Post-prostatectomy Radiotherapy: When, How, and Dose

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Adjuvant vs. Salvage RT

- “Adjuvant” RT - absence of clinical/ biochemical failure

- “Salvage” RT – clinical/ biochemical failure

Studies have shown advantage to *adjuvant* over *salvage RT*, but are these comparisons valid?
  - 2 different populations
  - By definition, salvage therapy group has declared themselves to have worse disease
### Adjuvant
- Margin (+)
- Path T3
- 64-66 Gy
- 3D-CRT or IMRT
- CTV = Prostate bed +/- SV bed
- PTV = CTV + 5-7mm depending upon practice
- Allow recovery of urinary control

### Salvage
- PSAF > 0.2 ng/mL
- Path features
- PSA kinetics
- 70 Gy
- 3D-CRT or IMRT
- CTV as per adjuvant RT
- PTV as per adjuvant RT
- Consider HT
- >72Gy if gross recurrence
Predicting clinical outcomes

Clinical factors
- cT-stage, biopsy Gleason, PSA

Pathologic factors
- Path stage, nodes, path Gleason, margins

Post-op PSA kinetics

PSAF interval, PSADT

Clinical outcomes
- LC, DM, DFS, OS
“Ideal” candidate for *adjuvant* RT

- Patient has expected longevity to see benefit
- Favorable clinical presentation
  - E.g. PSA <10, PSA velocity <2ng/ml per year

- *Favorable* pathologic features
  - Margin positive
  - Extra-prostatic extension (T3)
  - Prostatectomy Gleason ≤ 3+4
  - Node negative
  - No SVI (SVI+ still benefit)

- Urinary control stabilized

Increased risk of local failure

Lower competing risk of distant failure
Role of adjuvant RT for pathologic T3

- Multiple retrospective studies have shown a benefit to adjuvant RT for pT3N0

- 3 *randomized* studies have been completed
  - EORTC 22911
  - SWOG 8794/ INT0086
  - ARO 96-02/AUO AP 09/95
EORTC 22911-RCT Adjuvant 60 Gy

- 1005 men s/p RP w/ at least path T3 (capsular invasion, SVI), +Margin

- Randomized to adjuvant 60 Gy (50 sv+10 p) vs. late salvage
  - 8.9% of RT arm received no RT
  - 1% of observation arm received RT
  - Dose considered low by modern standards

- Biochemical (PSA >0.2) or clinical PFS (HR ~0.5)
- Median FU 10.6 y (closed early)

- Update shows significant improvement in PSA control & local control (but not clinical PFS)

Lancet 2005;366  Updated Lancet 2012;380
## EORTC 22911 path risk factors

<table>
<thead>
<tr>
<th></th>
<th>No RT N=503</th>
<th>RT N=502</th>
<th>Total N=1005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not pT3</td>
<td>0</td>
<td>0.4%</td>
<td>0.2%</td>
</tr>
<tr>
<td>ECE</td>
<td>25.2%</td>
<td>27.7%</td>
<td>26.5%</td>
</tr>
<tr>
<td>ECE + SVI</td>
<td>8%</td>
<td>5.2%</td>
<td>6.6%</td>
</tr>
<tr>
<td>ECE + M</td>
<td>33.6%</td>
<td>29.7%</td>
<td>31.6%</td>
</tr>
<tr>
<td>SVI</td>
<td>3.8%</td>
<td>4.6%</td>
<td>4.2%</td>
</tr>
<tr>
<td>SVI + M</td>
<td>1.6%</td>
<td>3.2%</td>
<td>2.4%</td>
</tr>
<tr>
<td>+M</td>
<td>15.7%</td>
<td>16.7%</td>
<td>16.2%</td>
</tr>
<tr>
<td>ECE, SV, M</td>
<td>12.1%</td>
<td>12.5%</td>
<td>12.3%</td>
</tr>
</tbody>
</table>
## EORTC 22911 10-year results

<table>
<thead>
<tr>
<th></th>
<th>PO RT</th>
<th>No RT</th>
<th>P- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local-regional</td>
<td>7.3%</td>
<td>16.6%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Clinical PFS or Death</td>
<td>70.3%</td>
<td>64.8%</td>
<td>0.0539</td>
</tr>
<tr>
<td>Clinical-PSA PFS or Death</td>
<td>60.6%</td>
<td>38.2%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

No difference in DM or OS (not primary endpoints)
10-year results

Biochemical PFS

Clinical PFS

Overall survival
Bolla, EORTC 22911

- Better PSA survival: 60% vs 38%
- Better locoregional control and salvage free survival
- Trend toward better clinical PFS: 83% vs 75%

- 84% of Observation group received salvage RT and/or HT at median PSA 1.7 and median interval 2.9 years.
- 56.4% of Observation group eventually received salvage XRT

- Increased Toxicity with XRT
This study may never show a difference in these endpoints. They were not the primary endpoints for this trial. The study was not powered to show this.
EORTC comments

• Primary endpoint was biochemical PFS
• RT dose low by modern standards
• ~30% of men had postop PSA > 0.2
• 84% of observation group received salvage RT (70Gy) and/or HT at median of 2.9 years

• Positive surgical margin w/ pT3 had most benefit
• Men < 70 years old had benefit in clinical PFS

• Increased Toxicity with XRT
SWOG 8794/ INT 0086

- Randomized 473 men w/ pT3N0 w/ at least one factor (ECE, SVI, +M) to adjuvant 60-64 Gy within 16 weeks vs. observation

- Primary endpoint metastasis-free survival
- Median FU 12.5 years
  - 32% of observation arm received RT at median of 2 years

- Significant improvement in PSA-FFS and RFS, MFS, OS

JAMA 2006;19 \rightarrow J Urol 2009;181.
<table>
<thead>
<tr>
<th></th>
<th>Observation</th>
<th>PO RT</th>
</tr>
</thead>
<tbody>
<tr>
<td># subjects</td>
<td>211</td>
<td>214</td>
</tr>
<tr>
<td>Median age</td>
<td>65.8</td>
<td>64.1</td>
</tr>
<tr>
<td>ECE and/or +M</td>
<td>67.7%</td>
<td>66.8%</td>
</tr>
<tr>
<td>SVI</td>
<td>10.9%</td>
<td>10.3%</td>
</tr>
<tr>
<td>ECE, SVI, +M</td>
<td>21.3%</td>
<td>22.9%</td>
</tr>
<tr>
<td>Gleason ≤6</td>
<td>46%</td>
<td>55%</td>
</tr>
<tr>
<td>Gleason 7</td>
<td>36%</td>
<td>33%</td>
</tr>
<tr>
<td>Gleason 8-10</td>
<td>18%</td>
<td>12%</td>
</tr>
<tr>
<td>Preop PSA &lt;10</td>
<td>53%</td>
<td>51%</td>
</tr>
<tr>
<td>Postop PSA &lt;0.2</td>
<td>58%</td>
<td>56%</td>
</tr>
</tbody>
</table>
### SWOG 8794 results

<table>
<thead>
<tr>
<th></th>
<th>PORT</th>
<th>OBS</th>
<th>HR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10-y</td>
<td>10-y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSA &lt;0.4</td>
<td>47%</td>
<td>23%</td>
<td>0.51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RFS</td>
<td>67%</td>
<td>48%</td>
<td>0.59</td>
<td>0.001</td>
</tr>
<tr>
<td>MFS</td>
<td>71%</td>
<td>61%</td>
<td>0.71</td>
<td>0.016</td>
</tr>
<tr>
<td>OS</td>
<td>74%</td>
<td>66%</td>
<td>0.72</td>
<td>0.023</td>
</tr>
</tbody>
</table>

*J Urol 2009;181*
Metastasis free survival: 71 vs. 61%

J Urol 2009;181
Overall survival: 74 vs. 66%
Quality of Life
- Initially Worse with XRT
- By 5 yrs, XRT>WW

SWOG 8794 comments

• Advantage in metastasis free survival AND overall survival to RT (despite lower than expected rates of mets)

• RT had increased side effects as expected but similar to observation arm at 5-years
• RT appeared to benefit even SVI +
• RT benefited men w/ postop detectable PSA but less so
• RT benefited men w/ Gleason >7 but less so

• 5-year **hormone-free survival** was 80% OBS vs. 91% RT (HR 0.44, p <0.001)
SWOG 8794: PSA-FFS by postop PSA
About 15% improvement even w/ postop PSA 0.2-1.0

<table>
<thead>
<tr>
<th></th>
<th>No RT</th>
<th>RT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. at risk</strong></td>
<td>≤ 0.2: 121, &gt; 0.2 and ≤ 1.0: 44, &gt; 1.0: 18</td>
<td>≤ 0.2: 121, &gt; 0.2 and ≤ 1.0: 57, &gt; 1.0: 11</td>
</tr>
<tr>
<td><strong>Event</strong></td>
<td>75, 35, 17</td>
<td>33, 39, 11</td>
</tr>
<tr>
<td><strong>5-year estimate</strong></td>
<td>77% 34% 0%</td>
<td>58% 27% 0%</td>
</tr>
<tr>
<td><strong>10-year estimate</strong></td>
<td>58% 27% 0%</td>
<td>10.3 2.4 0.2</td>
</tr>
<tr>
<td><strong>Median (years)</strong></td>
<td>10.3 2.4 0.2</td>
<td>10.3 2.4 0.2</td>
</tr>
</tbody>
</table>

Swanson JCO 2007; 25
SWOG 8794: PSA-FFS by Gleason
Gleason ≤ 7 benefited most

No RT  |  RT

<table>
<thead>
<tr>
<th>Gleason ≤ 7</th>
<th>No at risk</th>
<th>Event</th>
<th>5-year estimate</th>
<th>10-year estimate</th>
<th>Median (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 7</td>
<td>94</td>
<td>34</td>
<td>69%</td>
<td>60%</td>
<td>10.3</td>
</tr>
<tr>
<td>= 7</td>
<td>56</td>
<td>22</td>
<td>64%</td>
<td>39%</td>
<td>9.1</td>
</tr>
<tr>
<td>&gt; 7</td>
<td>20</td>
<td>12</td>
<td>44%</td>
<td>19%</td>
<td>4.3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gleason &gt; 7</th>
<th>No at risk</th>
<th>Event</th>
<th>5-year estimate</th>
<th>10-year estimate</th>
<th>Median (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 7</td>
<td>76</td>
<td>61</td>
<td>76%</td>
<td>69%</td>
<td>10.3</td>
</tr>
<tr>
<td>= 7</td>
<td>61</td>
<td>31</td>
<td>74%</td>
<td>64%</td>
<td>9.1</td>
</tr>
<tr>
<td>&gt; 7</td>
<td>31</td>
<td>31</td>
<td>72%</td>
<td>44%</td>
<td>4.3</td>
</tr>
</tbody>
</table>

Graph showing survival rates for Gleason ≤ 7 and > 7 groups with and without radiation therapy (RT).
## Adjuvant vs. Salvage

### Table 2. PSA Failure-Free Rates by Post-RP PSA Subgroup Among Patients Who Received Immediate or Delayed Radiation

<table>
<thead>
<tr>
<th>Post-RP PSA (ng/mL)</th>
<th>No. of Patients</th>
<th>5-Year PSA Failure-Free Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 0.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate XRT</td>
<td>122</td>
<td>77*</td>
</tr>
<tr>
<td>XRT at failure</td>
<td>34</td>
<td>38†</td>
</tr>
<tr>
<td>&gt; 0.2 and ≤ 1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immediate XRT</td>
<td>57</td>
<td>34*</td>
</tr>
<tr>
<td>XRT at failure</td>
<td>17</td>
<td>18†</td>
</tr>
</tbody>
</table>

Abbreviations: RP, radical prostatectomy; PSA, prostate-specific antigen; XRT, radiation therapy.

*Time to PSA failure = registration date to date of first PSA ≥ 0.4 ng/mL.
†Time to PSA failure = date of initiation of salvage RT to first subsequent date of PSA ≥ 0.4 ng/mL.

Swanson JCO 2007; 25
German study:
ARO 96-02/AUA AP 09/95

- Randomized 385 men w/ pT3N0 to adjuvant 60 Gy within 12 weeks vs. observation
- 20% men subsequently excluded b/c of detectable PSA

- Primary endpoint PSA-free survival
- Median FU 53.5 mos

- Significant improvement in PSA-FFS

Wiegel et la. J Clin Oncol 2009;27
Two steps in randomization

Randomly Assigned
(N = 388)

A:
“Wait and See”
(n = 194)

Eligible (n = 192)
Ineligible (n = 2)
Reason: immediate HT (n = 2)

B:
Radiotherapy 60 Gy
(n = 194)

Eligible (n = 193)
Ineligible (n = 1)
Reason: immediate HT

C:
Persistent PSA
(n = 78)
A: (n = 33)
B: (n = 45)

(n = 33)

Assigned:
“Wait and See”
Random: (n = 159)
Postoperative RT: 5
Given:
“Wait and See”: 154

Assigned
Postoperative RT
Random: (n = 148)
“Wait and See”: 34
(Reasons: refusal)
Given:
Postoperative RT: 114

Treatment

Outcome

Biochemical relapse
(n = 67)

Biochemical relapse
(n = 38)
Intent to treat (ITT) 1 vs. ITT 2
ITT2: 5-y PSA-FFS 54% vs. 72% (p=0.015)

Wiegel et al. J Clin Oncol 2009;27
Largest benefit in +M, PSA >10, SVI-, Gleason <7

<table>
<thead>
<tr>
<th>Subcategory</th>
<th>Radiotherapy n/events</th>
<th>Control n/events</th>
<th>RFS hazard ratio 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical margins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>negative</td>
<td>48/13</td>
<td>61/19</td>
<td>0.95 (0.47 to 1.93)</td>
</tr>
<tr>
<td>positive</td>
<td>100/25</td>
<td>97/47</td>
<td>0.41 (0.25 to 0.66)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>148</td>
<td>156</td>
<td>0.53 (0.36 to 0.80)</td>
</tr>
<tr>
<td>Test for heterogeneity: $\chi^2 = 3.74, df = 1, P = .05, I^2 = 73.2%$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: $P = .002$</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| PSA before RP     |                       |                  |                         |
| ≤10 ng/mL         | 78/18                 | 87/29            | 0.64 (0.36 to 1.16)     |
| >10 ng/mL         | 70/37                 | 70/20            | 0.43 (0.25 to 0.74)     |
| Total (95% CI)    | 148                   | 157              | 0.52 (0.35 to 0.77)     |
| Test for heterogeneity: $\chi^2 = 0.97, df = 1, P = .33, I^2 = 0\%$ |
| Test for overall effect: $P = .001$ |

| Stage             |                       |                  |                         |
| ptT3a/b           | 99/14                 | 101/26           | 0.34 (0.19 to 0.64)     |
| ptT3c             | 40/19                 | 43/24            | 0.77 (0.42 to 1.40)     |
| Total (95% CI)    | 139                   | 144              | 0.52 (0.34 to 0.80)     |
| Test for heterogeneity: $\chi^2 = 3.34, df = 1, P = .07, I^2 = 70.0\%$ |
| Test for overall effect: $P = .003$ |

| Gleason           |                       |                  |                         |
| Score ≤ 6        | 56/10                 | 57/23            | 0.42 (0.20 to 0.89)     |
| Score > 6        | 92/28                 | 102/44           | 0.59 (0.37 to 0.95)     |
| Total (95% CI)   | 148                   | 159              | 0.54 (0.36 to 0.80)     |
| Test for heterogeneity: $\chi^2 = 0.57, df = 1, P = .45, I^2 = 0\%$ |
| Test for overall effect: $P = .002$ |
German study toxicity

- Only one grade 3, no grade 4
- Only 2% grade 2 GU
- Only 1.4% grade 2 GI
ARO 96-02/AUA AP 09/95 comments

- Odd randomization: ITT 1 vs. 2
- Final randomized group (ITT2) all had undetectable postop PSA
- Total dose also low
- First study to use 3D-CRT
- Lowest toxicity
Ideal candidate for *adjuvant* RT

- Patient has expected longevity to see benefit
- Favorable clinical presentation
  - E.g. PSA <10, PSA velocity <2ng/ml per year
- *Favorable* pathologic features
  - Margin positive
  - Extra-prostatic extension (T3)
  - Prostatectomy Gleason ≤ 3+4
  - Node negative, no SVI

- Urinary control stabilized
- MDACC 66 Gy
Practical considerations

• Wait for optimal urinary control

• Utility of preop CT for postop RT planning

• Stricture now → stricture later
  – Conservative management (dilation, intermittent catheterization)

• Consider short-course HT w/RT (threshold RT dose for microscopic disease)
When to begin adjuvant RT
Predicting clinical outcomes - Salvage Rx

Clinical factors
- cT-stage, biopsy Gleason, PSA

Pathologic factors
- Path stage, nodes, path Gleason, margins

Post-op PSA kinetics

PSA failure interval, PSA doubling time

 Clinical outcomes
- LC, DM, DFS, OS
Local vs. Distant

• What is patient’s risk of occult distant mets?
  – Salvage local therapy in setting of metastatic disease likely has no benefit.

• Microscopic disease can manifest as a PSA failure and unlikely to be detected by current imaging studies.
Local vs. Distant

• Hopkins data (Pound et al):
  – Median time from PSAF to mets 8 yrs
  – Median time from mets to death was 5 yrs

• Factors associated with distant mets
  – Path Gleason $\geq 8$
  – PSAF $\leq 2y$
  – PSADT $\leq 10$ mos

JAMA 281, 1999
<table>
<thead>
<tr>
<th>FACTORS</th>
<th>5y METS-Free Survival %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gleason &lt; 8</strong></td>
<td>73 [65-80]</td>
</tr>
<tr>
<td>PSAF &gt; 2y</td>
<td>86 [74-92]</td>
</tr>
<tr>
<td>PSADT &gt; 10mos</td>
<td>69 [40-86]</td>
</tr>
<tr>
<td>PSAF ≤ 2y</td>
<td>76 [61-86]</td>
</tr>
<tr>
<td>PSADT ≤ 10mos</td>
<td>35 [16-56]</td>
</tr>
<tr>
<td><strong>Gleason 8-10</strong></td>
<td>40 [28-54]</td>
</tr>
<tr>
<td>PSAF &gt; 2y</td>
<td>60 [33-79]</td>
</tr>
<tr>
<td>PSAF ≤ 2y</td>
<td>31 [17-45]</td>
</tr>
</tbody>
</table>
PSA kinetics

- Other studies post-RP and post-RT have similar findings.
- PSADT important metric for DM and survival
  - e.g. D’Amico showed increased PC-specific death w/ PSADT < 3 mos (6y, HR=19.65)

- However, cutoff values are not absolute.
  - View in context of clinical situation.
Salvage Radiotherapy for Recurrent Prostate Cancer After Radical Prostatectomy

JAMA, March 17, 2004—Vol 291, No. 11

• Population
  – 501 pts at 5 US Tertiary Centers
  – Salvage XRT from 1987-2002
  – Rising PSA after prostatectomy

• Endpoint – Progression-Free Survival
  – PSA failure (>0.1 above nadir, confirmed by 2nd PSA)
  – Continued PSA increase
5 year PFS 48%

**Figure 1.** Kaplan-Meier Estimate of Progression-Free Probability After Salvage Radiotherapy
Path Gleason 8-10, (-) M, pre-RT PSA >2, PSADT<10 months, SVI

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preprostatectomy PSA level &gt;10 ng/mL</td>
<td>1.1 (0.8-1.4)</td>
<td>.73</td>
</tr>
<tr>
<td>Gleason score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-6</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>1.5 (0.98-2.2)</td>
<td>.06</td>
</tr>
<tr>
<td>8-10</td>
<td>2.6 (1.7-4.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Preradiotherapy PSA level, ng/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤1.0</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>1.1-2.0</td>
<td>1.2 (0.8-1.7)</td>
<td>.31</td>
</tr>
<tr>
<td>&gt;2.0</td>
<td>2.3 (1.7-3.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Negative surgical margins</td>
<td>1.9 (1.4-2.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PSA doubling time ≤10 mo</td>
<td>1.7 (1.2-2.2)</td>
<td>.001</td>
</tr>
<tr>
<td>Seminal vesicle invasion</td>
<td>1.4 (1.1-1.9)</td>
<td>.02</td>
</tr>
<tr>
<td>Extracapsular extension</td>
<td>1.2 (0.9-1.6)</td>
<td>.21</td>
</tr>
<tr>
<td>Positive lymph nodes</td>
<td>1.5 (0.7-3.0)</td>
<td>.32</td>
</tr>
<tr>
<td>Disease-free interval ≤12 mo</td>
<td>1.0 (0.7-1.3)</td>
<td>.71</td>
</tr>
<tr>
<td>Neoadjuvant androgen deprivation therapy prior to salvage radiotherapy</td>
<td>0.8 (0.5-1.1)</td>
<td>.16</td>
</tr>
<tr>
<td>Radiation dose &lt;6450 rad</td>
<td>1.0 (0.7-1.3)</td>
<td>.96</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; HR, hazard ratio; PSA, prostate-specific antigen. SI conversion factor: To convert rad to Gy, multiply rad values by 0.01.
Stephenson et al, conclusions

Poor predictors correlated with DISTANT METASTASES
(Local XRT does not address this)

Early Treatment is Better
(Best Prognosis in Patients with PSA<0.6)
Gleason, pre-RT PSA, margin status, PSADT

Stephenson et al. JAMA 291, 2004
Fig 2. Four-year progression-free probability after salvage radiotherapy for 1,326 patients who did not receive androgen-deprivation therapy before or during radiation therapy, stratified by preradiotherapy prostate-specific antigen (PSA), Gleason score, surgical margins, and PSA doubling time (PSADT). RT, radiotherapy; PFP, progression-free probability; CI, 95% CI.
Did he include a nomogram in this paper?

Also look at udpate of Hopkins experience. They seemed to show a benefit to salvage RT in pts w/ PSADT<6 mos...contrary to prior reports.

MD Anderson; 29/11/2009
Failure by PSA at initiation of salvage RT

Stephenson et al. J Clin Onc 2007; 25
14% HT before/during RT median duration of 4 months

Neoadjuvant androgen-deprivation therapy: Yes/No
Ideal candidate for *salvage* RT

- Patient has expected longevity to see benefit
- Favorable clinical presentation
  - E.g. PSA <10, PSA velocity < 2ng/ml per year
- Prostatectomy Gleason $\leq 3+4$
- Node negative, No SVI
- Margin positive
- Extra-prostatic extension
- Long interval to PSAF (e.g. $>2$ y, $>3$y?)
- PSADT $> 10$ months

- MDACC 70 Gy to CTV (+/- HT)
At simulation

Comfortably semi-full bladder (do NOT overfill...remember that these men are postop)
• Not overly distended rectum (+/- enema)
• Supine
• Leg immobilization
• Make sure patient is relaxed
• Scan from L5 through lesser trochanters
• 2-3 mm slices
• Consider “dry-run” simulation
Defining Structures

- Rectum
- Bladder
- Femoral heads
- CTV

- Use zoom
- Use window and level
- Use other planes of view (especially sag for apex)
Defining targets

- Use consensus guidelines as starting point
- Do NOT rely on surgical clips alone
- Preop imaging is the best if available
- Review op note, path report for gross size of prostate and site of positive margin
- Start inferiorly above UG diaphragm then up

- pT2 (no dz @ base) = prostate bed
- pT3a or pT2 w/ dz @ base = prostate bed +/- SV bed
- pT3b = prostate/SV bed (respecting tolerances)

- PTV = 7mm except 5-6 mm posteriorly
NOTE: Do **NOT** under-contour apex.

Almost all PZ, no capsule, common site for RT failures.

In very advanced cases, disease can track along membranous urethra.
Disease will not go through bladder wall, rectal wall, muscle
CTV

- Anterior-caudal:
  - Posterior edge of pubic symphysis

CTV

• Posterior-caudal:
  – Anterior rectal wall and levator ani
CTV

- Lateral-caudal:
  - Medial border of levator ani and obturator internus
CTV

• Anterior-cranial:
  – Posterior 1.5 cm of bladder wall
CTV

- Posterior-cranial:
  - Mesorectal fascia
CTV

- Lateral-cranial:
  - Sacrorectogenitopubic fascia
  - Lateral to neurovascular bundle
CTV

• Superior:
  – Superior most surgical clip or 5 mm above inferior border of vas deferens
Talk to surgeon about where clips were placed.

They may have little correlation to actual specimen.

MD Anderson; 29/11/2009
Defining Organs at Risk (OAR)

• **RECTUM:**
  From inferior ischium to anterior flexion of sigmoid
  Alternatively can use linear length of 10-11cm

• **BLADDER:**
  Entire bladder

• **FEMORAL HEADS:**
  Entire femoral head to lesser trochanter
PORT 66Gy to P+SV Beds

6600 Gy
6300 Gy
5940 Gy
5400 Gy
5000 Gy
During RT

- Kilovoltage 2D-2D matching on bone
- Check bladder filling before daily Rx w/ portable ultrasound
  - Too empty and too full are bad
- Intervene if lot of rectal gas
- CBCT is ok but may not be necessary
- Intent is to treat surgical bed
Patient example

- 62 yo M with rising PSA.
  - PSA 2.9 → 3.9
  - Clinical T2a
  - Biopsy: Gleason 3+3 and 3+4 in 7/12 Cores

- Robotic-assisted laparoscopic RP with bilateral nerve sparing and bilateral pelvic lymphadenectomy on 10/02/08
Again: Include probabilities of path endpoints using Partin tables as well as most recent Kattan nomogram.

MD Anderson; 29/11/2009
To maximize PSA control, what would you recommend?

(A) BILATERAL PELVIC LYMPH NODES:
Eleven lymph nodes, no tumor present.

(B) PROSTATE AND SEMINAL VESICLES:
PROSTATIC ADENOCARCINOMA, GLEASON SCORE 7 (3+4). (SEE COMMENT)
TUMOR EXTENDING TO THE MARGIN OF RESECTION.
NO EXTRAPROSTATIC EXTENSION PRESENT.
PROSTATIC INTRAEPITHELIAL NEOPLASIA (PIN), HIGH-GRADE.
Right and left seminal vesicles, no tumor present.
Segments of right and left vasa deferentia, no tumor present.
Include gross specimen size.

Also include extent of +M.

MD Anderson; 29/11/2009
• Patient declined adjuvant XRT; Feared further erectile dysfunction
• Dispositioned to PSA monitoring

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How do you calculate PSA-DT?
• Next Steps?

• Bone Scan: Low utility in this case
  – Questionable uptake in cervical spine
    • Cervical MRI: No evidence of metastasis

• Endorectal MRI:
  – No gross local recurrence
  – Questionable Mesorectal LN
    • (Biopsied – negative)
What is probability that bone scan will be revealing?

MD Anderson; 29/11/2009
SV beds received 48Gy, P bed boosted to 70Gy
What is the role of hormone therapy?

Look at the nomogram in Stephenson paper as well as the text. I think the nomogram may have a typo.

Also look at RTOG 96-04? Trial done, but not reported yet.

MD Anderson; 29/11/2009
POSTOP w/ IMRT/VMAT: Consider integrated boost

ADJUVANT: Prostate bed 64-66 Gy (32-33 fractions)

SALVAGE: Prostate bed 70Gy (35 fractions)

SV bed concurrently receives >57 Gy (35 fractions)
MDACC postop recommendations

• **ADJUVANT:**
  +M, path T3a-b 66 Gy

  Path node (+) no RP → 78 Gy to Prost/SV + HT
  Path node (+) s/p RP w/out +M → HT alone

• **SALVAGE RT (rising PSA)** 70 Gy (> 57Gy SV)

• Clinically palpable dz ≥72 Gy

• Consider short-term HT before and during RT
  – RTOG 9601 study w/ HT bicalutamide improved PFS & distant mets
  – EORTC conducting randomized study
Thank you