Magnetic resonance imaging in assessment of myometrial invasion and lymph node metastasis in endometrial carcinoma.

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ABSTRACT
Objectives: To evaluate the percentage agreement of MRI and histopathology findings in myometrial invasion and pelvic lymph node metastasis in endometrial carcinoma.
Materials and Methods: Eighty three patients of Govt. T. D. Medical College Alappuzha, identified as clinical suspects of cancer endometrium, were subjected to radiological evaluation with magnetic resonance imaging. For histopathological evaluation, hysterectomy and pelvic lymphadenectomy biopsies were taken. The study was conducted over a period of 18 months. Diagnostic validity of MRI was assessed using histopathology as gold standard. Furthermore, the main causes of error in staging based on MRI results was also analysed.
Results: Diagnostic accuracy of MRI with T2WI, DWI and DCE in assessing the depth of myometrial invasion was 94% in present study and the diagnostic accuracy of MRI for lymph nodal staging was 92.8% in present study and could be further increased by accounting ADC values in case of smaller lymph nodes.
Conclusion: DCE and DWI plays key role and has a significant added value to conventional MRI in staging endometrial cancer. DCE and DWI has high diagnostic accuracy in differentiating between benign and malignant uterine tumors, and nodal pathology. Combination of DWI and DCE MRI rather than using either of them helps in accurately staging the endometrial cancer by overcoming the pitfalls.

Keywords: Carcinoma endometrium, Magnetic Resonance Imaging(MRI), Dynamic Contrast Enhancement(DCE), Diffusion Weighted Imaging(DWI), FIGO, TNM, Myometrial invasion(MI).

BACKGROUND
Carcinoma of the endometrium is among the most common invasive gynecologic malignancies of the female genital tract. In developing countries it is the second most common gynecological malignancy, with incidence of 5.9/100000 while the incidence in India is about 4.3/100000. Endometrial carcinoma typically presents in postmenopausal women, with a peak incidence between 55 and 69 years. Postmenopausal bleeding is the most common presenting complaint and as such accounts for an earlier detection rate of the disease. Premenopausal patients may present with intermenstrual or abnormal menstrual bleeding, or incidentally detected as part of infertility investigations.
There are several risk factors for endometrial carcinoma which result in prolonged unopposed estrogen stimulation of the endometrial lining predisposing to endometrial neoplasia. Excess estrogen may be exogeneous (unopposed estrogen therapy) or endogenous, as in patients with obesity, ovarian malfunction due to polycystic ovarian syndrome, or estrogen-secreting tumors such as granulosa-cell and theca-cell tumors of the ovary. Nulliparity also increases the risk. Association between diabetes mellitus or hypertension in endometrial cancer has not been medically proved so far. Whereas Tamoxifen, a selective estrogen-receptor modulator used in the treatment of breast cancer, has an estrogenic effect on the endometrium and increases the risk of endometrial carcinoma and uterine sarcoma. The risk of developing endometrial cancer due to tamoxifen increases if, in addition, there is obesity; the risk is also dependent on the duration of treatment. Endometrial cancer may also occur as part of a hereditary disease, including hereditary non-polyposis colorectal cancer (HNPPC), also known as Lynch syndrome II.

The initial investigation is usually ultrasound of the pelvis, with careful assessment of the endometrial thickness. If the endometrium is thickened or if abnormal vaginal bleeding persists, sampling of the endometrial lining is undertaken as an outpatient procedure using the pipelle biopsy sampling technique, or may be done in the theatre as a hysteroscopic procedure with dilatation and curettage.
Endometrial cancer arises in the glandular component of the uterine epithelium. Endometrial carcinomas fall into two major histological categories: Type 1 tumors which are well or moderately differentiated, estrogen-dependent and tend to have a good prognosis; and Type 2 which are aggressive, non-estrogen-dependent tumors such as clear cell or serous subtypes. Ninety percent of endometrial carcinomas are endometrioid adenocarcinomas and are divided into three grades from Grade 1 (well differentiated) to Grade 3 (poorly differentiated, included in the Type 2 tumors). Less common histological subtypes, accounting for approximately 7% of cases, include clear cell carcinoma, and papillary serous carcinoma. The latter two histological subtypes and Grade 3 adenocarcinoma carry a worse prognosis. Rare tumors of mesenchymal origin account for approximately 3% of cases. These include endometrial sarcomas, malignant mixed Mullerian tumors (MMMT), adenosarcomas, and leiomyosarcomas. Gestational trophoblastic tumors are very rare and arise from abnormal proliferation of trophoblastic elements in the fertilized ovum.
The tumor can grow either as a polypoid mass within the uterine cavity or as a more diffuse thickening of the endometrial lining. Invasion of the myometrium occurs by direct spread through the superficial and deep layers and can extend up to the serosal surface. Tumors that penetrate the uterine serosa may directly invade adjacent organs and may also produce seedling metastases within the peritoneal cavity. Specific histological subtypes like clear cell, and papillary serous carcinomas, are particularly prone to...
peritoneal spread. Tumor can also extend down the endocervical canal, and may invade the cervical glandular epithelium or stroma. The uterus has a rich lymphatic network and blood supply, and in advanced diseases both lymph node metastases and blood borne deposits may occur. Hematogenous spread usually affects the liver, bones and brain. Tumors in the upper part of the uterine body metastasize to the common iliac and para-aortic lymph nodes. The mid and lower uterine body and the cervix drain to parametrial, paracervical and obturator lymph nodes, and then via the iliac chains to para-aortic lymph nodes. Ingual nodes may also be involved by spread along the round ligament or by metastasis from tumors of the lower vagina. In patients with recurrent disease, the most common sites of relapse are the lymph nodes, vagina, peritoneum, and the lung.

The five-year survival rate for patients with endometrial cancer overall is relatively high compared with other gynaecologic malignancies, with a five-year survival rate of 83% as most cases are detected at an earlier stage. Prognosis depends on the age of the patient, stage of disease at presentation and the histological subtype. High-grade endometrioid carcinoma, papillary serous adenocarcinoma, clear cell, or sarcomatous histology have an increased rate of recurrence and a poorer prognosis. Other poor prognostic factors include deep myometrial invasion, cervical invasion, lymph node involvement, and a high FIGO stage of disease.

The depth of myometrial invasion is one of the most important prognostic factors due to an association with nodal metastases. In patients with no myometrial invasion and low-grade histology, the five-year survival rate is 95%; whereas in patients with tumor invasion extending beyond the outer half of myometrium or having high grade histology, the five-year survival rate is 42%. Significant predictors of poor outcome in patients with recurrent disease are multiple sites of recurrence, hematogenous, peritoneal and nodal metastases, increasing age at primary surgery, high tumor grade and early relapse.

In this schema, preoperative information regarding the depth of myometrial invasion and nodal involvement is essential to tailor the surgical approach, which warrants the need for pre-operative imaging. Modern imaging provides important tools in the preoperative assessment of endometrial cancer and helps to optimize treatment planning and the surgery to be undertaken. Without imaging the surgeon has to rely on the preoperative tumour grade, which is often inadequate, to guide operative management. Therefore the role of magnetic resonance imaging (MRI) in endometrial carcinoma is in disease staging and treatment planning. MRI has been shown to be the most valuable imaging modality in this task, compared with endovaginal ultrasound and computed tomography, because of its intrinsic contrast resolution and multiplanar capabilities. It is also useful to stratify patients into low versus intermediate to high risk groups before the surgery. More recently lymph node specific contrast agents are also emerging as useful tools in determining metastatic nodal diseases, which helps to further tailor the surgery.

AIMS AND OBJECTIVES

To evaluate the percentage agreement of MRI and histopathology findings in myometrial invasion and pelvic lymph node metastasis in endometrial carcinoma.

REVIEW OF LITERATURE

UTERINE ANATOMY

- The upper two-thirds of the uterus above the level of the internal cervical os is referred to as the uterine corpus.
- The fallopian tubes and the round ligaments enter the uterus at the upper and outer cornu of the pear-shaped organ.
- The portion of the uterus that is above a line connecting the tubo-uterine orifices is referred to as the uterine fundus.
- The lower third of the uterus is called the lower uterine segment and the cervix

REGIONAL LYMPH NODES

The regional lymph nodes are paired (right and left), and each of the paired sites must be evaluated to determine stage and prognosis and to help direct therapy.

The regional nodes are as follows:
- Parametrial
- Obturator
- Internal iliac (hypogastric)
REGIONAL LYMPH NODES INVOLVED IN UTERINE CARCINOMA[1]

METASTATIC SITES
The vagina and lungs are the common metastatic sites. Intra-abdominal metastases to abdominal or pelvic peritoneal surfaces or the omentum are seen particularly with serous and clear cell tumors.

IMAGING
Magnetic resonance (MR) imaging currently is the preferred modality for local staging of endometrial cancer. Contrast-enhanced computed tomography (CT) scans do not have sufficient soft-tissue resolution to identify the tumor in the uterine corpus or to assess the depth of myometrial invasion.

Assessment of lymph node metastases on cross-sectional imaging is based on lymph node size, with nodes >1 cm in the short axial dimension considered abnormal. CT and MR imaging have been shown to perform equally well in assessing adenopathy. However, because there may be false positive causes of enlarged nodes from benign disease, positron emission tomography (PET)/CT is considered to be better in assessing lymph node metastases. Metabolically active lymph nodes of any size on PET/CT are considered metastatic. PET/CT is considered superior to other modalities in assessing for extra pelvic disease and bone metastases.[1]

CLINICAL CLASSIFICATION
TNM classification applies only to carcinoma and carcinosarcoma (malignant mixed mesodermal tumors). There should be histologic verification and grading of the tumor. Tumor involvement of the cervical stroma is prognostically important and affects staging (T 2). The new staging system no longer recognizes endocervical mucosal glandular involvement (formerly stage IIA ), because this does not affect prognosis. The location of the tumor and the depth of tumor invasion into the myometrium are of prognostic significance and should be included in the pathology report.

In category T1, the tumor is confined to the uterus. Category T1a involves <50% and category T1b involves >50% of the myometrium, which may be assessed on MR T1 weighted dynamic images. DWI(diffusion-weighted imaging) can also be used to assess the depth of myometrial invasion and also has shown promising results in assessing the depth of endometrial invasion.

In category T2, the tumor invades the cervix and may be seen on contrast-enhanced T1-weighted sequences.

In category T3a, the tumor involves the serosa or adnexa, whereas in T3b there is vaginal and parametrial involvement; this may be evaluated on contrast-enhanced T1 - and T2-weighted MR imaging sequences. The prognostic importance of malignant cells in peritoneal cytology samples has been debated and 2008 FIGO staging system stopped using peritoneal cytology for staging (formerly T3a, FIGO stage IIIA).

In category T4, the tumor infiltrates the bladder and rectal mucosa.

Regional nodal metastases are considered to be category N1 and can be assessed easily on CT or MR imaging. This size criterion for abnormality is taken as >1 cm in the short axial dimension.
REPORTING ANATOMIC STAGE OF TUMOR
Reports should describe the size and extent of the tumor and whether it involves the inner or outer half of the myometrium. Reporting of cervical and vaginal involvement is crucial, as treatment differs in these cases. It is also important to report extension through the serosa of the uterus or involvement of the ovaries and adjacent organs.[1]

IMAGING REPORT FORMAT
1. Primary tumor
   a. Size
2. Local extent
   a. Involvement of <50% or > 50% of the myometrium
   b. Involvement of the vagina and cervix
   c. Extra serosal extension
   d. Involvement of the ovaries and adjacent organs
3. Regional and distant lymph node involvement and extra pelvic disease

POTENTIAL ADVANTAGES OF PREOPERATIVE IMAGING:
1. Evaluation of the depth of myometrial invasion to predict the likelihood of advanced disease (ie, the incidence of lymph node metastasis is 2.5% in stage IA versus 15% to 45% in stage IB).
2. Diagnosis of gross cervical invasion, which requires preoperative radiation therapy or a different treatment plan (ie, radical hysterectomy instead of total abdominal hysterectomy).
3. Identification of suspicious lymph nodes to guide lymph node sampling at the time of surgery.
4. Detection of advanced disease.

FACTORS RECOMMENDED FOR TARGETED CLINICAL CARE
FIGO Stage
FIGO stage which parallels the AJCC stage, is used to assess the prognosis, and is used worldwide for documenting the patient status and outcome.

Grade
The aggressiveness of the tumor is related to the degree of histological differentiation of the glandular component.

Depth of Myometrial Invasion
Depth of myometrial invasion is an important prognostic factor and must be documented. Along with tumor grade, it can predict the probability of nodal metastasis and treatment outcome. Preoperative endometrial sampling may not correlate accurately with final tumor grade and depth of myometrial invasion.

Lymphovascular Space Invasion
The presence or absence of lymphovascular space involvement or invasion (LVI) of the myometrium is important. If present, LVI increases the probability of metastatic involvement of the regional lymph nodes. LVI should be recorded in the pathology report as a present, not identified, or indeterminate.

Peritoneal Cytology
The prognostic value of finding tumor cells in peritoneal “washings” remains controversial and requires further study. The newly adopted staging system[4] discontinued the use of positive cytology to alter the stage.

Estrogen and Progesterone Receptor Status
Estrogen and progesterone receptor status should be recorded if clinically appropriate, for future use in treatment with chemotherapy.

Tumor Suppressor and Oncogene Expression
Molecular profiling is becoming increasingly available, but its exact clinical utility is not yet known.

Nodal Disease
The presence or absence of metastatic disease in the regional lymph nodes is the most important prognostic factor in carcinomas clinically confined to the uterus. AJCC advocates the use of surgical/pathological assessment of nodal status whenever possible. The status of pelvic and para-aortic lymph nodes, if known, is an important predictor of outcome. The number of examined and positive nodes should be recorded if known.

Histopathologic Type
Serous and clear cell adenocarcinomas have a higher incidence of extrauterine disease at diagnosis than endometrioid adenocarcinomas. The risk of extraterine disease does not correlate with the depth of myometrial invasion in these histologic types, because nodal or intraperitoneal metastases may be found even in the absence of myometrial invasion. For these reasons, they have been classified as grade 3 tumors. For example-Endometrial intraepithelial carcinoma (EIC ) should be considered an invasive T 1 cancer, as it has been associated with metastatic disease and is not a “precancerous” lesion. Up to two-thirds of serous EIC s may be associated with extrauterine disease.[1]

Percentage of Nonendometrioid Cell Type in Mixed-Histology Tumors
The significance of the percentage of non-endometrioid cell types in mixed-histology tumors is unclear; however, this information may become important with future analytical studies.

Omentectomy Performed
Omentectomy should be considered for higher-grade lesions.

Morcellation
Intra-abdominal morcellation of a potentially cancerous organ should be avoided. However, with the increased use of minimally invasive techniques involving morcellation of the uterine specimen or subtotal removal, specimen integrity should be reported as morcellated versus intact and total (including the cervix) versus subtotal (supracervical) hysterectomy specimen.

**DEFINITIONS OF AJCC TNM [1]**

The AJCC recently established guidelines that will be used to evaluate statistical prediction models to grant endorsement for clinical use.[5]

The 2 systems used for staging endometrial cancer, the FIGO (International Federation of Gynecology and Obstetrics) system and the American Joint Committee on Cancer TNM staging system are basically the same. They both stage (classify) this cancer based on 3 factors:

- The extent (size) of the tumor (T): How far has the cancer grown into the uterus? Has the cancer reached nearby structures or organs?
- The spread to nearby lymph nodes (N): Has the cancer spread to the regional lymph nodes?
- The spread (metastasis) to distant sites (M): Has the cancer spread to distant lymph nodes or distant organs?

### T STAGING OF ENDOMETRIAL CANCER[1]

<table>
<thead>
<tr>
<th>T Category</th>
<th>FIGO Stage</th>
<th>T Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>Tumor confined to the corpus uteri, including endocervical glandular involvement</td>
<td></td>
</tr>
<tr>
<td>T1a</td>
<td>IA</td>
<td>Tumor limited to the endometrium or invading less than half the myometrium</td>
</tr>
<tr>
<td>T1b</td>
<td>IB</td>
<td>Tumor invading one half or more of the myometrium</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>Tumor invading the stromal connective tissue of the cervix but not extending beyond the uterus. Does NOT include endocervical glandular involvement.</td>
</tr>
<tr>
<td>T3</td>
<td>III</td>
<td>Tumor involving serosa, adnexa, vagina, or parametrium</td>
</tr>
<tr>
<td>T3a</td>
<td>IIIA</td>
<td>Tumor involving the serosa and/or adnexa (direct extension or metastasis)</td>
</tr>
<tr>
<td>T3b</td>
<td>IIIB</td>
<td>Vaginal involvement (direct extension or metastasis) or parametrical involvement</td>
</tr>
<tr>
<td>T4</td>
<td>IVA</td>
<td>Tumor invading the bladder mucosa and/or bowel mucosa (bullous edema is not sufficient to classify a tumor as T4)</td>
</tr>
</tbody>
</table>

### N STAGING OF ENDOMETRIAL CANCER[1]

<table>
<thead>
<tr>
<th>N Category</th>
<th>FIGO Stage</th>
<th>N Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
<td></td>
</tr>
<tr>
<td>N0(i=)</td>
<td>Isolated tumor cells in regional lymph node(s) no greater than 0.2 mm</td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>IIBC1</td>
<td>Regional lymph node metastasis to pelvis lymph nodes</td>
</tr>
<tr>
<td>N1mi</td>
<td>IIBC1</td>
<td>Regional lymph node metastasis (greater than 0.2 mm but not greater than 2.0 mm in diameter) to pelvic lymph nodes</td>
</tr>
<tr>
<td>N1a</td>
<td>IIBC1</td>
<td>Regional lymph node metastasis (greater than 2.0 mm in diameter) to pelvic lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>IIBC2</td>
<td>Regional lymph node metastasis to para-aortic lymph nodes, with or without positive pelvic lymph nodes</td>
</tr>
<tr>
<td>N2mi</td>
<td>IIBC2</td>
<td>Regional lymph node metastasis (greater than 0.2 mm but not greater than 2.0 mm in diameter) to para-aortic lymph nodes, with or without positive pelvic lymph nodes</td>
</tr>
<tr>
<td>N2a</td>
<td>IIBC2</td>
<td>Regional lymph node metastasis (greater than 2.0 mm in diameter) to para-aortic lymph nodes, with or without positive pelvic lymph nodes</td>
</tr>
</tbody>
</table>

Suffix (i=) is added to the N category when metastasis is identified only by sentinel lymph node biopsy.
**Definition of Distant Metastasis (M)**

<table>
<thead>
<tr>
<th>M Category</th>
<th>FIGO Stage</th>
<th>M Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td></td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>IVB</td>
<td>Distant metastasis (includes metastasis to inguinal lymph nodes, intraperitoneal disease, lung, liver, or bone). (It excludes metastasis to pelvic or para-aortic lymph nodes, vagina, uterine serosa, or adnexa).</td>
</tr>
</tbody>
</table>

**M Staging of Endometrial Cancer[1]**

**AJCC Prognostic Stage Groups**

<table>
<thead>
<tr>
<th>When T is...</th>
<th>And N is...</th>
<th>And M is...</th>
<th>Then the stage group is...</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>N0</td>
<td>M0</td>
<td>I</td>
</tr>
<tr>
<td>T1a</td>
<td>N0</td>
<td>M0</td>
<td>IA</td>
</tr>
<tr>
<td>T1b</td>
<td>N0</td>
<td>M0</td>
<td>IB</td>
</tr>
<tr>
<td>T2</td>
<td>N0</td>
<td>M0</td>
<td>II</td>
</tr>
<tr>
<td>T3</td>
<td>N0</td>
<td>M0</td>
<td>III</td>
</tr>
<tr>
<td>T3a</td>
<td>N0</td>
<td>M0</td>
<td>IIIA</td>
</tr>
<tr>
<td>T3b</td>
<td>N0</td>
<td>M0</td>
<td>IIIB</td>
</tr>
<tr>
<td>T1-T3</td>
<td>N1/N1mi/N1a</td>
<td>M0</td>
<td>IIIC1</td>
</tr>
<tr>
<td>T1-T3</td>
<td>N2/N2mi/N2a</td>
<td>M0</td>
<td>IIIC2</td>
</tr>
<tr>
<td>T4</td>
<td>Any N</td>
<td>M0</td>
<td>IVA</td>
</tr>
<tr>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
<td>IVB</td>
</tr>
</tbody>
</table>

**Histologic Grade (G)**

<table>
<thead>
<tr>
<th>G</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>GX</td>
<td>Grade cannot be assessed</td>
</tr>
<tr>
<td>G1</td>
<td>Well differentiated</td>
</tr>
<tr>
<td>G2</td>
<td>Moderately differentiated</td>
</tr>
<tr>
<td>G3</td>
<td>Poorly differentiated or undifferentiated</td>
</tr>
</tbody>
</table>

Carcinoma of the corpus uteri should be grouped according to the degree of differentiation of the endometrioid adenocarcinoma as follows:

<table>
<thead>
<tr>
<th>G</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>5% or less of a nonsquamous or nonmorular solid growth pattern</td>
</tr>
<tr>
<td>G2</td>
<td>6-50% of a nonsquamous or nonmorular solid growth pattern</td>
</tr>
<tr>
<td>G3</td>
<td>More than 50% of a nonsquamous or nonmorular solid growth pattern. Papillary serous, clear cell, and carcinosarcoma are considered high grade.</td>
</tr>
</tbody>
</table>
NOTES ON PATHOLOGICAL GRADING
1. Notable nuclear atypia exceeding that which is routinely expected for the architectural grade increases the tumor grade by 1 (i.e., 1 to 2 and 2 to 3).
2. Serous, clear cell and mixed mesodermal tumors are high risk and considered grade 3.
3. Adenocarcinomas with benign squamous elements (squamous metaplasia) are graded according to the nuclear grade of the glandular component.[1]

HISTOPATHOLOGIC TYPE

- Endometrioid adenocarcinoma, not otherwise characterized
- Endometrioid adenocarcinoma, variant (specify)
- Mucinous adenocarcinoma
- Serous adenocarcinoma
- Clear cell adenocarcinoma
- Mixed carcinoma (specify types and percentages)
- Squamous cell carcinoma
- Transitional cell carcinoma
- Small cell carcinoma
- Undifferentiated carcinoma
- Carcinosarcoma

T1a is a tumor limited to the endometrium or invading less than half the myometrium[1].
T1b is a tumor invading one half or more of the myometrium.[1]

T2 is a tumor invading the stromal connective tissue of the cervix but not extending beyond the uterus. It does not include endocervical glandular involvement.[1]
T3a is a tumor involving the serosa and/or adnexa (direct extension or metastasis). [1]
T3b is vaginal involvement (direct extension or metastasis) or parametrial involvement.

T4 is a tumor invading the bladder mucosa and/or bowel mucosa (bullous edema is not sufficient to classify a tumor as T4)[1]

ROLE OF MRI IN THE DIAGNOSTIC WORK-UP OF ENDOMETRIAL CANCER
According to the American College of Radiology (ACR) appropriateness criteria “MRI should be the preferred imaging modality for treatment planning, when available”, as it allows the best overall assessment of the disease [6].
The National Comprehensive Cancer Network (NCCN) guidelines advise MRI when the cervical invasion is suspected but also in pre-treatment evaluation of type II endometrial cancer [7]. The European Society of Urogenital Radiology guidelines recommends MRI in high and intermediate-risk cancers, in suspected advanced disease, and before lymph node sampling [8].
In 2015 a multidisciplinary European expert consensus meeting on endometrial cancer advised MR imaging in apparent stage I endometrial cancer to assess the depth of myometrial invasion when tailored lymph node dissection is performed. However, alternatively, expert ultrasound (US) and/or intraoperative pathological exams are other options [9]. Patients can be divided into three risk categories based upon histopathological tumor type and grade and depth of myometrial invasion [10].

There is increasing evidence that when findings of staging MRI and hysteroscopic biopsy are combined, women at high risk of lymph node metastases can be identified preoperatively [10-13]. In one study this yielded an accuracy of 81 % and was superior to combined transvaginal sonography (TVS) and hysteroscopic biopsy [13]. Another central preoperative finding in MRI is a cervical stromal invasion. This requires modification of the surgery technique including radical hysterectomy and pelvic and abdominal lymphadenectomy. Combined radiotherapy treatment is performed in most centers [9, 11].

MRI findings also contribute to triaging and guiding neoadjuvant therapy in advanced endometrial cancer in multidisciplinary consensus conferences[9,11].

**MRI PROTOCOL [28].**

### KEY POINTS IN MR STAGING OF ENDOMETRIAL CANCER

- Endometrial cancer is typically mildly hyperintense on T2-WI compared to normal myometrium [14].
- Subtype II tends to be inhomogeneous morphology with areas of hemorrhage and necrosis and is commonly diagnosed with deep myometrial invasion.
- Most tumors arise from the fundus and display exophytic expansion. Diffuse infiltrative growth is rarely found and which is characterized by diffuse myometrial thickening.
- Evaluation of the uterus at least in 2 planes using T2WI (maximal 4 mm slice thickness) along the uterine axis is mandatory to define the depth of myometrial invasion [9].
- The multiparametric approach of combining T2WI, DWI, and dynamic Gd MRI will render the most comprehensive approach to assess local tumor spread. It is most useful if radiologist supervision when images are obtained is not feasible or in less experienced readers.
- Cervical invasion is assumed when there is thinning or focal disruption of the hypointense signal of the cervical stroma and its continuity with the tumor. Stromal invasion, particularly when subtle is best identified in a plane perpendicular to the cervical canal.
- Invasion of the pelvic wall is suggested when the distance between the tumor and the pelvic wall including internal obturator muscle, levator ani, piriformis muscle, or iliac vessels is less than 3 mm.
- Rectum or bladder wall invasion is best evaluated in the sagittal plane. Preservation of the fat plane between tumor and bladder or rectum allows reliable exclusion of stage IVA.
- In aggressive tumor histologies (type II) careful assessment of the abdomen and pelvis for peritoneal deposits is warranted.[28]

### KEY POINTS IN LYMPH NODE IMAGING IN ENDOMETRIAL CANCER

- Regional nodes are pelvic and para-aortic lymph nodes. The latter may be the first manifestation of lymphatic spread.
- The rate of lymph node metastases in low-risk cancers is very low (2.4 %). It rises with increasing risk categories to 9 % in intermediate and 24 % in high risk categories [9, 11].
- Lymph nodes are easiest to depict on DWI due to their high SI on the high b value image.
- As DWI is limited in predicting lymph node metastases classical morphological criteria have to be combined for characterization. These include the short-axis diameter of pelvic lymph nodes with > 8 mm and abdominal lymph nodes > 10 mm. However, smaller lymph nodes with low ADC, irregular contours, necrosis, and clusters of lymph nodes may also be called suspicious of metastases [15].

**PITFALLS, CHALLENGES, AND HOW TO OVERCOME THESE**
A tumor involving more than half of the myometrial thickness is staged as IB. The area of the uterine cornua is physiologically thinner than the normal myometrium. Hence, particularly, when there is symmetrical invasion at this location it should not be overstaged[28].

In atrophic uteri and tumors isointense to myometrium, problem-solving modalities complementary to T2WI should be performed. For example- In DWI the angulation along the uterus should be identical to the T2W sequence. High-resolution 3D T1 WI at about 2–2.5 min after IV contrast media application may be best able to solve this problem [9].

If the depth of myometrial invasion is equivocal on T2WI and DWI, complementary GDT1 WI should be applied [16]

Thinned out endometrium due to tumor distension of the uterine cavity can make myometrial assessment challenging [17]. Though symmetry and smooth contours favor stage IA.

In endometrial cancer with coexisting adenomyosis or atypical uterine leiomyomas, the complementary use of both DWI and Gd is advised to assess the depth of myometrial invasion. Of note, both adenomyosis and some leiomyomas may show restricted diffusion, and leiomyomas may also be hypervascular. [28]

The double angulation technique provides a true orthogonal view of the uterus and may improve the assessment of myometrial invasion in rotated or tilted uteri. Thus, the problem of volume averaging artifacts can be reduced [18]

In equivocal lymph nodes, morphologic criteria should be combined with functional information. That is, enhancement pattern or ADC similar to uterine cancer support the diagnosis of nodal metastasis [28]

To reduce pitfalls in interpretation in DWI the findings should always be correlated with T2WI. The optimal high b value varies from field strength and vendors. It should be 800 mm/s [19] or more and is optimal when the fluid in the urinary bladder appears dark.[28]

**CLINICALLY CHALLENGING CONSTELLATIONS AND HOW TO AID WITH IMAGING**

- **Synchronous endometrial cancer and adnexal masses**

  Estrogen stimulation of the endometrium is a major risk factor for type I endometrial cancer. Thus hormone- active ovarian tumors and endometrial hyperplasia or endometrial cancer may be detected simultaneously. Coexisting endometrial cancer is reported in granulosa cell tumors and thecomas in 3–25 % of cases [20]. In imaging, granulosa cell tumors display a wide range from solid heterogeneous to multicystic masses. In contrast, thecomas display typical imaging features of well-delineated solid masses with low SI in T2WI MRI allows a specific diagnosis [21].

  More challenging is the constellation of endometrial cancer and a concomitant neoplastic ovarian mass. This may represent an independent ovarian neoplasm or metastases from the endometrial cancer. In endometrioid cancers, synchronous ovarian cancers are more likely to occur in premenopausal age and are often microscopic. The rare clear cell ovarian cancer which typically presents as a cystic mass with solid nodules protruding into the lesion may also be associated with endometrial cancer [22].

  In general, metastases to the ovaries seem more likely in type II endometrial cancer [23]. Furthermore, metastases from endometrial cancer rather than a second primary of the ovaries should be suspected if there is bilateral ovarian involvement or if the ovarian mass is small or if multi-nodularity is imaged in the ovaries [24]

- **Uterine cancer of unknown origin, endometrial or cervical cancer**

  Usually before the MRI staging, the origin of a uterine malignancy is known, based upon the clinical assessment and/or obtained histology. However, in a small subset of patients, e.g. one institution reported 3.2 %, the epicentre remains uncertain [25].

  At histology and even immunohistochemically the differentiation of endometrial from endocervical carcinoma may become challenging [26]. In this constellation, Radiology can assist in defining the origin by analyzing imaging features of the tumor and its local patterns of growth. Clinically, this information is pivotal as treatment regimens differ completely. In one study differentiation was feasible in 85 % (45/48) of cases [27].

  Features favoring endometrial cancer over the cervix are: the epicenter of the mass is in the endometrial cavity rather than in the cervix, depiction of the tumor growing within the endometrial cavity or hypovascularity in arterial phase in a small sized tumor [26]. However, some small sized cancers or type II cancers or sarcoma may be hypervascular, but the latter tends to be more heterogeneous. Whereas central necrosis, bladder invasion or ureterovesical fistulation favor the diagnosis of cervical cancer [28].

  In 2009, the European Society of Urogenital Radiology (ESUR) published guidelines for the staging of endometrial cancer (EC). The new guidelines recognized magnetic resonance imaging (MRI) as the imaging modality of choice for evaluating disease extent in patients with newly diagnosed EC [29].

  More recently, the European Society for Medical Oncology (ESMO) recommended that the initial surgical treatment of patients with EC should be tailored based on the risk of lymph node metastases, addressing the ongoing controversy regarding the role of lymphadenectomy [30–32].

  The major clinical challenge in the initial management of EC is to distinguish patients who are at intermediate to high risk of lymph node metastases from those at low risk to avoid over-treatment. The ESMO guidelines advise against lymphadenectomy in low-risk patients, i.e. grade 1 or 2 endometrioid adenocarcinomas without deep myometrial invasion (MI) [30,31]. In contrast, lymphadenectomy is suggested or recommended for intermediate and high-risk groups, respectively. Additionally, while further studies are needed, sentinel lymph node (SLN) sampling is now recognized as a potential alternative to lymphadenectomy [33].

  MRI can accurately assess the depth of MI and, thus, it is useful to stratify patients into low versus intermediate to high-risk groups before the surgery. Until recently, a combination of T2-weighted (T2WI) and dynamic contrast-enhanced imaging (DCE-MRI) was accepted as the best approach for local staging of EC [34,35]. However recent evidence suggests that diffusion-weighted imaging (DWI) also improves the evaluation of MI. As a result, DWI is now routinely used as an adjunct to T2WI and DCE-MRI [36–41]. Hence, the value of a tailored MR imaging protocol and a standardized imaging report is emphasized.[28]

  **Role of DCE-MRI**
Multiple studies have compared the performance of combined DCE-MRI + T2WI versus T2WI alone to stage EC, focusing in particular on the depth of myometrial invasion (MI) [36,37,39-51]. A meta-analysis demonstrated that DCE-MRI had similar sensitivity to T2WI but was more specific for the detection of deep MI [52]. On DCE-MRI, MI was best depicted during the equilibrium phase (2 min 30 seconds after iv contrast injection) [53,54]. DCE-MRI allows determining the presence of uninterrupted enhancement of the subendometrial zone which is best seen approximately 35–40 seconds following contrast injection. This information is useful when fertility-sparing management is being considered because it helps to exclude any MI, a key finding to confirm patient eligibility for conservative management [55]. Moreover, delayed DCE-MRI images (4–5 min after the injection) are optimal for the detection of cervical stromal invasion (CSI). [28]

Role of DWI

Multiple studies have demonstrated the added value of DWI for EC staging, particularly for assessing the depth of MI [36,37,39-41,44-48,51,55-59]. DWI is particularly useful in patients who cannot receive an intravenous injection of gadolinium-based contrast agents or have tumors that are isointense or hyperintense to the myometrium on contrast-enhanced images [44,14]. DWI is also useful in evaluating the depth of MI in the setting of concurrent adenomyosis [41]. The ESUR panel recommended including DWI to stage EC; at a minimum, the acquisition should include an axial oblique plane with the same orientation as axial oblique T2WI (i.e. perpendicular to the long axis of the uterus). The ESUR panel also endorsed the National Cancer Institute and prior ESUR consensus recommendations that advise a minimum of two b values with an optimal high b value of 800 to 1000 s/mm2 [60,61]. Several recent studies have compared DWI and DCE-MRI for the assessment of MI. Some found DWI to be superior to DCE-MRI; for example, Takeuchi et al. reported that DWI had an accuracy of 94% while DCE-MRI had an accuracy of 88% for detecting deep MI[41,44,45,14]. Other studies found no difference in the accuracy between the two techniques [62]. A meta-analysis by Andreano et al. reported no significant difference in the sensitivity or specificity between DWI and DCE-MRI for diagnosing deep MI [38]. A more recent and larger meta-analysis by Deng et al. confirmed the similar diagnostic performance of DWI to DCE-MRI; however, they also found that combined T2WI + DWI was superior to either DWI or DCE-MRI alone [63].

INTERPRETATION

FIGO MRI stage IA/IB

Stage IA is diagnosed if the tumor invades less than 50% of the myometrial thickness whereas stage IB is present if the tumor involves 50% or more of the myometrial thickness [64]. The depth of MI is best measured on the axial oblique images acquired perpendicular to the endometrial cavity. First, a line is drawn parallel to the presumed inner edge of the myometrium. Then, two lines are drawn: one measuring the entire thickness of the myometrium and the other measuring the maximum tumor extension into the myometrium. The ratio of the two lengths corresponds to the depth of MI [65]. The assessment of the depth of MI may be a challenge if a large endometrial tumor distends and thins out the myometrium or if an endometrial tumor is relatively isointense to myometrium on T2WI or if a tumor involves a cornu of the uterus where myometrium is physiologically thinner than elsewhere in the uterus, or if the uterine anatomy is distorted by leiomyomas and/or adenomyosis, under these circumstances DCE-MRI and DWI may be of particular value to improve the delineation of tumor margins and to avoid the overestimation of tumor extent. [28]

Schematic diagram of myometrial invasion [29].

FIGO MRI stage II

Cervical stroma invasion (CSI) is best assessed by evaluating both the sagittal and axial oblique planes that are acquired parallel and perpendicular to the long axis of the cervix, respectively. CSI is diagnosed when intermediate-SI tumor disrupts low-SI fibrous cervical stroma (CS) on T2WI. On DCE-MRI, CSI is indicated when the normal enhancement of CS is disrupted by a
hypoenhancing tumor, best seen on delayed phase images (4–5 min). On DWI, CSI is suspected when a tumor having high SI on high b value DWI and low SI on the apparent diffusion coefficient (ADC) map disrupts low-SI CS. [28]

FIGO MRI stage III—
Stage IIIA tumors invade the uterine serosa. They appear as intermediate-to-high-SI lesions that disrupt the normally smooth outer contour of the uterus on T2WI. One should be careful not to over stage IIIA when the tumor is isointense to the myometrium on T2WI. Contrast-enhanced imaging and DWI can improve the delineation of tumor margins and facilitate MR staging. Stage IIIA also includes direct tumor spread to the adnexa or ovarian metastases.
Stage IIIB tumors involve the parametria or the vagina by either direct invasion or metastatic spread. DWI is particularly useful for detecting small tumor deposits in the cervix and/or vagina. [28]
Stage IIIC disease is characterized by the presence of lymph node metastases and is subdivided based on pelvic (stage IIIC1) and/or para-aortic (stage IIIC2) lymph node involvement. The risk factors for lymph node metastases include the presence of high-risk histologic subtypes (grade 3 endometrioid adenocarcinoma and non endometrioid histologic types, i.e. carcinosarcoma, serous carcinoma or clear cell carcinoma), lymphovascular space invasion, deep MI, and CSI [66,67].
MRI has low sensitivity for the detection of lymph node metastases [68]. The assessment is largely based on size criteria where a short-axis diameter of greater than 8 mm in pelvic nodes and 10 mm in para-aortic nodes is taken to indicate tumoral involvement [68]. Other morphological features including round shape, spiculated margins, heterogeneous SI, SI similar to that of the primary tumor, or the presence of necrosis can be used to suggest the involvement in smaller nodes [44]. DWI aids in the detection of lymph nodes owing to their high SI on high b value images. However, there is a significant overlap between the ADC values of benign and malignant nodes and therefore the technique is currently used only as an adjunct to T2WI [69–73].

FIGO MRI stage IV—
Stage IV disease manifests with direct invasion of the bladder or rectal mucosa (stage IVA) or distant metastases (stage IVB). Preserved fat planes between the tumor and the bladder or rectum exclude stage IVA with high accuracy, alleviating the need for cystoscopy or rectosigmoidoscopy.

FIGO assessment[29]

**ROLE OF MRI IN INITIAL CLINICAL DECISION-MAKING**
A structured MRI reporting technique improves the report quality and facilitates the communication of clinically relevant information to a referring physician [61,74–79]
ROLE OF MRI IN THE SELECTION OF PATIENTS BEFORE FERTILITY-SPARING THERAPY

Approximately 5% of women who are diagnosed with EC fall under the age of 40 years [80]. If a patient is of childbearing age, desires fertility preservation, and has endometrium-confined grade 1 endometrioid adenocarcinoma or premalignant conditions (for example, atypical hyperplasia), conservative medical treatment with progestins (administered orally or via an intrauterine device) may be an option. Fertility-sparing management is controversial in patients with Lynch syndrome since their disease is due to genetic predisposition and may be less responsive to progestins [81]. In addition, there is evidence that patients with BMI greater than 25 kg/m² before or after progestogen treatment have a worse response to treatment and have a higher recurrence rate [82]. Thus MRI is useful before initiating conservative management to confirm that the disease is confined to the endometrium.

Recommended MR imaging algorithm for patients of childbearing age who are being considered for fertility preservation [29].

ROLE OF MRI FOR INITIAL TREATMENT PLANNING

The standard surgical procedures that simultaneously stage and treat EC include total hysterectomy, bilateral salpingo-oophorectomy with peritoneal washings, and pelvic plus para-aortic lymph node dissection. However, most patients present with FIGO stage I disease and are at low risk for lymph node metastases. The clinical benefit of lymphadenectomy in early-stage EC is controversial. Lymphadenectomy allows complete surgical staging and facilitates adjuvant treatment selection, potentially reducing the morbidity of unnecessary radiation therapy. However, lymphadenectomy carries a 7–10% risk of lymphocele development and a 23% risk of lower extremity lymphedema [82].

Several recent large prospective trials showed no survival benefit after lymphadenectomy in patients with early-stage grade 1 and 2 endometrioid adenocarcinoma [83-86]. Therefore, in patients with clinical stage I disease, the need for lymphadenectomy may be determined based on the presence of risk factors that increase the likelihood of lymph node metastases and subsequent recurrence [86-89].

The ESUR endorsed the ESMO recommendations to stratify stage I EC into four risk categories [30,32]. Accordingly, lymphadenectomy is not recommended in the low-risk group, i.e. stage I grade 1 or 2 endometrioid adenocarcinoma with less than 50% MI [30,32]. Lymphadenectomy is suggested or recommended for all other patients with newly diagnosed EC. In this schema, preoperative information regarding the depth of MI and histologic subtype is essential to tailor the surgical approach. MRI can assess the depth of MI, while histologic type and grade are determined by endometrial sampling [90]. Thus MRI protocol should be tailored according to the tumor histology and grade, patient preferences about fertility preservation.

Generally patients with grade 3 endometrioid adenocarcinoma and non-endometrioid histologies (carcinosarcoma, serous carcinoma, or clear cell carcinoma) are at high risk of extra-uterine spread including lymph node metastases. In such high risk groups, assessment for MI or CSI with MRI is less important, while the detection of extra-uterine disease is critical for treatment planning and assessment of DCE-MRI through the entire abdomen and pelvis should be performed; contrast-enhanced imaging is recommended but DCE-MRI is not required. Whereas in patients with grade 1 or 2 endometrioid adenocarcinoma, MRI should focus on evaluating the depth of MI and the presence of CSI. If image acquisition is unsupervised by the radiologist, DWI and contrast-enhanced images are recommended to assess MI and CSI. If image acquisition is supervised, DCE-MRI may only be necessary as an adjunct to DWI in challenging cases. In patients of childbearing age who desire fertility preservation and have grade 1 endometrioid cancer, DCE-MRI should be added to T2WI and DWI because the presence of intact subendometrial enhancement is useful to confirm an endometrium-confined disease.
Recommended MR imaging algorithm for newly detected endometrial cancer[29]

ASSESSMENT OF THE DEPTH OF MYOMETRIAL INVASION (MI) IN CHALLENGING CASES

Axial-oblique T2WI (a) and fused axial oblique T2-DWI (b) show a large tumor distending the endometrial cavity (white arrows) and compressing the myometrium; a continuous low signal intensity junctional zone is seen on both sets of images. (c) A smooth uninterrupted band of early sub endometrial enhancement on DCE-MRI helps to exclude myometrial invasion (arrows)[29]

Axial oblique T2WI (a) shows a large endometrial mass involving the right cornu of the uterus (white arrow). The tumor (black arrow) is isointense to the myometrium making it difficult to detect its margins. On T2WI, the tumor possibly extends to and abuts uterine serosa (white arrow). Contrast-enhanced T1WI (b) and fused axial T2WI-DWI (c) improve the delineation of tumor margins and show tumor extension into the outer half of the myometrium but no involvement of the uterine serosa consistent with FIGO IB disease (white arrow)[29]
TREATMENT SELECTION
Once a diagnosis of endometrial cancer has been established, the treatment of choice is total hysterectomy with bilateral salpingo-oophorectomy and surgical staging in the majority of cases. Lymph node status assessment is required for accurate staging and treatment planning. The detection of lymph node metastases in surgically staged patients varies between 8% and 33% depending on the quality of node dissection, pathologic assessment protocols, histologic subtype, and the clinical stage[110-112]. Increasing lymph node involvement is associated with the depth of myometrial invasion and the histologic grade of the tumor. The incidence of nodal metastases in patients with less than and greater than 50% myometrial invasion was 5% and 18%, respectively[110,113]. Knowledge of lymph node status assists in deciding adjuvant treatment and in radiotherapy planning. A systematic pelvic and para-aortic lymphadenectomy is associated with increased morbidity, more so in combination with radiotherapy when the incidence of serious complications can be up to 26%[114,115]. Thus, routine systematic pelvic and para-aortic lymphadenectomy for staging purposes is not recommended.12[116].

Staging lymphadenectomy can be avoided in endometrioid adenocarcinoma histology where the FIGO grade is 1 or 2 and the tumor is limited to the inner half of the myometrium, the cervical stroma is not involved and more recently, these cases are staged with the Sentinel lymph node (SLYMPH NODE) mapping algorithm[117]. The SLYMPH NODE mapping algorithm for staging has replaced lymphadenectomy in many practices worldwide and can be applied to almost all cases of apparent uterine-confined endometrial cancer regardless of FIGO grade or histotype[118]. Following a normal peritoneal survey, any suspicious lymph node should be removed and sent for histologic examination. In the absence of SLYMPH NODE mapping, myometrial invasion can be identified preoperatively using MRI to evaluate the need for lymphadenectomy[119]. Where MRI is not available, an intraoperative frozen section of the suspected region of the myometrium can be used to determine myometrial invasion in patients with grade 1–2 histology[120]. The aim of successful endometrial cancer surgery, when possible, is definitive treatment or, if surgery alone is not curative, to remove gross disease and accurately stage the patient to direct postoperative adjuvant therapies. In the majority of patients with grade 1 and 2 endometrioid histology, preoperative imaging will not significantly change the basic management or prognosis of these patients. However, imaging is helpful in patients with a suspected extrauterine disease where additional surgery is required for its removal or planning of adjuvant treatment. It is desirable to know the following information before the surgery:
1. Histology and grade.
2. Myometrial invasion (in cases where fertility preservation or ovarian preservation is considered).
3. Presence of resectable gross disease outside the uterus (enlarged ovary, nodes, and omental disease).
4. Presence of unresectable disease.
The possibility of finding extrauterine disease is higher in poorly differentiated endometrioid adenocarcinoma and non endometrioid carcinoma. In patients with serous histology, the extrauterine disease may be present in almost 50% of all cases. Ultrasound and MRI are used for evaluating the extent of local disease, while CT and PET are used for detecting lymph nodes or distant metastases[121]. Diffusion-weighted MRI (DWI-MRI) has also been used for detecting small metastatic deposits in lymph nodes and omentum. Extrauterine soft tissue involvement can be detected by transabdominal ultrasound, CT, MRI, and PET. Apart from preoperative staging, imaging is also used for planning adjuvant treatment and for detection of postoperative residual disease in high-risk patients (CT/PET-CT), monitoring and detecting recurrent disease (ultrasound, CT, MRI, and PET/PET-CT), and in post-treatment surveillance of asymptomatic patients with a high risk of relapse (PET/PET-CT).

Ultrasound
The uterine cavity and endometrium as well as the adnexa can be examined in great detail using transvaginal ultrasound. Transrectal ultrasound can also provide similar information and is useful in elderly patients with vaginal stenosis. Transabdominal ultrasound should be used in conjunction with transvaginal ultrasound if the uterus is large, and to avoid missing large ovarian or tubal pathology. Ultrasound examination of the uterus should be carried out systematically in a stepwise fashion[123]. Using a transvaginal ultrasound probe, the cervix should be examined in a sagittal plane for tumor invasion into the cervical stroma. The medias parametria should also be examined, followed by the entire body of the uterus from cornu to cornu in a sagittal plane, and from the cervix to the fundus in an axial plan. Tumor size should then be measured and, if possible, Gordon’s ratio (deepest invasion/normal myometrium ratio) measured at the area of deepest myometrial invasion[123]. Normal endometrium in a postmenopausal woman is smooth, usually, less than 1 mm thick, and has a thin hypoechoic layer between it and the myometrium. Although ultrasound can detect altered endometrium, it is not specific and histologic confirmation is always required. There is a higher likelihood of endometrial cancer with increasing thickness of the endometrium and postmenopausal status. In general, a cutoff value of 4–5 mm is indicative of carcinoma, with 96% sensitivity and 61% accuracy based on a meta-analysis by SmithBindman et al [124]. Furthermore, the heterogeneous echogenicity caused by areas of hemorrhage and necrosis and an irregular endometrial myometrial interphase that denotes myometrial invasion by cancer supports the diagnosis of endometrial cancer. Transvaginal ultrasound may also detect cervical stromal invasion. Transabdominal ultrasound can provide additional information, mostly related to the extrauterine disease.
Ultrasound images and schematic diagrams showing deepest invasion, the largest distance in any plane between endometrium-myometrium junction and maximum tumor depth, and corresponding normal myometrium assessed as the myometrial width aside of the deepest tumor invasion without fibroids; (a-b) deepest invasion/normal myometrium ratio ≥ 0.5 reflecting the deep invasion, histologically proven FIGO stage IB; (c-d) deepest invasion/normal myometrium ratio < 0.5 indicating superficial invasion, histologically proven FIGO IA.[123]

➢ **Computed tomography**
CT is less helpful in investigating abnormalities within the uterus. On CT, a gross suspicious endometrial mass may be seen as a hypodense lesion or an enlarged endometrial cavity that often cannot be distinguished from benign lesions. However, CT has a better multiplanar spatial resolution that is useful in visualizing the entire pelvic and abdominal cavity for enlarged nodes and gross soft tissue masses, as well as distant metastases in the lungs. In the absence of MRI or PET, CT should be requested if the extraterine disease is suspected in patients with high-grade histology, deep myometrial invasion, or a large uterus. Frequently, CT is ordered as a baseline investigation before a histologic diagnosis of endometrial cancer. The use of intravenous contrast helps identify vascular structures and soft tissue metastases and distinguishes lymph nodes from small bowel loops. A lymph node with a maximum short-axis diameter of greater than or equal to 10 mm is regarded as suspicious of metastatic disease. Nonetheless, the overall reported sensitivity in detecting nodal metastasis in CT is only about 40%. In a study conducted by Reich O et al., there was a positive correlation between the size of the positive lymph node and the size of the metastasis (P<0.01), 68 of 125 (54%) positive lymph nodes measured less than 10 mm in maximum short-axis diameter and 46 of 160 (29%) negative lymph nodes measured more than 10 mm in maximum short-axis diameter[125]. It was observed that patients with single metastatic nodes tend to have tumor deposits in nodes less than 10 mm. In patients with multiple positive nodes, 85% of patients had at least one positive node greater than 10 mm. In node-positive endometrial cancer patients the incidence of a single positive node was 25%–40% and multiple nodes were found in 60%–75% of patients. Therefore, CT should correctly detect more than 40% of node-positive patients. Additionally, a CT scan of the chest, abdomen, and pelvis as a preoperative investigation is useful for excluding unexpected anatomy that may result in modification of planned surgery.

➢ **Magnetic resonance imaging**
Where available, MRI is the imaging modality of choice for the anatomical study of the pelvis and abdomen. MRI is best suited to detect and evaluate endometrial cancer within the endometrial cavity; tumor infiltration into myometrium, endocervix, and gross extension into the parametrial and other pelvic tumor deposits. On T2-weighted images, endometrial cancer usually appears as intermediate signal intensity. Unlike normal endometrium, it does not have a uniform high signal owing to the presence of higher cellularity, necrosis, and hemorrhage within the tumor. The surrounding myometrium is composed of two distinct layers. The inner myometrial layer or “junctional zone” abuts the endometrium and appears as a low signal band, while the outer myometrium is more variable in appearance but usually of intermediate signal. Post intravenous contrast, the innermost myometrial layer enhances uniformly during the early dynamic phase as a continuous line or “sub endometrial stripe.” Disruption of the sub endometrial stripe or frank breach of the junctional zone is indicative of myometrial invasion. An intact junctional zone and a continuous band of early sub endometrial enhancement exclude deep myometrial invasion. Depth of myometrial invasion is related to the incidence of nodal metastasis. The incidence of nodal metastasis in patients with less than 50% and greater than 50% myometrial invasion was reported to be 5% and 18%, respectively[109]. A study comparing presurgical MRI images with histology showed the value of MRI in predicting the presence and depth of myometrial invasion and the potential utility of MRI in presurgical prognostication of patients
who may be suitable for more conservative treatment[119]. The sensitivity of MRI to distinguish superficial from deep myometrial invasion varies from nearly 60%–88%[126] and is limited in some situations such as very superficial invasion in premenopausal women or a large polypoid tumor extruding into the cervical canal [127,128]. The combination of T2-weighted and dynamic contrast-enhanced magnetic resonance images offers high accuracy for staging endometrial cancer in the range of 83%–91%. Endometrial cancer is best examined in the sagittal plane, providing longitudinal views of the uterus and cervix as well as surrounding structures such as bladder, rectum, and loops of bowel. T2-weighted MRI is the key sequence for evaluating myometrial invasion as it depicts the uterine zonal anatomy, with the intermediate signal-intensity tumor well delineated against the low-signal-intensity junctional zone. A minimum of at least two T2-weighted sequences in the sagittal, axial oblique or coronal oblique orientation (short and long axis of the uterine body) of the pelvis and one T1-weighted enhanced sequence acquired at 2 minutes ±30 seconds after intravenous contrast injection is recommended. Metastatic node detection with MRI is similar to a high-quality CT scan with variable sensitivity ranging from 38% to 89% and specificity ranging from 78% to 99% [129]. The combination of T2-weighted and dynamic contrast-enhanced magnetic resonance images offers high accuracy for staging endometrial cancer in the range of 83%–91%. If the cervical invasion is suspected, additional slice orientation perpendicular to the axis of the endocervical canal is recommended[130]. The presence of an intact enhancing cervical mucosa excludes cervical stromal invasion[131]. Multiparametric MRI including thin-section (3 mm) high-resolution multiplanar T2-weighted images and simple modifications, such as the addition of double oblique T2-weighted, diffusion-weighted, and dynamic (30, 60, 120 seconds, and 4 minutes) contrast-enhanced images, improves staging and treatment planning in patients with endometrial carcinoma[129]. Often these preoperative images are helpful not only in planning the primary surgery but also during deliberation of postoperative adjuvant radiotherapy for the presence of diverticula or any other variation in normal anatomy. However, DWI-MRI is increasingly routine in many centers, and higher field strength 3T MRI may significantly enhance the sensitivity of detecting metastatic lymph nodes by combining the size of node and relative apparent diffusion coefficient values[131]. Incorporating morphological features of nodal involvement best seen at high-resolution T2-weighted MRI include internal heterogeneity, spiculated nodal margins, necrosis, and signal intensity comparable to that in the primary tumor, improves the accuracy of evaluation in patients with rectal cancer and may apply to those with endometrial carcinoma[129]. DWI MRI is also sensitive in detecting early invasive extratubine and omental disease.

Normal zonal anatomy on T2-weighted MRI in (A) sagittal, (B) axial, and (C) coronal planes demonstrating high signal (bright) endometrium (arrowheads), low signal (darker) junctional zone or inner myometrium (solid white arrows), and intermediate signal (grey) outer myometrium (dotted arrows) [145].

Dynamic T1 fat-saturated post-contrast (Cii) shows disruption of sub endometrial stripe at anterior midbody of the uterus (dotted arrow) confirming my invasion. Cervical mucosal enhancement was preserved posteriorly but disrupted anteriorly (arrowhead)
confirming stromal invasion. Diffusion-weighted imaging (Ciii) highlights tumor extent and deep cervical stromal invasion but the absence of bladder wall invasion (arrowhead) [145].

Lymph node evaluation on MRI is enhanced by the combination of high-resolution T2 (A) and T1 (B) anatomical imaging and functional sequences including post-contrast T1 fat-saturated (C) and diffusion-weighted imaging (D) increasing nodal conspicuity and improving morphological assessment (arrowheads) [145].

Peritoneal metastatic nodular deposits (solid arrows) were demonstrated on axial T2 (A) and diffusion-weighted imaging (B) sequences in the same patient. Omental cake (arrowheads) on axial T2: (C) intermediate signal: grey and prominent restricted diffusion on diffusion-weighted imaging; (D): high signal: bright [145].

➢ Positron emission tomography-computed tomography

PET-CT is usually employed in the study of metastatic lymph nodes. It has high specificity in detecting metastatic nodes; however, its sensitivity is only modest and depends on the size of the metastatic deposit[132]. The detection rate of PET-CT was only 12% in metastatic lesions measuring 4 mm or less, but 100% when the deposit was 10 mm or larger[133]. It is not routinely employed in assessing intrauterine disease although it can detect the depth of myometrial invasion and extension into the endocervix reasonably well. In advanced stages, PET-CT helped detect metastatic deposits in the ovary and omentum and distant spread. In general, if the baseline MRI or CT scan suggests enlarged nodes and if one believes that removal of all positive nodes during
MATERIALS AND METHODS

Study design: Descriptive study with diagnostic test evaluation

Study period: January 2020 to June 2021

Study setting: Department of Radiodiagnosis and Department of Obstetrics and Gynecology, Govt. T.D. medical college Alappuzha - a tertiary care centre in Kerala. Most of the suspected cases of carcinoma endometrium is in the district and the surrounding rural areas are referred to this hospital, as there are no other higher referral centres available in government or private sector in the district.

Study population: Patients attending department of Obstetrics and Gynecology, and referred to department of Radiodiagnosis of T.D. Medical College Alappuzha, who are clinically suspected to have carcinoma endometrium , during the study period.

Inclusion criteria:
All patients with abnormal uterine bleeding with clinical suspicion of carcinoma endometrium, histologically proven endometrial cancer, sonologically suspected endometrial cancer with vaginal stenosis (without access for biopsy), uterine cancer of unknown origin in fractional curettage(endometrial versus endocervical), central pelvic mass likely malignant, rapidly enlarging uterus in postmenopausal age and suspected uterine neoplasm in CT, during the study period.

Exclusion criteria:
• Patients who are not willing to participate.
• Patients with contraindications for MRI.
• Patients with advanced disease requiring chemotherapy prior to surgery
• Patients with histopathology other than endometrial carcinoma such as carcinosarcoma and lieomyosarcoma
• Patients unsuitable for biopsy – Deranged hemostasis,not tolerating general anesthesia.
• Patients with unavailable, non-diagnostic or indeterminate histopathology reports.

Sample size and Sampling method:
A total number of 83 cases were enrolled in the study, which was calculated by the formula:

$$n = \frac{(Z_a + Z_{1-\beta})^2}{(\pi(1-\pi)(\rho_1 - \rho_0))^2} \left[ \frac{1}{\pi^2 + \pi(1-\pi)\rho_0} + \frac{2}{\pi(1-\pi)(1-\rho_0)} + \frac{1}{(1-\pi)^2 + \pi(1-\pi)\rho_0} \right]$$

$$\rho_0 = 0.5$$
$$\rho_1 = 0.75$$
$$\pi = 0.5$$
$$a = 5$$
$$1 - \beta = 80$$

According to study conducted by Fei Teng [11] et al, Kappa coefficient was taken has 0.758 and using the above formula sample size was calculated as 83.

PROCEDURE

The study commenced after the approval of the ethical committee of the institute. The participants were explained about the nature of the study and an informed written consent was obtained from all the study subjects in their mother tongue. Participant information sheet was be given to all the study subjects in their native language informing them about the procedure involved also making them aware that they can withdraw from the study any time they want and that this study would in no way influence their management in the hospital. Patients didn’t have to afford any additional financial burden by taking part in this study.

MAGNETIC RESONANCE IMAGING PROTOCOL

- **MRI scanner:** Siemens (MAGNETOM Aera), 1.5 T closed magnet
- **Coil:** Torso phased array RF coil (16 channels)
- **T2 weighted image:** TR 4000/TE 96 msec, Matrix 256 x256, FOV 200x100, Slice thickness 3.5mm.
- **T1weighted images** TR 400 /TE 9 msec, , 256 X 224 matrix, FOV 200x100, Slice thickness 3.5mm.

Optimal acquisition of MR images depends on good patient preparation. Motion artefacts caused by bowel peristalsis is reduced by instructing patients to fast 4 hours before the examination. Immediately before imaging patients must void their bladder to reduce movement and ghosting artefacts on T2-weighted images.

MR images are acquired with patients lying supine and a surface array multichannel coil to optimize image quality and reduce acquisition time.
MR Imaging Sequences and Planes used - The basic gynaecologic pelvic MR imaging protocol includes acquiring axial, sagittal, and coronal T2-weighted images. Axial T1- or T2-weighted images of the abdomen and pelvis are used to depict enlarged lymph nodes, hydronephrosis, and bone marrow abnormalities. High-resolution fat suppressed T2-weighted images are acquired in the axial oblique plane, perpendicular to the endometrium, allowing accurate assessment of myometrial invasion. Dynamic multiphase contrast material–enhanced imaging may be used to assess the local extent of endometrial carcinoma. Before administration of contrast material, fat suppressed T1-weighted MR images are acquired in the axial and sagittal planes. One and 2 minutes after administration of contrast material (gadopentetate dimeglumine (Magnevist; 0.1–0.2 mmol/kg body weight), they are acquired in the sagittal plane, and 3 minutes after contrast material administration, they are acquired in the axial oblique plane. Late contrast-enhanced fat suppressed T1-weighted images are obtained in the axial and sagittal planes approximately 5 min after contrast is administered.

(a) High-resolution sagittal T2-weighted FRFSE MR image shows the correct plane for prescribing the orthogonal axial images perpendicular to the endometrial cavity in patients with endometrial carcinoma. Solid line and arrow = long axis of the uterus, dashed lines = plane of acquisition for routine axial oblique sections.

(b) Coronal high-resolution FRFSE T2-weighted MR image shows that the body of the uterus is deviated to the right. The second oblique plane is prescribed perpendicular to the axis of the uterus in the coronal plane. The axis of the endometrial cavity in the coronal plane (solid line) and the acquisition plane of the oblique axial images (dashed lines) are seen. The combination of both acquisitions prescribed along the long axis of the uterus in the sagittal and coronal planes forms the double oblique axial image.

CASES
CASE 1:

SAGITTAL T2WI

SAGITTA L T1 C+
The above set of images shows a bulky uterus with thickened endometrium and a well-defined T2 intermediate signal intensity lesion which is showing diffusion restriction, hypoenhancement in DCE with less than 50% extension into the myometrium. No abnormal pelvic lymph nodes are seen in this patient.

**CASE 2:**
The above set of images shows large ill defined T2 heterogeneously hyperintense and hypoenhancing lesion in uterine cavity invading >50% of myometrium and reaching almost upto serosal surface with areas of diffusion restriction. No abnormal lymph nodes are seen in this patient.

CASE 3:
A case with endometrial cancer invading more than 50% of myometrium with no lymph node metastasis.

HISTOPATHOLOGICAL ANALYSIS
Surgical specimens were sectioned along the longitudinal plane of the uterus. Myometrial and cervical invasion are estimated macroscopically and microscopically and are classified according to FIGO guidelines as follows: stage IA, tumor confined to the uterus, <50% MI; stage IB, tumor confined to the uterus, ≥50% MI; or stage II, cervical stroma invasion. Lymph node dissection is performed with anatomic labelling into common, internal and external iliac, internal obturator and lumbo-aortic node groups by surgeons in the operating room. These lymph nodes are cut into parallel slices of 3–4 mm thickness and all nodal tissue is routinely processed and embedded in paraffin. Sections are stained with hematoxylin & eosin. The total number and anatomical site of lymph nodes, both metastatic and non-metastatic were documented.

DATA COLLECTION TOOLS
A semi-structured proforma was used for data collection (annexure 1).

STUDY VARIABLES
Exposure variables:
Age
DATA ENTRY AND ANALYSIS

Data was entered in Microsoft excel. Analysis of the data was done in SPSS version 20. Frequencies of variables, correlation between variables, sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated. Appropriate statistical tests were applied wherever applicable.

<table>
<thead>
<tr>
<th>Test Positive</th>
<th>Test Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>TP</td>
<td>FN</td>
</tr>
<tr>
<td>FP</td>
<td>TN</td>
</tr>
</tbody>
</table>

Table 1: Analysis of sensitivity, specificity, PPV and NPV
TP - True positive, TN - True negative, FP - False positive, FN - False negative, PPV - Positive predictive value, NPV - Negative predictive value

Sensitivity = (TP) / (TP+ FN)
Specificity = (TN) / (TN+FP)
Positive predictive value (PPV) = (TP) / (TP+ FP)
Negative predictive value (NPV) = (TN) / (TN+ FN)

Accuracy = (TN+TP)/ (TN+TP+FN+FP) = (No. of correct assessments) / (No. of all assessments)

RECEIVER OPERATING CHARACTERISTICS (ROC) ANALYSIS

ROC curve (Receiver-Operating Characteristics Curve) was plotted between sensitivity and 1- specificity. For a given diagnostic test, the true positive rate (TPR) against false positive rate (FPR) can be measured, where

TPR = TP/ (TP+FN)
FPR = FP/ (FP+TN)

TPR is equivalent to sensitivity and FPR is equivalent to (1 – specificity).

A point in ROC space is represented by a TPR and corresponding FPR, which shows the trade-off between sensitivity and 1-specificity. This means that, the increase in sensitivity is accompanied by a decrease in specificity or increase in false positive rates.

RESULTS AND ANALYSIS

Statistical analysis

All the data collected were coded and entered in Microsoft Excel sheet which was re-checked and analysed using SPSS statistical software version 22. Quantitative variables were summarised using mean and standard deviation (SD). Categorical variables were represented using frequency and percentage. Pearson Chi-square test and Fisher’s Exact test were used for comparing categorical variables between groups. Diagnostic characteristics of MRI was evaluated by comparing it with histopathological examination and sensitivity, specificity, PPV, NPV, accuracy. Percentage agreement of MRI and histopathology findings in myometrial invasion and pelvic lymph node metastasis in endometrial carcinoma was evaluated using kappa statistic. A p value of <0.05 was considered statistically significant.

Table 1: Characteristics of study subjects (N=83)

<table>
<thead>
<tr>
<th>Age-years</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>66.28±6.44</td>
</tr>
<tr>
<td>Median</td>
<td>66(62-72)</td>
</tr>
<tr>
<td>Age-no(%)</td>
<td></td>
</tr>
<tr>
<td>51-60 years</td>
<td>19(22.9)</td>
</tr>
<tr>
<td>61-70 years</td>
<td>42(50.6)</td>
</tr>
<tr>
<td>Complaints-no(%)</td>
<td>22(26.5)</td>
</tr>
<tr>
<td>-----------------</td>
<td>----------</td>
</tr>
<tr>
<td>AUB</td>
<td>83(100)</td>
</tr>
<tr>
<td>Attained menopause-no(%)</td>
<td>83(100)</td>
</tr>
<tr>
<td>Yes</td>
<td>83(100)</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Proven endometrial cancer-no(%)</td>
<td>83(100)</td>
</tr>
<tr>
<td>Yes</td>
<td>83(100)</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Myometrial invasion-no(%)</td>
<td>61(73.5)</td>
</tr>
<tr>
<td>&lt;50%</td>
<td>61(73.5)</td>
</tr>
<tr>
<td>&gt;50%</td>
<td>22(26.5)</td>
</tr>
<tr>
<td>Lymph node status-no(%)</td>
<td>71(85.5)</td>
</tr>
<tr>
<td>Involved</td>
<td>12(14.5)</td>
</tr>
<tr>
<td>Not involved</td>
<td>71(85.5)</td>
</tr>
<tr>
<td>Histopathological examination for myometrial invasion-no(%)</td>
<td>56(67.5)</td>
</tr>
<tr>
<td>&lt;50%</td>
<td>56(67.5)</td>
</tr>
<tr>
<td>&gt;50%</td>
<td>27(32.5)</td>
</tr>
<tr>
<td>Histopathological examination for lymph node involvement-no(%)</td>
<td>65(78.3)</td>
</tr>
<tr>
<td>Positive</td>
<td>18(21.7)</td>
</tr>
<tr>
<td>Negative</td>
<td>65(78.3)</td>
</tr>
</tbody>
</table>

Figure 1: Age

<table>
<thead>
<tr>
<th>Age</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>51-60 years</td>
<td>22.9</td>
</tr>
<tr>
<td>61-70 years</td>
<td>50.6</td>
</tr>
<tr>
<td>71-80 years</td>
<td>26.5</td>
</tr>
</tbody>
</table>

| Figure 1: Age |
Figure 2: Myometrial invasion

Figure 3: Lymph node status

Figure 4: Histopathological examination for myometrial invasion
Figure 5: Histopathological examination for lymph node involvement

Table 2: Comparison of myometrial invasion in MRI and histopathology

<table>
<thead>
<tr>
<th>Myometrial invasion in MRI</th>
<th>Histopathological examination for myometrial invasion</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50%</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>&lt;50%</td>
<td>56(91.8)</td>
<td>5(8.2)</td>
</tr>
<tr>
<td>&gt;50%</td>
<td>0</td>
<td>22(100)</td>
</tr>
</tbody>
</table>

*statistically significant

Table 3: Diagnostic characteristics of MRI for diagnosing myometrial invasion

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>100</td>
</tr>
<tr>
<td>Specificity</td>
<td>81.5</td>
</tr>
<tr>
<td>PPV</td>
<td>91.8</td>
</tr>
<tr>
<td>NPV</td>
<td>100</td>
</tr>
<tr>
<td>Accuracy</td>
<td>94</td>
</tr>
<tr>
<td>Kappa statistic</td>
<td>0.85</td>
</tr>
</tbody>
</table>

Figure 6: Comparison of myometrial invasion in MRI and histopathology

Table 4: Comparison of lymph node status in MRI and histopathology

<table>
<thead>
<tr>
<th>Myometrial invasion in MRI</th>
<th>Lymph node status in MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td>Myometrial invasion &lt;50%</td>
<td>56</td>
</tr>
<tr>
<td>Myometrial invasion &gt;50%</td>
<td>22</td>
</tr>
</tbody>
</table>

Figure 7: Comparison of lymph node status in MRI and histopathology
### Table 5: Diagnostic characteristics of MRI for diagnosing lymph node involvement

<table>
<thead>
<tr>
<th>Lymph node status in MRI</th>
<th>Histopathological examination for lymph node involvement</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Involved</td>
<td>Positive: 12(100) Negative: 0</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Not involved</td>
<td>Positive: 6(8.5) Negative: 65(91.5)</td>
<td></td>
</tr>
</tbody>
</table>

*statistically significant

### Table 6: Association of myometrial invasion with age

<table>
<thead>
<tr>
<th>Age group</th>
<th>Histopathological examination for myometrial invasion</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50%</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>51-60 years</td>
<td>17(89.5)</td>
<td>2(10.5)</td>
</tr>
<tr>
<td>61-70 years</td>
<td>28(66.7)</td>
<td>14(33.3)</td>
</tr>
<tr>
<td>71-80 years</td>
<td>11(50)</td>
<td>11(50)</td>
</tr>
</tbody>
</table>

*statistically significant

### Table 7: Association of lymph node status with age

<table>
<thead>
<tr>
<th>Age group</th>
<th>Histopathological examination for lymph node involvement</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>51-60 years</td>
<td>7(36.8)</td>
<td>12(63.2)</td>
</tr>
<tr>
<td>61-70 years</td>
<td>11(26.2)</td>
<td>31(73.8)</td>
</tr>
<tr>
<td>71-80 years</td>
<td>0</td>
<td>22(100)</td>
</tr>
</tbody>
</table>

*statistically significant

---

**Figure 7: Comparison of lymph node status in MRI and histopathology**

**Table 6: Association of myometrial invasion with age**

**Table 7: Association of lymph node status with age**
Figure 8: Myometrial invasion in different age groups

Figure 9: Lymph node status in different age groups

Table 7: Association of lymph node status with myometrial invasion

<table>
<thead>
<tr>
<th>Histopathological examination for myometrial invasion</th>
<th>Histopathological examination for lymph node involvement</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>&lt;50%</td>
<td>18(32.1)</td>
<td>38(67.9)</td>
</tr>
<tr>
<td>&gt;50%</td>
<td>0</td>
<td>27(100)</td>
</tr>
</tbody>
</table>

*statistically significant
DISCUSSION

In the present study, 83 patients with endometrial cancer (irrespective of the histologic grade) underwent MR imaging to assess myometrial invasion and lymph nodal involvement prior to surgery. All 83 patients underwent total hysterectomy, bilateral salpingo-oophorectomy and targeted pelvic lymph node sampling. Depth of myometrial invasion (confined to endometrium or inner half of the myometrium; deep invasion, invading the outer half of the myometrium), and presence of metastasis within the sampled lymph nodes were confirmed microscopically for all the 83 patients.

IMAGE ANALYSIS:

All patients were subjected to following MRI sequences:

- **FOR MYOMETRIAL INVASION:**
  1. T2 sequences of the pelvis: Sagittal and axial oblique two-dimensional T2W sequences through the uterus were obtained. Axial oblique T2W sequences were taken perpendicular to the endometrial cavity. The slice thickness ≤ 4 mm was used.
  2. DWI sequences: A minimum of two b values of 0 and 800–1000 s/mm² are recommended. The sagittal and axial oblique plane is obtained perpendicular to the endometrial cavity.
  3. Dynamic contrast-enhanced Imaging: Fat-saturated contrast-enhanced T1W sequence obtained 2 min 30 s after contrast medium administration is used for best tumor-to-myometrium contrast.

- **FOR LYMPH NODE INVOLVEMENT:**
  1. Axial T2WI from the renal hila to the pubic symphysis was taken.
  2. Axial DWI and ADC from the renal hila to the pubic symphysis was taken.

RESULTS:

Among 83 patients, endometrial cancer with less than 50% myometrial invasion was present in 61 patients (73.5%) and MI more than 50% was seen in 22 patients (26.5%). Lymph nodal metastasis was present in 12 patients (14.5%). All these 12 patients had myometrial invasion of more than 50%.

The presence of confounding factors relating to accurate estimation of the depth of myometrial invasion was noted for each case. These included the presence of:

- leiomyoma,
- adenomyosis,
- loss of junctional zone definition,
- poor tumor-to-myometrium contrast, and
- extension of tumor into the uterine cornua (10,21–24)[146-150].
SURGICAL HISTOLOGIC FINDINGS:
Post operative histologic examination revealed Myometrial invasion >50% in 27 patients and < 50% in 56 patients. Lymph nodes were found positive for malignancy in 18 patients and negative in 65 patients.

Diagnostic Performance of MR Imaging in Assessing Depth of Myometrial Invasion:
MRI for the assessment of depth of myometrial invasion had a diagnostic accuracy of 94% and sensitivity of 100%.

Confounding Factors in Assessing Depth of Myometrial Invasion:
Number of patients with confounding factors mentioned above

<table>
<thead>
<tr>
<th>CONFOUNDING FACTORS</th>
<th>NUMBER OF PATIENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>LEIOMYOMA</td>
<td>4</td>
</tr>
<tr>
<td>ADENOMYOSIS</td>
<td>NIL</td>
</tr>
<tr>
<td>LOSS OF JUNCTIONAL ZONE DEFINITION</td>
<td>7</td>
</tr>
<tr>
<td>POOR TUMOR TO MYOMETRIUM CONTRAST</td>
<td>1</td>
</tr>
<tr>
<td>EXTENSION OF TUMOR INTO THE UTERINE CORNUA</td>
<td>3</td>
</tr>
</tbody>
</table>

Among the factors mentioned above, the incorrect assessment of depth of myometrial invasion is seen in 10 patients- 7 with loss of junctional zone definition and 3 with tumor extending into cornua.
There was no association between incorrect assessment of the depth of myometrial invasion with MR imaging and other three confounding factors.
No other new factors confounded the present study interpretation.

DIAGNOSTIC PERFORMANCE OF MR IMAGING FOR LYMPH NODE INVOLVEMENT:
MRI for the assessment of lymph nodal status in the present study had diagnostic accuracy of 92.8%, specificity of 100%

In the present study, following criteria were taken into consideration for
1. 10 mm in short axis diameter for abdominal and 8 mm for pelvic lymph nodes as the threshold value
   Along with 1., presence of any one of the following was reported as positive on MR imaging
   2. Necrosis,
   3. Signal intensity similar to that of the primary tumor,
   4. Irregular borders and,
   5. Extraneural spread.

In the present study, incorrect estimation of lymph node involvement on MR as negative in 6 patients with small lymph nodes measuring approximately 4-5 mm on average.

RESULT ANALYSIS WITH PREVIOUS STUDIES:
The present study shows that MR imaging has higher diagnostic accuracy in assessing the depth of myometrial invasion and lymph nodal spread.

FOR ANALYSING THE DEPTH OF MYOMETRIAL INVASION:
The study done by Rechichi et al[45], which used DWI to assess the depth of myometrial invasion, found that DWI has sensitivity of 84.6%, which was calculated to be 100% in the present study.

Study by Ito et al[151] have shown that the addition of multiphase DCE-MRI to T2WI leads to a significant improvement in the accuracy of assessment of deep myometrial invasion, present study concurred with the facts.

Compared to multiple studies[146,43,14], the diagnostic accuracy of MR with DWI and DCE showed higher accuracy of 94% in assessing the depth of myometrial invasion.

Another study by Beddy et al[41], which included both DWI and DCE images for the assessment of myometrial invasion, had an accuracy of 90% compared to 94% in our study.

In the present study lymph nodes are not involved in the patients with <50% depth of involvement of myometrium which is consistent with the study conducted by Beddy et al[153] which concluded that depth of myometrial invasion is the most important morphologic prognostic factor for lymphnode metastasis.

FOR THE LYMPH NODAL METASTASIS:
In the present study we understaged lymph nodal status in 6 patients having an average lymph nodes size of 4-5 mm, which is on par with the study conducted by Theony et al[151], which concluded that even smaller lymph nodes are suspicious for malignancy due to micrometastasis.
Low ADC values can be used to accurately exclude metastases in such smaller lymph nodes [151].

PITFALLS AND HOW TO OVERCOME THEM:

1. Tumor involving more than half (>50%) of the myometrial thickness is staged as IB. The area of the uterine cornua is physiologically thinner than the normal myometrium. Hence, when it symmetrical invasion is present at this location, it should not be over staged[28]. In the present study we over staged 3 patients with extension into cornua.

2. In atrophic uteri and in tumours isointense relative to myometrium, problem solving modalities complementary to T2WI should be performed. High resolution 3D T1 WI at about 2–2.5 min after IV contrast media application may be best able to solve the problem [8].

3. If the depth of myometrial invasion is equivocal on T2WI and DWI, complementary GD T1 WI should be applied [18]. In the present study we used DCE MRI for all the patients to accurately assess the myometrial invasion.

4. Myometrial assessment in thinned out endometrium caused by tumorous distension of the uterine cavity by expansively growing cancers may be challenging [17].

5. In endometrial cancer and coexisting adenomyosis or atypical uterine leiomyomas the complementary use of both DWI and Gd is advised to assess the depth of myometrial invasion. Of note, both adenomyosis and some leiomyomas may show restricted diffusion, and leiomyomas may also be hypervascular[28]. In the present study we had 4 patients with uterine leiomyoma where we used DCE MRI for distinguishing it from the lesion.

6. Double angulation technique provides a true orthogonal view of the uterus and may improve assessment of myometrial invasion in rotated or tilted uterus. Thus, the problem of volume averaging artifacts can be reduced [15]. We used double angulation technique in the present study.

7. In equivocal lymph nodes morphologic criteria should be combined with functional information. Enhancement pattern or ADC similar to the uterine cancer support the diagnosis of metastasis [28].

8. To reduce pitfalls in interpretation in DWI the findings should always be correlated with T2WI. The optimal high b value varies from field strength and vendors. It should be 800 mm/s [19] or more and is optimal when the fluid in the urinary bladder appears dark[28].

9. In DWI the angulation along the uterus should be identical to the T2W sequence[8]. Angulation in DWI along the uterus in at least two planes, axial oblique and sagittal, identical to T2WI provides accurate assessment of myometrial invasion rather than single plane.

10. T2 Shine-through Effect: ADC values are always referred to avoid this pitfall.

11. Restricted Diffusion can be seen even in normal structures and non-malignant lesions. For example-normal proliferative endometrium, normal or reactive lymph nodes and retained mucus in an obstructed endometrial cavity. In these normal structures/ non malignant lesions other features like characteristic contrast enhancement on dynamic imaging in normal endometrium and retained mucus helps in differentiating benign from malignant lesions.

CONCLUSIONS

- MRI is a potent imaging tool assisting to triage treatment in women with endometrial cancer.
- The depth of myometrial invasion and lymph node metastases are the major findings to analyse in staging MRI.
- MRI with DWI and DCE plays an important role in assessing the depth of myometrial invasion with accuracy of 94%
- Diagnostic accuracy of MRI for lymph nodal staging is 92.8% in present study which can be further increased by accounting ADC values in case of smaller lymph nodes.
- Combination of DWI and DCE MRI rather than using either of them helps in accurately staging the endometrial cancer by overcoming the pitfalls.

LIMITATIONS

The study setting being a tertiary care centre, many cases were advanced carcinoma. Hence there is need for further studies before generalizations can be made.

REFERENCES


