ARROCase: Vaginal Cancer

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Overview

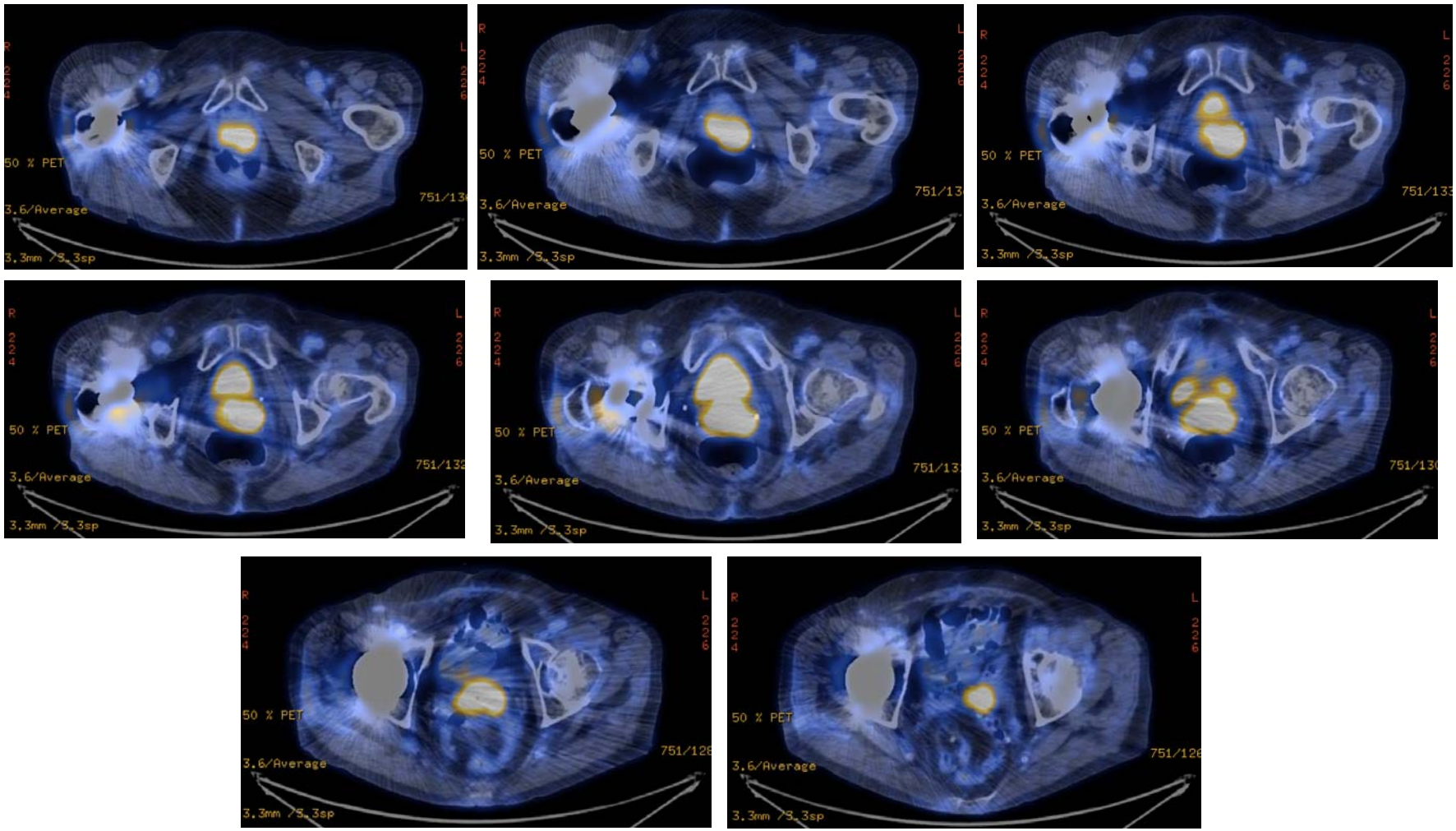
- Case Presentation
- Background
- Risk Factors
- Clinical Manifestations
- Workup
- Staging
- Management
- Surveillance and Follow up

Case Presentation

- CC: Vaginal discharge and spotting
- HPI: 82yo CF s/p hysterectomy 50 years ago for benign disease who c/o 6-month hx of vaginal discharge and spotting.
  - Gyn Onc's pelvic exam revealed extensive tumor involving the anterior and posterior wall of the vagina extending nearly to the introitus, sparing the urethral meatus. Rectovaginal exam confirmed paravaginal extension with thickening of the vaginal apex, suspicious for pelvic extension.
  - CT revealed surgically absent cervix and uterus with vaginal wall thickening, no LAD.

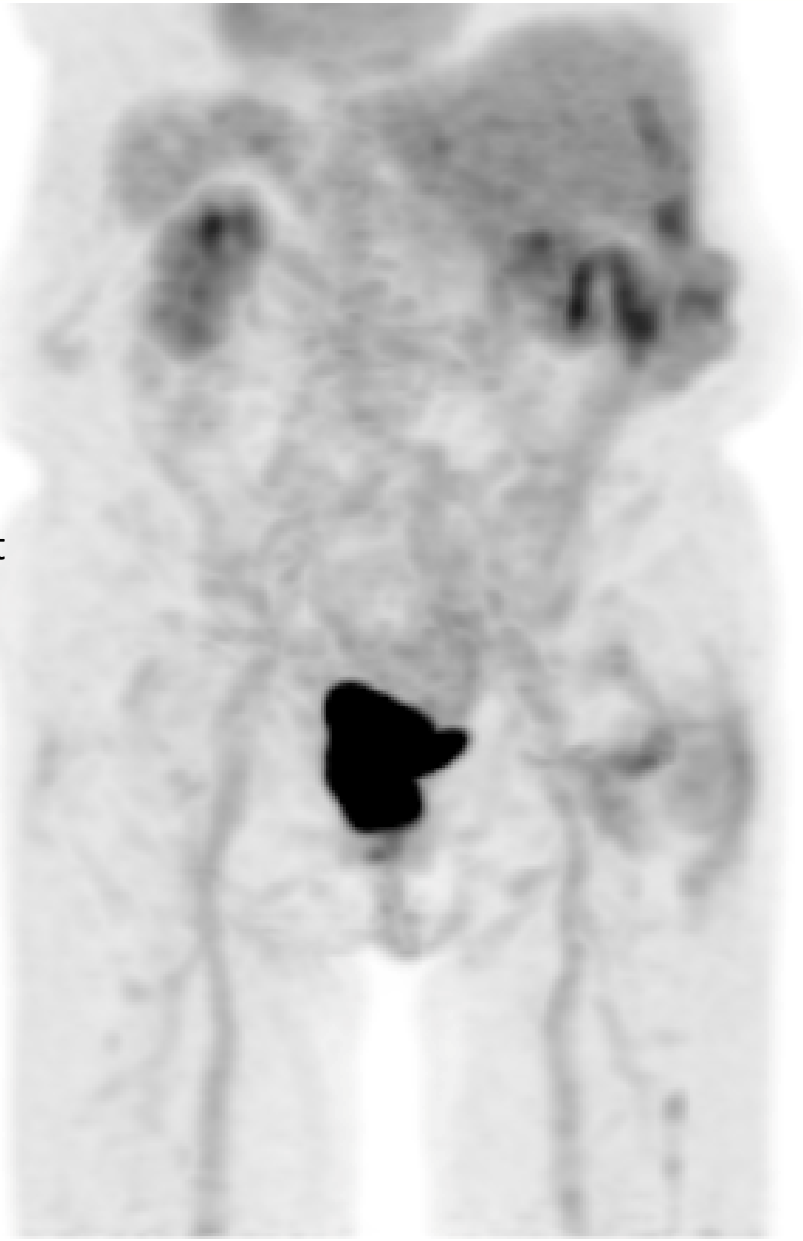
- PELVIC EXAM FINDINGS
  - Visual exam
    - Normal atrophic external female genitalia
  - Bimanual exam
    - firm circumferential mass beginning 1.5cm proximal to introitus extending entire length of the vagina without frank involvement of the urethral meatus
  - Speculum exam
    - poorly tolerated but confirmed BME
  - Rectovaginal exam
    - confirmed mild paravaginal extension bilaterally

PET-CT Scan



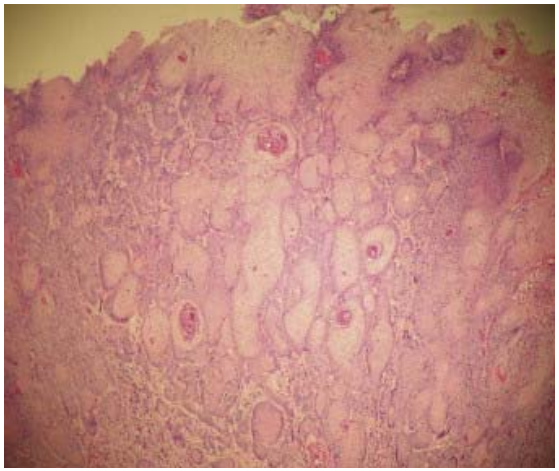
Maximum Intensity Projection (MIP): PA coronal view

-> more prominent on the left



Diagnosis

- Vaginal biopsy results
  - Squamous cell carcinoma
  - High grade
  - Less differentiated
  - Keratinization



Courtesy Tamara Kalir, MD, PhD, Phillips TL, Hoppe R, Roach M, et al. Leibel and phillips textbook of radiation oncology. Philadelphia: Elsevier/Saunders, 2010.

- FIGO Stage II (T2N0MO)

Staging

AJCC 7th Ed., 2010/FIGO 2008

TNM CATEGORIES	FIGO STAGES	DEFINITION	
Primary tumor (T)			
TX		Primary tumor cannot be assessed	
T0		No evidence of primary tumor	
T1	I	Tumor confined to vagina	
T2	**II**	**Tumor invades paravaginal tissues but not to pelvic wall**	
T3	III	Tumor extends to pelvic wall*	
T4	IVA	Tumor invades mucosa of the bladder or rectum and/or extends beyond the true pelvis (bullous edema is not sufficient evidence to classify a tumor as T4)	
Regional lymph nodes (N)			
NX		Regional lymph nodes cannot be assessed	
N0		**No regional lymph node metastasis**	
N1	III	Pelvic or inguinal lymph node metastasis	
Distant metastasis (M)			
M0		**No distant metastasis**	
M1	IVB	Distant metastasis	
ANATOMIC STAGE/PROGNOSTIC GROUPS			
Stage I	T1	N0	M0
Stage II	**T2**	**N0**	**M0**
Stage III	T1-T3	N1	M0
	T3	N0	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1

*Pelvic wall is defined as muscle, fascia, neurovascular structures, or skeletal portions of the bony pelvis. On rectal examination, there is no cancer-free space between the tumor and pelvic wall.

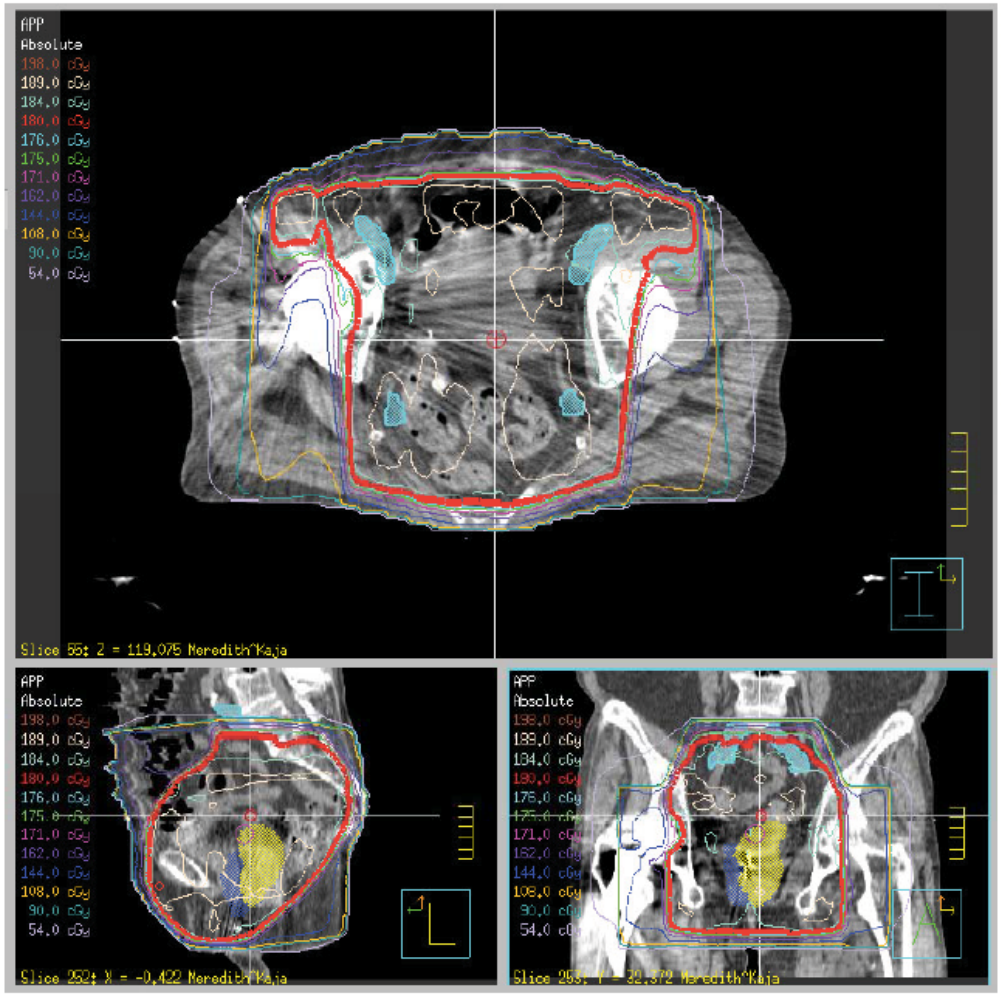
CLINICAL CASE IN RED.

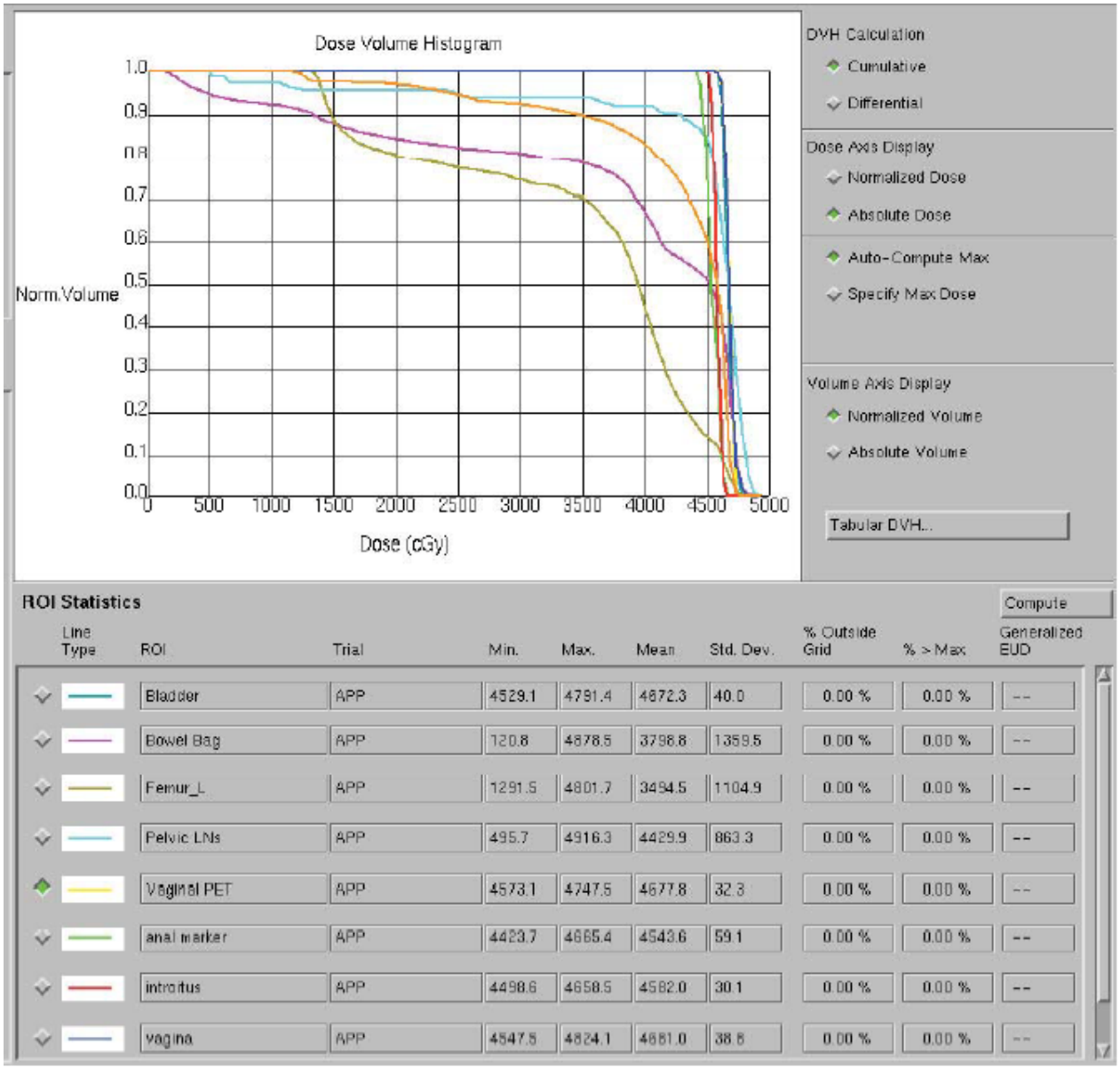
Case Definitive Tx Plan

- IMRT at outside hospital + Concurrent Chemotherapy (cisplatin) ➔ Interstitial Brachytherapy
  - IMRT with 45 Gy to the whole pelvis and inguinal nodes in 25 total fractions over 5 weeks
  - Interstitial vaginal high dose rate brachytherapy with 24 Gy in 4 total fractions with 2 planned insertions over 2 weeks

IMRT Planning

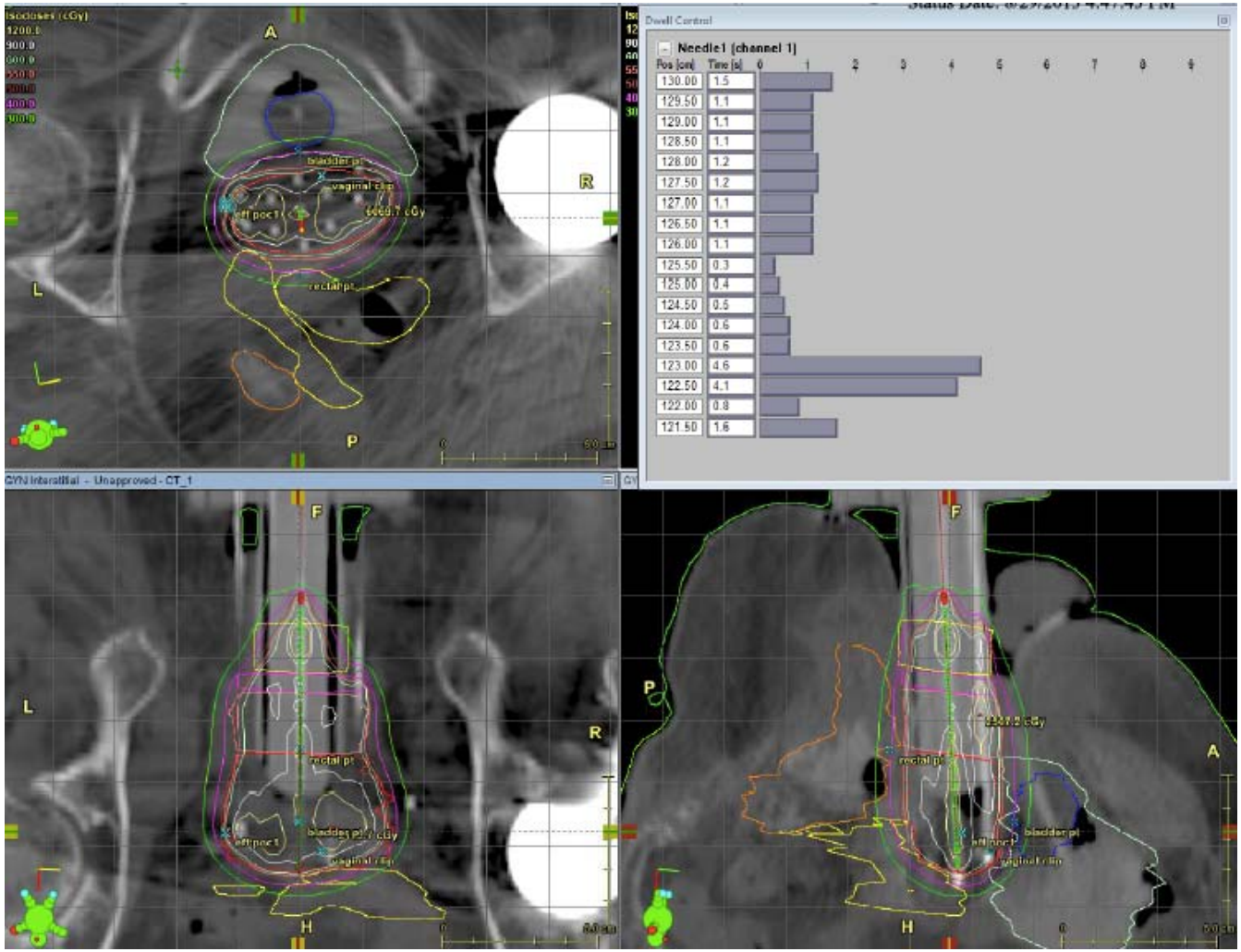
Outside Hospital



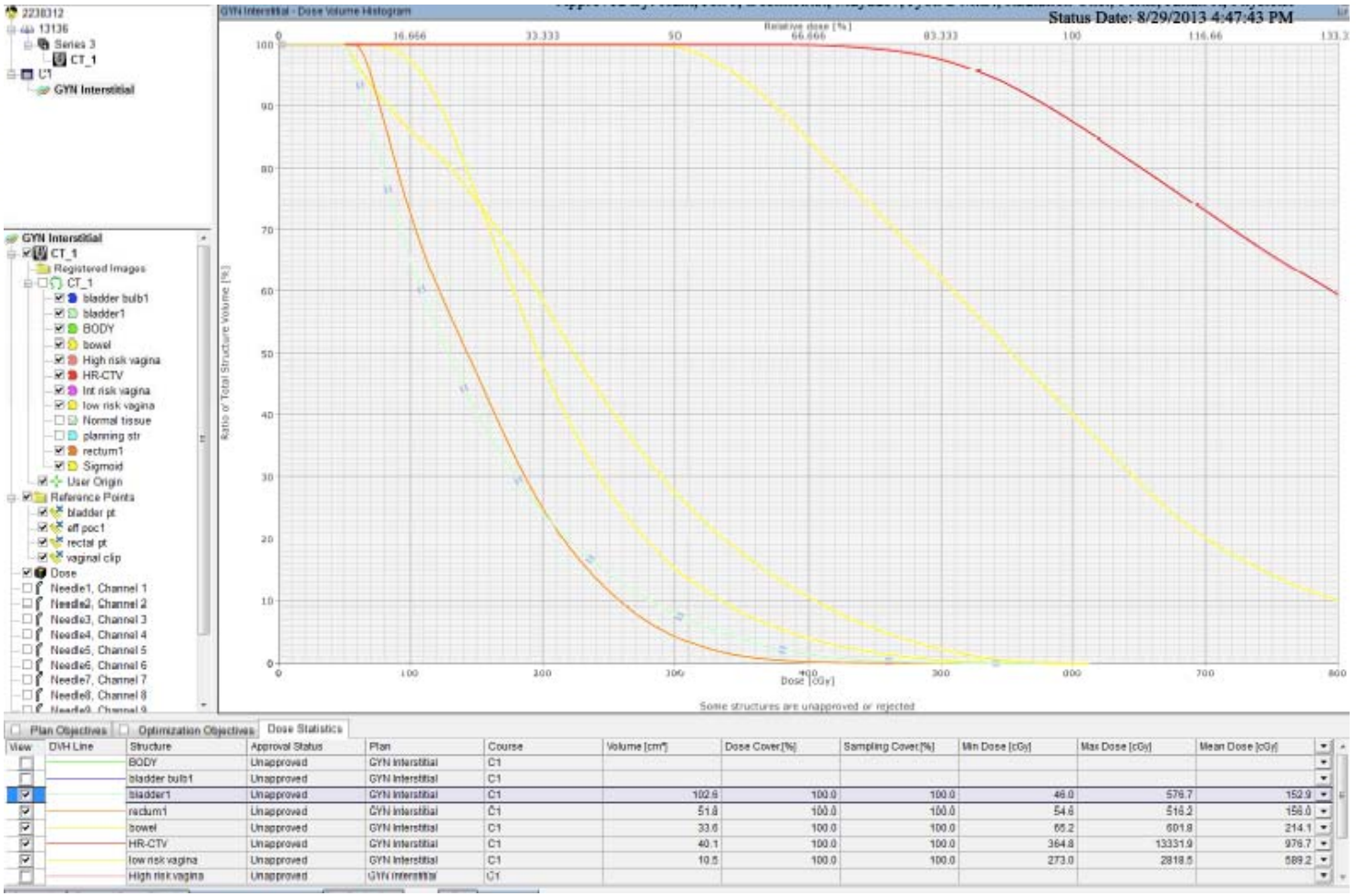


Line Type	ROI	Trial	Min.	Max.	Mean	Std. Dev.	% Outside Grid	% > Max	Generalized EUD
	Bladder	APP	4529.1	4791.4	4672.3	40.0	0.00 %	0.00 %	--
	Bowel Bag	APP	120.8	4878.5	3798.8	1359.5	0.00 %	0.00 %	--
	Femur_L	APP	1291.5	4801.7	3494.5	1104.9	0.00 %	0.00 %	--
	Pelvic LNs	APP	495.7	4916.3	4429.9	863.3	0.00 %	0.00 %	--
	Vaginal PET	APP	4573.1	4747.5	4677.8	32.3	0.00 %	0.00 %	--
	anal marker	APP	4423.7	4665.4	4543.6	59.1	0.00 %	0.00 %	--
	introitus	APP	4498.6	4658.5	4582.0	30.1	0.00 %	0.00 %	--
	vagina	APP	4547.5	4824.1	4661.0	38.6	0.00 %	0.00 %	--

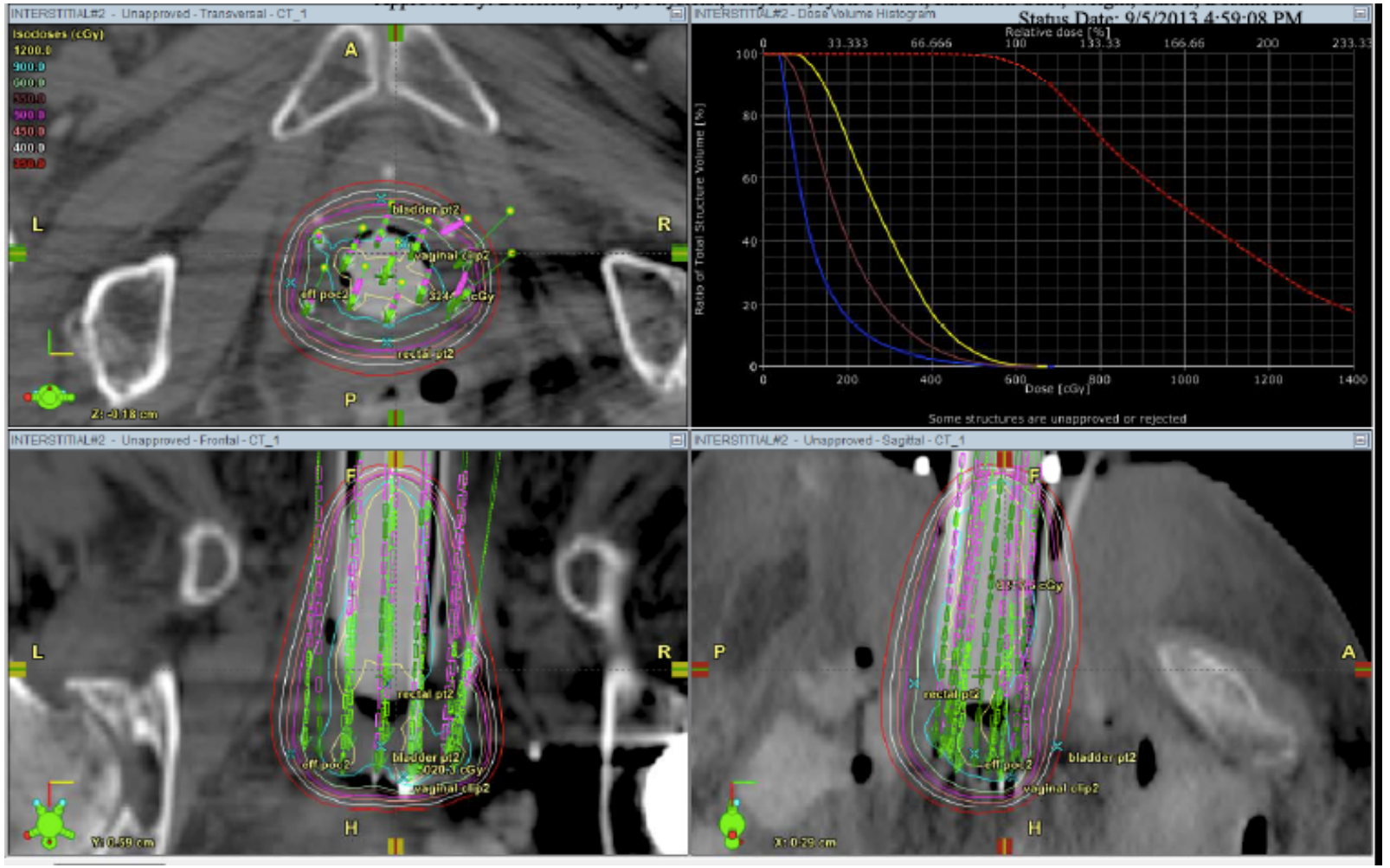
HDR Brachy Planning #1



HDR #1 DVH


GYN Interstitial - Dose Volume Histogram
Status Date: 8/29/2013 4:47:43 PM
Relative dose [%]
Ratio of Total Structure Volume [%]
Dose [cGy]
Some structures are unapproved or rejected
Plan Objectives
Optimization Objectives
Dose Statistics
View
DVH Line
Structure
Approval Status
Plan
Course
Volume [cm³]
Dose Cover [%]
Sampling Cover [%]
Min Dose [cGy]
Max Dose [cGy]
Mean Dose [cGy]
BODY Unapproved GYN Interstitial C1
bladder bulb1 Unapproved GYN Interstitial C1
bladder1 Unapproved GYN Interstitial C1 102.6 100.0 100.0 46.0 576.7 152.9
rectum1 Unapproved GYN Interstitial C1 51.8 100.0 100.0 54.6 516.2 158.0
bowel Unapproved GYN Interstitial C1 33.6 100.0 100.0 65.2 601.8 214.1
HR-CTV Unapproved GYN Interstitial C1 40.1 100.0 100.0 364.8 13331.9 976.7
low risk vagina Unapproved GYN Interstitial C1 10.5 100.0 100.0 273.0 2818.5 589.2
High risk vagina Unapproved GYN Interstitial C1

HDR Brachy Planning #2



Dosimetric Values

Interstitial #1

- ICRU Bladder point: 390 cGy
- ICRU Rectal point: 387 cGy
- D2cc Rectum: 310 cGy
- D2cc Bladder: 380 cGy
- D2cc Sigmoid: 180 cGy
- D2cc Bowel: 370 cGy

Interstitial #2

- ICRU Bladder point: 367 cGy
- ICRU Rectal point: 581 cGy
- D2cc Rectum: 480 cGy
- D2cc Bladder: 460 cGy
- D2cc Sigmoid: 430 cGy

Case Summary

- 82 WF with FIGO stage II (T2N0M0) vaginal cancer of squamous cell histology that was high grade, keratinized
- Treatment course
  - IMRT with 45 Gy to the whole pelvis and inguinal nodes in 25 total fractions over 5 weeks with concurrent cisplatin
  - Followed by interstitial vaginal high dose brachytherapy with 24 Gy in 4 total fractions with 2 planned insertions over 2 weeks.
- 1.5 years later, she remains without evidence of disease
- Treatment side effects
  - Mild vaginal foreshortening, no vaginal mucosal changes, no ulcerations

Background

- Primary vaginal cancer accounts for 3% of all malignant neoplasms of the female genital tract
  - Most are of squamous cell histology
  - Most are detected in women ≥ 60 yo
- Majority (75%) of vaginal malignancies are metastatic, which occur by direct extension or by lymphatic or hematogenous spread

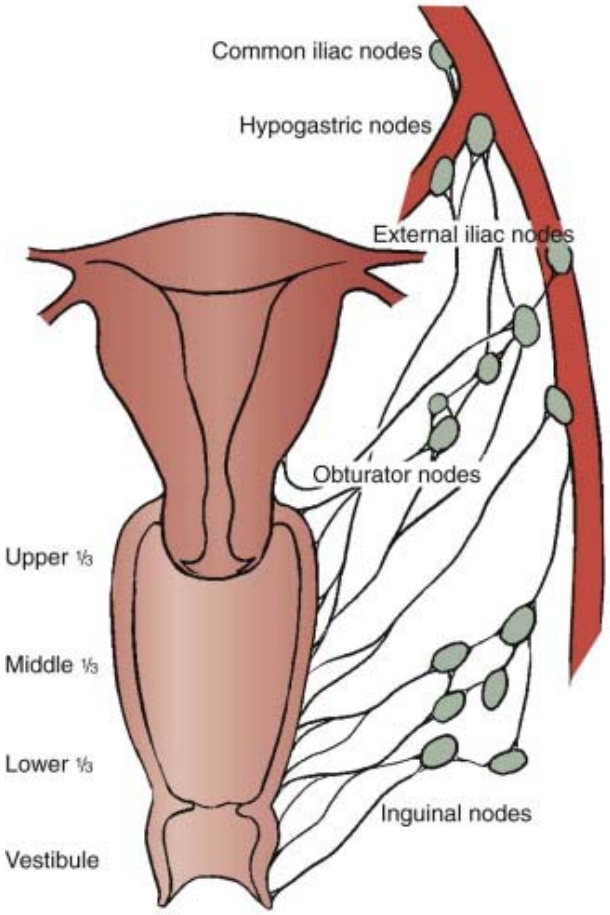
Risk Factors

- Most are mediated by HPV infection
- Same risk factors as cervical cancer
  - Number of lifetime sexual partners
  - Early age at first intercourse
  - Current smoker
- Many have a prior history of gynecologic malignancy

Clinical Manifestations

- Vaginal bleeding (most common)
- Discharge
- Pruritus
- Dyspareunia
- Pelvic pain
- Change in bowel/bladder habits
- Many are asymptomatic

Anatomy



Atlas of Human Anatomy illustrated by Frank Netter, MD

- Upper two thirds of the vagina drains to the obturator, internal, external and common iliac nodes
- Lower one third of the vagina drain to the inguinofemoral nodes
- Vaginal cancer is most often found in the posterior wall, superior one third of the vagina

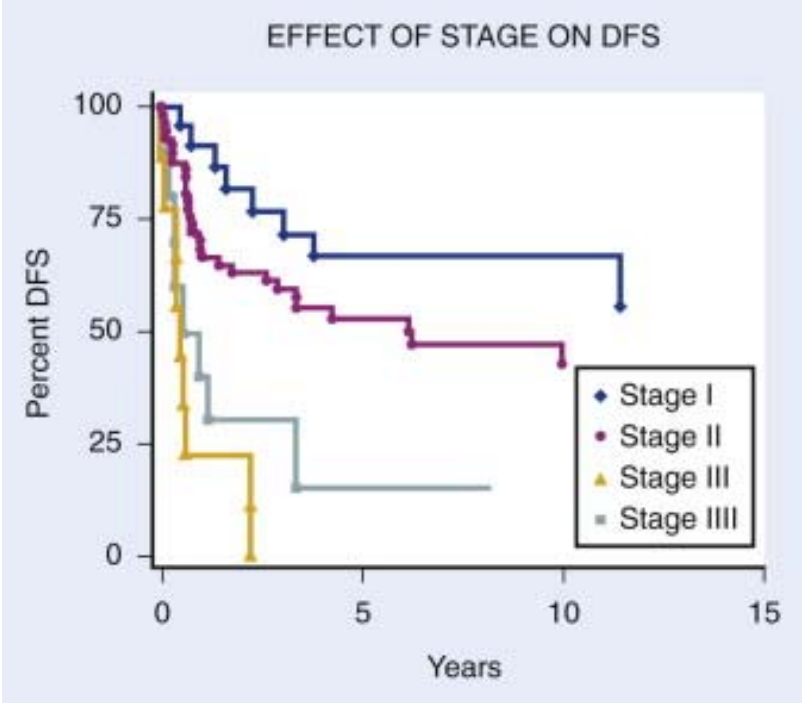
Workup for FIGO Staging

- Physical exam of pelvis and vagina
  - Speculum examination (rotate to observe posterior wall), vaginal palpation, bimanual pelvic, rectovaginal for staging
- Biopsy of suspicious lesions on vagina, vulva, cervical os, inguinal/femoral nodes
- Cystoscopy and/or proctosigmoidoscopy for locally advanced disease
- CXR, CBC, LFTs and ALP

Additional Workup for Management

- Advanced imaging does not contribute to FIGO staging
  - CT, MRI, PET/CT to assess extent of disease and treatment planning
- Note: cancer involving the vulva or cervix is not considered to be a vaginal primary

Overall DFS and Prognosis



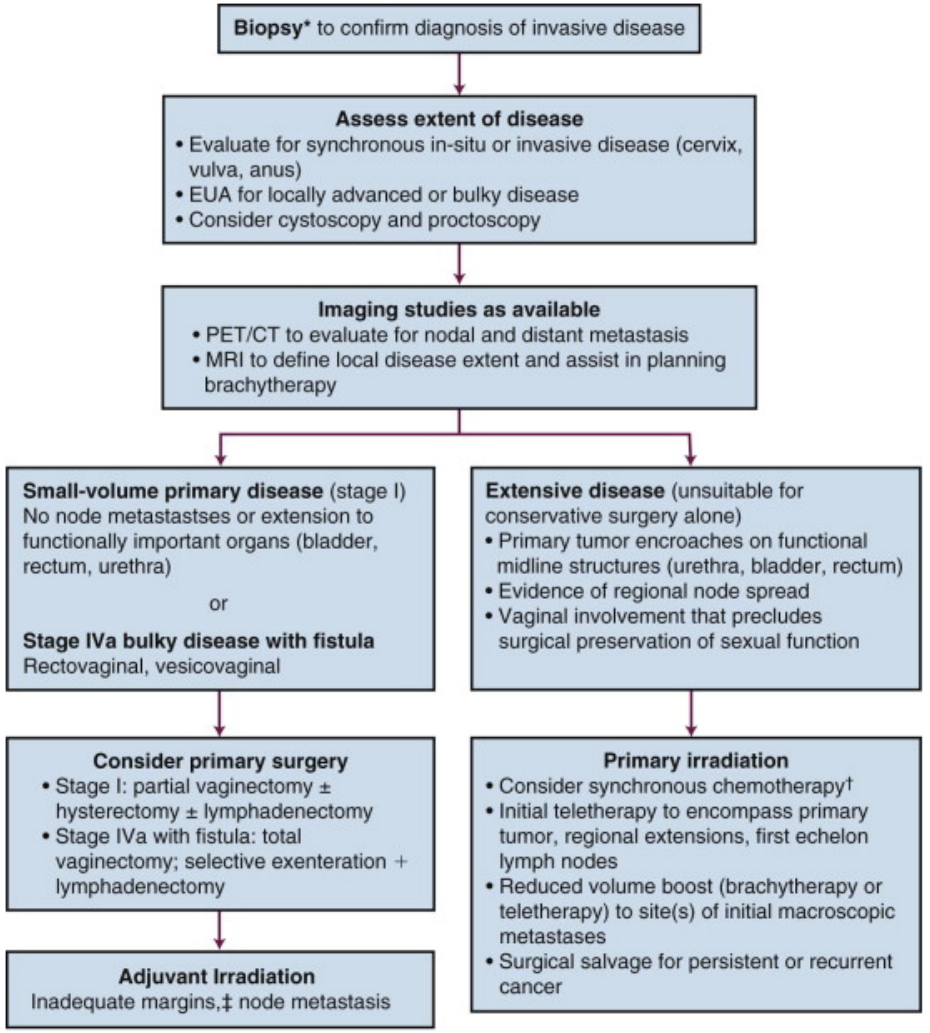
Stock RG, Chen ASJ, Seski J,et al: A thirty-year experience in the management of primary carcinoma of the vagina: Analysis of prognostic factors and treatment modalities. Gynecol Oncol 1995; 56: 45

- The most significant prognostic factor is anatomic staging, which reflects the extent of invasion into the surrounding tissue or of metastatic spread
- Other factors include >60 years of age, symptomatic at diagnoses, lesions of middle and lower 1/3 of vagina, poorly differentiated tumors, length of vaginal wall involvement

Screening

- While unproven, PAP smears of the vaginal vault in elderly women who have had hysterectomy for (pre)invasive cervical cancer is reasonable
- Insufficient evidence to recommend routine vaginal smear screening in women after total hysterectomy for benign disease

Standard Tx Options



Gunderson LL, Tepper JE Bogart JA. Clinical radiation oncology. Philadelphia, PA: Elsevier Saunders, 2012.

Definitive RT for Stage I

- ≤0.5cm: EBRT or IC ± IS, tx entire vaginal mucosa to 65 Gy with additional mucosal dose of 20-30 Gy to area of tumor involvement
  - Evidence
    - Overall, local control rates with brachytherapy alone range from 67-100%
    - 18% local failure rate with brachytherapy alone (Dancuart et al., 1988)
- >0.5cm: EBRT to whole pelvis ± inguinal LN to 45 Gy, followed by IS ± IC boost to tumor with 2cm radial margin to 70-80 Gy
  - Evidence
    - Tumor control the same with brachytherapy alone vs. EBRT followed by brachy (Perez et al., 1988)

Definitive RT for Stage II

- EBRT to whole pelvis ± inguinal LN to 45 Gy, followed by IS ± IC boost to tumor with 2cm radial margin to 70-80 Gy
  - Evidence
    - 36% pelvic tumor CR with brachytherapy alone vs. 67% CR with combined EBRT and brachytherapy (Perez et al., 1988)
    - 5-year PDC rate 84% and DSS rate 78% for Stage II receiving definitive RT (Frank et al., 2005)

Definitive RT for Stages III, IVA

- EBRT to whole pelvis + pelvic/inguinal LN to 45 Gy, followed by IS ± IC boost to tumor of 75-85 Gy and dose to lateral pelvic wall of 55 Gy to 60 Gy
  - Evidence
    - Only 20-30% of patients achieve local control. Pelvic recurrence occur more often than distant recurrences (Frank et al., 2005)

Chemoradiation

- No randomized trials
- Concurrent 5-FU and/or cisplatin chemotherapy with irradiation for advanced carcinoma (III, IVA, tumors larger than 4cm)
  - Evidence:
    - Cisplatin-based CRT 44% disease free over a mean follow-up time of 129 months (Frank et al., 2005)
    - 12 patients Stage II-IVA received CRT with Cisplatin, EBRT, brachytherapy; overall well tolerated; 5-year OS 66%, PFS 75%, locoregional PFS 92% (Samant et al., 2007)
    - 14 patients Stage I-III, non-surgical candidates, received CRT w 5-FU alone, w cisplatin or mitomycin-C; cancer control outcomes more favorable than prev studies with high dose RT alone (Dalrymple et al., 2004)

Considerations for the Post-Hysterectomy Patient

- 60% have had a previous hysterectomy
- Anatomical changes s/p hysterectomy
  - Small bowel tends to fall lower into the pelvis, increasing the likelihood of it being irradiated during treatment
  - Vaginal vault position varies more
- Technique to minimize under-dosing the target:
  - Fuse planning CT scans taken with full and empty bladder to estimate potential range of target volume positions
  - Fill the bladder with a fixed volume of saline using a Foley catheter immediately prior to treatment

Surveillance & Follow-up

- No reliable evidence that routine cytologic or imaging improves outcomes beyond PE and assessment of new symptoms
- Given the pt's locally advanced disease and tx regimen, consider pelvic exam and pap smear
  - q3months for year 1
  - q4months for year 2
  - q6months for years 3-5
  - then annually
- CXR annually for 5 years
- PET-CT if recurrence suspected

Salani et al., 2011

RT-Related Toxicities

Whole Pelvis EBRT

- Early
  - Diarrhea, bladder irritation (urgency, frequency, dysuria, hematuria, fatigue)
- Late
  - GI: change in bowel habits, rectal bleeding, stricture, ulcer, fistula
  - GU: chronic cystitis, urinary sx
  - Vaginal: stenosis, dryness, fibrosis, fistula
  - Fertility: ovarian dysfxn, menopause, poor uterine expansion
  - MSK: lumbosacral neuropathy and/or pelvic insufficiency fx

Interstitial Brachytherapy

- Vaginal stenosis, necrosis, rectovaginal and/or vesicular vaginal fistula formation, rectal injury, bladder, injury, vaginal bleeding, discharge, infection, hemorrhagic cystitis

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