

Locally-advanced cervical cancer

Author: Allison L. Matous, MD


Faculty sponsor: Shauna M. McVorrnan, MD

Dartmouth Cancer Center


Lebanon, NH

Epidemiology of cervical cancer in the US

Estimated Number* of New Cancer Cases and Deaths by Sex, US, 2023



Female		
Breast	297,790	31%
Lung & bronchus	120,790	13%
Colon & rectum	71,160	8%
Uterine corpus	66,200	7%
Melanoma of the skin	39,490	4%
Non-Hodgkin lymphoma	35,670	4%
Thyroid	31,180	3%
Pancreas	30,920	3%
Kidney & renal pelvis	29,440	3%
Leukemia	23,940	3%
All sites	948,000	



Female		
Lung & bronchus	59,910	21%
Breast	43,170	15%
Colon & rectum	24,080	8%
Pancreas	23,930	8%
Ovary	13,270	5%
Uterine corpus	13,030	5%
Liver & intrahepatic bile duct	10,380	4%
Leukemia	9,810	3%
Non-Hodgkin lymphoma	8,400	3%
Brain & other nervous system	7,970	3%
All sites	287,740	

US incidence of cervical cancer: 13,960
US mortality from cervical cancer: 4,310

©2023, American Cancer Society, Inc., Surveillance and Health Equity Science

Epidemiology of cervical cancer around the world

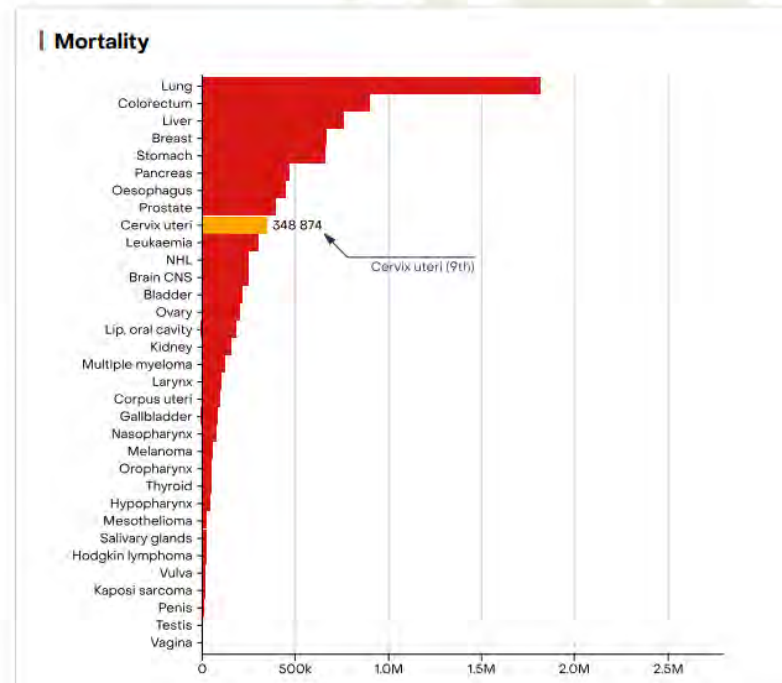
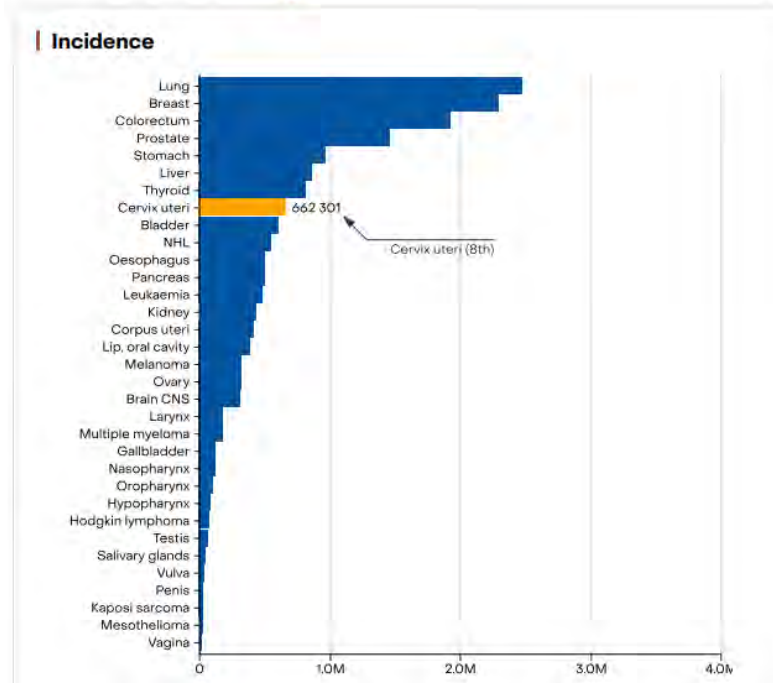
Incidence

Rank	Cases	ASR (World)
8	662 301	14.1

Mortality

Rank	Deaths	ASR (World)
9	348 874	7.1

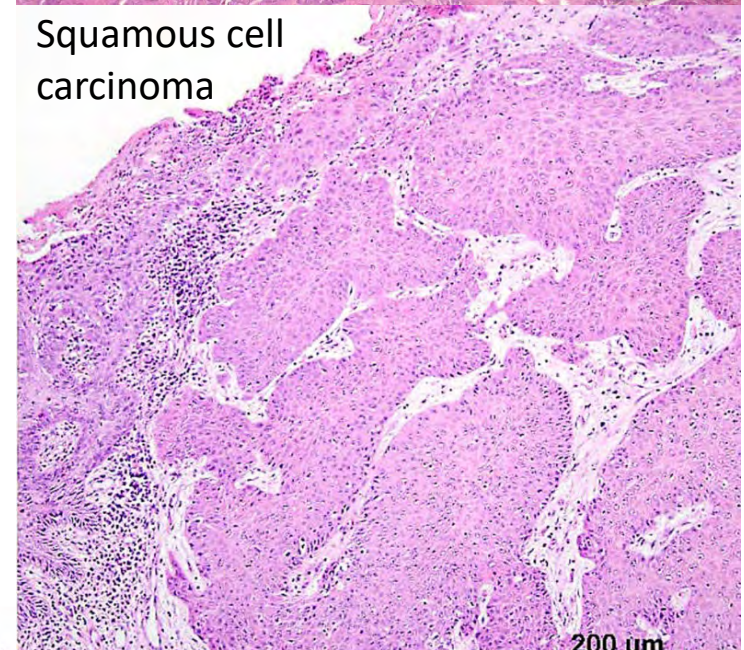
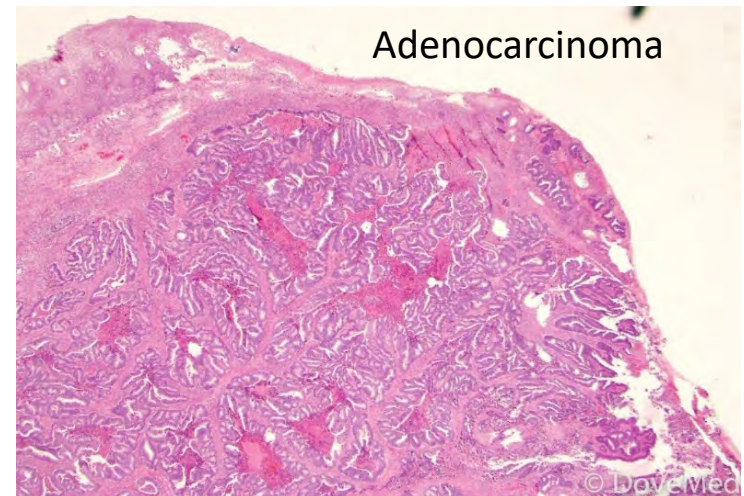
Cancer site ranking



Histology

- Squamous cell carcinoma (~80%)
- Adenocarcinoma
 - Mucinous
 - Endometrioid
 - Serous
 - Clear cell*
- Adenosquamous carcinoma
- Rare: small cell neuroendocrine, rhabdomyosarcoma, lymphoma

*Related to *in utero* exposure to DES

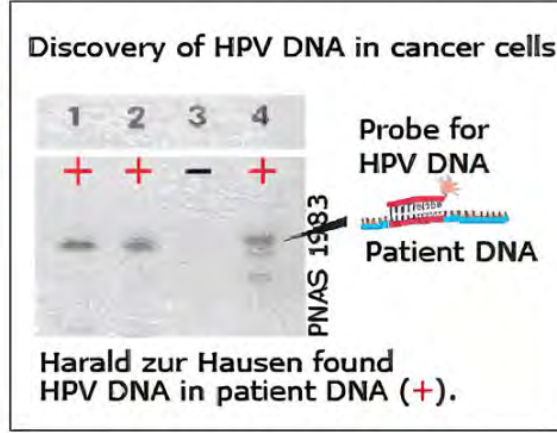
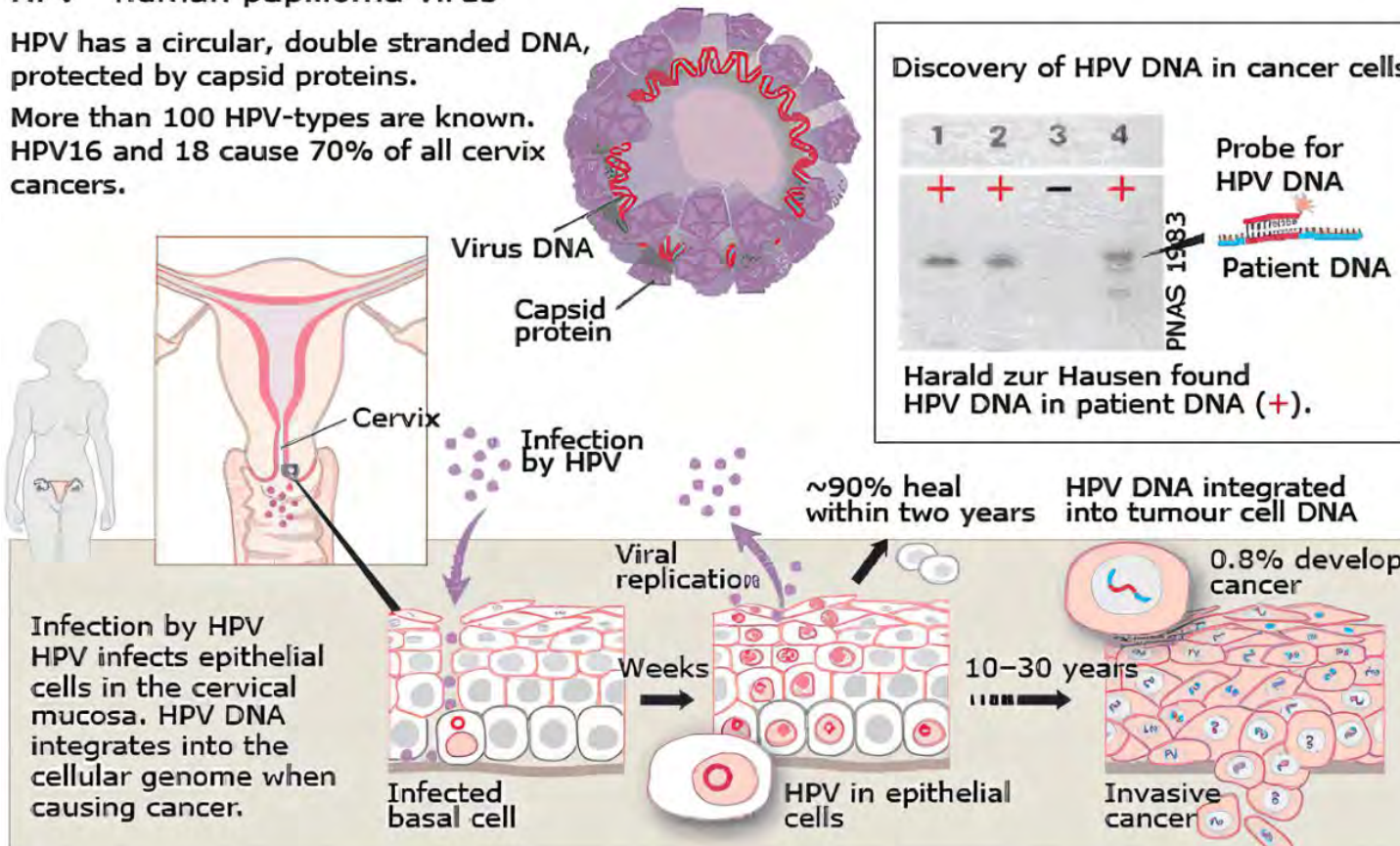


HPV infection is the primary agent responsible for > 95% of cervical cancers

HPV – human papilloma virus

HPV has a circular, double stranded DNA, protected by capsid proteins.

More than 100 HPV-types are known. HPV16 and 18 cause 70% of all cervix cancers.



Note, management does not differ by HPV status, but HPV-associated cancers have a better prognosis

Common high-risk subtypes: 16, 18, 31, 33

© The Nobel Committee for Physiology or Medicine 2008 Illustration: Annika Röhl

Case: A 40 F presents with heavy vaginal bleeding

- Reports bleeding started about 2 weeks ago and became so heavy that she presented to the ED
- Bleeding stopped after she was given medroxyprogesterone

Clinical pearls: Work-up

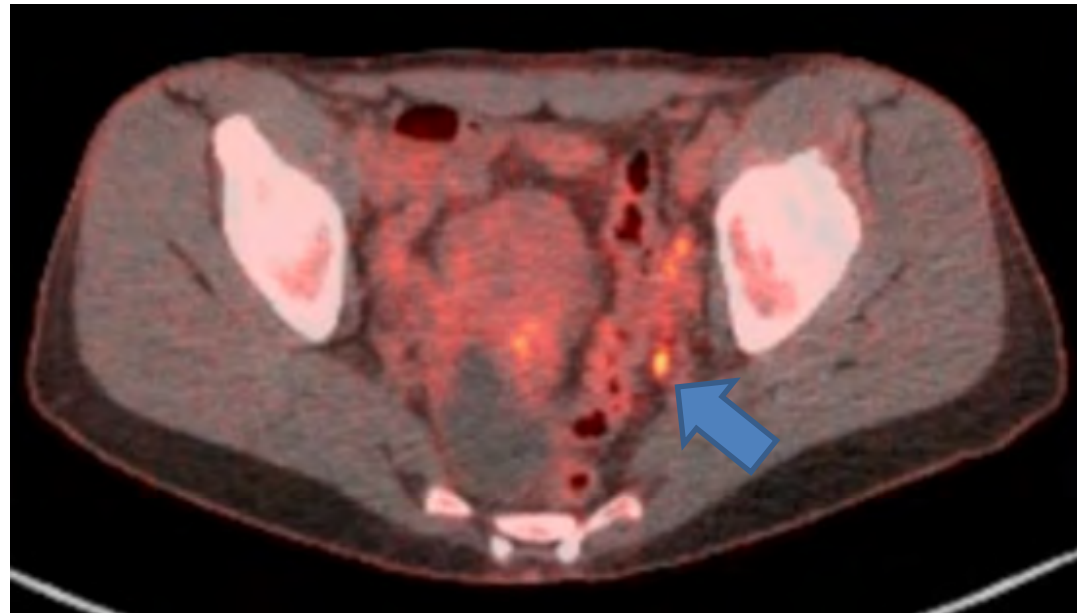
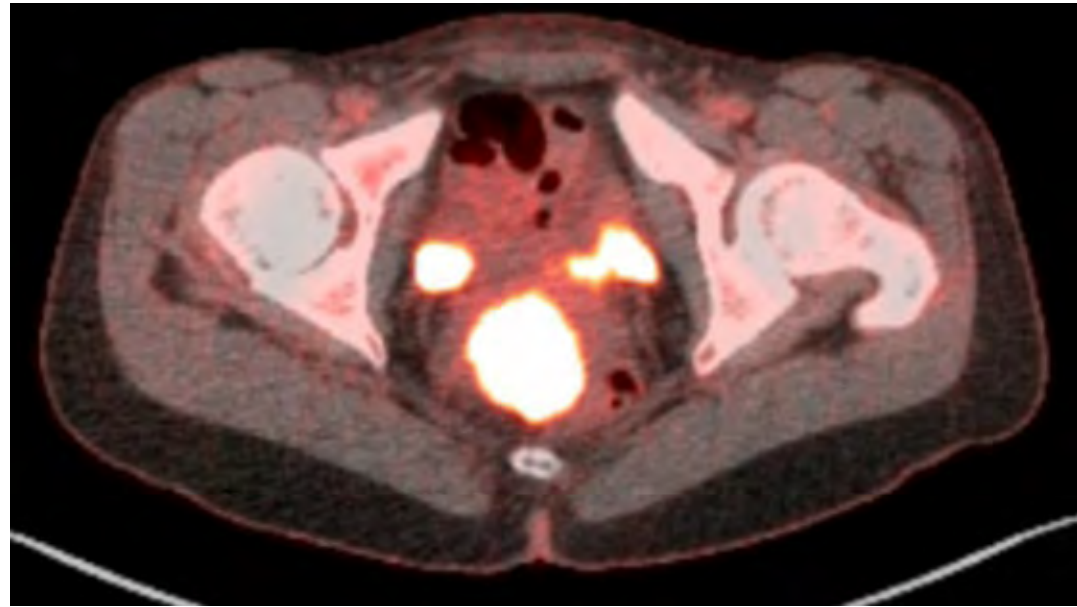


- H&P
 - Pelvic exam
 - Speculum
 - Bimanual
 - Rectovaginal exam – to assess for parametrial and rectovaginal septal involvement
 - Inguinal lymph nodes
- Labs: CBC, CMP
 - Pregnancy test if of child-bearing potential
 - Consider HIV test
- Cervical biopsy with HPV status
- Imaging:
 - Stage I:
 - PET / CT or CT chest / abdomen / pelvis
 - Pelvic MRI required if considering fertility-sparing surgery, otherwise pelvic MRI can be considered
 - Stage II - IVA:
 - Pelvic MRI
 - PET / CT or CT chest / abdomen / pelvis
- Additional workup (cystoscopy, proctoscopy, further imaging) dictated by clinical presentation

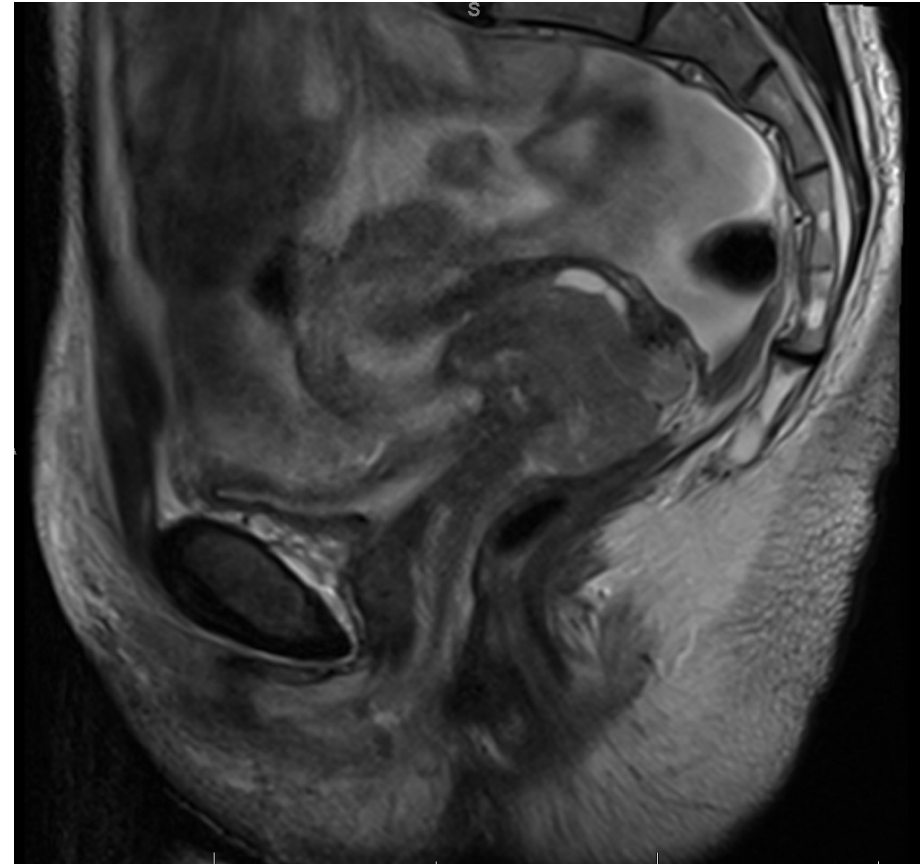
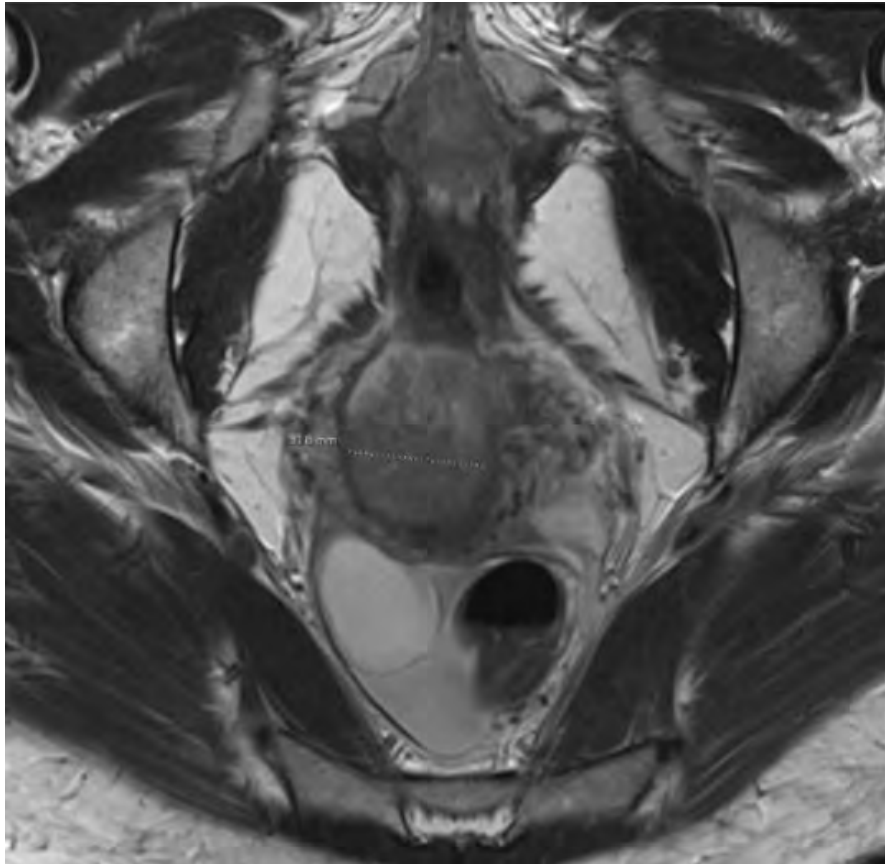
Physical exam

- Underwent pelvic US in the ED that revealed an 8 cm uterus, 5 mm endometrial stripe, mass in lower uterine segment
- Pelvic exam: 4 x 3 cm friable cervical mass without parametrial nodularity
- Cervical mass biopsy: invasive adenocarcinoma, **p16+**

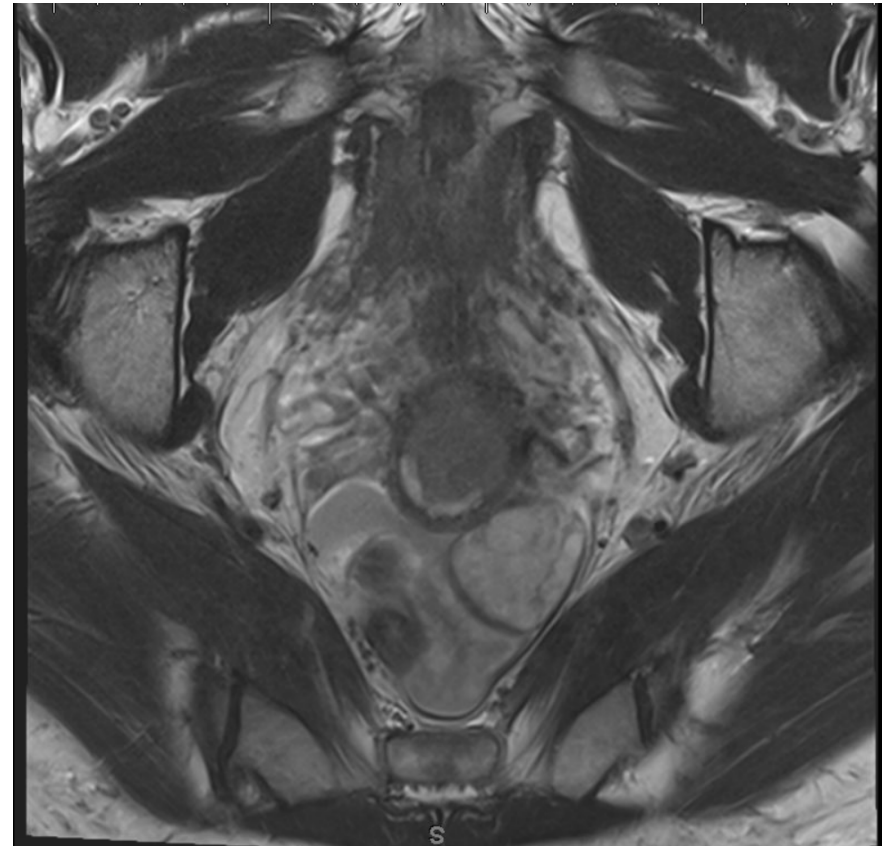
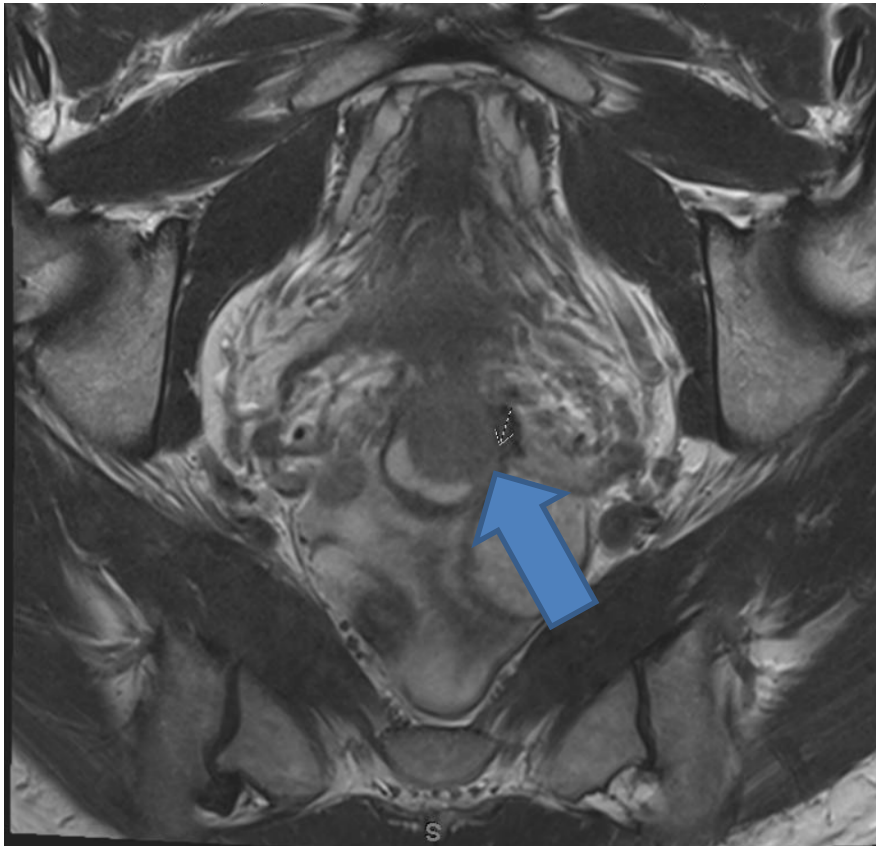
PET / CT:
Hypermetabolic 4
cm mass extending
into endometrium
and subcentimeter
left internal iliac LN



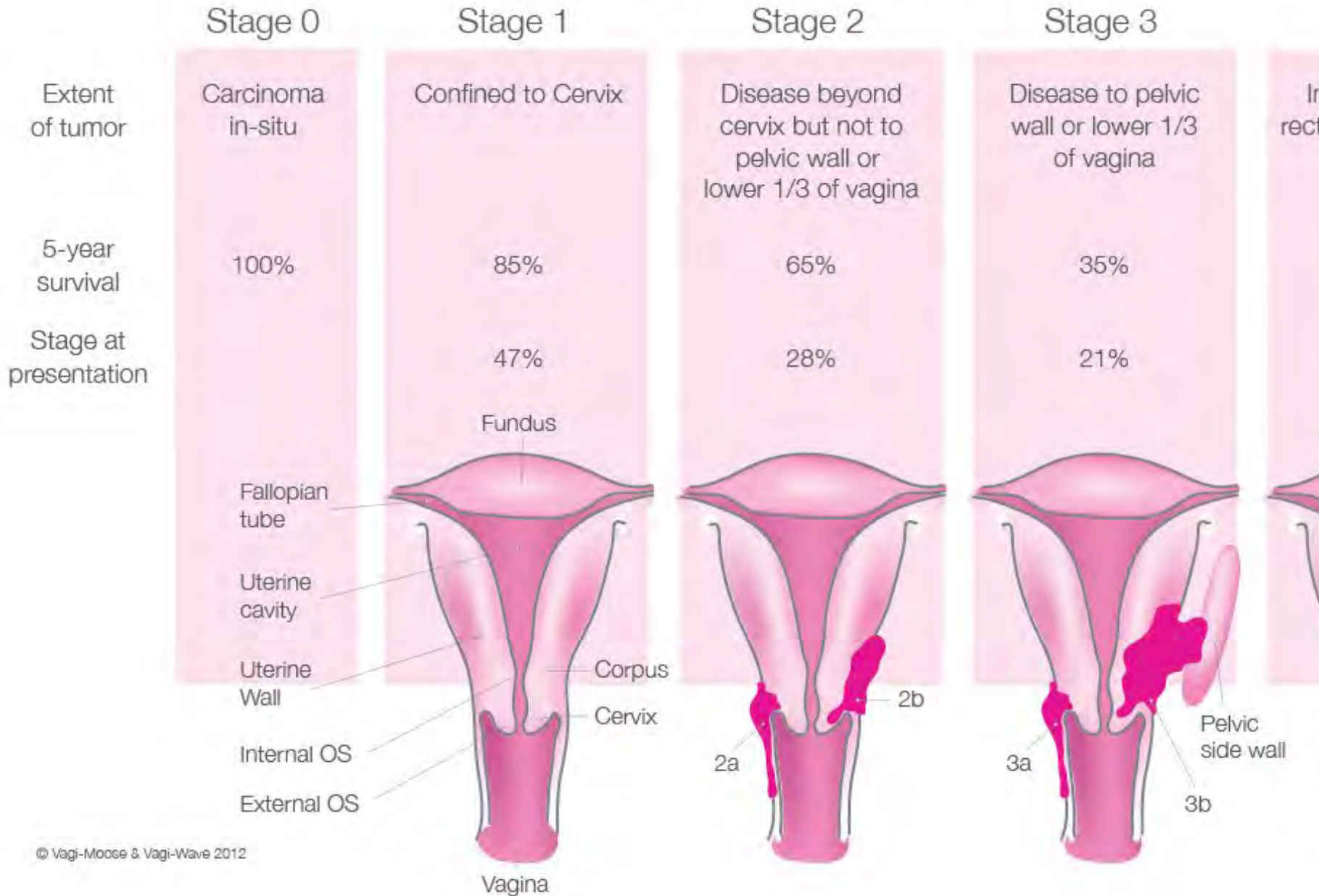
MRI pelvis: 5.0 x 2.0 x 3.1 cm cervical mass extending into lower uterus and upper 1/3 of vagina with parametrial invasion



MRI showing disruption of cervical stromal ring indicating parametrial extension



Staging of Cervical Cancer



FIGO stage I: carcinoma confined to the cervix*

*ignores extension into uterus

- Stage IA: diagnosed by microscopy, depth of invasion ≤ 5 mm
 - IA1: invasion ≤ 3 mm
 - IA2: Invasion > 3 but ≤ 5 mm
- Stage IB: limited to cervix but DOI > 5 mm
 - IB1: > 5 mm depth of invasion and up to 2 cm in greatest dimension
 - IB2: > 2 cm but up to 4 cm in greatest dimension
 - IB3: > 4 cm in greatest dimension

FIGO 2018

FIGO stage II: carcinoma extends beyond the cervix but NOT to lower 1/3 of vagina or pelvic wall

- Stage IIA: limited to upper 2/3 of vagina
 - IIA1: carcinoma \leq 4 cm in greatest dimension
 - IIA2: carcinoma $>$ 4 cm in greatest dimension
- Stage IIB: parametrial invasion

FIGO 2018

FIGO stage III: carcinoma involves lower 1/3 of vagina / extends to pelvis wall / causes hydronephrosis / involves regional LNs

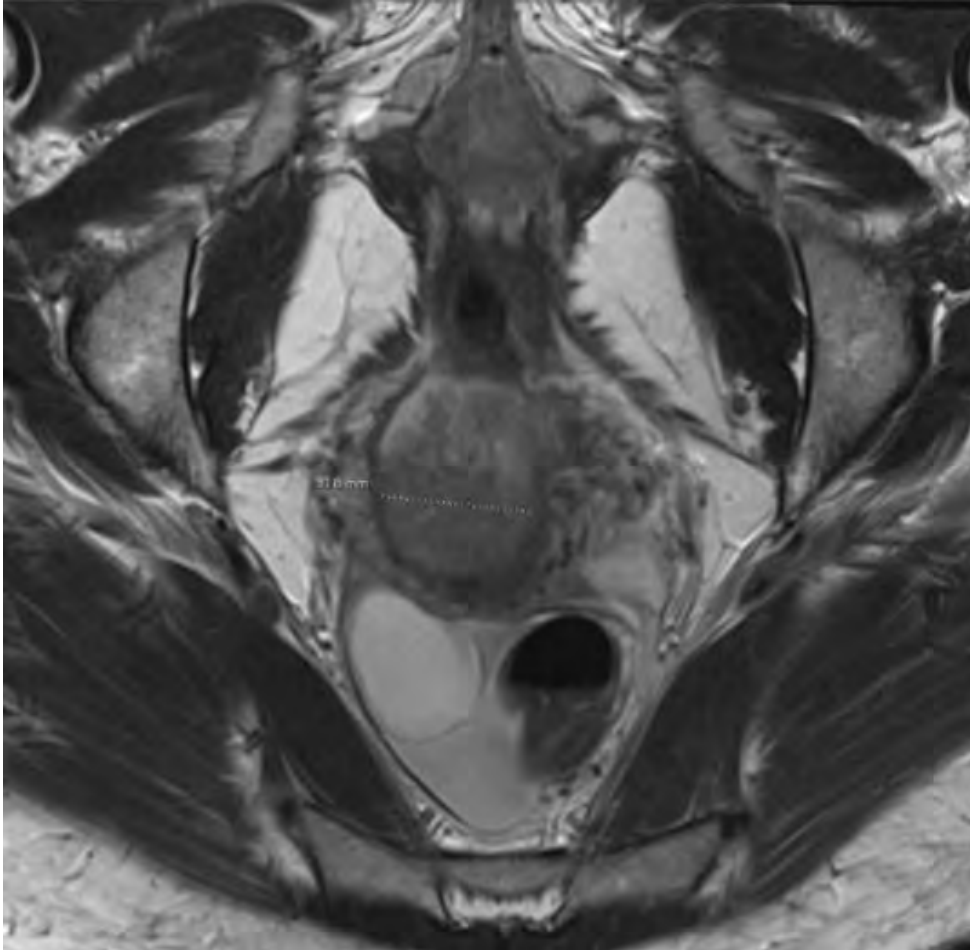
- Stage IIIA: involves lower 1/3 of vagina
- Stage IIIB: extends to pelvic wall and/or causes hydronephrosis or non-functioning kidney (unless known to be due to another cause)
- Stage IIIC: involves regional lymph nodes
 - IIIC1: pelvic lymph node involvement
 - IIIC2: para-aortic lymph node involvement

FIGO 2018

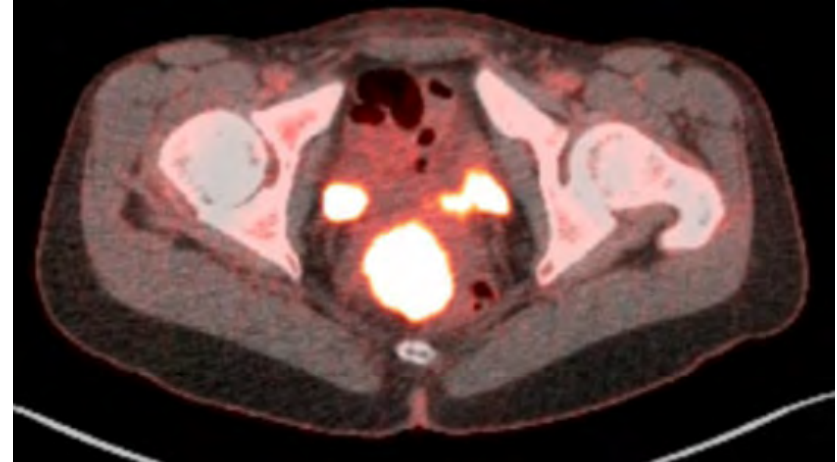
FIGO stage IV: carcinoma involves other organs

- Stage IVA: biopsy-proven spread to adjacent organs (rectum or bladder)
- Stage IVB: spread to distant organs

How would you stage our patient?



T2b: parametrial extension



N1: pelvic lymph node involvement

FIGO IIIC1

T2bN1M0

What is the optimal management of locally-advanced cervical cancer?: Lessons from the Landoni Experience

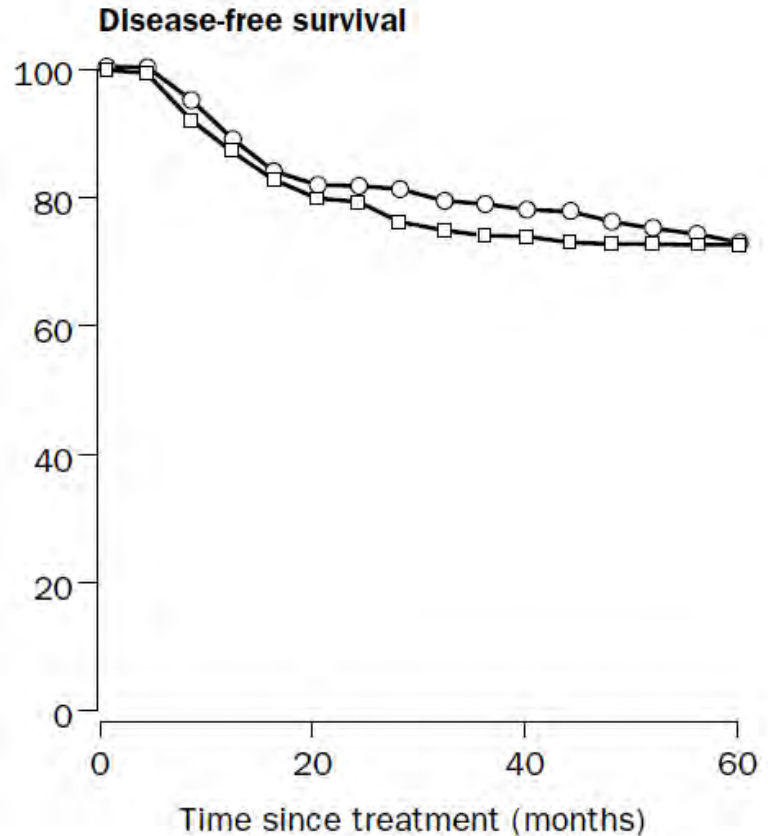
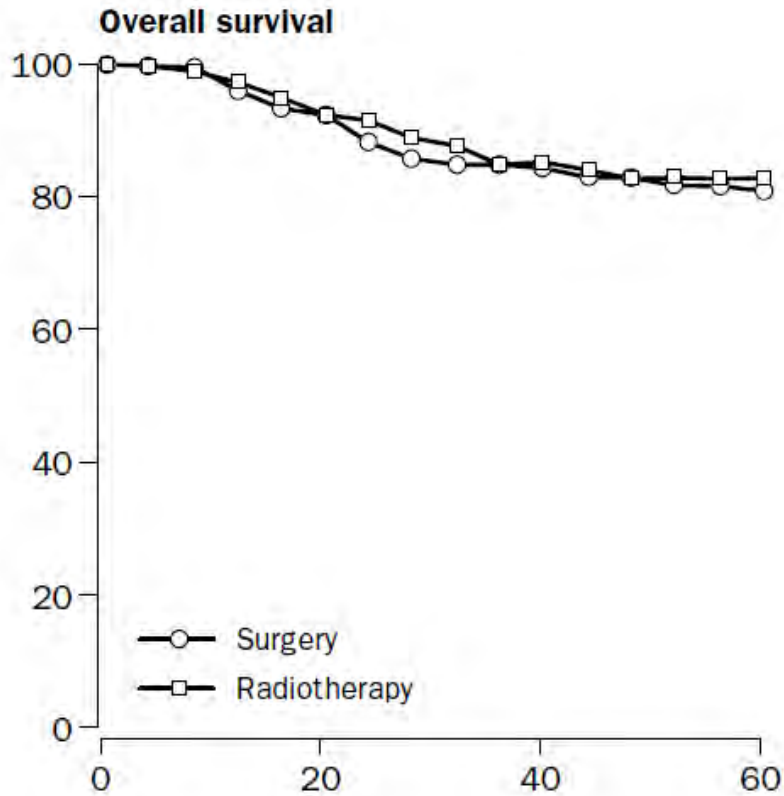
- Prospective, randomized study comparing RT vs radical hysterectomy +/- adjuvant RT for early-stage cervical cancer
- Population: FIGO IB – IIA
- Treatment:
 - RT: EBRT (40-53 Gy in 1.8 - 2.0 Gy fractions) + LDR boost (70–90 Gy to point A with Cs 137)
 - N = 167
 - Surgery: radical hysterectomy
 - N = 170

Indications for adjuvant RT: Stage pT2b or greater, < 3 mm of uninvolved cervical stroma, cut-through, positive lymph nodes

If node-positive: para-aortic nodes received 45 Gy with 5-10 Gy boost to involved node(s)

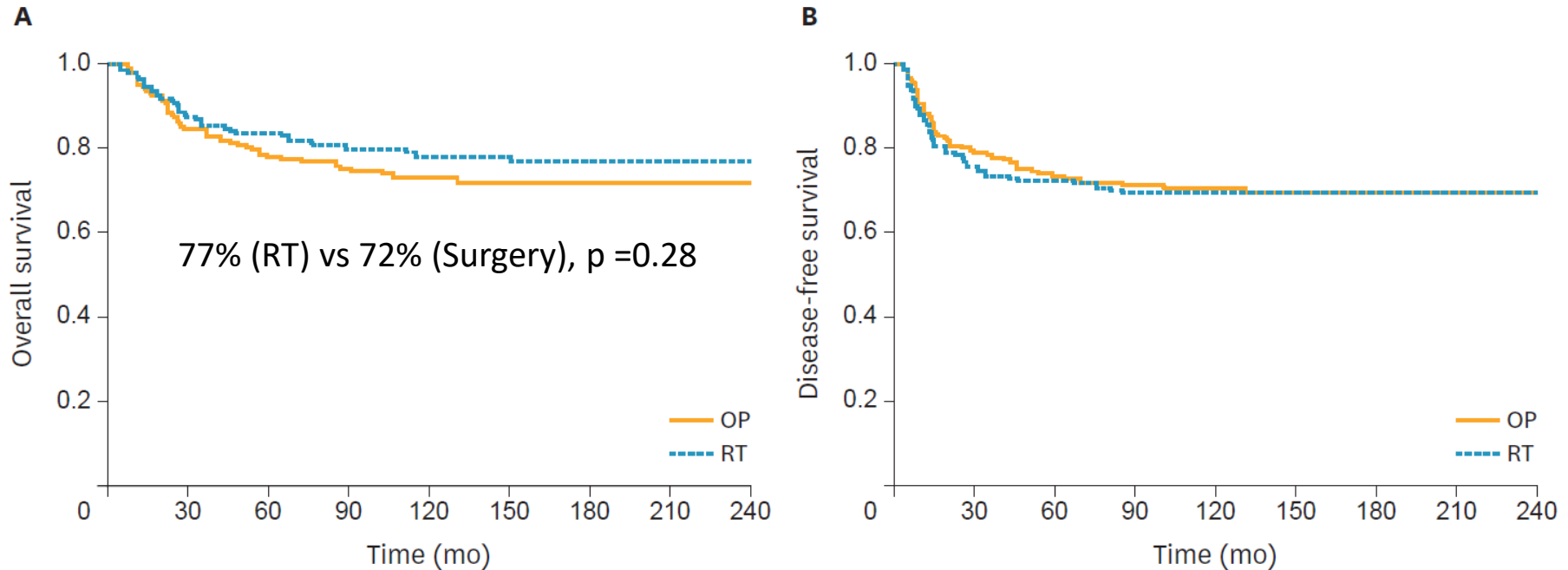
Landoni et al., 1997. *Lancet*.

No difference in 5-year OS or DFS



Landoni et al., 1997. *Lancet*.

No difference in 20-year OS or DFS



Note - 64% of surgical patients had adjuvant RT!

So oncologic outcomes are similar, but what about adverse effects?

Type of complication	Surgery	Surgery+RT	RT
No. of patients	61	108	158
Urologic			
Hydroureteronephrosis*	2 (3.3)	11 (10.1)	9 (5.6)
Ureteral fistula	1 (1.6)	-	-
Urinary incontinence	2 (3.3)	4 (3.7)	-
Atonic bladder	8 (13.1)	5 (4.6)	1 (0.6)
Actinic cystitis	-	7 (6.4)	9 (5.6)
Vascular			
Pulmonary embolism	2 (3.3)	1 (0.9)	-
Legs edema	-	12 (11.1)	1 (0.6)
Lymphocyst	5 (8.2)	5 (4.6)	1 (0.6)
Vascular lesion	1 (1.6)	-	-
Intestinal			
Rectal fistula	-	-	1 (0.6)
Bowel obstruction	-	6 (5.5)	2 (1.2)
Proctitis	-	-	14 (8.8)
Others			
Wound abscess	-	-	-
Abdominal hernia	4 (6.6)	4 (3.7)	2 (1.2)
Bone necrosis	-	1 (0.9)	-
Vaginal necrosis	-	-	1 (0.6)
Vaginal stenosis	-	1 (0.9)	2 (1.2)
Pelvic fibrosis	-	4 (3.7)	3 (1.8)
Uterine perforation	-	-	1 (0.6)
Peritonitis	-	1 (0.9)	-
Total	25 (40.7)	62 (56.4)	47 (29.0)

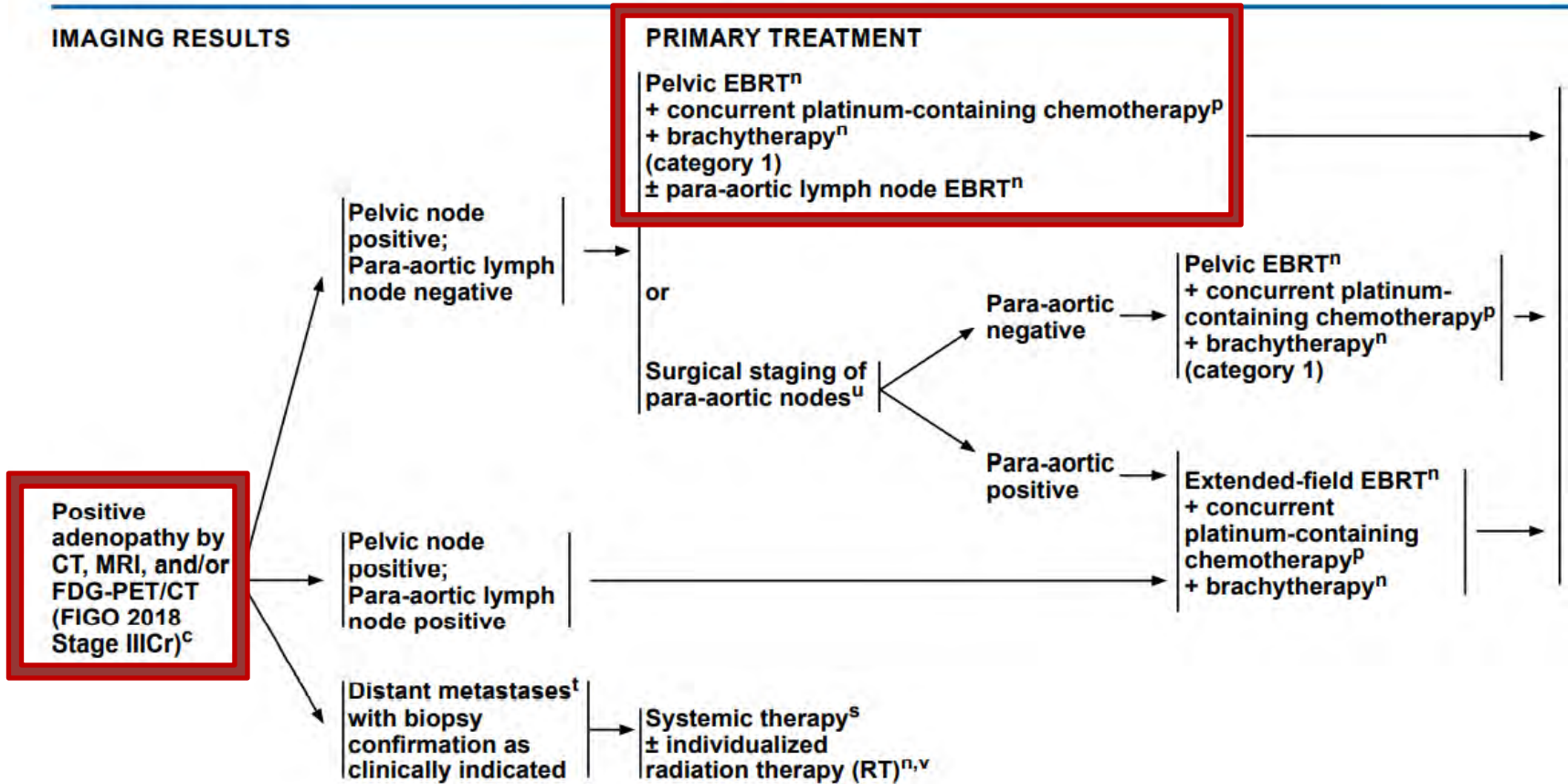
Landoni et al. 2017. *JGO*.

January 29, 2025

What did we learn from the Landoni experience?

Since complications are highest in patients who receive surgery + RT, patients should be appropriately selected for surgery (i.e. must have a low likelihood of requiring adjuvant RT) in order to reduce the complications associated with multi-modal therapy

NCCN guidelines



What's the evidence for concurrent cisplatin?

Trials to know:

GOG 123

GOG 109

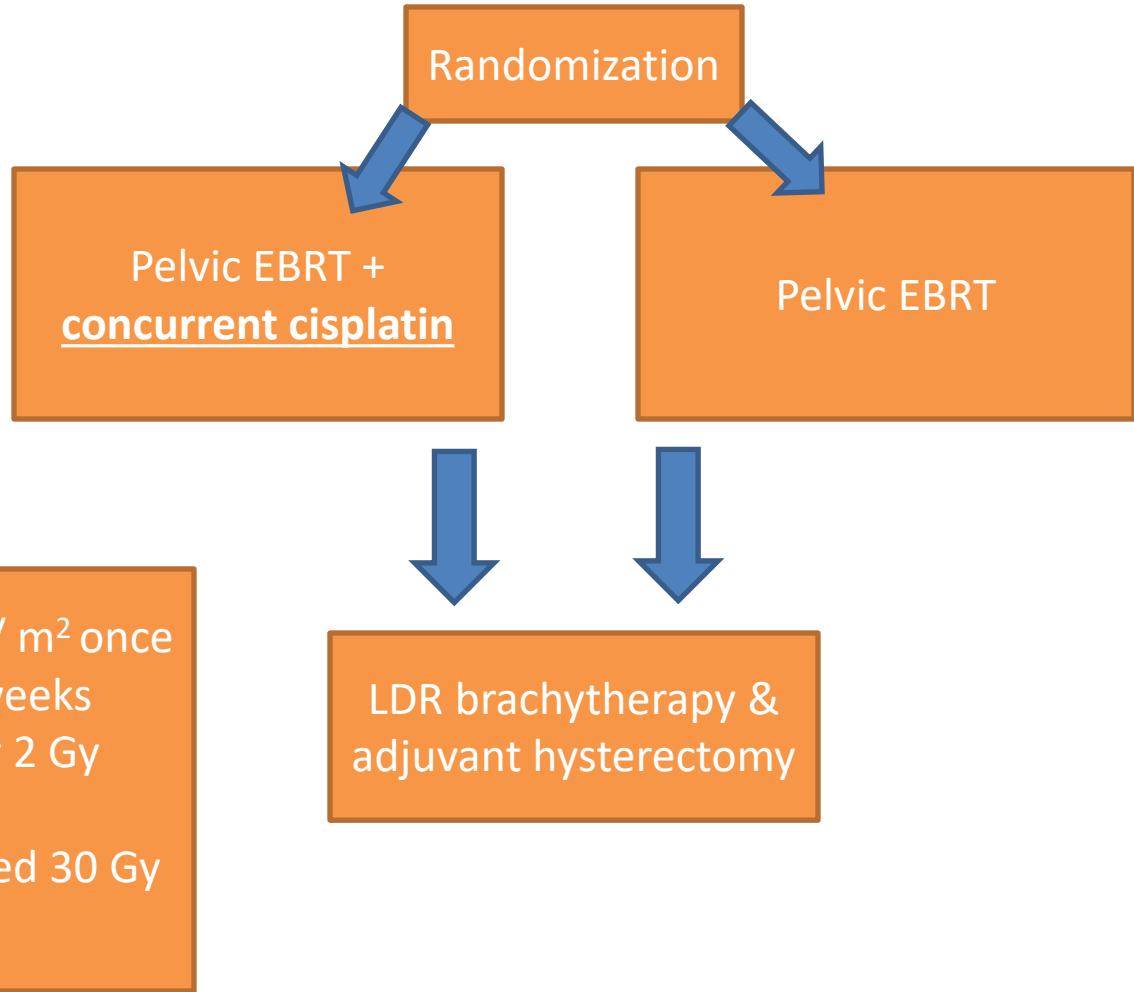
GOG 85 / SWOG 8695

GOG 120

RTOG 90-01

GOG 123

Population:
patients with bulky
stage IB cervical
cancer

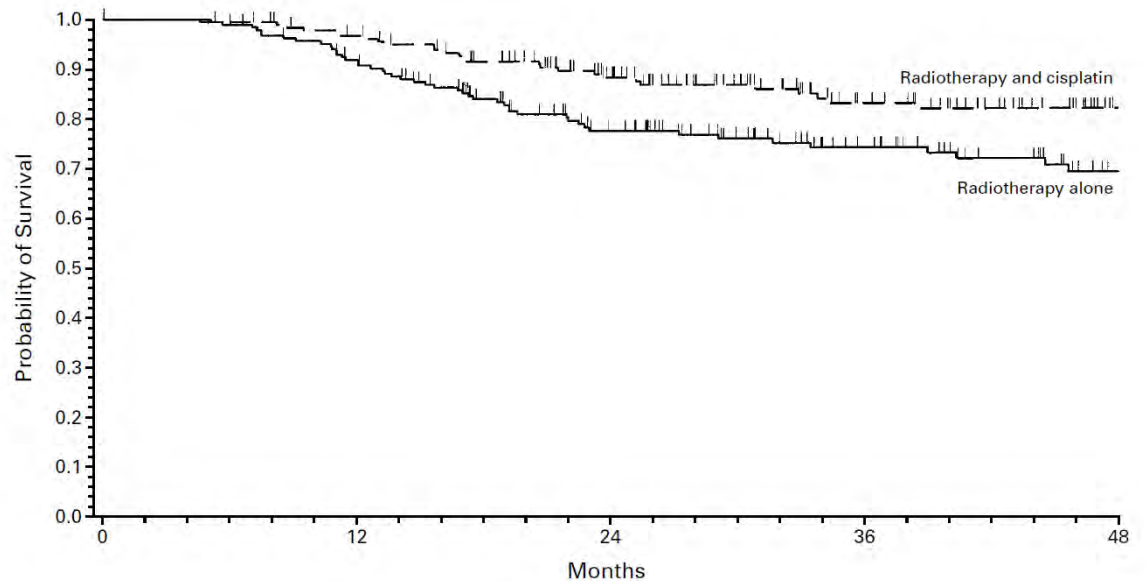
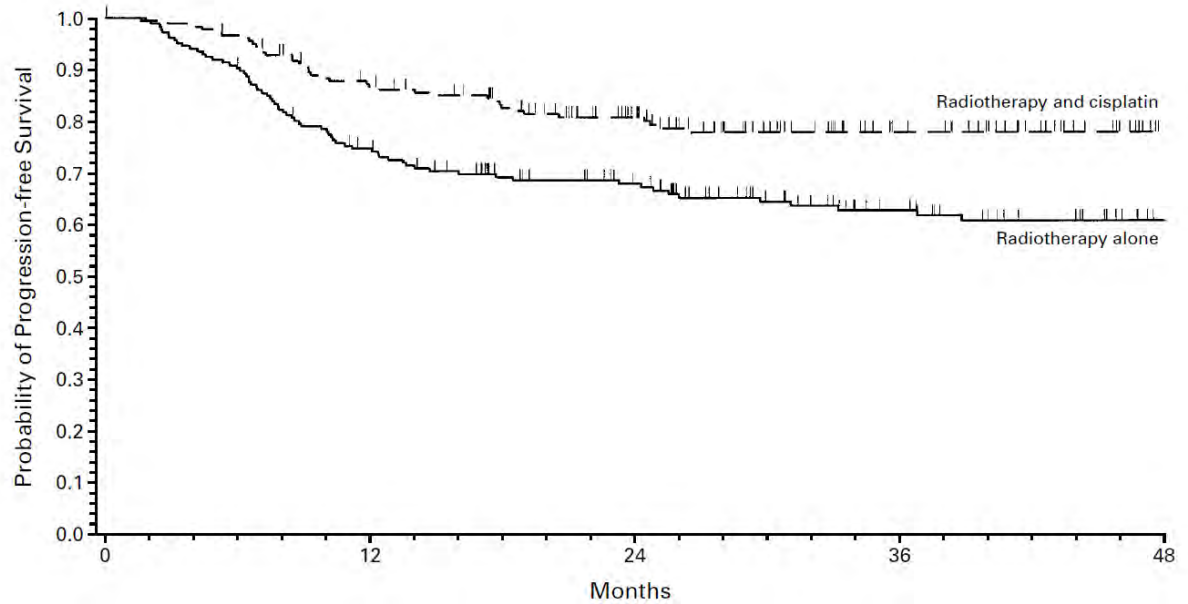


Cisplatin dosing: 40 mg / m² once weekly for up to 6 weeks
EBRT: 45 Gy in 1.8 or 2 Gy fractions
Brachytherapy prescribed 30 Gy to point A

Keys et al., 1999. *NEJM*.

January 29, 2025

Improved PFS and OS with cisplatin



Keys et al., 1999. *NEJM*.

January 29, 2025

GOG 109

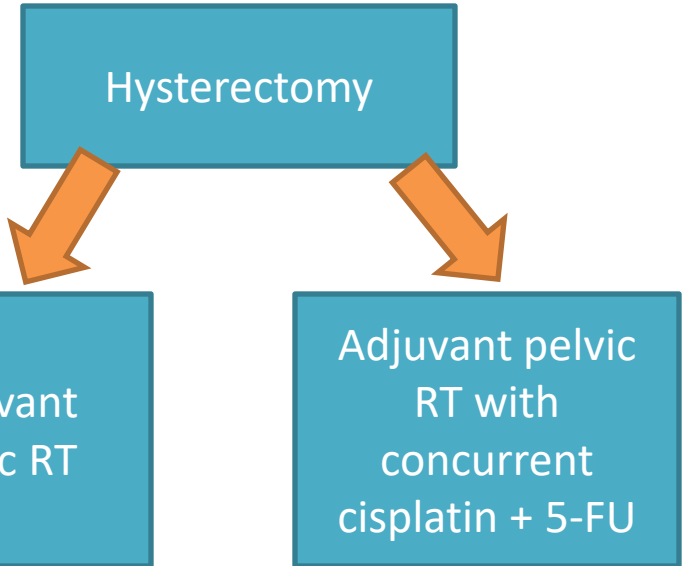
Population: patients with cervical cancer, stages IA2, IB, or IIA who underwent hysterectomy & had at least 1 of the following:

- **Positive margins**
- **Positive pelvic nodes**
- **Parametrial involvement**



Peters criteria

Cisplatin delivered as 70 mg / m² for 4 cycles



Peters et al., 2000. *JCO*.

Improved PFS and OS with cisplatin + 5-FU

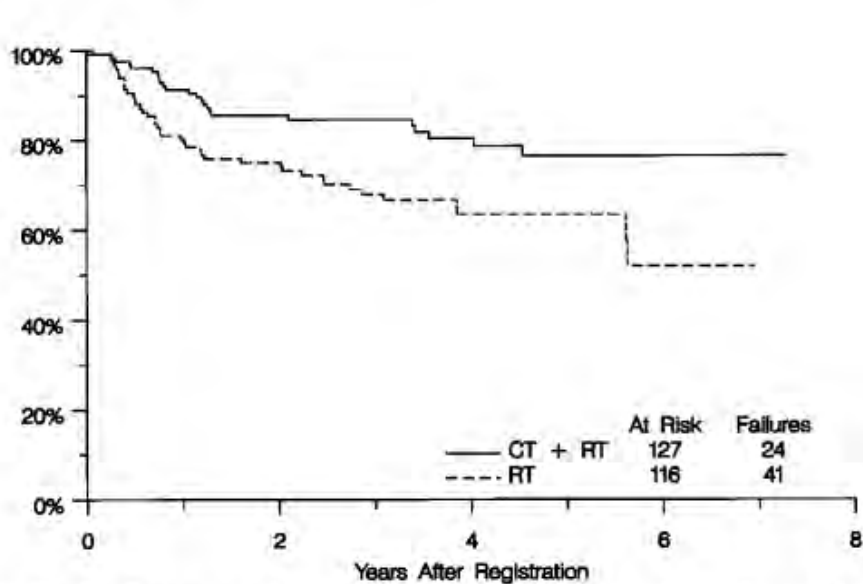


Fig 1. Progression-free survival for 127 patients randomized to receive CT + RT and for 116 patients randomized to receive RT alone.

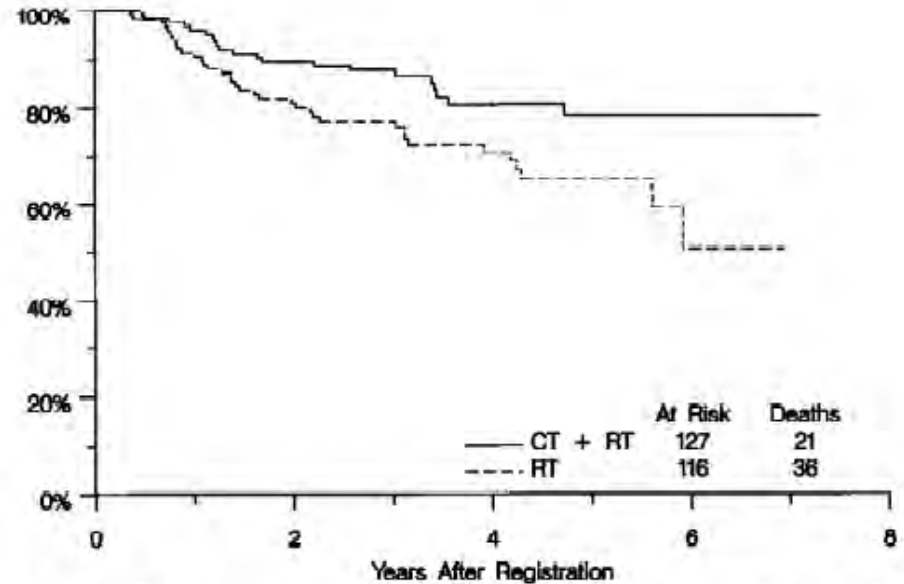


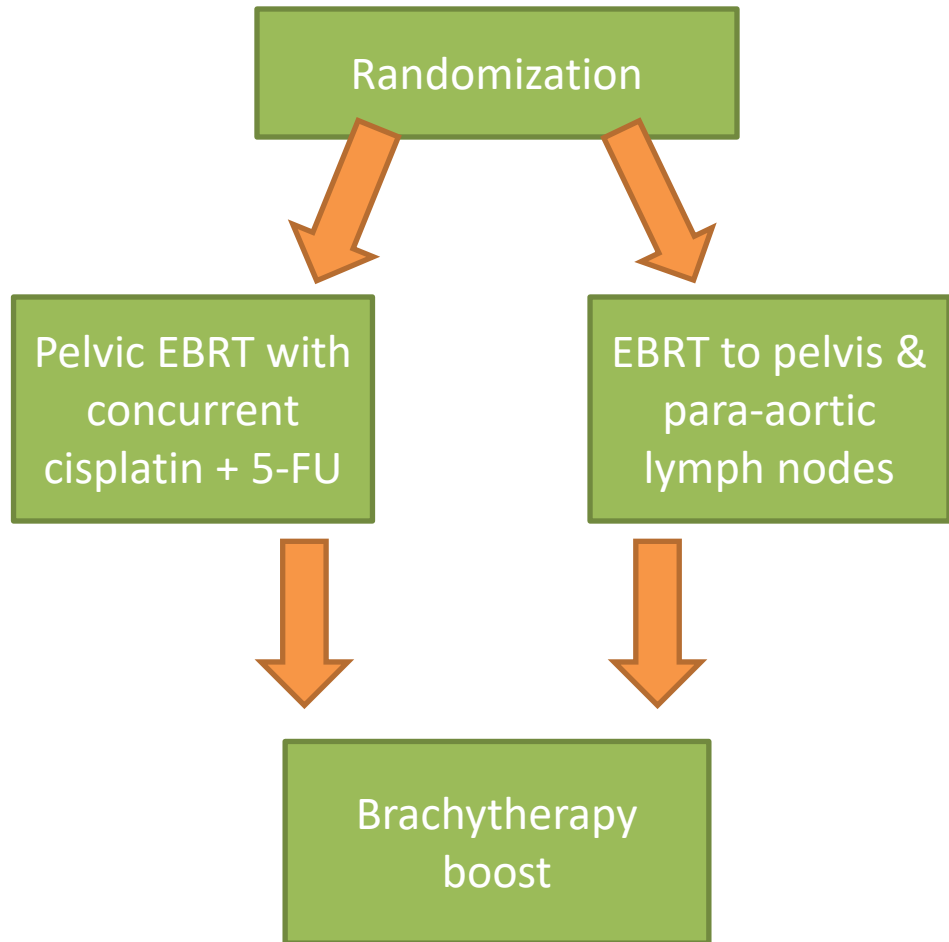
Fig 2. Overall survival for 127 patients randomized to receive CT + RT and for 116 patients randomized to receive RT alone.

Peters et al., 2000. *JCO*.

RTOG 90-01

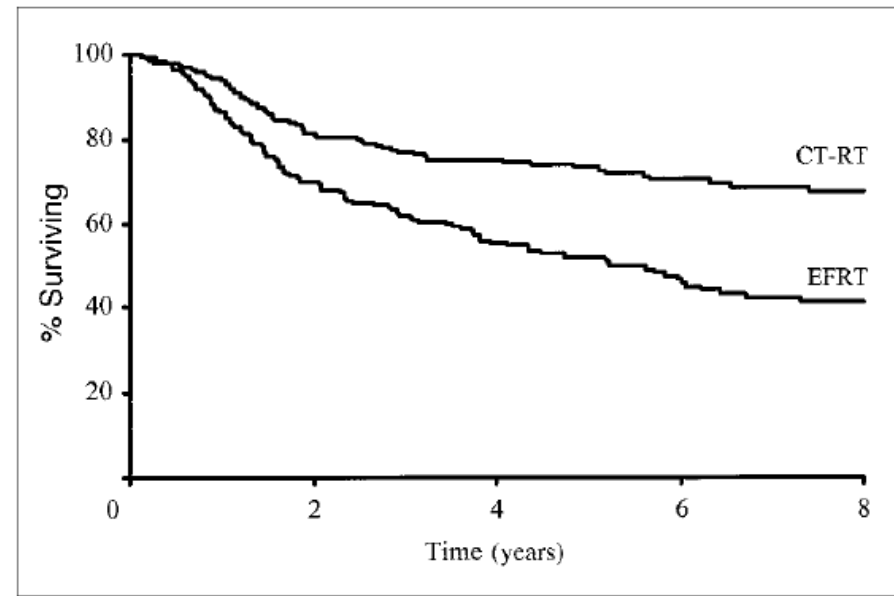
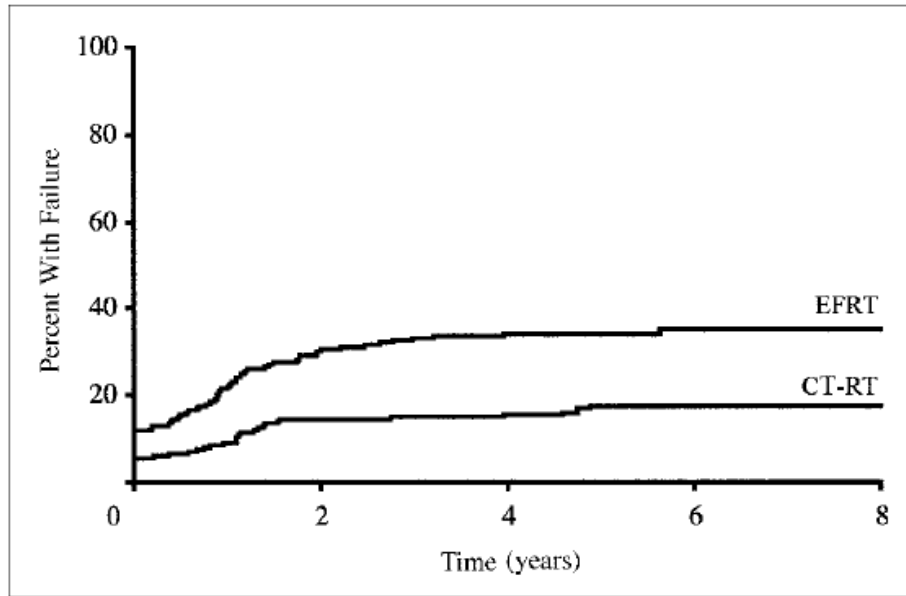
Population: patients with cervical cancer, stages IIB – IVA or stage IB- IIA with tumors at least 5 cm

EBRT delivered 45 Gy / 25 fx
Cumulative dose to Point A was 85 Gy
Cisplatin 75 mg / m² followed by 5-FU 4000 mg / m² over 96 hours delivered every 3 weeks for 3 cycles total



Eifel et al., 2004. *JCO*.

Lower rates of locoregional recurrence and improved OS with cisplatin + 5-FU



Eifel et al., 2004. *JCO*.

GOG 85 / SWOG 8695

Population: Patients with cervical cancer, stages IIB - IVA

EBRT delivered with conventional fractionation, with total dose depending on patient's stage
Cisplatin 50 mg / m² followed by 5-FU 4000 mg / m² delivered over 96 hours for 2 cycles
Hydroxyurea 80 mg / kg PO twice weekly

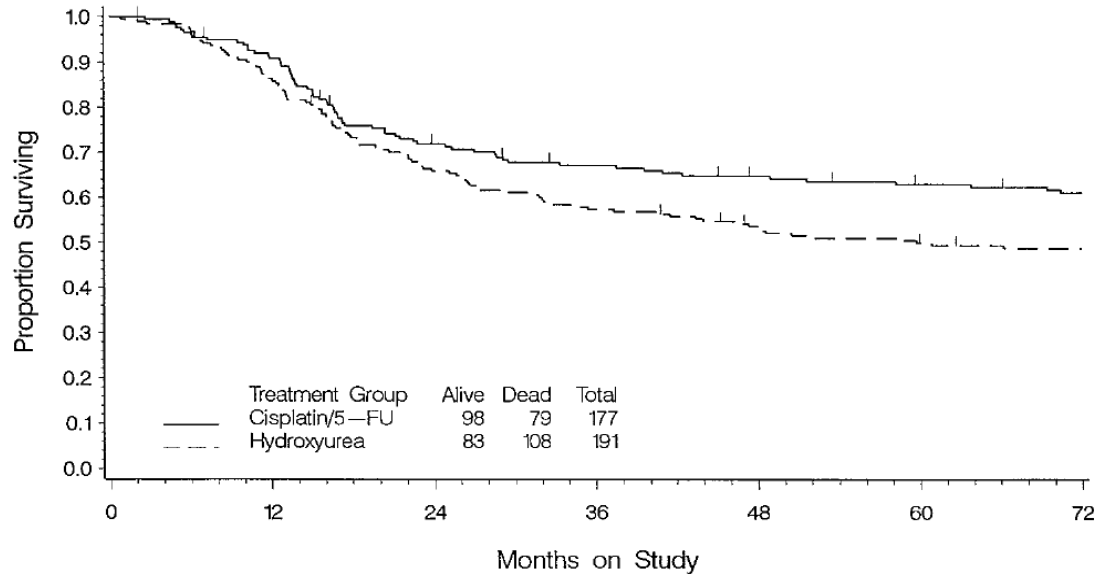
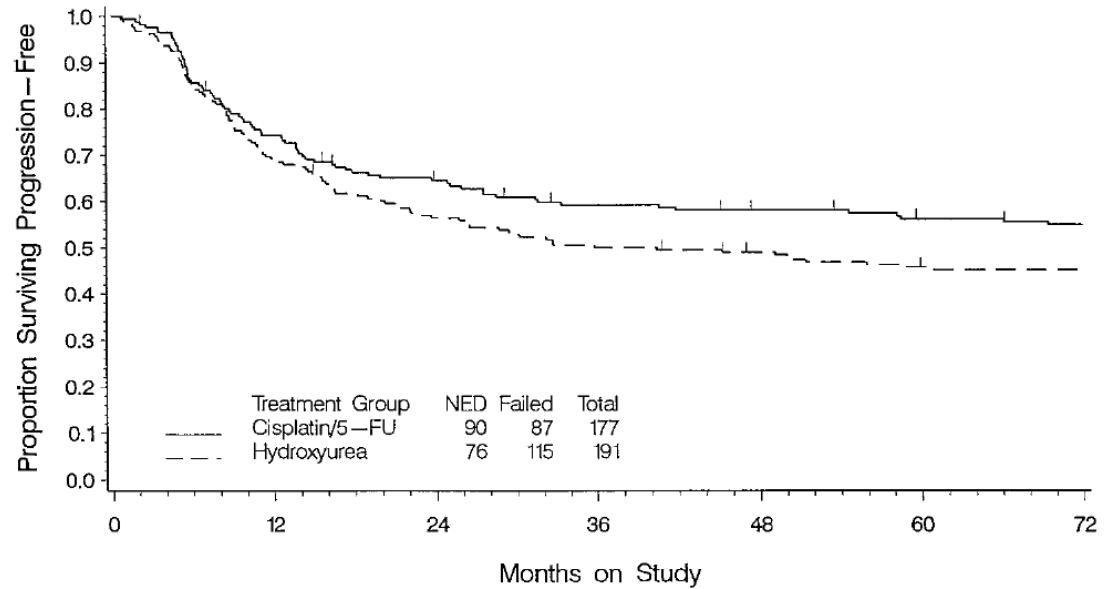
Randomization

Pelvic EBRT +/- brachytherapy boost with concurrent cisplatin + 5-FU

Pelvic EBRT +/- brachytherapy boost with concurrent hydroxyurea

Whitney et al., 1999. *JCO*.

Improved PFS and OS with cisplatin + 5-FU



Whitney et al., 1999. *JCO*.

GOG 120

Population: patients with cervical cancer, stages IIB - IVA

Randomization

Pelvic RT +
concurrent cisplatin

Pelvic RT +
concurrent cisplatin,
5-FU, & hydroxyurea

Pelvic RT +
concurrent
hydroxyurea

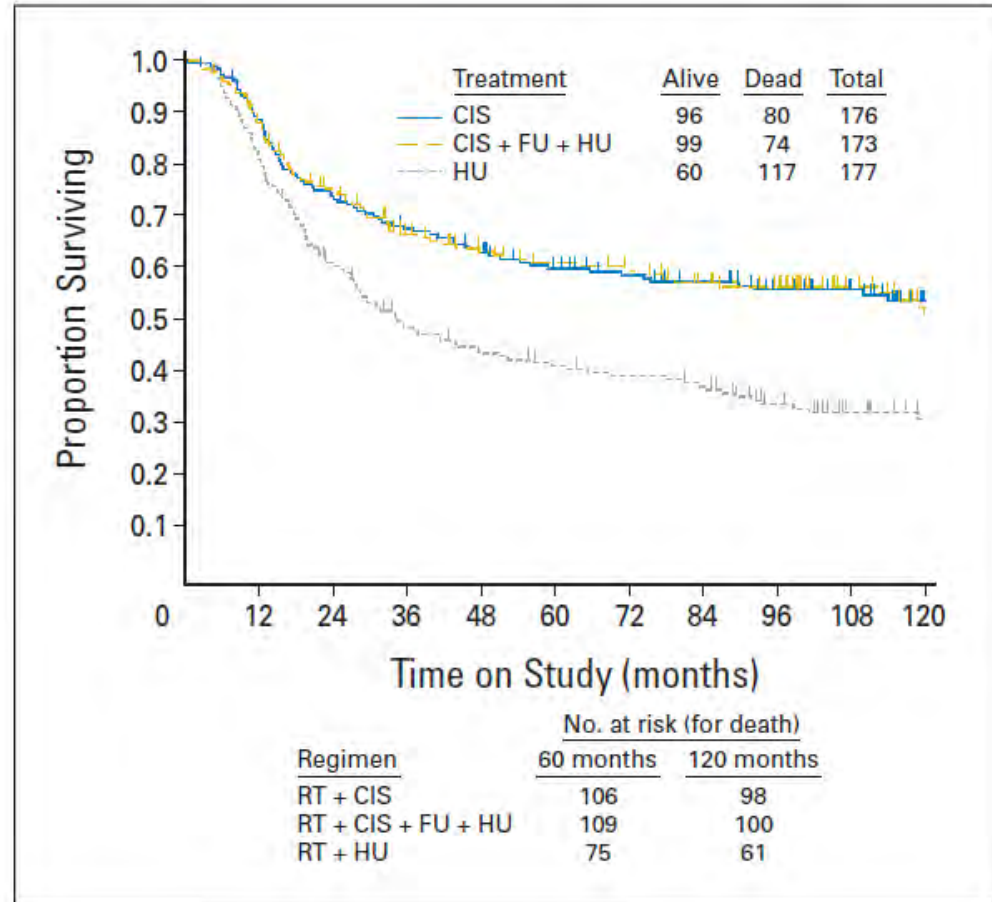
Pelvic RT included EBRT + LDR
brachytherapy boost,
cumulative dose depended on
patient stage

Rose et al., 2007. *JCO*.

January 29, 2025

Improved OS with cisplatin

OS benefit
seen for those
with stage IIB
and stage III
disease



Rose et al., 2007. *JCO*.

Results of these trial prompted -

NCI alert recommending EBRT with concurrent cisplatin

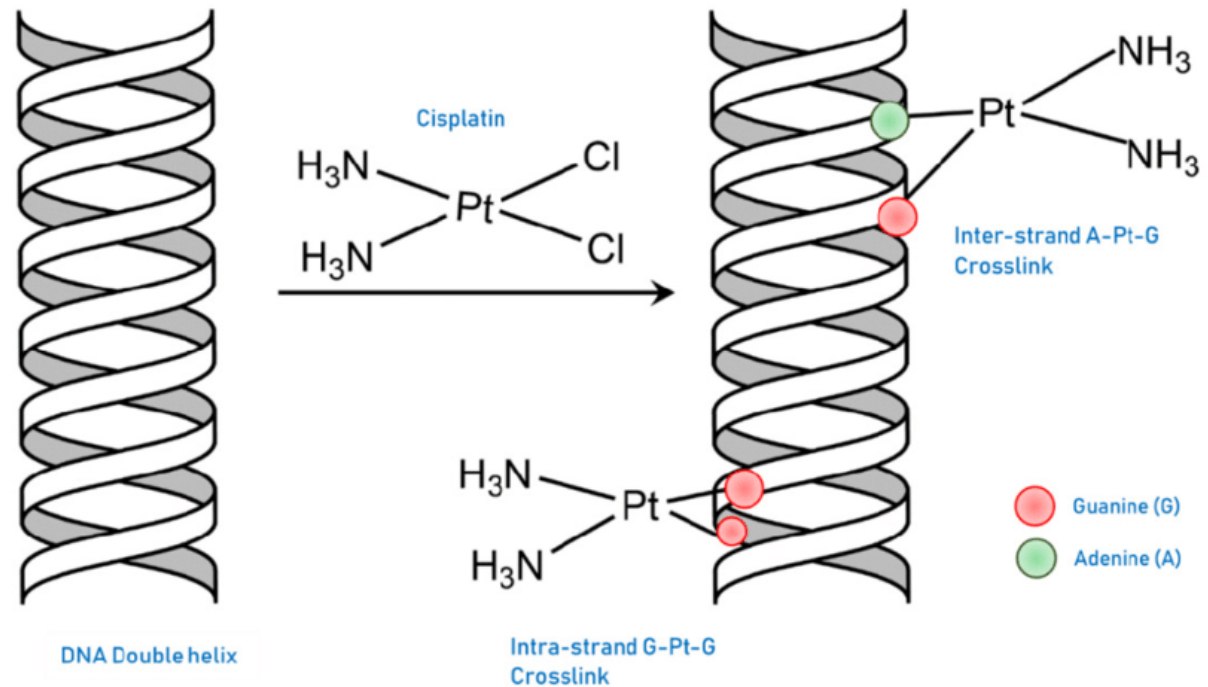
Absolute OS benefit at 5 years is 6% with platinum chemotherapy
Hazard ratio 0.81 in 1 meta-analysis

Reducing Uncertainties About the Effects of
Chemoradiotherapy for Cervical Cancer: A Systematic
Review and Meta-Analysis of Individual Patient Data From
18 Randomized Trials

Chemoradiotherapy for Cervical Cancer Meta-Analysis Collaboration

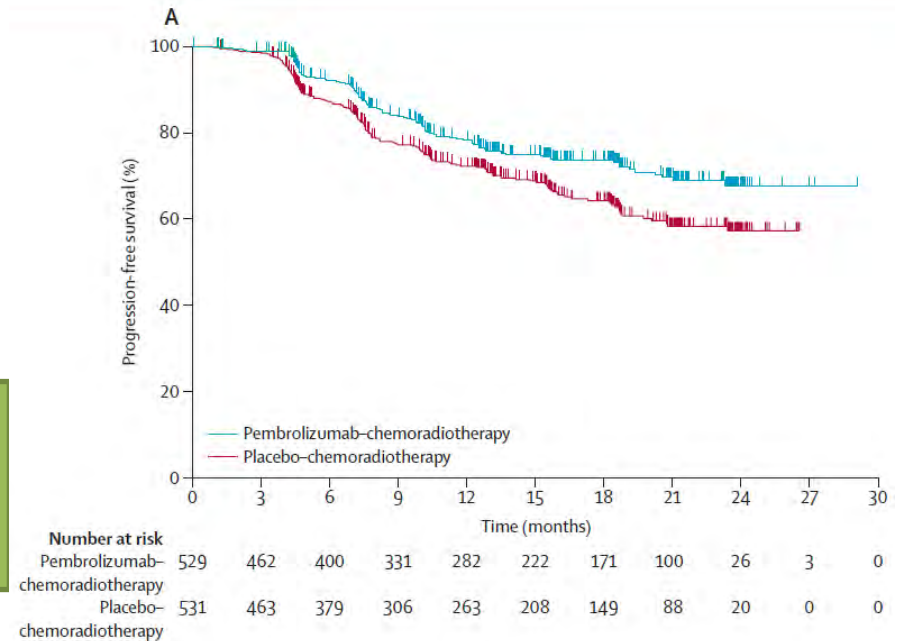
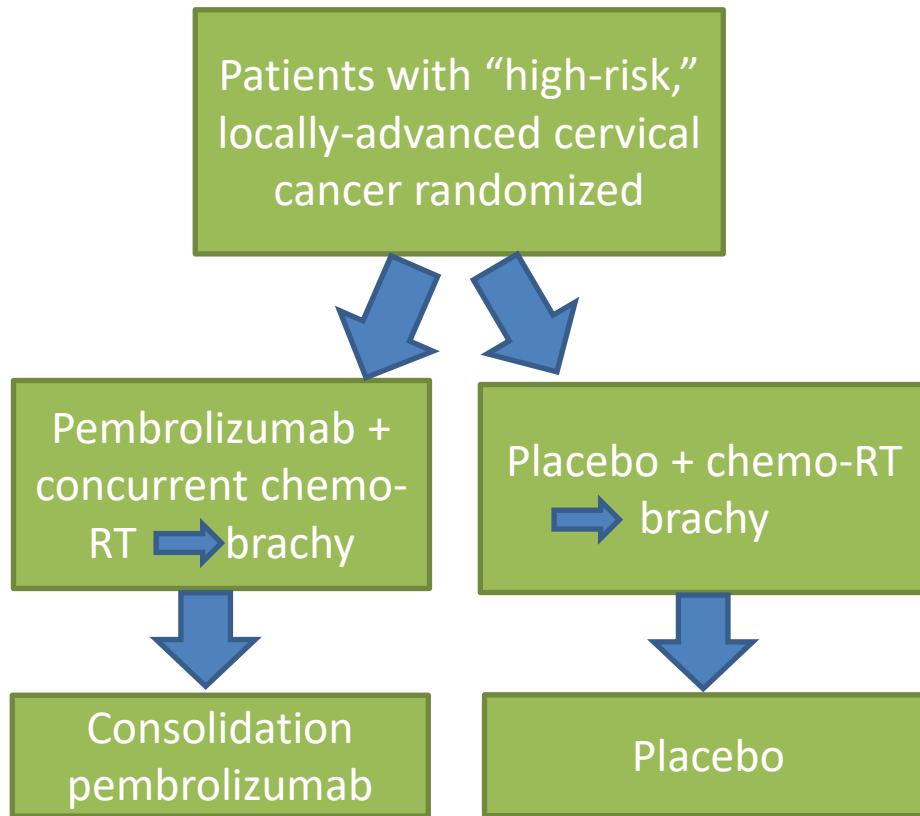
Cisplatin dosing

- 40 mg / m² weekly
- 5-6 weeks




In there a benefit with immunotherapy?: KEYNOTE A-18


- Randomized, double-blind, placebo-controlled phase III trial



Improved 2-year PFS with pembrolizumab (68%) compared to placebo (57%)

NCCN recommends *considering* concurrent + consolidative pembrolizumab when “high risk”:

- FIGO (2014) stage III – IVA  Note, FIGO 2014 staging is clinical and does not incorporate imaging
 - Category 1
- FIGO (2018) stage III – IVA
 - Category 2B



III The carcinoma has extended onto the pelvic sidewall. On rectal examination, there is no cancer free space between the tumor and pelvic sidewall. The tumor involves the lower third of the vagina. All cases of hydronephrosis or non-functioning kidney should be included unless they are known to be due to other causes.

IIIA Involvement of the lower vagina but no extension onto pelvic sidewall.

IIIB Extension onto the pelvic sidewall, or hydronephrosis/non-functioning kidney.

IV The carcinoma has extended beyond the true pelvis or has clinically involved the mucosa of the bladder and/or rectum.

IVA Spread to adjacent pelvic organs.

External beam radiotherapy course

- EBRT to pelvis
 - 45 Gy / 25 fractions to pelvis
 - SIB to 57.5 Gy to positive node
- Concurrent cisplatin

Simulation for EBRT

- Patient positioned head-first, supine, and with arms on chest and legs in neutral position
 - Superior border: above diaphragm
 - Inferior border: below ischial tuberosities
- 2 scans obtained to create an ITV
 1. Full bladder, no contrast
 2. Empty bladder, with IV contrast
- Empty rectum

A review of pelvic target volumes per EMBRACE II

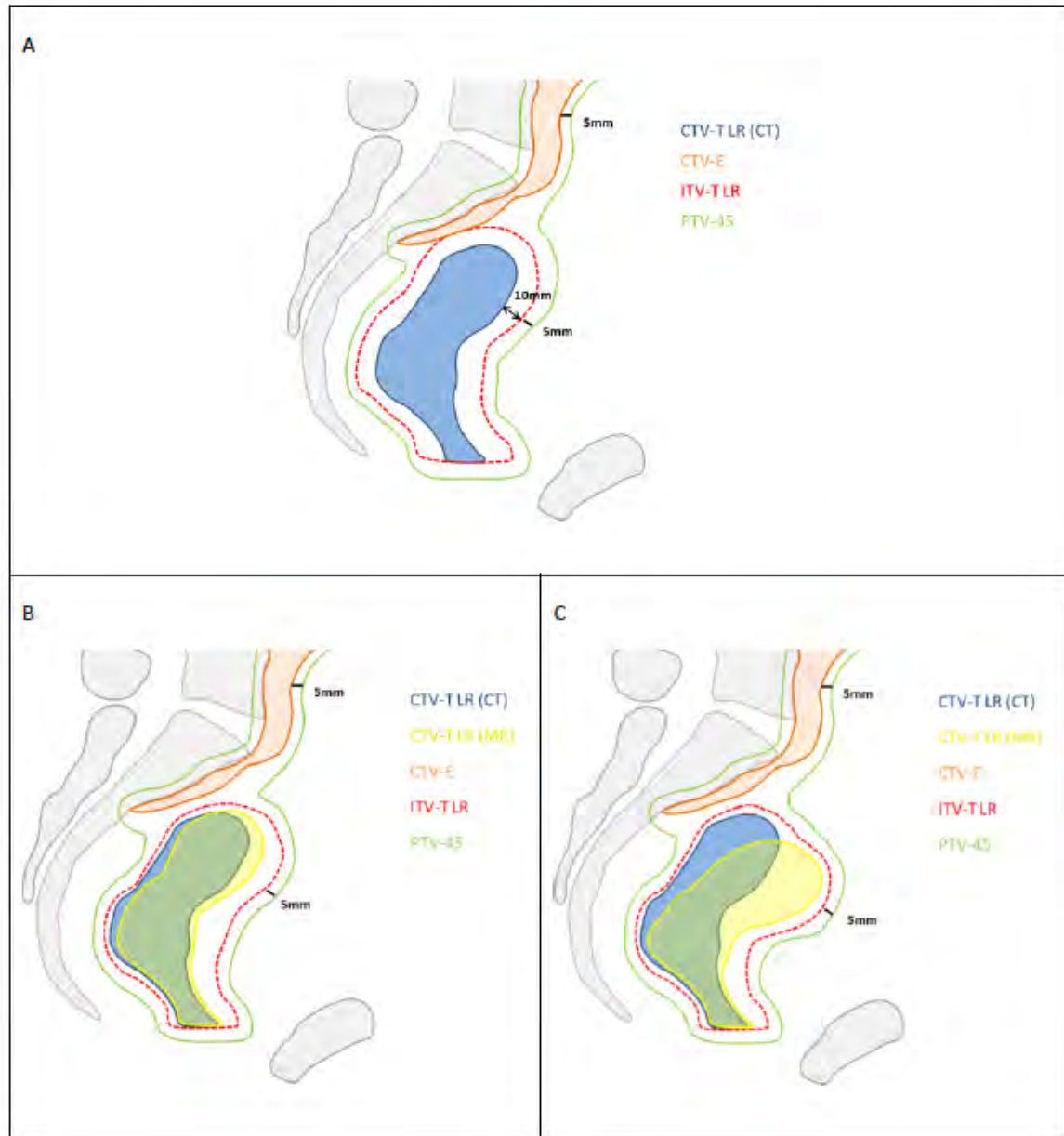
- GTV-T: cervical tumor as seen on MRI
- CTV-T HR: tumor and entire cervix
- CTV-T LR:
 - CTV-T HR + 5 mm anterior and posterior
 - Uterus
 - Parametria and involves nodes
 - Upper vagina
 - If pelvic wall, mesorectum, or other structures are involved, add 2 cm around CTV-T HR to include these structures
- ITV accounts for the position of the CTV-T LR on the empty & full bladder scans

Creating the ITV

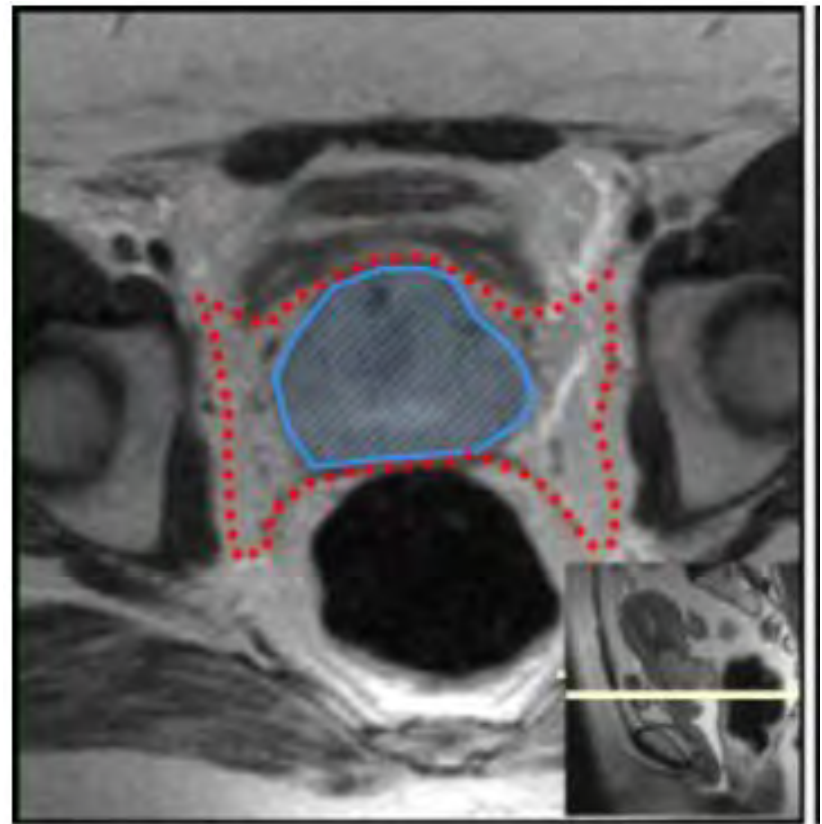
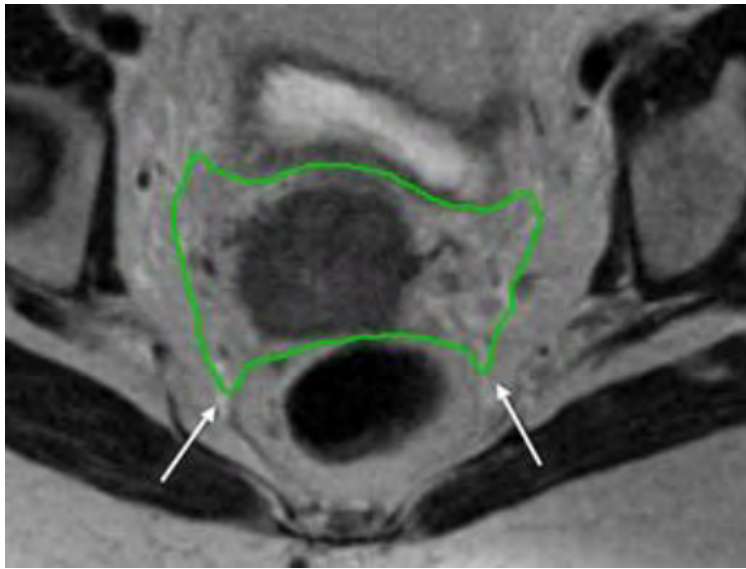
1. Fuse: empty & full bladder scans from simulation, MRI (T2 sequences)
 - Full bladder scan will be used for treatment planning, so draw on this
2. Contour cervical tumor as seen on MRI to create GTV-T
 - Incorporate other clinical & radiographic information as appropriate
3. Contour uninvolved cervix and add this to GTV-T to create CTV-T HR
4. Create CTV-T LR by creating 5 mm anterior & posterior expansions to CTV-T HR (but crop out of bladder & rectum)
 - Add parametria, uterus, upper vagina (ending volume 2 cm inferior to gross tumor) to CTV-T LR
5. Copy CTV-T LR as drawn on full bladder scan to ITV-T and adjust volumes based on empty bladder scan.
 - Goal is for ITV-T LR to include same structures when bladder is full or empty

Strategies to derive the ITV

- Standard margin applied to CTV (A)
- Individualized margin created based on anatomic changes seen on all planning imaging (B & C)



Borders of the parametria

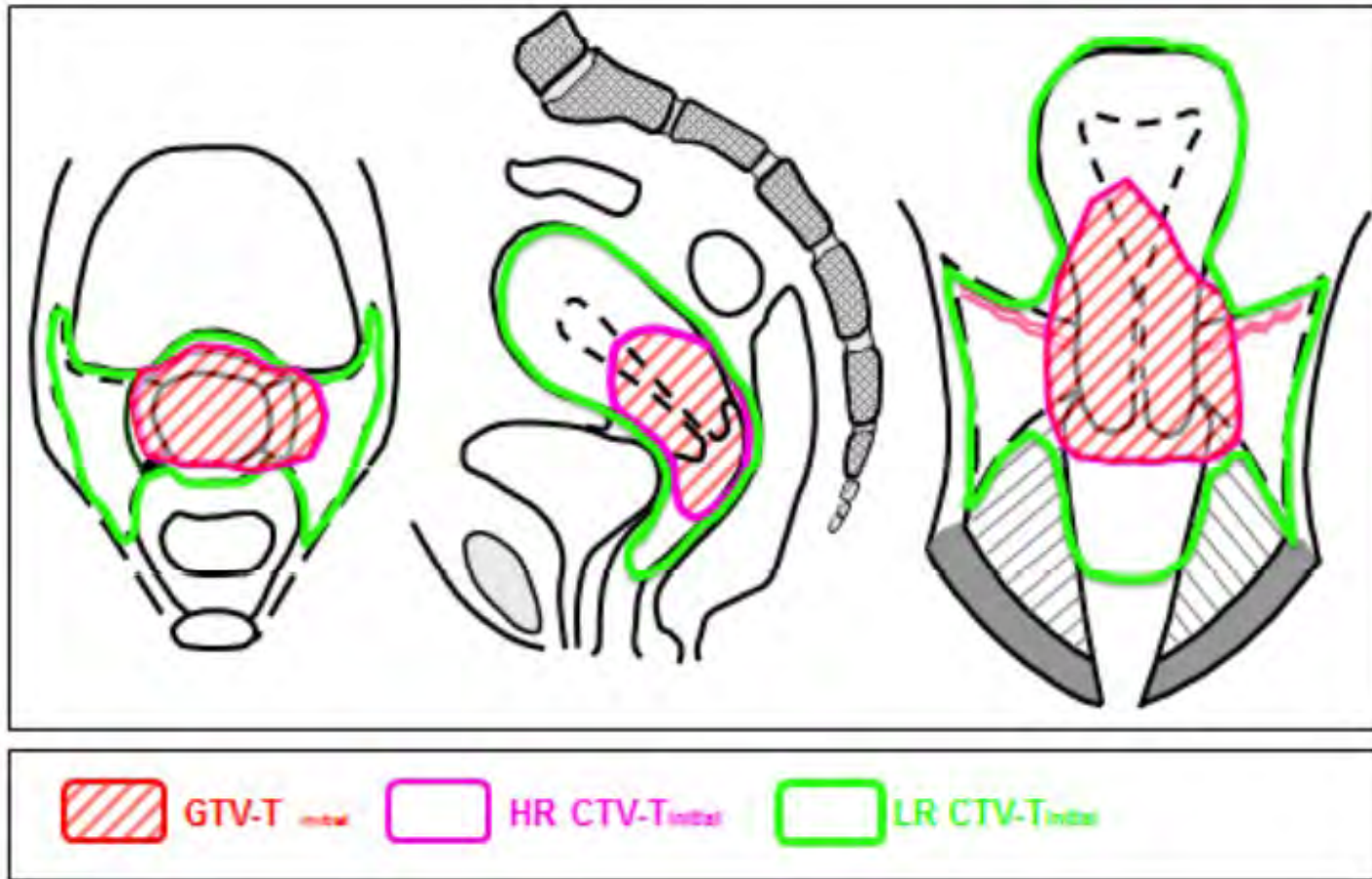


Anteriorly	Posterior wall of bladder or posterior border of external iliac vessel
Posteriorly	Uterosacral ligaments and mesorectal fascia (figure 6)
Laterally	Medial edge of internal iliac and obturator vessels
Superiorly	Top of fallopian tube/ broad ligament/uterine arteries. Depending on degree of uterus flexion, this may also form the anterior boundary of parametrial tissue.
Inferiorly	Urogenital diaphragm

Left: parametria delineated in green
Right: parametria delineated in red

Image credit: EMBRACE II

Sample target volumes per EMBRACE II

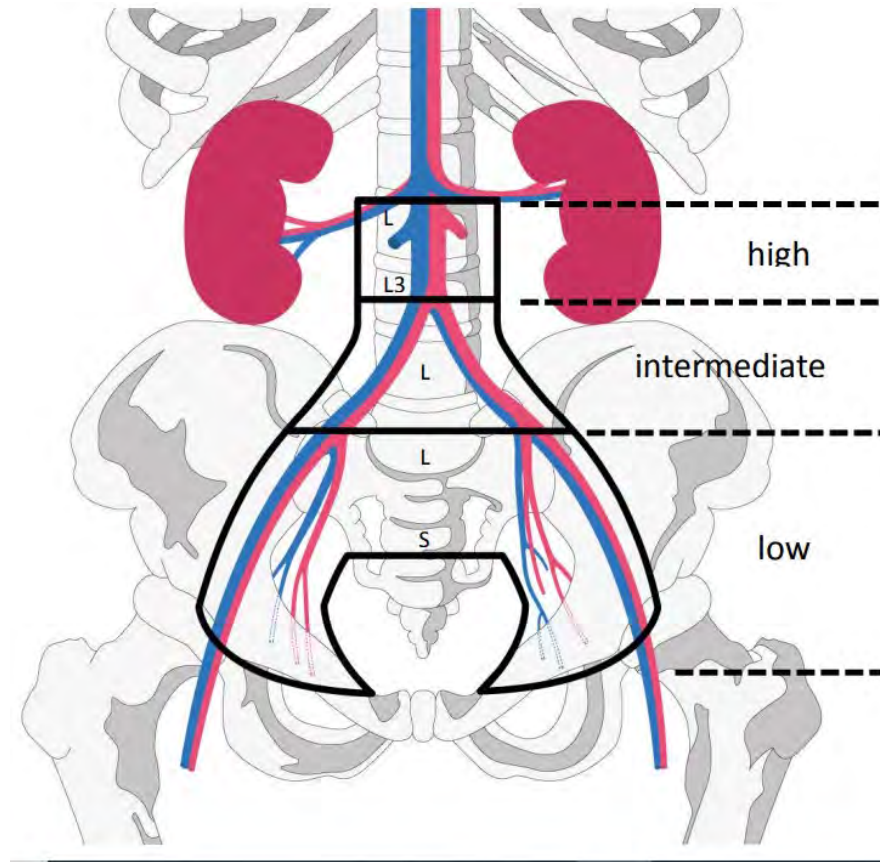


A deep dive on pelvic lymph node volumes per EMBRACE II

Risk Group LN	Definition	EBRT lymph node regions
Low Risk (LR LN)	Tumour size $\leq 4\text{cm}$ AND stage IA/IB1/IIA1 AND N0 AND squamous cell carcinoma AND no uterine invasion	“Small Pelvis” internal iliac external iliac obturator presacral
Intermediate Risk (IR LN)	Not low risk No high risk features ***Our patient fits this category***	“Large Pelvis” Nodes included in “Small Pelvis” and common iliac region (including the aortic bifurcation). In addition: <ul style="list-style-type: none"> • inguinal in case of distal vaginal involvement. • Mesorectal space in case of mesorectal nodes and advanced local disease
High Risk (HR LN)	Based on nodal pathology <ul style="list-style-type: none"> • ≥ 1 pathologic node at common iliac or above • OR ≥ 3 pathologic nodes 	“Large Pelvis + Para-aortic” Nodes included in “Large Pelvis” and para-aortic region with the upper border of CTV minimum at the level of renal veins (usually incl. L2), and at least 3 cm cranial of the highest pathological node in case of para-aortic nodes].

Contouring pelvic lymph nodes

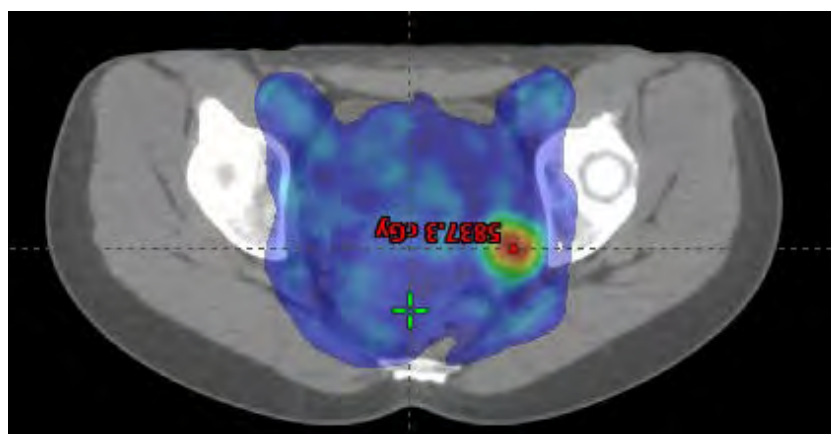
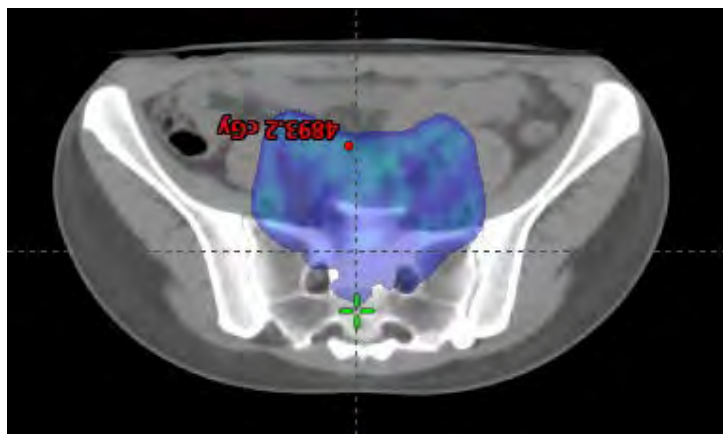
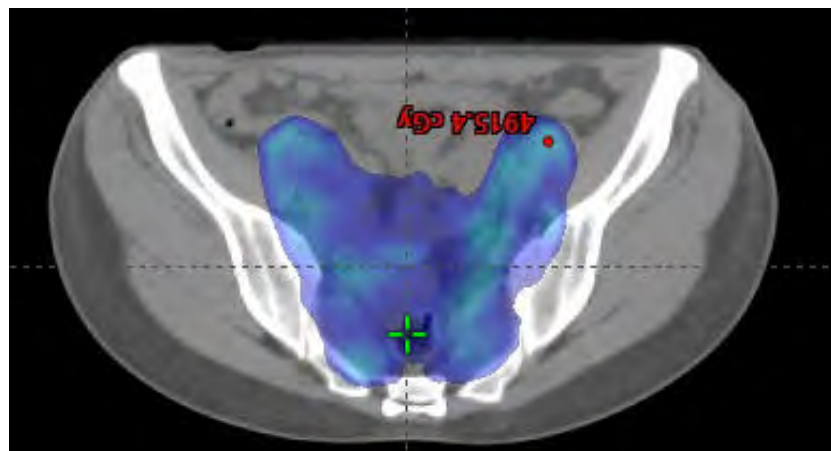
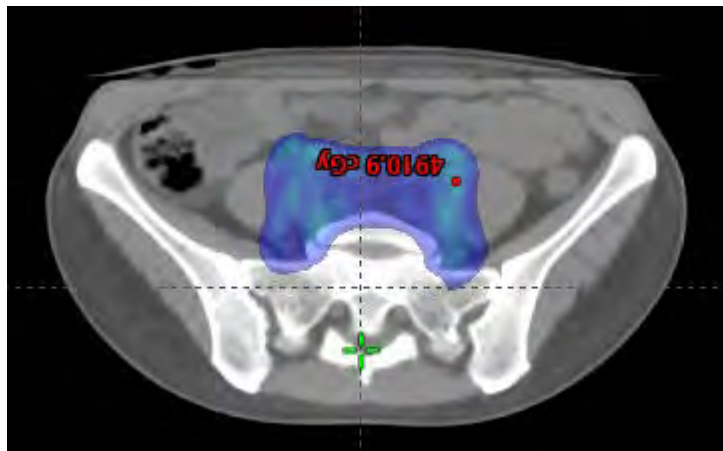
- CTV-E (elective nodal regions): 7 mm margin along the relevant vessels
 - Small pelvis
 - Large pelvis
 - Extended pelvic field
- GTV-N: pathologic nodes, can include margin up to 3 mm to create CTV-N



Planning considerations

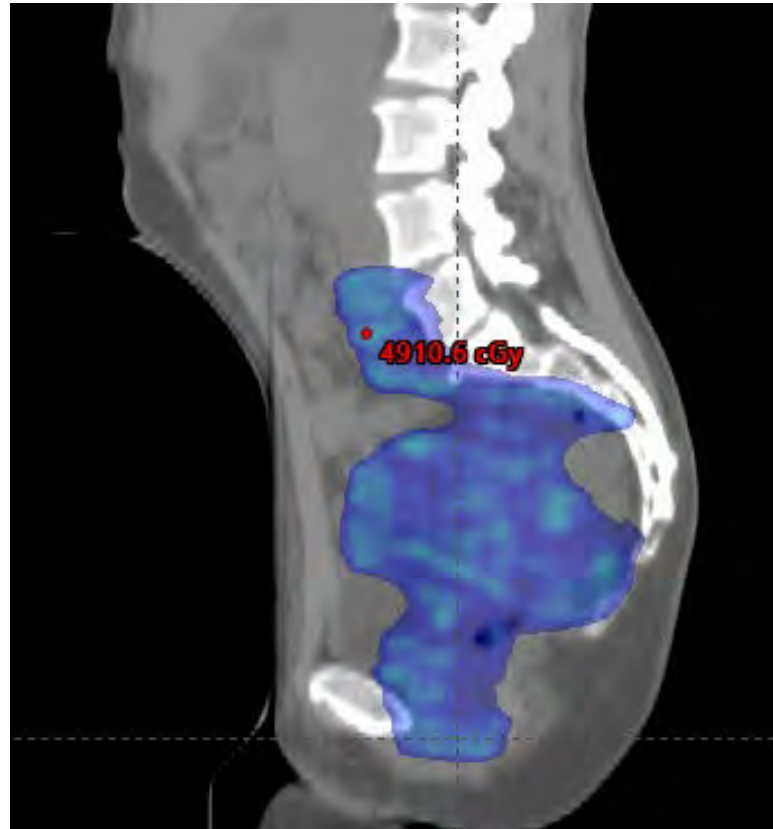
- Dose to pelvis – 45 Gy / 25 fx
 - EMBRACE I showed decreased morbidity with 45 Gy vs 50 Gy
- Dose to involved nodes – SIB 55 – 57.5 Gy
 - True pelvis: 2.2 Gy / fx for total dose of 55 Gy (EQD2 56 Gy)
 - Estimate 3-4 Gy EQD2 contribution from brachy for total EQD2 ~ 60Gy
 - Outside true pelvis: 2.3 Gy / fx for total dose of 57.5 Gy (EQD2 ~59 Gy)

Plan evaluation: EBRT

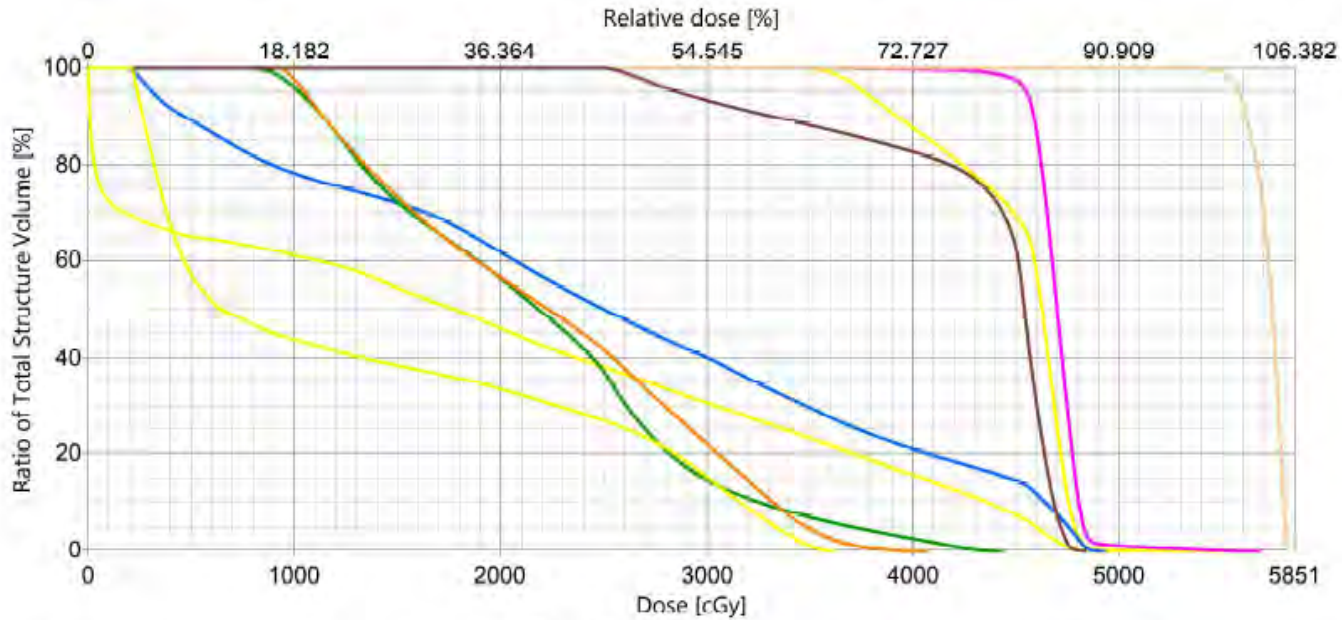


PTV45: CTV-T LR, pelvic nodes, pathologic nodes, 5 mm expansion
Positive nodes boosted to 57.5 Gy

Plan Evaluation: EBRT



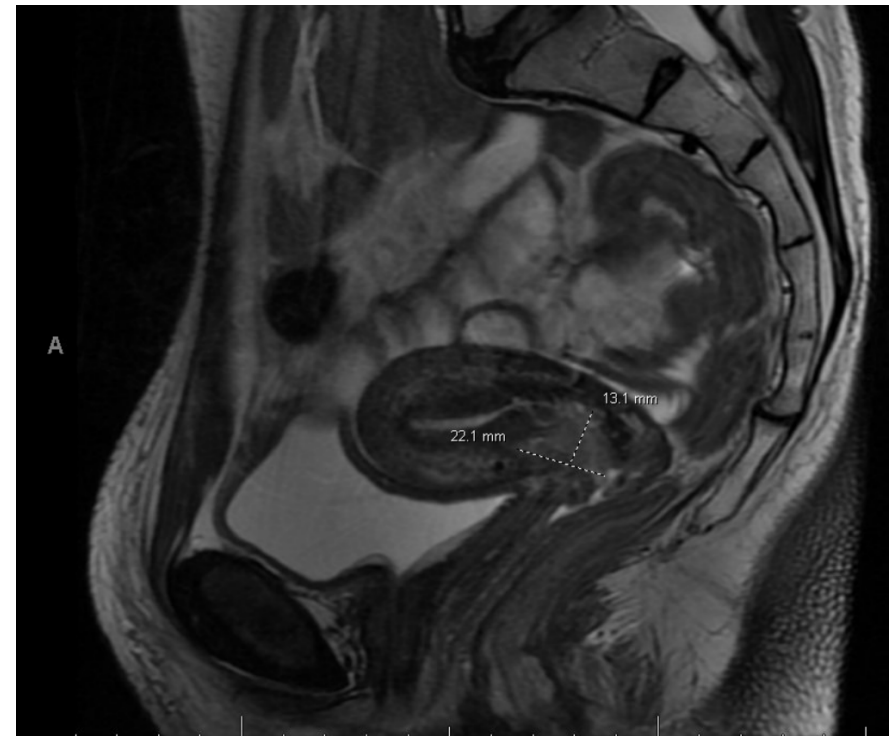
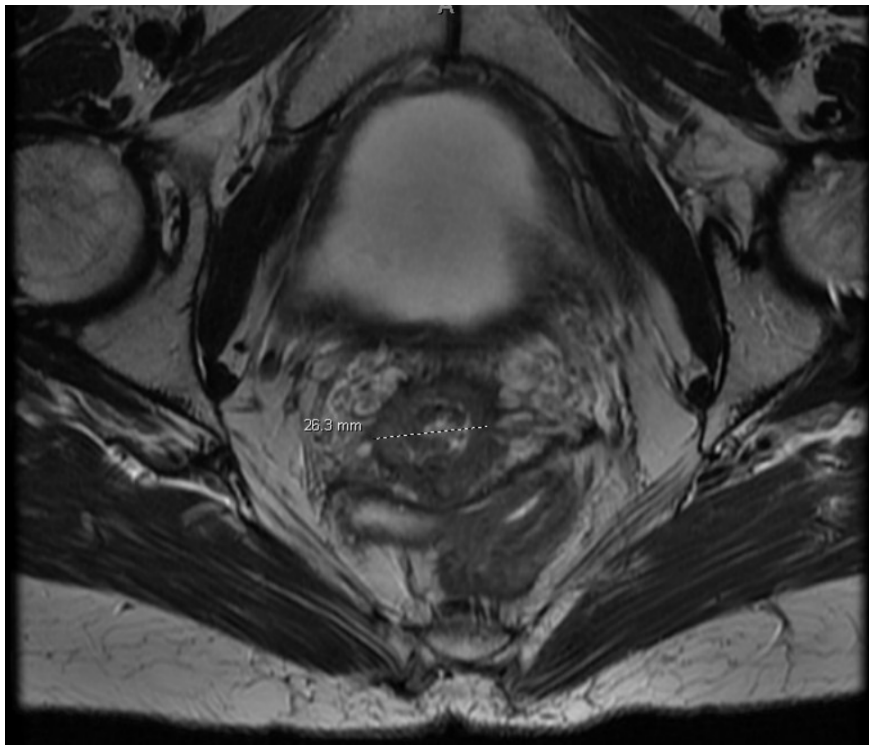
Pelvis - TPS DVH



Structure Color	Pelvis	Coverage	Sampling Coverage (%)	Volume (cc)	Min Dose (cGy)	Max Dose (cGy)	Mean Dose (cGy)
█	Bladder	100.00	100.00	216.43	3394.5	5469.3	4493.0
█	Bones	100.00	99.67	1919.62	0.0	5482.2	1899.1
█	Bowelbag	100.00	100.01	1028.93	174.8	4931.3	2534.7
█	FemoralHead_L	100.00	100.00	69.07	763.2	4437.9	2178.4
█	FemoralHead_R	100.00	100.00	72.58	916.0	4074.9	2225.1
█	plan_45 PLAN	100.00	100.01	1557.53	3002.7	5681.4	4697.4
█	PTV_LN	100.00	100.08	14.78	5396.0	5850.7	5724.0
█	Rectum	100.00	99.99	66.57	2500.7	4840.3	4316.3
█	SpinalCord1	100.00	100.17	13.87	205.5	3618.0	1361.1

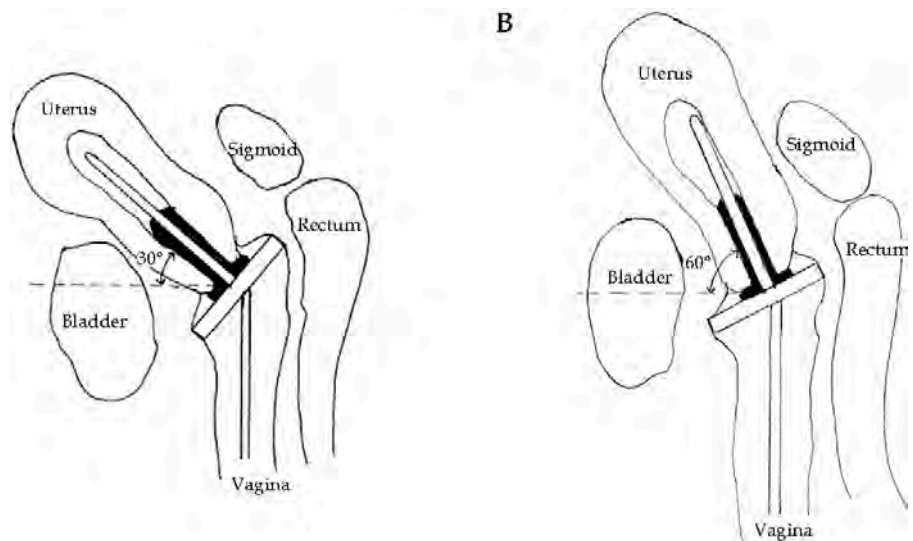
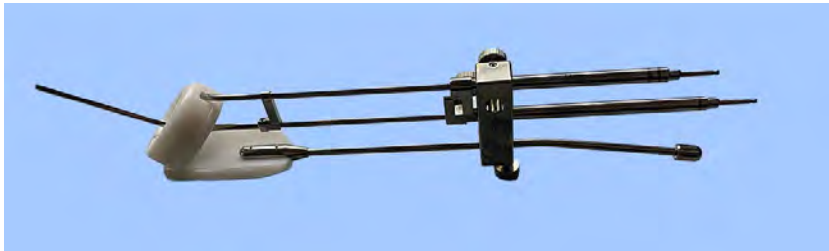
Restaging MRI following EBRT

Decreased size of cervical mass to 2.2 x 1.3 x 2.6 cm from 5 cm in greatest extension



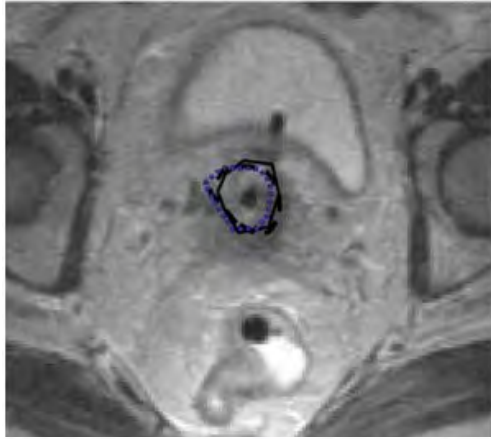
What's next? HDR brachytherapy boost via tandem & ring

- Goal: EQD2 D90 > 90 Gy to tumor
 - 85 Gy is acceptable
- Prescription: 7 Gy x 4 fractions
- HDR isotope: Ir-192

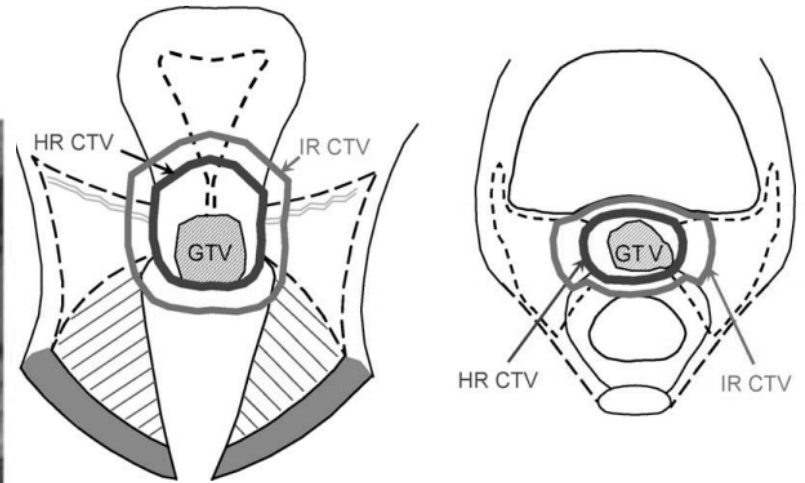
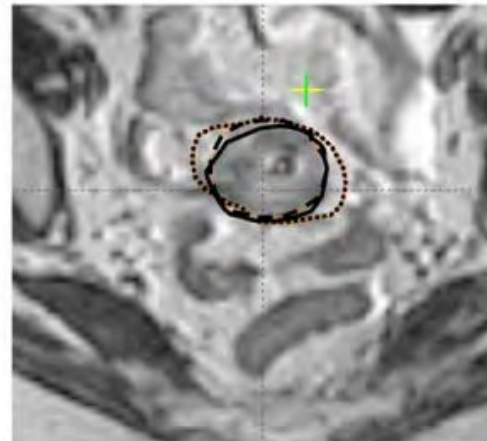
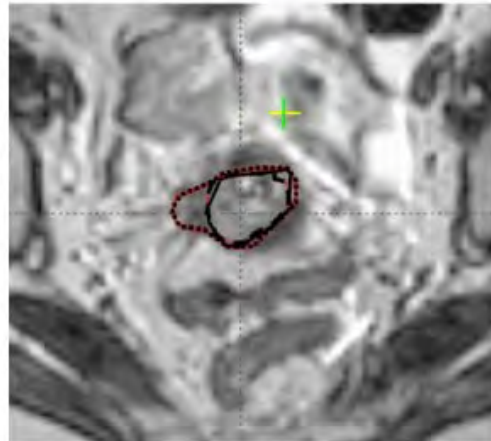
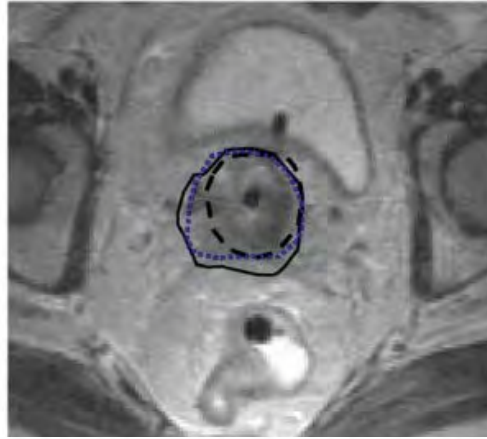


Brachytherapy Contouring

GTV



CTV-HR



GTV: residual tumor at time of brachy, as defined by MRI & exam

CTV HR: GTV + cervix

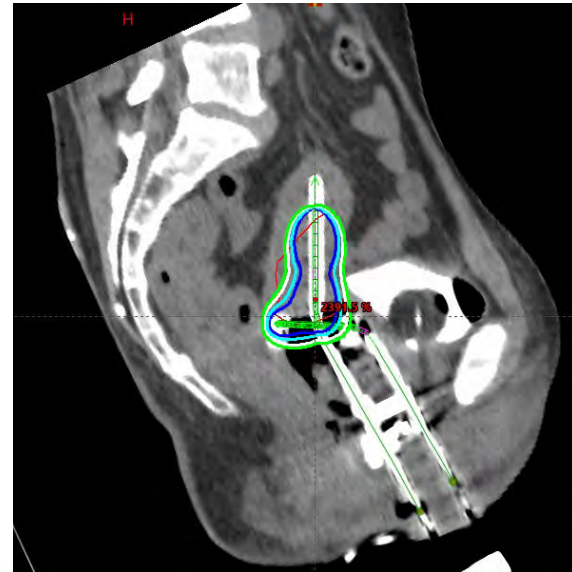
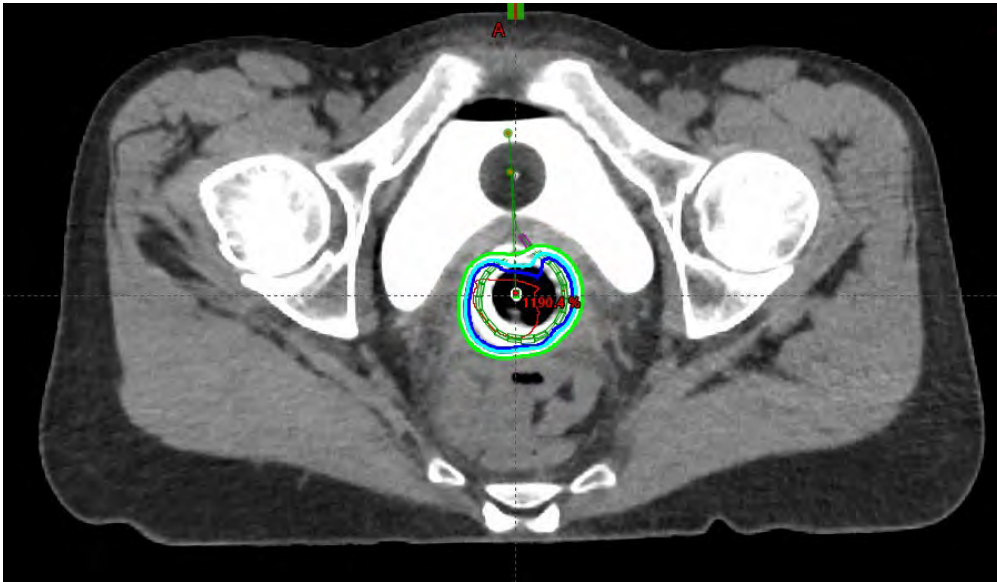
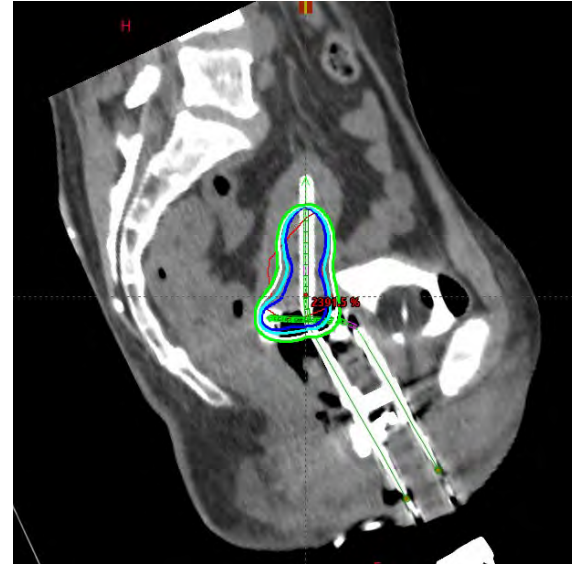
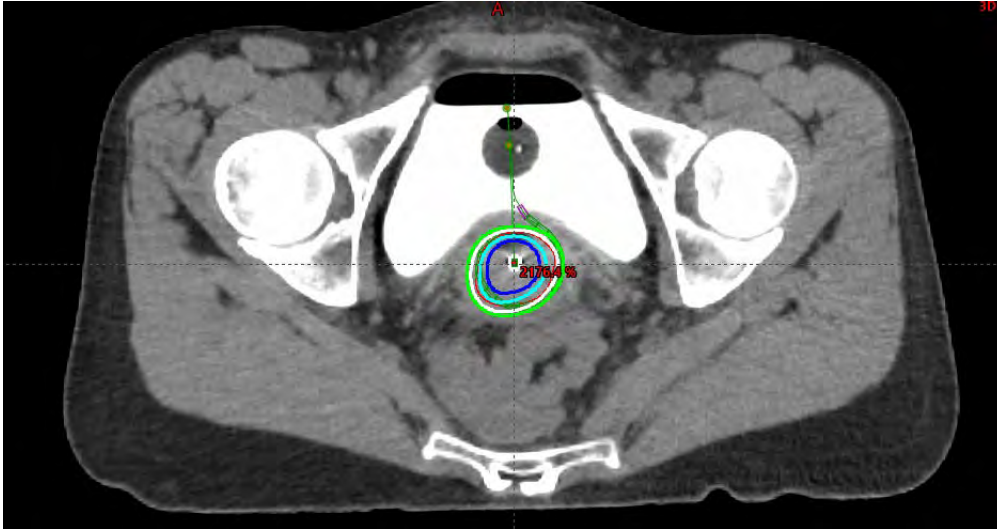
Note, **CTV IR** (intermediate risk CTV) is used in Europe & appears in GEC-ESTRO guidelines. This is defined as the CTV HR + 5– 5 mm margin.

For our patient, planning MRI was obtained after each tandem placement.

Haie-Meder, et al. 2005. *Radiotherapy & Oncol.*

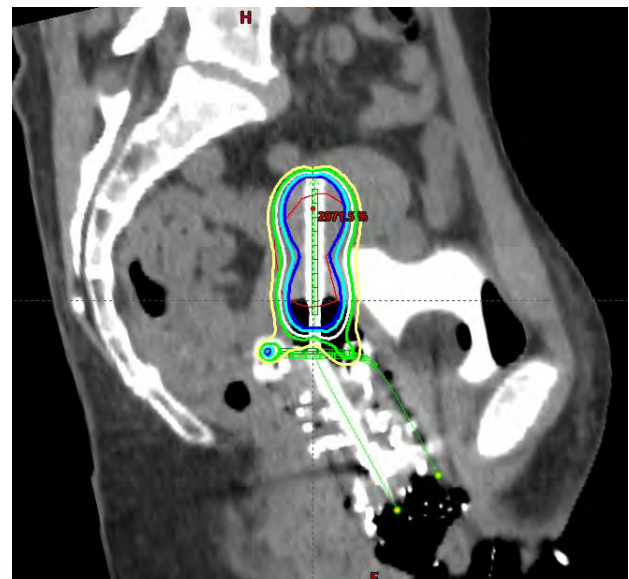
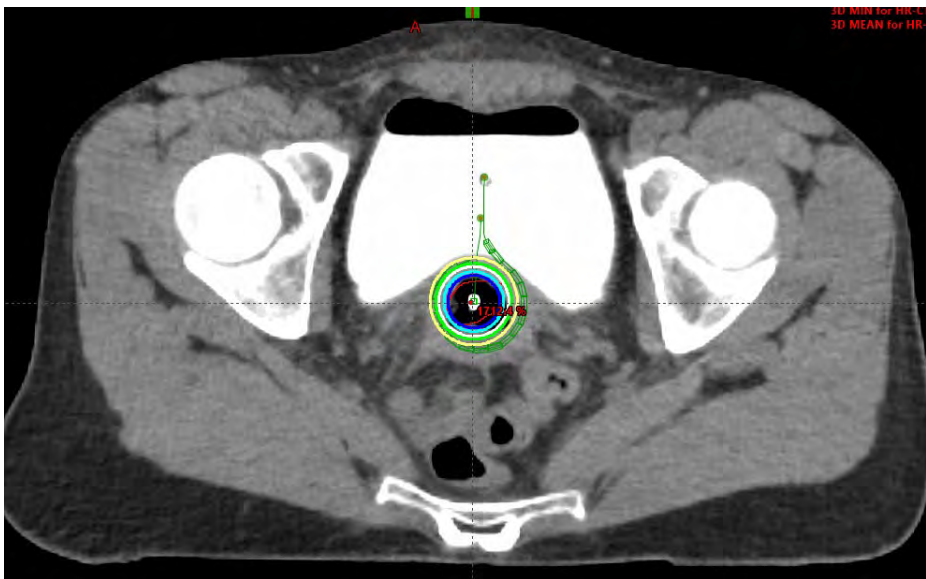
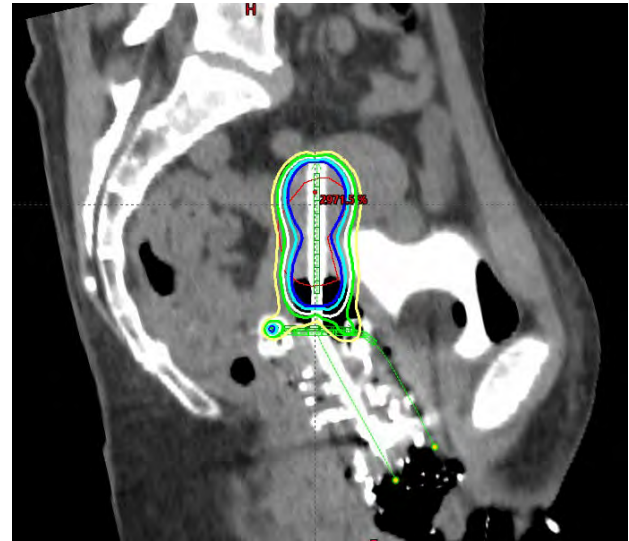
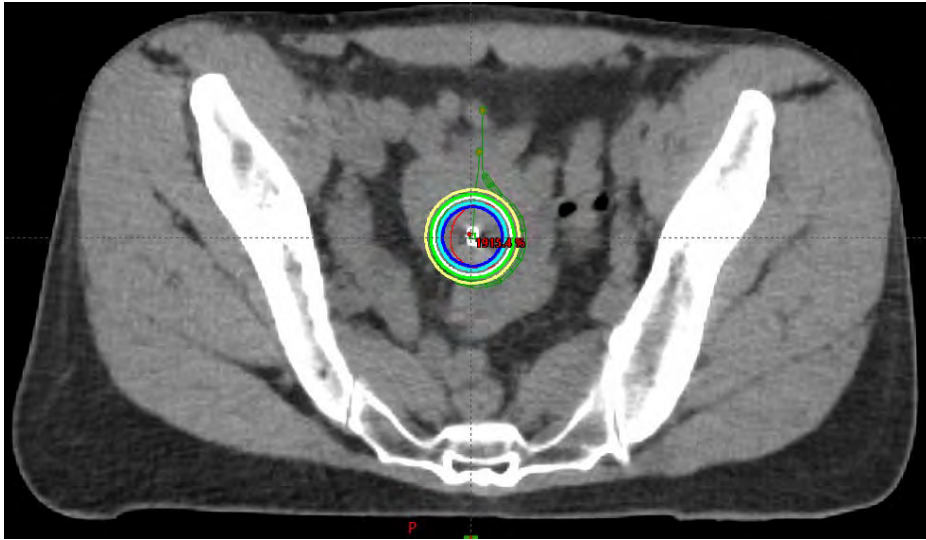
Fractions 1-2

White = 100% isodose line



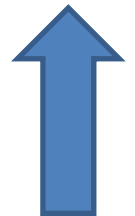
Fractions 3-4

White = 100% isodose line



EQD2 spreadsheet calculating dose across fractions

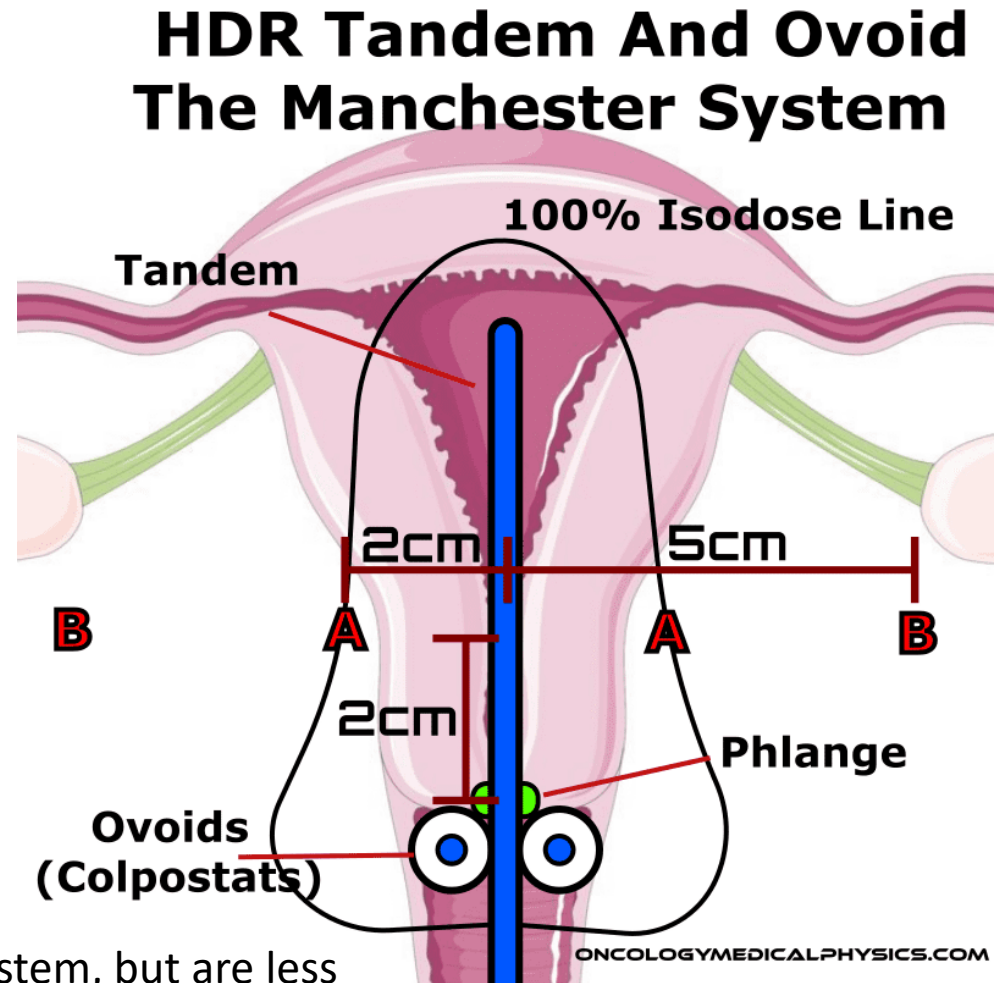
					Brachytherapy total	EBRT + Brachytherapy
Prescribed dose (Gy)	7.0	7.0	7.0	7.0		
Planning aim EQD2 ₁₀	9.9	9.9	9.9	9.9	39.7	83.9
CTV_{HR} [cm³]	19.4	19.4	12.5	12.5	16.0	3.5
D₉₀	7.2	7.2	7.2	6.8		
D ₉₀ EQD2 ₁₀	10.2	10.2	10.3	9.5	40.3	84.5



Dose was just shy of 85 Gy, but there was good coverage of the residual disease

Historical treatment points

- Point A, “point of limiting tolerance”: 2 cm superior to external cervical os & 2 cm lateral to tandem
- Point B: 3 cm lateral of Point A (lateral parametrium / obturator nodes)



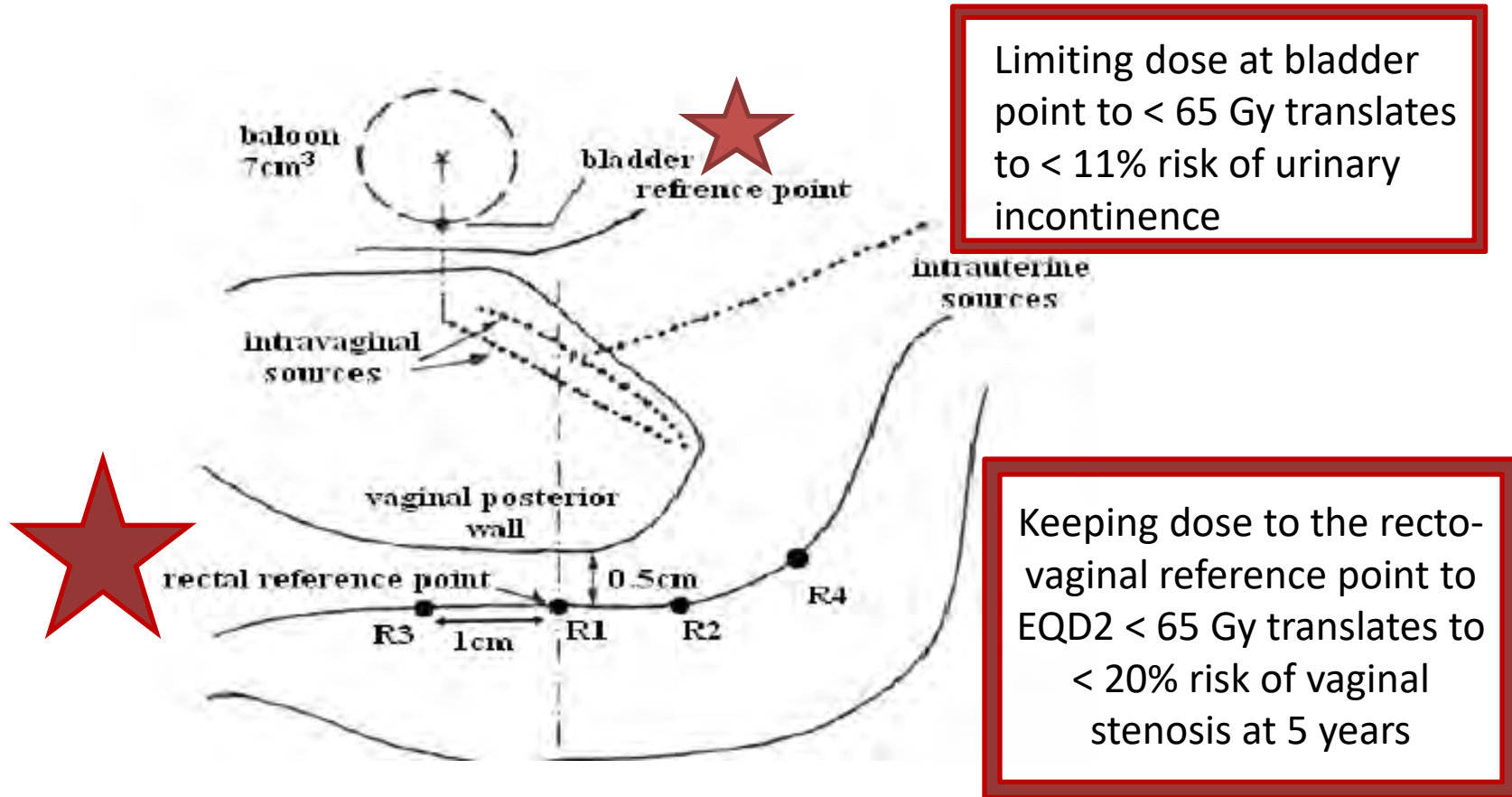
These points are from the Manchester system, but are less relevant in the age of 3D image-guided brachytherapy

Setting limits: OAR dose constraints per EMBRACE II

OAR	Bladder D _{2cm³} EQD ₂₃	Rectum D _{2cm³} EQD ₂₃	Recto-vaginal point EQD ₂₃	Sigmoid D _{2cm³} EQD ₂₃	Bowel D _{2cm³} EQD ₂₃
Planning Aims	< 80 Gy	< 65 Gy	< 65 Gy	< 70 Gy*	< 70 Gy*
Limits for Prescribed Dose	< 90 Gy	< 75 Gy	< 75 Gy	< 75 Gy*	< 75 Gy*

Note – EQD2 includes pelvic EBRT

Historical toxicity points



Recto-vaginal point: 5 mm posterior to vaginal wall at the midpoint of the ring

Bladder point: posterior Foley balloon at widest point, when inflated with 7 cc

Dose to OARs

Brachytherapy Total

BLADDER						
Bladder reference point	1.9	1.9	1.8	1.8		
ICRU EQD _{2,3}	1.8	1.8	1.8	1.8	7.2	59.3
D _{0.1cm³}	7.0	7.0	7.3	5.4		
D _{0.1cm³} EQD _{2,3}	13.8	13.8	15.2	9.2	52.0	104.1
D _{2cm³}	5.0	5.0	5.5	3.6		
D _{2cm³} EQD _{2,3}	8.1	8.1	9.3	4.8	30.2	82.3

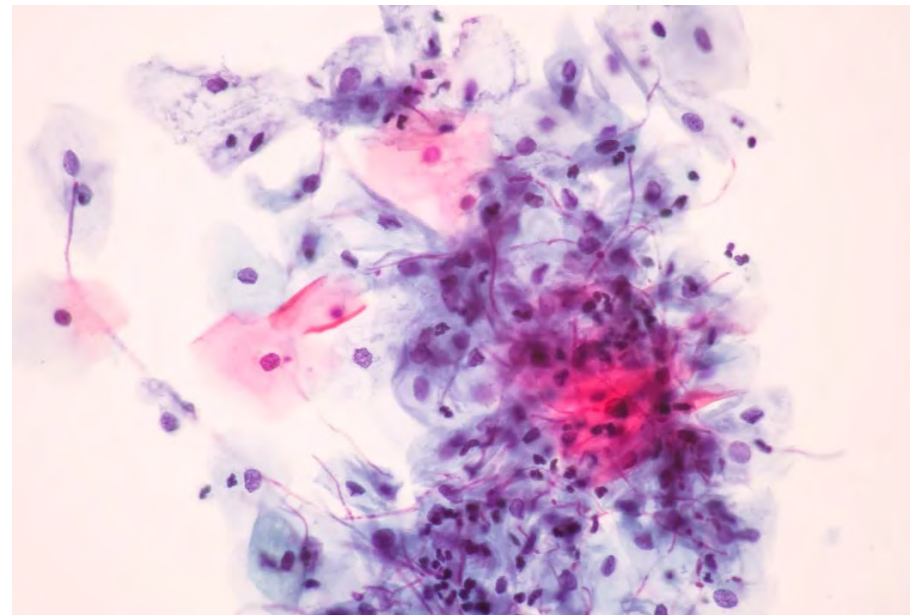
RECTUM						
Recto-vaginal reference point	3.3	3.3	2.1	2.1		
ICRU EQD _{2,3}	4.2	4.2	2.1	2.1	12.7	64.8
D _{0.1cm³}	3.8	3.8	2.5	2.2		
D _{0.1cm³} EQD _{2,3}	5.1	5.1	2.7	2.2	15.1	67.2
D _{2cm³}	2.8	2.8	2.0	1.6		
D _{2cm³} EQD _{2,3}	3.2	3.2	2.0	1.5	10.0	62.1

SIGMOID						
D _{0.1cm³}	5.8	5.8	3.8	3.5		
D _{0.1cm³} EQD _{2,3}	10.1	10.1	5.2	4.6	30.1	82.2
D _{2cm³}	4.0	4.0	2.7	2.7		
D _{2cm³} EQD _{2,3}	5.6	5.6	3.1	3.0	17.4	69.5

BOWEL						
D _{0.1cm³}	4.2	4.2	2.2	4.5		
D _{0.1cm³} EQD _{2,3}	6.0	6.0	2.2	6.8	21.1	73.2
D _{2cm³}	2.9	2.9	1.5	3.5		
D _{2cm³} EQD _{2,3}	3.4	3.4	1.4	4.6	12.8	64.9

What's next after the HDR boost? Cervical cancer surveillance & survivorship

- 1 month post-RT check to assess for resolution of acute effects
- PET and MRI 3 months s/p HDR
- H&P every 3 months for 2 years
- H&P every 6-12 months for 3-5 years
- Annual cytology with pap smears may be considered*



*value of detection of recurrent cervical cancer is limited, and accuracy of results may be affected in those who received pelvic radiation

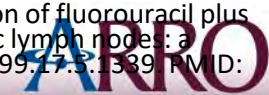
The vaginal dilator: An important component of post-treatment care

- Prevention of vaginal stenosis
- Allows for surveillance via physical exam
- Recommend use 2-3 times per week (3-5 minutes each time) for *at least 2 years*



References

- Chemoradiotherapy for Cervical Cancer Meta-Analysis Collaboration. Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: a systematic review and meta-analysis of individual patient data from 18 randomized trials. *J Clin Oncol*. 2008 Dec 10;26(35):5802-12. doi: 10.1200/JCO.2008.16.4368. Epub 2008 Nov 10. PMID: 19001332; PMCID: PMC2645100.
- Eifel PJ, Winter K, Morris M, Levenback C, Grigsby PW, Cooper J, Rotman M, Gershenson D, Mutch DG. Pelvic irradiation with concurrent chemotherapy versus pelvic and para-aortic irradiation for high-risk cervical cancer: an update of radiation therapy oncology group trial (RTOG) 90-01. *J Clin Oncol*. 2004 Mar 1;22(5):872-80. doi: 10.1200/JCO.2004.07.197. PMID: 14990643.
- Gunderson and Tepper, 8th ed.
- Haie-Meder C, Pötter R, Van Limbergen E, Briot E, De Brabandere M, Dimopoulos J, Dumas I, Hellebust TP, Kirisits C, Lang S, Muschitz S, Nevinson J, Nulens A, Petrow P, Wachter-Gerstner N; Gynaecological (GYN) GEC-ESTRO Working Group. Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. *Radiother Oncol*. 2005 Mar;74(3):235-45. doi: 10.1016/j.radonc.2004.12.015. PMID: 15763303.
- Keys HM, Bundy BN, Stehman FB, Muderspach LI, Chafe WE, Suggs CL 3rd, Walker JL, Gersell D. Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. *N Engl J Med*. 1999 Apr 15;340(15):1154-61. doi: 10.1056/NEJM199904153401503. Erratum in: *N Engl J Med* 1999 Aug 26;341(9):708. PMID: 10202166.
- Landoni F, Colombo A, Milani R, Placa F, Zanagnolo V, Mangioni C. Randomized study between radical surgery and radiotherapy for the treatment of stage IB-IIA cervical cancer: 20-year update. *J Gynecol Oncol*. 2017 May;28(3):e34. doi: 10.3802/jgo.2017.28.e34. Epub 2017 Feb 24. PMID: 28382797; PMCID: PMC5391393.
- Landoni F, Maneo A, Colombo A, Placa F, Milani R, Perego P, Favini G, Ferri L, Mangioni C. Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer. *Lancet*. 1997 Aug 23;350(9077):535-40. doi: 10.1016/S0140-6736(97)02250-2. PMID: 9284774.
- Lorusso D, Xiang Y, Hasegawa K, Scambia G, Leiva M, Ramos-Elias P, Acevedo A, Sukhin V, Cloven N, Pereira de Santana Gomes AJ, Contreras Mejía F, Reiss A, Ayhan A, Lee JY, Saevets V, Zagouri F, Gilbert L, Sehoul J, Tharavichitkul E, Lindemann K, Lazzari R, Chang CL, Lampé R, Zhu H, Oaknin A, Christiaens M, Polterauer S, Usami T, Li K, Yamada K, Toker S, Keefe SM, Pignata S, Duska LR; ENGOT-cx11/GOG-3047/KEYNOTE-A18 investigators. Pembrolizumab or placebo with chemoradiotherapy followed by pembrolizumab or placebo for newly diagnosed, high-risk, locally advanced cervical cancer (ENGOT-cx11/GOG-3047/KEYNOTE-A18): a randomised, double-blind, phase 3 clinical trial. *Lancet*. 2024 Apr 6;403(10434):1341-1350. doi: 10.1016/S0140-6736(24)00317-9. Epub 2024 Mar 20. PMID: 38521086.
- NCCN Guidelines Version 1.2025. Cervical cancer.
- Peters WA 3rd, Liu PY, Barrett RJ 2nd, Stock RJ, Monk BJ, Berek JS, Souhami L, Grigsby P, Gordon W Jr, Alberts DS. 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. *J Clin Oncol*. 2000 Apr;18(8):1606-13. doi: 10.1200/JCO.2000.18.8.1606. PMID: 10764420.
- Pötter R, Tanderup K, Kirisits C, de Leeuw A, Kirchheiner K, Nout R, Tan LT, Haie-Meder C, Mahantshetty U, Segedin B, Hoskin P, Bruheim K, Rai B, Huang F, Van Limbergen E, Schmid M, Nesvacil N, Sturdza A, Fokdal L, Jensen NBK, Georg D, Assenholt M, Seppenwoolde Y, Nomden C, Fortin I, Chopra S, van der Heide U, Rumpold T, Lindegaard JC, Jürgenliemk-Schulz I; EMBRACE Collaborative Group. The EMBRACE II study: The outcome and prospect of two decades of evolution within the GEC-ESTRO GYN working group and the EMBRACE studies. *Clin Transl Radiat Oncol*. 2018 Jan 11;9:48-60. doi: 10.1016/j.ctro.2018.01.001. PMID: 29594251; PMCID: PMC5862686.
- Rose PG, Ali S, Watkins E, Thigpen JT, Deppe G, Clarke-Pearson DL, Insalaco S; Gynecologic Oncology Group. Long-term follow-up of a randomized trial comparing concurrent single agent cisplatin, cisplatin-based combination chemotherapy, or hydroxyurea during pelvic irradiation for locally advanced cervical cancer: a Gynecologic Oncology Group Study. *J Clin Oncol*. 2007 Jul 1;25(19):2804-10. doi: 10.1200/JCO.2006.09.4532. Epub 2007 May 14. PMID: 17502627.
- Whitney CW, Sause W, Bundy BN, Malfetano JH, Hannigan EV, Fowler WC Jr, Clarke-Pearson DL, Liao SY. Randomized comparison of fluorouracil plus cisplatin versus hydroxyurea as an adjunct to radiation therapy in stage IIB-IVA carcinoma of the cervix with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology Group study. *J Clin Oncol*. 1999 May 17;17(5):1339-48. doi: 10.1200/JCO.1999.17.5.1339. PMID: 10334517.



Please provide feedback regarding
this case or other ARROcases to
arrocase@gmail.com