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The Role of Diffusion-Weighted Magnetic Resonance Imaging in Differentiating Benign and Malignant Breast Lesions: A Comprehensive Review

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Abstract

Breast magnetic resonance imaging (MRI) has emerged as a vital tool for detecting and characterizing breast lesions, particularly in differentiating benign from malignant tumors. This review explores the role of diffusion-weighted imaging (DWI) in breast MRI, highlighting its advantages over conventional imaging techniques. A systematic literature search was conducted across multiple databases, including PubMed and Scopus, to gather studies assessing DWI's sensitivity and specificity in breast cancer detection. The findings indicate that DWI provides high diagnostic accuracy, with a pooled sensitivity of 86.5% and specificity of 83.5%, comparable to dynamic contrast-enhanced MRI (DCE-MRI). Notably, utilizing apparent diffusion coefficient (ADC) thresholds can minimize unnecessary biopsies without compromising sensitivity. However, challenges remain in achieving standardization in DWI protocols, particularly regarding b-value selection and imaging techniques, which impact ADC accuracy. Advanced methodologies such as intravoxel incoherent motion (IVIM) and diffusion kurtosis imaging (DKI) have shown promise in enhancing diagnostic capabilities by providing deeper insights into tissue microstructure. This review underscores the importance of ongoing standardization efforts and collaboration among institutions to improve the reliability and applicability of DWI in clinical settings. In conclusion, DWI represents a transformative approach to breast cancer management, allowing for enhanced differentiation of lesions while reducing the need for invasive procedures. Further research and standardization are essential to optimize its use in routine clinical practice.

Keywords: *Breast MRI, Diffusion-Weighted Imaging, Benign Lesions, Malignant Tumors, Standardization.*

Introduction

Breast MRI has several benefits compared to conventional imaging methods, making it an essential instrument in diverse clinical situations [1]. Breast MRI is an advanced imaging modality with enhanced sensitivity for identifying breast malignancies, especially beneficial for high-risk screening and evaluating disease progression in confirmed cases. It is proficient in detecting initial cancers in metastatic contexts, analyzing pathologic nipple discharge, describing lesions, and evaluating breast implant integrity, making it an indispensable instrument in thorough breast care [2]. Recent improvements have resulted in the creation of shortened breast MRI procedures, providing an efficient method for cancer diagnosis while minimizing scan duration and expense [3].

In the field of breast MRI, diffusion-weighted imaging (DWI) has garnered considerable interest as a potential method for breast cancer diagnosis. DWI has some significant benefits compared to conventional approaches. This non-contrast approach obviates the need for contrast agents, hence mitigating possible

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dangers to patients and rendering it appropriate for those with intolerance to contrast media. The efficacy of DWI results in reduced scanning durations, hence improving patient comfort [4]. Moreover, DWI offers quantitative assessments via actual diffusion coefficient (ADC) values, which are essential for distinguishing among different lesion types. Numerous studies have validated the efficacy of DWI in breast cancer detection, exhibiting sensitivity and specificity comparable to dynamic contrast-enhanced MRI (DCE-MRI). The use of ADC thresholds with DCE-MRI has shown potential in minimizing superfluous biopsies [5, 6].

Notwithstanding its benefits, standardization continues to pose a hurdle in breast DWI. Diverse organizations have established rules and processes to guarantee uniformity and trustworthiness across various institutions and research. The selection of suitable b-values is essential for precise ADC readings. Recent studies indicate that breast density influences DWI image quality, highlighting the need for standardization across various breast forms [7].

Advanced DWI methodologies, including intravoxel incoherent motion (IVIM) and diffusion kurtosis imaging (DKI), provide deeper insights into tissue microstructure and microvasculature, hence augmenting its diagnostic efficacy. These approaches provide enhanced insights into tissue qualities, possibly augmenting the precision of breast cancer characterization and treatment strategies.

This review seeks to provide a thorough examination of the improvements and standardization initiatives in breast DWI. We will investigate the most recent approaches, address current problems, and analyze efforts designed to enhance consistency and reproducibility in breast DWI across various clinical environments. Through the examination of these advancements, we want to underscore the changing function of DWI in breast cancer management (Mansoor et al., 2020)

Quantitative DWI Metrics and ADC Thresholds in the Detection of Breast Cancer

A primary advantage of breast DWI is its capacity to provide excellent visibility and high specificity in differentiating malignant tumors from benign ones. The quantitative assessment facilitated by ADC values significantly aids in distinguishing between different lesion types [8]. Research has shown favorable outcomes for DWI when evaluating the sensitivity and specificity of various imaging modalities. Research indicated that DCE-MRI exhibited 100% sensitivity and 76.6% particularity, while DWI attained 82% sensibility and 86.8% specificity [9]. A recent systematic review encompassing 28 studies and 4406 lesions (1676 malignant, 2730 benign) across 3787 patients demonstrated that the pooled sensitivity and specificity of standalone DWI were 86.5% and 83.5%, respectively. In comparison with DCE-MRI, standalone DWI exhibited modestly lower sensitivity while maintaining similar specificity [10]. The integration of DCE-MRI and DWI produced excellent outcomes, achieving 96.8% susceptibility and 83.8% particularity, underscoring the efficacy of combining both methodologies [9]. Conversely, the amalgamation of DWI and T2WI represents a potential non-contrast technique. Research demonstrated that a decision tree using unenhanced sequences, including lesion margin and ADC, could differentiate malignant from benign lesions with AUCs ranging from 0.77 to 0.87 [11]. The integration of ADC and Kaiser scores may also be advantageous for novice radiologists [12].

The application of ADC criteria has shown to be an effective instrument in breast cancer detection, offering quantitative metrics to distinguish malignant from benign tumors. Malignant tumors have heightened cellularity and restricted water transport, leading to decreased ADC values in contrast to benign lesions or normal tissue. Meta-analyses indicate ADC values of 0.8–1.3 × 10^-3 mm²/s for malignant lesions, 1.2–2.0 × 10^-3 mm²/s for benign lesions, and 1.7–2.0 × 10^-3 mm²/s for normal breast tissue [13]. The recommended ADC thresholds for differentiating malignant from benign lesions typically range from 1.0 to 1.6 × 10^-3 mm²/s, despite significant overlap in these ranges. Nonetheless, appropriate thresholds may fluctuate based on variables such as MRI techniques and patient demographics. Consequently, ADC values must be interpreted judiciously with other imaging and clinical data, rather than used as an isolated diagnostic criterion [8]. These criteria may also decrease the incidence of superfluous biopsies, as shown in multi-center studies [5, 6].

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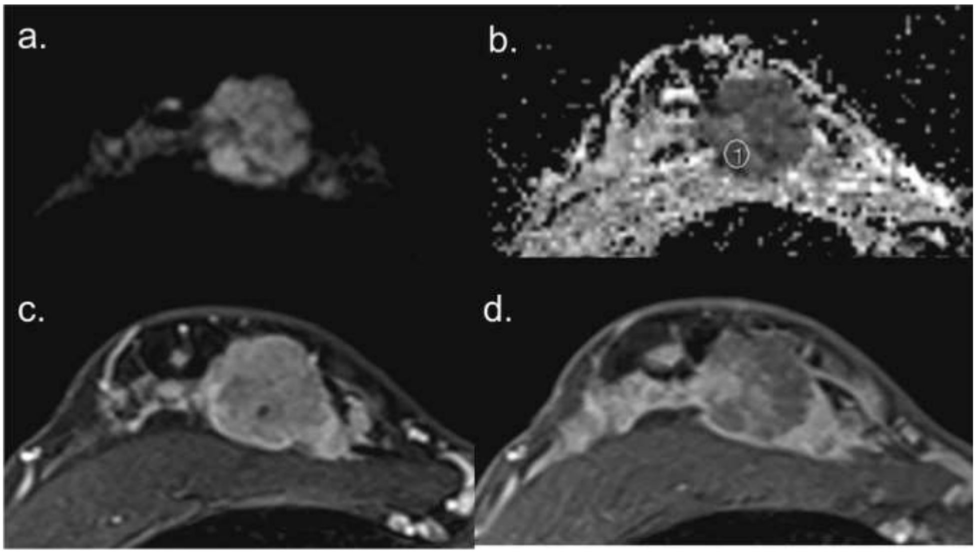
The ECOG-ACRIN study revealed that an ADC threshold of 1.53 × 10^-3 mm²/s (derived from b-values of 0 and 800 s/mm²) might decrease needless biopsies by 20.9% while preserving 100% sensitivity for malignancies. A multicenter investigation conducted by Clauser et al. indicated that an ADC threshold of 1.5 × 10^-3 mm²/s might exclude 46% of benign biopsies [5, 6]. A recent validation study indicates that utilizing the ADC cutoff may decrease biopsies by as much as 16%, albeit at the cost of diminished sensitivity for in situ and microinvasive disease manifesting as non-mass enhancement [13]. The classification of breast lesions using the Breast Imaging Reporting and Data System (BI-RADS) MRI based solely on ADC has also been contemplated, yet it currently possesses certain limitations [14-16]. Typically, low ADC levels signify malignant lesions, while high ADC values indicate benign lesions, as seen in Figure 1. This is mainly attributable to increased cellularity and more constrained water transport in malignant tumors [17]. This quantitative method enhances the diagnostic process, possibly increasing consistency and patient results.

Figure 1. Diffusion-weighted (DW) picture with a b value of 1000 sec/mm²

Association of ADC Levels with Hormone Receptor Activity

Meta-analyses of several studies have shown substantial connections between ADC values and hormone receptor status in breast tumors: Estrogen receptor (ER)-positive as well as progesterone receptor (PR)-positive malignancies often have lower ADCs compared to their negative counterparts. Cancers that are positive for human epidermal growth factor receptor 2 (HER2) often have elevated ADCs compared to those that are HER2-negative. Ki-67-positive neoplasms often exhibit reduced ADCs compared to Ki-67-negative neoplasms [17]. Nonetheless, significant variability exists across studies, underscoring the need for uniformity in research methodology and acquisition procedures.



Utilization of Diffusion-Weighted Imaging for Assessing Therapy Response in Breast Cancer

Neoadjuvant systemic therapy is often selected for locally progressed or particular types of breast cancer. DWI indicates tumor cellularity therefore water diffusivity and may identify tumor reaction to systemic therapy [18]. The ACRIN 6698 trial was conducted as a sub-study of the multicenter I-SPY 2 trial to evaluate the efficacy of DWI as an early indicator of breast tumors responding to neoadjuvant systemic chemotherapy. With an area under the recipient working characteristic curve (AUC) of 0.60 and 0.61, respectively, the percentage change in cancer ADC at mid-treatment (12 weeks) as well as following treatment was found to be a moderate predictor of abnormal complete response (pCR) in this study, which involved 242 women registered at 10 institutions. Recently, the findings from the Breast Multiparametric MRI for forecasting neoadjuvant treatment (BMMR2) challenge were reported [19,20]. The BMMR2 challenge used data from the I-SPY 2/ACRIN 6698 experiment to assess pCR prediction models derived from breast MRI. Three teams exceeded the ACRIN 6698 benchmark AUC of 0.78, attaining AUCs

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between 0.80 and 0.84 via diverse methodologies, including feature extraction and artificial intelligence, utilizing DCE-MRI and DWI either alone or in combination.

The assessment of increased tumor volume with contrast-enhanced MRI is shown to forecast the tumor's response to neoadjuvant treatment, albeit it is time-intensive. Recent research indicated that DWI-maximum intensity projection may serve as a substitute for contrast-enhanced MRI for tumor size evaluation, requiring a reduced processing time [21].

Standardization Initiatives in Breast Diffusion-Weighted Imaging (DWI)

The standardization of breast DWI has grown more crucial as the technology is more widely used in clinical practice. Diverse efforts, such as EUSOBI, DWIST, and QIBA, have established norms and methods to guarantee uniformity and dependability in breast DWI across various institutions and research [8,22,23].

The standardization standards generally delineate essential technological characteristics. They advocate for using magnetic field strengths of 1.5T or 3.0T with specialized breast coils to guarantee superior picture quality [24]. The field of view must cover both breasts, with the possibility of including the axillary area for thorough imaging. Standards for slice thickness exhibit minor variations but typically range from 3 to 5 mm. The selection of suitable b-values is essential for precise ADC measurements since ADC is greatly influenced by b-values (Figure 2).

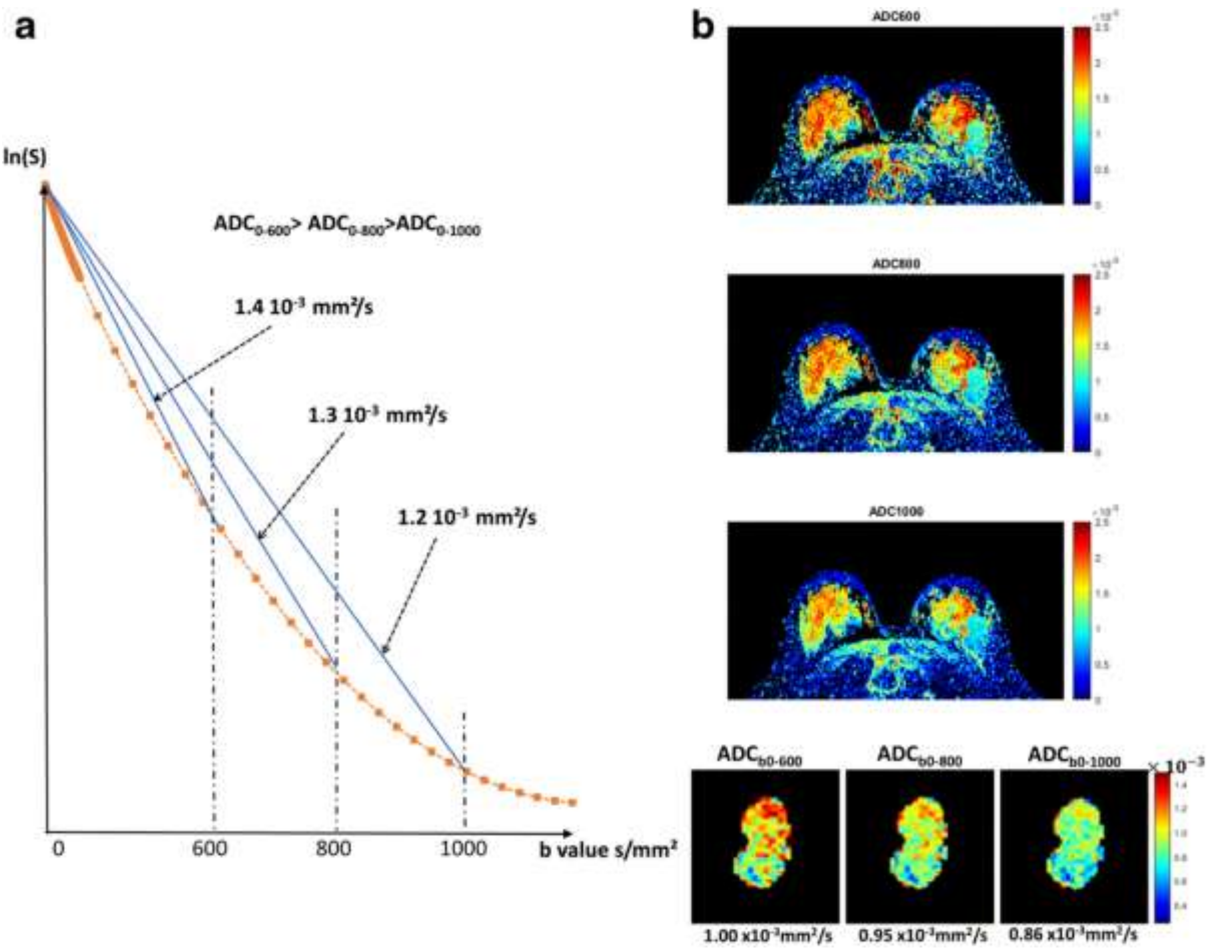

Figure 2. Decay of DWI signals concerning b value. Water diffusion in tissues leads to a reduction in the MRI signal proportional to the diffusion weighting of the MRI sequence, as shown by its b value. In pure water, the logarithm of the signal attenuation forms a linear relationship.

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The recommendations underscore the need for efficient fat suppression in breast DWI to prevent ADC underestimate and chemical shift abnormalities. Spectral adiabatic inverted recovery (SPAIR) is preferred over short-tau inverted recovery (STIR) because STIR may result in signal attenuation across all tissues, which may lead to inaccuracies in ADC estimates [25]. These initiatives seek to create baseline standards for equipment and imaging methods, essential for generating consistent findings across institutions. Nonetheless, difficulties remain, including inconsistencies in ADC measurements across several locations and equipment manufacturers [26]. Achieving agreement on the specifics of the protocol is still ongoing. The consensus on the ideal combination of b-values and imaging methodologies is in flux.

Differences in breast tissue structure and density influence the quality of DWI images. A recent study by Wielema M et al. indicates that DWI image quality improves with greater breast density, implying its potential efficacy for screening dense breasts, while highlighting the requirement for improvement in less dense breasts [7].

Prior studies also provide promising evidence for the reliability of DWI in therapeutic applications. A meta-analysis of 61 investigations, including 4778 patients and 5205 lesions, indicates that DWI consistently exhibits good diagnostic efficacy in distinguishing malignant from benign breast lesions, irrespective of differences in collection techniques or scanner types. DWI demonstrates an overall sensitivity of 90% and specificity of 86%, with little variation between 1.5T and 3.0T MRI units, effectively distinguishing between benign and malignant breast lesions regardless of variances in acquisition techniques or scanner types [27]. The findings are encouraging and indicate that while heterogeneity in ADC values across various locations and equipment may influence lesion definition, DWI remains efficient in distinguishing between malignant and benign breast lesions notwithstanding these discrepancies. However, ongoing cooperation and research in the domain are crucial to enhance and regulate breast DWI procedures, hence providing increased uniformity and dependability in the clinical setting.

Qualitative Assessment Techniques

Although quantitative techniques like as ADC measures are prevalent in breast DWI, qualitative approaches also contribute to lesion evaluation. Qualitative assessment entails the visual interpretation of diffusion-weighted (DW) pictures and apparent diffusion coefficient (ADC) maps, akin to the Prostate Imaging Reporting and Data System (PI-RADS) used in prostate imaging [28]. Our prior study indicated that multiple b-value diffusion-weighted imaging (5b-value DWI) demonstrated potential in evaluating breast lesions, exhibiting substantial observer concordance; however, its diagnostic efficacy (sensitivity 79.5–84.6%, specificity 62.5–64.3%) was inferior to that of combined MRI with dynamic contrast-enhanced imaging (sensitivity 97.4%, specificity 75.0–78.6%) [29].

Regarding lesion detection, prior studies on breast cancer identification using DWI alone have yielded inconsistent results concerning sensitivity and specificity [30]. However, a recent investigation assessed the impact of training on radiologists' efficacy in understanding unenhanced breast MRI with DWI for cancer identification [31]. Sixteen breast radiologists evaluated 96 breast images before and after a 2-hour training session. Results indicated that concise instruction markedly enhanced specificity (90.8–95.2%) and accuracy (83.5% to 85.9%), while inter-reader concordance also improved. The research indicates that specialized training may improve radiologists' proficiency in interpreting unenhanced breast MRI with DWI, suggesting its viability as an independent technique for breast cancer diagnosis. DWI identified a substantially greater number of clinically occult contralateral breast cancers (23 out of 30, 76.7%) with fewer biopsy recommendations compared to the combination of mammography and ultrasound (12 out of 30, 40.0%) in women with newly diagnosed breast cancer, indicating a superior cancer detection rate (2.0% vs 1.0%) and positive predictive value for biopsy (42.1% vs 18.5%) [32].

Recent research assessed the effect of dual interpretation of breast DWI on breast cancer detection [33]. This research included 378 women, of whom 41% had high-risk screening or surveillance MRI. Two breast radiologists assessed high- and low-b pictures together with ADC maps, enabling a quantitative assessment of the readers' choice. Each breast was classified as positive/suspect or negative by each reader, and instances deemed positive/suspect by one or more readers were considered positive. The findings indicated

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a sensitivity of 93% and a specificity of 86%, with a sensitivity of 71% for tumors measuring < 10 mm, suggesting the viability of DWI screening. Recent technological developments, like simultaneous multi-slice echo-planar diffusion-weighted imaging (SMS-DWI), may enhance lesion visibility [34]. Comprehensive multi-center research evaluating the screening efficacy of DWI is now underway in Korea [22], which will provide substantial evidence supporting DWI screening.

Advanced Methodologies in Diffusion-Weighted Imaging

In addition to conventional ADC measurements, sophisticated methods such as IVIM and non-Gaussian DWI may provide further insights into tissue microstructure and microvasculature. These techniques show potential in distinguishing malignant from benign breast lesions and forecasting metastatic breast cancer [17]. A meta-analysis of 16 studies assessing the diagnostic efficacy of IVIM-DWI in distinguishing breast tumors revealed that breast malignancies had considerably lower ADC and D values, with elevated f values in comparison to benign lesions. The D value demonstrated superior diagnostic efficacy, with a sensitivity of 86%, specificity of 86%, and an AUC of 0.91, in distinguishing breast cancers. IVIM-DWI parameters demonstrated superiority over ADC alone in differentiating breast cancers and may further discriminate invasive ductal carcinoma from ductal carcinoma in situ [35]. Diffusion kurtosis imaging (DKI) augments breast cancer assessment by quantifying non-Gaussian diffusion behavior at elevated b-values (>1000 s/mm2) via the kurtosis parameter (K), potentially enhancing the differentiation between malignant and benign lesions and offering insights into tumor characteristics that extend beyond conventional diffusion-weighted imaging, which generally employs b-values up to 1000 s/mm2 [36]. Recent studies indicate that DKI parameters, particularly elevated K values, may possess predictive significance in breast cancer, correlating with reduced distant disease-free survival [37]. These sophisticated diffusion methods have promise for enhancing diagnosis, therapy monitoring, and outcome prediction in breast cancer care.

Conclusions

In conclusion, breast DWI has had significant breakthroughs, enhancing its efficacy in detecting, characterizing, and discriminating breast lesions. The current standardization initiatives spearheaded by entities such as EUSOBI, DWIST, and QIBA are crucial for unifying imaging methods and improving diagnostic precision. As these initiatives advance, they will be crucial in promoting the widespread use of these imaging modalities and guaranteeing their dependability in clinical practice. The ongoing enhancement of standardizing methods is crucial for optimizing the efficacy of breast DWI in advancing patient treatment and outcomes.

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دور تصوير الرنين المغناطيسي بالانتشار في التمييز بين الآفات الحميدة والخبيثة في الثدي: مراجعة شاملة

الملخص

الخلفية :أصبح تصوير الرنين المغناطيسي للثدي أداة حيوية للكشف عن آفات الثدي وتوصيفها، لا سيما في التمييز بين الأورام الحميدة والخبيثة. تستعرض هذه المراجعة دور التصوير بالانتشار (DWI) في تصوير الرنين المغناطيسي للثدي، مع تسليط الضوء على مزاياه مقارنة بتقنيات التصوير التقليدية.

المنهجية :تم إجراء بحث منهجي في قواعد بيانات متعددة، بما في ذلك PubMed وScopus، لجمع الدراسات التي تقيم حساسية وخصوصية التصوير بالانتشار في الكشف عن سرطان الثدي.

النتائج :تشير النتائج إلى أن التصوير بالانتشار يوفر دقة تشخيصية عالية، بحساسية مجمعة تبلغ 86.5% وخصوصية مجمعة تبلغ 83.5%، وهي نتائج قابلة للمقارنة مع التصوير الديناميكي المعزز بالتباين .(DCE-MRI) ومن الجدير بالذكر أن استخدام قيم معامل الانتشار الظاهر (ADC) يمكن أن يقلل من الخزعات غير الضرورية دون المساس بالحساسية. ومع ذلك، لا تزال هناك تحديات في تحقيق توحيد بروتوكولات التصوير بالانتشار، خصوصًا فيما يتعلق باختيار قيم "b" وأساليب التصوير، مما يؤثر على دقة قيم ADC. وقد أظهرت منهجيات متقدمة مثل حركة الجسيمات داخل الفوكسل (IVIM) وتصوير التشتت الكرتوسي (DKI) وعودًا في تحسين القدرات التشخيصية من خلال تقديم رؤى أعمق في البنية الدقيقة للأنسجة.

الاستنتاجات :تؤكد هذه المراجعة على أهمية الجهود المستمرة لتوحيد المعايير والتعاون بين المؤسسات لتحسين موثوقية وقابلية تطبيق التصوير بالانتشار في البيئات السريرية. وفي الختام، يمثل التصوير بالانتشار نهجًا تحوليًا في إدارة سرطان الثدي، مما يسمح بتحسين التمييز بين الآفات وتقليل الحاجة إلى الإجراءات الجراحية. هناك حاجة ماسة إلى مزيد من البحث والتوحيد لتحسين استخدامه في الممارسة السريرية الروتينية.

الكلمات المفتاحية :تصوير الرنين المغناطيسي للثدي، التصوير بالانتشار، الآفات الحميدة، الأورام الخبيثة، التوحيد.