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BREAST IMAGING

REVIEW

The role of diffusion-weighted imaging in breast cancer: from diagnosis to treatment monitoring and follow-up

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ABSTRACT

Diffusion-weighted imaging (DWI) is a fundamental non-contrast sequence in multiparametric breast magnetic resonance imaging (MRI), measuring water diffusion to assess tissue microstructure. The derived apparent diffusion coefficient (ADC) effectively discriminates between malignant lesions, which typically exhibit lower ADC due to high cellularity, and benign ones. Advanced models, such as intravoxel incoherent motion, diffusion kurtosis imaging, restriction spectrum imaging (RSI), and time-dependent DWI, provide further quantification of micro-perfusion and tissue heterogeneity. This review covers technical advancements in DWI (including optimized single-shot echo-planar imaging, ultra-high b-value DWI, and synthetic DWI), its diagnostic performance [RSI achieves an area under the curve (AUC) of up to 0.982; DWI combined with other MRI sequences boosts the AUC to 0.960], and its clinical applications (predicting neoadjuvant chemotherapy response, with an AUC of up to 0.840; correlating with biomarkers such as estrogen receptor, progesterone receptor, and Ki-67; and non-contrast screening with a 99.5% negative predictive value). Artificial intelligence (AI) and radiomics further enhance its utility, with two-dimensional convolutional neural networks performing on par with radiologists (AUC ≈ 0.88). Limitations include artifacts, parameter variability, and poor resolution. Future directions involve ultra-high field MRI and AI-driven analysis. DWI is pivotal for personalized breast cancer care, though standardized protocols and further refinement are needed for broader clinical adoption.

KEYWORDS

Diffusion-weighted imaging, breast cancer, magnetic resonance imaging

Diffusion-weighted imaging (DWI) has emerged as a pivotal non-contrast magnetic resonance imaging (MRI) technique that measures the random motion of water molecules within biological tissues, providing unique insights into tissue microstructure at the cellular level. In breast imaging, DWI has transitioned from a research tool to an essential clinical component of multiparametric MRI (mpMRI) protocols, offering valuable functional information that complements conventional morphological assessment. The apparent diffusion coefficient (ADC) derived from DWI has demonstrated considerable utility in distinguishing malignant from benign breast lesions, with malignant tumors typically exhibiting restricted diffusion and lower ADC values due to increased cellularity, disrupted tissue architecture, and higher nuclear-to-cytoplasmic ratios.[1-3]

The clinical implementation of DWI in breast cancer management has expanded considerably, encompassing lesion characterization, prediction of molecular subtypes, assessment of treatment response, and evaluation of prognostic biomarkers. Technological advancements have addressed initial limitations related to image quality and resolution, paving the way for more sophisticated applications, including intravoxel incoherent motion (IVIM), diffusion kurtosis imaging (DKI), restriction spectrum imaging (RSI), and time-dependent DWI (T-dDWI).[4-7] These advanced techniques provide more nuanced information about tissue microstructure, perfusion characteristics, and diffusion heterogeneity beyond conventional ADC measurements.

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Recent developments in artificial intelligence (AI) and radiomics have further enhanced the potential of DWI, enabling the extraction of quantitative features that may not be perceptible to the human eye.[8-10] The integration of DWI into abbreviated MRI protocols and its potential role as a non-contrast screening tool represent promising directions for improving accessibility and reducing examination times while maintaining diagnostic accuracy.[11-13] This review comprehensively examines the technical advancements, diagnostic performance, and emerging applications of DWI in breast cancer, while addressing current limitations and future perspectives for clinical application.

Compared with previously published review articles focusing on breast DWI, this narrative review carries several distinctive strengths. First, this study integrates the newly emerging T-dDWI together with traditional ADC, IVIM, DKI, RSI, and mean apparent propagator (MAP)-MRI systems, forming a complete collation of mainstream quantitative diffusion models that previous reviews rarely fully covered. Second, a standardized comparative table is provided to differentiate the technical characteristics, applicable scenarios, and selection suggestions of each diffusion sequence intuitively, offering practical guidance for radiologists in daily clinical work. Third, we conduct targeted critical appraisal of heterogeneous and conflicting results among existing clinical studies and systematically elaborate confounding factors, including inconsistent scanning parameters, variable post-processing software, and publication bias, which lead to inconsistent research conclusions. Finally, we prospectively discuss the feasibility and unresolved challenges of multi-model diffusion MRI as a non-contrast screening tool for breast lesions, which provides unique forward-looking perspectives rarely emphasized in prior reviews.

Main points

- • Diffusion-weighted imaging (DWI) serves as a core non-contrast sequence for multiparametric breast MRI, and apparent diffusion coefficient (ADC) values assist in differentiating benign and malignant breast lesions.
- Advanced diffusion models achieve high diagnostic performance for breast lesions and enable further quantification of tissue microperfusion and heterogeneity.
- DWI and advanced diffusion models can predict neoadjuvant chemotherapy response, correlate with breast cancer biomarkers, and support non-contrast screening with high negative predictive value.
- Artificial intelligence and radiomics improve the diagnostic performance of breast DWI; artifacts, parameter variability, and poor resolution remain major limitations.

Literature retrieval and screening

All references cited in this narrative review were systematically retrieved from the following mainstream English-language electronic databases: PubMed, Embase, Web of Science, and Cochrane Library. The literature search was performed between January 2011 and May 2026. The retrieval keywords were grouped into three core modules and combined for advanced searching:

(1) Breast lesion and tumor keywords: breast cancer, breast neoplasm, breast lesion, invasive ductal carcinoma, Breast Imaging Reporting and Data System (BI-RADS);

(2) MRI keywords: diffusion-weighted imaging, DWI, apparent diffusion coefficient, ADC, intravoxel incoherent motion, IVIM, diffusion kurtosis imaging, DKI, restriction spectrum imaging, RSI, mean apparent propagator MRI, MAP-MRI, time-dependent diffusion MRI, T-dDWI;

(3) Outcome and evaluation keywords: diagnosis, differential diagnosis, molecular subtype, neoadjuvant chemotherapy, axillary lymph node metastasis, quantitative parameter, diagnostic performance.

Inclusion criteria: Original clinical observational studies, prospective and retrospective trials, and high-quality systematic reviews and meta-analyses focusing on breast DWI and advanced diffusion models published in English.

Exclusion criteria: Case reports, conference abstracts without full-text, *in vitro* and animal experimental studies, reviews lacking quantitative imaging outcomes, and duplicate publications.

Literature screening was conducted by two researchers. The screening process consisted of two stages: initial title and abstract screening to exclude irrelevant articles, followed by full-text evaluation of potentially eligible records. Disagreements on study eligibility were resolved through mutual discussion among the research team. It should be emphasized that this study is a narrative review rather than a formal systematic review. No prospective review protocol registration, quantitative meta-analysis, or standardized risk-of-bias assessment was implemented. The structured search strategy was adopted only to reduce literature selection bias and guarantee adequate comprehensiveness for narrative synthesis.

Technical advancements and standardization of diffusion-weighted imaging/intravoxel incoherent motion in breast cancer

The technical evolution of DWI in breast imaging has been marked by notable improvements in acquisition protocols, sequence optimization, and post-processing techniques. Standard single-shot echo-planar imaging (SS-EPI) remains the most widely used DWI sequence due to its rapid acquisition time and relative immunity to motion artifacts.[3] However, conventional SS-EPI is susceptible to distortions, susceptibility artifacts, and limited spatial resolution, particularly at higher magnetic field strengths. Technological innovations have addressed these challenges through the implementation of parallel imaging, compressed sensing technology, reduced field-of-view techniques, and advanced distortion correction methods.[7]

The standardization of DWI acquisition parameters across different MRI platforms and vendors represents a critical step toward ensuring reproducible and comparable quantitative measurements. A comprehensive two-site study evaluating IVIM biomarkers across different MRI vendors and software programs demonstrated that tissue diffusivity exhibited the highest consistency with coefficients of variation of 4.8% and 2.8% across sites, followed by perfusion fraction (14.5% and 18.9%) and pseudo-diffusivity (36.9% and 19.8%) (14). This investigation highlighted the translational potential of IVIM biomarkers while emphasizing the need for standardized acquisition and analysis protocols to minimize inter-platform variability.

Advanced diffusion models, including IVIM, DKI, and RSI, have expanded the diagnostic capabilities of DWI by separating diffusion effects from micro-perfusion and characterizing non-Gaussian diffusion behavior. Comparative studies between compartmentalized diffusion-weighted models have demonstrated that the three-compartment RSI model parameters showed superior diagnostic performance compared with the bi-exponential IVIM model in characterizing breast lesions and normal fibroglandular tissue.[5] The RSI-derived parameters F, CC, and C values achieved the highest area under the curve (AUC) values of 0.871, 0.982, and 0.863 for distinguishing malignant from benign lesions, malignant from normal tissue, and benign from normal tissue, respectively.

High b-value DWI, particularly at b-values ≥ 1,500 s/mm^2, has gained attention for improved lesion conspicuity and diagnostic specificity. Visual assessment of ultra-high b-value DWI (b: 2,500 s/mm^2) demonstrated substantial interobserver agreement (Fleiss kappa: 0.77) and higher diagnostic performance (AUC: 0.81) compared with conventional ADC measurements and lower b-value DWI.[12] The integration of ultra-high b-value DWI into abbreviated protocols showed promising results, with an approach combining b: 2,500 s/mm^2 DWI with native T1- and T2-weighted images achieving a negative predictive value of 99.5%, sensitivity of 97.4%, and specificity of 88.4%.[13]

Synthetic DWI has emerged as a feasible alternative to conventional DWI, providing higher tumor conspicuity and better cancer-to-parenchyma contrast ratios while maintaining comparable cancer detection rates.[15] The development of super-resolution techniques for ADC images, such as the double transformer-based network, has shown potential for enhancing resolution and improving radiomics analysis for tumor characterization.[16] These technical advancements collectively contribute to the ongoing refinement of DWI protocols, moving toward standardized, high-quality diffusion imaging that can be reliably implemented across clinical settings.

The diagnostic performance of diffusion-weighted imaging and advanced diffusion models in breast lesion characterization

The diagnostic performance of DWI in distinguishing malignant from benign breast lesions has been extensively validated across numerous studies. Conventional ADC values consistently demonstrate marked differences between malignant and benign lesions, with malignant tumors showing lower ADC values due to increased cellularity and microstructural alterations. A prospective study evaluating micro-structural metrics from T-dDWI reported that cell diameter, cell density, and intracellular volume fraction were significantly higher in malignant lesions than in benign lesions, and ADC was lower.[1] Among these parameters, cell density derived from T-dDWI achieved the highest diagnostic performance (AUC: 0.93), significantly outperforming conventional ADC (AUC: 0.79).

Advanced diffusion models, including IVIM, DKI, and RSI, have shown improved diagnostic accuracy compared with standard monoexponential DWI. A comparative study of compartmentalized diffusion-weighted models demonstrated that RSI-derived parameters outperformed IVIM parameters in differentiating malignant from benign breast lesions.[5] The combination of IVIM and RSI parameters achieved the highest diagnostic efficacy with AUCs of 0.893, 0.991, and 0.928 for distinguishing malignant from benign lesions, malignant from normal tissue, and benign from normal tissue, respectively.

The integration of DWI with established breast imaging reporting systems, such as the BI-RADS, has been shown to improve diagnostic specificity. A systematic review and meta-analysis investigating the added value of DWI compared with structured assessment of BI-RADS criteria using the Kaiser score found that adding DWI to a structured BI-RADS assessment increased specificity from 68.7% to 74.9%, though this improvement did not reach statistical significance.[17] However, other studies have demonstrated more substantial benefits, with the combination of high b-value DWI (b: 2,500 s/mm^2) and BI-RADS significantly increasing specificity from 25% to 73% while maintaining high sensitivity.[12]

Multiparametric approaches combining DWI with other functional MRI techniques have further enhanced diagnostic performance. The combination of ultrafast dynamic contrast-enhanced (DCE)-MRI semi-quantitative parameters with ADC achieved superior classification performance (AUC: 0.960) compared with either technique alone.[18] Similarly, the integration of amide proton transfer-weighted imaging with DKI demonstrated improved diagnostic efficacy (AUC: 0.893) compared with individual parameters.[2]

AI applications to DWI have shown promising results in lesion characterization. A deep learning study evaluating AI models for differentiating malignant from benign breast tumors using DWI without lesion segmentation found that a small two-dimensional convolutional neural network (2D CNN) achieved performance comparable with radiologists interpreting standard breast MR images (AUC: 0.88 vs. 0.86).[9] These findings suggest that AI-assisted DWI interpretation may reduce interpretation time and potentially improve diagnostic consistency.

The diagnostic value of DWI varies according to lesion morphology, with limited utility in non-mass enhancement (NME) lesions compared with mass lesions. A study focusing on NME lesions found that ADC mapping achieved modest diagnostic accuracy (AUC up to 0.71), with 31% of lesions presenting as NME on DCE-MRI unable to be evaluated with DWI.[19] This highlights the continued importance of DCE-MRI while suggesting that DWI may serve as a complementary rather than standalone technique for characterizing NME lesions.

Diffusion-weighted imaging for predicting and monitoring treatment response

DWI has demonstrated great potential for predicting and monitoring treatment response in patients with breast cancer undergoing neoadjuvant chemotherapy (NAC). The ability to identify responders early in the treatment course can guide therapeutic decisions and potentially avoid unnecessary toxicity in non-responding patients. Several studies have investigated the role of DWI-derived parameters as early biomarkers of treatment response.

The Breast Multiparametric MRI for Prediction of NAC Response challenge represented a major effort to identify image-based markers from mpMRI, including DWI, for predicting pathologic complete response (pCR) following NAC.[20] This initiative included 573 breast MRI studies from 191 women in the I-SPY 2/ACRIN 6698 trial, with several teams developing models that outperformed the benchmark established from the primary analysis. The top-performing entries achieved AUCs of 0.803, 0.838, and 0.840, utilizing various approaches ranging from feature extraction to deep learning methods that incorporated DCE and DWI alone or in combination.

Advanced analysis of DWI data using radiomics and machine learning has shown particularly promising results for response prediction. A study evaluating a machine learning model developed using radiomics data derived from physiologically decomposed (PD) DWI data achieved superior performance in predicting pCR following NAC compared with baseline and benchmark models.[8] The PD DWI model achieved an AUC of 0.89, demonstrating statistically significant improvements over baseline approaches and providing a greater net benefit according to decision curve analysis.

Changes in ADC values during treatment have been correlated with treatment response, with responding tumors typically showing earlier increases in ADC values than non-responders. This phenomenon is attributed to the breakdown of cell membranes and reduction in cellular density that occurs with effective treatment. The rate of ADC change with diffusion time (ΔADC) has

also been investigated as a potential biomarker, with Ki-67-positive cancers showing larger ΔADC values than Ki-67-negative cancers, suggesting that diffusion time may be a useful parameter to consider for breast cancer management.[21]

The integration of DWI with clinicopathologic features has further enhanced predictive performance for treatment response. Nomograms incorporating ADC values and clinicopathologic features demonstrated good performance in predicting axillary lymph node metastasis status before treatment, non-sentinel lymph node metastasis, and lymph node status after NAC.[22] For predicting pretreatment axillary lymph node status, the nomogram achieved an AUC of 0.90 in the training cohort and 0.86–0.90 in external testing cohorts.

DWI has also shown value in assessing tumor response beyond pCR prediction. Changes in diffusion parameters have been correlated with residual cancer burden and various pathologic response grading systems. The ability of DWI to provide functional information about tumor cellularity and microstructure makes it particularly suitable for monitoring treatment-induced changes, often preceding morphological alterations visible on conventional imaging.

The role of diffusion-weighted imaging in prognostic biomarker assessment and tumor heterogeneity

DWI has demonstrated significant correlations with established molecular prognostic biomarkers in breast cancer, providing non-invasive means to assess tumor biology and heterogeneity. A systematic review and meta-analysis including data from 52 studies examining ADC values in relation to hormone receptor status and prognostic biomarkers found significant differences in ADC values among different receptor statuses.[23] Estrogen receptor (ER)-positive, progesterone receptor (PgR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, and Ki-67-positive tumors consistently showed lower ADC values than their negative counterparts, reflecting the increased cellularity associated with more aggressive tumor biology.

The relationship between diffusion parameters and molecular subtypes extends beyond basic receptor status assessment. A study investigating the variation of ADC values with diffusion time according to breast tumor type and prognostic biomarker expression found that ADC values varied significantly with different diffusion times and correlated with molecular biomarkers, especially Ki-67.[21] Lower ADC values at short diffusion times (ADC_{short}) and standard ADC values ($ADC_{0–1,000}$) were observed in ER-positive compared with ER-negative cancers, and in PgR-positive compared with PgR-negative cancers.

MRI radiomics with machine learning has been applied to the challenging task of differentiating HER2 expression levels in a three-tiered classification system (HER2-zero, HER2-low, and HER2-positive). Although performance was suboptimal, radiomics models achieved AUCs of 0.757 for differentiating HER2-negative from HER2-positive tumors and 0.754 for differentiating HER2-zero from HER2-low tumors in the external test set.[24] Shapley Additive Explanations analysis identified early-phase DCE imaging features as having the strongest influence for both tasks, with T2-weighted imaging features also playing a prominent role.

The assessment of tumor heterogeneity through radiomics analysis of DWI data has provided insights into breast cancer biology and prognosis. Integrative radiomics clustering analysis of mpMRI data from 194 patients with breast cancer identified two distinct patient clusters associated with significant differences in molecular subtypes, particularly in Luminal A distribution, hormone receptor status, mean tumor size, lymph node metastasis, and edema.[10] This approach emphasizes the potential of mpMRI and radiomics-based cluster analysis to categorize tumors, uncover heterogeneity, and aid in personalized treatment strategies.

Advanced diffusion models, such as MAP-MRI, have shown promise in evaluating tumor microenvironment characteristics, including the tumor-stroma ratio (TSR). A prospective study demonstrated that MAP-MRI metrics, particularly radial non-Gaussianity, performed significantly better than ADC in assessing TSR status in breast carcinoma, achieving an AUC of 0.81 compared with 0.61 for ADC.[4] When combined with lymphovascular invasion, the model achieved 76% accuracy in discriminating high-TSR from low-TSR groups.

The ability of DWI to characterize tumor heterogeneity extends beyond molecular and cellular features to include spatial heterogeneity within tumors. Texture analysis and radiomics features derived from DWI have been correlated with genetic expression patterns, hypoxia markers, and other microenvironmental characteristics that influence tumor behavior and treatment response. These applications position DWI as a valuable tool for comprehensive tumor characterization that complements tissue sampling and may help guide targeted therapies.

Comparison of breast diffusion-weighted imaging models and clinical application recommendations

The principles, strengths, limitations, clinical value, and applicable scenarios of six mainstream breast DWI quantitative models are summarized in Table 1 below.

Emerging applications: radiomics, artificial intelligence, and non-contrast screening

The integration of radiomics and AI with DWI has opened new frontiers in breast cancer diagnosis and characterization. Radiomics involves extracting quantitative features from medical images that may not be perceptible to the human eye, providing a wealth of data for machine learning algorithms to identify patterns associated with specific pathological characteristics.[8,10] This approach has been applied to various clinical scenarios, including differentiation of molecular subtypes, prediction of treatment response, and assessment of tumor heterogeneity.

Deep learning applications to DWI have demonstrated remarkable capabilities in lesion detection and characterization. A comprehensive study evaluating different AI models for differentiating malignant from benign breast tumors using DWI without lesion segmentation found that a small 2D CNN achieved performance comparable with radiologists interpreting standard breast MRI.[9] The model achieved an AUC of 0.88 with specific data augmentation methods, with no significant difference in specificity (81.4% vs. 72.1%) or sensitivity (85.9% vs. 98.8%) compared with radiologists. These findings highlight the potential for AI-assisted DWI interpretation to reduce radiologist workload while maintaining diagnostic accuracy.

The application of AI extends to computer-aided diagnosis systems for triaging MRI-guided biopsies in preoperative patients with breast cancer. A multiparametric computer-aided diagnosis model incorporating clinical features and radiomic features from multiple MRI sequences, including DWI, correctly identified 48% of malignant additional lesions with a specificity of 98%.[39] Such systems have the potential to reduce unnecessary biopsies while ensuring that malignant

lesions are not missed, particularly in the context of screening women with extremely dense breasts where false-positive diagnoses are common.[40]

Non-contrast screening protocols based on DWI represent another emerging application with notable clinical implications. The development of abbreviated MRI protocols featuring ultra-high b-value DWI has shown promising results for breast cancer detection without contrast administration.[13] These protocols demonstrated high negative predictive value (≥ 97.0%) and sensitivity (≥ 92.1%) for lesion detection, though specificity was more limited (≥ 58.3%). The combination of high b-value DWI with native T1- and T2-weighted images improved performance, with the approach using b: 2,500 DWI achieving a negative predictive value of 99.5%, sensitivity of 97.4%, and specificity of 88.4%.

Table 1. Comparison of breast diffusion-weighted imaging models and clinical application recommendations

Models	Core principle	Main advantages	Main limitations	Clinical value	Clinical application recommendations
ADC[25-27]	Monoexponential model based on Brownian motion; requires two or more b-values.	Short scan time; only two b-values are needed; the most mature and widely applied technique; ADC maps directly visualize tissue diffusion differences.	Cannot distinguish perfusion effects from genuine diffusion signals; insufficiently characterizes the complexity of tissue microstructures.	Routine breast DWI; contrast-free breast cancer screening; pre-operative lesion assessment; neoadjuvant chemotherapy follow-up.	When rapid, accessible and standardized quantitative DWI metrics are needed; for patients unable to endure prolonged scanning; for multicenter large-cohort clinical trials.
IVIM[28-30]	Biexponential multi-b-value model; separates microcirculatory perfusion from pure water diffusion.	More accurate diffusion quantification than ADC, eliminating perfusion bias; simultaneously evaluates tumor cellularity and angiogenesis.	Prolonged scan acquisition (≥ 4 b-values); complicated computational processing; requires dedicated post-processing software.	Differentiation between benign and malignant lesions; non-invasive molecular subtype prediction; early neoadjuvant response evaluation; risk stratification of axillary lymph node metastasis.	When conventional ADC yields indeterminate diagnostic results; to assess tumor cellularity and angiogenesis; to predict molecular subtypes for individualized therapeutic planning.
DKI[31-33]	Non-Gaussian diffusion kurtosis model.	Assesses tumor histologic grade and proliferative activity; enables earlier and more sensitive neoadjuvant response evaluation.	Long scan time (≥ 3 b-values, including high b-values); high demand for sufficient signal-to-noise ratio; low b-value noise distorts kurtosis (K) value computation.	Differentiation between benign and malignant lesions; evaluation of histologic grade and proliferative activity; ultra-early neoadjuvant response prediction; assessment of intratumoral heterogeneity.	When assessment of tumor microstructure heterogeneity is required; for non-invasive evaluation of histologic grade and Ki-67 proliferation index; to predict response within one to two neoadjuvant cycles.
RSI[5,34,35]	Multi-b-value DWI with Laplace transform to generate a continuous spectrum of diffusion coefficients.	Comprehensively characterizes tissue diffusion features and cellular structural states; provides robust biomarkers for evaluating tumor invasiveness and prognosis.	Long scan time (≥10 b-values); complex mathematical computation; requires specialized post-processing software.	Differentiation between benign and malignant lesions; evaluation of tumor invasiveness and prognosis; tumor microenvironment heterogeneity assessment; neoadjuvant efficacy evaluation.	When full characterization of tissue diffusion heterogeneity is required; to stratify tumors by invasiveness and prognostic risk; when conventional ADC and DKI produce equivocal diagnostic outcomes.
MAP-MRI[4,36]	Multi-directional, multi-b-value DWI with Fourier transform to calculate the mean apparent propagator.	Fully characterizes tissue diffusion anisotropy; enables sensitive assessment of tumor invasiveness and fibrous tissue infiltration.	Extremely long scan time for multi-directional multi-b-value acquisition; complex computational reconstruction; requires dedicated post-processing software.	Assessment of tumor invasiveness and fibrous tissue infiltration; evaluation of tissue microstructure and diffusion anisotropy; neoadjuvant efficacy evaluation; prognosis prediction.	When assessment of fibrous tissue infiltration and diffusion anisotropy is required; to analyze water displacement distribution reflecting cellular microstructural features; to guide personalized surgical planning through comprehensive invasiveness evaluation.
T-dDWI[1,37,38]	Multi-b-value DWI acquisition with multiple diffusion times.	Superior diagnostic sensitivity for sub-centimeter early breast lesions; enables non-invasive simultaneous evaluation of tumor proliferation, histologic grade and molecular subtypes; facilitates ultra-early assessment of neoadjuvant treatment response.	Long scan time; complicated computation; requires specialized post-processing software.	Identification of early sub-centimeter breast lesions; non-invasive molecular subtype prediction; ultra-early neoadjuvant response assessment; non-invasive detection of axillary lymph node micro-metastasis.	When conventional DWI has insufficient sensitivity for tiny sub-centimeter lesions; to predict therapeutic response after one cycle of neoadjuvant chemotherapy; for non-invasive detection of axillary lymph node micro-metastasis.

ADC, apparent diffusion coefficient; IVIM, intravoxel incoherent motion; DKI, diffusion kurtosis imaging; RSI, restriction spectrum imaging; MAP-MRI, mean apparent propagator magnetic resonance imaging; T-dDWI, time-dependent diffusion-weighted imaging.

The potential of DWI as a standalone screening tool is further supported by studies comparing its performance with conventional mammography and ultrasound. In women with newly diagnosed breast cancer, DWI MRI detected significantly more contralateral breast cancers with fewer biopsy recommendations than combined mammography and ultrasound.[41] DWI showed a cancer detection rate of 2.0% compared with 1.0% for combined mammography and ultrasound, with higher positive predictive value for biopsies performed (42.1% vs. 18.5%).

Multi-modality fusion approaches combining DWI with other imaging sequences have shown improved classification performance compared with single-modality analysis. A multi-modality relation attention network with consistent regularization for breast tumor classification using DWI and ADC images achieved an AUC of 85.1%, accuracy of 86.7%, specificity of 83.3%, and sensitivity of 88.9%.[42] These results demonstrate the synergistic value of integrating information from multiple imaging sequences through advanced computational methods.

Limitations, challenges, and future perspectives

Despite the significant advancements and promising applications of DWI in breast cancer imaging, several limitations and challenges remain to be addressed for optimal clinical implementation. Technical challenges include the inherent limitations of EPI sequences, such as susceptibility artifacts, chemical shift artifacts, and limited spatial resolution, which can affect image quality and quantitative accuracy.[3,7] These issues are particularly pronounced in patients with implants, surgical changes, or in areas adjacent to the chest wall and axilla.

The standardization of acquisition protocols and analysis methods across different platforms and institutions represents a major challenge for widespread clinical adoption. As demonstrated by the evaluation of IVIM biomarkers across different MRI vendors and software programs, significant variability exists in quantitative parameters derived from different platforms.[14] This variability underscores the need for standardized protocols, harmonization techniques, and quality assurance procedures to ensure reproducible and comparable results across institutions.

The interpretation of quantitative diffusion parameters is complicated by the influence of various biological and technical factors. Tumor cellularity, necrosis, fibrosis, and microenvironment characteristics all affect diffusion measurements, but the specific contributions of each factor are not always clear.[21,23] Additionally, technical factors such as b-value selection, number of b-values, signal-to-noise ratio, and fitting algorithms can significantly impact quantitative parameter values and their clinical interpretation.

The limited spatial resolution of DWI remains a challenge for characterizing small lesions and NMEs. As noted in the study of NME lesions, 31% of lesions presenting as NME on DCE-MRI could not be evaluated with DWI, primarily due to non-visibility on DWI sequences.[19] This limitation highlights the current necessity of contrast-enhanced sequences for comprehensive breast MRI evaluation and the need for continued technical improvements in DWI resolution and lesion conspicuity.

The integration of advanced diffusion models into clinical practice faces challenges related to acquisition time, computational complexity, and clinical validation. Although techniques such as IVIM, DKI, RSI, and MAP-MRI have shown promising results in research settings,[4,5] their implementation in routine clinical practice requires optimization of acquisition protocols, development of streamlined analysis tools, and validation in large multicenter trials.

Future perspectives for DWI in breast cancer imaging include the continued development of ultra-high field strength MRI (≥ 7 T), which may provide improved signal-to-noise ratios and spatial resolution for diffusion imaging. The integration of AI and deep learning methods is expected to play an increasingly important role in image reconstruction, artifact reduction, and automated analysis.[9,16] Additionally, the combination of DWI with other functional imaging techniques, such as magnetic resonance spectroscopy, chemical exchange saturation transfer, and hyperpolarized MRI, may provide complementary information for comprehensive tumor characterization.

The potential role of DWI in screening populations, particularly as a non-contrast alternative for women at intermediate risk or with contraindications to contrast administration, warrants further investigation.[11,13] Large prospective trials are needed to establish the efficacy of DWI-based screening protocols and to define appropriate patient selection criteria, imaging interpretation guidelines, and follow-up recommendations.

Beyond the technical and translational obstacles outlined above, this narrative review also has inherent limitations. Potential publication bias exists across included studies, as investigations reporting favorable diagnostic performance of diffusion MRI biomarkers tend to be prioritized for publication, whereas studies yielding negative or non-significant results may remain unpublished, potentially leading to an overestimated diagnostic value of these imaging parameters. Moreover, there is substantial interstudy heterogeneity in MRI scanning parameters across research centers, and globally unified standardized acquisition and quantitative measurement pipelines for novel advanced diffusion techniques are still lacking. In addition, most AI radiomics models built on diffusion MRI data only undergo single-center internal validation; large multicenter external validation cohorts are scarce, leaving the generalizability of these models across diverse patient populations and MRI hardware platforms insufficiently verified.

Conclusion and outlook

DWI has evolved from an ancillary sequence in breast MRI to a core component of multiparametric breast MRI. It complements morphological assessment by providing functional information and has demonstrated significant clinical value in breast lesion characterization, treatment response prediction, prognostic biomarker evaluation, and tumor heterogeneity analysis. Technically, optimizations in acquisition protocols, reconstruction algorithms, and quantitative analysis methods have addressed early application limitations. Moreover, advanced diffusion models, such as IVIM, DKI, RSI, MAP, and T-dDWI, when combined with radiomics and AI technologies, have gone beyond the limitations of conventional ADC to enable deeper analysis of tissue microstructure.

Despite remarkable progress in DWI applications, challenges remain, including insufficient standardization, interpretation variations, and difficulties in clinical application. Additionally, limited by spatial resolution, its ability to visualize NME lesions is suboptimal, and contrast-enhanced sequences are still required for comprehensive assessment at this stage. In the future, with the development of ultra-high field strength MRI, advanced reconstruction technologies, and AI, as well as the advancement of contrast-free screening protocols based on DWI, the application scenarios of DWI in breast imaging will be further expanded. With the

accumulation of clinical evidence and the deepening of multidisciplinary collaboration among radiology, physics, oncology, and surgery, DWI will be more widely integrated into standardized clinical guidelines, providing stronger support for the accurate diagnosis of breast tumors, selection of treatment plans, and monitoring of treatment efficacy.

Footnotes

Conflict of interest disclosure

The authors declared no conflicts of interest.

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