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Reviews and Commentary
Review

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2018 FIGO Staging System for Uterine Cervical Cancer: Enter Cross-sectional Imaging

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Virtual Journal Club: RADY 401

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UNC SCHOOL OF MEDICINE Radiology

Learning objectives

By the end of this journal club, participants will be able to

- Identify components of cervical cancer staging
- Discuss advantages and disadvantages of various imaging modalities for cervical cancer staging
- Identify the best available imaging modality based on local availability

Two Quick Notes

1. This is a review article so the presentation will be slightly different than previous VJC presentations
2. Gender-neutral language is used when possible in recognition that not all patients with cervical cancer are female, and not all females have a cervix

Module Outline

I. Case
II. Background
III. Article Overview
IV. Clinical Questions
V. Key Points

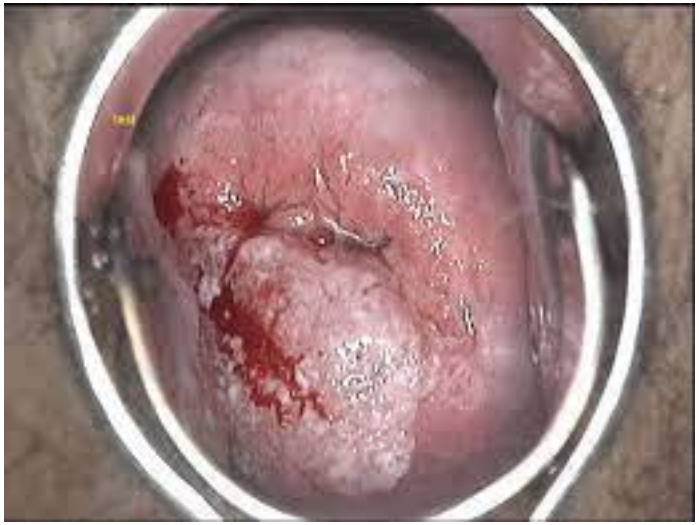
Case presentation

A 44yo G4P4004 female presented to HHA in 2019 for a routine pap smear.

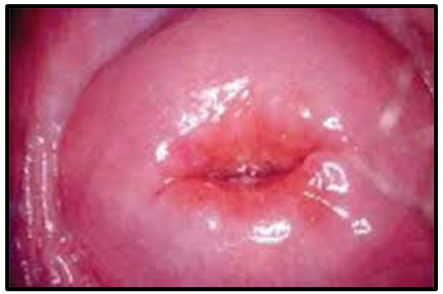
Per patient report, she had a normal pap in 2016.

She denies any abnormal bleeding and denies other GU complaints.

Case imaging



Pap smear: cervical cancer



Normal cervix for reference

Case questions (why we went to the literature)

What is the next step in this patient's workup?

When are specific imaging modalities used?

What options exist for imaging in resource-limited settings?

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Cervical Cancer

- Globally occurs in 12% of women
- Second most common cancer worldwide, most common in developing countries with 84% of cases in resource-limited areas
  - 14,500 news cases and 4,300 deaths per year in the US
  - 604,000 new cases and 342,000 deaths per year worldwide
- HPV is critical to development of cervical cancers
- 70% of cervical cancers are squamous cell, 35% are adenocarcinoma
- Overall 75% decrease in cases in resource-rich areas over 50 years

Cervical Cancer Risk Factors

- HPV
  - Early onset sexual activity
  - Multiple sexual partners or high-risk sexual partners
  - History of STIs
  - Early age at first birth (<20yr) or P3 or greater
  - History of vulvar or vaginal squamous intraepithelial neoplasia or cancer
  - Immunosuppression
- Non-NPV
  - Low SES
  - OCP use
  - Cigarette use (increased risk of squamous only(
  - Genetics

Cervical Cancer Continued

- Steps of cervical cancer development
  - Oncogenic HPV infections
  - Persistence of infection
  - Progressions of clonal epihelias cells from persistent viral infection to precancer
  - Development of carcinoma and invasion into the basement membrane
- HPV infection is very common, but cervical cancer develops in only a small proportion of infected patients
- Takes 10-15 years from infection until neoplasia development

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Article specifics

I. Purpose: To describe updates to the FIGO staging system for uterine cervical cancer, to describe imaging modalities for evaluation of UCC, and describe options in resource-limited settings

II. Journal: Radiology

III. Study type: Review

IV. # cases: NA

V. Data: FIGO Recommendations

FIGO Staging of GYN Cancers

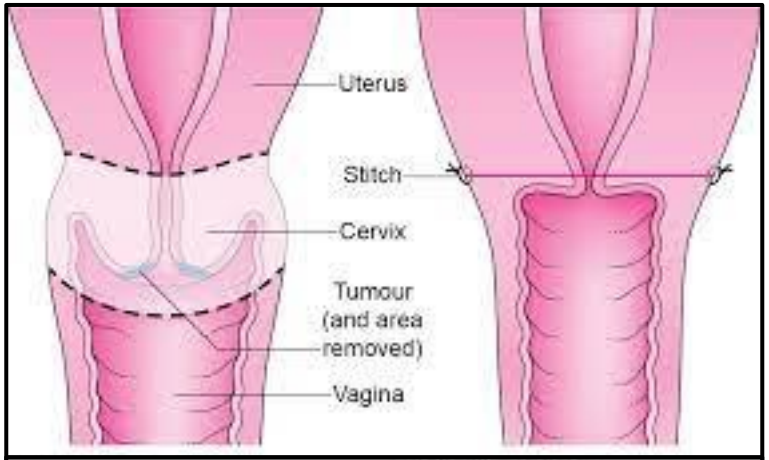
- Staging previously relied on surgery and pathology
- Clinical Staging was added in 2018
  - Pelvic exam
  - Bladder cystoscopy
  - Colposcopy
  - Imaging

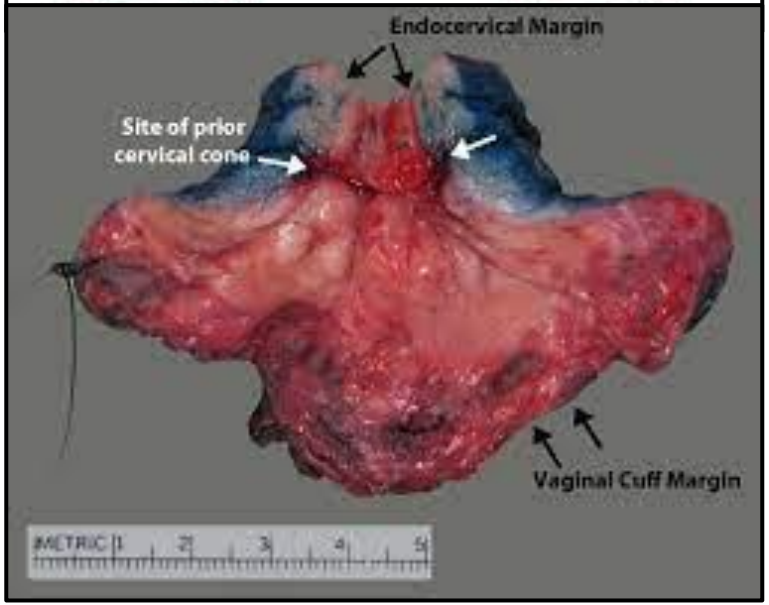
2018 FIGO Staging of Uterine Cervical Cancer

Stage	Description
I	Carcinoma is strictly confined to the cervix (extension to the uterine corpus should be disregarded)
IA	Invasive carcinoma that can be diagnosed only with microscopy, with maximum depth of invasion <5 mm
IA1	Stromal invasion <3 mm in depth
IA2	Stromal invasion ≥3 mm and <5 mm in depth
IB	Invasive carcinoma confined to the uterine cervix, with measured deepest invasion ≥5 mm
IB1*	Tumor measures <2 cm in greatest dimension
IB2*	Tumor measures ≥2 cm and <4 cm in greatest dimension
IB3*	Tumor measures ≥4 cm in greatest dimension
II	Carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall
IIA	Limited to the upper two-thirds of the vagina without parametrial involvement
IIA1	Tumor measures <4 cm in greatest dimension
IIA2	Tumor measures ≥4 cm in greatest dimension
IIB	With parametrial involvement but not up to the pelvic wall
III	Carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or nonfunctioning kidney and/or involves pelvic and/or para-aortic lymph nodes
IIIA	Involves the lower third of the vagina, with no extension to the pelvic wall
IIIB	Extension to the pelvic wall and/or hydronephrosis or nonfunctioning kidney from tumor
IIIC*	Involvement of pelvic and/or para-aortic lymph nodes, irrespective of tumor size and extent†
IIIC1*	Pelvic lymph node metastasis only
IIIC2*	Para-aortic lymph node metastasis
IV	Carcinoma has extended beyond the true pelvis or has involved (biopsy-proven) the mucosa of the bladder or rectum
IVA	Spread to adjacent pelvic organs
IVB	Spread to distant organs

Updates in 2018

- Maximal cross-sectional tumor diameter was previously measured with imaging and pathological exam, but clinical exam was added
  - Tumors 2-4cm (IB2) are twice as likely to be associated with death from cervical cancer as those <2cm (IB1)
  - IB1 more likely to be adenocarcinoma with low-grade histological features
  - IB2 more likely to be squamous cell carcinoma with high-grade histological features
- Assessment of abdominopelvic retroperitoneal lymph nodes
  - Pelvic lymph node mets correspond to stage IIIC1and para-aortic mets IIIC2
  - Lymphadenopathy at cross-sectional imaging is a major prognostic factor for survival





Radical Trachelectomy

- Fertility-sparing treatment where uterine cervix, parametria, and vaginal cuff are resected
- A cerclage is placed across the uterine isthmus to ensure cervical competency in future pregnancies
- Must be stage I disease (confined to the cervix)
- Tumor cannot extend into the uterine corpus
- Pelvic lymph nodes must be evaluated surgically and be negatives for mets

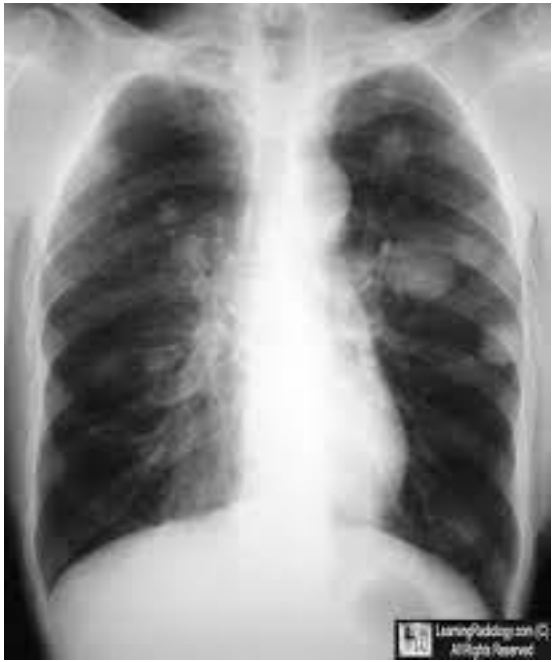
Resource Setting and Primary Target for Diagnosis*	FIGO Stage
Basic	
Chest radiography	
Lung metastases	IVB
Limited	
Pelvic US	
Tumor size	IB
Parametrial tumor spread	IIB
Abdominal US	
Hydronephrosis	IIIB
Chest radiography	
Lung metastases	IVB
Enhanced	
Abdominopelvic MRI†	
Tumor size	IB
Parametrial tumor spread	IIB
Tumor spread to pelvic sidewall	IIIB
Hydronephrosis	IIIB
Retroperitoneal adenopathy	IIIC
Chest radiography‡	
Lung metastases	IVB
Maximal	
Pelvic MRI	
Tumor size	IB
Parametrial tumor spread	IIB
Tumor spread to pelvic sidewall	IIIB
Torso fusion FDG PET/CT§	
Hydronephrosis	IIIB
Retroperitoneal adenopathy	IIIC
Distant metastases including lungs, peritoneum, extraretroperitoneal lymph nodes, and bones‖	IVB

Choice of Imaging based on resource availability for staging of patients with uterine cervical cancer

- Note.—Imaging is appropriate in women with tumor invasive to a depth greater than or equal to 5 mm. FDG = fluorodeoxyglucose, FIGO = International Federation of Gynecology and Obstetrics.
- *Complete description is available in reference 53.
- † Examination should include small field-of-view images tailored for soft-tissue evaluation of the central pelvis and large field-of-view images of the abdomen and pelvis to evaluate retroperitoneal lymph nodes and the renal collecting system.
- ‡ Abnormalities should be further evaluated with chest CT.
- § PET and CT images should be acquired with hybrid scanner and analysis should include fusion imaging. CT should be of diagnostic quality but use of iodinated contrast material is optional.
- ‖ Abnormalities should be confirmed with pathologic analysis.

Radiographic

- Chest radiography is PA and lateral views is performed to evaluate for pulmonary mets in patients with local to regionally advanced disease
- Lung nodules are most common, followed by pleural effusions or masses
- Radiography is first line (over CT) for chest imaging if PET/CT is NOT performed



Ultrasound

- Endovaginal or endorectal US can measure primary tumor size and assess for local spread into uterine cervical stroma (IB) or parametria (IIB)
- Tumor is typically homogenously solid and hypoechoic relative to uterine cervical stroma
- Transabdominal US can evaluate hydronephrosis (IIIB) – if cross-sectional imaging is not performed with CT, MRI, or PET/CT
- Closely correlates with MRI or pathological tumor size (IA2-IIA)
- Limited field of view, soft-tissue contrast can impeded accurate measurement

US versus MRI for Tumor Size and Parametrial Spread

Parameter	US*	MRI*
Tumor size <2 cm (FIGO stage <IB1)		
Sensitivity (%)	89 (71/80)	84 (67/80)
Specificity (%)	89 (91/102)	87 (89/102)
Tumor size >4 cm (FIGO stage >1B3)		
Sensitivity (%)	78 (25/32)	81 (26/32)
Specificity (%)	99 (148/150)	95 (143/150)
Parametrial extension (FIGO stage ≥IIB)		
Sensitivity (%)	77 (10/13)	69 (9/13)
Specificity (%)	98 (166/169)	92 (155/169)

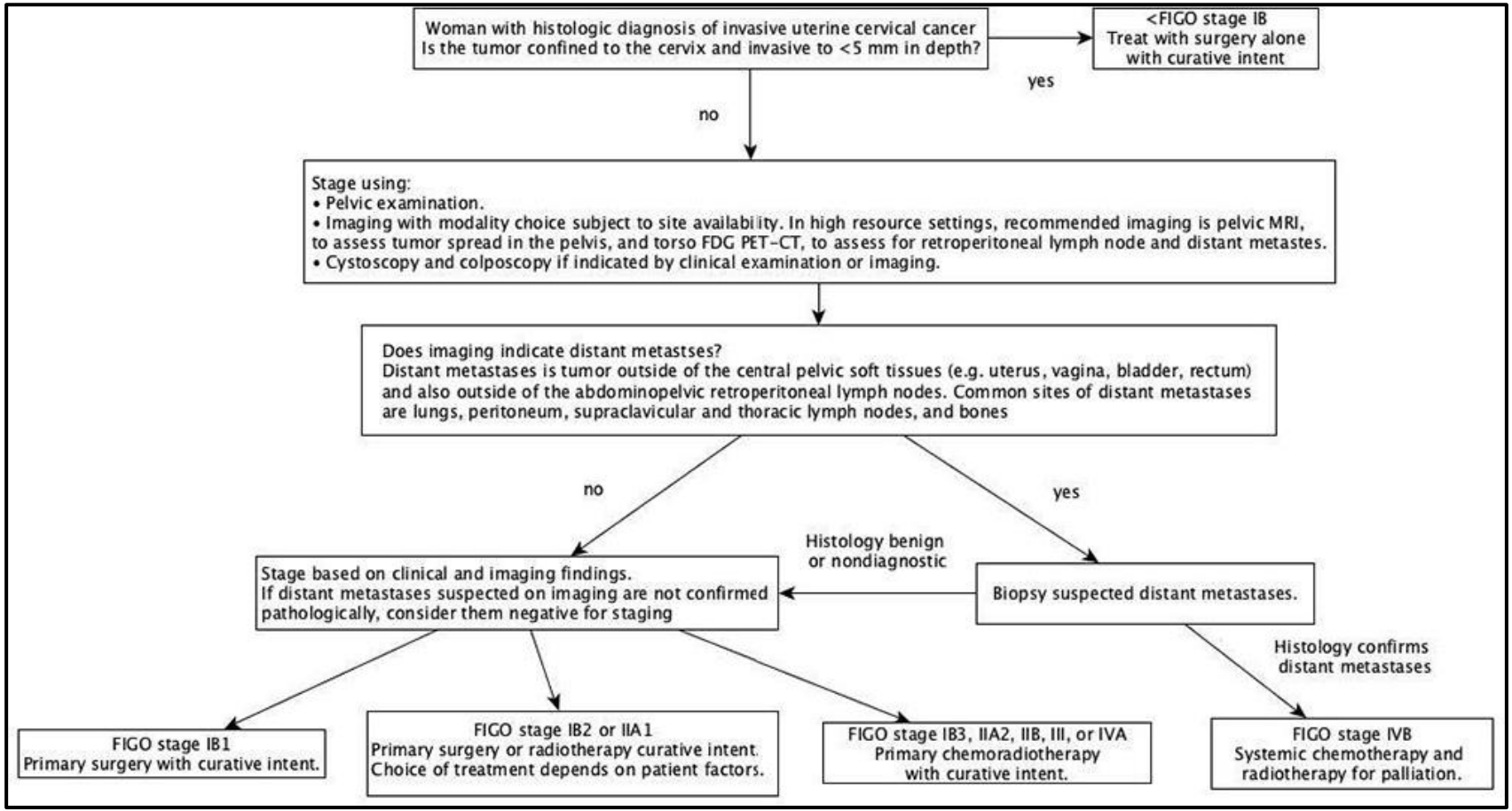
- Source.—Reference 54.
- Note.— Data in parentheses are primary ratios. Patient is clinically suspected to have low-stage disease (ie, less than International Federation of Gynecology and Obstetrics [FIGO] stage IIA).
- *Reference standard is pathologic analysis.

CT

- Abdominopelvic CT is used to evaluate retroperitoneal lymphadenopathy (IIIC)
  - Performed as PET/CT or when MRI is not available or contraindicated
  - Tumor is usually homogenously enhancing with normal cervical tissue
  - Tumor involvement “likely” if lymph nodes >1cm and “almost certainly” if >1.5cm

MRI

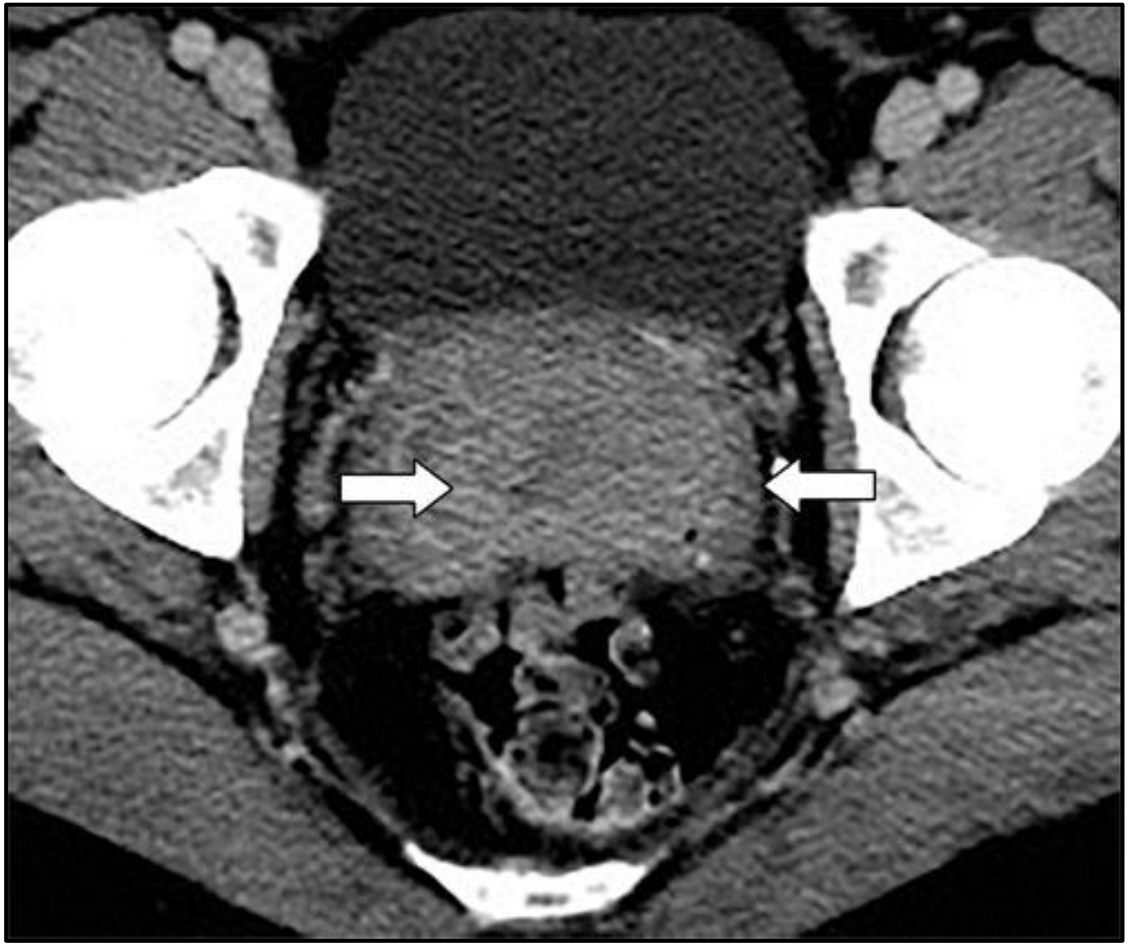
- Evaluates primary tumor as well as spread to soft tissues of the pelvis
- More closely correlates with pathologic tumor size than CT
- Multiplanar T2 images evaluate for tumor invasion into the parametria (stage IIB) and pelvic sidewall (stage IIIB)
  - Tumor, both primary and metastatic, is of intermediate signal intensity (ie, lower than fat but higher than myometrium or cervical stroma) and enhances less avidly than the normal
  - Some tumors, especially after cone biopsy, may be of too small a volume to be seen at MRI



Cervical cancer staging and patient triage with the FIGO 2018 staging system.
Recommended imaging according on resources available at the practice setting is described in Table 2.

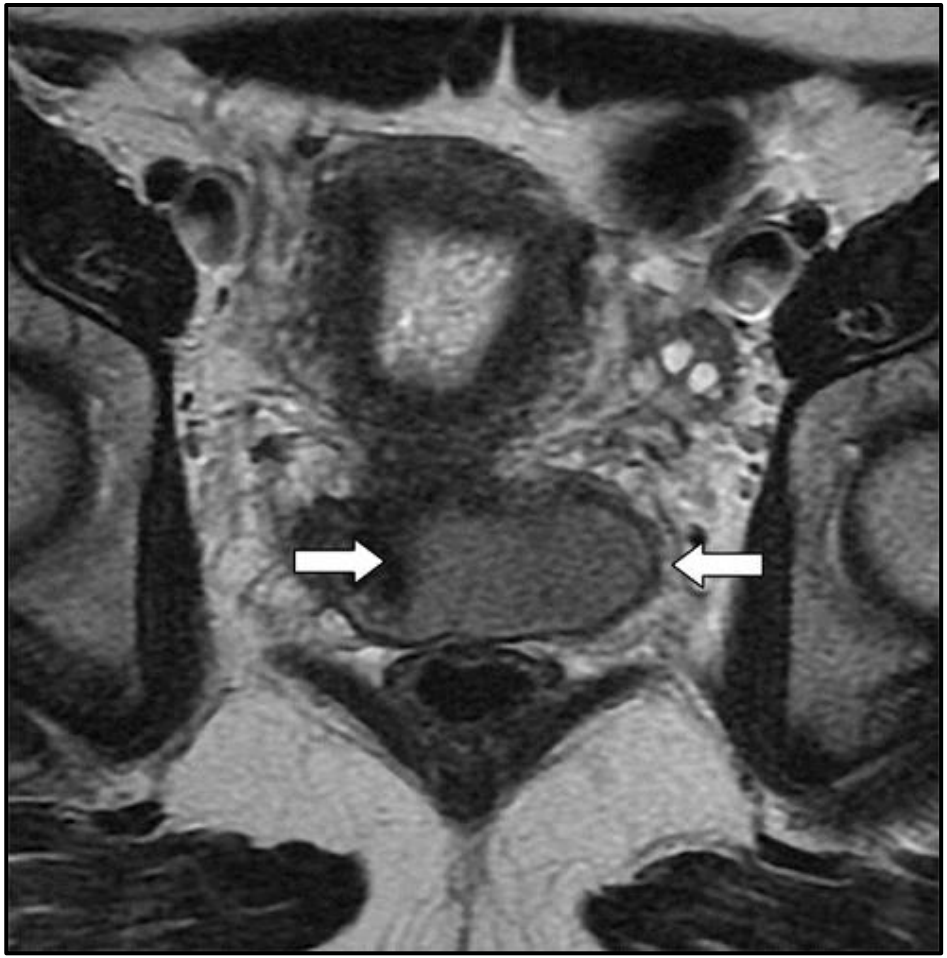
Contrast CT

Images show uterine cervical cancer at CT versus MRI. (a) Contrast--enhanced CT, (b)axial fast spin-echo T2-weighted MRI, and (c) axial T1 images after gadolinium-based contrast agent administration through pelvis of a woman with stage IB2 cervical cancer (arrows). Tumor size (stage IB and IIA), cervical stromal invasion (stage IA), and lack of parametrial spread (stage IIB) are assessed well with MRI but poorly with CT.



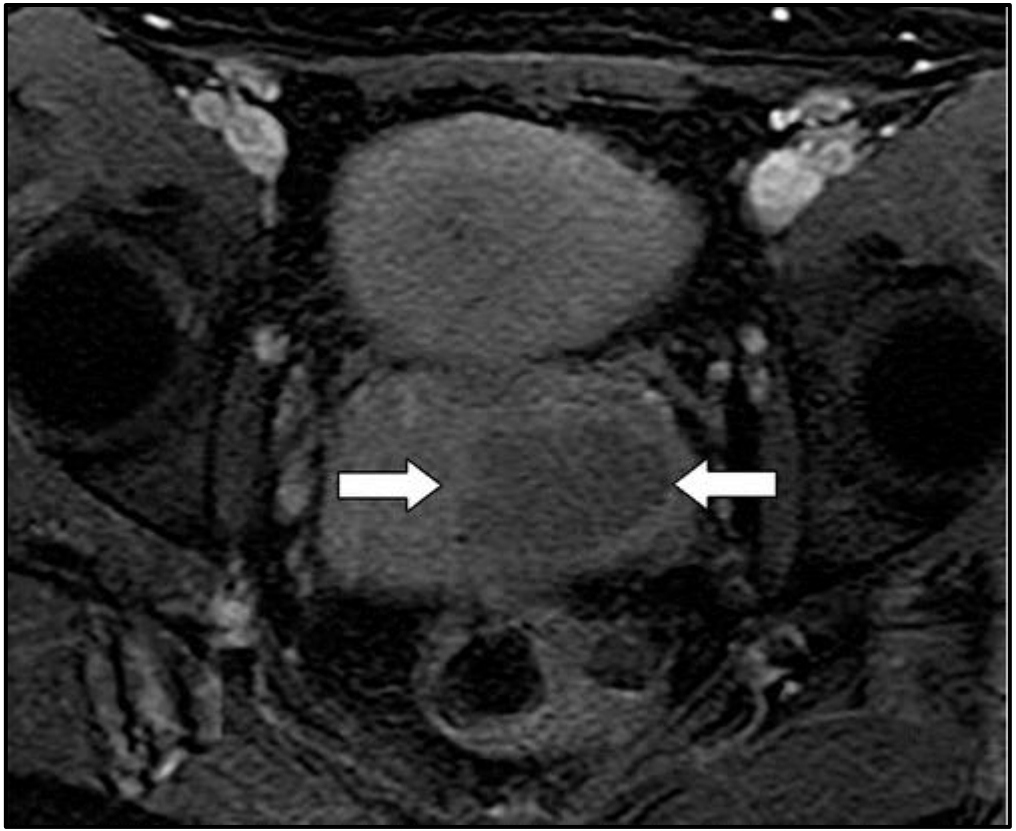
T2 MRI

Images show uterine cervical cancer at CT versus MRI. **(a)** Contrast--enhanced CT, **(b)axial fast spin-echo T2-weighted MRI,** and **(c)** axial T1 images after gadolinium-based contrast agent administration through pelvis of a woman with **stage IB2 cervical cancer (arrows). Tumor size (stage IB and IIA), cervical stromal invasion (stage IA), and lack of parametrial spread (stage IIB) are assessed well with MRI but poorly with CT.**



T1 with gadolinium-based contrast

Images show uterine cervical cancer at CT versus MRI. **(a)** Contrast--enhanced CT, **(b)**axial fast spin-echo T2-weighted MRI, and **(c) axial T1 images after gadolinium-based contrast** agent administration through pelvis of a woman with stage **IB2 cervical cancer (arrows). Tumor size (stage IB and IIA), cervical stromal invasion (stage IA), and lack of parametrial spread (stage IIB) are assessed well with MRI but poorly with CT.**



PET

- A meta-analysis of 72 studies involving 5042 women found that PET demonstrates a higher sensitivity (75%) and comparable specificity (98%) to MRI (sensitivity of 56% and specificity of 93%) and CT (sensitivity of 58% and specificity of 92%)

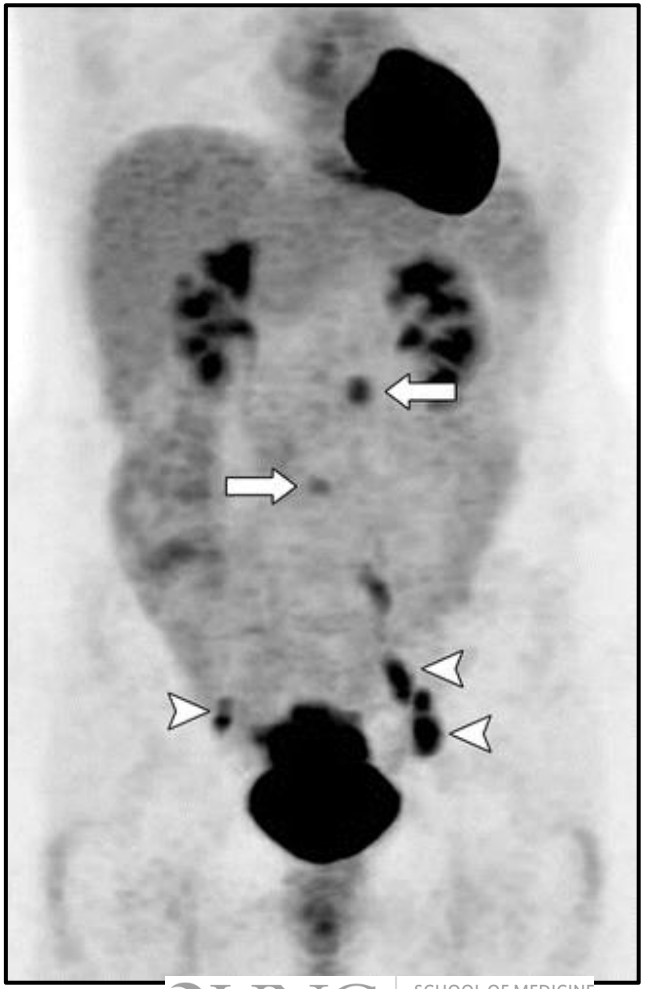
FDG PET/CT

- Obtained in same sitting
- Routinely performed from skull base through proximal thighs
- Negative oral contrast is use to minimize attenuation-correction artifact
- CT is acquired first, then PET is obtained caudocranially to minimize bladder filling or bowel peristalsis
- PET/CT is more sensitive than is CT alone, especially in depicting lymph nodes in the para-aortic stations
  - This can upstage the patient as well as expand the field of radiation treatment

- PET and PET/CT are best at predicting disease survival
  - A prospective cohort study of 560 patients found the risk of recurrent disease increased incrementally based one the most distant lymph node involvement at PET
    - hazard ratio of 2.40 (95% confidence interval: 1.63, 3.52) for pelvic, 5.88 (95% confidence interval: 3.80, 9.09) for para-aortic, and 30.27 (95% confidence interval: 16.56, 55.34) for supraclavicular involvement

PET

Images show uterine cervical cancer lymphadenopathy at fluorodeoxyglucose PET/CT versus CT. **(a) Coronal maximum intensity projection PET image in a patient clinically staged as IB shows hypermetabolic foci in pelvis (arrowheads) and abdomen (arrows), which at fusion PET/CT (not shown) correspond to retroperitoneal lymphadenopathy**. **(b, c)**, On concurrent contrast-enhanced CT images, hypermetabolic abdominal lymph nodes measure less than 1 cm in short axis and are morphologically normal. **Patient was staged as IIIC2 based on PET/CT.**



Contrast CT

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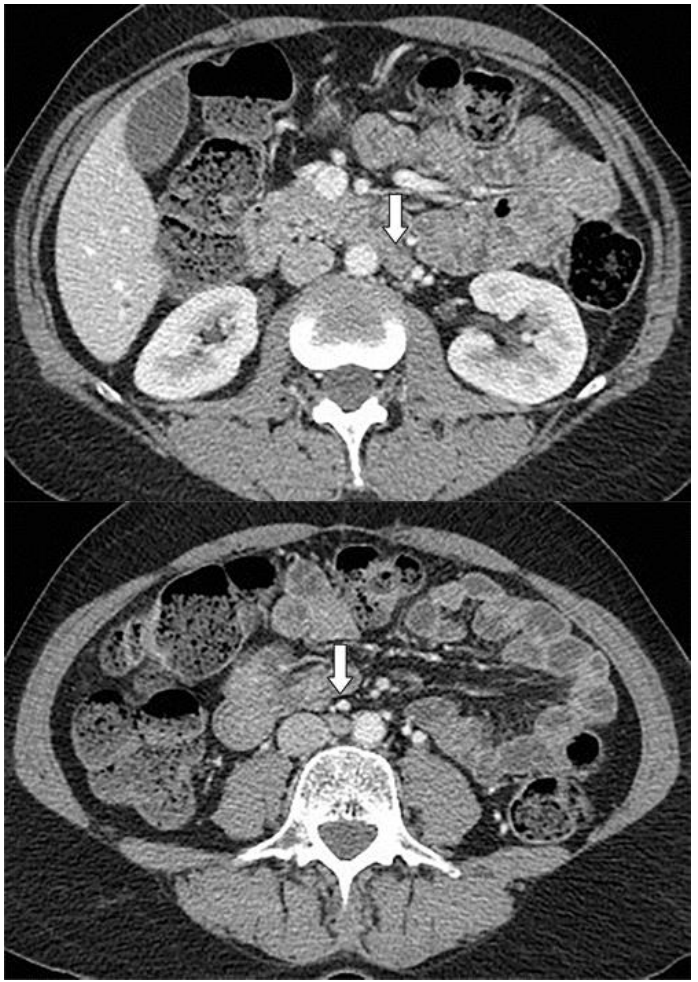

Choice of imaging

Resource Setting and Primary Target for Diagnosis*	FIGO Stage
Basic	
Chest radiography	
Lung metastases	IVB
Limited	
Pelvic US	
Tumor size	IB
Parametrial tumor spread	IIB
Abdominal US	
Hydronephrosis	IIIB
Chest radiography	
Lung metastases	IVB
Enhanced	
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Torso fusion FDG PET/CT§	
Hydronephrosis	IIIB
Retroperitoneal adenopathy	IIIC
Distant metastases including lungs, peritoneum, extraretroperitoneal lymph nodes, and bones‖	IVB

- Most cervical cancers are diagnosed in areas of the world without access to CT, MRI, or PET/CT
- There is limited access to brachytherapy and on-site pathology

But wait . . . (Limitations)

I. Recall that most cervical cancers are diagnosed in resource-limited settings with limited or no access to CT, MRI, PET/CT, brachytherapy, and pathologic analysis

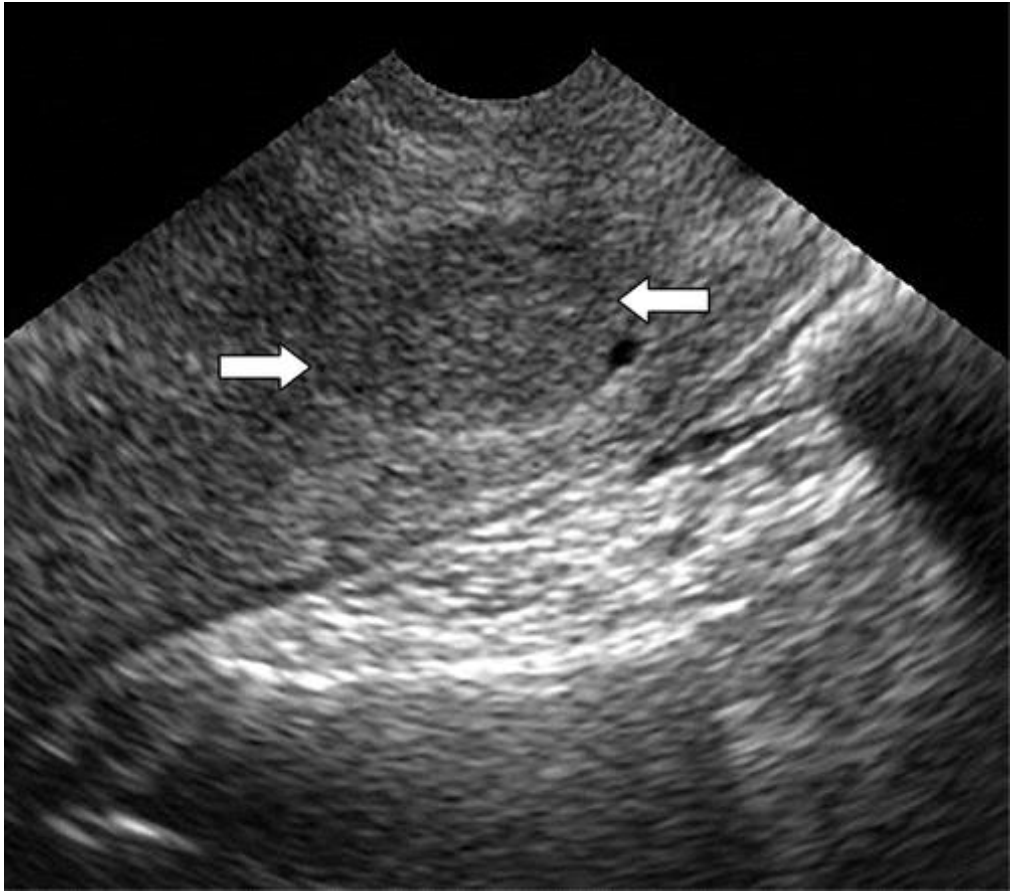
II. US is cheaper and portable making it ideal for resource-limited settings, however it is technician dependent

III. US is as effective as MRI – but only up to tumor size of 2 cm

IV. Guidelines call for multi-modal imaging, but areas may not have access to all types of imaging

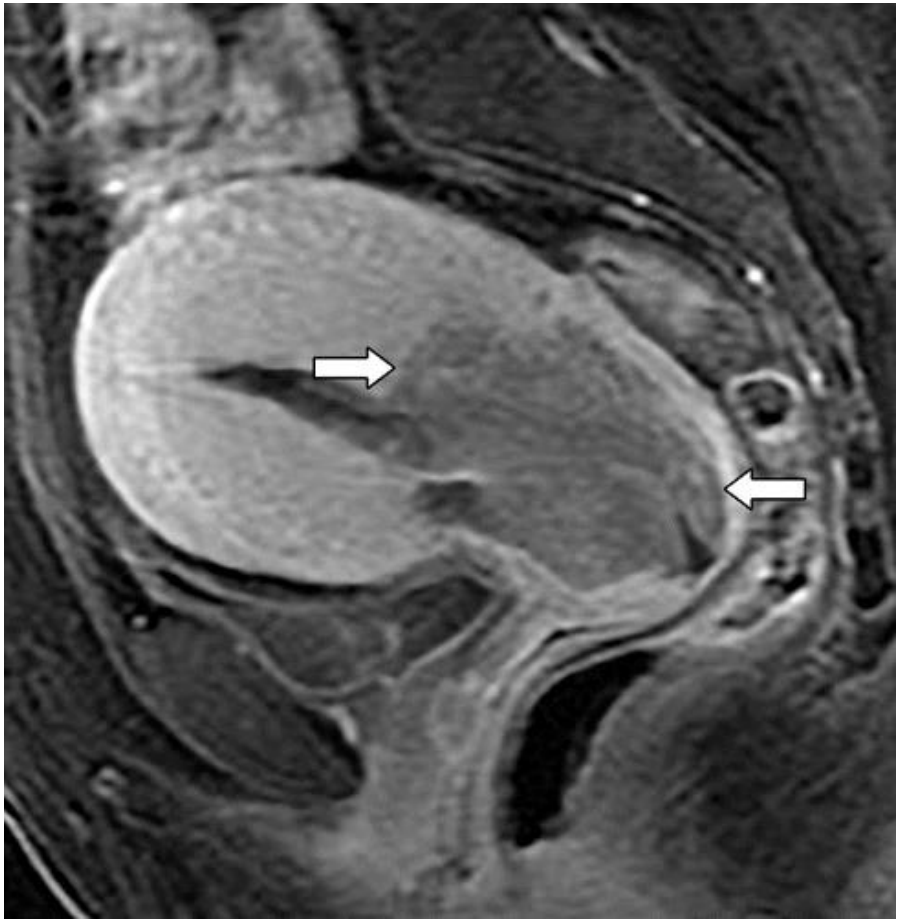
Ultrasound

Images show uterine cervical cancer size at US versus MRI. **(a) Sagittal endovaginal US image in a woman presenting with abnormal uterine bleeding shows 2.3-cm solid mass (arrows), pathologically diagnosed as invasive adenocarcinoma and initially staged as IB2**. **(b)** Sagittal MRI after gadolinium-based contrast agent administartion shows that tumor (arrows) extends into uterine corpus and measures 4.8 cm, corresponding to stage IB3.



MRI with gadolinium

Images show uterine cervical cancer size at US versus MRI. **(a)** Sagittal endovaginal US image in a woman presenting with abnormal uterine bleeding shows 2.3-cm solid mass (arrows), pathologically diagnosed as invasive adenocarcinoma and initially staged as IB2. **(b) Sagittal MRI after gadolinium-based contrast agent administartion shows that tumor (arrows) extends into uterine corpus and measures 4.8 cm, corresponding to stage IB3.**



Discussion

- Imaging is essential to the 2018 FIGO staging of uterine cervical cancer
- Retroperitoneal lymphadenopathy is now used in staging
- Cross-sectional imaging (PET/CT) should be used to assess nodal status
- Primary tumor size should be measured with MRI

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Clinical questions now . . .

What is the next step in this patient's workup?

When are specific imaging modalities used?

What options exist for imaging in resource-limited settings?

What does the Future Hold?

- Radiology
  - Fluorine 18 FDG PET/MRI allows PET and MRI to be obtained simultaneously
    - MRI is used to assess the primary tumor as PET identifies retroperitoneal and distant mets
    - Only 70% as specific as CT for lung nodules
    - 96% specific for FDG-avid lung nodules
- Primary Prevention
  - Increased access to HPV vaccines
- Secondary Prevention
  - Increased access to pap smears
  - New technologies for treating CIN I and II

Key points

I. US and MRI are more accurate at measuring primary tumor and assessing parametrial spread than CT or physical exam

II. PET/CT is more sensitive than CT or MRI at identifying mets in retroperitoneal lymph nodes

III. Torso PET CT is best for identifying distant mets that may change stage, prognosis, and/or treatment plan

IV. Retroperitoneal lymphadenopathy in abdomen and pelvis

V. Tumor size of 2cm (differentials IB1 vs IB2) is the cutoff for radical trachelectomy for fertility preservation

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