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ORIGINAL ARTICLE – OPEN ACCESS



# The Fusion of T2 Weighted MRI and Diffusion-Weighted Imaging in Evaluating the Depth of Myometrial Invasion in Endometrial Cancer

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ABSTRACT

**Objective:** To investigate the performance of fused T2WI-diffusion-weighted imaging (DWI) in the preoperative evaluation of the depth of myometrial invasion in endometrial cancer.

**Materials and Methods:** Twenty-nine patients with histologically proven endometrial carcinoma were enrolled in this study. All of them underwent a full magnetic resonance imaging exam including T2-weighted images and DWI with b values of 0, 500, and 1000 s/mm$^2$. The ADC value in endometrial cancer and normal endometrium of control cases was calculated. The myometrial invasion depth was judged in each sequence separately as well as by fused images, and was correlated with the surgical pathology results.

**Results:** In the evaluation of superficial myometrial invading lesions using the fused T2WI-DWI, the sensitivity was found to be 94.7%, specificity was 90%, and accuracy was 94.7%, while the values of about 90% sensitivity, 94.9% specificity, and 90% accuracy of fused T2WI-DWI in the evaluation of deep myometrial invading lesions were obtained. On the ADC maps, the mean ADC value of endometrial cancer was $0.9\pm0.17\times10^{-3}$ mm$^2$/s and the mean ADC value of normal endometrium of control cases was $1\pm0.11\times10^{-3}$ mm$^2$/s.

**Conclusion:** The fusion of T2WI and DWI showed a good noninvasive diagnostic method of staging of invasion and preoperative depth. It can be used as an alternative diagnostic tool for endometrial carcinoma staging with reduced cost and injection of a contrast agent.

**Keywords:** Endometrial carcinoma, MRI pelvis, diffusion MRI, fused T2WI- DWI

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## INTRODUCTION

Endometrial cancer is the second most common malignancy of the female genito-urinary system. According to the International Agency for Research on Cancer (Globocan 2018), uterine corpus cancer is the 6$^{th}$ most commonly occurring womens' cancer worldwide (1).

The management of endometrial cancer is primarily operative. It has emerged over the years from radical hysterectomy to more conservative surgery or conservative hormone treatment for early-stage endometrial cancer (2–5), with hysterectomy and surgical lymphadenectomy only performed in deep myometrial invasion cases (6–8).

Precise preoperative staging by evaluation of the depth of the myometrial invasion, which is the most important single prognostic factor of nodal and lymphovascular invasion, is crucial and can definitely affect the treatment planning (9–13).

Magnetic resonance imaging (MRI) has an established role in gynecologic imaging. Incorporation of diffusion-weighted imaging (DWI) into routine protocols for pelvic MRI have been endorsed to improve lesion characterization and disease mapping, thereby optimizing patient management (14).

Endometrial cancer appears as a hyperintense signal on high b values in the DWI, which changes into a hypointense signal on ADC maps as compared to the normal endometrium, and denotes restricted diffusion (15).

The aim of this work was to investigate the diagnostic accuracy of fused T2WI with DW MRI in the preoperative staging of early endometrial cancer.

## MATERIALS and METHODS

### Study Population

This prospective study included 29 patients referred from the gynecologic oncology center with pathologically proven endometrial carcinoma. Total hysterectomies were performed on all patients. The patient age ranged

from 45–80 years, while the mean age was 65 years. The primary symptoms are abnormal uterine bleeding, post-menopausal bleeding, and/or vaginal discharge.

The control group contains 36 patients with normal endometrium who underwent pelvic MRI for a non-gynecological reason.

The patients who did not encounter surgery or receive preoperative neoadjuvant chemotherapy or radiotherapy were excluded from the current study. The exclusion criteria extended to patients with a cardiac pacemaker, vascular clips, metal prostheses, or any other devices incompatible with MRI.

The Ethical Board Institute of the faculty of medicine at Cairo University approved the study in April 2015. Informed consents were acquired from all patients.

### MRI Protocol

The Achiva Philips: 32 Channel 1.5-Tesla scanner was used for the MRI examinations with a phased-array pelvic coil.

The examination protocol consisted of

**Precontrast Sequences**

- Axial oblique T1 weighted images (FOV: 250×274×211 mm; Slice thickness: 7 mm; Slice Spacing: 1.5 mm; Slice number: 25; TR: 450–650 ms; TE: 10–16 ms).
- Sagittal, coronal oblique T2 weighted images (FOV: 300×150×300 mm; Slice thickness: 5 mm; Slice Spacing: 1 mm; Slice number: 25; TR: 4000–7000 ms; TE: 110–120 ms) and axial oblique T2 weighted images (FOV: 250×274×211 mm; Slice thickness: 3 mm; Slice Spacing: 0.3 mm; Slice number: 32; TR: 4000–7000 ms; TE: 110–120 ms).
- Axial oblique DWI on 3 b-values (0/500/1000) (FOV: 320×260×200 mm; Slice thickness: 7 mm; Slice Spacing: 1 mm; Slice number: 25; TR: 1667 ms; TE: 61.97 ms).

**Postcontrast sequences**

- E-Thrive (T1 high resolution isotropic volume excitation fast gradient, 3D, & Fat-sat) (FOV: 271×255×252 mm; Slice thickness: 3 mm; 3D thickness: 3; Slice Spacing: 0 mm; Slice number: 84; TR: 4.5 ms; TE: 2.2 ms).

### MR Image Analysis

The T2WI and postcontrast T1WIs sequences were evaluated by expert radiologists having 5–10 years of experience. The DWIs were obtained separately, followed by the fused T2WI and DWI. The MRI analysis was done while the operators were blinded to the final histopathologic diagnosis.

A diagnosis of endometrial cancer is based on eliciting an increased or inhomogeneous signal on the T2WI and observing delayed mild enhancement on the contrast-enhanced sequences, as opposed to the normal myometrium, which shows intense homogeneous enhancement.

Restricted diffusion of endometrial cancer is evident by high signal intensity on the high b value (1000 s/mm$^2$), which eventually changed into low signal intensity on the ADC map.

The ADC value was calculated automatically via a manually placed largest region of interest (ROI), which provided the mean ADC value & MRDA (least ADC value/maximum restricted diffusion; MRDA) ($\times 10^{-3}$ mm/s).

T2-weighted MR images are used as a reference to exclude any necrosis from the measured ROI. Normal endometrial ADC measurement was done in the control cases for comparison and cutoff value estimation.

Localization of the deepest myometrial tumor invasion was done for each patient and subsequent classification into superficial (i.e., no or < half of myometrial thickness; stage IA) or deep myometrial invasion (> half of the myometrial thickness; IB) on T2WIs, DW images, as well as fused T2WIs/ DWI.

### Surgical Data and Histopathology

The included patients underwent total hysterectomy within 3 weeks after MR imaging.

According to the 2009 revised FIGO staging system for postoperative pathological staging, experienced pathologists evaluated the surgical specimens with special concern for the histologic type and tumor grades (well-differentiated, moderately differentiated, and poorly differentiated), depth of the uterine myometrial invasion, the cervical stromal, vaginal and parametrial involvement, and lymphatic and distant metastasis.

### Statistical Analysis

The analysis was done using: the SPSS version 23.0 software (IBM, Armonk, NY, USA). Quantitative data was summarized as maximum and minimum, and mean and standard deviation, while categorical data was represented using frequency and relative frequency (percentage). The sensitivity, specificity, and accuracy of T2 and fused WIs were also calculated and compared via the Pearson Chi-square $\chi^2$ test. A P-value of <0.05 was regarded as the statistically significant difference between the groups. The cut off ADC value for differentiation of malignant endometrial tumors from control cases was done via constructing an ROC curve with analysis of the area under curve.

## RESULTS

### Pathologic Findings

Out of 29 patients, 23 were pathologically proved to have endometrial carcinomas. The types were mostly endometrioid carcinomas, 1 case with clear cell adenocarcinomas, 2 cases with serous papillary carcinoma, and 3 cases with mixed endometrioid adenocarcinoma and serous papillary carcinoma. The histologic grades were: grade 1 in 15 cases (51.8%), grade 2 in 5 cases (17.3%), and grade 3 (G3) in 3 cases (10.3%).

The endometrial thickness ranged from 1.5 cm to 8 cm in its maximum thickness in the examined histopathologic specimens. A total of 19 cases showed a myometrial invasion of <50% myometrial thickness (i.e., superficial, stage IA) (65.5%), while deep invasion

(>50% myometrial thickness, IB) was found in 10 cases (34.5%).

Surgically, the FIGO stages were: stage IA (19), stage IB (7), stage II (2), and stage III (1).

The summary of the histopathology is shown in Table 1, 2, and 3.

**Table 1.** The pathology of endometrial carcinoma cases

| Type of tumor | n | % |
|---|---|---|
| Endometrioid adenocarcinoma | 23 | 79 |
| Grade 1 | 15 | 51.8 |
| Grade 2 | 5 | 17.3 |
| Grade 3 | 3 | 10.3 |
| Mixed endometrioid adenocarcinoma and serous papillary carcinoma | 3 | 10.3 |
| Serous papillary carcinoma | 2 | 6.8 |
| Clear cell carcinoma | 1 | 3.5 |
| Total | **29** | |

**Table 2.** The overall FIGO stage and depth of myometrium invasion of endometrial carcinoma cases

| Overall FIGO stage | n | % |
|---|---|---|
| IA | 19 | 65.5 (19/29) |
| IB | 7 | 24.1 (7/29) |
| II | 2 | 7 (2/29) |
| III | 1 | 3.4 (1/29) |
| Total | **29** | |

FIGO: Fédération Internationale de Gynécologie et d'Obstétrique

**Table 3.** The depth of myometrium invasion of endometrial carcinoma cases according to the postoperative pathology

| Depth of myometrial invasion | n | % |
|---|---|---|
| Superficial | 19 | 65.5 (19/29) |
| Deep | 10 | 34.5 (10/29) |

### MRI Findings

A distinct outline of the mass lesions, the exact extension, and an unambiguous contrast with the normal surrounding tissues are striking benefits of the fused T2WI-DW images. A total of 19 cases were approved pathologically with superficial invasion and 10 cases with deep invasion were identified. In T2WI, superficial invasion was found in 16 cases and deep invasion was identified in 6 cases. The accuracy of the overall invasion depth with T2 weighted imaging was 75.8% (22/29) and the false diagnosis was seen in 7 cases as follows; 3 cases of superficial invasion were diagnosed as deep myometrial invasion and 4 cases of deep myometrial invasion were diagnosed as a superficial myometrial invasion. In the fused T2WI-DW images, the superficial myometrial invasion was assessed successfully in 18 cases and deep myometrial invasion in 9 cases. The accuracy of the overall myometrial invasion depth was decided at 93.1% (27/29), as 2 cases were incorrectly diagnosed, including 1 case of superficial and 1 case of deep invasion. Table 4 summarizes the accuracy of the myometrial invasion with these 2 methods. A higher diagnostic accuracy, sensitivity, specificity, and positive and negative predictive values are found for the fused T2WI-DWI images as compared to T2WI alone (Fig. 1–3, Table 5).

The mean value of ADC of endometrial cancer, calculated from the ADC maps, was $0.9\pm0.17\times10^{-3}$ mm$^2$/s and the mean value of ADC of normal endometrium of control cases was $1\pm0.11\times10^{-3}$ mm$^2$/s. The ADC cutoff value for endometrial carcinoma was equal to or less than $0.6\times10^{-3}$ mm$^2$/s and showed a sensitivity of 69.9% and specificity of 77.1% ($p<0.001$) (Table 6) (Fig. 4).

## DISCUSSION

Various factors determine the prognosis of the endometrial carcinoma, including histologic grading, depth of myometrial invasion, and lymph nodes metastasis. A chief single prognostic factor that can be assessed preoperatively is the depth of myometrial invasion with 50% myometrial invasion as a cutoff that divides the FIGO

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

| Diagnosis | Concordance | Discordance | Accuracy (%) | 95%CI |
|---|---|---|---|---|
| T2WI | 22 | 7 | 75.8 (22/29) | 56.48 to 89.70 |
| T2WI-DWI | 27 | 2 | 93.1 (27/29) | 77.23 to 99.15 |

T2WI: T2 weighted images; DWI: Diffusion weighted imaging. Revised 2009 FIGO (Fédération Internationale de Gynécologie et d'Obstétrique) staging for carcinoma of the endometrium

**Table 5.** Sensitivity, specificity, and positive and negative predictive values for the diagnosis of the depth of myometrial invasion with T2WI and T2WI-DWI

| Diagnosis | Sensitivity (%) | Specificity (%) | Positive predictive value (%) | Negative predictive value (%) | Accuracy |
|---|---|---|---|---|---|
| Superficial invasion | | | | | |
| T2WI | 84.2 (16/19) | 60 (6/10) | 80 (16/20) | 66.67 (6/9) | 75.86 (22/29) |
| T2WI-DWI | 94.7 (18/19) | 90 (9/10) | 94.7 (18/19) | 90 (9/10) | 93.1 (**27**/**29**) |
| Deep invasion | | | | | |
| T2WI | 66.7 (6/9) | 80 (16/20) | 60 (6/10) | 84.2 (16/19) | 75.86 (22/29) |
| T2WI-DWI | 90 (9/10) | 94.7(18/19) | 90 (9/10) | 94.7 (18/19) | 93.1 (**27**/**29**) |

T2WI: T2 weighted images; DWI: Diffusion weighted imaging

**Table 6.** ADC value of endometrial cancer and control cases

| | Endometrial cancer | Control cases |
|---|---|---|
| Number | 29 | 36 |
| Mean ADC value | 0.9 | 1.0 |
| Minimum ADC value | 0.5 | 0.8 |
| Maximum ADC value | 1.3 | 1.3 |
| Standard deviation | 0.1732 | 0.1186 |

ADC: Apparent diffusion coefficient; 95% Confidence Interval (CI) 0.0275 to 0.1725 Significance value (p=0.0076); ADC cut off value for endometrial carcinoma is equal to or less than 0.6, as shown by the sensitivity and specificity

stage I into IA and IB. The patients with deep myometrial invasion are more liable to have pelvic lymph node metastasis and infiltration of the parametrium (13, 14, 16).

Fused T2WI-DWI allow the combined advantages of functional assessment of DWI and the morphological characterization of T2 WI using a simple operation, half a minute of processing time, and no more time needed for acquisition.

Many studies have used T2WI and DWI in conjunction (16–18) and reviews have concluded that the fused images are a well-recognized modality for unveiling the anatomical structures as well as obtaining the functional information with diagnostic accuracy improvement, even more so for local evaluation of pelvic malignancy recurrence (16–19).

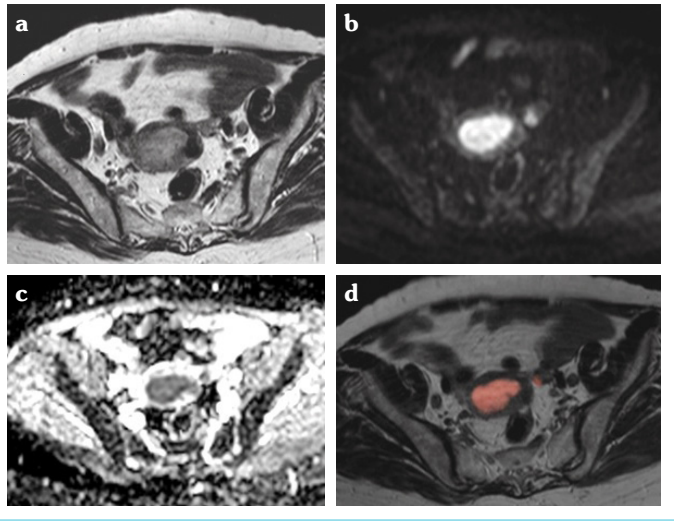


**Figure 1. Axial oblique T2WIs (a) shows an endometrial mass of intermediate signal intensity distending the endometrial cavity with the indistinct junctional zone (Stage IB). Axial oblique DWI at the b value of 1000 (b), ADC map (c), and T2/DW fused image (d) suggest deep myometrial invasion (>50%), i.e., Stage IB**

This study displayed that the fused T2WI-DWI images were remarkably ameliorating for the endometrial carcinoma staging through the accurate evaluation of myometrial invasion. The current study

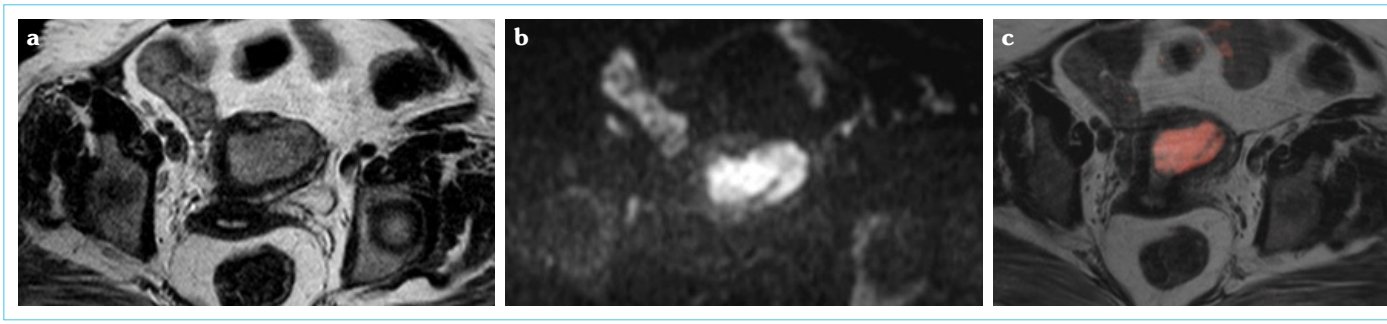


**Figure 2. Axial oblique T2WIs (a) with an endometrial mass of intermediate signal intensity is seen distending the endometrial cavity with the deep myometrial invasion at the fundus with an intact serosal surface. This was confirmed by Axial oblique DWI at a b value of 1000 (b) and a T2/DW fused image (c) (Stage IB)**

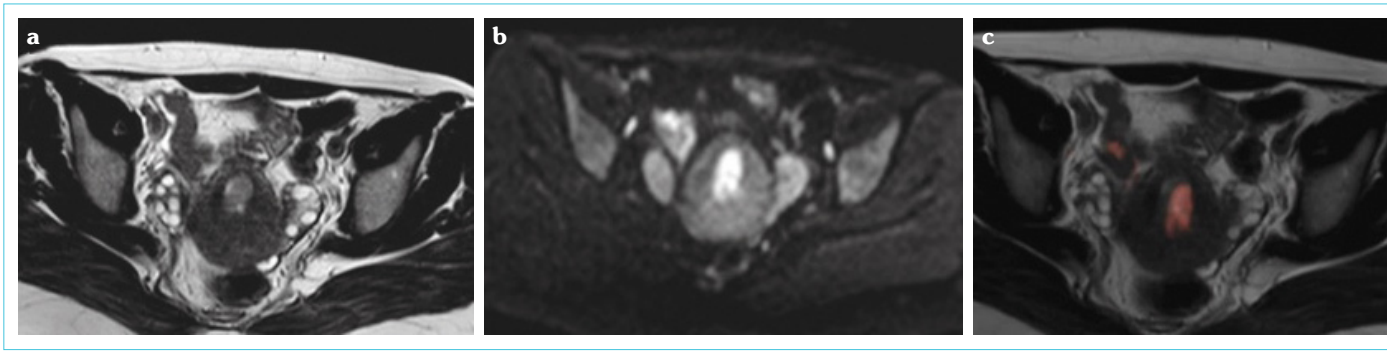


**Figure 3. Axial oblique T2WIs (a) shows relatively thickened endometrium with intermediate signal intensity. An intact junctional zone is noted. Axial oblique DWI is present at a b value of 1000 (b) and a T2/DW fused image (c) shows restricted diffusion with the interruption of the junctional zone posteriorly, suggesting superficial myometrial invasion which was confirmed by pathology, i.e., Stage IA**

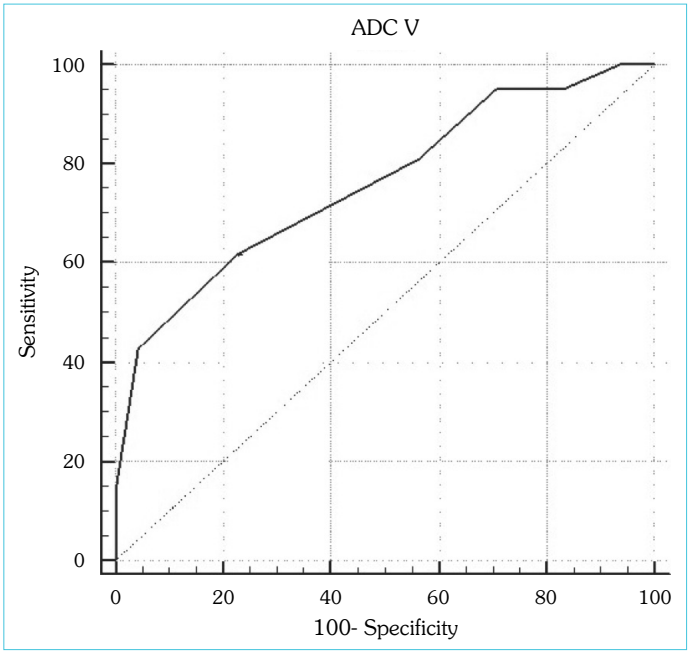


**Figure 4. ROC for ADC cut off value of endometrial cancer and control cases**

pectorial that fused T2WI-DWI images elicit a distinct outline of the mass lesions, the exact extension, and an unambiguous contrast with the normal surrounding tissues.

The sensitivity, specificity, and accuracy of fused T2WI-DWI in evaluating myometrial invading lesions were higher than that of T2 WI alone; for the superficial invasion they were 94.7%, 90%, and 94.7%, respectively, while for the deep myometrial invasion they were 90%, 94.7%, and 90%, respectively. The high diagnostic accuracy rate using T2WI for myometrial invasion depth assessment was consistent with previous studies (20–24).

Limitations to this study were the small number of cases evaluated and the exclusion of patients with advanced stage cancer, since they were not indicated for surgical treatment.

## CONCLUSION

The fusion of T2WI and DWI showed a good method for preoperative assessment of depth of myometrial invasion and accurate staging of early endometrial cancers.

**Ethics Committee Approval:** The Ethical Board Institute of the faculty of medicine at Cairo University approved the study in April 2015 (15-10-43).

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** OM wrote the manuscript and responsible for correspondence to journal. SF collected patient data and participated in its design. OM image processing and collection of patient's images. SF and OM participated in the design of the study and performed the statistical analysis. MH conceived of the study, and participated in its design and coordination and helped to draft the manuscript.

**Conflict of Interest:** The authors have no conflict of interest to declare.

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