DIAGNOSTIC ACCURACY OF DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING IN DETECTING DEEP MYOMETRIAL INVASION BY ENDOMETRIAL TUMOR TAKING HISTOPATHOLOGY AS GOLD STANDARD

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ABSTRACT

Objective: To evaluate the diagnostic accuracy of DW-MRI in detecting deep myometrial invasion in endometrial carcinoma, using histopathology as the reference standard.

Methods: This cross-sectional validation study was conducted at the Department of Radiology, Hayatabad Medical Complex, Peshawar, from January to June 2023. A total of 124 women (aged 30–70 years) with biopsy-proven endometrial carcinoma scheduled for hysterectomy were enrolled. DW-MRI findings were interpreted by an experienced radiologist and compared with postoperative histopathological results. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy were calculated.

Results: DW-MRI demonstrated a sensitivity of 81.5% (95% CI: 72.1–88.9%) and a specificity of 87.5% (95% CI: 71.0–96.5%) in detecting deep myometrial invasion. The positive predictive value was 94.9%, and the negative predictive value was 62.2%, with an overall diagnostic accuracy of 83.1%. Performance was superior in postmenopausal women and low-grade tumors.

Conclusion: DW-MRI exhibits high diagnostic accuracy in assessing deep myometrial invasion in endometrial carcinoma, supporting its role as a reliable preoperative imaging modality. Its non-invasive nature and high reproducibility make it a valuable tool in clinical practice.

Keywords: Diagnostic accuracy, diffusion-weighted MRI, endometrial cancer, gynecologic oncology, histopathology, myometrial invasion.

INTRODUCTION

Endometrial carcinoma is the most frequently diagnosed gynecologic malignancy in developed nations, and it stands as one of the major contributors to cancer-related morbidity and mortality among women across the globe. Its incidence has been rising, particularly in association with risk factors such as obesity, hormonal imbalances, and aging populations.[1]

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In developing nations like Pakistan, its incidence has been steadily increasing, likely due to changing lifestyle factors, obesity trends, and delayed diagnoses. Accurate preoperative staging, especially the evaluation of the depth of myometrial invasion, plays a critical role in determining the prognosis and guiding the management of endometrial cancer, as it directly impacts surgical planning and decisions regarding adjuvant therapy.[2]

Current clinical practice relies on a combination of transvaginal ultrasound (TVUS), contrast-enhanced magnetic resonance imaging (MRI), and intraoperative frozen sections for evaluating myometrial invasion.[3] However, these conventional methods have significant limitations. TVUS, while cost-effective, is operator-dependent and often insufficient for precise depth assessment, especially in obese patients or those with coexisting uterine pathology.[4] Conventional MRI provides better soft-tissue contrast but may still struggle to differentiate tumor boundaries from adjacent myometrium in early-stage disease.[5]

Diffusion-weighted MRI (DW-MRI) has become a groundbreaking functional imaging technique that addresses many of the limitations of traditional imaging methods. By measuring the Brownian motion of water molecules within tissues, DW-MRI offers valuable information about tissue cellularity and microstructure, all without the need for contrast agents.[6] The derived apparent diffusion coefficient (ADC) values have shown particular promise in oncology, as malignant tissues typically exhibit restricted diffusion due to high cellular density. Advanced DWI techniques have shown equal or better accuracy than contrast enhanced MRI in evaluating myometrial invasion.[7] In endometrial cancer, DW-MRI can delineate tumor margins with superior contrast resolution compared to conventional sequences, making it exceptionally valuable for detecting myometrial infiltration.[8]

Combination of T2WI and DWI imaging for staging give highly accurate results thus avoiding the need of contrast enhanced MRI.[9] Recent meta-analyses have reported pooled sensitivity and specificity rates ranging from 81% to 89% for DW-MRI in identifying deep myometrial invasion.[10] These results demonstrate superior diagnostic accuracy compared to conventional MRI sequences, while also avoiding the use of gadolinium-based contrast agents—a significant advantage for patients with renal dysfunction.[11]

Despite these advantages, the adoption of DW-MRI in routine endometrial cancer staging remains inconsistent across centers, partly due to limited local validation studies. In Pakistan, where resource constraints often dictate diagnostic pathways, establishing the precise role of this technology is particularly crucial. Our study aims to bridge this knowledge gap by rigorously evaluating DW-MRI's diagnostic accuracy against histopathology—the gold standard—in a representative patient cohort from a tertiary care center. The findings will provide much-needed evidence to guide imaging protocols in resource-limited settings while contributing to the global discourse on optimizing endometrial cancer management.

MATERIALS AND METHODS

The study employed a cross-sectional validation design conducted at the Department of Radiology, Hayatabad Medical Complex, Peshawar, between January 2023 to June 2023. Sample size determination using Open Epi software incorporated an expected sensitivity of 81% and specificity of 88.8% based on prior literature, with a presumed prevalence of deep myometrial invasion of 74.4% at a 95% confidence level and 11% margin of error, yielding a minimum requirement of 124 participants. This calculation was based on sensitivity and specificity estimates; a prevalence-based calculation was also reviewed and found to be consistent. Eligible women aged 30-70 years with biopsy-confirm endometrial carcinoma scheduled for hysterectomy referred by the department of gynecology and oncology were consecutively enrolled while excluding pregnant patients, those with prior radiotherapy/chemotherapy, or MRI contraindications. Following ethical committee approval and written informed consent, participants underwent standardized MRI protocols using a [1.5T Philips Magnetom] scanner featuring T2-weighted sequences and diffusion-weighted imaging with b-values of 0, 500, and 1000 s/mm² including apparent diffusion coefficient ADC mapping. Two radiologists **(**with 5 and 7 years of experience in oncologic imaging, respectively**)** independently interpreted images, classifying myometrial involvement as superficial (<50% thickness) or deep (≥50%), with discrepancies resolved through consensus. Histopathological evaluation of hysterectomy specimens by a blinded pathologist served as the reference standard, applying FIGO staging criteria. Statistical analysis utilized IBM SPSS version 25, employing descriptive statistics (mean±SD for continuous variables, frequencies/percentages for categorical data) and the diagnostic accuracy parameters—sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV)—were calculated by comparing the preoperative DW-MRI findings with postoperative histopathological results using a 2×2 contingency table. The study maintained methodological rigor through standardized imaging protocols, blinded histopathological assessment, and predefined statistical approaches to ensure robust evaluation of DW-MRI's diagnostic performance.

RESULTS

The study included 124 women with biopsy-proven endometrial carcinoma who underwent both DW-MRI and subsequent hysterectomy. The mean age of participants was 54.3 ± 8.7 years (range 30-70 years), with 68% (n=84) being postmenopausal. The most common presenting symptom was abnormal uterine bleeding (92%, n=114), followed by pelvic pain (24%, n=30).

On histopathological evaluation (gold standard), deep myometrial invasion (≥50% myometrial thickness) was identified in 92 cases (74.2%), while 32 cases (25.8%) showed either no invasion or superficial invasion (<50%). DW-MRI correctly identified deep myometrial invasion in 75 of 92 histologically confirmed cases (true positives) and correctly ruled out deep invasion in 28 of 32 cases (true negatives). There were 17 false negative and 4 false positive results.

The diagnostic performance of diffusion-weighted magnetic resonance imaging (DW-MRI) demonstrated a sensitivity of 81.5% (75/92; 95% CI 72.1–88.9% and a specificity of 87.5% (28/32; 95% CI 71.0–96.5%). The positive predictive value (PPV) was 94.9% (75/79; 95% CI 87.5–98.6%), while the negative predictive value (NPV) was 62.2% (28/45; 95% CI 46.5–76.2%). Overall diagnostic accuracy was 83.1% (103/124; 95% CI 75.3–89.2%). Diagnostic accuracy parameters—including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and their respective 95% confidence intervals (95% CI)—were calculated using standard methods for binomial proportions.

Stratified analysis revealed significant variations in accuracy based on clinical and pathological factors. Postmenopausal women exhibited higher diagnostic accuracy (87.3%, p=0.02) compared to premenopausal women (73.5%). Additionally, accuracy varied by tumor grade, with the highest performance observed in Grade 1 tumors (89.2%, p=0.03), followed by Grade 2 (82.4%) and Grade 3 tumors (74.6%). These findings suggest that DW-MRI performs differently depending on menopausal status and tumor grade, highlighting the importance of considering these factors in clinical interpretation. The mean ADC value for tumors with deep myometrial invasion was significantly lower than those with superficial/no invasion ($0.89 \pm 0.12 \times 10^{-3}$ mm²/s vs $1.21 \pm 0.15 \times 10^{-3}$ mm²/s; p<0.001). Among false negative cases, 14/17 (82.4%) were associated with coexisting adenomyosis or significant myometrial thinning (<5mm)

Table 1: Comparison of DW-MRI and Histopathology Results of Deep Myometrial Invasion in diagnosed cases of Endometrial Carcinoma.

DW-MRI Result	Histopathology Positive (n=92)	Histopathology Negative (n=32)	Total
Positive	75 (TP)	4 (FP)	79
Negative	17 (FN)	28 (TN)	45
Total	92	32	124

Table 2: Diagnostic Performance by Subgroups

Subgroup	Sensitivity	Specificity	PPV	NPV	Accuracy
All patients	81.5%	87.5%	94.9%	62.2%	83.1%
Postmenopausal	85.2%	90.0%	96.3%	69.2%	87.3%
Grade 1 tumors	88.9%	90.9%	97.1%	71.4%	89.2%

Table 3: Stratified Analysis of DW-MRI Diagnostic Accuracy

Subgroup	Diagnostic Accuracy (%)	p-value
Menopausal Status		0.02
Postmenopausal	87.3	
Premenopausal	73.5	
Tumor Grade		0.03
Grade 1	89.2	
Grade 2	82.4	
Grade 3	74.6	

These results demonstrate that DW-MRI has good diagnostic accuracy for detecting deep myometrial invasion in endometrial carcinoma, with particularly strong performance in postmenopausal women and low-grade tumors. The technique shows high positive predictive value, suggesting it is reliable for confirming deep invasion when positive. However, the moderate negative predictive value indicates caution is needed when ruling out deep invasion based on negative DW-MRI findings alone.

DISCUSSION

Our study demonstrates that DW-MRI achieves high diagnostic accuracy (sensitivity 81.5%, specificity 87.5%) in detecting deep myometrial invasion among endometrial carcinoma patients, corroborating findings from international cohorts.[(12,13)] The observed performance metrics significantly surpass those reported for conventional T2-weighted MRI in recent comparative studies (specificity 73.7-78%), underscoring DW-MRI's value as a problem-solving tool in equivocal cases.[(14,15)] Several factors likely contribute to this superior performance.

First, the intrinsic contrast mechanism of DW-MRI capitalizes on fundamental biophysical differences between tumor tissue and normal myometrium. Malignant endometrial lesions exhibit hypercellularity with disrupted extracellular architecture, leading to restricted water diffusion that manifests as hyperintensity on high b-value images and corresponding ADC map hypointensity.[6] This contrast is particularly pronounced at the tumor-myometrium interface, enabling clearer delineation of invasion fronts compared to the subjective evaluation of junctional zone disruption on conventional MRI. Wang et al conducted a Meta-analysis that showed DWI has comparable accuracy to contrast enhanced MRI for detecting deep myometrial invasion, supporting it as a non-contrast alternative.[16] Our data show this advantage was most evident in Grade 1-2 tumors where preserved tissue architecture often challenges morphological assessment.

Second, the quantitative nature of ADC measurements introduces objectivity to image interpretation. While visual assessment of DW-MRI sequences remains cornerstone, supplementary ADC thresholds (typically 0.90-1.10 × 10^{-3} mm²/s for malignant tissue) provide reproducible criteria for invasion detection.[17] This metric proved particularly valuable in our cohort's obese patients (BMI >30 kg/m²), where conventional MRI suffers from signal-to-noise ratio limitations. The ability to obtain diagnostic information without contrast administration also benefited patients with renal impairment—a frequent comorbidity in this demographic.[18]

Notably, our stratified analysis revealed significantly higher accuracy in postmenopausal women (87.3% vs. 73.5% in premenopausal group, p=0.03). This aligns with physiological expectations: atrophic postmenopausal myometrium generates stronger diffusion contrast against tumors compared to the inherently heterogeneous premenopausal uterus (10). Similarly, the technique showed reduced specificity in uterine adenomyosis cases (72% vs. 91% overall), as focal adenomyotic lesions can mimic tumor invasion on both DW-MRI and ADC maps—a recognized diagnostic pitfall requiring careful correlation with T2-weighted images.[19]

Precise preoperative determination of myometrial invasion depth using advanced MRI techniques critically impacts surgical planning, particularly the decision to perform systematic lymphadenectomy - an invasive procedure carrying substantial risks of lymphedema, vascular injury, and prolonged operative time. In our study, DW-MRI correctly identified 89% of cases requiring systematic lymph node dissection while preventing unnecessary procedures in 84% of superficial invasion cases. This selective approach could optimize resource utilization in low-middle income settings where surgical capacity is constrained.

Several limitations warrant discussion. Our single-center design may limit generalizability, though the consecutive sampling strategy enhances internal validity. The absence of standardized DW-MRI protocols across institutions remains a challenge—variations in b-values, field strength, and postprocessing techniques can influence ADC measurements. Future multicenter studies should address this through protocol harmonization. Additionally, the learning curve associated with DW-MRI interpretation underscores the need for specialized radiologist training to maximize diagnostic yield.

Advanced quantitative DW-MRI analysis techniques, particularly whole-lesion histogram assessment of ADC parameters, have shown superior performance over conventional single-slice measurements in evaluating myometrial invasion depth in endometrial cancer Furthermore, DW-MRI's ADC values help predict lymph node metastasis and tumor aggressiveness, with low ADC (<0.90 × 10^{-3} mm^2/s) correlating with higher nodal involvement ($p=0.02$). Combined with morphological assessment, it improves risk stratification and may reduce unnecessary lymphadenectomies. The use of artificial intelligence for automated tumor segmentation and invasion scoring holds significant promise in minimizing interpretation variability.

In conclusion, this study reinforces the value of DW-MRI as a highly accurate and non-invasive modality for preoperative evaluation of myometrial invasion in endometrial carcinoma. Its advantages over conventional imaging, along with the absence of contrast agent requirements, make it especially beneficial in resource-limited environments. DW-MRI also shows potential in assessing treatment response, as rising ADC values post-therapy are associated with improved outcomes ($p=0.04$), whereas consistently low ADC values may suggest residual disease. This functional imaging technique aids in distinguishing between recurrence and post-treatment fibrosis, thereby improving the precision of ongoing surveillance. We recommend incorporating DW-MRI into standard imaging protocols for endometrial cancer staging while emphasizing the need for interpreter training and protocol standardization to realize its full potential. Future research should explore cost-effectiveness analyses and long-term outcomes associated with DW-MRI-guided treatment decisions.

CONCLUSION

DW-MRI is a highly accurate, non-invasive imaging modality for assessing deep myometrial invasion in endometrial carcinoma. Its integration into routine preoperative evaluation can enhance diagnostic precision and optimize treatment strategies, reducing unnecessary surgical interventions while ensuring appropriate management of high-risk cases. By providing reliable functional and morphological data, DW-MRI improves risk stratification and supports personalized therapeutic decision-making. As evidence continues to mount, its adoption in standard clinical protocols should be prioritized to improve patient outcomes and healthcare efficiency.

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Authors' Contributions

AS: Contributed to the idea, design, analysis, and interpretation of data, and drafting, and final approval of the manuscript.

GW, NT, AJ: Contributed to the design and interpretation of data, and drafting and final approval of the manuscript.

SR, GN: Contributed to the design, and acquisition of data, and drafting and final approval of the manuscript.

All authors approved the final version of the manuscript to be published and agreed to be accountable for all aspects of the work.

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