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Diagnostic Comparison of MRI Sequences for Assessing Myometrial Invasion in Endometrial Cancer: A 1.5T MRI Study

Endometrium Kanserinde Miyometrial İnvazyonun Değerlendirilmesinde MRG Sekanslarının Tanısallığının Karşılaştırması: 1.5T MRG Çalışması

Ahmet Akçay* | **Abdusselim Adil Peker**

Bezmialem Vakıf University, Faculty of Medicine, Department of Radiology, İstanbul, Türkiye

Sorumlu Yazar | Correspondence Author
Ahmet Akçay
ahmetakcaymd@gmail.com
Address for Correspondence: Bezmialem Vakıf University, Faculty of Medicine, Department of Radiology, 34093, İstanbul, Türkiye

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ABSTRACT

Objective: To compare the diagnostic accuracy of T2-weighted, dynamic contrast-enhanced imaging, and diffusion-weighted imaging in assessing myometrial invasion depth in endometrial cancer and to determine if any sequence performs better.

Material and Method: In this retrospective study, 98 patients with histopathologically confirmed endometrial cancer underwent preoperative multiparametric pelvic magnetic resonance imaging scans using a 1.5-T machine between January 2018 and May 2024. The T2-weighted, dynamic contrast-enhanced, and diffusion-weighted imaging sequences were independently reviewed by an experienced radiologist blinded to pathology results to assess myometrial invasion depth (superficial vs. deep). Sensitivity, specificity, accuracy, negative predictive value, and positive predictive value were calculated. Statistical analyses included ROC curves and McNemar's test.

Results: T2-weighted, dynamic contrast-enhanced, and diffusion-weighted imaging showed high diagnostic accuracy for assessing myometrial invasion, with area under the curve values of 0.967, 0.954, and 0.916, respectively. T2-weighted images achieved the highest sensitivity (1.0) and specificity (0.934). While diffusion-weighted images and dynamic contrast-enhanced images demonstrated slightly lower accuracy compared to T2-weighted images, the differences were not statistically significant ($p>0.05$). However, both diffusion-weighted images and dynamic contrast-enhanced images had higher misclassification rates in cases with fibroids, adenomyosis, or indistinct junctional zones.

Conclusion: All three magnetic resonance sequences demonstrated high diagnostic accuracy for evaluating myometrial invasion in EC. Although T2-weighted images had slightly better diagnostic accuracy due to its superior anatomical detail, the differences were not statistically significant. In cases with confounding factors, combining T2-weighted, dynamic contrast-enhanced, and diffusion-weighted imaging improves diagnostic reliability.

Keywords: Endometrial cancer, MRI, myometrial invasion.

ÖZET

Amaç: T2 ağırlıklı, dinamik kontrastlı görüntüleme ve difüzyon ağırlıklı görüntüleme tekniklerinin endometrial kanserde miyometrial invazyon derinliğini değerlendirmedeki tanısal doğruluğunu karşılaştırmak ve herhangi bir dizinin daha iyi performans gösterip göstermediğini belirlemektir.

Gereç ve Yöntem: Bu retrospektif çalışmada, Ocak 2018 ile Mayıs 2024 tarihleri arasında histopatolojik olarak doğrulanmış endometrium kanseri tanısı konulan 98 hastaya preoperatif multiparametrik pelvik manyetik rezonans görüntülemeleri yapıldı. T2 Ağırlıklı, dinamik kontrastlı ve difüzyon ağırlıklı görüntüleme dizileri, patoloji sonuçlarından habersiz deneyimli bir radyolog tarafından bağımsız olarak incelenerek miyometrial invazyon derinliği (yüzeyel veya derin) değerlendirildi. Duyarlılık, özgüllük, doğruluk, negatif prediktif değer ve pozitif prediktif değer hesaplandı. İstatistiksel analizler ROC eğrileri ve McNemar testi ile yapıldı.

Bulgular: T2 Ağırlıklı, dinamik kontrastlı ve difüzyon ağırlıklı görüntüleme dizileri, miyometrial invazyonun değerlendirilmesinde yüksek tanısal doğruluk gösterdi; eğri altındaki alan değerleri sırasıyla 0,967, 0,954 ve 0,916 olarak bulundu. T2 Ağırlıklı seri, en yüksek duyarlılık (1,0) ve özgüllük (0,934) değerlerine ulaştı. Difüzyon ağırlıklı görüntüleme ve dinamik kontrastlı görüntüleme, T2 Ağırlıklı seriye kıyasla daha düşük doğruluk gösterdi, ancak aradaki fark istatistiksel olarak anlamlı değildi ($p>0,05$). Bununla birlikte, Difüzyon ağırlıklı görüntüleme ve dinamik kontrastlı görüntülemede, fibroid, adenomyozis veya belirsiz junctional zone gibi karışıklığa neden olan faktörler daha fazla yanlış sınıflandırmaya yol açmıştır.

Sonuç: Üç manyetik rezonans dizisi de endometrium kanserinde miyometrial invazyonun değerlendirilmesinde yüksek tanısal doğruluk göstermiştir. Daha fazla anatomik detay sunan T2 Ağırlıklı serinin, daha yüksek tanısal doğruluk sağladığı gözlemlenmiş; ancak diğer sekanslarla istatistiksel olarak anlamlı fark saptanmamıştır. Karışıklığa neden olan durumlarda, T2 Ağırlıklı serinin difüzyon ağırlıklı görüntüleme ve dinamik kontrastlı görüntüleme ile birlikte değerlendirilmesi tanısal doğruluğu artırmak için önerilmektedir.

Anahtar Sözcükler: Endometrium kanseri, MRG, miyometrial invazyon.

Introduction

Endometrial cancer (EC), frequently observed in older, postmenopausal women, is among the most prevalent gynecologic malignancies (1). Most cases of EC are diagnosed early, when the disease is limited to the uterus, due to the common symptom of vaginal bleeding (2). The surgical procedure and clinical management of EC are determined according to the stage of the disease. The pathological staging of EC is assessed using the FIGO classification system (3). In advanced EC, treatment may be extended with neoadjuvant chemotherapy and pelvic lymph node dissection, along with standard hysterectomy and bilateral salpingo-oophorectomy (2). Deep myometrial invasion, high cellular grade, cervical involvement, parametrial extension, lymph node metastasis, and the aggressive histological subtype of the tumor are critical factors indicating a poor prognosis and necessitating extensive surgical procedures in EC (2, 4). In cases with superficial myometrial invasion, if there are no other high-risk criteria present, hysterectomy and bilateral salpingo-oophorectomy are sufficient in terms of treatment (2). The diagnosis of EC is assessed through endometrial sampling using a Pipelle biopsy or dilation and curettage (D&C). Although preoperative endometrial biopsy has higher accuracy in detecting the degree of myometrial invasion, tumoral heterogeneity and insufficient sampling of the tumor tissue may lead to an underestimation of the stage of the disease (5). Magnetic resonance imaging (MRI) exhibits high soft tissue resolution, particularly when utilizing small field of view multiparametric scanning protocols. In this case, according to the guidelines, MRI is recommended for assessing endometrial cancer before surgery (2). Several studies in the literature have assessed MRI's accuracy in detecting the degree of myometrial invasion (6-9). Some studies evaluated MRI performance in a single session, while others evaluated the performance of two different MRI sequences separately. This study aims to individually assess all multiparametric pelvic MRI (mp-MRI) sequences, such as T2-weighted (T2W), diffusion-weighted (DWI), and contrast-enhanced T1-weighted (DCE) imaging, and to see if one works better than the others. Due to factors such as myometrial thinning, adenomyosis, and uterine fibroids, these MRI sequences may be affected, potentially leading to incorrect determinations regarding the degree of myometrial invasion.

Material and Methods

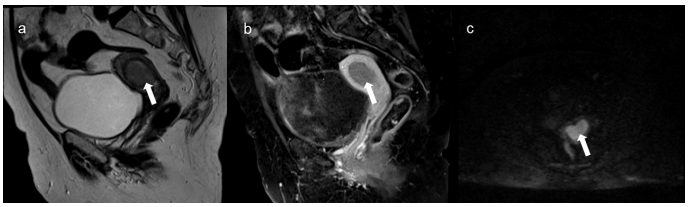
Approval for this study was obtained from Bezmialem Vakıf University Non-Interventional Research Ethics Committee (E-54022451-050.04-155766). Patients diagnosed with endometrial cancer who underwent preoperative pelvic mp-MRI between January 2018 and May 2024 were included. All subjects underwent surgery within five weeks after the MRI was obtained. Patients management was aligned with the ESMO guidelines (5). The exclusion criteria for this study included: 1. Significant image artifacts 2. Prior neoadjuvant chemotherapy 3. Tumors too small to be detected on MRI. All hysterectomy specimens were evaluated according to FIGO criteria, and the degree of myometrial invasion (superficial (<50%) and deep (>50%)) was compared with the findings from the individual multiparametric pelvic MRI sequences including T2W, DWI, DCE images. The MRIs were interpreted by an experienced abdominopelvic radiologist with six years of expertise, who was blinded to the histopathologic results. A total of 120 patients were initially considered for the study. However, 11 were excluded due to neoadjuvant chemotherapy, eight were excluded because of significant image artifacts, and five were excluded because their tumors were too small to detect on MRI. Ultimately, 98 patients were included in the study.

mp-MRI protocol

MRI scans were performed using a 1.5-T Siemens Avanto system. Patients were instructed to fast for a minimum of four hours before the procedure. No antispasmodic drugs were administered, and the patients' bladders were kept mildly distended throughout the process. The imaging protocol included T2-weighted images in the axial, coronal, and sagittal planes. For axial images, the TR/TE values were set at 5190/108, for coronal images at 4450/108, and for sagittal images at 4290/108. The field of view (FOV) was 420 mm for the axial and coronal planes, and 450 mm for the sagittal plane. The slice thicknesses were 5 mm, 4 mm, and 4.5 mm, respectively. Additionally, diffusion-weighted

imaging (DWI) was obtained with b-values of 50, 400, and 800 s/mm^2. The TR/TE value was 6600/81, with a FOV of 420 mm and a slice thickness of 5 mm. T1-weighted axial images (TR/TE: 716/10; FOV: 420 mm) were acquired both before and after contrast administration. Fat-saturated T1-weighted axial images were also taken using the same parameters. Gadolinium-diethylenetriamine pentaacetic acid was injected intravenously at a dose of 0.1 mmol/kg body weight. Afterward, contrast-enhanced images were obtained in the axial, coronal, and sagittal planes.

Figure I. The T2W image showed a hyperintense expansive mass in the endometrial cavity with no deep myometrial invasion, delineated from the hypointense junctional zone (a). The lesion appeared hypointense and distinct from the myometrium on the DCE image (b), and hyperintense with diffusion restriction, also clearly separated from the myometrium, on the DWI image (c).

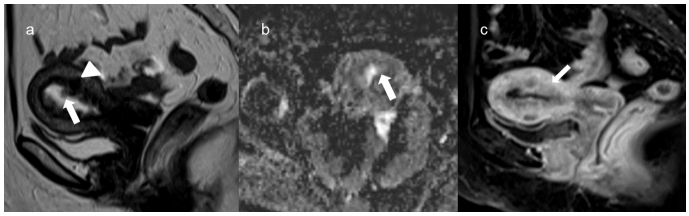


Analysis of MR images

Mp-MRI retrieved from the hospital database system were evaluated using a workstation. An experienced abdominopelvic radiologist with six years of experience interpreted the MRI scans and scored the degree of myometrial invasion (either superficial or deep) for each sequence.

On T2W images, the tumor showed an intermediate signal intensity, presenting as hypointense relative to the myometrium and hyperintense relative to the endometrium (Figure I). Tumor borders were carefully assessed in three T2-weighted plans simultaneously, especially when the tumor was close to uterine fibroids or adenomyosis with junctional zone enlargement. This was done to ensure accurate estimation of the depth of myometrial invasion, avoiding both underestimation and overestimation (Figure II). The tumor boundaries were determined by comparing the hyperintense signal intensity on DWI relative to the myometrium with the corresponding hypointense signal intensity on the ADC map. It was established whether the myometrial invasion was less than or greater than 50%. In DCE images, the tumor tissue, which appeared hypointense and exhibited less contrast enhancement compared to the myometrium, was identified to determine the degree of myometrial invasion. The boundaries of the EC within the myometrium were defined based on the signal characteristics described for each sequence. Following this, it was determined whether the myometrial invasion was less than or greater than 50%.

Figure II. The T2W image demonstrates a polypoid isointense mass within the endometrial cavity adjacent to hypointense adenomyomatosis, without evidence of myometrial invasion (a). Axial DWI reveals an iso-hyperintense lesion clearly delineated from the myometrium (b). The presence of adenomyosis, exhibiting a similar contrast-enhancement pattern as the mass, results in pseudo-invasion appearance into deeper myometrial layers(c).

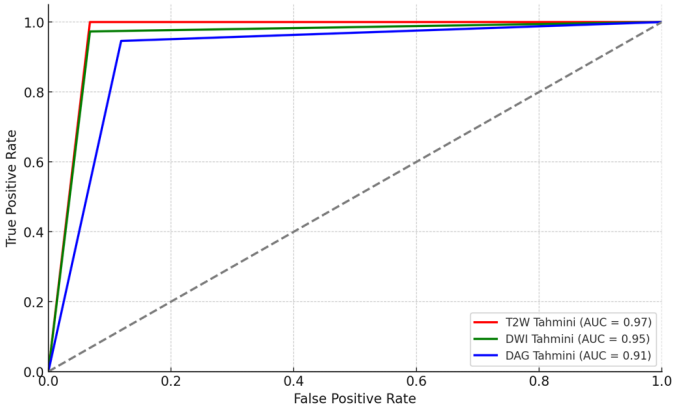


Statistical analysis

The statistical analysis in this study focused on evaluating the effectiveness of the T2W, DWI, and DCE MRI sequences in predicting the depth of myometrial invasion in cases of endometrial cancer. Continuous variables, such as patient age and tumor size, were described using measures like means, medians, and standard deviations. Age differences between patients with superficial and deep myometrial invasion were compared using an independent t-test. Diagnostic performance metrics, including sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV), were calculated for each MRI sequence. Receiver operating characteristic (ROC) curves were plotted, and the area under the curve (AUC) was reported along with 95% confidence intervals. To evaluate differences in diagnostic performance between sequences, McNemar's test was used, with statistical significance set at $p<0.05$. All analyses were conducted using SPSS software (IBM Corp.,

Version 28.0, 2021) and MedCalc version 19.6.1.

Figure III. ROC curves for T2W, DWI, and DCE sequences in predicting the depth of myometrial invasion.



Results

Among the 98 cases analyzed in this study, 61 (62%) presented with superficial myometrial invasion, while 37 (38%) exhibited deep myometrial invasion, as confirmed by pathological findings. The overall average age was 60.76 years, with a median age of 61 years. The average tumor size was 31.69 mm, with a median size of 28.5 mm.

The average age for patients with superficial myometrial invasion was 59.05 years (SD = 10.63), and the median age was recorded as 59 years. Conversely, the mean age of patients with deep myometrial invasion was 63.57 years (SD = 11.81), while the median age was 65 years. Although there was a noticeable difference in age distributions, the independent t-test showed that this difference was not statistically significant (*p=0.053*)

This study evaluated the effectiveness of T2W, DWI, and DCE MR sequences in estimating the extent of myometrial invasion in cases of endometrial cancer (Table I). The T2W sequence showed the best performance, with a sensitivity of 1.0, specificity of 0.934, and positive and negative predictive values (PPV and NPV) of 0.902 and 1.0, respectively (*p<0.001*). The DWI sequence also showed high performance, with sensitivity, specificity, PPV, and NPV of 0.973, 0.934, 0.900, and 0.983, respectively (*p<0.001*). Although the DCE sequence exhibited lower performance compared to the other sequences, it still demonstrated satisfactory results, with values of 0.946, 0.885, 0.833, and 0.964, respectively (*p<0.001*).

Accuracy rates for the T2W, DWI, and DCE sequences were similarly high, at 0.972, 0.965, and 0.938, respectively. ROC analysis revealed AUC values for T2W, DWI, and DCE of 0.967 (95% CI: 0.932–0.992), 0.954 (95% CI: 0.908–0.984), and 0.916 (95% CI: 0.855–0.957), respectively (Figure III). Cohen's Kappa analysis indicated strong agreement between the sequences, with values of 0.958 for T2W, 0.947 for DWI, and 0.905 for DCE. The pairwise comparison of the MRI sequences revealed p-values of 0.7272 for the comparison between T2W and DWI, 1.0000 for T2W and DCE, and 0.6875 for DWI and DCE, indicating no statistically significant differences in their performances.

Regarding misclassifications, T2W overestimated 1 case (false positive) and underestimated 1 case (false negative). DWI overestimated 2 cases and underestimated 1 case, while DCE exhibited the highest discrepancy, with 4 overestimated and 2 underestimated cases. In cases of incorrectly staged tumors on MRI, confounding factors such as cornual location (n = 2), concomitant adenomyomatosis (n = 2), and the presence of myoma uteri (n = 1) were identified.

Discussion

This study evaluated the diagnostic accuracy of T2W, DWI, and DCE MR sequences in determining the depth of myometrial invasion in cases of endometrial cancer. Our findings indicated that all three sequences provided high diagnostic accuracy, with T2W

Table I. Diagnostic performance of MR sequences in predicting depth of myometrial invasion

MR sequences	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)	AUC	p value
T2W	100	93.4	97.2	90.2	100	0.967	*<0.001*
DWI	97.3	93.4	96.5	90.0	98.3	0.954	*<0.001*
DCE	94.6	88.5	93.8	83.3	96.4	0.916	*<0.001*

PPV: positive predictive value, NPV: negative predictive value, AUC: area under the curve, T2W: T2 weighted imaging, DWI: diffusion-weighted imaging, DCE: dynamic contrast-enhanced imaging

demonstrating the highest overall performance. These results are consistent with the study that highlights the critical role of T2W MRI in accurately delineating myometrial invasion (10,11). There were no substantial differences noted in the performances of the sequences. However, obtaining images on three axes and the high contrast resolution helped better delineate anatomical boundaries, especially in challenging tumors located in the cornual region where the myometrium is thin. This is thought to have contributed to the higher success rate of the T2W sequence.

Similarly, a study conducted with 3T MRI reported, similar to our findings, that while there was no statistically significant difference in the performance of the sequences, DWI showed better diagnostic performance than T2W images (12). This difference may be attributed to the higher technical capacity of 3T MRI machines, which provide a better signal-to-noise ratio and improved contrast resolution.

DWI demonstrated a 97% accuracy rate with an AUC of 0.954 in predicting the degree of myometrial invasion, which is consistent with the literature (13). Studies in the literature have reported that diagnostic performance improves when DWI sequences are evaluated in conjunction with T2W sequences (14,15). Although in this study each sequence was assessed separately, it is predicted that a combined evaluation with T2W could enhance diagnostic performance due to its high contrast resolution and signal-to-noise ratio. In the literature, a study similar to ours reported no significant difference between DWI and DCE in determining the extent of myometrial invasion (16). However, a meta-analysis demonstrated that DWI was superior to DCE in detecting the depth of myometrial invasion (17). This finding is thought to be related to technological advancements that have improved the contrast resolution of DWI. Additionally, DWI enables differentiation between malignant tumors and benign lesions such as uterine fibroids and adenomyosis, which may exhibit similar contrast enhancement to tumors but, unlike tumors, do not show diffusion restriction. These factors likely contribute to the superior performance of DWI in detecting myometrial invasion. Additionally, in our study, it was observed that in tumors with cornual localization, particularly in postmenopausal patients with myometrial thinning, assessment errors may arise when relying solely on axial DWI. This highlights the importance of high-resolution T2W imaging obtained in three planes, which proved to be more effective in accurately determining the depth of myometrial invasion in such cases.

DCE images showed an accuracy of 94% and an AUC of 0.916 in evaluating the extent of myometrial invasion in endometrial cancer. Additionally, as highlighted in previous studies, the absence of interruption in early-phase subendometrial enhancement plays a key role in identifying tumors confined to the endometrial cavity, which holds particular significance in the planning of fertility-sparing surgeries (18). Although the other two sequences (T2W, DWI) exhibited better diagnostic performance, the difference in diagnostic accuracy was not statistically significant. Conditions such as fibroids, adenomyosis, and an indistinct junctional zone led to misinterpretation of myometrial invasion depth on DCE. Similar to our findings, the study by Beddy et al. also reported that DCE images could result in incorrect radiological assessments in the presence of accompanying lesions, while DWI showed better performance (13). Therefore, since accompanying lesions with contrast enhancement patterns similar to EC that are located near the tumor-myometrium interface may lead to misinterpretation on DCE images, DWI and T2W images should be used to assist in the evaluation of these cases.

Preoperative staging in EC is essential for predicting patient prognosis and guiding treatment decisions (2,4). Assessment of myometrial invasion depth using MRI in the preoperative setting has been integrated into clinical guidelines for EC (2,19). In our study, all imaging sequences demonstrated high diagnostic accuracy for evaluating myometrial invasion depth, with no significant differences in AUC values 0.967, 0.954, and 0.916 for T2W, DWI, and DCE, respectively. However, in a few cases where discrepancies between sequences were observed, T2W images showed the highest concordance with pathology results. While there is no clear consensus in the literature, our findings from a 1.5T MRI indicate that the high-resolution T2W sequence may be more effective than the others (10-12). This is likely because it provides superior anatomical detail and

allows for evaluation across multiple planes. DWI and DCE, which offer functional insights into tumor biology, are also important components of the EC imaging protocol, and our results indicate that these sequences provide comparable diagnostic accuracy to T2W. However, in cases where factors such as cornual location, fibroids, adenomyosis, or an indistinct junctional zone may lead to inaccurate assessment of myometrial invasion depth, it is crucial to evaluate all sequences together for accurate staging.

There are several limitations to this study. First, the study was performed with a 1.5-T MRI scanner, which may have influenced diagnostic performance when compared to 3T MRI systems, known for their higher resolution and better signal-to-noise ratio. Second, the study did not evaluate interobserver variability, as all MRI sequences were interpreted by a single radiologist. Third, the sample size, although sufficient for the study design, limits the generalizability of the findings to broader populations. Additionally, this was a retrospective study, and further prospective studies are needed to confirm these results and evaluate the impact of different MRI protocols on diagnostic performance. Lastly, the exclusion of patients who had undergone neoadjuvant chemotherapy may limit the applicability of the findings to more advanced cases of endometrial cancer.

In conclusion, this study demonstrates that T2W, DWI, and DCE MRI sequences all have high accuracy in assessing myometrial invasion in endometrial cancer. Although the differences in performance were not statistically significant, T2W showed a slight advantage due to its superior anatomical detail and ability to assess the tumor in multiple planes. DWI also performed well, providing valuable functional information. In cases with complicating factors such as fibroids or adenomyosis, combining T2W and DWI is recommended to enhance accuracy and reduce the likelihood of misinterpretation. Further studies with larger sample sizes and 3T MRI systems are required to confirm and strengthen these findings.

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