Magnetic Resonance Imaging of Benign and Malignant Uterine Neoplasms

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Benign and malignant uterine masses can be seen in the women. Some of these are asymptomatic and incidentally discovered, whereas others can be symptomatic. With the soft tissue contrast resolution magnetic resonance imaging can render a definitive diagnosis, which can further help streamline patient management. In this article we show magnetic resonance imaging examples of benign and malignant masses of the uterus and their treatment strategies.

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Introduction

A myriad of tumors occur in the uterus. In this article we will discuss the benign and malignant uterine tumors, with a focus on magnetic resonance imaging (MRI) features, pathology, and treatment.

Benign

Fibroids

Uterine fibroids (leiomyomas or myomas) are the most common pelvic tumors in women, seen predominantly in African-Americans.¹⁻³ Fibroids appear, grow, and regress during life, especially during reproductive age, pregnancy, and postpartum period, and are seen in 35% of menstruating women.²⁻³ Associated risk factors include early menarche age, nulliparity, old age at first pregnancy, obesity, diabetes, hypertension, and family history. Although generally asymptomatic, fibroids may cause abnormal bleeding, pelvic pain, pressure, and infertility, which often reduce or disappear after menopause.²

Fibroids arise from uterine smooth muscle myometrium, composed of disordered smooth muscle cells and abundant extracellular matrix. Grossly, fibroids vary in size and number.¹⁻² They are classified as (1) submucosal (adjacent to or in the uterine cavity), (2) intramural (entirely within the myometrium), and (3) subserosal (distort the outer contour or surface of the uterus). Moreover, subserosal and submucosal fibroids can be pedunculated (attached to the uterus by a stalk), extending from the external uterine surface or within the uterine cavity (intracavitary); pedunculated fibroids can rarely tors, leading to infarction (Fig. 1).³⁻⁵

The myometrium, exposed to repeated hormonal influences during reproductive years, is vulnerable to mutations. In fact, the single-gene somatic defect (MED12 mutation) is seen in most fibroids. Chromosomal rearrangements are often complex and diverse, explaining the variable growth, dormancy, and regression, and also the heterogeneous response to medical therapy. Fibroids commonly undergo degeneration, particularly if they outgrow their blood supply. Types of degeneration include hyaline, myxoid, cystic, red (carneous or hemorrhagic), and sarcomatous.¹⁻²

MRI is the most accurate imaging technique for fibroid detection and localization. Nondegenerated fibroids classically appear as well-defined, rounded homogeneous masses, with decreased T2-weighted signal intensity and intermediate T1-weighted signal intensity compared with normal myometrium. Cellular fibroids (with more cellular compound and less extracellular matrix) have high T2 signal intensity and greater enhancement.¹⁻⁴ Some fibroids have a rim of T2 hyperintensity related to dilated lymphatics, veins, or edema that may
It should be noted that this T2 signal is not considered degeneration.

The presence of degeneration may alter the appearance of the fibroid in MRI. Hyaline degeneration is the most common, occurring in more than 60% of the fibroids. On MRI, hyalinization within the fibroid is characterized by diffuse decreased T2 signal. Cystic degeneration, found in 4% of fibroids, is seen on MRI as well-defined areas of internal fluid (high T2 signal intensity, Fig. 3). Myxoid degeneration represents cystic foci of gelatinous material, either abundant or interspersed between smooth muscle cells. On MRI, myxoid degeneration also shows low T1 signal and high T2 signal intensity, but in postcontrast images it may have minimal enhancement around the mucinous lakes or clefts (Fig. 4). Red degeneration is related to massive hemorrhagic infarction, resulting in coagulative necrosis, and it is most often found during pregnancy or is related to oral contraceptives. On MRI, red degeneration has variable signal intensity, with diffuse T1 hyperintensity and variable T2 signal intensity or even a peripheral halo of T1 hyperintensity and T2 hypointensity. Calcifications are found in 4% of fibroids and appear as hypointense, nonenhancing areas on all MRI sequences.
Lipoleiomyomas, rare and seen only in 0.8% patients, are thought to reflect a variant of fibroids containing macroscopic fat. On MRI, these tumors follow fat signal on all sequences, characterized by T1 and T2 hyperintensity, signal loss on fat-saturated sequences, and India ink artifact on out-of-phase imaging (Fig. 5). Currently, there are no reliable imaging criteria for accurate diagnosis of degeneration into or de novo leiomyosarcoma.

Rare and unusual fibroid growth patterns, such as atypical extraterine locations and aggressive invasive growth, have been described: intravenous leiomyomatosis (growth into veins); metastasizing leiomyoma (spread to distant organs, especially lung); diffuse leiomyomatosis (diffuse growth throughout the uterine parenchyma, usually innumerable small nodules symmetrically enlarging the uterus); peritoneal disseminated leiomyomatosis (dissemination throughout the peritoneal cavity); retroperitoneal leiomyomatosis (growth in the retroperitoneum, usually broad ligament); and parasitic leiomyomatosis (when a pedunculated leiomyoma loses its connection by torsion and attaches to other structure with parasitic vessels).

Therapeutic approaches for uterine fibroids include expectant management, medical treatment, surgery (myomectomy or hysterectomy), uterine artery ligation or uterine artery embolization (UAE), and high-intensity focused ultrasound ablation. Management depends on many factors, including fibroid size; number and location, as well as the presence of symptoms; patient age; and childbearing desire. Hysterectomy is the definitive treatment of fibroids, though minimally invasive procedures such as embolization and ablation are becoming useful, uterine-sparing alternatives.

MRI is important in pretreatment and posttreatment fibroid evaluation. For example, cervical fibroids may not respond to UAE because of alternate blood supply; nonenhancing fibroids are also less likely to respond. Treatment of pedunculated fibroids should be avoided particularly if the stalk is less than 2 cm, as they can detach after treatment. Following therapy, a decrease in uterine and fibroid volume and coagulative...
necrosis of fibroids indicate response (Fig. 6). On MRI, treated fibroids become smaller, with well-defined T1 signal of increased intensity, and more homogeneous T2 signal without enhancement in the intensity. Continued growth after treatment raises a concern of malignancy.3

**Polyps**

Endometrial polyps, seen in 10%-40% of women, are the most common pathologic lesions of the uterine corpus.9 They often present with abnormal premenopausal or postmenopausal bleeding.10

Endometrial polyps are benign localized overgrowths of the endometrium; they consist of stroma of dense fibrous tissue or smooth muscle cells, thick-walled vessels, and endometrial glands.9,11 The endometrial polyps vary in size and can be multiple in 20% of the cases. Patients treated with tamoxifen have an increased incidence (8%-36%) of polyps.11,12 Most polyps are small and incidental, but can be associated with endometrial hyperplasia and carcinoma.9,10,12

On MRI, polyps are generally well-circumscribed (70%), isointense on T1 signals, and hypointense on T2 signals (80%) relative to normal endometrium.11 Polyps typically have rapid early and persistent enhancement or gradually increasing enhancement, though the degree of enhancement varies with respect to the outer myometrium (strong = 17.5%, moderate = 52.5%, and weak = 30%).11 In few cases, a stalk can be seen, particularly when outlined by intracavitary fluid (Fig. 7).9,12,13

Polyps can also have a central fibrous core (low T2 signal intensity), intratumoral cysts (discrete smooth-walled cystic structure of high T2 signal intensity), and hemorrhage (high T1 signal intensity), described by Hase et al11 in 75%, 55%, and 35%, respectively.9,11 Central fibrous core and intratumoral cysts favor benign polyps, whereas endometrial invasion, necrosis, and irregular internal "cystic" areas suggest endometrial cancer.9 Polyps, in contrast to endometrial cancer, typically enhance avidly.11,14 Polyps demonstrate less restricted diffusion than malignant lesions; Fujii et al15 reported a mean apparent diffusion coefficient value of 1.44 ± 0.34 for benign lesions and 0.98 ± 0.19 for malignant lesions with an accuracy of 92%.15-18

Endometrial polyps are typically removed to alleviate symptoms and to evaluate for atypical hyperplasia or carcinoma or both.10,12 The risk of malignancy is related to polyp size and patient age. In the past, treatment was hysterectomy, but today, minimally invasive procedures such as hysteroscopic polypectomy, endometrial ablation, and postoperative insertion of a levonorgestrel intrauterine device are used.10

**Adenomyosis**

Adenomyosis, seen in 21%-47%, is more common in premenopausal multiparous women.19-22 Two-thirds of patients are asymptomatic, experiencing menometrorrhea, dysmenorrhea, and pelvic pain.19,21,22 Associations with endometrial surgery, multiparity, and tamoxifen are reported.19,21,22

Figure 6 A 43-year-old woman before and after uterine artery embolization. Sagittal T2-weighted MR images: (A) preuterine and (B) postuterine artery embolizations show marked reduction in uterus and fibroid size. It should be noted that the individual fibroids become smaller, more well defined, and homogenous in signal intensity after embolization (asterisk).
Adenomyosis is defined as ectopic endometrial mucosa within the myometrium and adjacent smooth muscle hypertrophy. It often coexists with other hormone-dependent pelvic lesions, namely fibroids, deep pelvic endometriosis, polyps, and endometrial hyperplasia. Adenomyosis can be focal (with one or several foci) or diffuse (with numerous foci spread throughout the myometrium), superficial or deep (penetrating more than one-third of the myometrium), and is often asymmetric. Adenomyoma represents a nodular aggregate of endometrial glands with compensatory hypertrophy of surrounding myometrium.

MRI has a sensitivity of 70%-88%, specificity of 86%-93%, and accuracy of 85%-90% for diagnosis of adenomyosis. Findings include (1) globular uterus with regular contours; (2) asymmetric myometrial thickening (more common of the posterior wall); (3) focal or diffuse junctional zone (JZ) thickness ≥12 mm; (4) greatest JZ to myometrium thickness ratio >40%-50%; and (5) myometrium foci of high T2 signal intensity and sometimes T1 signal intensity. JZ thickening more than 12 mm is highly predictive of adenomyosis (Fig. 8); JZ <8 mm practically excludes the diagnosis. A thickness between 8 and 12 mm is indeterminate and additional findings should be evaluated. The high-T2-signal-intensity foci reflect dilated fluid-filled endometrial glands (Fig. 8). This sign is highly specific, but seen in only approximately half of the cases.

JZ thickness varies in response to several conditions that need to be considered to avoid misdiagnosis. The JZ thickens with age up to approximately 50 years and then starts to thin, being thinner or absent during the menopause. During the menstrual cycle, JZ thickness is variable; it is the thickest between 8 and 16 days. Pregnancy, contraceptive pills, and gonadotropin-releasing hormone agonist cause the JZ to get thin or even disappear. Myometrial contractions, focal wedge-shaped areas of low T2 signal intensity, which bulge the uterine cavity, cause pseudothickening of the JZ and mimic adenomyosis, though they can be differentiated by their transient nature.

Adenomyoma is seen on MRI as a poorly defined mass-like lesion of low T2 signal intensity containing internal high T2 signal intensity (and occasionally T1 signal) foci (Fig. 8). Like fibroids, adenomyomas can be intramyometrial, subserosal, and submucosal, including intracavitary growth (polypoid adenomyoma). Hemorrhagic cystic adenomyosis (adenomyotic cyst) is related to bleeding of adenomyosis, characterized on MRI by high T1 signal intensity reflecting hemorrhage or even fluid-fluid levels.

Treatment of adenomyosis depends on the presence of symptoms, patient age, and future childbearing desire. Asymptomatic women do not require treatment. Medical treatment consists of hormonal therapy or nonsteroidal anti-inflammatory drugs or both. Surgical options include hysterectomy, myomectomy or adenomyoma excision.

Figure 7 A 37-year-old woman with endometrial polyp. (A) Sagittal T2-weighted MR image shows the polyp (asterisk) with stalk arising from the endometrium (arrow). Axial T2-weighted (B) and fat-suppressed contrast-enhanced (C) MR images show the avidly enhancing polyp with stalk arising from the endometrium (arrow). Well-circumscribed T2 hypointense fibroid with heterogeneous enhancement (asterisk) should be noted. The patient also incidentally has diffuse infiltrating rectal cancer.
myometrial reduction, and endometrial ablation or resection. UAE may improve or resolve symptoms, especially the short-term ones, though with increased risk of recurrence. Recently, high-intensity focused ultrasound ablation has shown promising results for adenomyosis treatment. MRI, reduction of uterine size, decrease in JZ thickness, and infarction of focal lesions can be seen following treatment.

Endometrial Hyperplasia

Endometrial hyperplasia has an incidence of 133 per 100,000 woman-years, and 389 per 100,000 woman-years in women aged between 50 and 54 years. In patients with normal menstrual cycle, endometrial hyperplasia is seen in 0.5%-5%. In patients with abnormal bleeding, endometrial hyperplasia is found in 2.5% and most of them are postmenopausal. It commonly results from unopposed estrogen or sequential estrogen-progesterone hormone replacement therapy. Endometrial hyperplasia can occur in premenopausal women with polycystic ovary disease and anovulatory cycles. Obesity and tamoxifen therapy are known risk factors. Endometrial hyperplasia is characterized by excessive endometrial gland proliferation, with an increased glands to stroma ratio. Endometrial hyperplasia is a precursor to endometrial carcinoma. The most widely used histologic classification system (World Health Organization) evaluates architectural features and cytologic atypia to identify precursor lesions: 1—simple hyperplasia; 2—complex hyperplasia; 3—simple hyperplasia with atypia; and 4—complex hyperplasia with atypia. Progression rates to carcinoma are 1%, 3%, 8%, and 29% for the 4 precursor classifications, respectively. In women undergoing hysterectomy for biopsy-proven atypical endometrial hyperplasia, approximately 40% have concomitant carcinoma on surgical pathology.

MRI is generally used only for problem solving, to exclude other diagnoses, like adenomyosis. The imaging appearance is nonspecific and may parallel early endometrial carcinoma, cystic atrophy, and endometrial polyps. In postmenopausal women, an endometrial thickness of 5 mm or more identifies 95% of all carcinomas and an endometrial thickness less than 4 mm has a 1% probability of cancer. In premenopausal women, there are no reliable criteria for differentiating benign and malignant endometrial hyperplasia.

Figure 8 A 35-year-old woman with adenomyosis and focal adenomyoma. Sagittal and axial T2-weighted (A) MR image shows thickening of the junctional zone greater than 12 mm (white line) and more focal mass-like area compatible with an adenomyoma (asterisk) containing characteristic T2 hyperintense foci (arrow).

Figure 9 A 51-year-old woman with tamoxifen-induced endometrial hyperplasia and diffuse polyps. Sagittal T2-weighted MR image shows heterogeneous thickening of the endometrium related to hyperplasia and polyps in a patient treated with tamoxifen.
On MRI, endometrial hyperplasia is typically diffuse, with a well-defined endometrial-myometrial interface (Fig. 9). The thickened endometrium is isointense or slightly hypointense on T2 relative to normal endometrium (Fig. 9). On dynamic contrast-enhanced (DCE)-MRI, endometrial hyperplasia shows progressive enhancement, enhancing similar to or greater than adjacent myometrium. 

Diffusion weighted imaging (DWI) has been shown to be helpful in differentiating malignant from benign lesions, including endometrial hyperplasia, with reported sensitivity and specificity of 95% and 90%, respectively. 

Endometrial thickening is evaluated by curettage or biopsy. Management options can be surgical and nonsurgical. Surgical options include hysterectomy, and nonsurgical options include hormonal therapy (progesterone) and followed by imaging or endometrial sampling or both. Total hysterectomy is the current treatment of atypical endometrial hyperplasia.

**Malignant**

**Endometrial Cancer**

Endometrial carcinoma is the most common gynecologic and 10th most common malignancy, with an incidence of 24.6 per 100,000 women per year. It is most common in women aged 45-74 years, with median age at diagnosis of 62 years. Most of the endometrial cancers are diagnosed at an early stage (68%) with 5-year survival rate of 81.5% overall, 17.5% for metastatic disease, and 95.1% for localized disease. Symptoms include abnormal uterine bleeding and vaginal discharge. The main risk factor is exposure to unopposed estrogen, exogenous (hormone replacement) or endogenous (anovulation in polycystic ovary syndrome, estrogen-producing tumors, and excessive peripheral conversion in adipose tissue in obesity). Tamoxifen, nulliparity, infertility, early menarche, and late menopause are also known risk factors.

Combined or progesterone-based oral contraceptive pills are protective. Lynch syndrome (hereditary nonpolyposis colon cancer) and Cowden syndrome have increased risk of endometrial cancer.

Endometrial carcinomas are classified into 2 major types (type I and type II). Type I tumors comprise 80% and include grade 1 or 2 endometrioid histology. These tumors are hormone responsive and have favorable prognosis. Type II tumors comprise 10%-20% and include grade 3 endometrioid and nonendometrioid carcinomas (serous, clear cell, mucinous, squamous, transitional cell, mesonephric, and undifferentiated). These tumors are of higher grade and have poor prognosis, without clear association to estrogen stimulus. Endometrioid carcinoma has a different genetic profile from that of nonendometrioid neoplasms. The former shows microsatellite instability and specific mutations of PTEN, K-ras, and β-catenin genes, whereas in the latter, p53 mutations predominate.

MRI in diagnosis and staging of endometrial carcinoma uses a multiparametric approach, including high-resolution T2-weighted, DW, and DCE image acquisitions. The tumor shows intermediate T2 signal intensity relative to normal endometrium, and mildly T2 hyperintensity compared with myometrium, the latter of which helps determine the depth of myometrial invasion. On quantitative evaluation, apparent diffusion coefficient value is lower in endometrial carcinoma (0.86-0.98) than in normal endometrium (1.28-1.65), indicating restricted diffusion.

Cervical stromal involvement is defined as less than or greater than 50% thickness of the myometrium, is best assessed on DCE images, as JZ thinning in postmenopausal patients, and underlying adenomyosis or fibroids can confound assessment on T2-weighted images alone. Cervical stromal involvement is characterized by extension into the cervix, best seen in T2-weighted (sagittal) or DCE images. High-resolution T2-weighted imaging has a 55%-77% accuracy for staging. The addition of DCE improves accuracy to 83%-98%.

Endometrial cancer spreads via different routes (direct, lymphatic, transstubal peritoneal seeding, or hematogenous). Metastases to paraaortic lymph nodes before pelvic lymph nodes can occur via gonadal vessels. The involvement of lymph nodes based on size criteria has substantial limitations.
Incorporation of morphologic features (internal heterogeneity, spiculated margins, necrosis, and signal intensity comparable to that of the primary tumor) improves lymph node evaluation. The incidence of nodal involvement correlates with depth of myometrial invasion: 3% if less than 50% myometrial invasion, 46% if greater than 50%.12,34,35 The management of endometrial cancer is based on stage of the disease. The International Federation of Gynecology and Obstetrics (FIGO) recommendation is total hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and paraaortic lymphadenectomy, peritoneal washing, and omental biopsy.32,35 However, in patients with early stage disease, the role of lymphadenectomy is controversial and these women may be appropriately treated with minimally invasive laparoscopic hysterectomy and bilateral salpingo-oophorectomy, decreasing morbidity and hospital stay.32,35 In selected patients with cervical or vaginal involvement, adjuvant radiation therapy may be used. Chemotherapy is reserved for advanced disease.44

Uterine Sarcomas
Uterine sarcomas are a rare and heterogeneous group of tumors that account for 5%-8% of all uterine malignancies, and include leiomyosarcoma, endometrial stromal sarcoma (ESS), and malignant mixed epithelial and mesenchymal tumors (MEMTs). ESS and leiomyosarcoma are composed of purely nonepithelial components, whereas MEMTs are composed of epithelial and mesenchymal components. The clinical presentation is nonspecific but these tumors classically present as rapidly growing masses, which may be accompanied by vaginal bleeding and abdominal or pelvic pain.45-49 Associations include African-American ethnicity, long-term tamoxifen therapy, and previous pelvic irradiation.47
Leiomyosarcomas are a common subtype, representing 40%, and arising from the myometrial smooth muscle.46-48 Diagnosis is based on atypia, mitosis, and tumor necrosis.46,48 They are usually solitary intramural masses and may arise rarely from a fibroid.46-48 Less than 0.5% of uteri removed for presumed fibroids have incidental leiomyosarcoma. Pathologically, it can be difficult to distinguish leiomyomas with abundant mitosis from well-differentiated leiomyosarcomas.46 ESSs arise from endometrial stroma, accounting for 10%-15% of uterine sarcomas and are characterized by resemblance to endometrial stroma with cells of varying atypia (well differentiated or low grade to undifferentiated or high grade).46,48 Extrauterine ESS may originate in endometriosis.46 Association with tamoxifen and estrogen use has been reported.47 MEMTs can be benign (adenofibromas and adenomyomas) or malignant (adenosarcomas, carcinosarcomas, and carcinofibromas). In adenosarcomas, the epithelial component is benign and mesenchymal component malignant; in carcinofibromas the epithelial component is malignant and mesenchymal component benign; in carcinosarcomas both components are malignant. The mesenchymal aspect of MEMTs can have homologous (elements normally found within the uterus) or heterologous components (elements not usually seen within the uterus, including benign or malignant cartilage, fat, bone, and rhadoid tissues).46,49
Carcinosarcoma, formerly called malignant mixed müllerian tumor, is the most common uterine sarcoma, representing nearly 50% of all uterine sarcomas and 2%-3% of all uterine malignancies.45,46,48-50 This tumor behaves more like endometrioid adenocarcinoma than like sarcoma, with common risk factors and similar patterns of clonality, lymphatic metastases, and recurrence; however, the prognosis is generally poor.46,48 It is accepted that carcinosarcoma represents metaplastic transformation of carcinoma to sarcoma; some researches argue that the carcinosarcoma represents an aggressive form of endometrial carcinoma.45,46,49 Associations to long-term tamoxifen therapy and previous pelvic irradiation have been reported.12,45,49
The 5-year survival rates vary according to the histologic type. Leiomyosarcomas for example, range from 18.8%-68%,
ESSs from 25%-98%, and MEMTs from 22%-39% (carcinosarcomas) to more than 80% (adenosarcomas).\textsuperscript{47,50,51} Imaging differentiation of leiomyosarcomas from leiomyomata is difficult. The most common MRI appearance is a large infiltrating myometrial mass with irregular, ill-defined margins; heterogeneous T1 signal; intermediate- to high-intensity T2 signal; and heterogeneous enhancement owing to areas of necrosis and hemorrhage (Fig. 12).\textsuperscript{37,48} These characteristics do not differentiate it from benign degenerating fibroids.\textsuperscript{48,52} Rapid growth remains suspicious for leiomyosarcoma though not reliable.\textsuperscript{47,48,53} In a large retrospective study (n = 580), less than 3% of leiomyosarcomas showed rapid growth and leiomyosarcoma was discovered in just 1 woman among 371 women with rapidly growing masses (presumed fibroids).\textsuperscript{53} Restricted diffusion and T2 signal of the mass have shown potential for differentiating benign from malignant tumors.\textsuperscript{54} ESS frequently appears as a polypoid endometrial mass on MRI, with low-intensity T1 and heterogeneous T2 signals. These tumors involve the myometrium and have a tendency for lymphatic and vascular invasion, appearing as worm-like bands of low-intensity T2 signal within areas of myometrial involvement.\textsuperscript{47,48} Compared with endometrial carcinoma, ESS is larger with more delayed contrast enhancement, irregular nodular margins, and nodular extension into the myometrium.\textsuperscript{47,48}

Malignant mixed mullerian tumors have similar imaging characteristics to those of endometrial carcinoma.\textsuperscript{45,47,48} MRI findings of carcinosarcoma have been described mainly in case series; these tumors are generally well defined with the tumor epicenter in the endometrium (88%), cervix (8%), or myometrium (4%), and can present even as prolapsed uterine tumors (Fig. 13).\textsuperscript{45,49,50,55,56} The tumor typically has high-intensity or heterogeneous T2 signal relative to myometrium and can have intratumoral T1 hyperintensity related to hemorrhage. Enhancement pattern varies, though delayed heterogeneous enhancement contrasts with the relative hypoenhancement of more common endometrial carcinomas.\textsuperscript{45}

The primary treatment of uterine sarcoma is surgery. Pelvic lymphadenectomy and adjuvant radiotherapy are usually performed, even in early stage disease, owing to the high incidence of lymph node involvement and pelvic recurrence. Chemotherapy may be indicated, especially in MEMTs, owing to the epithelial component.\textsuperscript{48,50}

\textbf{Figure 12} A 63-year-old woman with rapidly growing pelvic mass, diagnosed with leiomyosarcoma in the context of multiple fibroids. Sagittal T2-weighted (A) and contrast-enhanced fat-suppressed T1-weighted (B) images show markedly heterogeneous appearing fibroid (arrow in A) containing irregularly enhancing internal soft tissue (arrow in B).

\textbf{Figure 13} A 61-year-old woman with uterine carcinosarcoma. Sagittal T2-weighted MR image shows the classic prolapse of a polypoid uterine mass (arrow) into the vagina or vulva, known as the “broccoli sign.” Abnormal heterogeneous thickening of the endometrial cavity related to combined tumor and blood products (asterisk) should be noted.
Gestational trophoblastic disease

Gestational trophoblastic disease (GTD) has abnormal trophoblastic proliferation and comprises a spectrum of lesions with varying malignant potential. GTD is divided into 5 main types: (1) hydatidiform mole, (2) invasive mole, (3) choriocarcinoma, (4) placental-site trophoblastic disease (PSTD), and (5) epitheloid topoblastic disease.

The clinical presentation, laboratory findings, and prognosis vary among the different types of GTD, with moles most commonly manifesting as vaginal bleeding or as missed or incomplete abortions. Gestational hypertension in the first trimester is virtually diagnostic of hydatidiform mole. Overall, 80%-85% of molar pregnancies follow a benign course without local recurrences or metastases, 15%-20% locally invasive, and 3%-5% developing metastases. Vaginal seeding is seen in up to 30% of the cases. Metastases are primarily hematogeneous, most commonly to the lungs (76%-87%), liver (10%), and brain (10%), and tend to be hypervascular with propensity to hemorrhage.

Hydatidiform moles, either complete or partial, result from aberrant fertilization and represent 80% of all GTDs, with an incidence of 0.6-1.1 per 1000 pregnancies. Both subtypes are premalignant, with 15% of complete moles and 0.5%-1.0% of partial moles undergoing malignant transformation. The invasive lesions include invasive mole, choriocarcinoma, and PSTD; epitheloid topoblastic disease is a rare variant of PSTD. Hydatidiform moles and choriocarcinoma arise from villous trophoblast, which produces β-hCG, whereas PSTD arises from interstitial trophoblast. The term gestational trophoblastic neoplasia or persistent trophoblastic neoplasia refers to invasive GTD, including invasive mole, choriocarcinoma, and PSTD.

Complete moles are characterized by absence of an embryo and severe villous swelling and trophoblast hyperplasia, resembling a bunch of grapes. Partial moles usually have an embryo that may survive up to the second trimester and exhibit less intense villous swelling and patchy hyperplasia. Invasive moles extend into or beyond the myometrium, considered locally invasive nonmetastasizing neoplasm. Choriocarcinoma represents malignant trophoblast proliferation, arising from any type of pregnancy (50% from moles, 25% term or preterm, and 25% aborted or ectopic) and occurring in 1 of 20,000-50,000 pregnancies. It is highly malignant with extensive necrosis and hemorrhage and early vascular invasion resulting in metastases even if the primary tumor is small.

Diagnosis of GTD is based on clinical history and examination, quantitative β-hCG titers, and pelvic ultrasonography. MRI does not play a role in routine evaluation but may be used for problem solving and better delineating extent of myometrial and extraterine invasion in invasive mole and choriocarcinoma. In 25%-40% of patients with complete moles, theca lutein cysts are seen, resulting in bilateral multicystic ovarian enlargement.

MRI of molar pregnancy is nonspecific, and difficult to be distinguished from those of retained products of conception. Findings include expansion of the endometrial cavity containing heterogeneous low-intensity T1 and high-intensity T2 signal with multiple cystic spaces representing hydropic villi, with enhancement of tumor and surrounding cystic spaces (Fig. 14). Invasive moles infiltrate and disrupt the JZ and myometrium on T2-weighted and postcontrast images. However, loss of zonal anatomy may also be observed after missed or incomplete abortions or recent curettage.

The management of patients with GTD varies according to histologic subtype. Molar pregnancies are treated preferably by suction curettage. β-hCG, an excellent tumor biomarker, is useful in tumor surveillance and recurrence. Invasive mole and choriocarcinoma are treated primarily with chemotherapy. Other recommendations for chemotherapy include...
Persistently elevated or rising hCG levels and metastatic disease.\textsuperscript{57-59} Surgery and radiotherapy are reserved for high-risk patients.\textsuperscript{59}

Other Uncommon Uterine Malignancies (Small Cell Cancer and Lymphoma)

Neuroendocrine Tumor (Small Cell Cancer)

Small cell carcinoma is a group of malignant neoplasms showing neuroendocrine differentiation, mainly arising in the lung and digestive tract.\textsuperscript{66-68} In the uterus, small cell carcinomas are rare, accounting for less than 1% of all endometrial malignancies.\textsuperscript{66-70} On pathology, these tumors are characterized by sheets of small densely packed cells, hyperchromatic nuclei, high nuclear-to-cytoplasmic ratio, and positive markers for neuroendocrine differentiation on immunohistochemistry.\textsuperscript{66,67,69-72} Uterine small cell carcinomas exhibit aggressive behavior, local invasion, extraterine spread, early lymph node involvement, and distant metastasis at diagnosis.\textsuperscript{66,67,71-73}

Clinically, the most common symptoms include abnormal vaginal bleeding and pelvic pain.\textsuperscript{67,69,73} Uterine small cell carcinomas may produce and secrete metabolically active amines and peptides and cause paraneoplastic syndromes, including syndrome of inappropriate secretion of antidiuretic hormone, retinopathy, Cushing syndrome, and membranous glomerulonephritis.\textsuperscript{66,68,69,71,73} These tumors have been described in a wide age range of women (23-84 years), with a mean age of 60 years.\textsuperscript{67,69} The prognosis is poor and most patients present with advanced disease.\textsuperscript{67,69,72,73}

MRI features of uterine small cell carcinoma are limited to case reports, and generally speaking indistinguishable from those of other uterine neoplasms.\textsuperscript{66-73} Typically, the tumor is seen as an intracavitary mass, frequently associated with diffuse myometrium invasion and extrauterine spread.\textsuperscript{66,67,69} On MRI, the tumor usually has low T1 and high T2 signal intensity.\textsuperscript{66-69,72,73} The tumor may demonstrate irregular heterogeneous enhancement because of tumor infiltration, hemorrhage, and necrosis,\textsuperscript{68,67,73} though a homogeneous enhancement resembling lymphoma has also been described.\textsuperscript{66} Enlarged lymph nodes and distant metastasis are commonly found at diagnosis.\textsuperscript{66,67,73}

The treatment of uterine small cell neuroendocrine carcinomas includes chemotherapy along with local treatment, which may be surgery, radiotherapy, or both. The surgical approach typically is total hysterectomy and pelvic lymphadenectomy. Hormonal therapy and octreotide are also sometimes used.\textsuperscript{69-72}

Lymphoma

Uterine lymphoma may be primary or secondary. Distinguishing primary from secondary lymphoma is important as they differ in treatment and prognosis.\textsuperscript{74} Involvement of the female reproductive organs in secondary lymphoma has been reported in 40% of cases in autopsy series, whereas primary uterine lymphomas are rare, representing less than 1% of extranodal lymphomas.\textsuperscript{74,75} Most of the primary uterine lymphomas are non-Hodgkin lymphomas, the most common being diffuse large B-cell and follicular lymphoma.\textsuperscript{74} By pathology, tumor is characterized by infiltrates of lymphocytes and plasma cells in the uterine stroma.\textsuperscript{74,76} These tumors are difficult to detect on Papanicolaou test as they may not involve the epithelium. For this reason, primary lymphoma usually is a large lesion at diagnosis.\textsuperscript{74} Lymphoma infiltrates the uterus, causing diffuse enlargement without disruption of the uterine architecture; polypoid lesions are less common. Local spread is most common to the vagina and bladder.\textsuperscript{74-76} The age range of presentation is broad (20-80 years) with a mean age of 40 years, and most patients present with vaginal bleeding.\textsuperscript{74,75}

MRI is a useful imaging modality to assess the extent of uterine lymphoma.\textsuperscript{74} Lymphoma causes homogeneous enlargement of the uterus with preservation of the zonal architecture on T2-weighted images, though loss of zonal

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**Figure 15** A 23-year old with gestational trophoblastic disease, after treatment with chemotherapy. Sagittal T2-weighted (A) and contrast-enhanced fat-suppressed T1-weighted (B) images show decrease in size and enhancement of the previously seen uterine mass (arrow) compatible with treatment response.
anatomy and endometrial disruption have also been described. 

Typically, the lesion has a low to intermediate T1 signal and high T2 signal intensity. Though no imaging findings have been described on DWI in uterine lymphoma, lymphomas in general show restricted diffusion because of hypercellularity and little extracellular space. The tumor typically enhances homogenously, though it can be heterogeneous. Differentiating lymphoma from other pelvic malignancies is crucial to prevent unnecessary surgery. Standard treatment is with chemotherapy or radiation therapy.

### Conclusion

A wide spectrum of benign and malignant pathologies occur in the uterus. MRI is helpful in delineating the anatomy, extent of growth in both benign and malignant diseases, staging of common and uncommon primary uterine malignancies, and response to targeted and systemic treatment.

### References

65. S h a hS H ,J a g a n n a t h a nJ P ,K r a j e w s k iK ,e ta l :U t e r i n e s a r c o m a s :T h e na nd