

Myometrial invasion and overall staging of endometrial carcinoma: assessment using fusion of T2-weighted magnetic resonance imaging and diffusion-weighted magnetic resonance imaging

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Background: The age of onset of endometrial carcinoma has been decreasing in recent years. In endometrial carcinoma, it is important to accurately assess invasion depth and preoperative staging. Fusion of T2-weighted magnetic resonance imaging (T2WI) and diffusion-weighted magnetic resonance imaging (DWI) may contribute to the improvement of anatomical localization of lesions.

Materials and methods: In our study, a total of 58 endometrial carcinoma cases were included. Based on the revised 2009 International Federation of Gynecology and Obstetrics staging system, a fusion of T2WI and DWI was utilized for the evaluation of invasion depth and determination of the overall stage. Postoperative pathologic assessment was considered as the reference standard. The consistency of T2WI image staging and pathologic staging, and the consistency of fused T2WI and DWI and pathologic staging were all analyzed using Kappa statistics.

Results: Compared with the T2WI group, a significantly higher diagnostic accuracy was observed for myometrial invasion with fusion of T2WI and DWI (77.6% for T2WI; 94.8% for T2WI-DWI). For the identification of deep invasion, we calculated values for diagnostic sensitivity (69.2% for T2WI; 92.3% for T2WI-DWI), specificity (80% for T2WI; 95.6% for T2WI-DWI), positive predictive value (50% for T2WI; 85.7% for T2WI-DWI), and negative predictive value (90% for T2WI; 97.7% for T2WI-DWI). In summary, T2WI-DWI fusion exhibits higher diagnostic accuracy with respect to staging relative to T2WI only (81.0% for T2WI; 94.8% for T2WI-DWI).

Conclusion: Fused T2WI-DWI may represent a noninvasive, lower cost approach for the effective assessment of myometrial invasion and staging of endometrial carcinoma.

Keywords: endometrial carcinoma, T2WI, DWI, myometrial invasion, magnetic resonance imaging, fusion, staging

Introduction

A 5-year survival rate of 96% has been reported for stage I endometrial carcinoma patients, and 17% for stage IV patients.¹ About 75% of endometrial cancer patients are in stage I when they start their treatments.² Laparoscopic surgery and conservative hormone treatment are recent options in the treatment of early-stage endometrial cancer cases,³⁻⁵ although some investigators have advocated another surgical method, surgical lymphadenectomy, in cases of deep myometrial invasion.⁶⁻⁸ Accurate assessment of the myometrial invasion depth and endometrial cancer staging prior to surgery is very important for patients and definitely affect treatment planning and subsequent prognosis.⁹⁻¹² In 2009, the Committee of the International Federation of Gynecology

and Obstetrics (FIGO) revised the FIGO staging system (1988 version) for endometrial carcinoma, providing a better treatment basis for endometrial carcinoma.^{13,14}

Magnetic resonance imaging (MRI) is a more accurate approach for the assessment of endometrial carcinoma staging compared with ultrasonography and CT before surgery.^{15–19} In fact, many studies have shown that dynamic contrast-enhanced MRI (DCE-MRI) is a good choice of imaging modality for predicting invasion depth. However, the role of DCE-MRI in overall staging is still controversial, and some researchers have suggested that there was no benefit.^{20–22} A retrospective study found that DCE-MRI did not improve diagnostic performance relative to viewing T2-weighted imaging (T2WI) independently with respect to predicting invasion depth,²³ and DCE-MRI – depending upon the contrast agent used – may involve greater costs and risks. As for endometrial carcinoma, some studies have shown that diffusion-weighted imaging (DWI) exhibits better performance than DCE-MRI in assessing myometrial invasion.^{24–26} Therefore, it is necessary to find a simpler and more cost-effective imaging modality.

The combination of T2WI and DWI fuses morphologic and functional observations, which can improve the anatomical localization of lesions, and the entire procedure takes <30 s. Fused images possess many other advantages, such as simplicity of operation, intuitiveness of images, and noninvasiveness, and the combination of T2WI and DWI has been used in many studies.^{27–30} Reports have shown that the fused images are a very good modality for displaying anatomical structure and functional information, and improve the accuracy of diagnosis. The high accuracy of fused T2WI-DWI images has been useful in assessing locally recurrent pelvic malignancies.²⁷

No data are currently available about the use of fused T2WI-DWI in assessing invasion depth and stage of endometrial carcinoma. Hence, in this study, we aim to investigate the performance of 3T fused T2WI-DWI ($b=1,000$ s/mm²) prior to surgery, which could lessen the overall patient burden.

Materials and methods

Cases

We obtained the approval of the Tianjin First Center Hospital Medical Ethics Committee and received informed consent from enrolled cases. Fifty-eight endometrial carcinoma patients treated at our hospital from April 2013 to January 2016 were included in this investigation. The average patient age was 60.41 ± 7.75 years (range, 45–78 years). No patient had previously received hormone replacement therapy. A total of 58 cases were enrolled, based on our inclusion criteria of:

- 1) the diagnosis of endometrial carcinoma being confirmed by biopsy after surgery; 2) patients having not received any other surgical or non-surgical treatments; 3) completion of the MRI examination before surgery, including conventional unenhanced MRI and DWI examination; 4) the time interval between surgery and MR examination being <2 weeks; and 5) the presence of detailed clinical medical records.

MRI

All MRI examinations were conducted using a 3T MRI system (Trio Tim; Siemens Medical Systems, Erlangen, Germany), 1–2 weeks prior to surgery. A 32-channel, phased array body coil was utilized. Relative parameters were as follows: axial T1WI (repetition time [TR]=630 ms, echo time [TE]=11 ms, field of view [FOV]=200×200 mm, matrix=256×320, number of excitation [NEX]=3, 23 scanning layers); axial T2WI (TR=4,000 ms, TE=101 ms, FOV=200×200 mm, matrix=256×320, NEX=3, 23 scanning layers); sagittal and coronal T2WI with fat suppression sequence (TR=4,000 ms, TE=92 ms, FOV=200×200 mm, matrix=256×320, NEX=3). Axial DWI data were obtained through a single-shot, echo-planar technique, with TR=5,000 ms, TE=81 ms, matrix=128×128, NEX=3, and FOV=200×200 mm; the diffusion sensitive factor b -value was 1,000 s/mm². Sequences were performed with identical section thickness and a gap in axial planes. This study was performed with normal respiration.

Image analysis

One radiologist, with 15 years of experience in gynecologic radiology, read images independently without the knowledge of clinical and pathologic information; and MRI images were reviewed in random order during the diagnostic process. We used image processing software on a MR post-processing workstation (Siemens Syngo 2010A). Myometrial invasion and staging were analyzed using T2WI and fused T2WI-DWI. The radiologist assessed the following parameters: 1) invasion depth, 2) cervical stromal involvement, 3) bilateral adnexa and vaginal or other pelvic organ involvement, 4) presence of enlarged lymph nodes, and 5) presence of distant metastatic disease. The invasion depth was defined as the distance between the inner myometrial interface and the invasion point. We categorized invasion depth of <50% of the myometrial thickness as superficial invasion, and extension $\geq 50\%$ of the myometrium as deep invasion.

Histologic analysis

All patients were treated surgically, and the time interval between MR examination and surgery was <2 weeks. Histopathologic characteristics of the lesions were observed by

an experienced pathologist, and the following were evaluated: uterine myometrial invasion; presence or absence of cervical stromal involvement; complete or incomplete serous membrane; vaginal and parametrial involvement; and lymph node metastasis and distant metastasis. These factors are in accordance with 2009 revised FIGO staging system for postoperative pathologic staging.

Statistical analysis

Statistical analysis software (IBM SPSS Statistics for Windows, version 19.0; IBM Corp., Armonk, NY, USA) was used for data processing. To analyze the infiltration depth, we calculated data accuracy, sensitivity, specificity, and positive and negative predictive values using T2WI and fused T2WI-DWI. Accuracy comparisons between T2WI and fused T2WI-DWI images were performed via χ^2 test. The consistency of T2WI images staging and pathologic staging, and the consistency of fused T2WI-DWI images staging and pathologic staging were all analyzed using Kappa statistics. The criteria for the Kappa statistics were >0.75 (excellent agreement) and <0.4 (poor agreement). A P -value <0.05 was considered to show a statistically significant difference between the groups.

Results

Histopathologic diagnoses

Histopathologic diagnoses are listed in Table 1. Of 58 endometrial carcinoma cases, postoperative histologic assessment revealed 51 cases with endometrioid adenocarcinoma, 2 cases with clear-cell differentiation, 1 case with adenocarcinoma and papillary differentiation, and 4 cases with a mixed pattern. In addition, there were 43 cases with stage IA endometrial carcinoma; 8 cases with stage IB, 3 cases with stage II, and 4 cases with stage III. Forty-five cases were classified

as having superficial invasion and 13 cases as deep invasion. None had lymph node metastasis or local spread of cancer upon histopathologic examination.

Assessment of depth of invasion

Fused T2WI-DWI images showed obvious boundaries of lesions, extent of involvement, and a clear contrast with surrounding normal structures. Pathology confirmed 45 cases with superficial invasion and 13 cases with deep invasion. Superficial invasion was determined correctly in 36 cases (accuracy rate of 80%) and deep invasion in 9 cases (accuracy rate of 69.2%) with T2WI. The accuracy of overall depth of invasion was 77.6% (45/58) with T2WI; 13 cases were wrongly diagnosed, including 9 cases of superficial invasion that were mistaken for deep myometrial invasion, and 4 cases of deep myometrial invasion that were mistaken for superficial myometrial invasion. Superficial myometrial invasion was correctly determined in 43 cases (accuracy of 95.6%) and deep myometrial invasion in 12 cases (accuracy of 92.3%) with T2WI-DWI fused images. The accuracy of overall depth of myometrial invasion was determined at 94.8% (55/58); 3 cases were misdiagnosed, including 2 cases of superficial myometrial invasion that were mistaken for deep invasion, and 1 case of deep invasion that was mistaken for superficial invasion. The accuracy of the assessment of myometrial invasion with these 2 methods is compared in Table 2. Fused T2WI-DWI images had higher diagnostic accuracy, sensitivity, specificity, and positive and negative predictive values compared with T2WI (Table 2).

Staging of endometrial carcinoma

For overall staging, 51 patients had tumors confined to the uterus, 3 patients had cervical stromal invasion, 4 patients had tumor invasion into serosa or adnexa, and no patient had enlarged lymph nodes or the presence of distant metastatic disease. We correctly staged 47 patients (81%) with endometrial carcinoma using T2WI. Of patients who were incorrectly

Table 1 Surgical histopathologic characters

	Data	Percentage (%)
Overall FIGO stage		
IA	43	74.1 (43/58)
IB	8	13.8 (8/58)
II	3	5.17 (3/58)
III	4	6.90 (4/58)
Myometrial invasion		
Superficial	45	77.6 (45/58)
Deep	13	22.4 (13/58)
Histologic subtype		
Endometrioid	51	87.9 (51/58)
Clear cell	2	3.4 (2/58)
Serous papillary	1	1.7 (1/58)
Mixed	4	6.9 (4/58)

Abbreviation: FIGO, International Federation of Gynecology and Obstetrics.

Table 2 Sensitivity, specificity, and positive and negative predictive values for diagnosis of the depth of myometrial invasion with T2WI and T2WI-DWI

Diagnosis	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Superficial invasion				
T2WI	80 (36/45)	69.2 (9/13)	90 (36/40)	50 (9/18)
T2WI-DWI	95.6 (43/45)	92.3 (12/13)	97.7 (43/44)	85.7 (12/14)
Deep invasion				
T2WI	69.2 (9/13)	80 (36/45)	50 (9/18)	90 (36/40)
T2WI-DWI	92.3 (12/13)	95.6 (43/45)	85.7 (12/14)	97.7 (43/44)

Abbreviations: DWI, diffusion-weighted imaging; T2WI, T2-weighted imaging.

Table 3 Endometrial carcinoma staging with T2WI and fused T2WI-DWI images compared with pathologic results

T2WI/ T2WI-DWI	Pathologic diagnoses			
	IA	IB	II	III
IA	35/41	3/1	0/0	0/0
IB	8/2	5/7	0/0	0/0
II	0/0	0/0	3/3	0/0
III	0/0	0/0	0/0	4/4

Abbreviations: DWI, diffusion-weighted imaging; T2WI, T2-weighted imaging.

staged, 8 cases were over-staged (stage IA mistaken for stage IB) and 3 cases were under-staged (stage IB for stage IA). We correctly staged 55 patients (94.8%) with endometrial carcinoma using fused T2-weighted and DW images. Two cases were over-staged (stage IA for stage IB) and 1 case was under-staged (stage IB for stage IA). The accuracy rate for staging endometrial carcinoma stage I was 78.4% (40/51) with T2WI and 94.1% (48/51) with fused imaging. The overall staging accuracy rate was 81% (47/58) with T2WI and 94.8% (55/58) with fused imaging (Table 3; Figure 1). In stage I endometrial carcinoma cases, 8 cases that were wrongly diagnosed with T2WI were correctly diagnosed with T2WI-DWI fused images (Figures 2 and 3). Therefore, fused T2WI-DWI images exhibited higher diagnostic accuracy than T2WI in the assessment of tumor staging. Statistical analyses revealed that results of endometrial carcinoma staging obtained from fused images and pathologic findings were more consistent than those obtained from T2WI images and pathologic findings (Table 4).

Discussion

We demonstrated that fused T2WI-DWI images were acceptable for assessing invasion depth, and significantly improved the staging of endometrial carcinoma. Our study illustrated that fused T2WI-DWI images showed obvious lesion boundaries, the extent of invasion, and depicted a clear contrast with the surrounding normal structures. This modality is therefore advantageous for the detection, localization, and assessment of invasion depth and tumor staging.

The sensitivity, specificity, and accuracy of fused T2WI-DWI in evaluating superficial myometrial invading lesions were 95.5%, 92.3%, and 95.6%, respectively; for evaluating deep myometrial invading lesions, the sensitivity, specificity, and accuracy of fused T2WI-DWI were 92.3%, 95.5%, and 92.3%, respectively. These values were higher than the results for T2WI. The diagnostic accuracy rate of evaluating invasion depth using T2WI was high and consistent with previous reports in the literature.^{14,31,32} To our knowledge, investigators who used fused T2-weighted and DW images for evaluation did not report overall staging of endometrial cancer (2009 stage). In this study, with fused T2-weighted and DW images, we diagnosed the overall staging of 58 patients with an accuracy rate of 94.8% (55/58), which was better than T2WI, particularly with respect to stage I endometrial carcinoma. The accuracy for stage IA and IB were 95.3% and 87.5%, respectively, which was also significantly higher than T2WI. The fused images manifested higher diagnostic consistency and correlated well with pathologic findings. There are some reasons, however, for misjudgments (ie, overstaging and understaging). The lesions appear as significantly higher signals than muscles, which generally can be diagnosed on T2WI only, but it is relatively difficult to diagnose the lesions when they appear as iso-intense or the contrast signal is not obvious; this can lead to misdiagnosis or stage misjudgment (such as in Figure 3). In addition, interpretation of staging is compromised with concomitant conditions on MR images, such as tumor at cornus uteri, fibroid, or adenomyosis – these can interfere with the assessment of the lesions and easily lead to misdiagnosis. Fused T2-weighted and DW images, therefore, exhibit distinct advantages in diagnosing these lesions.

Extensive research has shown that DCE-MRI is an imaging modality for predicting deep endometrial invasion.^{22,33} However, a retrospective study found that with regard to the prediction of deep myometrial invasion, DCE-MRI did not improve diagnostic performance when viewed independently with T2W images.²³ In addition, since DCE-MRI is



Figure 1 Magnetic resonance images of an endometrial cancer patient (stage IA).

Notes: (A) T2-weighted image shows irregular endometrial thickening and appears as heterogeneous signals. (B) DW image shows a lesion with a high signal. (C) Fused T2WI-DWI image shows clear anatomical structures and the lesion shows good contrast from the surrounding normal tissue.

Abbreviations: DWI, diffusion-weighted imaging; T2WI, T2-weighted imaging.

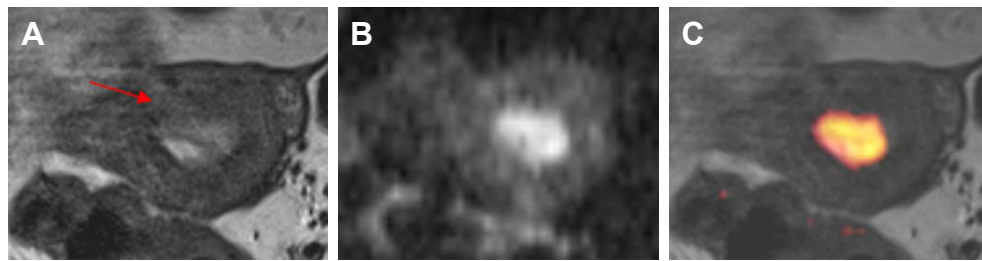


Figure 2 A 56-year-old woman with endometrial carcinoma (pathologic stage is IA).

Notes: (A) T2-weighted image shows that the myometrial signal was heterogeneous (arrow), and we judged the depth of myometrial invasion to be greater than one-half of the myometrial thickness, classifying this case stage as stage IB using T2WI. (B) DWI image shows that the extent of the lesion was limited. (C) Fused T2WI-DWI image shows clear margins of the tumor and depth of invasion to be less than one-half of the myometrial thickness.

Abbreviations: DWI, diffusion-weighted imaging; T2WI, T2-weighted imaging.

performed using a contrast agent, it involves greater risk and financial cost to the patient.

Noninvasive DWI depicts differential molecular diffusion movements of water within various tissues. With DWI, increased cellularity and fewer mesenchymal structures between the glands in endometrial carcinomas may restrict water diffusion when compared with a normal endometrium.^{25,34} Endometrial cancer is observed as hyperintense areas that are depicted as hypointense on the apparent diffusion coefficient map.³⁵ Several research groups have analyzed the usefulness of DWI in the detection and assessment of myometrial invasion in endometrial cancer.^{26,36} Researchers have reported that staging errors were excluded when incorporating DWI, and conventional MRI based on the fusion of DWI lesions for endometrial cancer is more sensitive for the effective assessment of lesions.³⁴

Fused T2WI-DWI image is objective because it fuses morphologic and functional images to improve the anatomical localization of lesions in DWI. The anatomy is often not visualized clearly, and this may predispose it to the misdiagnosis of small lesions.³⁷ However, our 3T MRI scan shows higher signal-to-noise ratio and soft tissue resolution than low-field intensity MRI, which can then

resolve this problem. The entire processing time for the fusion operation is <0.5 min. Also, the use of fused images has many other advantages, such as simplicity of operation, intuitiveness of images, noninvasiveness, and repeatability. Fused T2-weighted and DW images have been used in many other abdominal and pelvic tumor studies as well.^{27–30} Results have shown that fused images are very good for displaying anatomical structures and can provide functional information, thereby improving the accuracy rate of diagnosis.

There are several limitations to our study. First, a very limited number of cases were included in the current study; therefore, investigations with larger sample sizes and multicenter studies need to be conducted in the future. Second, we only included a few patients with advanced stage (IV) cancer because most of the patients were diagnosed and treated at earlier stages, with the fast development of medical science and financial conditions. Third, most patients with advanced stage cancer underwent radiochemotherapy without having the opportunity for surgical treatment. These limitations made it difficult for us to retrieve the appropriate pathologic samples and results that we required, which are very important in measuring the accuracy rates for stage IV patients.



Figure 3 A 60-year-old woman with endometrial carcinoma (pathologic stage, IB).

Notes: (A) It was difficult to judge the depth of myometrial invasion with the T2-weighted image. (B) DWI image shows the great extent of the high signal lesion. (C) Fused T2WI-DWI image shows clear margins of the tumor, and the depth of myometrial invasion to be greater than one-half of the myometrial thickness; the diagnosis was clearly stage IB.

Abbreviations: DWI, diffusion-weighted imaging; T2WI, T2-weighted imaging.

Table 4 Diagnostic accuracy rate of endometrial carcinoma staging with T2WI and T2WI-DWI

Diagnosis	Concordance	Discordance	Accuracy (%)	κ -value	P-value
T2WI	47	11	81.0 (47/58)	0.601	0.023
T2WI-DWI	55	3	94.8 (55/58)	0.881	

Abbreviations: DWI, diffusion-weighted magnetic resonance imaging; T2WI, T2-weighted magnetic resonance imaging.

Conclusion

The fusion of T2WI and DWI exhibited potential advantages in the noninvasive evaluation of invasion depth and preoperative staging. As an alternative approach to diagnosing endometrial carcinoma, this method reduces the cost and does not require the use of a contrast agent.

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Disclosure

The authors report no conflicts of interest in this work.

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