GYNECOLOGIC CANCER and RADIATION THERAPY

Jon Anders M.D.
Radiation Oncology
Brachytherapy

- Comes from the Greek *brakhus* meaning short
- Brachytherapy is treatment at short distance
- Intracavitary vs interstitial
  - i.e. gyn vs prostate
Brachytherapy

• Originally used Radium-226
  – Manufactured as needles and tubes
  – Half life of 1600 years
  – Decays to Radon
Brachytherapy

- Low dose rate (LDR) done with Cesium-137 sources with a half life of about 30 years
- Decays to solid Barium
Brachytherapy

- High dose rate (HDR) delivered with Iridium-192 source with a half life of 73.8 days
Brachytherapy

• Most commonly used for
  – Post-operative endometrial cancer
  – Intact bulky or locally advanced cervical cancer

• Other sites include
  – Prostate (Palladium or Iodine seeds)
  – Breast cancer
Endometrial Cancer
Endometrial Cancer

### Staging

<table>
<thead>
<tr>
<th>TNM CATEGORY</th>
<th>FIGO STAGE</th>
<th>PRIMARY TUMOR (T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1a</td>
<td>IA</td>
<td>Tumor limited to endometrium or invades less than one-half of the myometrium</td>
</tr>
<tr>
<td>T1b</td>
<td>IB</td>
<td>Tumor invades one-half or more of the myometrium</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>Tumor invades stromal connective tissue of the cervix but does not extend beyond uterus**</td>
</tr>
<tr>
<td>T3a</td>
<td>IIIA</td>
<td>Tumor involves serosa and/or adnexa (direct extension or metastasis)</td>
</tr>
<tr>
<td>T3b</td>
<td>IIIB</td>
<td>Vaginal involvement (direct extension or metastasis) or parametrial involvement</td>
</tr>
<tr>
<td>T4</td>
<td>IVA</td>
<td>Tumor invades bladder mucosa and/or bowel mucosa (bullous edema is not sufficient to classify a tumor as T4)</td>
</tr>
</tbody>
</table>

* FIGO staging no longer includes Stage 0 (Tis)  
** Endocervical glandular involvement only should be considered as stage I and not Stage II.

<table>
<thead>
<tr>
<th>TNM CATEGORY</th>
<th>FIGO STAGE</th>
<th>REGIONAL LYMPH NODES (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td></td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td></td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>IIIC1</td>
<td>Regional lymph node metastasis to pelvic lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>IIIC2</td>
<td>Regional lymph node metastasis to para-aortic lymph nodes, with or without positive pelvic lymph nodes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TNM CATEGORY</th>
<th>FIGO STAGE</th>
<th>DISTANT METASTASIS (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td></td>
<td>No distant metastasis (no pathologic M0; use clinical M to complete stage group)</td>
</tr>
<tr>
<td>M1</td>
<td>IVB</td>
<td>Distant metastasis (includes metastasis to inguinal lymph nodes intraperitoneal disease, or lung, liver, or bone. It excludes metastasis to para-aortic lymph nodes, vagina, pelvic serosa, or adnexa)</td>
</tr>
</tbody>
</table>
Endometrial Cancer

- Completely staged vs not
- Risk of positive pelvic nodes GOG 33
  – Creasman data from 1987

<table>
<thead>
<tr>
<th></th>
<th>Gr 1</th>
<th>Gr 2</th>
<th>Gr 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrium</td>
<td>0%</td>
<td>3%</td>
<td>0%</td>
</tr>
<tr>
<td>Inner</td>
<td>3%</td>
<td>5%</td>
<td>9%</td>
</tr>
<tr>
<td>Middle</td>
<td>0%</td>
<td>9%</td>
<td>4%</td>
</tr>
<tr>
<td>Deep</td>
<td>11%</td>
<td>19%</td>
<td>34%</td>
</tr>
</tbody>
</table>
Endometrial Cancer

• PORTEC
  – PRT of postoperative radiation for pT1 endometrial cancer
  – Pts had TAH/BSO but no lymph node dissection
  – Grade 1 with deep invasion, all grade 2, and grade 3 with superficial invasion
Endometrial Cancer

• PORTEC
  – Randomized to pelvic XRT vs. no further tx
  – Local failure:
    • XRT – 4%
    • No RT – 15%
    • P<0.001
  – Survival
    • XRT – 80%
    • No RT – 86%
Endometrial Cancer

- GOG 99
  - PRT of postoperative pelvic XRT vs no further tx for intermediate risk endometrial cancer
  - TAH/BSO
  - Lymph node dissection done
  - Stage IB, IC, IIA
  - Grade 1-3
Endometrial Cancer

• GOG 99
  – Local failure
    • XRT – 2%
    • No RT – 12%
  – Endometrial cancer deaths
    • XRT – 5%
    • No RT – 7%
Endometrial Cancer

• GOG 99
  – Risk factors
    • Age
    • LVS
    • G 2/3
    • >1/3 invasion
Endometrial Cancer

• PORTEC – 2
  – PRT of postoperative pelvic XRT vs vaginal brachytherapy for high intermediate risk endometrial cancer
  – Pts had TAH/BSO but no lymph node dissection
  – Age > 60 and stage IC grade 1-2 or stage IB grade 3
  – Any age with stage IIA grade 1-2 or grade 3 with < 50% invasion
Endometrial Cancer

- **PORTEC – 2 site of first failure**
  - Pelvic relapse @ 3 years
    - VBT – 3.6%
    - Pelvic XRT – 0.7% (p=0.03)
  - Vaginal relapse @ 3 years
    - VBT – 0.9%
    - Pelvic XRT – 2%
  - Distant failure @ 3 years
    - VBT – 6.4%
    - Pelvic XRT – 6%
Endometrial Cancer

- Overall survival @ 3 years
  - 90.4% vs 90.8%
- Patient reported quality of life better after VBT than pelvic XRT
Endometrial Cancer

- Standard of care has now become vaginal brachytherapy treatments for most intermediate risk disease.
- Vaginal cuff brachytherapy directs radiation toward the lymphatic channels of the upper 3-4 cm of vagina.
Endometrial Cancer

- LDR treatments done with colpostats alone
- Required a hospital stay of 2-3 days with 1-2 insertions
Endometrial Cancer

- HDR treatments done with a cylinder
- Depending on source strength treatment can take from 3 – 12 minutes
- 3 treatments done 2-3 times per week
Endometrial Cancer

- A dose of 700cGy is prescribed to a depth of 5mm
- CT used for planning
Endometrial Cancer
Endometrial Cancer

• Morbidity of treatment
  – Vaginal shortening or narrowing
  – Vaginal dryness
  – Mild incontinence
  – Bowel obstruction
  – Fistula formation (bladder or bowel)
  – Vaginal necrosis
Cervical Cancer
### Cervical Cancer

**Staging**

<table>
<thead>
<tr>
<th>TNM Category</th>
<th>FIGO Stage</th>
<th>PRIMARY TUMOR (T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td></td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td></td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1s</td>
<td>*</td>
<td>Carcinoma <em>in situ</em> (preinvasive carcinoma)</td>
</tr>
<tr>
<td>T1</td>
<td>I</td>
<td>Cervical carcinoma confined to uterus (extension to corpus should be disregarded)</td>
</tr>
<tr>
<td>T1a**</td>
<td>IA</td>
<td>Invasive carcinoma diagnosed only by microscopy. Stromal invasion with a maximum depth of 5.0 mm measured from the base of the epithelium and a horizontal spread of 7.0 mm or less. Vascular space involvement, venous or lymphatic, does not affect classification</td>
</tr>
<tr>
<td>T1a1</td>
<td>IA1</td>
<td>Measured stromal invasion 3.0 mm or less in depth and 7.0 mm or less in horizontal spread</td>
</tr>
<tr>
<td>T1a2</td>
<td>IA2</td>
<td>Measured stromal invasion more than 3.0 mm and not more than 5.0 mm with a horizontal spread 7.0 mm or less</td>
</tr>
<tr>
<td>T1b</td>
<td>IB</td>
<td>Clinically visible lesion confined to the cervix or microscopic lesion greater than T1a/IA2</td>
</tr>
<tr>
<td>T1b1</td>
<td>IB1</td>
<td>Clinically visible lesion 4.0 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T1b2</td>
<td>IB2</td>
<td>Clinically visible lesion more than 4.0 cm in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>II</td>
<td>Cervical carcinoma invades beyond uterus but not to pelvic wall or to lower third of vagina</td>
</tr>
<tr>
<td>T2a</td>
<td>IIA</td>
<td>Tumor without parametrial invasion</td>
</tr>
<tr>
<td>T2a1</td>
<td>IIA1</td>
<td>Clinically visible lesion 4.0 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T2a2</td>
<td>IIA2</td>
<td>Clinically visible lesion more than 4.0 cm in greatest dimension</td>
</tr>
<tr>
<td>T2b</td>
<td>IIB</td>
<td>Tumor with parametrial invasion</td>
</tr>
<tr>
<td>T3</td>
<td>III</td>
<td>Tumor extends to pelvic wall and/or involves lower third of vagina, and/or causes hydronephrosis or non-functioning kidney</td>
</tr>
<tr>
<td>T3a</td>
<td>IIIA</td>
<td>Tumor involves lower third of vagina, no extension to pelvic wall</td>
</tr>
<tr>
<td>T3b</td>
<td>IIIB</td>
<td>Tumor extends to pelvic wall and/or causes hydronephrosis or non-functioning kidney</td>
</tr>
<tr>
<td>T4</td>
<td>IVA</td>
<td>Tumor invades mucosa of bladder or rectum, and/or extends beyond true pelvis (bullous edema is not sufficient to classify a tumor as T4)</td>
</tr>
</tbody>
</table>

* FIGO staging no longer includes Stage 0 (Tis)

**All macroscopically visible lesions—even with superficial invasion—are T1b/IB.
Cervical Cancer

• Staging

• Recommended exams
  – Palpation
  – Inspection
  – Cloposcopy
  – Endocervical curettage
  – Hysteroscopy
  – Cysto and procto
  – Intravenous urography
  – Plain films of lungs and bones
Cervical Cancer

• Staging
  – Lymph nodes assessed by CT, MRI, PET, or lymphangiography may not be used to determine clinical stage as they are not universally available
  – They can be used to develop a treatment plan
Cervical Cancer

• 90% of squamous cell cancers contain HPV DNA

• Most frequent types are 16 and 18
Cervical Cancer

• Stage II and III disease was historically treated with radiation alone.

• In the past 15 years concurrent chemotherapy and radiation have become the standard
Cervical Cancer

• For 1B tumors there is debate about the most appropriate treatment
• Landoni published a randomized trial comparing radical surgery vs radiotherapy for stage Ib-IIa disease
Cervical Cancer

• The 5 year overall and disease free survival was identical for both groups
• 84% of patient with cervical size >4cm and 54% of patients with cervical size <4cm received post-op radiation due to pathologic risk factors
• GU morbidity was highest in the combined group
Cervical Cancer

• Radiation therapy consists of two components
  – External beam
  – Intracavitary implants
Cervical Cancer

• External beam radiation
  – Treatment of the primary tumor and pelvic lymph nodes
  – Small doses of radiation delivered mon-fri for 5 weeks
  – Concurrent with weekly platinum
Cervical Cancer

- Traditionally a four field technique was used
Cervical Cancer

• Today IMRT is more frequently used in an attempt to spare bladder and bowel when possible
Cervical Cancer
Cervical Cancer

- Intracavitary implant using the Fletcher-suite applicator
Cervical Cancer

- Dose prescribed to Point A
Cervical Cancer
Cervical Cancer

- For LDR treatment
  - Patients taken to the OR for placement
  - 2-3 day stay in the hospital depending if one or two implants are done
Cervical Cancer

- HDR treatment done as outpatient
- Five treatments
- Conscious sedation
- CT for planning
Cervical Cancer
Cervical Cancer

- **Good implant**
  - **Tandem**
    - Roughly midway between the sacral promontory & symphysis pubis - (LAT)
    - Should bisect the ovoids (LAT)
    - Not rotated - (PA)
  - **Ovoids**
    - Inferior to the Foley bulb and at the level of the femoral heads - (LAT)
    - Are superimposed - not rotated - (LAT)
    - Rest just within the bony pelvis - (PA)
  - **Packing**
    - q 1 mm packing, ↓ rectal dose by 12% from one ovoid
Cervical Cancer

The investigators reported about 75% pelvic tumor control in 118 patients with stage IIIB and III carcinoma of the uterine cervix. The major complication rates were 6 with less than 4500 mg-hr, 16% with 4500 to 4999 mg-hr, 28% with 5500 mg-hr, and 87% with higher intracavitary doses (combined with 45 to 50 Gy to the whole pelvis).
Cervical Cancer

- Morbidity of treatment
  - Vaginal stenosis or foreshortening
  - Chronic cystitis and proctitis
  - Incontinence and urethral stricture
  - Bowel obstruction
  - Fistula formation (bladder or rectum)
Cervical Cancer

• Morbidity of treatment
  – Risk of rectal complications may plateau after 3-5 years
  – Risk of urinary complications has a positive slope of approximately 0.3% per year
Cervical Cancer

• Morbidity of treatment
  – NCI published risk of second malignancy of 0.5% at 15 years
Thank you very much