Role of MRI Diffusion Weighted Imaging in the Diagnosis of Malignant Uterine Tumors

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Abstract

MRI has a pivotal and established role in detection and staging of gynecological malignancy. Diffusion-Weighted Imaging (DWI) can demonstrate abnormal signals emitted by pathologic foci based on differences in molecular diffusion. It also permits the quantitative evaluation of the Apparent Diffusion Coefficient (ADC) that may be useful for distinguishing between malignant and benign tissues and for monitoring therapeutic outcomes. On this basis, the aim of this study was to assess the added value of DWI and ADC values in the evaluation of gynecological malignancy.

Material and Methods: Twenty patients with suspected gynecological pathology were examined by MRI. Site of origin of the lesion (corporal or cervical), zonal distribution, lesion size, lesion shape, and signal characteristics were determined. The bladder, rectum, pelvic side wall muscles and lymph nodes were evaluated for each study. Descriptive statistical values such as sensitivity, specificity, and positive and negative predictive values were measured for each MR imaging finding.

Results: MR stage was comparable to operative stage in all cases. The sensitivity and specificity of DWI in detection of abnormal endometrium was 100%. DWI and ADC maps allow differentiation of benign from malignant zones of cervix with sensitivity and specificity of 100%. Sensitivity of the ADC in assessment of regional nodal spread was 100% with specificity of 67%.

Conclusion: Conventional MRI findings in conjunction with DWI and quantitative measurement of the Apparent Diffusion Coefficient (ADC) are effective method in the diagnosis and staging of gynecological cancer.

Key Words: Uterine – DWI – ADC value.

Introduction

GYNECOLOGICAL cancers encompass a diverse group of tumors with different epidemiological and pathological features, clinical presentations and treatment strategies. Worldwide, cervical cancer is the second most common cancer among women, with an estimated 493,000 new cases (or 9.7% of cancer in women) and 274,000 deaths (or 9.3% of cancer deaths in women) in the year 2002 and a five-year prevalence of 1.4 million cases. About 83% of the cases occur in developing countries, where cervical cancer accounts for 15% of all cancers in women, with a cumulative risk of 1.5% (1 in 67) by age 64 [1].

Endometrial cancer is the seventh most common cancer among women, with an estimated 199,000 new cases (3.9% of cancer in women) and 50,000 deaths (1.7% of cancer deaths in women) in the year 2002 and a five-year prevalence of 776,000 cases. In contrast with cervical cancer, endometrial cancer is relatively more common in developed countries. About 69% of the cases occur in developed countries where it accounts for 5.9% of all cancers in women, with a cumulative risk of 1.3% (1 in 77) by age 64 [1]. MRI has a pivotal and established role in detection and staging of gynecological malignancy. The exquisite soft tissue resolution of MRI allows accurate demonstration of tumor size, location, extension and nodal involvement. Despite excellent clinical utilization to date, conventional T1 and T2 sequences cannot provide information about tumor microenvironment [2].

Although Diffusion-Weighted Imaging (DWI) now plays an important role in the diagnosis of brain disorders [3-5], it has not been fully applied to body imaging because the images become distorted by its sensitivity, resulting in misregistration attributable to chemical-shift artifacts. Advances in parallel imaging techniques have reduced image distortion and increased the Signal-to-Noise Ratio (SNR), rendering body DWI feasible [6]. DWI can
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demonstrate abnormal signals emitted by pathologic foci based on differences in molecular diffusion. It also permits the quantitative evaluation of the Apparent Diffusion Coefficient (ADC) that may be useful for distinguishing between malignant and benign tissues and for monitoring therapeutic outcomes [7-13].

Aim of the work:
The purpose of this study was to assess the added value of DWI and ADC values in the evaluation of gynecological malignancy.

Patients and Methods

The study was conducted in the Department Of Diagnostic Radiology of Assiut University Hospital. Twenty female patients with their ages ranged from 5-75 years old “mean age was 40 years” were recruited from the Department of Obstetrics and Gynecology and were examined by MRI in the period between July 2014 and March 2015.

The presenting symptom was irregular uterine bleeding “10 patients”, post menopausal bleeding “9 patients” and pelvi-abdominal mass “1 patient”.

Patient preparation:

Before MRI examination, the patients were routinely questioned about any of the conditions which may be a contraindication for an MRI examination such as cardiac pace makers, metallic intracranial or thoracic surgical clips and metallic prosthetic implants [especially ferromagnetic hip prosthesis]. The patients were instructed to remove any metal object [e.g. jewelry, hair pins] and change into a cotton gown for examination.

Fasting for a minimum of 6 hours before the examination was routinely recommended to reduce intestinal motion.

An informed consent was obtained.

Technique:

MR imaging was performed on a 1.5 T superconducting MR imager unit. An abdominal phased array coil was used in all patients. The following sequences were obtained:

1- A multiplanar Fast Field Echo (FFE) localizer upon which the remaining pulse sequences were planned.

2- Axial T2W fast spin echo MR imaging from the renal hilum to the symphysis pubis (TR range/effective TE range, 3500/90-110; echotrain length, 8; slice thickness, 4-6mm; gap, 1-2mm; field of view, 24-38cm; excitations (NSA), 3; and matrix, 304 X 512).

3- Sagittal T2W fast spin echo MR imaging from one femoral head to the other (TR range/effective TE range, 3500/90-110; echotrain length, 8; slice thickness, 4-6mm; gap, 1-2mm; field of view, 24-38cm; excitations (NSA), 3; and matrix, 304 X 512).

4- Coronal T2W fast spin echo MR imaging of the pelvis from the aortic bifurcation to the symphysis pubis (TR range/effective TE range, 3500/90-110; echotrain length, 8; slice thickness, 4-6mm; gap, 1-2mm; field of view, 24-38cm; excitations (NSA), 3; and matrix, 304 X 512).

5- Axial T1 W spin echo MR imaging from the renal hilum to the symphysis pubis (TR range/TE range, 400-640/10-14; slice thickness, 5-8mm; gap, 1-2mm; field of view, 24-38cm; excitations (NSA), 1-2; matrix, 256 X 256; and respiratory compensation).

6- Axial Short Tau Inversion Recovery (STIR) sequence was used in cases where lesions of high signal intensity in both T1-and T2-weighted sequences were found (TR range/TE range, 1500/15; slice thickness, 4-6mm; gap, 1-2mm; field of view, 24-38cm; excitations (NSA), 1-2; and matrix, 256 X 256; and respiratory compensation).

7- Axial DWI using spin-echo-type single-shot echo planar imaging with the following parameters: B-value=0, 250, 500, 750 and 1000ms/mm², TR/TE=3000-4000/60-68ms, a 3-4mm slice thickness/no gap, a 24-to 45-cm FOV, and a 102 X 128-128 X 192 matrix.

Anterior saturation bands were routinely placed over the anterior abdominal wall to reduce respiratory motion artifacts.

The images of all pulse sequences were then hard copied.

MRI image analysis:

All MR images were reviewed by two radiologists. If there was a difference in opinion, it was resolved by taking unbiased opinion from a third radiologist.

Site of origin of the lesion (corporeal or cervical), zonal distribution, lesion size, lesion shape, and signal characteristics were determined.

In endometrial lesions the following findings were observed: The presence of a mass (defined as any focal abnormality with thickening of the
endometrium), myometrial invasion (superficial <50% of myometrial thickness, deep >50% of myometrial thickness), fibrous core (low signal intensity stripe or center on T2W images), intratumoral cysts (discrete, smooth walled, cystic structures of high T2 signal intensity within the mass), necrosis within the mass (irregular high T2W signal intensity within the mass), fluid in endometrial cavity, and integrity of the parametrium.

In cervical lesions zonal origin (mucosal or stromal) of the lesion, its site, size, signal intensity, shape, presence of cysts, or necrosis within the mass, integrity of the parametrium and uterine trizonal anatomy were also assessed.

In all cases the thickness of the endometrium, junctional zone, and myometrium were measured using cross-hair cursor on the monitor.

The bladder, rectum, pelvic side wall muscles (levator ani, obturator internus, and pyriformis muscles) and lymph nodes were evaluated for each study.

Bladder invasion was diagnosed when tumor extends directly to the serosal surface of the bladder wall, causing either focal wall thickening and/or interruption or alteration of the normal low signal intensity on T2W images. Rectal infiltration was similarly assessed. Tumor extension to the pelvic side wall muscles was diagnosed when the tumor was extended to and was continuous with the involved muscles with loss of the intervening fat planes. Associated changes of signal intensity within the muscles were considered confirmatory findings.

Lymph node assessment: Lymph nodes greater than 1 cm in greatest diameter was considered pathologic. Presence of intranodal necrosis (high T2W irregular zone inside) was considered confirmatory finding.

Other findings looked for was the presence of ascites, peritoneal and/or omental implants.

**DWI and ADC analysis:**

Patients who had high signal intensity endometrium on DWI and low signal intensity on ADC images were taken as diffusion positive and patients who had high or low signal on DWI and high signal on ADC images were taken as diffusion negative. True positives were patients who had diffusion positive endometrium and histopathologically proved to have endometrial malignancy. True negatives were those patients who had endometrium which was negative on both diffusion imaging and histopathology. False positive patients had diffusion positive endometrium but the histopathology reported benign findings. False negatives were defined as patients who were diffusion negative but histopathology reported them as endometrial malignancy.

Because DW images are intrinsically T2-weighted, the T2 shine-through effect can in fact cause problems in image interpretation. According to previous reports [14], DW images obtained with a high b-value in our study were evaluated in reference to corresponding ADC maps to avoid this pitfall: When hyperintensity on high b-value images corresponded to a low ADC value, tumor was diagnosed; conversely, the hyperintense area on high-b-value images that corresponded to a high ADC value was not considered an expression of tumor tissue.

**Statistical analysis:**

Descriptive statistical values such as sensitivity, specificity, and positive and negative predictive values were measured for each MR imaging finding.

**Results**

**Surgical and histopathological findings:**

Twenty patients were included in the study. Ten patients with malignant endometrial masses, 9 patients with cervical carcinoma and 1 patient with rhabdomyosarcoma.

The corporeal lesions 4 masses were diagnosed as stage I, another 6 was diagnosed as stage III. Of stage I cases less than 50% of the thickness of the myometrium was infiltrated in 2 cases. In the other 2 cases more than 50% of the myometrial thickness was infiltrated. In one case of endometroid adenocarcinoma a synchronous left ovarian endometroid carcinoma was evident. In the other 5 stage III cases of endometrial carcinoma parametrial infiltration was evident.

No cervical involvement was evident. Invasion of the rectum or the UB was not evident in any patient. No pelvic wall infiltration was evident.

Nine cases with stage IIB cervical carcinoma were operated. In all cases stromal invasion was evident with parametrial infiltration. In five of them, vaginal infiltration was evident. Enlarged regional lymph nodes were evident in 3 patients. Nodal metastases were pathologically identified in the 3 cases.

No evidence of rectal or vesical infiltration was operatively detected, in any case.
Fig. (1): Patient aged 58 years old complains of post menopausal bleeding. (A,B) Sagittal and coronal T2W images. (C-G) Axial T2W, T1W, DWI and ADC map. A barrel shaped lesion is seen involving the entire circumference of the cervix replacing the full thickness of its stroma with obliteration of the normal low signal intensity of the anterior and posterior vaginal walls and bilateral parametrial infiltration. Enlarged right iliac nodes are seen with fluid intensity in the largest node “suggesting degeneration”. In DWI the lesion shows high signal intensity with low signal intensity in ADC map. The degenerated right iliac node shows high signal intensity in DWI and ADC images. Operative and histopathological diagnosis was stage IIB cervical adenocarcinoma with iliac nodal metastases.

Fig. (2): A 5 year old patient complaining of pelvi-abdominal swelling. (A-C) Axial, sagittal and coronal T2W images (D,E) Axial DWI and ADC map. A sizeable solid mass with lobulated outlines is seen involving the uterine body, the cervix and upper vagina with obliteration of the utero-vesical fat planes and recto-uterine space. In DWI the lesion shows high signal intensity with low signal intensity in ADC images Tru-cut needle biopsy revealed uterine rhabdomyosarcoma.
Fig. (3): Patient aged 45 years old complaining of irregular uterine bleeding. (A,B,D) Sagittal, coronal, and axial T2W. (C) Axial T1 W, (E,F) DWI and ADC map. A moderately hyperintense solid lesion involving the entire thickness of the posterior wall of the cervix obliterating the posterior fornix and the normal low signal intensity of the muscle layer of the upper part of the posterior vaginal wall. The right parametrial infiltration is well appreciated in axial T1W images. The lesion exhibits high signal intensity in DWI images with low signal intensity in ADC images. Operative and histopathological diagnosis was stage IIB squamous cell cervical carcinoma.

**MR imaging findings:**

On MR imaging 10 cases of malignant endometrial lesions were diagnosed. In all cases endometrial lesion can be identified either in the form of irregular endometrial thickening (7 cases) or endometrial masses (3 cases). The intensity of the endometrial lesion was generally low in T2W images. Foci of necrosis (irregular intra-tumoral foci of higher T2W signal intensity) were identifiable on four cases.

In all cases the junctional zone was infiltrated either partly or totally, as identified by interruption of its normal low T2W signal intensity.

In cases of endometrial carcinoma more than 50% of the depth of the myometrium was penetrated in 8 cases while in 2 cases less than 50% of the myometrial thickness was infiltrated.

In one patient widening of the internal os by the endometrial lesion was evident suggesting cervical involvement.

In the case of endometroid adenocarcinoma a left ovarian mass with thick low signal intensity walls in T2W images and mixed solid/cystic intensity of its center. Infiltration of the parametrium in other stage III cases, evidenced by irregular interface between the tumour and parametrium and stranding of the latter was evident.

In cases of cervical carcinoma, stromal invasion was evident in all cases, with parametrial infiltration in terms of irregular tumor/parametrium interface. Involvement of the upper vagina was evidenced by loss of the normal low signal intensity of the muscle layer in T2W imaging.

No vesical infiltration can be detected on MR imaging. Lateral pelvic wall and pelvic floor infiltration was similarly absent.

In 3 cases, bilateral iliac adenopathy was evident with positive metastatic nodes identified at histopathology.

In the patient with uterine rhabdomyosarcoma tissue diagnosis was obtained via a Tru-cut needle biopsy. Surgery was postponed.

MR stage was comparable to operative stage in all cases. In all patients with endometrial carcinoma the lesion was diffusion positive being hyperintense on DW images and low on ADC images. The mean ADC value for abnormal endometrium was $0.730\pm0.215 \times 10^{-3} \text{mm}^2/\text{sec}$ at b-value of $1000\text{sec/mm}^2$. The sensitivity and specificity of DWI in detection of abnormal endometrium was 100%.

Malignant cervical tissue demonstrates restricted diffusion and hence reduced ADC values when
compared to normal tissue. The mean ADC value for cervical malignancy was $0.890 \pm 0.112 \times 10^{-3}$ mm$^2$/sec at b-value of 1000 sec/mm$^2$. DWI and ADC maps allow differentiation of benign from malignant zones of cervix with sensitivity and specificity of 100%. There was no statistically significant difference in the ADC values between adenocarcinoma and squamous cell carcinoma. Moreover the regional nodal disease was readily identified at DWI. In 2 cases the enlarged nodes demonstrate high signal intensity in DWI with low signal intensity in ADC images. In the third case with metastatic regional adenopathy the enlarged nodes were showing high signal intensity in DWI and ADC images due to necrosis. Sensitivity of the ADC in assessment of regional nodal spread was 100% with specificity of 67%.

Table (1): Summarizes the pathologic findings in the twenty patients.

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<th>Finding</th>
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<tr>
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<td>Adenocarcinoma</td>
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Fig. (4): Patient aged 60 years old and complains of post menopausal bleeding. (A-C) Sagittal, axial and coronal T2W images, (D,E) Axial DWI and ADC map. An irregular sessile lesion of low signal intensity is seen within the uterine cavity extending into the internal cervical os and eroding the junctional zone in the right lateral uterine wall with thinned out myometrium thereby. In DWI the lesion shows high signal intensity and in ADC images it shows low signal intensity. Operative and histopathological diagnosis was stage IB endometrial adenocarcinoma.

Fig. (5): A 70 year old patient complaining of post menopausal bleeding. (A-C) Sagittal, axial T2W and T1W images, (D,E) Axial DWI and ADC map. An irregular lesion of low T2W signal is seen diffusely involving the endometrial cavity with junctional zone and posterior uterine wall myometrium infiltration. A left ovarian solid lesion is seen exhibiting low T1W signal and high T2W signal with thick low signal intensity rim. In DWI the endometrial and ovarian lesions show high signal intensity with low signal intensity in ADC images. Diagnosis was stage IB endometroid carcinoma with endometroid carcinoma of the ovary.
Discussion

MRI examination is a useful modality for staging and evaluation of gynecologic malignancy in general and uterine malignancy in particular. The DW-MRI method has been introduced to cancer diagnostics in the recent years, and this has widened the diagnostic capabilities of MRI.

In our study 10 patients with pathologically proven endometrial carcinoma were included. In all the patients the endometrial lesion exhibits high signal intensity in DWI with low signal intensity in ADC images with sensitivity and specificity of 100%. The mean ADC value for abnormal endometrium was $0.730\pm0.215 \times 10^{-3}\text{mm}^2/\text{sec}$ at b-value of $1000\text{sec/mm}^2$. Similar results were reported by Shen et al., [15] where the mean ADC of endometrial carcinoma of 24 cases was $0.864 \times 10^{-3}\text{mm}^2/\text{sec}$, Inada et al., [16] where the mean ADC value of endometrial cancer was $0.97\pm0.19 \times 10^{-3}\text{mm}^2/\text{sec}$, Tamai et al., [17] who reported that the mean ADC value of endometrial cancer was $0.88 \pm 0.16 \times 10^{-3}\text{mm}^2/\text{sec}$ and Fujii S. et al., [18] who reported ADC value of endometrial carcinoma of $0.98\pm0.21 \times 10^{-3}\text{mm}^2/\text{sec}$. The specificity and sensitivity in our study was higher than the reported sensitivity and specificity by Fujii S. et al., [18] “84.6% and 100%” and Inada Y. et al., [16], “overall detection sensitivity was 96%”. This can be explained by the later stage disease at presentation of the patients included in our study making the possibility false positive results less likely.

Nine patients with pathologically proved cervical carcinoma were included in our study. The in all the patients the cervical lesion exhibits high signal intensity in DWI with low signal intensity in ADC images with sensitivity and specificity of 100%. The mean ADC value for abnormal endometrium was $0.890\pm0.112 \times 10^{-3}\text{mm}^2/\text{sec}$ and Inada et al., [15] where the mean ADC of cervical carcinoma of 24 cases was $1.09 \times 10^{-3}\text{mm}^2/\text{sec}$ and Fujii S. et al., [18] who reported ADC value of cervical carcinoma of $1.05 \times 10^{-3}\text{mm}^2/\text{sec}$ at b-value of $1000\text{sec/mm}^2$. This values agrees with the published reports by Liu et al., [19] “mean ADC value=0.88 \times 10^{-3}\text{mm}^2/\text{sec}”, Naganawa et al., [20] “mean ADC value=1.09 \times 10^{-3}\text{mm}^2/\text{sec}”, Kilickesmez et al., [21] “mean ADC value=1.05 \times 10^{-3}\text{mm}^2/\text{sec}”, McVeigh et al., [22] “mean ADC value=1.09 \times 10^{-3}\text{mm}^2/\text{sec}”, Xue et al., [23] “mean ADC value=1.08 \times 10^{-3}\text{mm}^2/\text{sec}”, Hoogenbam et al., [24] “mean ADC value=0.86-1.15 \times 10^{-3}\text{mm}^2/\text{sec}”, Payne et al., [25] “mean ADC value=1.38 \times 10^{-3}\text{mm}^2/\text{sec}”, Chen YB [26] “mean ADC value=1.38 \times 10^{-3}\text{mm}^2/\text{sec}”. The sensitivity and specificity in our patients were 100% with similar reported results by Chen YB [26], “Sensitivity: 96% and Specificity: 100%”, Kilickesmez et al., [21] “Sensitivity: 96% and Specificity: 94.5%”, Hoogendam et al., [24] “Sensitivity: 91-97% and Specificity: 91-100%” and Payne et al., [28] “Sensitivity: 98% and Specificity: 93%”. The diagnostic performance of DWI in lymph node assessment in our work “sensitivity: 100% and specificity: 67%” was different from that reported by Chen YB et al., [26] “sensitivity: 83% and specificity: 74%” possibly due small number of cases with lymph node disease in our study.

Despite of the lack of published data about the diagnostic performance of DWI in assessment of urogenital rhabdomyosarcoma yet its DWI and ADC appearance was concordant with the established data in distinction of benign and malignant genital tract tumors.

Conclusion:

Conventional MRI findings in conjunction with DWI and quantitative measurement of the Apparent Diffusion Coefficient (ADC) are effective methods in the diagnosis and staging of gynecological cancer.

DWI can provide excellent tissue contrast and may be able to demonstrate malignant tumors. ADC values may be valuable in distinguishing between malignant and benign lesions.

Future work should be directed by the potential of DWI in assessment of degree of differentiation of malignant gynecologic tumors which significantly affects the post-therapeutic outcome and overall survival.

References


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الملخص العربي

يلعب التصوير بالرنين المغناطسي دوراً محورياً في كشف وتحديد مراحل الورم الخبيث لأمراض النساء. التصوير باستخدام خاصة

الانتشار يمكن أن يظهر إشارات غير طبيعية متعلقة من بؤر مرضية على أساس الاختلافات في الانتشار الجزيئي. كما يسمح التقييم الكمي

لمعالجات الانتشار في التمييز بين الأنسجة الخبيثة والحميدة ورصد النتائج العلاجية. على هذا الأساس، كان الهدف من هذه الدراسة هو تقييم

القيمة الدالة لحصيبة الانتشار والتقييم الكمي في تقييم الأورام الخبيثة لأمراض النساء.

المواد والأساليب: تم فحص عشرون من المرضى المشتبه بإصابتهم بأمراض نسائية عن طريق التصوير بالرنين المغناطيسي، تم تحديد

موقع مشاكل الورم، وتوزيع المنطقة، حجم الورم وكيفية الانتشار. المثلث، المستقيم، عضلات جدار الحوض الجانبي والعقد الليفاوية تم

تقييمها في كل حالة. تم قياس القيم الإحصائية الوصفية مثل القيمة والرقمية، والقيم التنبؤية الإيجابية والسلبية لكل علاج من علاجات التصوير

بالرنين المغناطيسي.

النتائج: كانت مرحلة التشخيص بالرنين المغناطيسي متميزة لمرحلة الورم جراحياً في جميع الحالات. وكانت حساسية وخصوصية خاصة

الانتشار في الكشف عن بطانة الرحم غير الطبيعية 100%. خاصة الانتشار والتقييم الكمي لمعالجات الانتشار سمحت في الفترات بين المناطق

الحميدة من الخبيثة من عمق الرحم مع حساسية وخصوصية 100%. وكانت حساسية خاصة الانتشار في تقييم الانتشار العقد الليفاوية 100%

مع خصوصية 100%

الاستنتاج: نتائج التصوير بالرنين المغناطيسي التقليدية جنبًا إلى جنب مع استخدام خصعة الانتشار والتقييم الكمي لمعالجات الانتشار

هو وسيلة فعالة في تشخيص وتحديد مراحل الورم الخبيثة للجهاز التناسلي للمرأة.