Preoperative assessment of deep myometrial and cervical invasion in endometrial carcinoma: Comparison of magnetic resonance imaging and gross visual inspection

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This study aimed to evaluate the accuracy of magnetic resonance imaging (MRI) in the detection of deep myometrial invasion and cervical extension by endometrial carcinoma. We also aimed to compare MRI results to surgical staging of endometrial carcinoma. Forty women with a histologic diagnosis of endometrial carcinoma underwent a preoperative pelvic MRI. In 33 cases intraoperative gross visual inspection (GVI) of the surgical specimen was also evaluated. The results obtained were compared with the histologic diagnosis. Pathologic evaluation of the myometrium determined that superficial invasion was present in 25 patients and deep invasion in 15. The uterine cervix was found to be involved in 12 cases. The accuracy, sensitivity, and specificity of MRI and GVI were 93%/91%, 80%/77%, and 100%/100%, respectively, in detecting deep myometrial invasion and 80%/79%, 33%/36% and 100%/100%, respectively, in determining cervical invasion. When the Kappa statistical measurement was applied, the results from each technique, MRI and GVI, showed an agreement on the evaluation of myometrial and cervical invasion by endometrial carcinoma. In conclusion, MRI, in this series, was demonstrated to be a reliable method for preoperative endometrial carcinoma “imagiological staging”. The high accuracy achieved by MRI and GVI suggests that they may be used interchangeably.

KEYWORDS: cervical invasion, endometrial carcinoma, gross visual inspection, magnetic resonance, myometrial invasion.

In Portugal, endometrial carcinoma occupies second place among the gynecological malignancies, in contrast to other developed countries(1). Abnormal vaginal bleeding facilitates its diagnosis at an initial phase(1,2).

Several prognostic factors can modify the therapeutic orientation of endometrial carcinoma, such as histologic subtype, microscopic grade of differentiation, and stage of the disease. Endometrial sampling can predetermine the morphology of the tumor, but myometrial and cervical invasion data are only available during surgery(2,3) or by imaging techniques. Since 1988, the Cancer Committee of the International Federation of Gynecology and Obstetrics (FIGO) preconized surgical staging for endometrial carcinoma(4).

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Preoperative knowledge of tumor invasiveness is important as it allows referral of patients to oncologic surgery centers\(^3,5\) where more extensive surgery can be performed. Deep myometrial and cervical invasion are associated with an increased risk of pelvic and para-aortic lymph node metastases\(^1,6\).

Pelvic magnetic resonance imaging (MRI) is an imaging technique accepted in the characterization of pelvic tumors due to its multiplanar capacity and to its excellent resolution of soft tissue contrast\(^7–10\). Significant accuracy of MRI evaluation of tumoral invasion of the myometrium (superficial/deep) as well as tumoral extension to the cervix has been described in the literature\(^7,11–24\).

In most centers, surgical staging preconized by FIGO is done by intraoperative consultation in order to estimate the extent of spread of a known endometrial carcinoma. This consultation may be done by gross visual inspection (GVI) combined with frozen sections\(^25,26\).

In this work we performed a prospective study to evaluate the accuracy of MRI and GVI in endometrial carcinoma (invasion of the deep myometrium and of the uterine cervix). We also aimed to compare these two different approaches.

**Patients and methods**

**Patients**

We studied 40 patients with endometrial carcinoma treated in the Department of Gynecology of the Portuguese Institute of Oncology between July of 1998 and August of 1999. The patients were 45–83 years of age (mean = 63.2 years). Six were premenopausal (one was on contraceptives), and 34 were postmenopausal (three were receiving hormonal replacement therapy and one was taking tamoxifen for breast cancer). Patients underwent surgery from 0 to 78 days (mean = 26 days) after pelvic MRI examination.

All the patients were submitted to abdominal hysterectomy and bilateral salpingo-oophorectomy, with pelvic lymphadenectomy in 13 and selective para-aortic lymphadenectomy in seven. Twenty-six cases were classified as stage I, eight as stage II, five as stage III and one as stage IV endometrial carcinoma (FIGO staging classification\(^40\)). The histologic diagnosis and the tumor grade are shown in Table 1.

**Magnetic resonance**

MRI was performed with a 1.0-Tesla superconducting magnet (model Gyroscan NT; Philips, Eindhoven, Netherlands), using a body coil. In each exam axial T1-weighted (TR/TE = 427/8 ms) and axial and sagittal T2-weighted (TR/TE = 5952/150 ms) images were acquired. The parameters were two acquisitions, a matrix of 256 × 256, with 5-mm slice thickness and 0.5-mm interslice gap.

After unenhanced T1-weighted and T2-weighted images were obtained, a dynamic study during rapid manual endovenous administration of 0.1 mm/kg gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany). A turbo-FLASH technique was used, with 14/6.9 ms (TR/TE), with a flip angle of 40° and a 256 × 256 matrix, with multisection in the sagittal plane of the uterine corpus and acquisition of images each 20 s during 3 min.

The images were interpreted prospectively by a radiologist (TC) prior to surgery. The appraised parameters were: depth of myometrial invasion and extension to the cervix. The evaluation of these variables was done on the images obtained by any of the sequences, selecting the image that demonstrated the highest certainty or determination of more advanced stage.

Invasion of the myometrium was divided in superficial (equal to or less than 50% of the thickness of the myometrium) and deep (more than 50% of the thickness of the myometrium). The tumor was classified as superficial if rupture was observed, there was irregularity of the junctional zone, or when the internal surface of the myometrium was irregular in the dynamic study. It was considered deep invasion when the tumor was observed reaching the external half of the myometrium.

Cervical invasion was considered to be present when widening of the internal os and cervical canal and/or abnormal signal intensity was observed in the cervical canal; cervical epithelium disappeared partly or totally; and/or disruption of the normal low signal intensity of junctional zone in the cervix on sagittal T2-weighted images was visualized. In the dynamic study, the cervical invasion was determined when interruption of the contrast enhancement by the epithelium or the cervical stroma was detected.

<table>
<thead>
<tr>
<th>Table 1. Comparison of the histologic diagnosis and the tumor grade</th>
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<tbody>
<tr>
<td>Histopathologic type</td>
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<tr>
<td>Endometrioid adenocarcinoma</td>
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<tr>
<td>Papillary serous adenocarcinoma</td>
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<tr>
<td>Clear cell carcinoma</td>
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<tr>
<td>Mucinous adenocarcinoma</td>
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<tr>
<td>Mixed malignant müllerian tumor</td>
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<tr>
<td>Glassy cell carcinoma</td>
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<td>Undifferentiated carcinoma</td>
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Fig. 1. Images of a 61-year-old woman with deep myometrial invasion. A) Axial T2-weighted image (left), sagittal T2-weighted image (center) and sagittal dynamic MR image after contrast (right). The uterus is mostly occupied by the tumor, with thinning of the myometrium (arrow) caused by deep myometrial invasion. Differentiation of tumor from residual myometrium is easy in the late phase of dynamic MRI. B) Gross specimen. Hysterectomy specimen with a polypoid tumor occupying the endometrial cavity (left). Whole mounted sagittal section of the endometrial cavity filled with a polypoid tumor invading the myometrium (H & E) (center). Aggregates of tumor cells invading the external half of myometrium (H & E 200×) (right).

Fig. 2. Histologic stage I endometrial carcinoma with deep myometrial invasion in a 51-year-old woman. A) Axial T2-weighted image (left), sagittal T2-weighted image (center) and sagittal dynamic gadolinium enhanced image (right). The images demonstrate the tumor extending into the outer half of the myometrium, signifying deep myometrial invasion. Demonstration of myometrial invasion anteriorly is better on the dynamic study image than on the T2-weighted images. B) Section of the uterine wall with an adenocarcinoma invading the external half of myometrium (arrow) (H & E 1×).

Fig. 3. Images of a 77-year-old woman with deep myometrial invasion. A) Axial T2-weighted image (left) and sagittal T2-weighted image (center) show an expanded central zone of high signal intensity. The junctional zone is not interrupted and the surface is smooth, which indicates no myometrial invasion. In the sagittal dynamic MR image after contrast (right) the lesion is shown as a low-signal area and there is a high-signal-intensity, outer stripe of normal myometrium, a finding suggestive of stage I cancer with superficial myometrial invasion. B) Well-differentiated neoplastic glands infiltrate singly through the myometrium without reactive stroma (H & E 200×).
Gross visual inspection

The surgical specimen of the uterus was examined immediately after surgical resection in 33 cases studied by MRI (83%) by a pathologist who was unaware of the results of the MRI.

The uterus was sectioned in the midsagittal plane and the myometrium was cut at regular intervals in order to determine tumor presence and the extent of myometrial invasion (≤ 50% or > 50%). The invaded myometrial thickness was compared with total myometrial thickness. The uterine cervix was also examined for evaluation of tumor extension. Patients were treated accordingly with GVI staging.

All cases were reviewed by a pathologist (AF), blinded to the MRI report, and the results of MRI and GVI were compared to the microscopic study.

Statistical analysis

The accuracy, sensitivity, and specificity of MRI and GVI results were characterized, taking the pathological report as “standard” [sensitivity = TP/(TP + FN), specificity = TN/(TN + FP), and accuracy = (TP + TN)/(TP + TN + FP + FN), where TP is the true positive, TN is the true negative, FN is the false negative, and FP is the false positive(27)].

The Kappa statistic was used to evaluate the amount of agreement. This measure is scaled from 0 to 1, and Landis and Koch(28) proposed the following interpretation for intermediate values (below 0.0 – poor; 0.00–0.20 – slight; 0.21–0.40 – fair; 0.41–0.60 – moderate; 0.61–0.80 – substantial; 0.81–1.00 – almost perfect).

Results

In the 40 cases studied by pelvic MRI, 12 cases were classified as deep invasion of the myometrium and 28 as superficial invasion. The pathologic study of the surgical specimens confirmed those 12 cases as having deep myometrial invasion (Figs 1 and 2). In three patients that MRI determined superficial invasion of the myometrium, the histologic analysis found deep invasion.

Among the three understaged cases, one had a 61-day interval between MRI and the surgery (median interval between the exam and surgery = 26 days) and the tumor was grade 3. In the other case, the invasion of the external half of the myometrium consisted of small isolated tumoral foci (Fig. 3). In the third case an intramural leiomyoma was present in the left horn, making evaluation difficult.

In two cases, no myometrial invasion was found in the histologic examination (stage IA). In both cases MRI and GVI also failed to show myometrial invasion.

Regarding cervical extension MRI did not detect tumoral extension to the uterine cervix in 36 cases and found invasion in four cases (Fig. 4). The pathologic study of the surgical specimens found cervical invasion in 12 cases, including the four cases recognized by MRI. In the eight patients in whom MRI understaged cervical invasion, one case was stage IIB and the other seven cases showed only endocervical epithelial invasion (Figs 5 and 6). No overestimation occurred with MRI.

The general accuracy of MRI for deep myometrial invasion was 93% and for cervical invasion 80%. The positive and negative predictive values for deep myometrial invasion were 100% and 89%, respectively; for cervical invasion the positive and negative predictive values were 100% and 78%, respectively (Table 2).

Kappa statistic revealed agreement between the results of MRI for invasion of the external half of the myometrium and the tumoral extension to the uterine cervix and the histologic findings (k = 0.8333 and k = 0.4118, respectively).

GVI was performed in 33 patients, finding invasion
of the external half of the myometrium in 10 cases and 23 cases without deep myometrial invasion. Twenty cases were confirmed histologically, three cases being understaged by GVI. Only in four cases did GVI determine cervical extension. Histology found nine cases with cervical extension. No macroscopic overestimation of tumor extension occurred.

The general accuracy of GVI for invasion of the external half of the myometrium was 91% and for cervical invasion was 79%. The positive and negative predictive values for deep myometrial invasion were 100% and 87%, respectively; for cervical invasion the positive and negative predictive values were 100% and 76%, respectively (Table 3).

Kappa statistic showed that an agreement existed between the results of GVI for invasion of the external half of the myometrium and for extension to the uterine cervix and the histologic evaluation ($k = 0.8016$ and $k = 0.4324$, respectively).

**Discussion**

Endometrial carcinoma is the second most common gynecological malignancy in Portugal and abnormal vaginal bleeding usually permits its detection at an early stage$^{(1,2)}$. Since 1988, surgical staging of endometrial carcinoma was proposed by FIGO$^{(4)}$ and both treatment and prognosis are strongly related to the stage of the disease. High risk factors, such as high tumor grade, deep myometrial invasion, and extension to cervix, indicate those patients who should undergo pelvic and para-aortic lymph node dissection.

In stage I of disease, the depth of invasion of the myometrium is related to the incidence of lymph node metastases which increases from 3% in superficial invasion of the myometrium to 40% or more in deep invasion$^{(1,29)}$. A preoperative knowledge of the absence or presence of deep myometrial invasion and/or cervical invasion is very important in treatment planning$^{(2,8,30)}$.

The importance of MRI in endometrial carcinoma staging has been well recognized. MRI studies allow tumor visualization, determine the degree of myometrial invasion, and also evaluate cervical extension, obtaining good accuracy in endometrial tumor evaluation$^{(31)}$.

In previously published series, the accuracy of the T2-weighted images in the determination of myometrial invasion by endometrial carcinoma varied between 67.9% and 82%$^{(10,11,16,32)}$. The use of a dynamic study after administration of endovenous contrast increases the accuracy to 85% and 91%$^{(10,32)}$, respectively.

In this MRI study, we used T2-weighted images sequences and dynamic studies to evaluate the depth of myometrial invasion and cervical extension. An option for those images where invasion was more clearly demonstrated or deeper was used for staging.
though T2-weighted images were used in the majority of the cases in order to determine the depth of myometrial invasion, the dynamic study after administration of endovenous contrast was extremely helpful in those cases where the junctional zone was not clearly visualized.

Our results are in keeping with other series\cite{10,32}. We obtained an accuracy of 93% in the evaluation of deep myometrial invasion and an accuracy of 80% regarding cervical extension. High-grade tumor progression and the presence of leiomyoma are well known artifacts that decrease accuracy. MRI sensitivity determining tumoral cervical extension was low (33%). Possible explanations for this result may be related to the very small endocervical tumoral foci that were detected by careful and extensive pathologic sampling of uterine cervix and/or with MRI coil characteristics. However, when cervical stromal invasion was present, MRI was able to detect it in 75% of the cases (3 out of 4). The clinical impact of endocervical superficial invasion does not imply a modification in surgical treatment (no need for radical hysterectomy)\cite{5,33,34}, according to Bigelow et al. and Surwit et al. Regarding the type of coil used, in the literature, pelvic phased array coil is commonly referred to improve the quality of the obtained images\cite{35,36}.

Surgical staging proposed by FIGO is done in the majority of oncologic centers, as well as in our institution, by gross and frozen section examination of the hysterectomy specimen. In the literature, the reported accuracy of gross visual inspection (superficial/deep invasion), achieves values between 85% and 91%\cite{25,26,37,38}. Our results are similar as we obtained an accuracy of 93% when evaluating deep myometrial invasion.

As in the MRI evaluation GVI had lower accuracy on the evaluation of tumoral cervical extension. The obtained accuracy of 79% is in accordance with other series\cite{22–24,39}.

In our series, no overestimation occurred with evaluation of tumoral invasion. The great experience of the senior pathologists who performed GVI may be an explanation for the absence of overestimation.

In conclusion, in this cohort, a very similar accuracy level was obtained by the two different approaches in the evaluation of endometrial carcinoma invasion. MRI is an adequate method for determine the depth of myometrial invasion (\(K = 0.8333\)) and cervical extension (\(K = 0.4118\)) in endometrial carcinoma staging, and can replace GVI in those centers where pathology is not available on site. The presurgical knowledge of endometrial carcinoma invasiveness may also help to select patients that will benefit from being submitted to surgery in an oncologic center. The fact that MRI is more sophisticated and expensive method may reduce its applicability.

### References


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**Table 2.** Indexes of the accuracy of MRI for correct determination of deep myometrial and cervical invasion  

<table>
<thead>
<tr>
<th></th>
<th>Accuracy (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV(^a) (%)</th>
<th>NPV(^b) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI—Deep myometrial invasion</td>
<td>92.5</td>
<td>80.0</td>
<td>100.0</td>
<td>100.0</td>
<td>89.3</td>
</tr>
<tr>
<td>MRI—Cervical invasion</td>
<td>80.0</td>
<td>33.3</td>
<td>100.0</td>
<td>100.0</td>
<td>77.7</td>
</tr>
</tbody>
</table>

\(^a\)PPV, positive predictive value; \(^b\)NPV, negative predictive value; \(\text{MRI, magnetic resonance imaging.}\)

**Table 3.** Indexes of the accuracy of gross visual inspection for correct determination of deep myometrial and cervical invasion  

<table>
<thead>
<tr>
<th></th>
<th>Accuracy (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV(^a) (%)</th>
<th>NPV(^b) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GVI—Deep myometrial invasion</td>
<td>90.9</td>
<td>76.9</td>
<td>100.0</td>
<td>100.0</td>
<td>87.0</td>
</tr>
<tr>
<td>GVI—Cervical invasion</td>
<td>78.8</td>
<td>36.4</td>
<td>100.0</td>
<td>100.0</td>
<td>75.9</td>
</tr>
</tbody>
</table>

\(^a\)PPV, positive predictive value; \(^b\)NPV, negative predictive value; \(\text{GVI, gross visual inspection.}\)

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