A MRI scoring system for predicting endometrial vs cervical origin in patients with bulky uterine masses of indeterminate histology

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Purpose

In a small but important subset of patients with newly diagnosed uterine cancer, there is an overlap between endometrial and cervical cancer histology and routine biopsy results are inconclusive for determining the origin of the tumour. The use of specific immunohistochemical (IHC) stains like vimentin, estrogen receptors, carcinoembryonic antigen (CEA) and p16 can differentiate between these two histological entities, but in cases of high grade or undifferentiated adenocarcinomas, especially when curettage or biopsy samples are small, even specific IHC stains may fail to provide a definitive diagnosis [1,2].

Discrimination between cervical and endometrial carcinoma is of critical importance because of differences in therapeutic approach. Erroneous diagnoses may compromise patients’ prognosis [3,4]. The aim of our study was to record all MRI features of bulky uterine cancers, involving both cervix and uterine corpus and to attempt to identify those features that favour the diagnosis of endometrial or cervical cancer. Using as standard of reference final surgicopathological results or repeated tumor biopsies and IHC stains, we aimed to design a MRI scoring system, based on specific MRI features, which has the potential to predict the origin (cervix or endometrium) of large uterine cancers with indeterminate histology.
Methods and materials

Study population

Seventy-seven patients, with newly diagnosed biopsy-confirmed uterine tumours, involving both cervix and corpus on MR images were retrospectively selected to be evaluated in our study. Exclusion criteria included patients with microscopic disease, tumours located exclusively at the cervix or the endometrium and patients with sarcomas. The age of the patients was 29-83 years (mean: 57.9 years). Tumour maximal diameter on MRIs, ranged from 2.5-14cm (mean: 5.8cm).

Diagnostic biopsy or curettage was performed in all patients. Initial biopsy results were positive for endometrial cancer in 14/77 and positive for cervical cancer in 43/77 patients. In 20/77 patient initial histology was inconclusive for determining the origin of uterine tumour (cervix vs endometrium).

Final biopsy results in 58/77 patients were positive for cervical cancer and in 19/77 were positive for endometrial cancer. In 4 surgically treated patients, initial biopsy definite for endometrial cancer (no ICH used), examination of the surgical specimen revealed poorly differentiate cervical cancer. In one surgically treated patient, with pre-op biopsy consistent with poorly differentiate endocervical adenocarcinoma (no ICH used), final histology showed a high grade adenocarcinoma of endometrial origin.

MRI studies

Pelvic MRIs were performed with a 1.5 T unit with the use of a phased-array body coil.

High-resolution turbo spin-echo (TSE) T2-weighted (T2-w) sequences were obtained in the sagittal, axial and axial oblique (perpendicular to the long axis of the cervix) planes (TR/TE: 3500/90). Axial TSE T1-weighted (T1-w) (TR/TE/NSA: 400/13/1) and TSE T2-w images (TR/TE: 2000/80) were obtained from the pelvis to the renal hilum to assess lymph node status. Sagittal dynamic T1-w contrast-enhanced images (DCE-MRI) were obtained every 17 sec for a total scan duration of 3 min (TR/TE/flip angle:15/42/30°). Axial or sagittal T1-w fat-suppressed contrast-enhanced images (TR/TE: 400/14) were also performed.

All MRIs were evaluated blindly by two radiologists experienced in female pelvic imaging. Based on readers’ experience and on literature review [5-9], the following ten tumour features were selected for evaluation and recorded by each radiologist independently: tumour location, perfusion pattern (early arterial and late phase on dynamic contrast-
enhanced-DCE images), presence of a rim (complete or partial) of enhancement at the periphery of the tumour, mass within the endometrial cavity, depth of myometrial invasion #50%, distended, fluid-filled endometrial cavity, invasion of parametria, pelvic wall or pelvic organs.

In cases of disagreement a consensus was reached.

**Standard of Reference**

Final diagnosis of endometrial or cervical cancer was established with histological examination of the surgical specimen in 26/77 patients. In 36 of the remaining 51 patients who were treated conservatively, final diagnosis based on cervical biopsy or endometrial curettage; in 15/51 patients with inconclusive biopsy results, final diagnosis based on IHC stains.

**Statistical analysis**

Kappa (K) values were calculated to assess inter-rater reliability. The MRI features found by consensus from the two readers were tested for their ability to discriminate between cervical and endometrial cancer by comparing with final histology results. The sensitivity (SE), specificity (SP) and positive likelihood ratio (PLR) were calculated for every discriminant MRI parameter.

In order to assess the discriminant ability of significant MRI criteria, a score was assigned according to PLR values: for PLR ranging from 1 to 2 a score equal to 1 was assigned, for PLR ranging from 2 to 5 a score of 2 was assigned and for PLR ranging from 5 to 10 a score of 3 was assigned. Scores were positive for those MRI criteria more frequently observed with cervical cancer and negative for those more frequently observed with endometrial cancer. The final score for every patient was tested against final histology results using ROC analysis; optimal cut-off for a MRI scoring system discriminating between cervical and endometrial cancer was calculated. The optimal cut-off of the MRI scoring system was tested in cases with indeterminate initial biopsy results. Statistical significance was set at 0.05.
Results

We found seven MRI features with significantly discriminant predictive ability (p< 0.001) for cervical versus endometrial cancer. Tumor location, tumor hypervascularity on early DCE-MRI and full depth cervical stromal invasion showed the highest SE and SP values in discriminating between the two uterine primaries, with high level of agreement amongst the two radiologists. The presence of mass within the endometrial cavity was a less significant imaging feature of cervical cancer with only acceptable K values. A distended endometrial cavity, deep (>50%) myometrial invasion and presence of an enhancing rim at the periphery of the tumour had significant discriminant predictive value (p<0.001), however they were less sensitive or specific compared to the above MRI features. The highest possible likelihood ratio (PLR) was found for the assigned location (PLR=6) followed by perfusion pattern on early DCE-MRI (PLR=3).

On the basis of the PLR, a seven-feature MRI scoring system was designed to help readers predict the histology of a bulky uterine cancer. MRI scoring system values are presented in the following table:

<table>
<thead>
<tr>
<th>MRI features</th>
<th>Assigned score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor assigned cervical location</td>
<td>3</td>
</tr>
<tr>
<td>Tumor assigned uterine body location</td>
<td>-3</td>
</tr>
<tr>
<td>Hypervascularity on early arterial DCE-MRI</td>
<td>2</td>
</tr>
<tr>
<td>Hypovascularity on early arterial DCE-MRI</td>
<td>-2</td>
</tr>
<tr>
<td>*Mass in endometrial cavity</td>
<td>-2</td>
</tr>
<tr>
<td>*Retained secretions</td>
<td>2</td>
</tr>
<tr>
<td>*Myometrial invasion #50%</td>
<td>-2</td>
</tr>
<tr>
<td>*Full depth cervical stromal invasion</td>
<td>2</td>
</tr>
<tr>
<td>*Peripheral enhancing rim</td>
<td>1</td>
</tr>
</tbody>
</table>

T.A.S #4 = cervical cancer

T.A.S score <4 = endometrial cancer

*when these features are absent no MRI score is assigned
Abbreviation: TAS=Total Assigned Score

ROC analysis estimated the optimal cut-off value of the scoring imaging system regarding tumour origin. Applying a cut-off # 4 for cervical origin and < 4 for endometrial origin, the discriminative ability of the MRI scoring system had 96.6% SE, 100% SP, 100% NPV and 90.5% PPV. When the MRI scoring system was applied to all patients, 75/77 cases (97.4%) were correctly classified (Fig. 1-5). Only two cases of cervical cancer had a < 4 MRI score. In the first case (MRI score = 2, indicative of endometrial cancer) suboptimal DCE-MRI due to patient motion artifact may have been responsible for the false results. In the second patient, a MRI score equal to 3 was assigned (indicating endometrial origin) but surgicopathological examination was consistent with adenosquamous carcinoma of the cervix (Fig. 6).

When the scoring system was applied to 20 cases with poorly differentiated adenocarcinomas of unclear origin (cervix vs endometrium), all cases were correctly classified. Additionally, when the MRI scoring system applied to four surgically treated patients with erroneous pre-op initial histology for tumor origin, all patients were correctly diagnosed.

Limitations

Limitations of our study included the retrospective nature and the relatively small study population. In this study, MRI interpretation was performed only by radiologists experienced in imaging of the female pelvis. Validation of the MRI scoring system as a tool applied by general radiologists is needed. An important limitation is that in 51/77 of our study patients, IHC and not surgery was performed to define tumor origin. Immunohistochemistry is, however, the appropriate alternative method for differentiating endometrial from cervical carcinomas when surgery is not an option.
Fig. 1: 62-year-old woman, who presented with vaginal bleeding. Sagittal T2-w image shows a bulky mass involving both cervix and uterine body (arrows). Since most of the tumour mass involves the cervix, a cervical location was assigned (AS=+3). Note the presence of two small fibromas in the uterine fundus. Abbreviation: AS=assigned score
Fig. 2: Corresponding sagittal early arterial DCE-MRI of the same patient as in Fig. 1, shows a hypovascular tumour (AS=-2) within the endometrial cavity (AS=-2), involving >50% of the uterine myometrial thickness (AS=-2). No parametrical involvement was detected (not shown). Total assigned MRI score was -3, highly indicative of endometrial carcinoma. Final surgicopathological examination confirmed the diagnosis. Abbreviation: AS=assigned score

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**Fig. 3:** 77-year-old woman with vaginal bleeding. Pre-op biopsy was consistent with endometrial carcinoma. Sagittal T2-w image shows a bulky mass involving both cervix and uterine body (arrows). The bulky mass involves the cervix to a higher degree than the endometrial cavity, therefore a cervical location was assigned (AS=+3). Abbreviation: AS=Assigned score

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Fig. 4: Corresponding sagittal early arterial DCE-MRI of the same patient as in Fig. 3 shows the hypervascular tumour (AS=+2), extending within endometrial cavity (AS=-2) and involving more than 50% of total myometrial thickness (AS=-2). Retained secretions within endometrial cavity are also noted (AS=+2).

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Fig. 5: Axial T2-w image of the same patient as in Fig.3 and Fig.4 shows full cervical stromal invasion and extension of the tumor to the parametrial tissues (arrows) (AS=+2). Total assigned MRI score for this patient was +5, highly indicative of cervical cancer. Final surgicopathological examination was consistent with high grade squamous cell carcinoma of cervical origin.

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Fig. 6: 63-year-old woman with biopsy-confirmed cervical carcinoma, FIGO IB1. Early arterial DCE-MRI clearly demonstrates a hypervascular mass extending beyond the internal os (arrow). The assigned MRI score was 3, indicative of uterine carcinoma of endometrial origin. Adenosquamous carcinoma of the cervix was found on final surgicopathological examination.

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Conclusion

The proposed MRI-scoring system may potentially help radiologists standardize their reports and accurately predict tumour origin in patients with uterine tumours of indeterminate histology.
References


