

ROLE OF MRI IN THE STAGING OF TUMORS OF THE UTERINE CERVIX

Fathy A. Tantawy MD *, **Mostafa Shafek MD ****, **Doaa I. Hassan MD*** and
Heba A. El Sayed*

(Radiodiagnosis* and gynaecology ** departments, Faculty of Medicine, Zagazig University).

ABSTRACT

Cervical cancer is the worldwide leading cause of cancer-related death of women, especially in developing countries. The International Federation of Gynecology and Obstetrics recommends staging during surgery, however, surgical-pathologic staging would not be feasible in cases of more advanced cancers. Generally, in these cases, the staging is performed by means of clinical and gynecological examination and basic imaging studies. However, such an approach fails to demonstrate the actual extent of the disease, and does not include significant prognostic factors such as tumor volume, stromal invasion and lymph node involvement. Magnetic resonance imaging has increasingly been utilized in cervical cancer staging, since at early stages of the disease its performance may be compared to intraoperative findings and, at advanced stages, it shows to be superior to the clinical evaluation. Additionally, magnetic resonance imaging presents an excellent imaging resolution for the different densities of pelvic structures, does not require ionizing radiation, is comfortable for the patient, improves de staging, allowing the early detection of recurrence and the identification of reliable prognostic factors which contribute to the therapeutic decision making process and results prediction with an excellent cost-effectiveness.

Aim: To asses the role of MRI in the accurate staging of cancer cervix compared with the clinical FIGO staging.

Patients And Methods: A total number of 37 patients with untreated first diagnosed cervical cancer scheduled for MRI. MRI data were compared to the data of the clinical FIGO stage using our golden standard as referance .

Results: Our study revealed that MRI can accurately stage the cervical cancer if compared to the clinical FIGO staging system.

Conclusions: Magnetic resonance imaging is the imaging modality of choice for staging the primary cervical tumour, evaluate response to treatment and detect tumour recurrence and potential complications. Adequate patient preparation, protocol optimization and MRI reporting expertise are essential to achieve high diagnostic accuracy.

Keywords: Cancer cervix – MRI- Figo staging criteria.

INTRODUCTION

Uterine cervical cancer is the third most common gynaecological malignancy after endometrial and ovarian cancers. Nearly 80% of cervical cancer occurs in the developing countries and most patients are diagnosed with the disease at an advanced stage, thus not suitable for surgical staging (1).

It affects the female genital tract in middle age group between 45 and 55 years (2).

Histologically, squamous cell carcinoma is the commonest type. Other types are adenocarcinoma, adenoid-cystic, adenoid-basal, and small cell carcinoma are described (3).

The greatest difficulties in the clinical examination of patients with cervical cancer are accurate estimation of tumour size, the assessment of parametrial and pelvic side wall invasion, and the evaluation of lymph node metastases which are recognized important prognostic factors. Despite these inherent limitations of the clinical examination, uterine cervical cancer is the only gynaecological cancer still largely staged clinically, in accordance with the classification of the International Federation of Gynaecology and Obstetrics (FIGO) (1).

Preoperative MR imaging criteria are not formally included in the revised FIGO staging system because cervical carcinoma is most prevalent in developing countries, where imaging resources are limited, However, the revised FIGO

staging system acknowledges the benefits of staging on the basis of MR imaging findings and encourages its use when available (4) .

MR imaging has been shown to accurately delineate the local extent of disease and depict extrauterine tumor spread. MR imaging accurately depicts the depth of myometrial invasion and cervical stromal invasion and may depict metastatic spread, including peritoneal deposits (4) .

Lymph node metastasis is the most common form of extrauterine disease

spread and is the strongest predictor for recurrence (4) .

Diffusion-weighted imaging sequences are designed to detect alterations in thermally induced random (Brownian) motion of water molecules within tissues . The degree of such motion, also known as diffusion, as measured with diffusion-weighted imaging relates to the mean path length traveled by water molecules within a specific time interval. The degree of signal loss is proportional to the degree of water motion (mean diffusional path length), with the greatest signal loss seen with bulk water (5).

Diffusion is quantified by a parameter, the apparent diffusion coefficient (ADC; unit mm²/s), which is usually presented as a quantitative parametric map as gray-scale images. On ADC maps, tumors usually demonstrate low ADC

values and appear as low signal intensity area compared with normal tissue (6).

PATIENTS AND METHODS

The study population included a total of 37 patients, from 23 to 80 years. The study was conducted over a period of 23 months, starting from september 2012 to august 2014.

Patients were referred to the radiodiagnosis department from the gynaecology department in Zagazig university hospital. Verbal consent was taken from all the patients as well as detailed explanation of the study technique and its value were conducted in full details to all patients before the examination start.

The duration of the disease illness at time of performing the MRI studies varied from 23 year to 80 years (Mean 59 years). All of the patients were first time diagnosed having cervical carcinoma with no prior interference.

All of our patient underwent complete clinical examination as well as full history taking. The clinical evaluation was reviewed by a skillful gynecologist first before being aware of the MRI findings of each patient.

For patients who underwent surgery (up to stage IIA), the histopathological stage was used as the gold standard. For patients who did not undergo surgery, the gold standard stage was set on a review consensus between the two gynaecologists after correlation with MRI findings and other investigations.

Technique MR and DW IMAGING were done by using 1.5 tesla super conducting MR imager (Achieva, Philips Medical System. MRI study was done with the patients in the supine position using the standard a pelvic surface array multichannel coil.

Patient preparation Ideally, the patient is asked to empty the bladder before going on the MR scanner. A full bladder may degrade T2-weighted images because of ghosting and motion artifacts.

1) The conventional MR sequences were done as the following:

- 1) Sagittal T2WI (TR4400-4800/TE110).
- 2) Axial T2WI (TR4400-4800/TE110).
- 3) Coronal T2WI (TR4400-4800/TE110).
- 4) Axial T1WI (TR148-597/TE2-15).
- 5) Coronal T1WI (TR148-597/TE2-15).

The previous sequences were done with slice section 5 mm thickness with 1mm gap and Field of view (FOV) 230 mm.

2) 7 cases with very small lesion or those with suspected urinary bladder invasion were given

contrast agent. The contrast media used in the conventional MR examination was Gd-DTPA (Gadolinium). The dose: IV 0.1- 0.2mmol/kg body weight. Post contrast T1 fat sat axial, coronal and sagittal spine echo sequences.

3) For 31 of the cases DWI images were done at (b: 0,500,1000)with ADC value calculated mm²/second.

RESULT

The study group comprised of 37 patients, with a mean age of 59 years (range 23 to 80 years).

Squamous cell carcinoma was present in 78.4% (29/37) of the patients, followed by adenocarcinoma in 21.6% (8/37) cases.

MRI growth pattern was Anterior wall 10.8 %, Posterior wall 5.4% and Combined 83.7 %.

The overall accuracy of MRI in staging carcinoma of cervix 94.6 % (35/37), and that of clinical FIGO staging was 40 % (15/37). MRI was inaccurate in 5.4 % (2/37) cases. Out of these two patients, in which MRI was wrong, it was unable to detect urinary bladder invasion in one case and to detect distant metastasis in another case.

Out of the 37 cases, 3 cases showed additional significant MRI data representing 8 % of the studied group, one showed bilateral ovarian solid lesion, one showed complicated ovarian cyst and the last one had avascular necrosis of the hip joint.

Out of the 37 cases of the studied group the most common presenting symptom was offensive watery discharge representing 37.8 % followed by post menopausal bleeding 29.7%.

MRI reported 100% sensitivity and specificity in the detection of vaginal invasion, parametrial invasion as well as pelvic side wall invasion.

MRI also reported 66 % sensitivity and 100 % specificity in detection of urinary bladder wall invasion, 50 % sensitivity and 100 % specificity in detection of distant metastasis.

The cut-off short-axis diameter for an enlarged node was considered 10 mm on MRI, and we performed CT-guided lymph nodal biopsy in all such cases. All the cases with enlarged LN more than 10 mm were positive for metastasis except in one patient who had two enlarged common iliac LNs proved to be non metastatic by biopsy.

31 out of 31 cases underwent diffusion weighted MRI showed restricted diffusion with reduced ADC value if compared to the normal cervical tissue with the mean ADC value 795.4 ± 59.1 mm²/s.

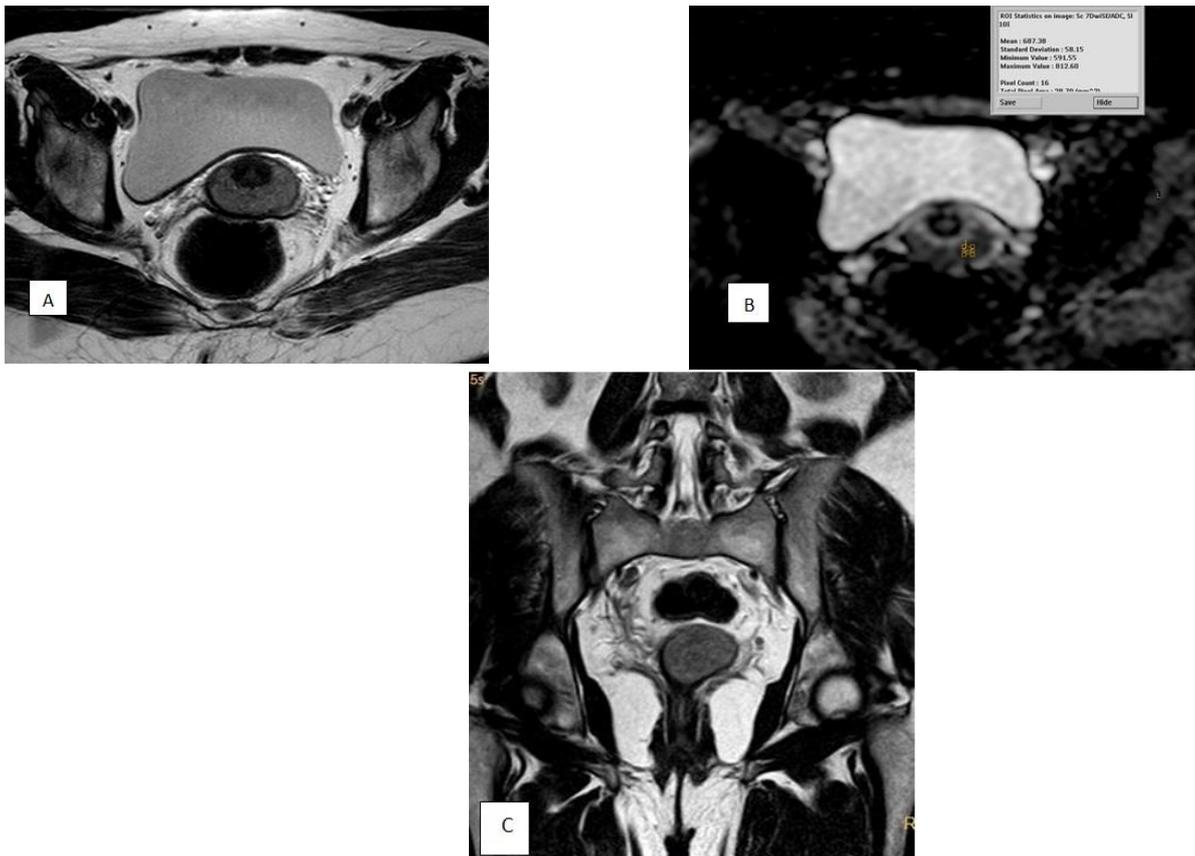


Figure 1: 33 years old patient with stage IIA cervical mass proved pathologically to be squamous cell carcinoma, (A and c) axial and coronal T2WI shows well defined isointense cervical mass with clear upper vagina as well as preserved peripheral hypointense stromal ring denoting absence of para metrial invasion. (B) ADC map showing low ADC value measures $687.3 \times 10^{-3} \text{ mm}^2/\text{s}$.

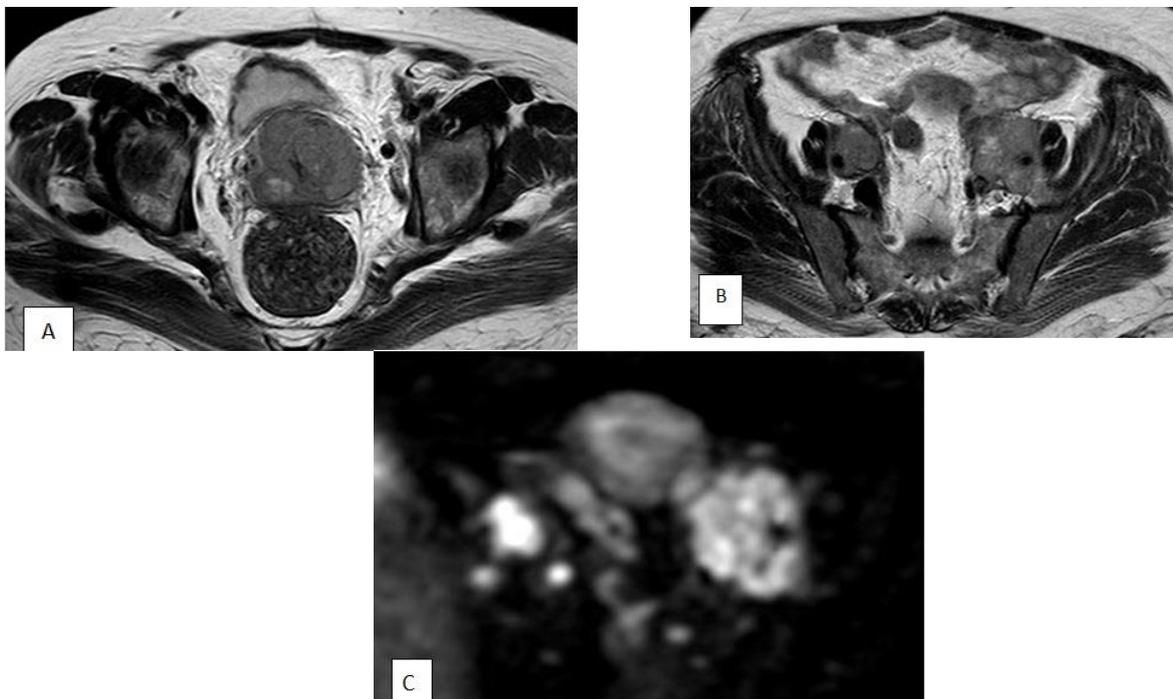


Figure 2: 73 years old patient with cervical cancer stage IIB proved pathologically to be squamous cell carcinoma (A) Axial T2- weighted MR image shows a tumor with intermediate signal intensity replacing the normal low-signal-intensity cervical stroma with interruption of the low-signal-intensity cervical stromal ring. (B) Axial T2- weighted MR image at different level shows bilateral deep pelvic LNs. (C) DWI shows bilateral high SI lesions of restricted diffusion corresponding to the enlarged LNs.

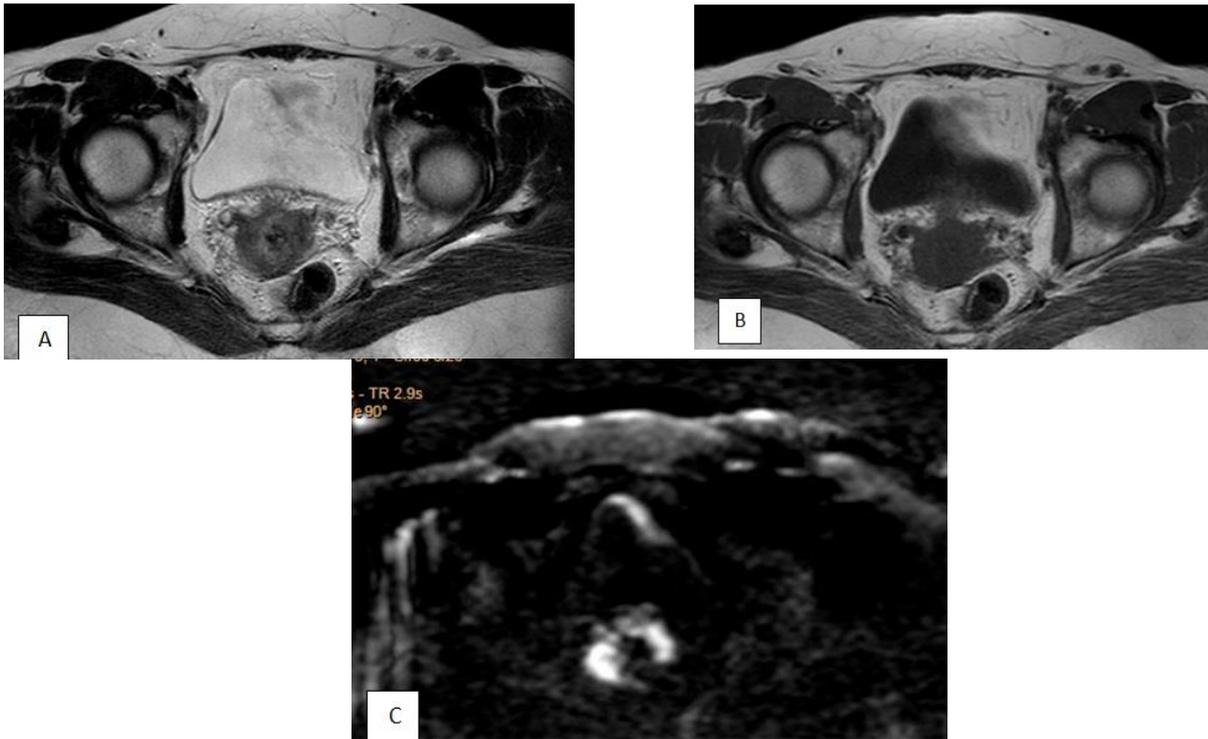


Figure 3: 53 years old patient with stage IIB cervical cancer proved to be squamous cell carcinoma (A and B) axial T2 and T1WI showing cervical mass displaying iso SI on T2 and low SI on T1, note the interruption of the hypointense ring on T2 images denoting para metrial invasion. (C) Axial DW showing restricted diffusion .



Figure: 4 47 years old patient with cervical cancer stage IV A proved to be adenocarcinoma. (A) Sagittal T2WI shows isointense cervical mass extending upwards into the endometrial cavity and downwards to the upper vagina. (B and C) Sagittal T1 fat sat with contrast and axial T1 demonstrate the mass invading the posterior UB wall.

DISCUSSION

Nearly 80% of cervical cancer patients are diagnosed with the disease at an advanced stage, thus not suitable for surgical staging stated by Corinne et al (1) and with our with most of our cases were beyond stage IIA the corner stone for surgical interference.

Study done by Nilu et al (7) and Tejinder et al(8) reported that the mean age of the studied group was 46 years and 51 years with average (range 28 to 65 years) and(21-80 years) respectively. In our current study the mean age of the studied group was 58 years with average 23 to 80 years

The commonest histological type of cervical carcinoma is squamous cell carcinoma, which accounts for 78.4% of our cases followed by and adenocarcinoma was 21.6 %.

The study of Mohammed et al (9) reported that the most common pathological type of the examined cervical mass was the squamous cell carcinoma representing 73.3% of the total studied cervical malignancy, This incidence was nearly compatible by the study done by Nilu et al (7) reporting that Squamous cell carcinoma was present in 90.7% (68/75) of the patients, followed by adenocarcinoma in 9.3% (7/75) cases, and with the study done by Harpreet et al stating that Eighty percent to 90% of cervical carcinomas are of squamous cell origin.

Cervical cancer was identified in our study as a mass of intermediate to hyperintense on T2WI (figure 1) keeping with Yoshikazu et al (10) and Mohammed et al (9) reported that cervical cancers appear as hyperintense masses on T2-weighted images regardless of histopathologic type.

We investigated the accuracy of MRI at 1.5T, as a convenient, complete method for allocating patients with invasive cervical carcinoma to best possible treatment, resulting in overall accuracy of 94.6 % in a study of 37 compared to that of clinical FIGO staging was 59 % (22/37), MRI was inaccurate in 5.4 % (2/37) cases.

By using MRI at 1.5T in 67 cases Nilu et al (7) had addressed that the overall accuracy of MRI in staging carcinoma of cervix was 89.3% (67/75), and that of clinical FIGO staging was 61.3% (46/75), Evis et al (11) reached an overall staging accuracy of of MRI ranges from 75% to 96% .

Parametrial invasion is the main determinant whether the appropriate management would be surgical or radiation. The intact hypointense stromal ring of about 3-mm thickness has a negative predictive value of 100% in excluding parametrial invasion. Claudia et al (12), Mangal et al (13) and Nilu et al (7) reported that intact T2-

hypointense stroma ring has a high negative predictive value for parametrial invasion and is between 94% and 100% (figure 2 and 3) .

MRI is highly sensitive in the detection of vaginal invasion reporting 100 % sensitivity in both stage IIA and IIIA. The signs of vaginal involvement is better characterized on high-resolution T2- weighted sequences, showing the segmental interruption of the normal hypointense signal of the vaginal wall, or yet a hyperintense vaginal thickening (tumor), or the mass itself in contiguity with the vaginal wall . Vaginal invasion corresponds to stage IIA; when this invasion extends up to the lower vaginal third, corresponds to stage IIIa, this is also was reported by Claudia et al (12) stating that MRI has 93 % sensitivity in the detection of vaginal invasion .

Our study reported only 66% sensitivity with 100 % specificity in detection of urinary bladder wall invasion (IVA), the lower sensitivity in comparison to Mohamed et al (9) reported 100 % sensitivity and 100% specificity of UB invasion (figure 4) this obvious difference in MRI sensitivity may be attributed to one patient refusing to have IV contrast for better assess of UB invasion .

Van Vierzen et al (14) found that the combination of pre-contrast and post-contrast MR images doesnot improve staging accuracy except in the assessment of bladder and rectal wall invasion.

Staging of cervical cancer is still based on clinical FIGO criteria can be erroneous in up to 32% of patients with the greatest difficulties in the clinical evaluation of patients with cervical cancer are the assessment of parametrial and pelvic sidewall invasion reported by Evis et al (11) as well as our study where FIGO clinical criteri were wrong in 40 % (15 out of 37 cases) , most of them missing the para metrial invasion and underestimating the patient stage.

MRI had an advantage of picking other significant data that may or may not alter the treatment therapy, in our study 3 out of 37 cases had concurrent illness that was not suspected clinically (1/37 or 2.8 %) had bilateral solid ovarian lesions , (1/37 or 2.8 %) had complicated ovarian cyst and (1/37 or 2.8 %) had AVN of the right hip, both of th ovarian lesions proved to be malignant .

Nilu et al (7) picked up 4.4% (3/67) patients had another disease along with cancer of cervix, two had ovarian neoplasia (2/23 or 8%) which was clinically interpreted as parametrial invasion and one patient had illiopsis abscess (1/23 or 4%) which was also not suspected clinically.

Cervical cancers show restricted diffusion and tend to have lower ADC than normal cervical tissue accepted by Sayan et al (15) and ours showing 100 % of cases (31/31) showed restricted diffusion with lower ADC value than normal cervical tissue.

There is no significant difference in the ADC value among the different pathological types with the mean ADC value $.791 \times 10^{-3} \text{ mm}^2/\text{s}$ in cases with squamous cell carcinoma and $.796 \times 10^{-3} \text{ mm}^2/\text{s}$ in cases with adenocarcinoma. Disagreeing with the study done by Elena et al (6) claiming that adenocarcinomas typically have high cellular density and so would be expected to have lower ADC values.

The accuracy of MRI in the current study is fairly high in the detection of pelvic node metastasis from uterine cervical carcinoma with ten millimetres is the considered upper limit for short axis of normal pelvic nodes, our study showed (12/12 or 100 %) of pathologically proven metastatic LN with the short axis diameter was more than 10 mm. This size criterion has been widely accepted by Mohammed et al (9), Claudia et al (12) and Nilu et al (7).

Finally in agreement with Tejinder et al (8), Evis et al (11) and Nilu et al (7) FIGO staging may not be a true representation of the correct volume of disease and therefore, does not provide prognostic insight into the potential of the disease

CONCLUSION

Even though MRI is not utilized by the majority of oncology services for staging uterine cervix tumors, and, up to this moment, it has not been officially approved by FIGO yet, it is the best imaging method in terms of accuracy for assessment of tumors, and plays an essential role in the therapeutic planning and follow-up.

MRI has shown to be better than the clinical examination, and, when utilized as the initial staging method, reduces the number of invasive procedures and radiological studies such as urography, cytoscopy and rectosigmoidoscopy, with lower cost for the management of the disease. Additionally, the correct assessment of the tumor extent and volume allows optimizing the planning of the fields for external pelvic radiotherapy and brachytherapy.

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يعد سرطان عنق الرحم الثالث من حيث الانتشار في اورام الحوض لدي السيدات يسبقه سرطان المبيض و سرطان بطانة الرحم و هو اكثر انتشارا في دول العالم الثالث .
هنالك العديد من الاخطاء في تقييم مراحل سرطان عنق الرحم اعتمادا علي الفحص السريري للمرضي قد يصل الي ٦٥ % في بعض الاحيان.

الاتحاد الدولي لطب النساء والتوليد توصي بتقييم مرحله الورم و مدي انتشاره أثناء الجراحة، ومع ذلك، لن يكون ممكنا في حالات سرطان الأكثر تقدما التي يتم قيها إجراء التدرج عن طريق الفحص السريري واللجوء الي التصوير الطبي. في كثير من الاحيان يفشل هذا النهج للتدليل على مدى الفعلي للمرض، ولا تشمل العوامل النذيره مثل حجم الورم، والغزو اللحمية وتورط العقدة الليمفاوية. وقد استخدم على نحو متزايد التصوير بالرنين المغناطيسي في تشخيص و تدرج المراحل المختلفه للمرض ، و يظهر الرنيني المغناطيسي قدره كبيره علي التقييم الفعلي لمرحلة المرض بالاضافه الي مدي انتشاره في الغدد الليمفاويه داخل او خارج الحوض لتكون متفوقة على التقييم السريري. بالإضافة إلى ذلك، لا يتطلب التصوير بالرنين المغناطيسي الإشعاع المؤين، و هو مريح للمريض و يسمح بالكشف المبكر عن تكرار الورم.

لقد ازداد استخدام الرنين المغناطيسي في تقييم اورام الحوض لدي السيدات خصوصا في العقدين الاخيرين فهو مع الفحص السريري للمريض سوف يعطينا تقيما دقيقا لمراحل سرطان عنق الرحم.