, Chen X, Wei X, Diao Y, et al. Synthetic MRI with quantitative mappings for identifying receptor status, proliferation rate, and molecular subtypes of breast cancer. Eur J Radiol 2022; 148: 110168. DOI: 10.1016/j.ejrad.2022.110168.
77. Yuen S, Monzawa S, Yanai S, Matsumoto H, Yata Y, Ichinose Y, et al. The association between MRI findings and breast cancer subtypes: focused on the combination patterns on diffusion-weighted and T2-weighted images. Breast Cancer 2020; 27: 1029-1037.
78. Zhang Q, Zhao Y, Nie J, Long Q, Wang X, Wang X, et al. Pretreatment synthetic MRI features for triple-negative breast cancer. Clin Radiol 2023; 79: e219-e226. DOI: 10.1016/j.crad.2023.10.015.
79. Tomaszewski MR, Gillies RJ. The biological meaning of radiomic features. Radiology 2021; 298: 505-516.
80. Lafcı O, Celepli P, Seher Öztekin P, Koşar PN. DCE-MRI radiomics analysis in differentiating luminal A and luminal B breast cancer molecular subtypes. Acad Radiol 2022; 30: 22-29.
81. Slavkova KP, Patel SH, Cacini Z, Kazerouni AS, Gardner AL, Yankeelov TE, Hormuth DA 2nd. Mathematical modelling of the dynamics of image-informed tumor habitats in a murine model of glioma. Sci Rep 2023; 13: 2916. DOI: 10.1038/s41598-023-30010-6.
82. Xie T, Zhao Q, Fu C, Bai Q, Zhou X, Li L, et al. Differentiation of triple-negative breast cancer from other subtypes through whole-tumor histogram analysis on multiparametric MR imaging. Eur Radiol 2019; 29: 2535-2544.
83. Corrias G, Micheletti G, Barberini L, Suri JS, Saba L. Texture analysis imaging "what a clinical radiologist needs to know". Eur J Radiol 2022; 146: 110055. DOI: https://doi.org/10.1016/j.ejrad.2021.110055.
84. van Timmeren JE, Cester D, Tanadini-Lang S, Alkadhi H, Baessler B. Radiomics in medical imaging – "how-to" guide and critical reflection. Insights Imaging 2020; 11: 91. DOI: 10.1186/s13244-020-00887-2.
85. Du T, Zhao H. Habitat analysis of breast cancer-enhanced MRI reflects BRCA1 mutation determined by immunohistochemistry. Biomed Res Int 2022; 2022: 9623173. DOI: 10.1155/2022/9623173.
86. Leithner D, Horvat JV, Marino MA, Bernard-Davila B, Jochelson MS, Ochoa-Albiztegui RE, et al. Radiomic signatures with contrast-enhanced magnetic resonance imaging for the assessment of breast cancer receptor status and molecular subtypes: initial results. Breast Cancer Res 2019; 21: 106. DOI: 10.1186/s13058-019-1187-z.
87. Leithner D, Bernard-Davila B, Martinez DF, Horvat JV, Jochelson MS, Marino MA, et al. Radiomic signatures derived from diffusion-weighted imaging for the assessment of breast cancer receptor status and molecular subtypes. Mol Imaging Biol 2020; 22: 453-461.
88. Horvat JV, Iyer A, Morris EA, Apte A, Bernard-Davila B, Martinez DF, et al. Histogram analysis and visual heterogeneity of diffusion-weighted imaging with apparent diffusion coefficient mapping in the prediction of molecular subtypes of invasive breast cancers. Contrast Media Mol Imaging 2019; 2019: 2972189. DOI: 10.1155/2019/2972189.
89. Chang Y C, Ackerstaff E, Tschudi Y, Jimenez B, Foltz W, Fisher C, et al. Delineation of tumor habitats based on dynamic contrast enhanced MRI. Sci Rep 2017; 7: 9746. DOI: 10.1038/s41598-017-09932-5.
90. Gillies RJ, Balagurunathan Y. Perfusion MR imaging of breast cancer: insights using "habitat imaging". Radiology 2018; 288: 36-37.
91. Kim JJ, Kim JY, Suh HB, Hwangbo L, Lee NK, Kim S, et al. Characterization of breast cancer subtypes based on quantitative assessment of intratumoral heterogeneity using dynamic contrast-enhanced and diffusion-weighted magnetic resonance imaging. Eur Radiol 2022; 32: 822-833.
92. Kim M, Park JE, Kim HS, Kim N, Park SY, Kim YH, Kim JH, et al. Spatiotemporal habitats from multiparametric physiologic MRI distinguish tumor progression from treatment-related change in post-treatment glioblastoma. Eur Radiol 2021; 31: 6374-6383.
93. Cho HH, Kim H, Nam SY, Lee JE, Han BK, Ko EY, et al. Measurement of perfusion heterogeneity within tumor habitats on magnetic resonance imaging and its association with prognosis in breast cancer patients. Cancers (Basel) 2022; 14: 1858. DOI: 10.3390/cancers14081858.
94. Zhang L, Fan M, Wang S, Xu M, Li L. Radiomic analysis of pharmacokinetic heterogeneity within tumor based on the unsupervised decomposition of dynamic contrast-enhanced MRI for predicting histological characteristics of breast cancer. J Magn Reson Imaging 2022; 55: 1636-1647.
95. Wang H, Zeng L, Wu H, Tian J, Xie H, Zhang L, et al. Preoperative vascular heterogeneity based on dynamic susceptibility contrast MRI in predicting spatial pattern of locally recurrent high-grade gliomas. Eur Radiol 2024; 34: 1982-1993.
96. Feng S, Yin J. Dynamic contrast-enhanced magnetic resonance imaging radiomics analysis based on intratumoral subregions for predicting luminal and nonluminal breast cancer. Quant Imaging Med Surg 2023; 13: 6735-6749.

97. Lu H, Yin J. Texture analysis of breast DCE-MRI based on intratumoral subregions for predicting HER2 2+ status. Front Oncol 2020; 10: 543. DOI: 10.3389/fonc.2020.00543.
98. Xu R, Yu D, Luo P, Li X, Jiang L, Chang S, Li G. Do habitat MRI and fractal analysis help distinguish triple-negative breast cancer from non-triple-negative breast carcinoma. Can Assoc Radiol J 2024; 75: 584-592.
99. Ren W, Xi X, Zhang X, Wang K, Liu M, Wang D, et al. Predicting molecular subtypes of breast cancer based on multi-parametric MRI dataset using deep learning method. Magn Reson Imaging 2024; 117: 110305. DOI: 10.1016/j.mri.2024.110305.
100. Wang X, Hu X, Wang C, Yang H, Hu Y, Lan X, et al. Automatic segmentation and molecular subtype classification of breast cancer using an MRI-based deep learning framework. Radiol Imaging Cancer 2025; 7: e240184. DOI: 10.1148/rycan.240184.
101. Ba ZC, Zhang HX, Liu AY, Zhou XX, Liu L, Wang XY, et al. Combination of DCE-MRI and NME-DWI via deep neural network for predicting breast cancer molecular subtypes. Clin Breast Cancer 2024; 24: e417-e427. DOI: 10.1016/j.clbc.2024.03.006.
102. Huang G, Du S, Gao S, Guo L, Zhao R, Bian X, et al. Molecular subtypes of breast cancer identified by dynamically enhanced MRI radiomics: the delayed phase cannot be ignored. Insights Imaging 2024; 15: 127. DOI: 10.1186/s13244-024-01713-9.