Radiotherapy for Endometrial Cancer

Dr. Satyajit Pradhan

Dept. Of Radiotherapy & Radiation Medicine

Institute of Medical Sciences

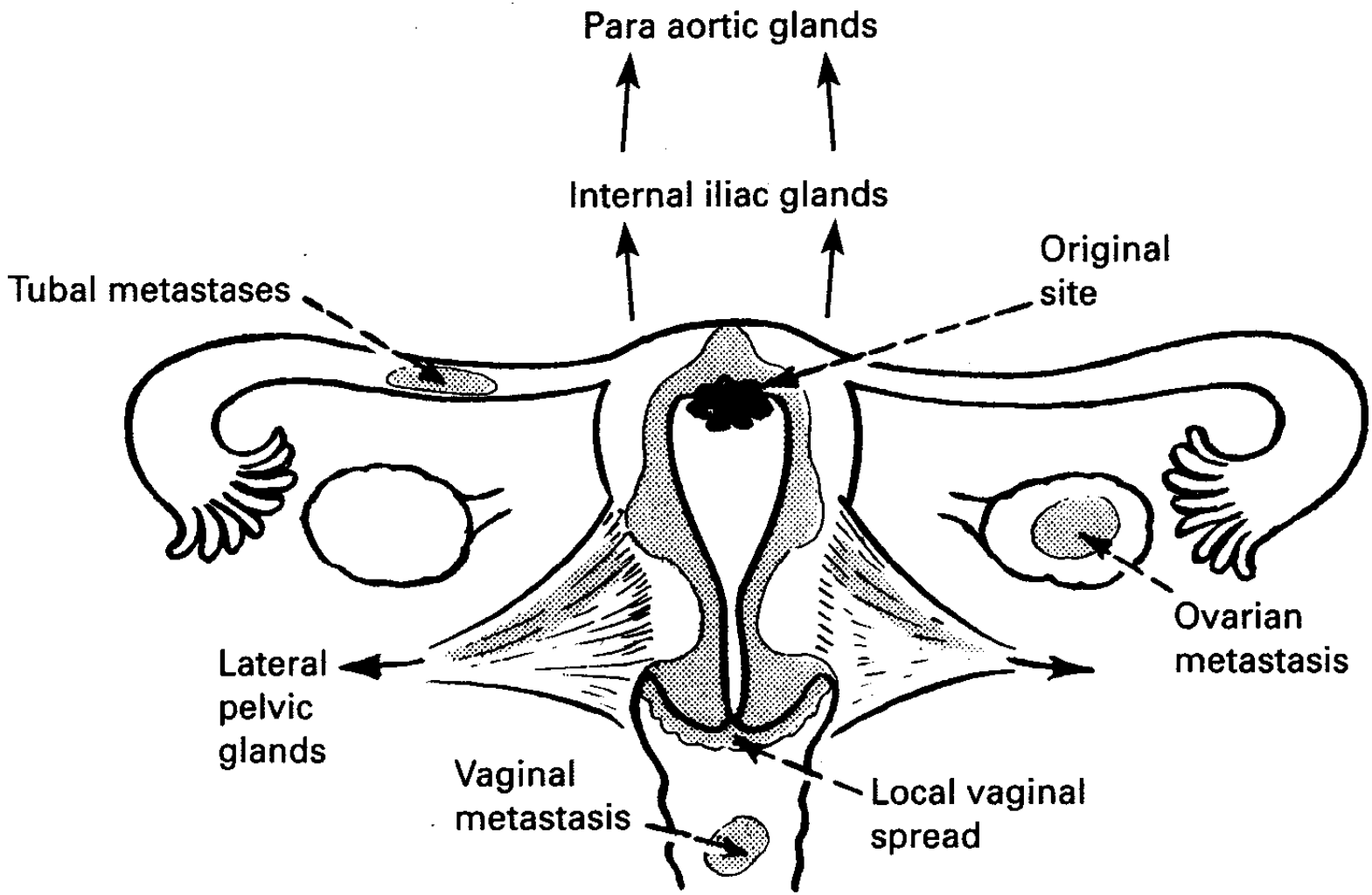
Banaras Hindu University

Varanasi-221 005

EPIDEMIOLOGY

GLOBOCAN 2012 data:

- Second most common gynaecological malignancy in developed countries
- 6th most common cancer amongst females-estimated 319600 new cases
- 5% of all cancers in women & 2% of total cancer cases
- Incidence rates highest in Northern America and lowest in South Central Asia
- Incidence rates low in India
- Peak incidence 60-70 years
- Median age 61-63
- 75-80% diagnosed in an early stage



Most metastases occur in adjacent structures and peritoneum. In advanced cases distant metastases do occur, most commonly in lung, but occasionally in liver, vertebrae or other bones and in supraclavicular lymph nodes.

HISTOLOGY

- **Carcinoma (94%)**
  - Endometrioid (75-80%)
  - Adenosquamous (4%)
  - Papillary Serous (3%)
  - Clear Cell (<4%)
  - Mucinous (9%)
  - Secretory(<2%)
- **Sarcoma (6%)**
  - Carcinosarcoma (60%)
  - Leiomyosarcoma (30%)
  - Endometrial Stromal Sarcoma (10%)
  - Adenosarcoma (<1%)

HISTOLOGICAL GRADE	DEFINITION
G1- WELL DIFFERENTIATED	5% or less tumour in solid sheets. Overall risk of pelvic & paraaortic lymph node mets 3% & 1.5%
G2- MODERATELY DIFFERENTIATED	6-50% tumour in solid sheets. Pelvic & paraaortic nodes 10%
G3- POORLY DIFFERENTIATED	>50% tumour in solid sheets. Pelvic & paraaortic lymph node involvement 30% & 20%

CLINICAL FEATURES

More than 90% of patients with Endometrial Cancer report having symptoms of

- Postmenapausal bleeding
- Menorrhagia
- Foul smelling vaginal discharge

Advanced Cases

- Constipation
- Lower extremity lymphoedema
- Abdominal distension - ascites due to peritoneal mets
- Cough hemoptysis - lung mets
- Jaundice - liver mets

DIAGNOSTIC WORKUP

Gold Standard - Endometrial Tissue Sampling

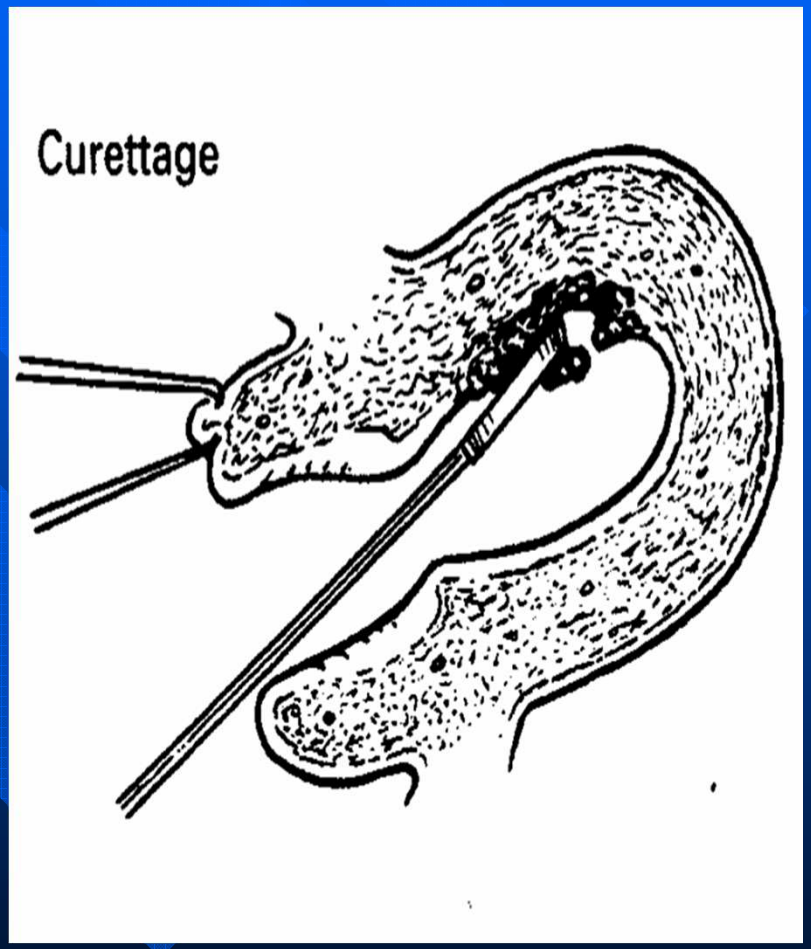
- Biopsy
- Dilatation and Curettage
- Trans Vaginal Ultrasound
- CT scan
- MRI
- PET Scan
- CA 125

EVALUATION AND STAGING WORKUP

- Routine Blood & Urine tests
- Chest X- ray
  - rule out metastasis
  - evaluate cardiopulmonary status
- IVP
- Barium Enema (patients with advanced disease)
- Cystoscopy,
- Proctosigmoidoscopy

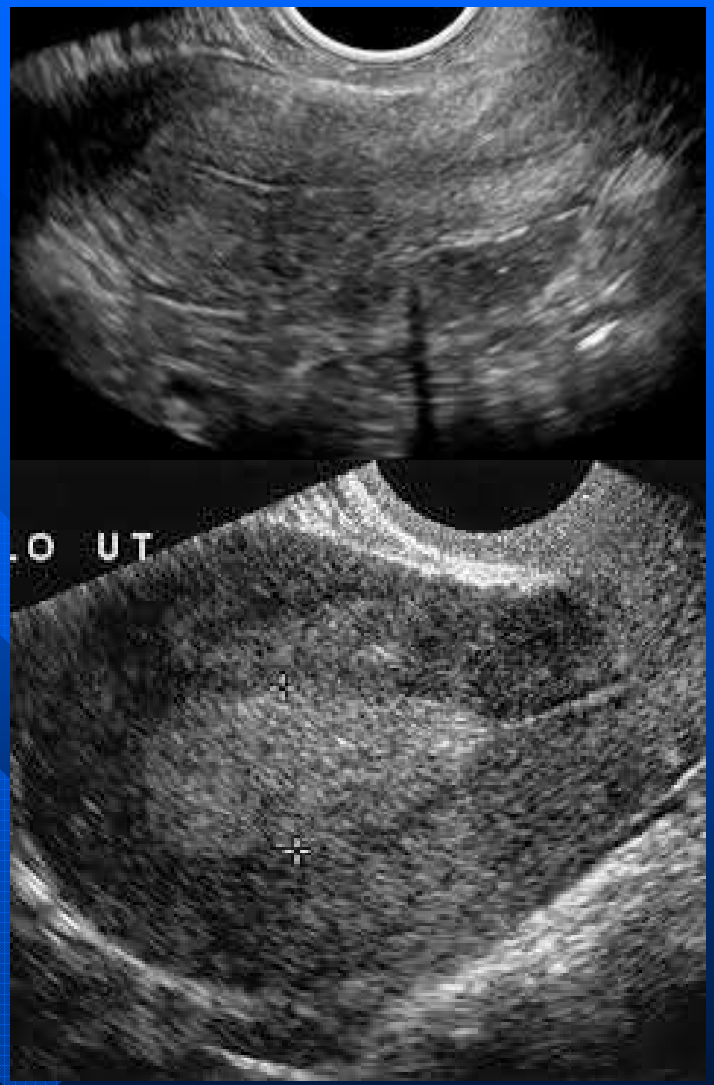
Endoemtrial Biopsy, D&C

- OPD basis
- Endometrial biopsy / Aspiration Curettage with Endocervical sampling
- Fractional D&C - if Endometrial biopsy or Aspiration curettage is negative



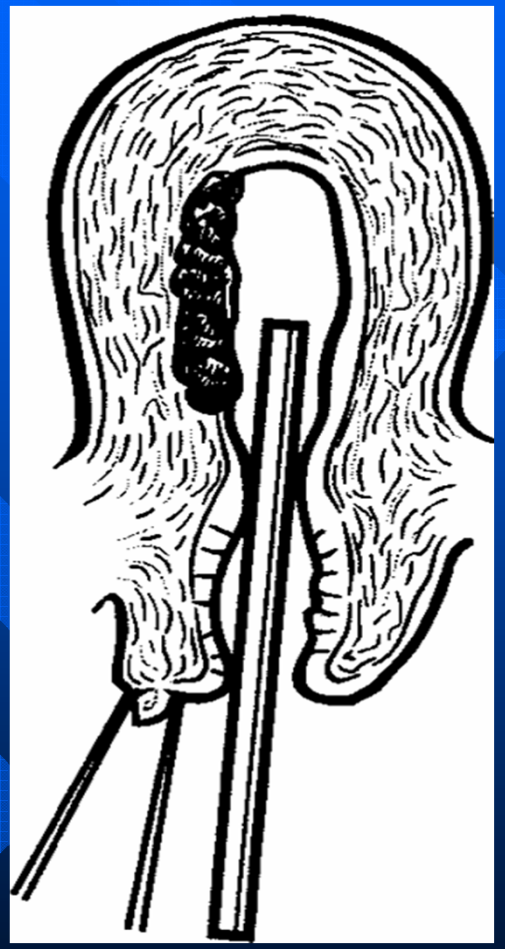
TV US

- Transvaginal ultrasound- superior to conventional USG
- Useful in determining depth of myometrial invasion (60-76%)
- Overall accuracy in determining invasion – 79%
- Endometrial thickness of more than 5mm is considered to be abnormal.



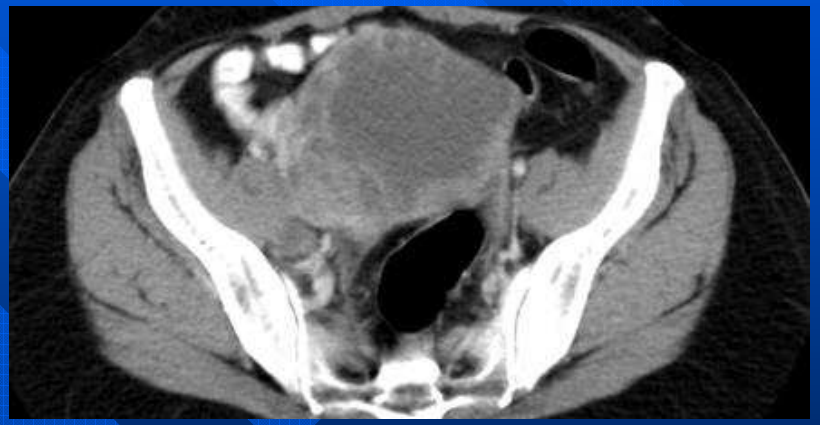
Hysteroscopy

- Considered when TVU is abnormal but biopsy inconclusive or non-diagnostic
- Sensitivity reported - 60-95% compared to D&C obtained at same time
- Specificity 50-99%
- Should be used sparingly - may contribute to extrauterine spread of disease

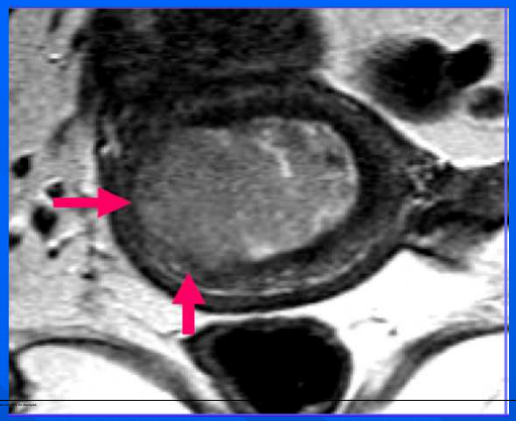


CECT

- Endometrial Ca – may show diffuse thickening or hypodense mass relative to normal myometrium
- Cervical involvement seen as >3.5cm enlargement with low attenuation areas in stroma
- Parametrial extension – loss of periureteral fat
- Sidewall extension - <3mm intervening fat between soft tissue mass & pelvic side wall
- Overall accuracy of 76% in detecting myometrial invasion



MRI



Recommended as part of preop evaluation of Endometrial ca.

- Better than CT in determining myometrial invasion- considered as most accurate
- Used in monitoring Endometrial status in those on tamoxifen

STAGING

- Clinical staging used before 1988 - on basis of fractional biopsy specimen & EUA
- Surgical staging initiated on small scale in 1973
- Surgical Staging System approved at 1988 FIGO
- Revised Surgical Staging system 2009 FIGO

CLINICAL STAGING

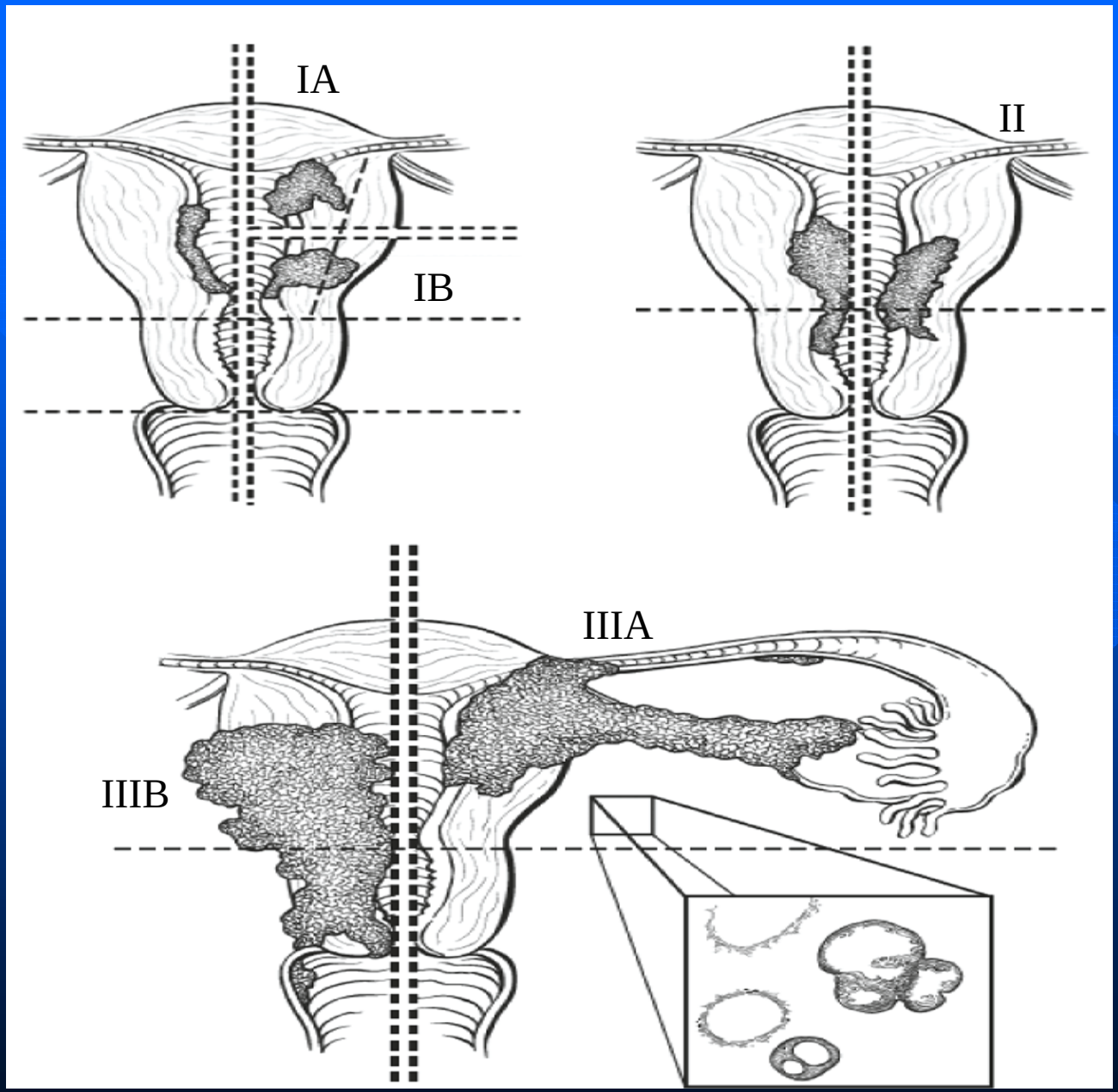
Before 1988 - **Clinical Staging**

- Stage I - tumor limited to uterus
  - IA if length was ≤8 cm
  - IB if length was >8 cm
- Stage II when cervix was involved
- Stage III when disease extension beyond uterus/cervix was limited to the true pelvis
- Stage IV
  - IVA when extension beyond true pelvis or involvement of bladder or rectum
  - IVB when distant spread

This system applicable to few patients who cannot have surgery & are treated with definitive radiation

Endoemetrial Cancer Surgical Staging System: FIGO 1998	
Stage I	Tumour limited to Uterus
IA Grades 1-3	Limited to endometrium
IB Grades 1-3	Invasion to <50% of myometrium
IC Grades 1-3	Invasion to ≥50% of myometrium
Stage II	Extension to Cervix but not beyond Uterus
IIA Grades 1-3	Endocervical glandular involvement only
IIB Grades 1-3	Cervical stromal invasion
Stage III	Extension outside uterus/cervix with/without regional metas.
IIIA Grades 1-3	Invades serosa or adnexum or +ve peritoneal cytology
IIIB Grades 1-3	Vaginal metastasis
IIIC Grades 1-3	Metastases to pelvic and/or periaortic LN
Stage IV	
IVA Grades 1-3	Invasion of bladder and/or bowel mucosa
IVB	Distant metastases including Intra-abdominal and/or inguinal LN

Revised Endoemetrial Cancer Surgical Staging System: FIGO 2009	
Stage I	
IA Grades 1-3	Tumor limited to endometrium or invasion <50% myometrium (includes endocervical glandular involvement)
IB Grades 1-3	Invasion to ≥50% myometrium (includes endocervical glandular involvement)
Stage II	
II Grades 1-3	Cervical stromal invasion
Stage III	
IIIA Grades 1-3	Tumor invades uterine serosa and/or adnexae
IIIB Grades 1-3	Vaginal and/or parametrial involvement
IIIC1 Grades 1-3	Metastases to pelvic LN.
IIIC2 Grades 1-3	Para-aortic and/or pelvic LN involvement.
Stage IV	
IVA Grades 1-3	Invasion of bladder, bowel mucosa or both
IVB	Distant metastases including Intra-abdominal spread or inguinal LN


IA
IB
II
IIIA
IIIB

PROGNOSTIC FACTORS

- **Age**- older age worse outcome. Age ≥60 years predictive of local-regional recurrence
- **Race**- White women fare better. Incidence of high-risk tumors more in African American
- **Histologic Subtype**- FIGO Ann. Report-5-year survival rate higher for Endometrioid adenoca. compared to serous & clear-cell cancer
- **Grade**- Grade directly affects depth of myometrial penetration & frequency of LN involvement
- **Myometrial Involvement**- Regardless of grade-1% of tumors limited to endometrium have LN involvement; 25% pelvic and 17% para-aortic involvement with deep penetration
- **LVI positive tumors-** 4 fold, increase in pelvic LN metastases, & 6 fold, increase in PAN metastases. More frequent relapses, & poorer outcome

PROGNOSTIC FACTORS

- **LUS involvement** - GOG study-doubling of incidence of pelvic nodal involvement - 8% to 16% & increase in PAN involvement from 4% to 14% when tumour from / involved isthmus
- **Cervical Stromal Involvement**
- **Peritoneal Cytology** - literature on true impact of +ve peritoneal cytology is mixed. Association of malignant cytology with other adverse prognostic factors
- **Adnexal /Serosal involvement** - Associated with greater pelvic/ para aortic LN involvement
- **Pelvic & Para-Aortic Lymph Node Involvement** -major predictor of outcome
- **Molecular Prognostic Factors**
  - ❖ Overexp. of p53 & HER-2 -advanced stage & poorer outcome
  - ❖ PTEN mut;- early stage, nonmetastatic dis. favourable surv.

SURGICAL MANAGEMENT

Surgery the main treatment for Endometrial Ca

- Simple hysterectomy
- Bilateral salpingo-oophorectomy (BSO)
- Inspection of the pelvic & abdominal cavities
  - Biopsy of any suspicious extrauterine lesions
  - Peritoneal washings in most cases
- Surgical assessment of lymph nodes ranges
  - Palpation
  - Biopsy of suspicious nodes
  - Pelvic & para-aortic lymphadenectomy

ROLE OF RADIATION THERAPY

Radiation therapy - significant role in management of Endometrial Ca

- Radiation Therapy:
  - Adjuvant T/t after surgery
  - Definitive T/t- medically inoperable/ local recurrence
- Past: most treated with Preop ICBT ±EBRT followed by hyst. Merit in patients with gross cervical involvement
- Nowadays: undergo surgery first-depending on prognostic features from pathology review RT need determined.
- Recent years- data from prospective RCT addressing management issues in Endometrial Ca.
- Unlike Cervical Ca. data in Endometrial Ca. less conclusive

Role of RT in Stages I and II

- Treatment options in early-stage Endometrial Ca. after hysterectomy:
  - Observation
  - Intravaginal RT
  - Pelvic RT
- **IVRT** preferred approach at MSKCC- best Therapeutic Ratio
- **Observation**
  - Best morbidity profile
  - Increased risk of local recurrence
  - Not the best Therapeutic Ratio
- **Pelvic RT**:
  - Recurrence reduction- very effective
  - Morbidity profile higher than IVRT

Radiation Therapy Recommendations for Early Stage Disease Based on Risk Factors

- Trial results in early-stage Endometrial Ca - Pelvic RT an excessive treatment for most patients
- Treatment recommendations-individualized based on risk factors
- Observation, IVRT or Pelvic RT- risk of vaginal & pelvic recurrence to be assessed
- Vaginal recurrence- data from randomized trials- adjuvant IVRT alone sufficient to control potential microscopic disease
- PORTEC-2- IVRT as good as pelvic RT in controlling vaginal recurrence (0.9% vs. 1.9%, ; p = .97) -patients in this trial at high risk for vaginal recurrence

Radiation Therapy Recommendations for Early Stage Disease Based on Risk Factors

- Swedish randomized trial - IVRT alone sufficient for vaginal control
- How best to reduce pelvic recurrence-more controversial.
- For patients at **low risk of pelvic lymph node involvement:** Endometrioid Gr-1 or 2 with no or minimal myometrial invasion-neither lymphadenectomy nor pelvic RT likely to be of significant benefit
- Those with **higher risk of LN involvement:** need to have LN surgically assessed /receive pelvic RT to control potential microscopic disease
- Two PORTEC trials and Swedish trial- risk of pelvic recurrence only 2% to 6% even in absence of lymphadenectomy

No Myometrial Invasion, Grades 1 and 2

- Risk of vaginal recurrence almost negligible.
- PO pelvic or intravaginal RT unlikely to add to final outcome,
- **RT not routinely recommended to this group of patients**

No Myometrial Invasion, Grade 3

- Risk of LN metastasis not very high.
- Offered either IVRT alone or observation at MSKCC

Less Than 50% Myometrial Invasion, Grades 1 and 2

- Most common stage subgroup of all endometrial cancers
- PORTEC I, MSKCC, Sorbe et al., Straughn et al, Horowitz et al.- low rate of vaginal and pelvic recurrence - RT of limited use
- Either observation or IVRT a reasonable option
- Two important issues to address:
  - Older patients higher rates of vaginal /pelvic relapse
  - LVI - higher chance of vaginal recurrence
- MSKCC-patients ≥60 years old or have LVI - recommended to have IV RT

Less than 50% Myometrial Invasion, Grade 3

- Horowitz et al. and Fanning- no vaginal or pelvic recurrence in patients with <50% myometrial invasion Gr 3 treated with hysterectomy and lymphadenectomy + IVRT
- MSKCC- IV RT irrespective of lymphadenectomy

≥50% Myometrial Invasion, Grades 1 and 2

- POTEC-I-Risk of vaginal recurrence with surgery alone-not minimal in this group
  - 10% for those with grade 1 and 13% for Gr 2
  - 5-year vaginal recurrence rates for patients treated with pelvic RT were 1% and 2% for Gr1 and Gr2
  - Vaginal Control- Pelvic RT not superior to IVRT
- PORTEC-2 & Swedish Trial-Omission of Pelvic RT increased pelvic recurrence risk

≥50% Myometrial Invasion, Grades 3

- Very few recommend surgery alone for these patients
- GOG 99 trial: factors associated with an increased recurrence rate (25% at 5 years)
  - (a) Increasing age
  - (b) Moderate to poorly differentiated tumor grade
  - (c) Presence of LVI
  - (d) Outer 1/3 myometrial invasion

  Subgroup of patients with high intermediate risk (HIR) defined:
  - (a) at least 70 years age with only 1 of other risk factors
  - (b) at least 50 years of age with any 2 of other risk factors
  - (c) any age with all 3 of other risk factors
- At MSKCC- patients with HIR risk as per GOG 99, offered PO pelvic RT even with negative lymphadenectomy

  If not HIR, then IVRT considered, only in setting of adequate lymphadenectomy- minimum of 10 nodes

Cervical Involvement

- Distinction between gross & occult cervical involvement
- **Gross involvement:**
  - Increases risk of parametrial extension & spread to pelvic lymph nodes - similar to primary cervical cancer
  - Undergo radical hysterectomy and pelvic lymph node dissection **or**
  - PreOP RT including pelvic RT and ICBT followed by simple hysterectomy
- **Occult cervical involvement:**
  - Simple hysterectomy ±lymphadenectomy & adjuvant RT most often pelvic RT & IVRT
  - Pitson et al - 68% 5-year DFS, pelvic relapse was 5.8%

Cervical Involvement

- Emerging data on role of IVRT alone in some patients with occult cervical involvement who also had surgical lymph node staging. In these series, patients treated with IVRT alone were highly selected
- **Endocervical glandular involvement:** no longer considered stage II
  - PORTEC-2 patients randomized to pelvic RT or IVRT
  - MSKCC patients - IVRT alone, especially if no other adverse features / if they had lymphadenectomy
- **Cervical stromal invasion:**
  - Gr 1 & 2 & depth <50%-IVRT if adequate lymphadenectomy
  - Gr 3 & deep stromal invasion-pelvic RT irrespective of lymphadenectomy

Treatment Recommendations at MSKCC for Stage I & II Patients with Endometrioid Cancer

Extent/Grade	1	2	3
No MI invasion	Observation	Observation	IVRT or Observation[a]
<50% invasion	IVRT or Observation[a]	IVRT or Observation[a]	IVRT
>50% invasion	IVRT	IVRT	IVRT or IMRT[b]
Endocervical Gland	IVRT	IVRT	IVRT or IMRT[b]
CSI <50%	IVRT	IVRT	IVRT or IMRT[b]
CSI >50%	IMRT	IMRT	IMRT

[a]Observation offered in patients <60 years old and without lymph node invasion
[b]IMRT if High to Intermediate Risk

Role of RT in Stage III

- **Isolated adnexal involvement** treated with pelvic RT- outcome reasonably good
- If **pelvic node involvement** (IIIC) only major risk factor, T/t with PO pelvic RT- 60%-72% long-term survival rate
- Stage IIIC disease, by virtue of **para-aortic node inv.**- particularly high-risk group- After surgery generally treated with extended-field RT to encompass pelvis & para-aortic regions
- Whether safe to omit RT after adequate surgical LN staging in patients with stage IIIC EC -addressed in study from Mayo Clinic- need for PO RT even after adequate surgical staging
- Many patients with stage III disease fail in abdomen- investigators have evaluated whole-abdomen irradiation (WAI) in these patients-GOG study

Systemic Therapy Recommendations Based on Risk Factors

Isolated Positive Peritoneal Cytology

- Generally recommend IVRT and Megace

Early-Stage Serous and Clear-Cell Cancer

- Tend to spread in fashion similar to ovarian cancer- high propensity for upper abdominal relapse
- Important to perform comprehensive surgical staging
- Patients with surgically staged early disease- IVRT with concurrent Carboplatin/Paclitaxel

Early-Stage High-Risk Endometrioid Adenocarcinoma

- Adjuvant CT in addition to RT

Systemic Therapy Recommendations Based on Risk Factors

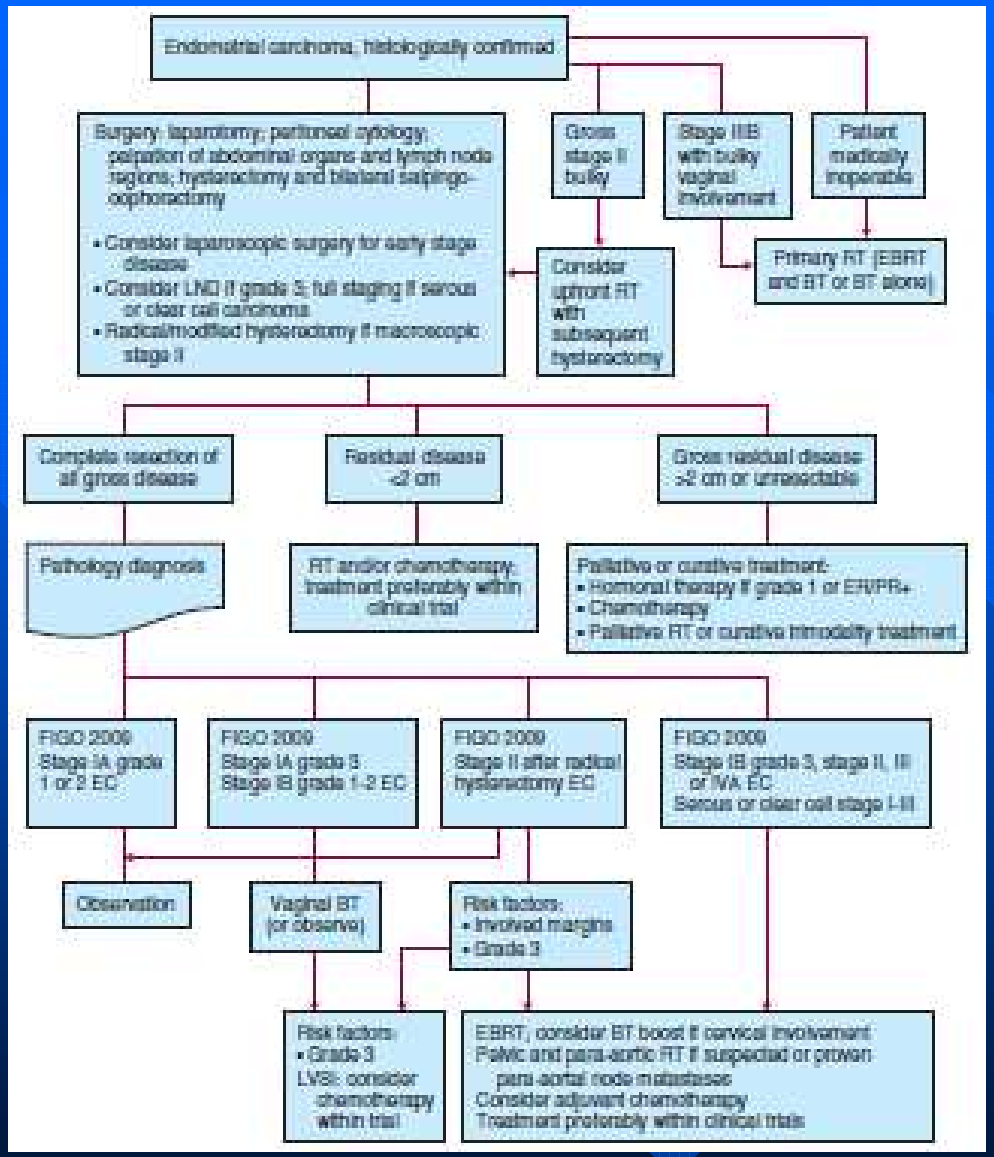
Stage IIIA

- Results of PO EBRT in isolated adnexal/serosal involvement generally good

  Distant relapse-26% to 33% - need for adj. systemic therapy
- At MSKCC,concurrent CTRT followed by Carboplatin/Taxol similarly to the RTOG 9708T

Stage IIIC

- Outcome of patients with isolated LN involvement (especially pelvic nodes), treated with PO pelvic RT - relatively good
- At MSKCC- recommend CTRT followed by Carboplatin/ Paclitaxel to try reduce risk of recurrence further
- When extranodal involvement (i.e. +ve washing, adnexa/ serosal, and vaginal/parametrial involvement) in this subset- CT alone might be better



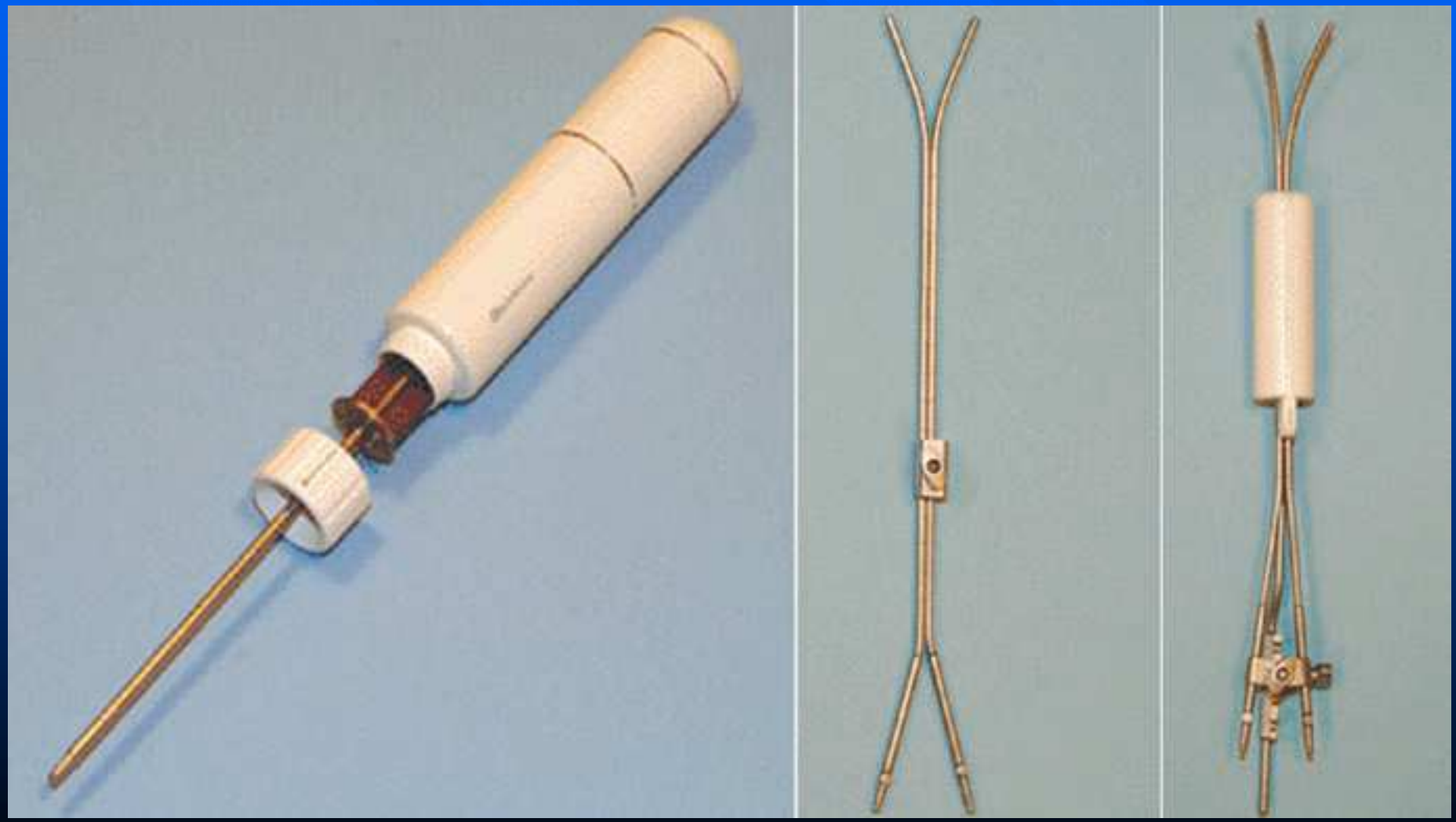
Treatment algorithm for patients with endometrial carcinoma

RADIATION THERAPY TECHNIQUES

Intravaginal Radiation

- Purpose - deliver highest dose of radiation to vaginal mucosa, limit dose to the surrounding normal structures
- HDR brachytherapy using ^{192}Ir sources - preferred method of delivering IVRT
- Applicator used generally a cylinder
- Treatment on an outpatient basis without need for anesthesia
- At MSKCC - treatment 4 to 6 weeks PO depending on vaginal cuff healing
- Longer for vaginal cuff to heal after LAVH/BSO and robotic hysterectomy than after TAH/BSO
- 3 fractions of 7 Gy - total dose of 21 Gy
- Interval between each fraction - 1 to 2 weeks

Vaginal Cylinder and Y Applicator for Endometrial Brachytherapy Applications



Intravaginal Radiation

- **Dose prescription:** 0.5-cm depth from the mucosal surface
- Delivered usually using 3-cm-diameter cylinder- treat 4 to 7 cm of vagina - depending on depth of invasion & Tumor Gr.
- Grade 3, serous or clear-cell carcinoma- length of vagina treated generally 7 cm (average length of vagina after simple hysterectomy about 10 cm).
- Grade 1 or 2 Endometrioid Adenoca. - treated vaginal length
  - 4 cm if myometrial invasion <50%
  - 5 cm for >50% myometrial invasion
  - 6 cm for cervical involvement

Intravaginal Radiation

- Dose per fraction lowered to 6 Gy instead of 7 Gy if diameter of cylinder <3 cm. Done to avoid very high dose of radiation to vaginal mucosa
- The dose per fraction is also lowered to 4 to 5 Gy when pelvic radiation added
- IVRT with LDR ^{137}Cs sources-

  60 Gy to vaginal mucosa **or**

  30 to 35 Gy to 0.5-cm depth from vaginal mucosa

External Beam Radiation

Pelvic Radiation

Conventional Pelvic RT

- **Simulation:**
  - Small bowel opacified using oral contrast
  - Vaginal marker used to define the vaginal cuff
  - Rectum opacified with barium or CT-compatible contrasts
  - Usually prone position- displace small intestines from field
- **Target volume:**
  - Pelvic lymph nodes, & proximal 2/3 vagina
  - Presacral nodes not included unless gross cervical involvement
- High-energy LINAC (15 MV) - sparing of skin and sc. tissue

External Beam Radiation

Pelvic Radiation

Conventional Pelvic RT

- **Beam arrangement:** ideal is 4-field pelvic-box - reduce dose to small intestines & to some extent bladder and rectum
- **AP/PA fields:**
  - Superior border is L5-S1
  - Inferior border is bottom of obturator foramina
  - Lateral border - 2 cm beyond widest point of inlet of true bony pelvis
- **Lateral fields:**
  - Anterior border- in front of pubis symphysis
  - Posterior border at least at S2-3
  - Superior & Inferior borders-same as for AP/PA fields

External Beam Radiation

Pelvic Radiation

Conventional Pelvic RT

- **Dose:**
  - All fields treated daily to dose of 1.8 Gy
  - Total dose of 50.4 Gy when pelvic radiation is used alone
  - 45 Gy when combined with IVBT

External Beam Radiation

Pelvic Radiation

Intensity-Modulated RT

- MSKCC-PO IMRT used for most patients with endometrial cancer who need pelvic RT
- Simulation:
  - Supine position
  - Immobilized using Aquaplast
  - Oral & rectal contrasts for better visualize small & large intestines
  - Contrast in vaginal cuff to better visualize upper vagina

External Beam Radiation

Pelvic Radiation

Intensity-Modulated RT

- **Volumes:**
  - Pelvic LN poorly visualized by CT when normal-defined by encompassing the contrast-enhanced blood vessels
  - Modified 7 mm margin around contrast-enhanced vessels -a good surrogate target for pelvic LN (Taylor *et al*.)
  - Nodal CTV- modified 7mm margin (excluding bowel & muscles) recommended around iliac vessels
  - Nodal PTV- An additional expansion of 7 mm all around nodal CTV generally recommended
  - Vaginal PTV- outlining contrast enhanced vaginal cuff & adding a 3-cm margin-account for impact of bladder & rectal filling, as well as vaginal motion

External Beam Radiation

Extended Field Radiation

- Patients with documented +ve PAN
- CT simulation crucial- for accurate delineation of kidneys, small bowel & liver in addition to nodal target
- Nodal Target: Pelvic, pericaval, interaortocaval nodes & PAN defined by contrast-enhanced blood vessels
- Preferred approach - four-field box technique over AP/PA- to lower dose to the small intestines. Attention to dose to kidneys from four-field arrangement
- **Borders:**
  - Lower border- as in pelvic radiation
  - Upper border - extended usually to T12-L1 interspace
- **Dose:** 45.0 Gy at 1.8 Gy or 1.5 Gy if acute GI toxicity
- MSKCC- IMRT preferred choice for extended-field RT

External Beam Radiation

Whole-Abdomen Radiation

- **Target:**
  - Whole peritoneal cavity
  - Adequate coverage of diaphragm
  - Adequate margin during all phases of normal respiration
  - Minimal to no liver shielding
- **Fields:**
  - AP/PA open fields standard approach
  - Five HVL kidney blocks placed on PA field only (if patient lying supine) from start of treatment
- **Border:**
  - Upper border -usually 1 cm above the diaphragm
  - Lateral borders- beyond peritoneal reflections
  - Lower border- usually at bottom of obturator foramen

External Beam Radiation

Whole-Abdomen Radiation

- **Dose:**
  - Usually 30.0 Gy at 1.5 Gy/#
  - 19.8-Gy boost to pelvis at 1.8 Gy/#
  - Cone down boost:

    Paraaortic region generally to total dose of 45 Gy

    Pelvis to 50 Gy
- IMRT higher & more uniform doses delivered with potentially less toxicity

COMPLICATIONS OF RADIATION TREATMENT

Pelvic Radiation

- PORTEC-1 randomized trial:
  - Overall Grades 1 to 4 late complications

    26% in RT group *vs* 4% in observation group ($p < .0001$)

    Grades 1 & 2 - 22%

    Grades 3 & 4 - 3%

    AP/PA fields & 4 field box; 30% vs 21% ($p = .06$)
  - QoL (Noute *et a*l.):

    Pelvic RT significant ($p < .01$) & clinically relevant higher rates of urinary incontinence, diarrhea, and fecal leakage- more limitations in daily activities

    Increased symptoms reflected by frequent use of incontinence materials after pelvic RT (day & night use, 42.9% *vs*. 15.2% for surgery alone; $p< .001$)

COMPLICATIONS OF RADIATION TREATMENT

Pelvic Radiation

- Chronic Lymphoedema- GOG 99 - lymphadenectomy- randomized to surgery alone compared to PO RT: 2.5% *Vs* 5%
- Sacral insufficiency fractures (SIFs) - potential complication of pelvic RT in gynaecologic cancers
- Morbidity rate of conventional pelvic RT could be reduced by using IMRT:
  - Mundt et al. - significant reduction in acute & chronic GI toxicity - IMRT *Vs* conventional radiation
  - MSKCC - IMRT associated with less bowel obstruction (BO) than conventional RT

COMPLICATIONS OF RADIATION TREATMENT

Whole-Abdomen Radiation

- Toxicity of WAR more pronounced than that of pelvic radiation- not as high as expected.
- GOG study 122

  RT arm- GI toxicity- not >2% for Grade 4

  not >11% for Grade 3

  Liver toxicity- 1% Grade 4

  Cardiac toxicity- 4% Grade 4 in CT arm

COMPLICATIONS OF RADIATION TREATMENT

Intravaginal RT

- IVRT limits dose to normal structures, such as bowels & bladder
- Special attention paid to:
  - Depth of prescription
  - Dose per fraction
  - Length of vagina treated
  - Diameter of cylinder used
- Swedish Trial: IVRT arm
  - Intestinal toxicity - 2.3 % Gr-1, 0.4% Gr-2
  - Urinary tract toxicity: 20.2% Gr-1, 2.7% Gr-2, 0.8% Gr-3
  - Vaginal toxicity: 4.1% Gr-1, 0.8% Gr-2, 0.8% Gr-3

COMPLICATIONS OF RADIATION TREATMENT

Intravaginal RT

- Sorbe and Smeds:15% late complication rate & very high incidence of vaginal stenosis after PO HDR IVRT

  Attributed to:
  - High dose per fraction of 6 to 9 Gy
  - Dose prescribed at 10 mm from surface of cylinder- very high vaginal mucosal, bladder, and rectal doses
- PORTEC-2: IVRT *Vs* Pelvic RT
  - Better social functioning (p= .005) & lower symptom scores for diarrhea, fecal leakage, need to stay close to toilet, & limitation in daily activities due to bowel symptoms (p = .001)
  - No diff. in sexual functioning /symptoms in T/t groups; Sexual functioning lower & symptoms more frequent in both T/t groups compared to norm population


THANK YOU