Abdominal Radiology (2019) 44:2557–2571
https://doi.org/10.1007/s00261-019-01984-7

REVIEW

MRI of cervical cancer with a surgical perspective: staging, prognostic implications and pitfalls

Patricia Balcacer[1] · Arvind Shergill[1] · Babak Litkouhi[2]

Published online: 22 March 2019

Abstract

Learning objectives Magnetic resonance imaging (MRI) of the pelvis is the most reliable imaging modality for staging, treatment planning, and follow-up of cervical cancer; and its findings may now be incorporated into the International Federation of Gynecology and Obstetrics Federation (FIGO) 2018 clinical staging of cervical cancer. It is imperative that radiologists are familiar with the imaging appearance of the different stages of cervical cancer as well as the post-treatment changes and imaging pitfalls given the respective clinical manifestations, treatment regimens, and prognosis of an accurate diagnosis. In addition to the different stages of cervical cancer, we address the imaging techniques for diagnosis, staging and treatment implications as well as the changes of the new FIGO staging system.

Background The use of MRI to diagnose and stage cervical cancer is steadily increasing and the new FIGO stagi ng system, previously based on clinical examination, now allows the staging or change of staging based on the imaging findings. MRI can evaluate the extent of disease because of its excellent contrast resolution for pelvic tissues and organs, high accuracy and detailed elaboration of the cervical/uterovaginal anatomy.

Content Relevant anatomy, including normal MRI appearance of the cervix, parametria and pelvic ligaments; different stages of cervical cancer on MRI with prognostic and therapeutic implications; MRI sequences, other imaging modalities used in the staging and follow-up, treatment of different stages and the appearance of the cervix and cervical cancer post-treatment. Since clinical implications and therapeutic strategies for cervical cancer treatment vary tremendously according to degree of tumor extension, familiarity with relevant MRI techniques and findings is essential for radiologists.

Summary It is important that radiologists interpreting pelvic MRI are aware with the different stages of cervical cancer to provide useful information regarding treatment and prognosis. Pitfalls regarding the interpretation of tumor extension can interfere with an accurate diagnosis and have significant therapeutic implications.

Keywords Cervical cancer · FIGO cervical staging · Cervical cancer staging

Introduction

The International Federation of Gynecology and Obstetrics Federation (FIGO) staging system of cervical cancer was introduced in 1958 and most recently revised in 2018, reflecting an increased knowledge of cancer biology and prognostic factors, and thus allowing for improved risk stratification. The new 2018 FIGO system highlights the utility of imaging, and permits its use, when available, as part of clinical staging. This revised staging system recognizes the importance of tumor size in terms of metastatic risk (stage IB1, IB2, and IB3 tumors), and incorporates the status of regional lymph nodes (both radiographically and pathologically detected) in staging (designated stage IIIC1/C2) [1].

Cervical cancer

Cervical cancer is the second most common cancer in women worldwide, with approximately 500,000 new cases and 250,000 deaths annually [2]. In the United States, the incidence of cervical cancer has significantly decreased

✉ Patricia Balcacer
pbalcacer@gmail.com

[1] Division of Abdominal Imaging, Department of Radiology, Beth Israel Deaconess Medical Center- Harvard Medical School, Boston, MA, USA

[2] Department of Obstetrics, Gynecology, and Reproductive Sciences, Yale School of Medicine, New Haven, CT, USA

secondary to robust screening for premalignant lesions with Pap smears and HPV testing. As a result, 80–90% cases of cervical cancer are now diagnosed in developing countries, where screening programs do not exist. Of the patients diagnosed with cervical cancer in the United States, approximately half have never had screening or did not get screened within 5 years preceding diagnosis [3].

Almost all subtypes of cervical cancer are caused by human papilloma virus (HPV). Squamous cell carcinoma accounts for approximately 75% of cervical carcinomas. The other 25% include adenocarcinomas and adenosquamous carcinomas (20%), as well as small cell neuroendocrine carcinomas (< 5%). Although still infrequent when compared to squamous cell carcinoma, the incidence of adenocarcinoma is increasing, which may be in part due to suboptimal detection of glandular lesions by Pap smear. There is controversy regarding the significance of histology in terms of outcomes, and the current staging system does not differentiate between histologic types (in contrast to uterine corpus cancers). With the exception of neuroendocrine tumors and other rare subtypes, management remains largely the same regardless of histology [4, 5].

Unlike endometrial and ovarian cancer, the staging of cervical cancer is clinical. In the past, the FIGO staging system only permitted fairly low-cost testing, such as exam under anesthesia (EUA), pathology from cervical conization, cystoscopy, proctoscopy, IVP, and X-ray of the chest, to stage the disease. Computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET), though commonly utilized in making treatment decisions, were not part of the previous staging system. However, recognizing this, the new 2018 FIGO cervical cancer staging permits imaging and pathological finding to be incorporated into disease staging, where available [1].

Anatomy of the cervix

The cervix is the lower portion of the uterus, and typically measures two to five centimeters in length. Unlike the uterine corpus, the body of the cervix is mainly fibrous, with little smooth muscle. The cervix connects the lower uterine segment to the vaginal vault, where the portion that extends into the vagina is known as the portio vaginalis or ectocervix. The ectocervix is lined by stratified squamous epithelium, while the epithelium of the supravaginal endocervix is composed of columnar glandular cells. Metaplasia develops at the squamocolumnar junction, also called the transformation zone. In this region, under the influence of estrogen and other factors, and in the setting of high-risk HPV, columnar cells can transform into squamous cells. This metaplastic process, in the presence of high-risk HPV, appears to be the key event of cervical cancer tumorigenesis [5, 6].

Intraperitoneally, the cervix is covered anteriorly by the bladder and its peritoneum in the anterior cul-de-sac. The vesicocervical space is a potential space located between the cervix and bladder. This potential space extends caudally as the vesicovaginal space and is bound laterally by the vesicocervical or vesicouterine ligaments, also known as the bladder pillars. Posteriorly, the peritoneum over the cervix extends to the cul-de-sac of Douglas, with the lateral margin being the uterosacral ligaments. Laterally, the cardinal ligaments extend to the pelvic sidewall. These three-paired ligaments, namely the vesicouterine, uterosacral and cardinal ligaments, are commonly referred to as the parametrium, and are traversed by the pelvic ureter [7].

MRI imaging of cervical cancer

Normal appearance of the cervix

The normal cervix demonstrates four distinct layers on T2WI, best appreciated on sagittal view. The central endocervical mucosa, which is contiguous with the endometrium, appears hyperintense on T2WI. The plica palmatae, subjacent to the hyperintense mucosa, demonstrates moderately hyperintense T2 signal. The middle fibromuscular stroma is hypointense on T2WI, and contiguous with the hypointense junctional zone of the uterus in most women. The outer fibromuscular stroma demonstrates hypointense to intermediate intensity T2WI, and is contiguous with the outer myometrium [8] (Fig. 1).

High-resolution T2-weighted imaging is the mainstay for tumor detection as it best depicts cervical tumors and their extension into the uterus, parametrium and adjacent organs. Cervical cancer typically appears as a hyperintense T2 mass compared to the background hypointense T2 signal of the cervical stroma. A visible cervical mass indicates stage IB or higher, and it can be variable in appearance, often appearing exophytic, infiltrating, or barrel shaped (Figs. 2, 3 and 4). Oblique axial T2WI planned perpendicular to the cervical long axis provides more accurate assessment of stromal involvement and parametrial invasion. Fat-suppressed T2 sequences can be helpful for the evaluation of parametrial involvement [8, 9]. The MRI protocols are tailored per institution and ours is shown in Table 1.

The role of gadolinium

There is wide variation in the literature regarding use of IV gadolinium-based agents, however, some studies have shown that the detection of small tumors may be improved due to early enhancement relative to cervical stroma on dynamic contrast-enhanced (DCE) [10] (Fig. 2) MRI is

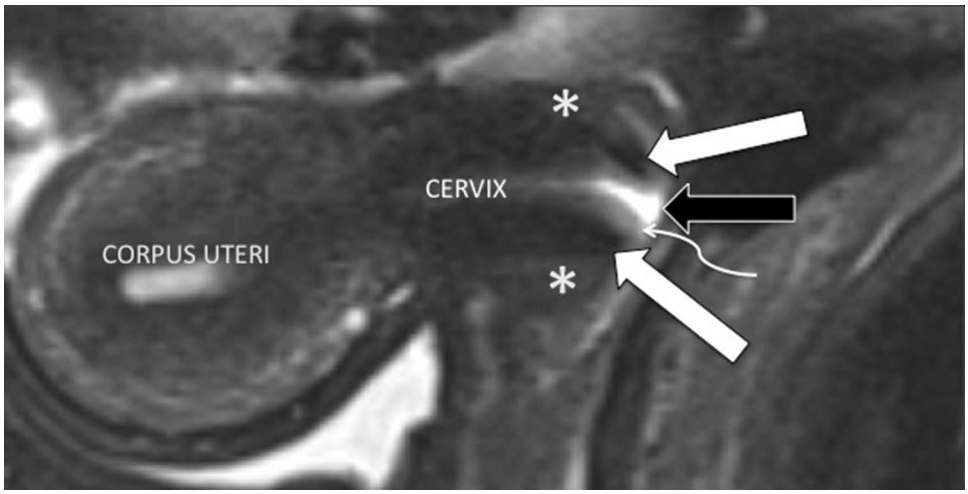

Fig. 1 Anatomy of the cervix. Sagittal T2 Fat-sat shows the MRI anatomy of the normal cervix. Hyperintense T2 endocervical canal (black arrow), hypointense T2 fibrous stroma (block arrows), and intermediate T2 signal of smooth muscle (asterisks). Please note plica palmatae subjacent to the endocervical mucosa (curved white arrow)

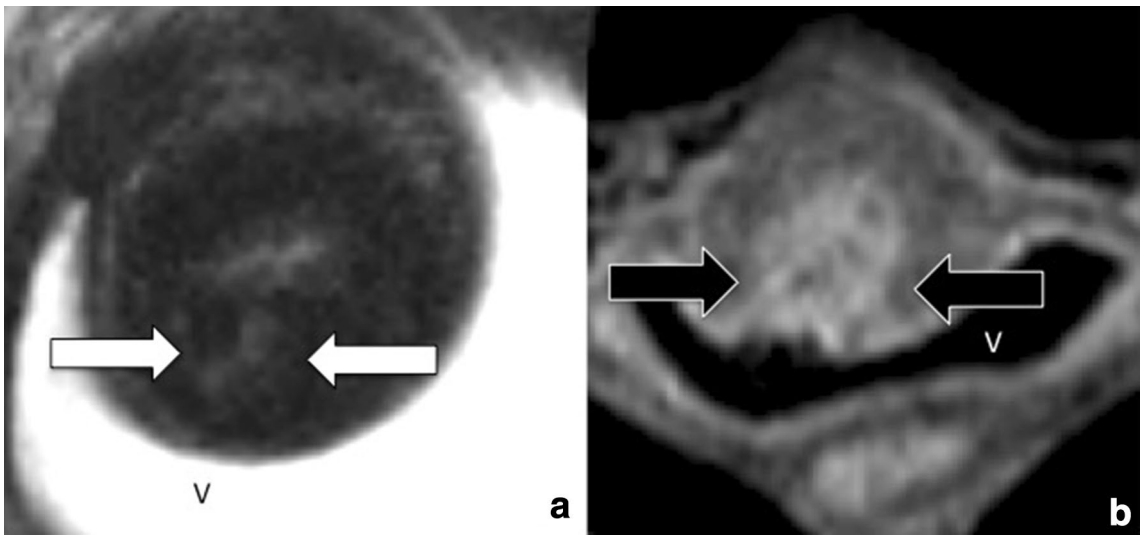

Fig. 2 Oblique axial T2 (**a**) and axial T1 post-contrast (**b**) demonstrate a subtle cervical neoplasm that is poorly defined, mildly hyperintense on T2 (white arrows) and more conspicuous after administering IV contrast (black arrows). Please note distended vagina with sonographic gel (V)

being used as a tool for the detection of tumor recurrence and post-radiotherapy changes [11].The use of gadolinium is helpful in the detection of residual tumor after neoadjuvant treatment; however, benign conditions such as edema, inflammation and necrosis induced by radiation could mimic residual tumor post treatment [12].

DCE MRI has been shown to be superior to conventional T1WI post gadolinium. A recent study [13] DCE MRI has value in identifying complete and incomplete response after neoadjuvant treatment. A time-signal intensity curve steeper than that of myometrium is significantly associated with the presence of residual tumors, which is in line with the typical early and strong enhancement of nontreated cancers. Applying DCE could identify the absence of residual tumor and potentially avoid unnecessary surgery [14].

Diffusion-weighted imaging (DWI)

The detection and evaluation of cervical cancer is typically carried out on the T2WI, which show the highest anatomical detail owing to their excellent intrinsic tissue contrast resolution. A potential pitfall in the evaluation of cervical cancer is discerning the T2 hyperintense tumor from peritumoral

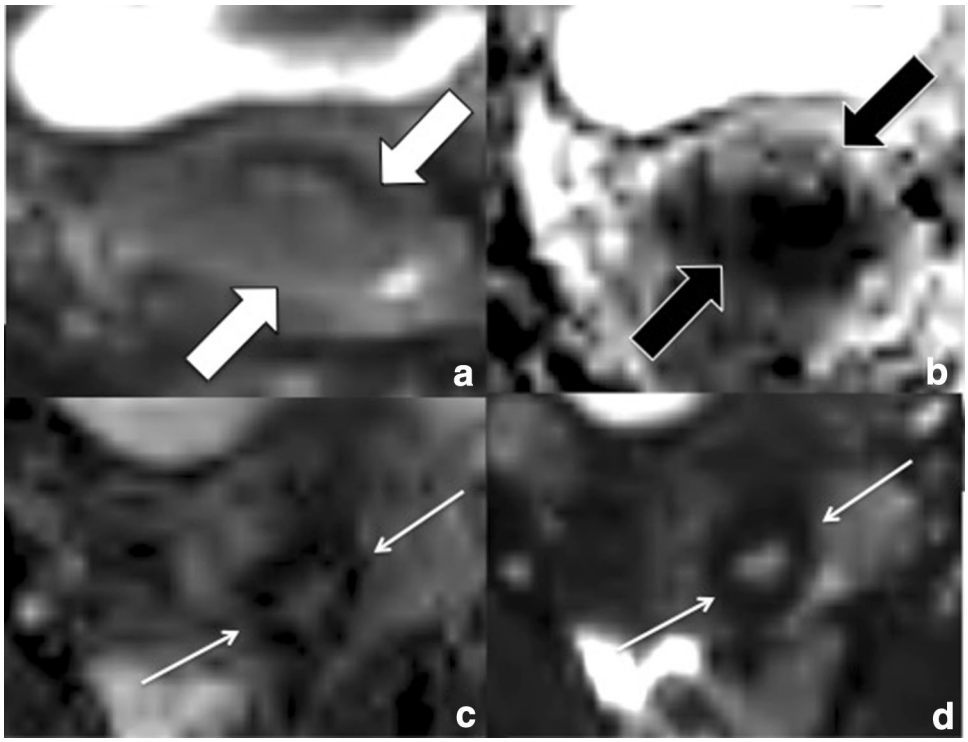

Fig. 3 Diffusion-weighted images (DWI) and apparent diffusion coefficient (ADC) map. Axial DWI (**a**) demonstrates abnormal hyperintense signal of a cervical mass (white block arrows) with corresponding hypointense signal on ADC (**b**) representing restricted diffusion (black block arrows). Compare with the hypointense ring of the normal cervix (white thin arrows) in both DWI (**c**) and ADC (**d**)

Table 1 MRI protocol used at our institution for cervical cancer staging

Pre-scan preparation
60 ml of surgilube: intravaginal via Foley catheter or catheter syringe
Antiperistaltic agent Glucagon (1 mg): Half dose before study: other half during pre-contrast image acquisition
Technical details
Slice thickness: 4 mm, 3 mm for high-resolution sequences
Field of view (FOV): 24-32 cm
Sequences
3-plane localizer
Axial T1 in/out phase (straight to whole pelvis): TR 175 ms; TE: 1.3/2.5 ms*; slice thickness 5 mm
Axial T2 FRFSE (straight to whole pelvis): TR 6000 ms; TE 120 ms; slice thickness 4 m m
Sagittal T2 FRFSE: (TR 5500 ms; TE 120 ms; FOV 24 cm; slice thickness 4 mm
Oblique T2 FSE (perpendicular to mass-can be axial or coronal oblique): TR 4000 ms; TE 120 ms; slice thickness 4 mm
Oblique DWI non-BH (b800) (perpendicular to mass-can be axial or coronal oblique)
Sagittal oblique DWI Non-BH (b500)
Oblique 3D FSPGR pre and post contrast: TR: 4 ms; TE 1.7 ms; slice thickness 3.6 mm.
Contrast: gadolinium based agent, no timing run required (25 s scan delay)
Oblique 3D fat-sat T1 post-contrast (3 Phases: Image Phases at 0:0, 0:50, 1:35 s)
Sagittal 3D fat-sat T1 post-contrast (to include uterus)
Optional sequences
Oblique 3D Fat-Sat T1 post contrast (perpendicular to mass)
Abbreviations
BH: breath-hold; DWI: diffusion weighted imaging; TR: repetition time; TE: time echo; FOV: field of view
FSE: fast-spin echo
FRFSE: fast recovery fast spin echo
FSPGR: fast spoiled gradient echo
3D: 3-dimensional
*3: tesla

edema, leading to increased risk of overstaging, based on incorrect tumor size, and the consequent changes in management [15].

Diffusion-weighted imaging (DWI) helps differentiate between tumor tissue and reactive changes. Cervical cancer demonstrates lower ADC values (i.e., more restricted diffusion) than does the normal cervical tissue (Fig. 3), hence DWI may allow for more accurate staging of cervical cancer by depicting more accurate determination of depth of invasion and status of nodal involvement [16]. DWI may be helpful because it can distinguish tumor from peritumoral edema, improving the accuracy of tumor measurement. Similarly, DWI may represent a powerful adjunct for differentiating between metastatic and non-metastatic lymph nodes, as it reflects differences in cellularity [17].

The correlation between DWI features and recurrence-free survival is well known [18]. The response to neoadjuvant therapy can be assessed qualitatively by observing high-signal intensity on high-b-value DW and quantitatively with ADC value measurement. Some failed to demonstrate a 'cutoff' ADC associated with complete response [19]; other studies [20, 21] have found a significant difference for median ADCs between cervical cancer and normal cervix before treatment and in responders versus nonresponders to neoadjuvant treatment. Overall, DWI may help identify patients at greater risk of early recurrence after treatment and has the potential ability to help differentiate between complete and incomplete response to neoadjuvant treatment [11].

MRI staging of cervical cancer

Stage I

Stage IA Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion < 5 mm.

- *1A1* Measured stromal invasion < 3 mm in depth.
- *1A2* Measured stromal invasion ≥ 3 mm and ≤5 mm in depth.

Stage 1B Invasive carcinoma with a measured depth of stromal invasion ≥ 5 mm, or with a clinically visible tumor, limited to cervix (Fig. 4):

- *1B1* A clinically visible tumor < 2 cm in greatest dimension, or a subclinical (i.e. microscopic) lesion with ≥ 5 mm depth of stromal invasion
- *1B2* Invasive carcinoma ≥ 2 cm and < 4 cm in greatest dimension.
- *1B3* Invasive carcinoma ≥ 4 cm in greatest dimension.

There is a limited role for imaging of stage IA tumor since these tumors are identified histologically and by definition are not clinically visible. MRI and additional imaging (PET, see below) is typically performed for larger stage IB

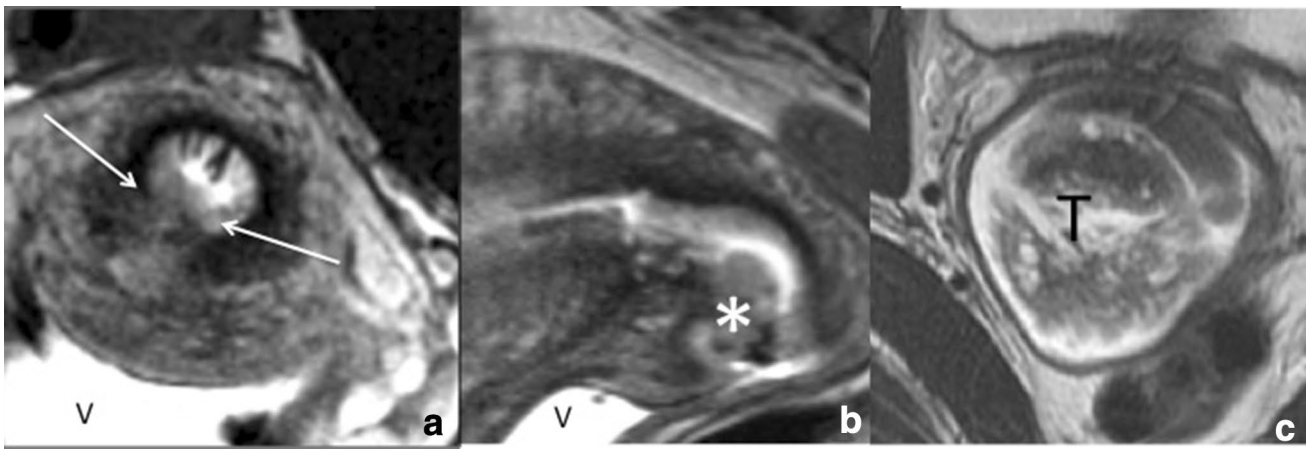

Fig. 4 Stage IB: Earliest detectable stage on imaging. Axial T2 (**a**) demonstrate a stage IB1 tumor disrupting the T2 stroma and measuring less than 2 cm (arrows). Sagittal T2 (**b**) shows a stage IB2, hyperintense cervical cancer (asterisk) measuring 2 cm. Axial T2 (**c**) demonstrates a stage IB3, a 5 cm cervical cancer with papillary fronds (T) without vaginal invasion. Note vaginal distention with sonographic gel (V). Pathology of the IB3 mass was consistent with villonodular subtype of cervical cancer

tumors (e.g. IB2 and IB3), and is also commonly performed for smaller clinical lesions (e.g. IB1–IB2) in patients planning on undergoing uterine/fertility-sparing radical trachelectomy to better define the extent of endocervical tumor.

Stage II

Tumor is seen beyond the cervix into the upper two thirds of the vagina (IIA) or into the parametrium (IIB).

IIA Extension into the upper two thirds of the vagina (Fig. 5)

– *IIA1* < 4 cm greatest dimension.
– *IIA2* 4 cm greatest dimension.

IIB Parametrial invasion, but not extending to the pelvic sidewall (Fig. 6).

Parametrial invasion is indicated by disruption of the normal hypointense signal of the cervical stromal ring, often seen as a spiculated tumor–parametrium interface, nodular tumor extension into the parametrium, or tumor encasement of the periuterine vasculature.

The preservation of the hypointense stromal ring on T2WI has a highly negative predictive value for parametrial invasion [22]. The disruption of the cervical stromal ring could be erroneously overstaged as parametrial invasion. To avoid this pitfall, it is important to remember that the delineation of the cervical fibromuscular stroma and the parametria is the thin T2 intermediate/hypointense outer margin of the cervix, rather than the more hypointense cervical stroma (Fig. 6). When tumor involves the portio vaginalis, disruption of the vaginal wall is also suggestive of parametrial involvement [13].

The specificity of MRI in detecting parametrial invasion decreases with larger tumors, particularly when tumor size is greater than 4 cm. This results from peritumoral edema, which manifests as T2 hyperintense signal that gives the appearance of cervical stromal disruption [23, 24].

Vaginal involvement by the cervical mass is best evaluated at the time of clinical examination. On MRI, vaginal involvement manifests as disruption of the normal hypointense T2 W vaginal wall by hyperintense or intermediate signal of the tumor. Post-contrast T1WI is helpful in demonstrating hypoenhancing tumor within the vagina. The use of vaginal gel is commonly used in pelvic protocols. The use and potential benefits have not been widely tested, though a study [25] showed that when vaginal gel is utilized, there is improved accuracy in staging of early cervical cancer. In our experience, distending the vagina with sonographic gel helps in the evaluation of vaginal involvement by tumor (Fig. 4).

Stage III

Tumor involves the lower third of the vagina or pelvic sidewall. The updated 2018 FIGO staging system designates involvement of the regional lymph nodes as stage IIIC (whether identified by imaging or pathology).

IIIA No extension into pelvic sidewall, tumor extends into the lower third of the vagina (Fig. 7).

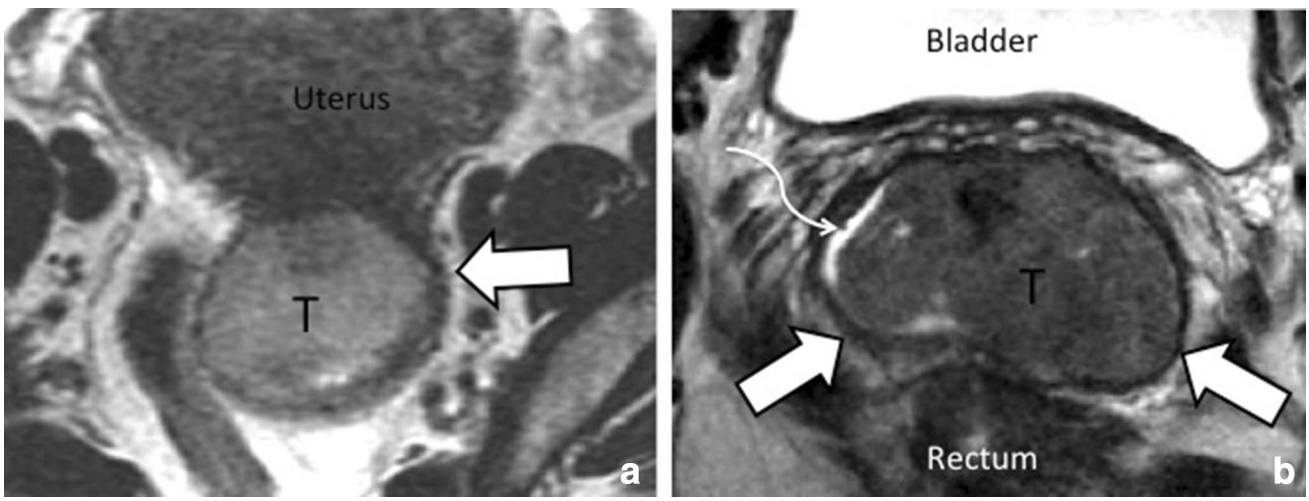

Fig. 5 Stage IIA. Axial T2 (**a**) shows stage I1A1 (< 4 cm), and axial T2 (**b**) shows stage IIA2 (> 4 cm) cervical neoplasms (T) in two different patients. The tumors have T2 intermediate/hyperintense signal and extend into the upper vagina with gel (curved arrow), however, there is no parametrial extension. Note intact T2 hypointense cervical stroma and vaginal wall surrounding the tumor in both cases (block white arrows)

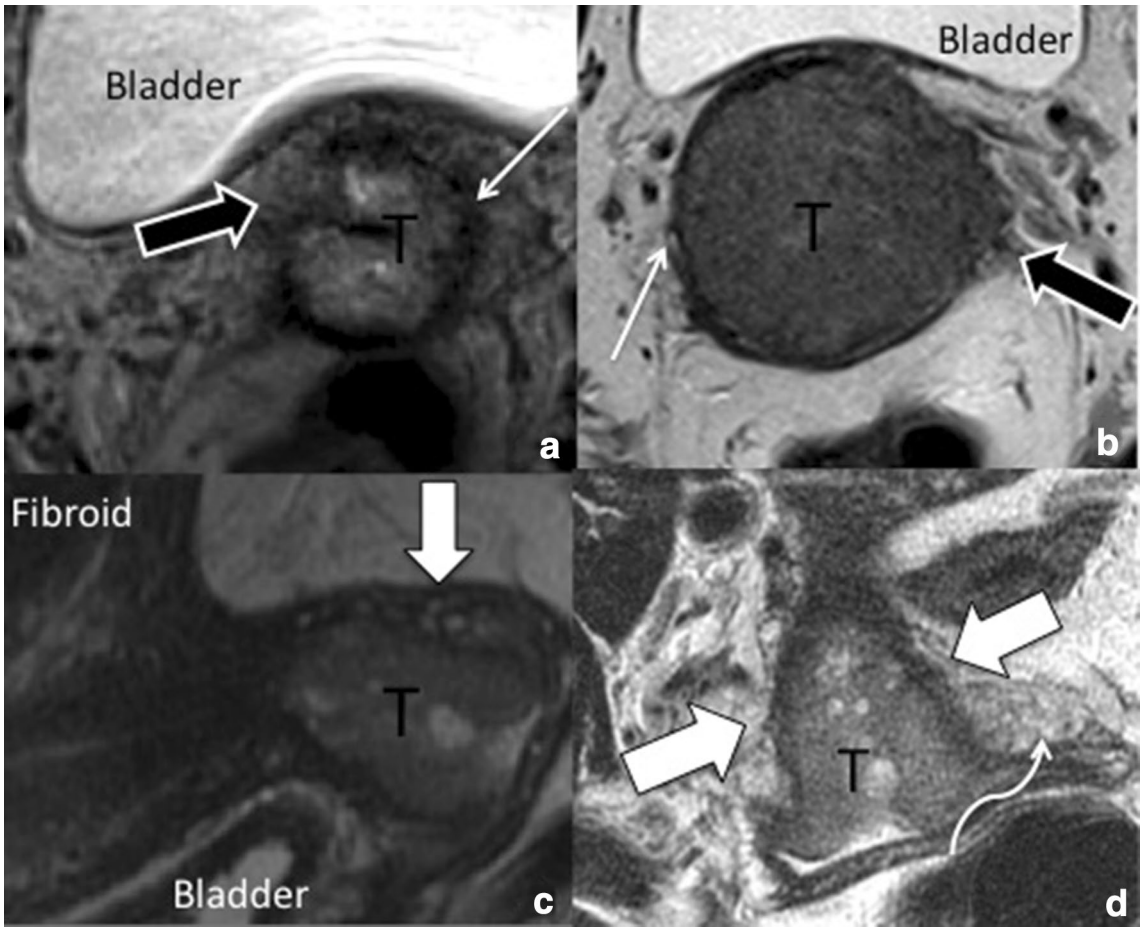

Fig. 6 Stage IIB. Axial T2 images in two different patients (**a**, **b**) show disruption of the T2 hypointense cervical stroma (block black arrows) by cervical cancer (T). Note portions of preserved T2 hypointense stroma (thin arrows). Compare to sagittal T2 (**c**) and corona] T2 (**d**) in stage IIA, showing a cervical mass (T) with preserved T2 hypointense outer margin of the fibromuscular stroma and no extension into the parametria (block white arrows). Please also note "haziness" adjacent to the cervix which may be confused with tumor involvement (curved arrow)

IIIB Extension into the pelvic sidewall or ureteral involvement with hydronephrosis caused by tumor. The presence of pelvic sidewall invasion is indicated by tumor extension into the iliac vasculature, internal obturator, piriformis or levator ani muscles. A dilated ureter, obstructed by tumor is considered pelvic sidewall invasion (Fig. 7).

When tumor extends into the inferior third of the vagina, a more complex and extensive strategy for radiation therapy planning is needed [26]. The accuracy of MRI in determining vaginal invasion ranges from 83 to 94%. The decreased accuracy is a result of vaginal wall edema, which can mimic tumor involvement. Again, this would be best resolved on clinical exam [23].

IIIC Involvement of pelvic and/or para-aortic lymph nodes, regardless of tumor size and extent (Fig. 8).

– *III C1* Pelvic lymph node metastasis only.
– *IIIC2* Para-aortic lymph node metastasis.

* The notations r (imaging) and p (pathology) are used to indicate the method used to allocate the case to Stage IIIC. For example, if imaging shows pelvic lymph node metastasis, the stage is IIIC1r, and if confirmed with pathology, IIIC1p.

Stage IV

The tumor extends into the bladder or rectum (*biopsy proven* bladder or rectal mucosal involvement) and/or beyond the true pelvis.

IVA Extension into adjacent bladder or rectum (Fig. 9)
IVB Distant metastases (Fig. 9).

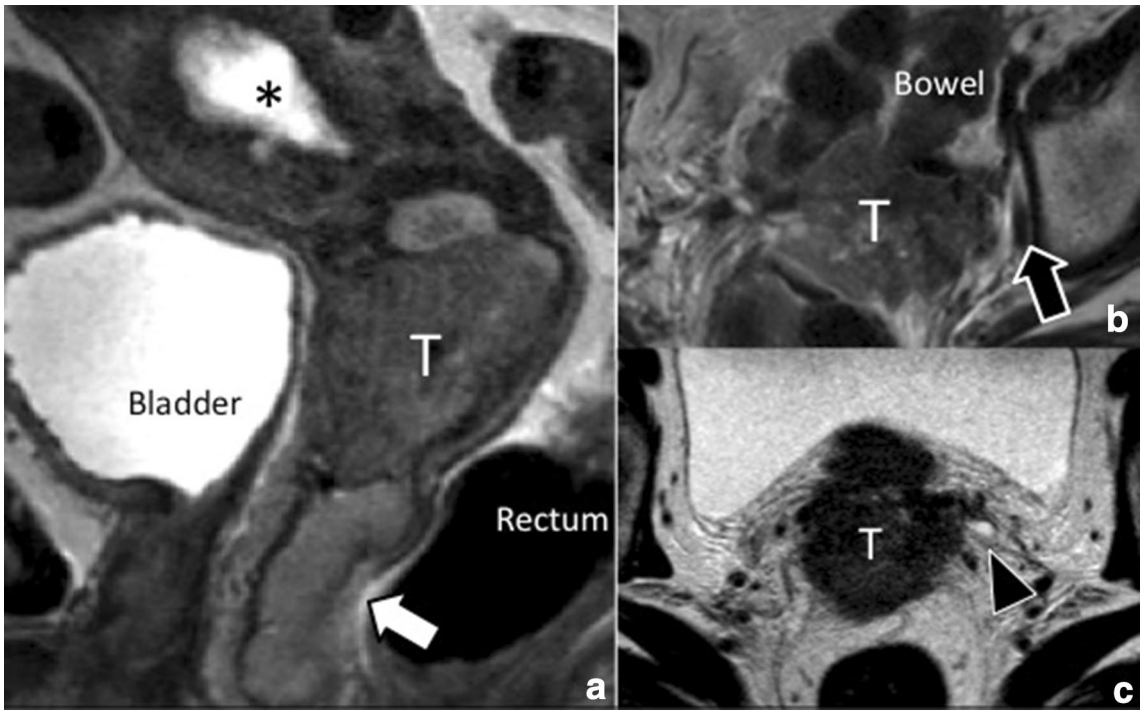

Fig. 7 Stage Ill in three different patients. Sagittal T2 (**a**) demonstrates stage IIIA of a biopsy-proven tumor-extending into the lower third of the vagina (block white arrow). Note obstruction of the corpus uteri (*). Axial T2 (**b**) shows a different heterogeneous cervical mass (T) extending abutting the left internal obturator muscle (block black arrow), consistent with pelvic side-wall involvement (stage IIIB). Axial T2 (**c**) shows obstruction of the left ureter (arrowhead) by the cervical mass (T), also consistent with pelvic side-wall invasion (stage IIIB)

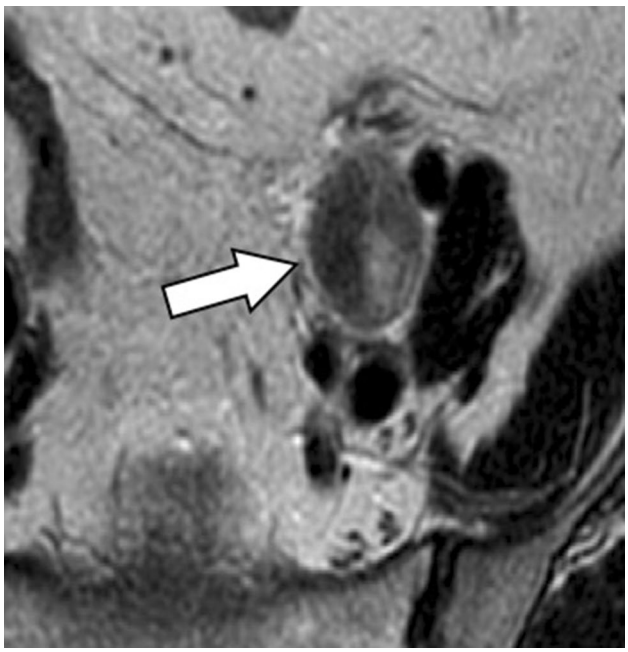

Fig. 8 Example of pelvic adenopathy. An enlarged heterogeneous left common iliac lymph node consistent with malignant adenopathy (arrow). The morphology of the lymph node such as round shape, heterogeneous signal, necrosis and spiculated margins are associated with malignant lymph nodes regardless of size

Tumor involvement of the bladder is depicted as disruption of the hypointense bladder wall by the mass. Direct invasion of the rectum by the cervical mass is uncommon, as the pouch of Douglas separates the posterior fornix of the vagina from the rectum. Rectal invasion is indicated by disruption of the T2 hypointense rectal wall by hyperintense tumor, which can then protrude into the rectal lumen [27] (Fig. 9b).

The preferred route for rectal invasion is via the uterosacral ligaments [28]. False positives occur when tumor abuts the rectum or bladder wall without mucosal invasion or when bladder wall edema mimics tumor involvement (i.e. bullous edema). Bullous edema commonly noted cystoscopically or on imaging, does not constitute IVA disease [29]. The accuracy of MRI ranges between 71 and 100% for bladder, and 88–91% for rectal invasion, respectively. MRI has also demonstrated a high negative predictive value (up to 100%) for exclusion of bladder and rectal invasion, therefore, the need for cystoscopy and endoscopic staging procedures is not mandated by FIGO if the staging MRI is negative for tumor involvement of these structures [30].

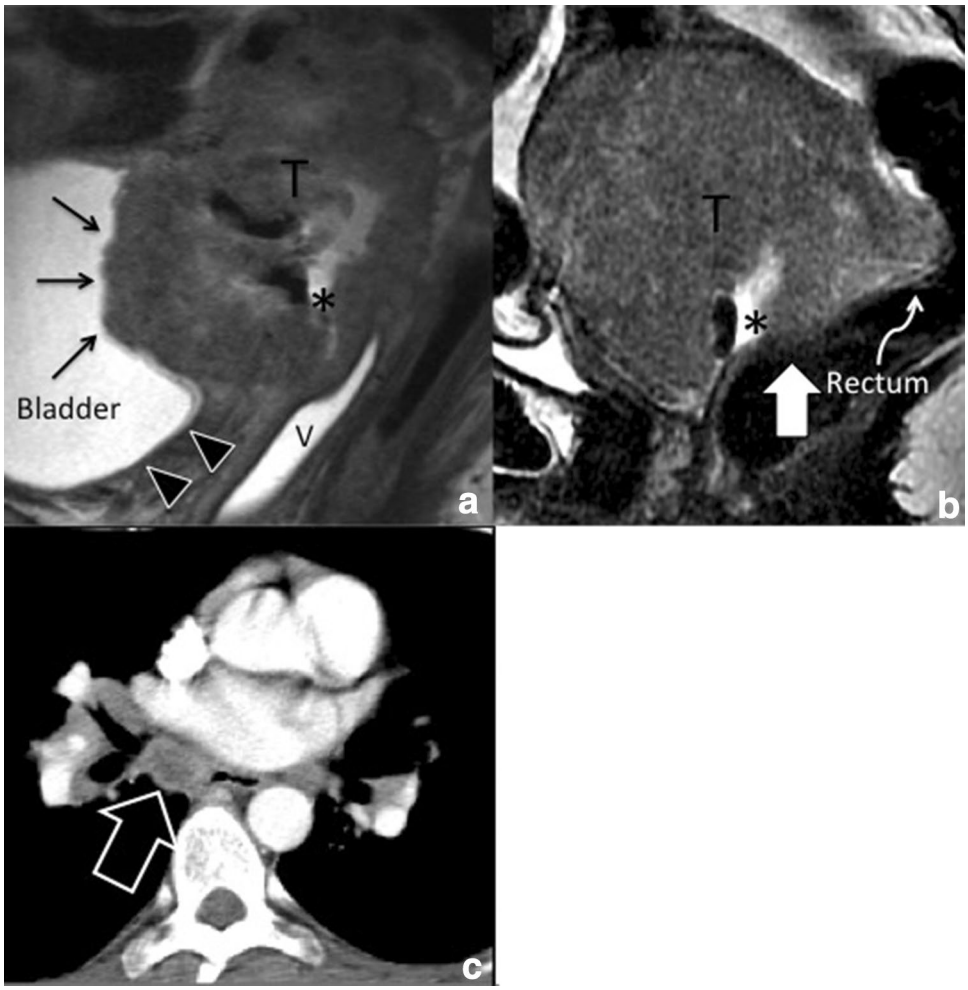

Fig. 9 Stage IV. Sagittal T2 demonstrate large cervical tumors (T) with internal gas and fluid (*) in different patients. Bladder wall invasion (**a**) shown by disruption of the normal bladder wall (black arrowheads) by tumor extending into the lumen (thin arrows). Rectal wall invasion (**b**) in a different cervical mass extending into the rectal lumen (block arrow). Compare to the preserved rectal wall more superiorly (curved arrow). Axial CT chest (**c**) demonstrates mediastinal adenopathy (block black arrow)

Clinical staging and implications of MRI

The revised FIGO staging now incorporates imaging evaluation in addition to clinical examination, according to available resources. MRI is the best method of radiologic assessment of primary tumors greater than 10 mm and has the ability to identify additional prognostic factors, which can guide the choice of treatment modality.

Treatment of cervical cancer depends on the stage (Table 2). Prognostic factors are taken into consideration when considering the radicality of surgery, whether a fertility-sparing procedure is an option, and whether chemo-radiation would be the preferred primary treatment. Principally, it is best to avoid radical surgery, followed by adjuvant chemo-radiation (for negative prognostic factors such as lymph node metastases), as the short- and long-term complications from this can be significant. Surgical treatment is the preferred modality for the treatment of small, early Stage 1B1/IB2 and IIA1 lesions. Depending on the substage, this could include cone biopsy ± simple extrafascial hysterectomy, versus radical hysterectomy or radical trachelectomy (for uterine/fertility preservation) for larger lesions. Lesion size (i.e. IB1 vs. IB2) suggests whether fertility-sparing and minimally invasive surgery are appropriate options [31]. More advanced lesions (e.g. IB3 and higher), are typically treated with chemo/radiation therapy. Imaging provides valuable clinical information during treatment planning [32, 33].

A shortcoming of the previous FIGO clinical staging system is the accurate assessment of parametrial invasion, tumor size, depth of invasion, and lymph node metastases by low-cost means (e.g. exam under anesthesia, IVP). These are key factors in predicting the need for adjuvant chemo-radiation therapy after radical surgery, which, as outlined above, is a circumstance clinicians aim to avoid. Accordingly, when available, the 2018 FIGO staging system permits imaging to assess for these factors. Studies have shown an estimated error rate with clinical staging of up to 25% for stage I and II disease, and 40% for more advanced stages. Additionally, there is a high inter and intra-observer variation in clinical pelvic examination [34]. An accurate pretreatment evaluation of parametrial

Table 2 Revised FIGO Staging

Stage	Description
I	Carcinoma strictly confined to cervix (extension to uterine corpus disregarded), diagnosed only by microscopy
IA	
IA1	Measured stromaL invasion < 3 mm in depth
IA2	Measured stromal invasion > or = 3 mm and < 5 mm in depth
IB	
IB1	Invasive carcinoma ≥ 5 mm depth of stromal invasion, and < 2 cm in greatest dimension
IB2	Invasive carcinoma ≥ 2 cm and < 4 cm in greatest dimension
IB3	Invasive carcinoma ≥ 4 cm in greatest dimension
II	Carcinoma invades beyond uterus, but has not extended onto lower third of vagina or pelvic wall
IIA1	Involvement limited to upper two-thirds of vagina without parametrial involvement, Invasive carcinoma < 4 cm in greatest dimension
IIA2	> 4 cm in greatest dimension
IIB	
IIB	With parametrial involvement, but not up to pelvic wall
III	Carcinoma involves lower third of vagina and/or pelvic wall and/or causes hydronephrosis or nonfunctioning kidney and/or involves pelvic and/or para-aortic lymph nodes
IIIA	
IIIA	Carcinoma involves lower third of vagina, no extension to pelvic wall
IIIB	
IIIB	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney (unless known to be due to another cause)
IIIC	
IIIC	Involvement of pelvic and/or para-aortic lymph nodes, irrespective of tumor size and extent (with r (imaging) and p (pathology) notations)
IIIC1	Pelvic lymph node metastasis only
IIIC2	Para-aortic lymph node metastasis
IV	Carcinoma extends beyond true pelvis or involves (biopsy proven) the mucosa of the bladder or rectum
IVA	
IVA	Spread to adjacent pelvic organs
IVB	
IVB	Spread to distant organs

invasion is crucial for both treatment planning and patient outcome [35].

A recent meta-analysis [22] of 3254 patients studied in 40 papers revealed that the pooled sensitivities for the detection of parametrial invasion and advanced disease in cervical carcinoma are significantly higher for MRI than for clinical exam, although the specificities of both are high and comparable. Despite the heterogeneity among the studies, they concluded that MRI is significantly better at excluding parametrial invasion and advanced disease compared to clinical examination.

Tumor size is also essential for prognosis and subsequent patient management [17]. Clinically visible lesions, and those with larger dimensions, are allocated to Stage IB and subgroups bases on the maximum diameter of the lesion. However, extension to the uterine corpus is disregarded for staging purposes at it does not in itself alter either the prognosis or management. Tumor volumes measured on MRI have been shown to give an accurate representation of true pathological tumor diameter within the cervix when compared with the anatomic pathological specimen. The FIGO measurement on EUA correlates poorly with average MR tumor diameter [36].

In a retrospective study [37] of 183 patients between 2003 and 2006, pretreatment staging MRI changed both the initial FIGO clinical staging and treatment planning and achieved a greater impact in higher tumor stages. In addition to more accurate tumor size and parametrial invasion assessment, MRI plays an important role in obese patients, who are generally more difficult to examine clinically. Besides staging, MRI can also help identify patients who may be candidates in deciding fertility-preserving surgery with radical trachelectomy by identifying a cervical length greater than 2.5 cm and tumor which is less than 2 cm in size and greater than 1 cm from the internal os [38].

Assessment of lymphadenopathy

Lymph nodal involvement is one of the most important prognostic factors in cervical cancer (Fig. 8). Pelvic lymphadenectomy is performed as a component of radical surgery given the high frequency of lymph node involvement [38, 39]

Although not part of the previous FIGO staging, it is recognized that the presence of lymph nodal metastases decreases the overall 5-year survival rates by 35–40% [40]. It was also found to be an important predictor for local control and, in one series [41], lymph nodal involvement was the most important predictor of overall survival. This and similar data led to changes in the 2018 FIGO staging system, with the presence of regional lymph nodes metastases designated as stage IIIC [42].

The traditional accepted MRI criteria for diagnosing metastatic pelvic lymph nodes is a shortest axis lymph node of greater than 1 cm, which has revealed a relevantly low sensitivity (30–73%). Overall, the sensitivity and specificity for detection of lymph node metastases by MRI widely ranges from 38–89% and 78–99%, respectively. Additional features that can be used to identity suspicious nodes include round shape, irregular margins, heterogeneous T2 signal, or the presence of necrosis [43].

DWI has emerged as a new technique for detecting pelvic lymph metastases in patients with cervical cancer. Additionally, the quantitative assessment can be performed by the measurement of the ADC. However, despite multiple studies that analyzed the feasibility of diagnosing metastatic adenopathy, the findings are inconclusive [44, 45]. In a recent meta-analysis [46], in regards of the performance of DWI in lymph node metastases in 1021 patients, DWI appears useful for differentiation between metastatic and benign lymph nodes in patients with uterine cervical cancer. Given the heterogeneity of the studies analyzed and lack of a standard protocol among the institutions, large, multi-centric and prospective studies with standardized diffusion protocols are still needed for further change in routine clinical applications.

Assessment of treatment response

Role of MRI

MR imaging is 78% accurate in evaluation of tumor response; in 22% of patients, however, benign conditions are not distinguishable from tumor [8]. There is no consensus in the reviewed literature regarding indication of MRI for routine follow-up of cervical carcinoma after chemoradiation or surgery. After trachelectomy, MRI at 6 months and 1 year is advised due to high recurrence rate fertility sparing [41] [47].

MR criteria for a complete response include: (a) No lesion seen in the cervix or in the adjacent anatomic areas, (b), homogeneous hypointense cervical stroma and (c) homogeneous and delayed intravenous contrast uptake of the cervix [26] (Fig. 10).

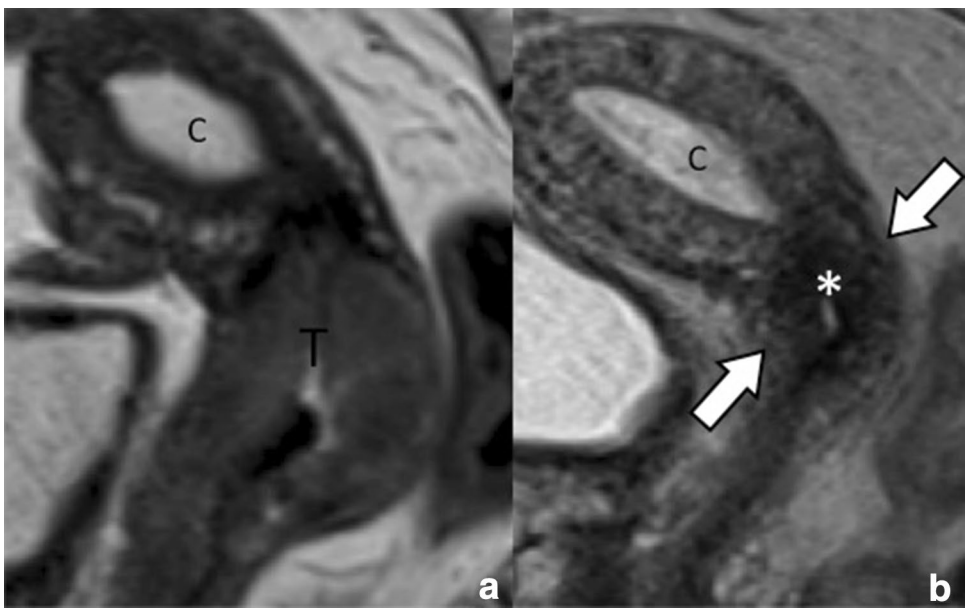

Fig. 10 Treatment response. Sagittal T2 (**a**) demonstrates a large cervical mass (T) obstructing the corpus uteri (C) before treatment. Sagittal T2 (**b**) after radiation demonstrates resolution of the mass and new visualization of the T2 hypointense cervical stroma (*). Note improved obstruction of the corpus (C) and small cervix post-radiation (block arrows)

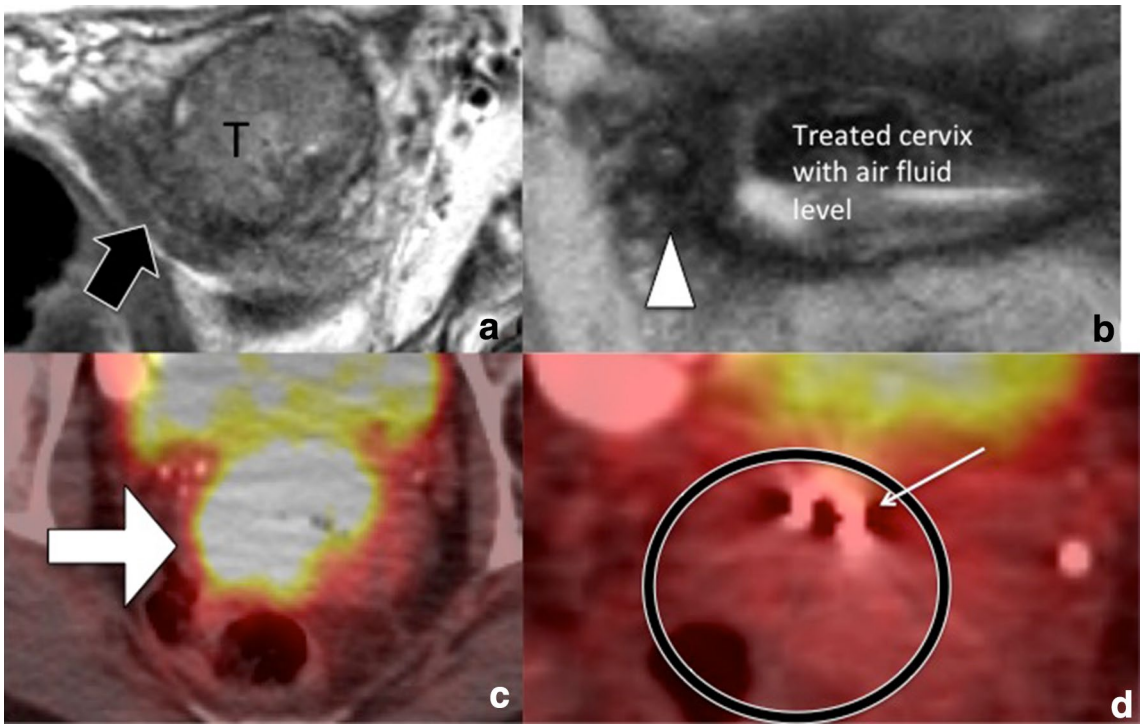

Fig. 11 Pitfall of residual tumor. Axial T2 pre-treatment (**a**) shows a large tumor (T) with parametrial extension (black arrow) and corresponding FDG avidity on PET–CT (white arrow) (**b**). Axial T2 post-treatment (**c**) demonstrates improvement of the mass with heterogeneous residual signal in the right parametrium (arrowhead). PET–CT post treatment done simultaneously (**d**) demonstrates no FDG activity (circle), compatible with complete response. Please note fiducials (white arrow)

Role of PET–CT

Combining metabolic PET images with anatomic CT has proven highly accurate in identifying the presence of regional lymph node involvement as well as extrapelvic disease extension. PET–CT has been found to be useful for initial staging, assessment of therapy response, and detection of recurrence in patients with cervical cancer [48] (Figs. 11, 12). The initial staging may be improved by providing information on extrapelvic and para-aortic sites, such as thoracic adenopathy, lung, bone, peritoneum, omentum, adrenal gland, and liver and also helps in treatment planning with external beam radiotherapy for patients with locally advanced cervical cancer [34].

Role of PET–MRI

In general, FDG-PET is combined with low-dose CT images. The contrast resolution of CT is inferior to that of MRI, therefore, if local treatment is suspected based on PET–CT, MRI is necessary for adequate treatment planning. The pitfalls of MRI alone in the detection of residual or persistent disease is complicated by the false-positive results that can occur by inflammation-induced edema, necrosis and post-radiation induced fibrosis. The combination of MRI and FDG-PET results in a more accurate diagnosis, staging and follow-up of cervical cancer [49]. Additionally, FDG-PET is able to assess lymph node metastasis, potentially resulting in better treatment decisions after radiation treatment [50].

Conclusion

The staging system of cervical cancer remains clinical, but the new revised 2018 FIGO staging systems also permits, when available, imaging and pathology data to assign or change the stage. MRI is the modality of choice for local–regional staging of cervical cancer, evaluating the response to treatment and detecting tumor recurrence and potential complications. The combination with PET or PET–CT and other imaging modalities can also depict a more accurate detection of pathological lymph nodes, providing important information about prognostic factors in this disease.

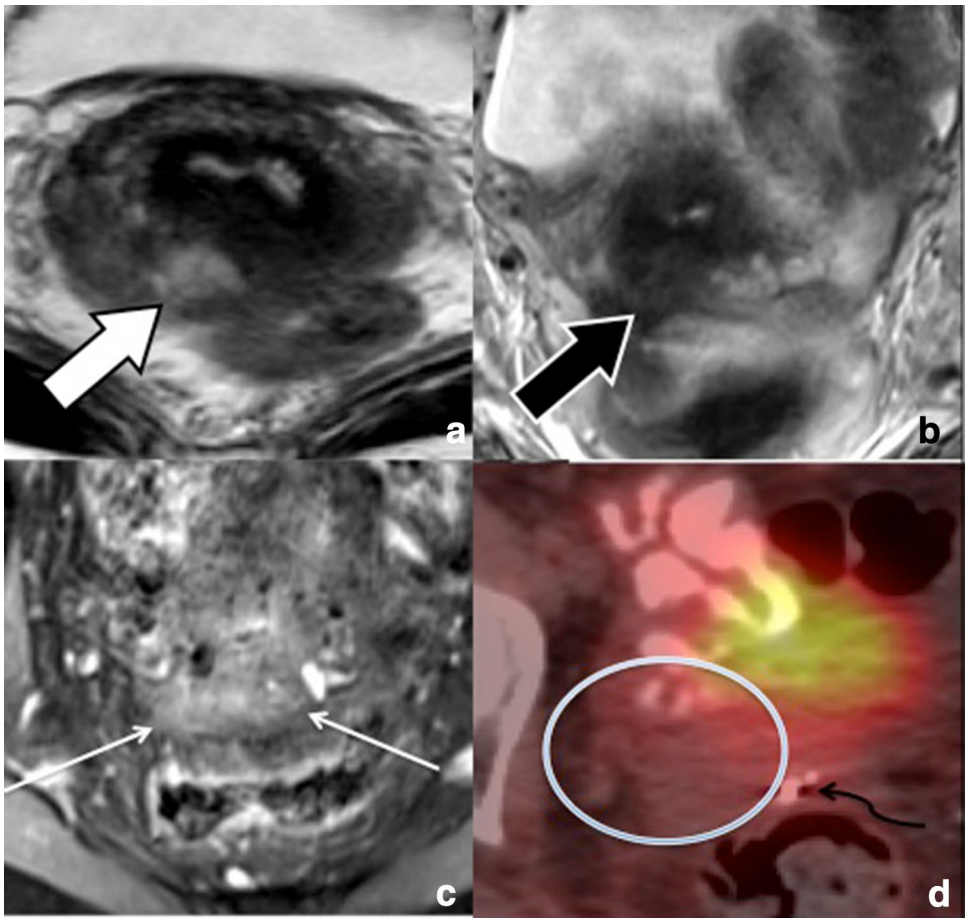

Fig. 12 Pitfall of residual tumor. Axial T2 (**a**) demonstrates a hyperintense cervical mass in the right posterolateral cervix before treatment (block white arrow). Axial T2 (**b**) of the same patient after treatment demonstrates abnormal intermediate T2 signal (block black arrow) with corresponding enhancement shown (thin white arrows) (**c**), concerning for residual tumor. PET–CT (**d**) performed shortly after demonstrates no FDG uptake (circle) at the level of the cervix, adjacent to a fiducial marker (curved arrow) consistent with complete response

References

1. Bhatla N, Berek JS, Cuello Fredes M, Denny LA, Grenman S, Karunaratne K, et al. Revised FIGO staging for carcinoma of the cervix uteri. Int J Gynaecol Obstet. 2019 Jan 17;68(16-20):394.
2. Ferlay J, Shin H-R, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. Wiley Subscription Services, Inc., A Wiley Company; 2010 Jun 17;127(12):2893–917.
3. Herrington CS. Recent advances in molecular gynaecological pathology. Histopathology. Blackwell Publishing Ltd; 2009 Sep;55(3):243–9.
4. Li N, Franceschi S, Howell-Jones R, Snijders PJF, Clifford GM. Human papillomavirus type distribution in 30,848 invasive cervical cancers worldwide: Variation by geographical region, histological type and year of publication. Int J Cancer. Wiley Subscription Services, Inc., A Wiley Company; 2011 Feb 15;128(4):927–35.
5. Wingo SN, Gallardo TD, Akbay EA, Liang M-C, Contreras CM, Boren T, et al. Somatic LKB1 mutations promote cervical cancer progression. Aziz SA, editor. PLOS ONE. 2009;4(4):e5137.
6. Bahrami A, Hasanzadeh M, Shahidsales S, Farazestanian M, Hassanian SM, Moetamani Ahmadi M, et al. Genetic susceptibility in cervical cancer: From bench to bedside. J Cell Physiol. 2018 Mar;233(3):1929–39.
7. Kurman RJ. Blaustein's Pathology of the Female Genital Tract. Kurman RJ, editor. New York, NY: Springer Science & Business Media; 2011, p155-191.
8. Choi SH, Kim SH, Choi HJ, Park BK, Lee HJ. Preoperative magnetic resonance imaging staging of uterine cervical carcinoma: results of prospective study. Journal of Computer Assisted Tomography. 2004 Sep;28(5):620–7.
9. Ma DJ, Zhu J-M, Grigsby PW. Change in T2-fat saturation MRI correlates with outcome in cervical cancer patients. Int J Radiat Oncol Biol Phys. 2011 Dec 1;81(5):e707–12.
10. Thomsen HS. Guidelines for Contrast Media from the European Society of Urogenital Radiology. American Journal of Roentgenology. American Roentgen Ray Society; 2003 Dec;181(6):1463–71.
11. Jalaguier-Coudray A, Villard-Mahjoub R, Delouche A, Delarbre B, Lambaudie E, Houvenaeghel G, et al. Value of Dynamic Contrast-enhanced and Diffusion-weighted MR Imaging in the Detection of Pathologic Complete Response in Cervical Cancer after Neoadjuvant Therapy: A Retrospective Observational Study. Radiology. Radiological Society of North America; 2017 Aug;284(2):432–42.
12. Vincens E, Balleyguier C, Rey A, Uzan C, Zareski E, Gouy S, et al. Accuracy of magnetic resonance imaging in predicting residual disease in patients treated for stage IB2/II cervical carcinoma with chemoradiation therapy. Cancer. 2008 Oct 15;113(8):2158–65.
13. Dhoot NM, Kumar V, Shinagare A, Kataki AC, Barmon D, Bhuyan U. Evaluation of carcinoma cervix using magnetic resonance imaging: correlation with clinical FIGO staging and impact on management. J Med Imaging Radiat Oncol. Blackwell Publishing Asia; 2012 Feb;56(1):58–65.
14. Houvenaeghel G, Lelievre L, Buttarelli M, Jacquemier J, Carcopino X, Viens P, et al. Contribution of surgery in patients with bulky residual disease after chemoradiation for advanced cervical carcinoma. Eur J Surg Oncol. 2007 May;33(4):498–503.

15. Balleyguier C, Sala E, Da Cunha T, Bergman A, Brkljacic B, Danza F, et al. Staging of uterine cervical cancer with MRI: guidelines of the European Society of Urogenital Radiology. Eur Radiol. Springer-Verlag; 2011 May;21(5):1102–10.
16. Lin G, Ho K-C, Wang J-J, Ng K-K, Wai Y-Y, Chen Y-T, et al. Detection of lymph node metastasis in cervical and uterine cancers by diffusion-weighted magnetic resonance imaging at 3T. J Magn Reson Imaging. Wiley Subscription Services, Inc., A Wiley Company; 2008 Jul;28(1):128–35.
17. Malayeri AA, Khouli El RH, Zaheer A, Jacobs MA, Corona-Villalobos CP, Kamel IR, et al. Principles and applications of diffusion-weighted imaging in cancer detection, staging, and treatment follow-up. RadioGraphics. Radiological Society of North America; 2011 Oct;31(6):1773–91.
18. NaNakamura K, Joja I, Nagasaka T, Fukushima C, Kusumoto T, Seki N, et al. The mean apparent diffusion coefficient value (ADCmean) on primary cervical cancer is a predictive marker for disease recurrence. Gynecologic Oncology. 2012 Dec;127(3):478–83.
19. McVeigh PZ, Syed AM, Milosevic M, Fyles A, Haider MA. Diffusion-weighted MRI in cervical cancer. Eur Radiol. Springer-Verlag; 2008 Jan 12;18(5):1058–64.
20. Naganawa S, Sato C, Kumada H, Ishigaki T, Miura S, Takizawa O. Apparent diffusion coefficient in cervical cancer of the uterus: comparison with the normal uterine cervix. Eur Radiol. Springer-Verlag; 2004 Nov 5;15(1):71–8.
21. Heo SH, Shin SS, Kim JW, Lim HS, Jeong YY, Kang WD, et al. Pre-Treatment Diffusion-Weighted MR Imaging for Predicting Tumor Recurrence in Uterine Cervical Cancer Treated with Concurrent Chemoradiation: Value of Histogram Analysis of Apparent Diffusion Coefficients. Korean Journal of Radiology. 2013;14(4):616.
22. Thomeer MG, Gerestein C, Spronk S, van Doorn HC, van der Ham E, Hunink MG. Clinical examination versus magnetic resonance imaging in the pretreatment staging of cervical carcinoma: systematic review and meta-analysis. Eur Radiol. Springer-Verlag; 2013 Jul;23(7):2005–18.
23. Kraljević Z, Visković K, Ledinsky M, Zadravec D, Grbavac I, Bilandzija M, et al. Primary uterine cervical cancer: correlation of preoperative magnetic resonance imaging and clinical staging (FIGO) with histopathology findings. Coll Antropol. 2013 Jun;37(2):561–8.
24. Kim M, Suh DH, Kim K, Lee HJ, Kim YB, No JH. Magnetic Resonance Imaging as a Valuable Tool for Predicting Parametrial Invasion in Stage IB1 to IIA2 Cervical Cancer. Int J Gynecol Cancer. 2017 Feb;27(2):332–8.
25. Atcı N, Özgür T, Öztürk F, Dolapçıoğlu KS. Utility of intravaginal ultrasound gel for local staging of cervical carcinoma on MRI. Clin Imaging. 2016 Dec;40(6):1104–7.
26. Csutak C, Ordeanu C, Nagy VM, Pop DC, Bolboaca SD, Badea R, et al. A prospective study of the value of pre- and post-treatment magnetic resonance imaging examinations for advanced cervical cancer. Clujul Med. 2016;89(3):410–8.
27. Gill BS, Kim H, Houser CJ, Kelley JL III, Sukumvanich P, Edwards RP, et al. Extended Clinical Outcomes of 3D High-Dose-Rate Intracavitary Brachytherapy with MRI-Based Planning for Treatment of Cervical Cancer. Brachytherapy. 2014 Mar;13:S33.
28. Testa AC, Moro F, Pasciuto T, Moruzzi MC, Di Legge A, Fuoco G, et al. PRospective Imaging of CErvical cancer and neoadjuvant treatment (PRICE) study: role of ultrasound to assess residual tumor in locally advanced cervical cancer patients undergoing chemoradiation and radical surgery. Ultrasound Obstet Gynecol. 2018 Jul;52(1):110–8.
29. Testa AC, Di Legge A, De Blasis I, Moruzzi MC, Bonatti M, Collarino A, et al. Imaging techniques for the evaluation of cervical cancer. Best Practice & Research Clinical Obstetrics & Gynaecology. 2014 Jul;28(5):741–68.
30. Mitchell DG, Snyder B, Coakley F, Reinhold C, Thomas G, Amendola M, et al. Early invasive cervical cancer: tumor delineation by magnetic resonance imaging, computed tomography, and clinical examination, verified by pathologic results, in the ACRIN 6651/GOG 183 Intergroup Study. J Clin Oncol. 2006 Dec 20;24(36):5687–94.
31. Rockall AG, Qureshi M, Papadopoulou I, Saso S, Butterfield N, Thomassin-Naggara I, et al. Role of Imaging in Fertility-sparing Treatment of Gynecologic Malignancies. RadioGraphics. Radiological Society of North America; 2016 Nov;36(7):2214–33.
32. Peters WA, Liu PY, Barrett RJ, Stock RJ, Monk BJ, Berek JS, et al. Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix. JCO. 2000 Apr;18(8):1606–13.
33. Matsuo K, Machida H, Mandelbaum RS, Konishi I, Mikami M. Validation of the 2018 FIGO cervical cancer staging system. Gynecologic Oncology. 2019 Jan;152(1):87–93.
34. Kaur H, Silverman PM, Iyer RB, Verschraegen CF, Eifel PJ, Charnsangavej C. Diagnosis, staging, and surveillance of cervical carcinoma. American Journal of Roentgenology. American Roentgen Ray Society; 2003 Jun;180(6):1621–31.
35. Rockall AG, Ghosh S, Alexander-Sefre F, Babar S, Younis MTS, Naz S, et al. Can MRI rule out bladder and rectal invasion in cervical cancer to help select patients for limited EUA? Gynecologic Oncology. 2006 May;101(2):244–9.
36. Monk BJ, Tian C, Rose PG, Lanciano R. Which clinical/pathologic factors matter in the era of chemoradiation as treatment for locally advanced cervical carcinoma? Analysis of two Gynecologic Oncology Group (GOG) trials. Gynecologic Oncology. 2007 May;105(2):427–33.
37. Shen G, Zhou H, Jia Z, Deng H. Diagnostic performance of diffusion-weighted MRI for detection of pelvic metastatic lymph nodes in patients with cervical cancer: a systematic review and meta-analysis. Br J Radiol. The British Institute of Radiology; 2015 Aug;88(1052):20150063.
38. Bouchard-Fortier G, Reade CJ, Covens A. Non-radical surgery for small early-stage cervical cancer. Is it time? Gynecologic Oncology. 2014 Mar;132(3):624–7.
39. Kato R, Hasegawa K, Torii Y, Udagawa Y, Fukasawa I. Factors affecting platinum sensitivity in cervical cancer. Oncol Lett. Spandidos Publications; 2015 Dec;10(6):3591–8.
40. Leblanc E, Narducci F, Frumovitz M, Lesoin A, Castelain B, Baranzelli MC, et al. Therapeutic value of pretherapeutic extraperitoneal laparoscopic staging of locally advanced cervical carcinoma. Gynecologic Oncology. 2007 May;105(2):304–11.
41. Atahan Il, Onal C, Ozyar E, Yiliz F, Selek U, Kose F. Long-term outcome and prognostic factors in patients with cervical carcinoma: a retrospective study. International Journal of Gynecological Cancer. Blackwell Publishing Inc; 2007 Jul;17(4):833–42.
42. Sironi S, Buda A, Picchio M, Perego P, Moreni R, Pellegrino A, et al. Lymph node metastasis in patients with clinical early-stage cervical cancer: detection with integrated FDG PET/CT. Radiology. Radiological Society of North America; 2006 Jan;238(1):272–9.
43. McMahon CJ, Rofsky NM, Pedrosa I. Lymphatic Metastases from Pelvic Tumors: Anatomic Classification, Characterization, and Staging. Radiology. Radiological Society of North America, Inc; 2010 Jan;254(1):31–46.
44. Kim JK, Kim KA, Park B-W, Kim N, Cho K-S. Feasibility of diffusion-weighted imaging in the differentiation of metastatic from nonmetastatic lymph nodes: early experience. J Magn Reson Imaging. 2008 Sep;28(3):714–9.

45. Kim HS, Kim CK, Park BK, Huh SJ, Kim B. Evaluation of therapeutic response to concurrent chemoradiotherapy in patients with cervical cancer using diffusion-weighted MR imaging. J Magn Reson Imaging. 2013 Jan;37(1):187–93.
46. Kuang F, Yan Z, Li H, Feng H. Diagnostic accuracy of diffusion-weighted MRI for differentiation of cervical cancer and benign cervical lesions at 3.0T: Comparison with routine MRI and dynamic contrast-enhanced MRI. J Magn Reson Imaging. John Wiley & Sons, Ltd; 2015 Oct;42(4):1094–9.
47. McEvoy SH, Nougaret S, Abu-Rustum NR, Vargas HA, Sadowski EA, Menias CO, et al. Fertility-sparing for young patients with gynecologic cancer: How MRI can guide patient selection prior to conservative management. Abdominal Radiology. 3rd ed. Springer US; 2017 May 20;42(10):2488–512.
48. Schwarz JK, Rader JS, Huettner PC, Watson MA, Grigsby PW. Molecular Characterization of FDG-PET Metabolic Response in Cervical Cancer. International Journal of Radiation Oncology*Biology*Physics. 2007 Nov;69(3):S115.
49. Mongula JE, Bakers FCH, Vöö S, Lutgens L, van Gorp T, Kruitwagen RFPM, et al. Positron emission tomography-magnetic resonance imaging (PET-MRI) for response assessment after radiation therapy of cervical carcinoma: a pilot study. EJNMMI Res. SpringerOpen; 2018 Jan 2;8(1):1.
50. Siva S, Deb S, Young RJ, Hicks RJ, Callahan J, Bressel M, et al. 18F-FDG PET/CT following chemoradiation of uterine cervix cancer provides powerful prognostic stratification independent of HPV status: a prospective cohort of 105 women with mature survival data. Eur J Nucl Med Mol Imaging. 2015 Nov;42(12):1825–32.