Seminoma of the testis: Current role of radiotherapy

Andrew K. Lee, MD, MPH
Associate Professor
Department of Radiation Oncology
• Make sure it is seminoma
• Know which staging system
• Stage I and II curable by relatively low doses of radiation
• 2nd malignancies happen but rare
• Salvage chemo effective
Radiation therapy after orchiectomy

• Stage I
  – XRT (para-aortic 20Gy)
  – Observation (size, rete testis+, age)
  – Carboplatin alone

• Stage II
  – XRT (Dog-leg 20 Gy + Boost node 6-10Gy)
  – Chemotherapy for bulky disease (>5cm)

• Residual disease after chemotherapy
Seminoma

~40% of germ cell tumors

- Classic (pure)
  - Syncytiocytotrophoblastic
- Anaplastic (WHO 3+ mitoses/HPF)
- Spermatocytic

- Princess Margaret data suggests more relapses w/ anaplastic, but others have not shown difference in outcome based on pathology.
Natural history

Usually local

- ~80% of seminomas present as stage I.
- ~15% stage II.

Orderly nodal spread

- PA nodes, renal hilar nodes, mediastinum, SC

<5% have spread beyond PA nodes @ presentation (e.g. liver, lung, bone, brain).

Radiosensitive
Nodal drainage

- Usually not to inguinal/iliacs unless prior disruption and collaterals have formed.
- Scrotum does drain to superficial inguinal.

- Right testicular vein joins IVC few cm below Rt renal vein.
- Left enters into Lt renal vein.
Staging

• AJCC
• Royal Marsden
• Walter-Reed
• M.D. Anderson
No seminoma is considered poor risk

**TABLE 43-4. AJCC Staging System**

<table>
<thead>
<tr>
<th>Primary Tumor (pT)</th>
<th>N0</th>
<th>N1-3</th>
<th>Stage IIA,B</th>
<th>N1-2, nodes &lt;5cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor limited to the testis and epididymis without vascular/lymphatic invasion</td>
<td>Tumor limited to the testis and epididymis with vascular/lymphatic invasion, or tumor extending through the tunica albuginea with involvement of the tunica vaginalis</td>
<td>Tumor may invade the tunica albuginea but not the tunica vaginalis</td>
<td>Tumor invades the spermatic cord with or without vascular/lymphatic invasion</td>
<td>Tumor invades the scrotum with or without vascular/lymphatic invasion</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regional Lymph Nodes (N)</th>
<th>Clinical</th>
<th>Distant Metastasis (M)</th>
<th>Serum Tumor Markers (S)</th>
<th>RT for stage I and IIA,B</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
<td>MX</td>
<td>Distant metastasis cannot be assessed</td>
<td>N0 T N1-3 M0 S1-3</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis with a lymph node mass 2 cm or less in greatest dimension; or multiple lymph nodes, none more than 2 cm in greatest dimension</td>
<td>M0</td>
<td>No distant metastasis</td>
<td>Any T N0 T N1-3 M0 S1-3</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or multiple lymph nodes, any one mass greater than 2 cm but not more than 5 cm in greatest dimension</td>
<td>M1</td>
<td>Distant metastasis</td>
<td>Any T N0 T N1-3 M0 S1-3</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis with a lymph node mass more than 5 cm in greatest dimension</td>
<td>M1a Nonregional nodal or pulmonary metastasis</td>
<td>LDH*</td>
<td>Stage 0 T N0 M0 S0</td>
</tr>
<tr>
<td>N1-2</td>
<td>nodes &lt;5cm</td>
<td>M1b Nonpulmonary visceral metastasis</td>
<td>HCG (mIU/mL)</td>
<td>Stage 1 T N0 M0 S0</td>
</tr>
<tr>
<td>SX</td>
<td>Marker studies not available or not performed</td>
<td>AMP (ng/mL)</td>
<td>Stage 2</td>
<td>T N0 M0 S0</td>
</tr>
<tr>
<td>≤1.5 N*</td>
<td>and &lt;5000</td>
<td>≤1000</td>
<td>Stage 3</td>
<td>T N0 M0 S0</td>
</tr>
<tr>
<td>1.5-10 N*</td>
<td>or 5000-50,000</td>
<td>1000-10,000</td>
<td>Stage 4</td>
<td>T N0 M0 S0</td>
</tr>
<tr>
<td>&gt;10 N*</td>
<td>or &gt;50,000</td>
<td>&gt;10,000</td>
<td>Stage 5</td>
<td>T N0 M0 S0</td>
</tr>
</tbody>
</table>

---

**Note:**


# TABLE 43-3. Modified Royal Marsden Hospital Staging System

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>No clinical evidence of metastases beyond the testicle</td>
</tr>
<tr>
<td>Stage II</td>
<td>Infradiaphragmatic lymph node metastases</td>
</tr>
<tr>
<td>II A</td>
<td>Maximum diameter $&lt; 2 \text{ cm}$</td>
</tr>
<tr>
<td>II B</td>
<td>Maximum diameter $&gt; 2 \text{ but } &lt; 5 \text{ cm}$</td>
</tr>
<tr>
<td>II C</td>
<td>Maximum diameter $&gt; 5 \text{ but } &lt; 10 \text{ cm}$</td>
</tr>
<tr>
<td>II D</td>
<td>Maximum diameter $&gt; 10 \text{ cm}$</td>
</tr>
<tr>
<td>Stage III</td>
<td>Supradiaphragmatic nodal involvement</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Parenchymal metastatic disease</td>
</tr>
</tbody>
</table>

MDACC staging

• Stage I    Tumor confined to testis & adnexae (rete, epididymis, cord).
• Stage II   Nodal mets below diaphragm.
  • IIA  < 10 cm
  • IIB  ≥ 10 cm
• Stage III  Supradiaphragmatic nodes.
• Stage IV   Hematogenous mets.
Surgery

- “Radical inguinal orchiectomy with high ligation of the spermatic cord.”
- No biopsy
- No “trans-scrotal” approach
Stage I therapy options

- Surveillance

- RT to PA nodes (+/- pelvic nodes)

- Chemo (Carboplatin vs RT)
  - 5-y RFS ~96-94%
  - Fail primarily in para-aortics
Surveillance: Pooled Analysis

- 638 stage I pts managed w/ orchidectomy and surveillance at PMH, Royal Marsden, Danish, Royal London
- Median FU 7 years
- 5 year Relapse-free rate 82.3%
  - (121 relapses)

» JCO 20:4448-52, 2002
Pooled analysis – Multivariate analysis

• Tumor size ($\leq 4$ cm vs. $>4$ cm)
  4cm cutoff used but probably a continuum

• Rete testis invasion

• Having both features worse than one
# Pooled analysis:
**Predictors of 5-year relapse-free rate**

<table>
<thead>
<tr>
<th></th>
<th>Rete testis (-)</th>
<th>Rete testis (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>T ≤4 cm</strong></td>
<td>87.8% HR = 1.0</td>
<td>85.6% HR = 1.7</td>
</tr>
<tr>
<td><strong>T &gt;4 cm</strong></td>
<td>83% HR = 2.0</td>
<td>68.5% HR = 3.4</td>
</tr>
</tbody>
</table>
Relapse-free rate

Fig 4. Relapse-free rate based on number of adverse prognostic factors.
Surveillance- Prognostic Factors (Considerations from MDACC)

• Post-orchiectomy elevation in B-HCG and spermatic cord involvement associated with increased relapses in patients treated w/ infradiaph RT

• These 2 factors did not significantly impact OS, but may be predictive of occult stage II disease.
  • [Dosmann. IJROBP 26:381,1993]
MDACC considerations cont...

- One would expect that PA RT would eradicate occult infradiaphragmatic nodal dz.
- Possible that there were more supradiaphragmatic failures?
- Occult non-seminomatous component?
- Authors do not recommend altering RT but rather closer FU
Best candidates for surveillance

- Smaller primary
- No rete testis invasion
- Older patient
- Reliable patient

- Consider frequency of FU scans (~$30K for 5 years vs. ~$20K for RT)
- If fail, then either bigger RT fields or BEP/EP
MRC TE19/EORTC 309852 RCT: XRT vs. Carboplatin (x1)

- 1477 men randomized to XRT (PA or Dog-leg, 30-20Gy, n=904) vs. Carboplatin x 1 (7 x GFR+25, n=573)
- 3-y RFS 95.9% vs. 94.8%
- Slightly less 2\textsuperscript{nd} primary GCT w/ carbo 5-y 1.96% vs. 0.54%
- No OS difference

Oliver et al. Lancet 2005;366
Update w/ median FU 6.5y showed non-inferiority, but….

5-y RFS 96% vs. 94.7% for XRT and carbo, respectively
Carbo reduced contralateral GCTs (HR=0.22, p=0.03)
but relatively few absolute events (n=2 vs. 15)

GFR calculated using EDTA (n=357) or creatinine clearance w/ 24-hour urine (n=212)
If GFR normal, then dose AUC x 7
If >99% of the AUC x 7 dose given, then RFS 96.1%
If lower dose, then RFS only 92.6%

Oliver et al. J Clin Oncol 2011;29
Carboplatin

• Long-term results and effects pending
• Need high enough dose
• Still had more PA failures
• Requires similar FU and imaging as surveillance group for now
• Some may be salvaged w/ RT alone

• Not clear on baseline factors…most might have done well w/ surveillance…dilute the findings?
Stage I - RT field size

• Anatomically, dog-leg seems too extensive.
• Randomized data shows that in most men with stage I that para-aortic RT is sufficient.

• Patients with prior history of pelvic/inguinal surgery/trauma should still receive ipsilateral pelvic field
Stage I - RT field size

- **MRC** [Fossa. JCO 17:1146, 1999]
- **N=478 stage I (T1-3) pure seminomas (ABD CT -, AFP-)**
- **Radical orchiectomy followed by randomization to:**
  - Dog leg (T11-mid obturator) vs. PA only (T11-L5)
  - 200cGy x 15 = 3000 cGy.
## Results

<table>
<thead>
<tr>
<th></th>
<th>All relapses</th>
<th>Pelvic relapses</th>
<th>Deaths</th>
<th>3 y OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog-leg (n=242)</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>Para-aortic (n=236)</td>
<td>9</td>
<td>4 (p=0.04)</td>
<td>1</td>
<td>99.3%</td>
</tr>
</tbody>
</table>
Updated results 10.7 years

- 5-year relapse free survival the same 96%
- Only 1 death from seminoma on PA arm
- Only 1 relapse >3 years after entry on PA

Mead et al. JNCI 2011;103:241
Can you go smaller?

- Kiricutz et al. [IJROBP 35:293, 1996]
- N=86 stage I treated w/ orchiectomy and PA to L1-L5 w/ 4 field technique.
- Median dose 30 Gy.
- Median FU 63 mos.
- 4.7% relapse rate (all outside field).
- 10 y DFS and OS 95% and 100%
When should you go bigger?

• Pelvic/inguinal:
  – Prior pelvic/inguinal surgery/trauma
  – Cryptorchidism
  – Scrotal surgery/violation

• Scrotal field:
  – Scrotal invasion
<table>
<thead>
<tr>
<th></th>
<th>No. Inguinal Pts./Total No. Pts. (%)</th>
<th>No. Scrotal Violation Pts./Total No. Pts. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All pts.:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local recurrence</td>
<td>4/976 (0.4)</td>
<td>6/206 (2.9)*</td>
</tr>
<tr>
<td>Distant recurrence</td>
<td>100/867 (11.5)</td>
<td>23/181 (12.7)</td>
</tr>
<tr>
<td>Survival</td>
<td>893/976 (91.5)</td>
<td>191/206 (92.7)</td>
</tr>
<tr>
<td>Stage I disease:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local recurrence</td>
<td>1/707 (0.1)</td>
<td>2/151 (1.3)</td>
</tr>
<tr>
<td>Distant recurrence</td>
<td>73/745 (9.8)</td>
<td>19/158 (12.0)</td>
</tr>
<tr>
<td>Survival</td>
<td>683/711 (96.1)</td>
<td>140/142 (98.6)</td>
</tr>
<tr>
<td>Seminoma:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local recurrence</td>
<td>0/469 (0.0)</td>
<td>1/77 (1.3)</td>
</tr>
<tr>
<td>Distant recurrence</td>
<td>26/491 (5.3)</td>
<td>4/86 (4.6)</td>
</tr>
<tr>
<td>Survival</td>
<td>519/545 (95.2)</td>
<td>94/99 (95.0)</td>
</tr>
<tr>
<td>Nonseminomatous germ cell tumor:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local recurrence</td>
<td>1/245 (0.4)</td>
<td>1/62 (1.6)</td>
</tr>
<tr>
<td>Distant recurrence</td>
<td>74/376 (19.7)</td>
<td>19/95 (20.0)</td>
</tr>
<tr>
<td>Survival</td>
<td>374/431 (86.8)</td>
<td>97/107 (90.6)</td>
</tr>
</tbody>
</table>

* p < 0.05.
Effect of adjuvant therapy following scrotal violation

*From:* Capelouto: J Urol, Volume 153(3S)

<table>
<thead>
<tr>
<th></th>
<th>No. Treatment/ Total No. (%)</th>
<th>No. No Treatment/ Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local recurrence</td>
<td>1/95 (1.0)</td>
<td>1/44 (2.3)</td>
</tr>
<tr>
<td>Distant recurrence</td>
<td>12/95 (12.6)</td>
<td>2/44 (4.5)</td>
</tr>
<tr>
<td>Survival</td>
<td>95/95 (100)</td>
<td>43/44 (97.7)</td>
</tr>
</tbody>
</table>
Stage I - RT dose 20 Gy

- 15-40 Gy have been used.
- “Standard” dose ~ 25 Gy.
- PMH: 25 Gy in 20 fxns with ~100% in-field control.

- Randomized data shows that 20 Gy is similar to 30 Gy (MRC TE19)
MRC (TE18) randomized trial
30 Gy vs. 20 Gy for Stage I

- Randomized 1094 men (1995-98) to 30Gy/15fx vs. 20Gy/10 fx.
  - T10/11 to L5/S1 (88% of men)
  - Ipsilateral pelvic RT for prior inguino-pelvic or scrotal surgery

- Median FU 7 years
- RFS for 30 vs. 20 Gy were 95.1% vs. 96.8%, respectively
- 10 and 11 relapses, respectively (2-y difference 0.7%)

- Difference in morbidity
  - Moderate-severe lethargy 20 vs. 5%
  - Inability for normal work 46 vs. 28%

JCO 23, 2005. Updated JNCI 2011;103
MDACC old technique

- T10-L5 inclusive
- 25 Gy

Top of T10 w/ older techniques (Cobalt-60, prescribing to mid-plan, one field a day, divergence into thorax) may have contributed to increase cardiac-related death

Radiation exposure to abdominal organs/organs and divergence into thorax

Stage I-MDACC current technique

• T12 - L5 inclusive (avoid inferior heart)
• 2 Gy x 10 = 20 Gy
• AP/ PA with high energy photons or PA protons
• Add pelvic/inguinal field for prior inguinal surgery or cord invasion
• Add pelvic-inguinal-scrotal for scrotal violation.
Protons reduced dose to all organs compared to x-rays (photons)…would result in 5-fold reduction in 2nd cancers
Stage II - Non-bulky

• Node positive.
• In general, this is considered < 5 cm
  – IIA, B
• MDACC includes < 10 cm.
  – IIA
• Can be treated w/ postop RT.
• Relapse rate ~ 10-20% and OS ~90%.
Stage II (non-bulky)- RT

- PA + Ipsilateral pelvis
- Stage IIA (< 2cm) 20-25 Gy
- Stage IIB (2-5cm) 20-25 Gy + 6-10 Gy boost
- Give 2-3 cm margin on gross dz.
- Failures salvaged w/ chemotherapy
## Results of RT for Non-bulky stage II

<table>
<thead>
<tr>
<th>Institution</th>
<th>Number of Patients</th>
<th>Five-Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.D. Anderson Cancer Center(^6)</td>
<td>55</td>
<td>95% OS</td>
</tr>
<tr>
<td>Mallinckrodt Inst. of Radiology(^24)</td>
<td>33</td>
<td>97% OS</td>
</tr>
<tr>
<td>Princess Margaret Hospital(^37)</td>
<td>40</td>
<td>94% DF</td>
</tr>
<tr>
<td>Cross Cancer Institute(^45)</td>
<td>20</td>
<td>85% DF</td>
</tr>
<tr>
<td>Royal Marsden Hospital(^12)</td>
<td>39</td>
<td>95% OS</td>
</tr>
<tr>
<td>Dr. Daniel den Hoed Cancer Center(^3)</td>
<td>29</td>
<td>91% OS</td>
</tr>
</tbody>
</table>
Mediastinal RT for Stage II

- Largely abandoned
- Number of studies showing RFS but no OS benefit
- Chance of salvage w/ CTx is high
- Increased toxicity w/ larger field
- May inhibit future systemic therapy
- More intercurrent deaths (cardiac & pulmonary toxicity)
  
  » PCS [Hanks. IJROBP 24:913,1992]
Stage II – Bulky >5cm

- In general > 5-10 cm (II C,D)  
  (Not MDACC staging)
- Several studies have shown inferior control rates w/ infradiaphragmatic RT (PMH).
- Other studies have shown good control rates with more extensive fields, but no OS advantage due to potential RT toxicity (MDACC)
**PMH** [JCO 16:290, 1998]

### Table 3. Relapse by Stage: Radiation Therapy as Initial Treatment

<table>
<thead>
<tr>
<th>Stage</th>
<th>Total</th>
<th>Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIA</td>
<td>40</td>
<td>4</td>
</tr>
<tr>
<td>IIB</td>
<td>24</td>
<td>3</td>
</tr>
<tr>
<td>IIC</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>IID</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>&gt; 5 cm</strong></td>
<td><strong>80</strong></td>
<td><strong>16 (20%)</strong></td>
</tr>
</tbody>
</table>


Fig 2. Relapse rate and size of retroperitoneal lymph node disease.
16 patients relapsed.

Isolated SC relapse in 5% (5 pts w/ one embryonal ca on biopsy).

7/64 patients w/ IIA/B relapsed (3 w/ isolated SC).

Table 4. Sites of Relapse

<table>
<thead>
<tr>
<th>Site</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retroperitoneal lymph nodes</td>
<td>2</td>
</tr>
<tr>
<td>Bone</td>
<td>4</td>
</tr>
<tr>
<td>Left supraclavicular lymph nodes</td>
<td>7</td>
</tr>
<tr>
<td>Lung/mediastinum</td>
<td>4</td>
</tr>
<tr>
<td>Other (including liver, axilla)</td>
<td>3</td>
</tr>
</tbody>
</table>

NOTE. Some patients relapsed in more than one site.
Fig 3. Relapse rate in patients with IIC/D disease based on postorchiectomy treatment.
MDACC reccs from this study

• PA + Pelvic (+/- left supraclav) for MDA stage IIA

• PA field: T12-L5 inclusive (thoracic duct)
• 20 Gy (2 Gy x 10) to elective sites
• Boost gross dz w/ 6-10 Gy
• Lt S/C: AP field, 6 MV, 6-8cm field, prescribed to 100%
Stage II (Bulky >5-10cm) - Treatment

- In general, treated with orchiectomy and platinum-based therapy (e.g. cisplatin, etoposide or BEP).
- Some large tumors MAY be controlled by RT, but field size/ dose may be too large.
- With large bulk, ~15% will relapse within irradiated field. Another 25% distantly.
- Bulk may be predictive of distant failure.
Residual post-chemo disease

- Controversial
- 60-80% will have residual mass 1 month after CTx.
- Some may regress over months-years.
- ~ 85% of time = fibrosis (15% viable ca)
- > 10 cm @ presentation tend to recur at site of bulky disease (~85% of time)
2 patterns of regression

• “Tumor implodes around great vessels and obliterates radiographic planes. Residual disease merges w/ great vessels, the psoas m and other RP structures…poorly defined…usually fibrosis”

• “Well delineated and distinct…may be resectable…high incidence of residual seminoma.”

Proposed treatment options

• Options:
  – Observation (miss tumor)
  – Biopsy
  – RT (needlessly irradiate most patients)
  – Surgery (can be difficult)
MSKCC

- N=55 w/ residual seminoma after chemo
- 58% (32/55) had resection and 42% (23/55) had biopsies
  - Surgery w/ in 4 WEEKS of completion of CTx
- If < 3cm, then 0/28 had viable tumor.
- If ≥ 3cm, then 8/30 (30%) had viable tumor.
MSKCC part II

- 6/8 pts w/ positive histology actually had resection of “well-defined” mass
- 4 seminomas
- 2 teratomas
- All six are NED, but 3 got RT and 1 got RT + CTx.
MSKCC recommendation

• For < 3cm, close observation with tx at time of progression.
• For ≥ 3 cm, options are observation, RT, surgery.
• Authors favor surgery to “define response, resect viable tumor…and direct further treatment.”
Does RT make a difference in outcome?

- Duchesne et al. [Eur J Ca 33:829,1997]
- Multi-institutional retrospective study
- N= 302 w/ metastatic seminoma w/ normal AFP (> 50% stage II) s/p CTx +/- RT
- No difference in PFS (88%) w/ RT
- Absolute 3y PFS benefit of RT was estimated at 2.3% for platinum-based pts.
Size and RT

- Median residual size for no RT 3cm [1-11cm]
- Median residual size for RT 2.9cm [0.5-20cm]

- Trend for increased progression w/ increased size of residual, but not statistically significant.
MDACC

- No standard treatment...individualize
- Consider observing lesion ≤ 3 cm
  - especially if ill-defined
- Consider treating lesion > 3 cm
  - Especially if well-defined
- If give RT, then 20-25 Gy to involved fields
  - Allow time for regression
  - May not affect PFS
  - Possible non-seminomatous elements (30%?)
PET and residual disease

- Austrian and German [JCO 19:3740,2001]
- Prospective and multi-institutional trial
- 33 pts w/ ≥ 1cm post-CTx residual had PET scan (median 44 days post-CTx)
- PET correlated w/ path (9) and/or clinical FU (28)
Table 3. Specificity, Sensitivity, and Positive and Negative Predictive Value for Detecting Viable Tumor in Residual Postchemotherapy Lesions by FDG PET and Maximum Transverse Diameter of the Residual Lesion (≤ 3 cm or > 3 cm)

<table>
<thead>
<tr>
<th></th>
<th>FDG PET</th>
<th>Size ≤ or &gt; 3 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specificity</td>
<td>1</td>
<td>0.75</td>
</tr>
<tr>
<td>95% confidence interval</td>
<td>0.877-1</td>
<td>0.551-0.893</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.89</td>
<td>0.78</td>
</tr>
<tr>
<td>95% confidence interval</td>
<td>0.517-0.997</td>
<td>0.4-0.972</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>0.97</td>
<td>0.91</td>
</tr>
</tbody>
</table>
When patient is on RT

- Nausea ~10-40%
- Leukopenia < 15% (more w/ dog-leg)
- Diarrhea 5-15% (more w/ dog-leg)
- Dyspepsia < 5%

[MRC trial. JCO 17, 1999]

* I rarely see any significant side effects w/ 200cGy x 10
After patient completes RT

- Most relapses will occur w/in 18-24 months
- Late relapses (10 y) have been reported but rare
- FU schedule…depends on stage and presenting factors:
  - Every 4-6 months for 1 year
    - B-HCG, AFP, LDH, CBC, BUN/Cr
    - BP, CXR, ABD-P CT (Q 3-6 x 2 y)
  - Every 6-12 month for years 2-4
  - Annually thereafter if desired
Fertility

• Internal scatter w/ DL field < 1% of prescription dose (JCRT)
• At baseline, a significant portion of pts (~1/3) will have difficulty w/ fertility (motility, count, morphology)
  – Even extremely low RT doses may be problematic for these men.
• Post-RT, most men (~2/3) who wish to have children are able to do so.
MRC trial-toxicity

- Acute toxicity (N/V, leukopenia) was slightly less in PA only arm.

<table>
<thead>
<tr>
<th></th>
<th>2\textsuperscript{nd} malig.</th>
<th>Median time to nl sperm count</th>
<th>Azospermia @ 18 mos.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog-leg</td>
<td>1</td>
<td>20 months</td>
<td>35%</td>
</tr>
<tr>
<td>PA</td>
<td>2</td>
<td>13 months</td>
<td>11%</td>
</tr>
</tbody>
</table>
2nd malignancies

2nd testis tumor ~4% total

  – Nearly 29,000 survivors of testicular ca
    • Actuarial risk of any 2nd ca (excluding contralateral testis) was 16% @ 25 y (expected 9.3%).
  – Half were seminomas
    • Among RT alone: O/E = 1.45 at 20 years
    • Older RT techniques
2nd malignancies

- GI malignancies RR = 2-3x
- Leukemia
  - w/ RT only: RR = 2-3+ (contrary to other studies)
  - w/ any Chemotherapy: RR = 10+

- Retroperitoneal sarcomas are relatively rare
Late toxicities

- Peptic ulcer disease (5-10%)
  - 7% in MRC trial
  - 10-40 weeks after
  - May increase w/ doses > 30-45 Gy and prior history
Thank you