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Fertility-Sparing For Young Patients With Gynecologic Cancer: How MRI Can Guide Patient Selection Prior to Conservative Management

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Abstract

Historically, cancer treatment has emphasized measures for the “cure” regardless of the long-term consequences. Advances in cancer detection and treatment have resulted in improved outcomes bringing to the fore various quality of life considerations including future fertility. For many young

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cancer patients, fertility preservation is now an integral component of clinical decision-making and treatment design.

Optimal fertility-sparing options for young patients with gynecologic cancer are influenced by patient age, primary cancer, treatment regimens, and patient preferences. Possible approaches include embryo or oocyte cryopreservation, ovarian transposition, conservative surgery, and conservative medical treatment to delay radical surgery. These may be used alone or in combination to maximize fertility preservation.

Awareness of the various fertility-sparing options, eligibility criteria, and the central role of Magnetic Resonance Imaging (MRI) in the proper selection of patients will enable radiologists to produce complete clinically relevant imaging reports and serve as effective consultants to referring clinicians. Knowledge of the potential imaging pitfalls is essential to avoid misinterpretation and guide appropriate management.

Keywords

Oncofertility; Fertility preservation; Magnetic Resonance Imaging; Gynecologic cancer; Cancer

Introduction

Cancer survivorship has improved over the years and increasingly there are many young survivors including both children and women of reproductive age. It is estimated that in 2016, 10% of cancer survivors in the United States will be younger than 40 years (1). As such, quality of life issues including fertility preservation have become increasingly valuable to patients, families, and physicians. In the evaluation and treatment of cancer, there has been a paradigm shift leading to the emergence of oncofertility, a new field that recognizes the psychosocial impact of cancer-related infertility, bridges oncology with reproductive research, and assists patients to make informed decisions regarding cancer treatment and future fertility (2, 3).

Physicians need be familiar with the latest fertility-sparing approaches to effectively counsel women of reproductive age or parents/guardians of pediatric patients (4). Fertility-preserving options are influenced by the patient's age, primary cancer, planned treatment, participating male partner or patient preferences regarding the use of donor sperm, and time interval to the initiation of therapy (4, 5). For appropriately selected patients with non-gynecologic or gynecologic cancer, fertility-sparing options include assisted reproductive technologies and ovarian transposition (5). For appropriately selected patients with gynecologic cancer, fertility-sparing surgeries such as conization or trachelectomy for cervical cancer, cystectomy or unilateral salpingo-oophorectomy (USO) for ovarian tumors, and conservative medical endocrine treatment for endometrial cancer are also possible (5).

Selection of the appropriate fertility-preserving option for the optimal benefit and safety of the patient depends on accurate cancer staging. MRI (magnetic resonance imaging) is particularly well suited to play an important role for assessing patient eligibility. MRI has unique utility for evaluation of gynecologic malignancies, particularly local staging of

cervical and endometrial cancer (6) and characterization of sonographically indeterminate adnexal masses (7).

This review gives an overview of fertility-sparing options currently available to young patients with gynecologic cancers, illustrates the essential role of MRI in evaluating these options, and highlights the key imaging findings to include in the imaging report to address selection criteria.

General eligibility considerations in identifying suitable candidates for fertility preservation are summarized in Table 1.

Part I: Fertility-Sparing Using Assisted Reproductive Technologies

All newly diagnosed cancer patients desiring future biological offspring require prompt consultation with a reproductive endocrinologist before the start of potentially fertility-impairing therapy (gonad-removing surgery, gonadotoxic chemotherapy, or radiation) (4).

Embryo and oocyte cryopreservation are the two most established artificial reproductive technologies utilized for fertility preservation (4). These approaches involve ovarian stimulation to induce development of multiple follicles, ultrasound-guided transvaginal oocyte retrieval, in-vitro fertilization (if embryo cryopreservation is chosen), and finally cooling to subzero temperatures for use at a later time (8).

While both embryo and oocyte cryopreservation are standard of care for reproductive age women and post pubertal girls, oocyte cryopreservation does not require a participating male partner or donor sperm, thereby permitting greater reproductive autonomy. Oocyte cryopreservation is therefore particularly well suited for single women, post-pubertal girls, or any patients with religious or ethical objections to embryo freezing (4, 8).

Two additional available methods include 1) ovarian tissue cryopreservation with the intent of future implantation, and 2) retrieval of immature oocytes, in-vitro maturation, and vitrification (rapid cooling to avoid ice formation) (4, 9). While still undergoing refinement, these are the only approaches available to pre-pubertal girls as they obviate the need for ovarian stimulation and sexual maturity (4, 9). The potential concern is reintroduction of cancer cells during implantation (4, 9). Thus, this approach is avoided in patients with an inherent predisposition to ovarian cancer or malignancies with moderate-to-high risk of ovarian metastases (e.g., leukemia, Ewing's sarcoma, neuroblastoma, gastric, colon, and breast cancers) (9, 10).

Embryo and oocyte cryopreservation may be associated with ovarian hyperstimulation syndrome (OHSS), an exaggerated response to ovarian stimulation resulting in increased capillary permeability (11). Clinical signs/symptoms, imaging findings (ovarian size, presence of ascites, and pleural effusions), and biochemical parameters are combined to grade OHSS as mild, moderate, or severe (12). The mild form is common whereas severe OHSS accounts for only 0.1–2% of cases (12).

Imaging stigmata of OHSS include symmetric enlargement of both ovaries by multiple variable-sized follicular and corpus luteal cysts. Ovaries acquire a characteristic ‘spoke wheel’ appearance due to multiple peripheral ovarian cysts surrounding the central ovarian stroma (11, 13, 14) (Figure 1). Enlarged cystic ovaries should not be mistaken for cystic ovarian neoplasm (14). Presence of ascites indicates that OHSS is at least moderate in severity. Possible OHSS complications include thromboembolism and ovarian torsion (11, 15, 16).

Part II: Fertility-Sparing Using Ovarian Transposition

Ovaries are extremely radiosensitive, with the effective sterilizing dose decreasing with age (17). The extent of the damage depends on patient age, cumulative dose to the ovaries, fractionation, and type of concurrent chemotherapy. Pelvic radiation also induces damage to a patient’s uterus consisting of changes to the muscles and vasculature, and hormone-resistant endometrial insufficiency, thereby leading to increased risk of infertility, miscarriage, and intrauterine growth retardation (18, 19). Women with a heavily irradiated uterus may require a surrogate (carrying of a pregnancy by a third party) (20).

Ovarian transposition (surgical placement of the ovaries outside the radiation field) is performed to preserve ovarian function in patients planned for lower abdominal and pelvic radiation (21). Recent evidence implicates fallopian tubes as a primary precursor of high-grade serous ovarian and peritoneal cancer.(22) Fallopian tubes are now often removed at the time of ovarian transposition to reduce the risk of ovarian cancer. The benefits of this approach remain to be proven.

Cervical cancer is the most common indication for ovarian transposition in reproductive age women, with vaginal and rectal cancers being less common indications (21). Similar to ovarian tissue cryopreservation and implantation, ovarian transposition is not recommended for patients with an inherited predisposition to ovarian cancer or malignancies at moderate-to-high risk of ovarian metastases (23, 24).

Ovarian transposition successfully preserves ovarian function in 65–94% of patients (23). Various factors such as patient age, radiation scatter, transposition locations, vascular pedicle status, types of radiation, and adjuvant chemotherapy impact the rate of success. To maximize fertility preservation, oocyte cryopreservation may be performed prior to ovarian transposition (8).

To confirm patient eligibility for ovarian transposition, MRI (and occasionally Positron Emission Tomography-Computed Tomography, PET/CT) is useful to delineate disease extent and exclude ovarian involvement.

Various transposition locations can be considered depending on the size/location of radiation field (Figure 2). In patients with cervical cancer, ovaries are often placed into the paracolic gutters or anterior to the psoas muscles above the pelvic brim (21). Transposed ovaries are frequently marked with surgical clips to facilitate visualization during radiation planning.

On imaging, transposed ovaries appear as ovoid structures with follicles adjacent to surgical clips (25). Ovarian cysts and peritoneal inclusion cysts are common following ovarian transposition (Figure 2) (21, 25). Depending on the phase of ovulatory cycle, transposed ovaries may demonstrate physiologic fluorine 18-fluorodeoxyglucose (FDG) avidity on PET/CT (Figure 2). This should not be misinterpreted as metastatic disease (26). Metastases to transposed ovaries are extremely rare and have the same imaging features as metastases to non-transposed ovaries (23).

Part III: Suggested Tailored MRI Protocols for the Initial Work-Up of Gynecologic Cancers and Adnexal Lesions

MRI is the preferred imaging modality for the assessment of cervical and endometrial cancer (6). It is also the best problem-solving imaging technique for the characterization of adnexal masses indeterminate at ultrasonography, US (7, 27, 28). It is essential to tailor MR imaging protocols to the individual needs of the patient to provide accurate and complete information for optimal patient selection and initial treatment design.

Patient Preparation

Patients are encouraged to fast 4–6 hours prior to their MRI appointment and empty their bladder before the examination to reduce peristalsis-related motion artifacts. An anti-peristaltic agent is administered intramuscularly or intravenously at the start of the examination to further reduce peristalsis (6).

Patients are imaged in the supine position with 1.5-Tesla magnet and a multi-channel phase-array receiver coil. Endovaginal receiver coils are not in use routinely; however, they substantially increase the signal-to-noise ratio and can aid the evaluation of small cervical lesions including their detection, assessment of size, endocervical extent, and presence of parametrial invasion (29–32). The opacification of the vagina with gel is optional in women with cervical cancer (33).

Tailored MR Imaging Protocols (Table 2)

Large field-of-view T1-weighted (T1WI) $\pm$ T2-weighted (T2WI) images from the top of the kidneys to the iliac crests are acquired to exclude hydronephrosis, para-aortic lymphadenopathy, and osseous metastases (6, 33, 34). Axial T1WI of the pelvis without and with fat saturation are useful to distinguish blood from fat (28).

High-resolution small field-of-view T2WI in minimum two orthogonal planes is the cornerstone of local tumor staging. In patients with cervical cancer, these are usually obtained in the sagittal plane and axial oblique plane (perpendicular to the endocervical canal) (6, 33); the coronal oblique plane (parallel to the endocervical canal) may be optionally added (35). In patients with endometrial cancer, T2WI are obtained in the sagittal and axial oblique planes with the latter acquired perpendicular to the endometrial cavity (6, 34). In case of an adnexal mass, sagittal, axial, and axial oblique T2WI are obtained with axial oblique plane being parallel to the endometrial cavity, “ovarian axis” (27, 28).

“Ovarian axis” images can help to confirm the ovarian origin of the mass by laying out the gonadal vessels leading to the ovaries.

Diffusion weighted imaging (DWI) is an integral part of the imaging protocol (6, 36). The standard DWI includes a minimum of two sets of images with b-values of 0 and 800 sec/mm² to suppress high-SI (signal intensity) from freely diffusing water (using urinary bladder SI as a reference); apparent diffusion coefficient (ADC) maps are generated thereafter (6). In patients with endometrial and cervical cancer, sagittal, and axial oblique DWI are acquired in the same orientations as T2WI and are useful to detect myometrial invasion (endometrial cancer) and delineate tumor margins (cervical cancer). Coronal oblique DWI (parallel to the endocervical canal) may be included in the cervical protocol (35). Axial DWI is used for adnexal mass assessment.

DWI should always be interpreted in conjunction with other sequences such as T2WI and contrast-enhanced images. It is particularly important with adnexal masses because both benign (endometrioma, mature cystic teratoma) and malignant ovarian masses can show diffusion restriction (high SI on high b-value images and low SI on ADC maps).

Dynamic contrast-enhanced MRI (DCE-MRI) is also a part of the MR imaging protocol. While DCE-MRI is currently optional with newly diagnosed cervical cancer, it improves tumor-to-cervical stromal contrast in patients with small tumors (<2 cm), which is useful in patients being considered for fertility preservation (33, 37). DCE-MRI is essential for local staging of endometrial cancer and for characterization of adnexal lesions (27, 38). In case of endometrial cancer, DCE-MRI is acquired in the sagittal plane with delayed contrast-enhanced images being acquired in the axial oblique plane. In case of an adnexal mass, DCE-MRI is acquired axially using either dynamic multiphase approach or perfusion imaging. The latter is acquired for at least 3 minutes with temporal resolution under 15 seconds (39–42). Perfusion images are processed by placing regions of interest (ROIs) on the most avidly/rapidly enhancing component of the ovarian mass and on the outer myometrium resulting in one of three types of time-intensity curves (using the enhancement of the outer myometrium as a reference) (42). Type 1 curve, slow low level of enhancement without plateau, suggests benignity. Type 3 curve, rapid high level of enhancement (faster than that of the myometrium), indicates probable malignancy. An in-between Type 2 curve, moderate level of enhancement with a plateau, may point to a borderline ovarian tumor. The advantage of perfusion imaging over traditional dynamic multiphase acquisition is not yet proven.

Part IV: Fertility-Sparing Management of Cervical Cancer

Cervical cancer is the fourth most common cancer in women worldwide with the highest incidence in developing countries (43). It is one of the few common gynecologic malignancies with a predilection for women of reproductive age. In the United States, from 2009 to 2013, nearly 40% of new cases occurred in women younger than 45 years (44).

Traditionally, radical surgery was the only treatment option available to most women with early stage cervical cancer. The infrequent finding of parametrial invasion at radical

hysterectomy in patients with cervix-confined tumors ≤ 2 cm led experts to suggest that patients with small tumors can be treated less aggressively (45). Fertility-sparing surgery has emerged as an option in appropriately selected young women desiring fertility and is endorsed by both the European Society of Medical Oncology (ESMO) and the National Cancer Care Network (NCCN) (46–48). Conservative surgery affords the opportunity for pregnancy and achieves long-term oncologic results similar to traditional radical surgery (49).

The International Federation of Gynecology and Obstetrics (FIGO) staging system for cervical cancer is based largely on clinical examination and suffers from the well-documented limitations pertaining to the accuracy of staging (50, 51). MRI is the best imaging modality to detect and demonstrate tumor size, endocervical extent, depth of cervical stromal invasion (CSI), and parametrial and nodal involvement; thus it overcomes FIGO limitations and is integral to the assessment of patient eligibility for conservative management of cervical cancer (47, 52–55).

Conservative Surgical Management

Fertility-sparing surgery starts with pelvic lymph node evaluation (pelvic lymphadenectomy or sentinel lymph node mapping), and, if no lymph node metastases are detected at frozen sections, continues with the resection of the cervix (cone resection, simple trachelectomy, or radical trachelectomy) (48, 56).

Cone resection or cone biopsy is an en bloc removal of the ectocervix and endocervical canal (47). Radical trachelectomy consists of cervical, vaginal cuff, and parametrial resection, followed by the creation of an isthmic vaginal anastomosis (Figure 3). Simple trachelectomy is similar to radical trachelectomy except parametrial resection is avoided. Intraoperative frozen sections are sent to confirm ≥ 1 cm tumor-free margin between the tumor and internal cervical os (minimum 0.5 cm for some centers) (56–58). Radical trachelectomy can be performed vaginally (Dargent's procedure) or abdominally using open, laparoscopic, or robot-assisted approaches. Cervical cerclage is placed to prevent premature delivery from cervical incompetence (59).

Stage IA1 tumors without lymphovascular space invasion (LVSI) are managed with cone biopsy alone (with negative margins). Stage IA1 tumors with LVSI or Stage IA2 tumors are approached with pelvic lymph node assessment and cone resection or radical trachelectomy. Stage IB1 tumors ≤ 2 cm are managed with pelvic lymph node assessment combined with cone resection or simple trachelectomy (if LVSI is absent) or radical trachelectomy (if LVSI is present) (48).

Fertility-sparing surgery is most validated for tumors ≤ 2 cm (47). Larger stage IB1 lesions (2–4 cm) have a higher risk of extra-cervical spread and increased likelihood of recurrence after radical vaginal trachelectomy (Dargent's procedure) (59). Therefore, these women are usually selected for abdominal radical trachelectomy or neoadjuvant chemotherapy plus conservative surgery (48, 60). Conservative management is considered unsafe for patients with Stage IB2 and Stage IIA1 disease (48).

Patient Eligibility Criteria and Role of MRI (Table 3 and Figure 4)

1. Tumor Characteristics—Patients should have confirmed invasive cervical cancer of squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma histology (47). Patients with small cell neuroendocrine tumors (aggressive behavior) and gastric type minimum deviation adenocarcinoma or adenoma malignum (rare and challenging to diagnose) are ineligible (47).

2. Tumor size 2cm (some centers accept 4 cm, particularly if tumor is exophytic)—Tumor size directly affects patient eligibility. MR imaging can accurately measure tumor size including cranio-caudal dimension, which presents a challenge at clinical examination.

On T2WI, cervical cancer appears as an intermediate-SI lesion that may disrupt low-SI cervical stroma (Figures 5 and 6) (61). On DWI, the tumor has high SI on high-b-value images and low SI on ADC maps relative to the cervical stroma (62). While DCE-MRI is not required for initial staging, small tumors may enhance earlier than adjacent stroma with most tumors being iso or hypointense on delayed images (37, 63, 64).

Tumor should be measured relative to the cervical axis with its size reported in three dimensions. On T2WI, the tumor size is reported to be within 0.5 cm of the surgical size in 70–90% of cases (65–67). Prior procedures can lead to overestimation secondary to edema, inflammation, and granulation tissue. The addition of DWI and DCE-MRI to T2WI may increase tumor conspicuity and aid the detection/size assessment of small tumors (32, 35, 37, 68).

Pattern of tumor growth may occasionally influence eligibility particularly in patients with larger tumors >2 cm (58). Therefore, the imaging report should indicate if the tumor is exophytic (grows outward and does not encroach on the endocervical canal), endophytic (grows inward along the endocervical canal), or a combination of both (61).

3. Tumor-to-internal os distance 1 cm (some centers accept 0.5 cm)—The ideal distance between the superior margin of the tumor and the internal os is 1 cm to allow for a 1 cm of healthy cervical stroma between internal os and surgical anastomosis (56). This maximizes local tumor control and increases the success of pregnancy by reducing the risk of cervical incompetence, ascending infection, and premature delivery. Some centers accept 0.5 cm as the minimum margin (57).

Tumor-to-internal os distance is difficult to assess clinically, but can be determined accurately on MRI (69). The internal os is seen as the waist of the uterine contour where low SI cervical stroma changes into intermediate SI myometrium (sagittal T2WI) and as the entrance of uterine vessels (axial or coronal oblique T2WI) (Figures 4 and 5). MRI excels at identifying patients who are unlikely to undergo successful fertility-sparing surgery because of close proximity of the superior tumor margin to the internal os (65, 69–71). In a recent study, all patients with tumor within 5 mm of internal os and 60% of patients with tumor within 6–9 mm of internal os required radical hysterectomy due to close surgical margin. In contrast, all patients with tumor-to-internal os distance of at least 1 cm underwent successful

fertility-preserving surgery (69). Thus, MRI can identify high-risk patients who may have a better chance at fertility preservation if managed with neoadjuvant chemotherapy plus conservative surgery approach. The addition of DWI and DCE-MRI to T2WI can aid the assessment of endocervical extent through enhanced conspicuity of tumor margins (32, 35, 37).

Some patients have had prior excisions. Cervical length, measured on sagittal T2WI from the internal to external os, should ideally be > 2.5 cm and minimum 2 cm (33, 72). If extra cone biopsy is contemplated, this information is important to avoid cervical incompetence and future preterm delivery.

4. Depth of cervical stromal invasion < 50% (some centers accept any degree of CSI)—Deep stromal invasion (invasion of outer third) is associated with a higher recurrence rate and shorter survival (73, 74). In patients considered for fertility preservation, it is preferable that the tumor involves less than half of stromal thickness. This criterion is not strictly enforced because clinical assessment is a challenge and MRI evaluation is imprecise (55, 69).

Stromal invasion is present when intermediate-SI tumor disrupts low-SI stroma (Figures 5 and 6) (61). When T2WI is used, the sensitivity for the detection of deep stromal invasion is moderate at best (ranging from 50 to 75%) probably because of the difficulty in differentiating tumor from postsurgical inflammation and edema (69). Literature suggests that DCE-MRI may aid the assessment because stromal invasion can appear as early focal enhancement within otherwise hypo-enhancing stroma (63, 64).

5. Absence of parametrial invasion—Tumor spread beyond the cervix is a contraindication to conservative surgery (56). MRI is superior to clinical examination for identifying parametrial invasion (54). On T2WI, the presence of an intact rim of low-SI stroma surrounding the cervical tumor virtually excludes parametrial invasion (6). Parametrial invasion is present if the tumor disrupts low-SI stroma either focally or diffusely, results in nodular or spiculated tumor-to-parametrial interface, or encases peri-uterine vessels (Figure 6) (75). Parametrial invasion may be overestimated occasionally due to post-procedural edema and inflammation.

6. Absence of lymph node metastases—Presence of nodal metastases is an important adverse prognostic factor with pelvic and para-aortic regions being most commonly involved (76). If intra-operative frozen sections from sentinel lymph node sampling or pelvic lymphadenectomy indicate metastatic lymph nodes, primary chemoradiotherapy is usually the optimal treatment approach (56, 59).

Size is the main imaging criterion to detect nodal metastases with 1.0 cm short axis diameter being the most commonly used threshold for both pelvic and para-aortic lymph nodes (52, 77). Other suspicious morphologic features include round shape, irregular borders, loss of fatty hilum, SI similar to primary tumor, and presence of necrosis (77). Similar to CT, conventional MRI has high specificity but only modest sensitivity for identifying nodal

metastases; this is primarily due to the inability to detect metastasis in normal-sized lymph nodes (52, 77).

Functional techniques (DWI, MRI enhanced with lymph-node specific contrast agents, and PET/MRI) may improve the detection of nodal metastases independent of size (78–81). Lymph nodes appear as discreet high SI ovoid structures on high b-value DWI increasing their conspicuity and facilitating detection. A recent meta-analysis suggests that DWI with ADC values may potentially increase sensitivity, but lack of standardized DWI protocols, overlap in ADC values of reactive and malignant nodes, and variability in ADC cut-off values limit applicability in daily clinical practice (79).

PET/MRI including PET/MRI-DWI is increasingly used in clinical practice, but both clinical applications and technical optimization are ongoing. This approach has the potential to provide a “one-stop-shop” evaluation of the primary tumor and lymph nodes (80, 81).

Part V: Fertility-Sparing Management of Endometrial Cancer

Endometrial cancer is the fifth most common cancer in women worldwide (82). It is the most common gynecologic cancer in developed countries and its incidence is increasing (1, 82). Although it presents most frequently in postmenopausal women, up to 7% of cases occur in patients younger than 45 years (83). The main risk factor is prolonged unopposed exposure to endogenous or exogenous estrogens (84). Younger patients are more likely to be obese, nulliparous, or have underlying conditions such as polycystic ovarian syndrome, all of which elevate endogenous estrogens (85, 86).

Endometrial cancer is often symptomatic early on and most patients are diagnosed at Stage I (tumor confined to the uterine corpus) (87). The standard management for apparently early stage disease is total hysterectomy and bilateral salpingo-oophorectomy (secondary to hormonal sensitivity of most endometrial cancer) with nodal assessment (sentinel lymph node mapping algorithm or pelvic $\pm$ para-aortic lymphadenectomy) (88, 89).

Conservative Medical Management

Fertility-sparing treatment is increasingly accepted as an alternative for young women who have disease limited to the endometrium and want to maintain their reproductive potential (88, 89). Patients should be counseled that conservative management is not a standard treatment and close follow-up is a must (88, 89). MRI is essential to confirm eligibility by excluding myometrial invasion and tumor extension beyond the uterine corpus (90).

Conservative treatment consists of progestins administered orally or via a levonorgestrel-coated intrauterine device (91, 92). Assessment of treatment response is performed at 6 and 9 months with dilation and curettage (D&C) and MRI (88, 89, 93). Approximately 75% of patients respond to therapy, but 30–40% recur (94–97). Responders at 6 months are encouraged to attempt immediate pregnancy that has the added benefit of decreasing the rate of recurrence (91, 95). Maintenance therapy for additional 6 months is offered to women who want to delay pregnancy (91). Non-responders at 9 to 12 months and those who recur after initial response should be referred for total hysterectomy (91). Ovaries may be

preserved in selected cases, i.e., patients younger than 45 years with no genetic predisposition for ovarian cancer such as BRCA mutation or Lynch Syndrome (89).

After completion of child bearing, patients should undergo total hysterectomy due to the high risk of recurrent endometrial cancer (88, 89).

Patient Eligibility Criteria (All Must Be Satisfied) and Role of MRI (Table 4)

1. Tumor and Patient Characteristics—Patients must have a well-differentiated (FIGO grade 1) endometrioid adenocarcinoma or premalignant conditions (atypical hyperplasia or endometrial intraepithelial neoplasia) (88, 89). Histologic characteristics must be obtained by D&C since this approach is more accurate than pipelle biopsy for the assessment of tumor grade (98).

Testing for Lynch Syndrome is advised for all women with endometrial cancer, particularly patients younger than 50 years who have significant family history of endometrial and/or colorectal cancer, or patients who have suspicious pathologic features at immunohistochemistry or microsatellite instability screening (88). It is controversial whether conservative management is appropriate for women with Lynch Syndrome because the predisposing factor is genetic (mutations in DNA mismatch repair genes), and hormonal therapy may be ineffective (91).

2. Endometrium-confined disease

○ **Absence of any myometrial invasion:** MRI is critical to confirm that tumor is confined to the endometrium (Figure 7). On T2WI, endometrial cancer has the same or lower SI than the normal endometrium and stands out against low SI inner myometrium (junctional zone, JZ) (99, 100). On DCE-MRI, most tumors enhance homogeneously, as well as slower and less intensely than the myometrium, with peak myometrial enhancement and maximal tumor-to-myometrium contrast occurring about 90–120 seconds after intravenous administration of contrast medium (101, 102). On DWI, tumor has high SI on high-b-value images and low SI on ADC maps relative to the myometrium (103–106).

Diagnostic clues that are useful to confirm endometrium-confined disease include uninterrupted low-SI band of JZ on T2WI and a continuous rim of sub-endometrial enhancement (SEE, thin layer of early enhancement of inner JZ) on DCE-MRI acquired within first minute of intravenous administration of contrast medium (100, 101, 107). If SEE is not present, the inner surface of the enhanced myometrium should be smooth and sharply demarcated (Figure 7) (101).

Recent data suggest that DWI is also highly accurate for assessing the presence and depth of myometrial invasion (105, 106, 108, 109). DWI alone does not provide sufficient anatomic detail and is best interpreted in conjunction with T2WI (Figure 7). In fact, fused images (T2WI + DWI) are superior to DCE-MRI alone or T2+DCE-MRI for detecting any myometrial invasion (105). Thus, a combination of T2WI + DWI + DCE-MRI is recommended in routine clinical practice for the most comprehensive and accurate assessment (6).

Several pitfalls exist. First, myometrial invasion may be under- or overestimated in the presence of leiomyomas and adenomyosis which distort normal uterine zonal anatomy (36). Second, myometrial invasion may be overestimated in the uterine cornua, where the myometrium is thinner than elsewhere in the uterus. Third, some tumors enhance similar to the myometrium. Lastly, peri-tumoral enhancement (early irregular enhancement around the tumor) can disrupt SEE and falsely indicated myometrial invasion (107). These pitfalls may be avoided or diminished if T2WI, DWI, and DCE-MRI are interpreted in conjunction with each other (38, 107, 108, 110).

○ **Absence of cervical stromal invasion:** Infiltration of the cervical stroma (Stage II) is associated with a higher risk of lymph node metastases and adverse prognosis (111, 112). On T2WI, cervical stromal invasion is suspected when intermediate-to-high-SI tumor disrupts low-SI cervical stroma (100). On DCE-MRI, stromal invasion is suggested when hypo-enhancing tumor interrupts continuous enhancement of cervical epithelium ($\pm$ stoma), best seen 1.5 to 4 minutes after intravenous administration of contrast medium (100, 113). Both T2WI and DCE-MRI suffer from modest sensitivity with false positive findings observed when the tumor distends endocervical canal. On the other hand, a recent report suggests that DWI is both highly sensitive and more accurate than either T2WI or DCE-MRI (114). The absence of cervical stromal invasion is indicated by the smooth tumor-cervical stromal interface on high b-value images.

○ **Absence of synchronous primary ovarian cancer or ovarian metastases:** In approximately 10% of cases endometrial cancer may manifest with synchronous primary ovarian cancer or metastasis to the ovaries (115–118). The detection and differentiation between the two entities are critical for patient management and prognostication (117). Recent studies using targeted gene panels suggest that the majority of ovarian cancers in patients with endometrial cancer are in fact metastases to the ovaries (119, 120). Young women with ovarian involvement from either cause are not amenable to conservative management.

Careful MR imaging assessment of both adnexa is crucial if fertility-sparing management is being contemplated. Ovaries should be inspected for signs of malignancy as discussed further in Part VI of this manuscript. The distinction between synchronous primary ovarian carcinoma versus metastasis is an ongoing challenge at imaging (121). The presence of a large endometrial tumor and a small ovarian lesion may favor metastasis, whereas a small endometrial tumor and a large unilateral complex ovarian mass $\pm$ endometriosis raises the possibility of a synchronous primary ovarian malignancy (121).

○ **Absence of lymph node metastasis:** Lymph node metastases are rare in early-stage endometrial cancer (84, 89, 122, 123). When they occur, the most common sites of involvement are pelvic and para-aortic nodal regions. MRI assessment of lymph node status in endometrial cancer parallels and faces similar challenges as that of cervical cancer (124).

Part VI: Fertility-Sparing Management of Ovarian Tumors

Most ovarian cancers manifest in postmenopausal women as advanced-stage disease. However, a substantial subset occurs in reproductive age women, with the incidence rising with age (125). Majority of ovarian malignancies in young women are germ cell tumors and epithelial borderline tumors, with invasive epithelial ovarian cancers and sex-cord stromal tumors being less common (126, 127).

Conservative Management

Surgery is the cornerstone of the initial management of ovarian tumors. The goals are to resect the ovarian tumor to attain accurate histologic diagnosis, comprehensively stage apparently early stage disease, or cytoreduce advanced-stage disease (128). Preoperative imaging can aid the characterization, map the extent of disease, and guide surgical approach (i.e. laparoscopy versus laparotomy) (128). The review of intraoperative frozen-sections by an expert gynecologic pathologist is invaluable to tailor surgical procedures based on the histologic information. Fertility-sparing surgery, defined as unilateral salpingo-oophorectomy (USO) with preservation of the uterus and contralateral ovary, is possible for most young women who desire future fertility and have any stage malignant germ cell tumors, sex-cord stromal tumors, borderline tumors or have early stage epithelial carcinomas (129–133).

Malignant germ cell tumors—Five percent of germ cell tumors are malignant; the rest are benign mature cystic teratomas. Malignant germ cell tumors manifest in very young women (younger than 20 years) and are the most common ovarian malignancy in this age group (Figure 8, and Figure 9) (127). Dysgerminomas and immature teratomas are the most frequent, followed by yolk sac and mixed tumors (134). Most patients present with Stage I (ovary-confined) disease and have >90% 5-year overall survival; even advanced-stage disease has a good prognosis due to high chemosensitivity making fertility preservation possible (135).

Conservative surgery for malignant germ cell tumors is considered appropriate regardless of histologic subtype and FIGO stage (129, 130). USO is combined with comprehensive peritoneal staging. Advanced-stage disease is debulked although extensive resections are avoided due to chemo-responsiveness. Lymphadenectomy can be omitted if lymph nodes are macroscopically normal (129). Adjuvant platinum-based chemotherapy is advised for most malignant germ cell tumors; exceptions are Stage I pure dysgerminoma and well-differentiated Stage I immature teratoma (129, 130).

Sex-cord stromal tumors—Most malignant sex-cord stromal tumors are comprised of granulosa cell tumors (70%) and Sertoli-Leydig tumors (132). Granulosa cell tumors (GCTs) are subdivided into adult (95%) and juvenile (5%) types. Adult type manifests mostly in perimenopausal women, whereas juvenile type predominates in pre-pubertal girls. Sertoli-Leydig tumors affect women younger than 30 years and are the most common androgen-producing ovarian tumors (with 30% being hormonally active) (Figure 10) (136). The majority of sex-cord stromal tumors are unilateral and ovary-confined at diagnosis with >90% 5-year overall survival rate for Stage I disease (132). Fertility-sparing surgery for

patients with sex-cord stromal tumors is similar to that of malignant germ cell tumors (129, 130, 137). Endometrial curettage is mandatory in patients with granulosa cell tumors to rule out synchronous endometrial carcinoma (secondary to estrogen excess production by the tumor) (129). Adjuvant platinum-based chemotherapy is considered for patients with either high-risk Stage I disease or Stage > I disease (129, 132).

Borderline ovarian tumors—Borderline ovarian tumors commonly manifest in premenopausal women (average age: 38 years) (138). Serous followed by mucinous borderline tumors are the most common histologic subtypes (139). While most mucinous borderline tumors are confined to a single ovary at presentation, serous borderline tumors may involve both ovaries (15–40%), develop peritoneal implants (35%), and at times involve lymph nodes (Figure 11) (139). Young women with borderline tumors are amenable to fertility-sparing surgery regardless of FIGO stage as long as there are no invasive peritoneal implants (i.e., low-grade serous ovarian cancer). Unilateral serous borderline tumors are approached with ovarian cystectomy or USO. Mucinous borderline tumors require USO due to their large size and to exclude intra-epithelial carcinoma (140–143) (144). Bilateral serous borderline tumors are managed with bilateral cystectomy or combined USO and contralateral cystectomy (140). These procedures are combined with appendectomy (if mucinous histology) and comprehensive peritoneal staging to exclude low-grade serous ovarian cancer (which is a contraindication to conservative fertility-sparing management).

Epithelial ovarian cancers—Epithelial ovarian cancers are most common in postmenopausal women; however, around 12% of cases manifest in women younger than 45 years (125). Most patients present with advanced staged disease making these the most lethal of all gynecologic cancers (1). Young women with early stage disease and a strong desire for fertility may be offered fertility-sparing management. Patients with unilateral ovarian involvement (Stage IA or IC disease) and favorable histology (serous, mucinous, endometrioid, or mixed histologic subtypes) or Stage IA clear cell carcinoma (less favorable histology) may be candidates for USO plus comprehensive peritoneal staging and lymphadenectomy. Adjuvant platinum-based chemotherapy is required for Stage IA clear cell carcinoma and Stage IC tumors (131, 133). Bilateral ovarian involvement (Stage IB) and extra-ovarian spread preclude conservative management (131, 133).

General diagnostic approach based on clinical and imaging data

Patients with concerning symptoms and/or pelvic mass undergo pelvic ultrasonography and assessment of serum tumor markers (serum human chorionic gonadotropin (hCG), α -fetoprotein (AFP), lactate dehydrogenase (LDH), inhibin, and CA-125) (128, 145–148). Elevation of these markers can aid diagnosis; normal levels don't rule out ovarian tumor. Elevated AFP or hCG are virtually diagnostic of malignant germ cell tumors (134). CA-125 can be raised with epithelial tumors (both borderline and invasive types), although non-neoplastic conditions including endometriosis, pelvic inflammatory disease, and uterine leiomyoma may also cause nonspecific elevation. Inhibin may serve as a useful marker of granulosa cell tumor (132).

Pelvic ultrasonography is the best imaging modality for the initial assessment of a suspected adnexal mass. When sonographic findings are suspicious for malignancy, a patient should be referred to a gynecologic oncologist and undergo staging CT, which is the current standard of care. Preoperative CT helps surgical planning by demonstrating the extent of disease including unilateral or bilateral ovarian involvement, presence and distribution of peritoneal implants, lymphadenopathy and distant metastases.

Up to 25% of adnexal mass cannot be characterized with US as definitely benign or definitely malignant (146, 147). In this setting, MRI is the most accurate and cost-effective imaging modality (7, 149). In addition to lesion characterization, MRI shows the presence of preserved ipsilateral ovarian tissue (important if cystectomy is being considered), evaluates contralateral ovary, detects and maps peritoneal implants, and demonstrates enlarged lymph nodes facilitating clinical decision-making with regard to fertility-sparing surgery.

The European Society of Uroradiology has recently proposed an updated step-by-step algorithmic approach to assist the interpretation of multi-parametric MRI acquired to characterize sonographically indeterminate adnexal masses (Figure 12) (27). This approach helps to characterize adnexal masses as probably-definitely benign, probably-definitely malignant, or indeterminate (40). It relies on the evaluation of lesion origin, morphology and SI on conventional sequences (T1WI, FST1WI, T2WI), SI on high b-value DWI (800 sec/mm²), and enhancement characteristics/kinetics on DCE-MR (27).

In the first step, conventional T1WI and T2WI are reviewed to divide adnexal masses into one of three broad categories: T1 “bright” masses, T2 solid masses, and complex cystic or cystic-solid masses (27, 28). T1 “bright” masses require further assessment with fat saturated T1WI to differentiate fat from blood. If fat is observed within adnexal mass (high SI on TWI that suppresses after fat saturation), the differential diagnosis is narrowed to frequent mature cystic teratoma or rare malignant immature teratoma. Mature teratoma often presents as a cystic mass filled with fatty sebaceous fluid and may contain coarse tooth-like calcifications (best seen on CT) allowing confident diagnosis of a benign mass (134). In contrast, immature teratoma is typically a solid-cystic mass with small foci of fat, cysts filled with simple fluid, and scattered fine calcifications (best seen on CT) (134).

If a T1 “bright” mass contains blood products (high SI on T1WI that persists after fat saturation) and demonstrates no solid components, the differential diagnosis can be narrowed to benign entities such as a hemorrhagic cyst or endometrioma. If solid components are detected within a T1 “bright” mass further evaluation is performed as for a complex cystic/cystic-solid mass (described below) (27).

If a T2 solid mass is identified, the most likely origin (i.e. ovarian, uterine, or other) should be determined. Findings suggestive of ovarian origin are the ovarian beak sign and absent normal ipsilateral ovary. Features indicative of uterine origin are the uterine claw sign, “bridging vessel” sign (if pedunculated leiomyoma), and normal ipsilateral ovary (27).

T2 solid masses are divided further into homogenous T2 “dark” masses (SI similar to that of skeletal muscle) or heterogeneous T2 “intermediate” masses (SI higher than that of skeletal muscle). If a homogenous T2 dark mass has low SI on high b-value DWI, benign etiology

(ovarian fibroma or cystadenofibroma) is likely (27, 42). Heterogeneous T2 “intermediate” masses present a diagnostic challenge since differential diagnosis is broad and includes a variety of benign and malignant entities. Although confident diagnosis is not always possible, knowledge of patient age and serum tumor markers in combination with key MR imaging features can be useful. For example, dysgerminoma (most common malignant germ cell tumor) is suggested by young patient age, elevated LDH $\pm$ HCG, and heterogeneous T2 “intermediate” mass that contains fibro-vascular septa with low SI on T2WI and avid enhancement (134).

Purely cystic lesions or cystic lesions with few thin septa can be confidently diagnosed as benign (40). In contrast, complex cystic and cystic-solid masses require comprehensive assessment utilizing conventional sequences, DWI, and contrast-enhanced imaging (preferably DCE-MRI). This group includes adnexal masses caused by infection (pelvic inflammatory disease) and ovarian tumors including borderline tumors and invasive ovarian cancers (27, 28).

MR imaging features of overtly malignant ovarian masses are well established and include mixed cystic-solid mass, irregular or nodular thick septa and walls, intermediate SI solid components on T2WI, high SI on high b-value DWI, and contrast enhancement (40, 42, 149–151). The distinction between borderline and invasive tumors is an important and clinically relevant issue because epithelial ovarian cancer is amenable to conservative management only if confined to a single ovary whereas borderline tumors, particularly serous histology, are amenable to fertility-preservation even in the presence of bilateral ovarian involvement and peritoneal spread (130). Unfortunately, this differentiation presents an ongoing diagnostic challenge since these tumor types can have overlapping MR features such as a cystic-solid mass with intermediate SI solid component(s) on T2WI and contrast enhancement.

The presence of papillary projections (enhancing solid finger-like projections) is one architectural feature that is common to serous borderline tumors and suggests the diagnosis (152). On T2WI, papillary projections range from small low-to-intermediate SI lesions to larger lesions with characteristic internal branching low SI fibrous stalk and high SI peripheral clumps (Figure 11) (152). Emerging evidence also indicates that addition of DWI and DCE-MRI may facilitate the differentiation between borderline and invasive tumors. On DWI, solid components of borderline tumor have lower-SI on high b-value images and higher mean ADC values than invasive tumor (153). On DCE-MRI acquired using perfusion technique (as described in Part III), moderate initial enhancement followed by a plateau (Type 2 curve) may indicate borderline tumors, whereas rapid intense early enhancement with subsequent washout (Type 3 curve) may suggest malignant mass (27, 39–42). However, the advantage of perfusion imaging over traditional dynamic multiphase approach remains to be proven.

Conclusion

Fertility-sparing approaches are now included in various treatment guidelines (including ESMO and NCCN) and are increasingly accepted as safe for appropriately selected

reproductive age women with gynecologic cancer. MRI plays an important role in preoperative workup and proper selection of patients who are being considered for conservative fertility-sparing management of cancer. Radiologists should be familiar with various fertility-sparing options and their eligibility criteria in order to provide comprehensive and clinically relevant imaging reports and to serve as effective consultants for their clinical colleagues.

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Abbreviations

ADC Apparent Diffusion Coefficient

D & C	Dilation and Curettage
DCE-MRI	Dynamic contrast-enhanced MRI
DWI	Diffusion-weighted Imaging
ESMO	European Society for Medical Oncology
ESUR	European Society of Urogenital Radiology
FDG	Fluorodeoxyglucose
FIGO	International Federation of Gynecology and Obstetrics
FST1WI	Fat saturated T1WI
JZ	Junctional Zone
LVSI	Lymphovascular Space Invasion
MRI	Magnetic Resonance Imaging
NCCN	National Comprehensive Cancer Network
OHSS	Ovarian Hyperstimulation Syndrome
PET/CT	Positron Emission Tomography-Computed Tomography
PET/MRI	Positron Emission Tomography-Magnetic Resonance Imaging
USO	Unilateral Salpingo-oophorectomy
ROI	Region of Interest
SEE	Subendometrial Enhancement
SI	Signal Intensity
T1WI	T1-weighted Images
T2WI	T2-weighted Images
US	Ultrasonography

Figure 1.

31-year-old woman with cervical cancer and ovarian hyperstimulation. A. A drawing shows the spoke-wheel appearance of hyperstimulated ovaries with multiple peripheral cysts centered on ovarian stroma. B. Axial T1WI shows symmetrically enlarged bilateral ovaries with low SI cysts; some cysts contain high SI blood products (white arrow). C. Axial oblique T2WI shows symmetrically enlarged bilateral ovaries with high SI cysts peripherally and edematous stroma centrally (black arrow); some cysts contain low SI foci due to blood products (white arrow). Note the small volume ascites (white arrowhead) and primary cervical tumor (black arrowhead). D. Axial oblique contrast-enhanced image shows symmetrically enlarged ovaries. Ovaries contain peripheral cysts (black arrow) with wall enhancement and enhancing central stroma. Note the absence of enhancing nodular septa or nodules. Primary cervical tumor is also seen (black arrowhead).

Figure 2.

A. Drawing depicts common transposition locations for the ovaries. B. 48-year-old woman with cervical cancer who underwent ovarian transposition and definitive chemoradiation. Axial T2WI demonstrates transposed left ovary that re-migrated down into the pelvis (white arrow). It contains a dominant follicle, and is surrounded by a peritoneal inclusion cyst (black arrow). Transposed right ovary is not illustrated on this image. C and D. 32-year-old woman with cervical cancer and ovarian transposition prior to definitive chemoradiation. C. Coronal T2WI shows transposed ovaries in lower paracolic gutters (white arrows). D. Composite axial FDG-PET/CT image in the same patient demonstrates physiologically increased FDG uptake in the transposed right ovary (white arrow) and no increased FDG uptake in the transposed left ovary (white arrowhead).

Figure 3.

A. Drawing portrays cone biopsy/resection (en bloc resection of ectocervix and endocervical canal) and vaginal/abdominal radical trachelectomy (resection of cervix, adjacent parametria and a cuff of the upper vagina). B. The remaining uterus is anastomosed to the vagina with a resultant isthmic vaginal anastomosis.

Figure 4. Drawings illustrate the location of the internal os seen as the waist of the uterine contour where low SI cervical stroma changes to intermediate SI myometrium (A) and as the entrance of uterine vessels (B).

Figure 5.

31-year-old woman with Stage IB1 cervical cancer. A. Sagittal T2WI demonstrates endophytic intermediate-SI tumor (white arrow). The tumor borders are obscured by post-cone resection changes making it challenging to accurately determine tumor size and endocervical extent. B and C. The tumor margins (white arrow) are more clearly defined on DWI and contrast-enhanced images, respectively, facilitating assessment of tumor size (2 cm in maximum dimension) and extent (1 cm caudal to internal os). D and E. Axial oblique and coronal oblique T2WI illustrate the location of internal os marked by the entrance of the uterine vessels (white arrows). F. Sagittal T2WI in the same patient after radical trachelectomy shows the normal appearing uterine remnant and isthmic vaginal anastomosis (white arrow).

Figure 6.

37-year-old woman with Stage IB1 cervical cancer. A. Sagittal T2WI demonstrates 2.7 cm endophytic intermediate-SI tumor (white arrow). B and C. Axial oblique T2WI and fused (T2WI + DWI) images, respectively, show tumor extension to the internal os and left parametrial invasion (black arrows). The internal os is demarcated as the entrance of the uterine vessels (white arrows).

Figure 7.

40-year-old woman with new onset menorrhagia and D&C demonstrating FIGO grade 1 endometrioid adenocarcinoma. A and B. Sagittal and axial oblique T2WI demonstrate intermediate-SI tumor in the endometrial cavity and preserved smooth interface between the tumor and low-SI junctional zone (white arrows). C and D. Sagittal and axial oblique fused (T2WI + DWI) images confirm smooth interface between the tumor and junctional zone (white arrows). E and F. Sagittal early (E) and delayed DCE-MRI (F) images show intact band of junctional zone enhancement (black arrows) and smooth tumor-to-myometrium interface (black arrow), respectively.

Figure 8.

23-year-old woman with dysgerminoma who presented with low back pain and elevated serum LDH and β -HCG. A and B. Axial and sagittal T2WI show solid intermediate-SI adnexal mass with low-SI fibrovascular septa (white arrows). C and D. Axial DWI and ADC map demonstrate diffusion restriction. E. Axial contrast-enhanced image shows solid enhancing adnexal mass with avidly enhancing fibrovascular septa (black arrows).

Figure 9.

13-year-old teenager with immature cystic teratoma who presented with lower abdominal pain and no elevation in serum tumor markers. A and B. T1WI and FST1WI demonstrate left adnexal mass with small high-SI focus (white arrow) on T1WI (A) which becomes low-SI on FST1WI (white arrow) (B). C, D, and E. Axial T2WI, fused (T2WI + DWI), and contrast-enhanced images show complex predominantly cystic left adnexal mass with multiple cystic components and thickened and/or nodular septations with restricted diffusion and enhancement F. The same patient presented several years prior with right adnexal mass. Sagittal contrast-enhanced CT image obtained at that time shows a large cystic-solid right

adnexal mass with several small foci of fat (white arrow) and small scattered calcifications (black arrow).

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Figure 10.

25-year-old woman with Sertoli-Leydig tumor who presented with pelvic discomfort and elevated serum testosterone. A. Axial T2WI shows intermediate-SI predominantly solid mass with few small cystic areas. B and C. Axial fused (T2WI + DWI) and ADC images demonstrate diffusion restriction within the solid portion of the mass. D. Axial contrast-enhanced image shows enhancement within the solid portion of the mass.

Figure 11.

20-year-old woman with bilateral serous borderline ovarian tumors who presented with lower abdominal pain and elevated serum CA-125 level. A. Axial T2WI of the right adnexa shows cystic and solid right adnexal mass with large branching papillary projections (black arrow) extending into the pouch of Douglas. B. Axial T2WI of the left adnexa shows small cystic lesion with small intermediate-SI papillary projections (black arrow). C and D. Axial fused (T2WI + DWI) images demonstrate restricted diffusion within papillary projections (white arrows). E and F. Axial contrast-enhanced images show enhancement within these papillary projections (white arrows).

Figure 12.

A diagram illustrates an algorithmic approach to the characterization of sonographically indeterminate adnexal masses using multi-parametric MRI. This approach is based on the recently updated ESUR guidelines (27).

Table 1

General Eligibility Considerations in Identifying Suitable Candidates for Fertility Preservation (adapted from reference [8])

✓ Appropriate cancer stage
✓ Desire to preserve fertility
✓ Reproductive age (upper age limit varies from 40 to 45 years)
✓ No known significant impairments to fertility
✓ Patient compliance with treatment and follow-up

Table 2

Tailored MR Imaging Protocols for the Initial Work-Up of Gynecologic Cancers and Adnexal Lesions

Patient Preparation, Positioning, and Coil Selection				
<ul style="list-style-type: none"> ✓ Fast 4–6 hours before ✓ Empty the bladder ✓ Anti-peristaltic agent administration (IM or IV) ✓ Supine position ✓ 1.5-Tesla magnet ✓ Multi-channel phase-array receiver coil ✓ Optional <ul style="list-style-type: none"> ○ Endovaginal receiver coils for small cervical lesions ○ Vaginal opacification with gel for cervical cancer 				
Tailored MR Imaging Protocols				
✓ Large FOV T1WI ±T2WI	• From the top of the kidneys to the iliac crests (Upper abdomen)			
✓ T1WI without and with fat saturation	• Pelvis, Axial plane			
	Cervical cancer	Endometrial cancer	Adnexal mass	
✓ High-resolution small FOV T2WI	<ul style="list-style-type: none"> • Sagittal plane • Axial oblique plane perpendicular to the endocervical canal) • Optional: Coronal oblique plane (parallel to the endocervical canal) 	<ul style="list-style-type: none"> • Sagittal plane • Axial oblique plane perpendicular to the endometrial cavity) 	<ul style="list-style-type: none"> • Sagittal plane • Axia plane • Axial oblique plane (ovarian axis) 	
✓ DWI and ADC map	<ul style="list-style-type: none"> • Sagittal plane • Axial oblique plane in the same orientations as axial oblique T2WI • Optional: Coronal oblique DWI (parallel to the endocervical canal) 	<ul style="list-style-type: none"> • Sagittal plane • Axial oblique plane in the same orientations as axial oblique T2WI 	<ul style="list-style-type: none"> • Axial plane 	
✓ DCE-MRI	<ul style="list-style-type: none"> • Useful for assessment of small tumors • DCE-MRI: Sagittal plane • Delayed CE: Axial oblique plane 	<ul style="list-style-type: none"> • DCE-MRI: Sagittal plane • Delayed CE: Axial oblique plane 	<ul style="list-style-type: none"> • Axial plane 	

Abbreviations: IM = intramuscular, IV = intravenous, MR = magnetic resonance, FOV = field of view, T1WI = T1-weighted Images, T2WI = T2-weighted Images, DWI = Diffusion Weighted Imaging, ADC = Apparent Diffusion Coefficient, DCE-MRI = Dynamic Contrast-Enhanced MRI, CE = Contrast Enhancement

Table 3**Cervical Cancer: Eligibility Criteria For Fertility-Sparing Management**

Tumor Characteristics	
✓ Invasive squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma	
○ <i>Not eligible:</i> Small cell neuroendocrine tumor or gastric type minimum deviation adenocarcinoma	
Criteria Evaluated at MRI	
✓ Tumor size ≤ 2 cm	
(Some centers accept tumor size ≤ 4 cm, particularly if exophytic)	
✓ Tumor-to-internal os distance ≥ 1 cm	
(Some centers accept ≥ 0.5 cm)	
✓ Cervical stromal invasion (CSI) < 50%	
(Some centers accept: any degree of CSI)	
✓ Absence of parametrial invasion	
✓ Absence of lymph node metastases	

Table 4

Endometrial Cancer: Eligibility Criteria For Fertility-Sparing Management (All Criteria Must Be Met)

Tumor Characteristics	
✓	Well-differentiated (FIGO Grade 1) endometrioid adenocarcinoma (by D&C)
✓	Premalignant conditions <ul style="list-style-type: none"> ◦ Atypical hyperplasia ◦ Endometrial intraepithelial neoplasia
Patient Characteristics	
✓	No contraindications to progestins
Criteria evaluated at MR Imaging	
✓	Disease confined to the endometrium: <ul style="list-style-type: none"> ◦ Absence of any myometrial invasion ◦ Absence of cervical stromal invasion ◦ Absence of synchronous primary ovarian cancer or ovarian metastases ◦ Absence of lymph node metastases

Abbreviations: FIGO = FIGO - The International Federation of Gynecology and Obstetrics, D&C = dilation and curettage, MR = magnetic resonance