PORT after RP

Adjuvant

Or

Salvage
RT after RP

- 40-50% PSA relapse after RP in HR
- Definition: PSA should be undetectable within 6 weeks of RP
- Initial PSA is measured 6-12 weeks after RP
- AUA defines biochemical recurrence as PSA >0.2 after RP with second confirmation level >0.2
PORT

• Timing after RP
  • Adjuvant means immediate RT after RP for a very low or undetectable PSA; reserved for high risk features such as ECE, positive margins and SVI
  • Salvage means delayed RT for rising or persistently elevated PSA after RP or LR; success depends on PSA level, PSA doubling time and time to failure (and other risk factors)
Adjuvant RT after RP

• Rationale:
  • The overall risk of adverse factor after RP such as ECE, +ve margin or SVI up to 50%
  • Increased LF with high risk features
  • Adjuvant RT eradicates residual microscopic disease in the surgical bed
Adjuvant RT after RP

- **Pros:**
  - Improve local control (AND OS) by eradicating persistence disease in the prostate bed
  - Salvage treatment less effective than adjuvant RT?
  - Reduced risk of LF and PSA relapse
  - Reduction in distant metastasis
  - Delayed need for AD
Adjuvant RT after RP

- Cons:
  - Unnecessary RT for many patients
  - Increased morbidity
  - No survival benefit
  - Salvage possible if detected early
  - Financial cost
Adjuvant RT after RP

- SWOG randomized trial: n=425; pT3N0
- RT 60-64 Gy vs observation after RP
- Median Follow-up: 10.6 years
- OS similar; DM 8% vs 17% (p<.01)
- Median PSA RFS: 10 vs 3 years (p<.001)
- Adverse events: 24% vs 12%
  - Rectal (3.3% vs 0%), ureth. Strict. (18% vs 10%) and total urinary incontinence (6% vs 3%)
SWOG: analysis of treatment failure

- Predominant failure after RP is LOCAL (22% vs 8%)
- PSA < 0.2: BF 72% to 42%, LF 20% to 7% and DF 12% to 4% with adjuvant RT
- PSA 0.2 < 1.0: BF 80% to 73%, LF 25% to 9% and DF 16% to 12%
- PSA > 1.0: BF 94% vs 100%, LF 28% vs 9% and DF 44% vs 18%
**SWOG: analysis of treatment failure**

<table>
<thead>
<tr>
<th>Table 2. PSA Failure-Free Rates by Post-RP PSA Subgroup Among Patients Who Received Immediate or Delayed Radiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-RP PSA (ng/mL)</td>
</tr>
<tr>
<td>≤ 0.2</td>
</tr>
<tr>
<td>Immediate XRT</td>
</tr>
<tr>
<td>XRT at failure</td>
</tr>
<tr>
<td>&gt; 0.2 and ≤ 1.0</td>
</tr>
<tr>
<td>Immediate XRT</td>
</tr>
<tr>
<td>XRT at failure</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.
Adjuvant RT after RP (updated results)

- EORTC trial: n=1005; ≥ 1 path risk factors
- RT 60 Gy within 16 weeks vs wait and see
- Median Follow-up: 10.6 years
- OS and DM similar
- BPFS 60.6% vs 41.1% (p<0.0001)
- LC significantly improved; (LF 16.6% vs 7.3%)
- Grade 3 toxicity 5.3% vs 2.5%; p=0.052
  - ASTRO 2010
Adjuvant RT after RP

- German trial: ARO-96-02: n=385; pT3
- Undetectable PSA: n=307
- RT 60 Gy vs WS
- Median Follow-up: 40 months
- bNED 81% vs 60% (p<0.0001)
- Late rectal toxicity 3% (grade 2)
## Summary of PORT trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Inclusion criteria</th>
<th>Patients (n)</th>
<th>Median follow-up (y)</th>
<th>Biochemical progression-free survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EORTC 22911 (9)</td>
<td>pN0M0 tumors and ≥1 pathologic risk factors: capsular perforation, positive surgical margins, seminal vesicle invasion</td>
<td>1,005 (968 eligible)</td>
<td>5</td>
<td>74 vs. 52</td>
</tr>
<tr>
<td>SWOG 87-94 (10)</td>
<td>pT3N0M0 tumors and ≥1 pathologic risk factors: capsular perforation, positive surgical margins, seminal vesicle invasion</td>
<td>431 (425 eligible)</td>
<td>10.6</td>
<td>&lt;0.0001. 65 vs. 36 (median, 10.3 vs. 3.1) ≤0.001</td>
</tr>
<tr>
<td>German trial (11)</td>
<td>pT3 R0 or R1 tumors</td>
<td>385 (307 with undetectable PSA)</td>
<td>4.5</td>
<td>72 vs. 54</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
</tbody>
</table>
Summary of PORT trials (contd)

<table>
<thead>
<tr>
<th>Clinical progression-free survival (%)</th>
<th>Metastasis-free survival (%)</th>
<th>Overall survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>85 vs. 75</td>
<td>94 vs. 94</td>
<td>92 vs. 93</td>
</tr>
<tr>
<td>0.004</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>61 vs. 47</td>
<td>Median, 14.7 vs. 13.2</td>
<td>Median, 14.7 vs. 13.8</td>
</tr>
<tr>
<td>0.001</td>
<td>0.06</td>
<td>0.16</td>
</tr>
<tr>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>
SWOG update
Journal of Urology 2009

Figure 1. Metastasis-free survival by treatment arm
SWOG update
Journal of Urology 2009

Figure 2. Survival by treatment arm
SWOG update
Journal of Urology 2009

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Events/N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-Prostatectomy PSA*</td>
<td></td>
</tr>
<tr>
<td>Undetectable</td>
<td>106/249</td>
</tr>
<tr>
<td>Detectable (&gt;0.2)</td>
<td>76/127</td>
</tr>
<tr>
<td>Gleason Score**</td>
<td></td>
</tr>
<tr>
<td>Gleason 2-6</td>
<td>66/167</td>
</tr>
<tr>
<td>Gleason 7-10</td>
<td>73/155</td>
</tr>
<tr>
<td>Extent of Disease</td>
<td></td>
</tr>
<tr>
<td>Extracapsular or + Margins</td>
<td>133/286</td>
</tr>
<tr>
<td>Seminal Vesicle Involved</td>
<td>74/139</td>
</tr>
<tr>
<td>Overall</td>
<td>207/425</td>
</tr>
</tbody>
</table>

Hazard Ratio (Radiotherapy vs. Observation)

* Missing for 49 patients, ** Missing for 100 Patients
Size of box and diamond symbols are proportionate to sample size

Figure 3. Metastasis-free survival HR estimates and corresponding 95% CI for subsets of patients based on baseline risk factors
Figure 4. Metastasis-free survival for radiotherapy arm stratified by PSA status after prostatectomy.
Meta-Analysis of RCTs for adjuvant RT

Schema of the RCTs

- pT3 R0-1 or pT2 R1 pN0 (SM+, ECE, or SVI)
- Prostate CA post RP

RANDOMIZATION

- EORTC 22911 n=1005
- SWOG 8794 n=425
- ARO 96-02 n=307

Adjuvant RT
Observation
Meta-Analysis of RCTs for adjuvant RT

• Conclusions:
  • No path sub-group identified that fails to benefit from adjuvant RT including pT3R0
  • OS in SWOG trial in all groups including SM+, ECE+ and SVI+ considered individually
  • Further study for adjuvant RT is warranted in pT2 R1 disease
Salvage RT

- Stephenson et al JCO 2007
  - Largest salvage studies n=1540
  - 6 yr PFP after salvage RT 45%
  - Factors associated with post-RT progression
    - preRT PSA > 2.0
    - PSA DT ≤ 10 months
    - Negative SM
    - GS 8-10
  - Early salvage (at low PSA) more effective than late
Salvage RT

• Trock et al JAMA 2008
  • Retrospective comparison of
    • salvage RT (n=160) RT+ HT (n=78) or observe (n=397)
    • Med FU after RP and recurrence 9 & 6 yrs
    • Salvage RT: 3-fold reduction in PCSM vs observation
    • No benefit of adding HT (retrospective)
    • Benefit most in PSADT < 6mths and GS 8-10
    • Interestingly, this group is mostly denied salvage RT
Salvage RT

- Recommendations based on these trials:
  - Early salvage RT for rising PSA after RP
  - Not appropriate to wait for PSA to reach higher levels
  - No subgroups identified as yet where salvage RT could be considered futile (?even HR benefit from salvage although less likely to be cured)
  - Role of HT in combination with RT not clear
ADT CONCURRENT WITH SALVAGE RT

ASCO Post following publication of EORTC 22911 (PFS benefit for adj RT) → These remaining issues include questions about the optimal timing of irradiation (adjuvant vs early salvage), and whether there is a benefit of more aggressive therapy in the salvage setting, such as androgen deprivation therapy in combination with irradiation and/or extending the radiation field to include the pelvic nodes and prostate bed. These questions are being explored in the RADICALS-HD, RAVES, GETUG-17, EORTC 22043, RTOG 9601, and RTOG 0534 trials.
A PHASE III TRIAL OF RADIATION THERAPY WITH OR WITHOUT CASODEX IN PATIENTS WITH PSA ELEVATION FOLLOWING RADICAL PROSTATECTOMY FOR \( pT3N0 \) CARCINOMA OF THE PROSTATE

**Schema**

<table>
<thead>
<tr>
<th>S</th>
<th>Neoadjuvant Hormone Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>1. No</td>
</tr>
<tr>
<td></td>
<td>2. Yes</td>
</tr>
<tr>
<td>R</td>
<td>Positive Surgical (inked) Margins</td>
</tr>
<tr>
<td></td>
<td>1. No</td>
</tr>
<tr>
<td></td>
<td>2. Yes</td>
</tr>
<tr>
<td>A</td>
<td>PSA Nadir after Surgery &lt;0.5 ng/ml</td>
</tr>
<tr>
<td></td>
<td>1. No</td>
</tr>
<tr>
<td></td>
<td>2. Yes</td>
</tr>
<tr>
<td>I</td>
<td>Entry PSA level</td>
</tr>
<tr>
<td></td>
<td>1. 0.2 to 1.5 ng/ml</td>
</tr>
<tr>
<td></td>
<td>2. 1.6 to 4.0 ng/ml</td>
</tr>
</tbody>
</table>

**Notes**

- **Radiation Therapy**: 64.8 Gy in 36 fx (1.8 Gy in 5 daily sessions per week) to the original prostate volume, the tumor resection bed and the proximal membranous urethra.
- **Casodex or Placebo**: Patients will receive either one (150 mg) tablet of Casodex or placebo in a double-blinded fashion p.o. daily for two years beginning immediately upon, or just prior to, the initiation of irradiation.

**BCRFS at 7 yrs**: RT+ADT=57% vs. RT=40% (\( p<0.01 \))

**DM rate at 7 years**: RT+ADT=7.4% vs. RT=12.6% (\( p<0.04 \))

**ASTRO 2010 Report** (Too few events to assess survival yet)
Recent trials

• RTOG 9601 reported at ASTRO 2010; median FU: 7 yrs
• N=771 with pT3N0 or pT2N0 (+ve margins) with elevated PSA post-RP
• RT+AAT (bicalutamide for 24mth) vs RT alone (64.8Gy)
  • DM: 7.4% vs 12.6% (p<0.04); OS 91% vs 86%
  • FFP: 57% vs 40% p<0.0001 (GS<7 63% vs 50%; GS 7 55% vs 39% and GS 8-10 56% vs 26%)
• Late grade 3 and 4 GI/GU toxicity similar; cardiac 2.8% vs 1.8%
• Liver toxicity and Gynecomastia (mostly grades I/II; 89% vs 15%) higher
GETUG-AFU 16 (positive for PFS)

Phase III RCT short-term HT + RT for salvage after RP

**Background:** RT is the standard as salvage treatment after RP. The role of HT is not demonstrated to date. This trial assessed the efficacy of RT alone vs RT+HT on PFS for patients with BR after RP.

**Methods:**
- 743 pts with rising PSA after RP and undetectable PSA post-op
- Treated 2006-2010
- Patients were randomized (1:1; stratification on risk factors at RP and type of planned RT) to:
  - RT alone (66Gy on prostate bed +/- pelvic irradiation according to pN status and risk of initial node involvement), OR
  - RT+HT (goserelin, for 6 months)
- Assuming 5-year PFS of 45% for RT arm, the trial required 369 pts per arm to detect an improvement of 12% on PFS in RT+HT arm (90% power and 5% alpha risk). BR was evaluated according to ASTRO-consensus.

**Results:**
- Median age: 67yo
- Baseline characteristics:
  - pT2ac: 54%, pT3ac: 46%
  - gleason > 6: 76%
  - positive margins: 51%
  - seminal vesicles involvement 13%
  - PSA doubling time at relapse was > 6 months in 74%.
- Median follow-up was 63.1 months
- 216 events were notified (138 in RT vs 78 in RT+HT)
- The intent to treat analysis showed an **improved 5-yr PFS** of 62.1% vs 79.6% for RT+HT (p < 0.0001).
- 5-yr OS was 94.8% for RT vs 96.2% for RT+HT (p = 0.18).
- Cause of death was progressive disease in 2.1% pts on RT arm vs 0.8%.
- TOXICITY: Acute toxicities occurred more frequently in RT+HT arm (89% vs 79%). No difference was found in grade ³3 acute toxicities (1.9% vs 2.2%) and late toxicities (18.8% vs 21.9%). No toxic death was observed.

**Conclusions:** GETUG-AFU 16 is the first randomized trial comparing RT vs RT+ short HT as salvage treatment for BR after RP with undetectable post-op PSA. RT+HT significantly improve the 5-yr PFS without increasing acute or late grade 3 toxicities. A longer follow up is required to quantify the impact on OS but RT+HT could be considered as the standard in this situation.
Ongoing Phase III RCTS to address immediate adj vs. early salvage after RP:

- Radiotherapy and Androgen Deprivation in Combination After Local Surgery-Hormone Duration (RADICALS-HD)
  - UK and NCIC; aiming for 4000 patients
  - The trial has two randomizations steps:
    - Timing of RT
      - ADT for 6mon vs. no ADT
    - RT dose of 66 Gy to the prostatic fossa
  - Primary endpoint: 10-yr prostate-cancer-specific survival

- Radiotherapy Adjuvant Versus Early Salvage (RAVES)
  - Australia and New Zealand (TROG 08.03)
  - (Arm 1) Adjuvant RT (ART) commenced within 4 months of RP.
  - (Arm 2) Active surveillance with early salvage RT (SRT). The trigger for SRT is PSA level ≥ 0.2ng/ml. RT should commence as soon as possible (no later than 4 months) following the first PSA measurement ≥ 0.2ng/mL.
  - RT = 64Gy in 32 fractions to the prostate bed
  - Primary outcome = biochemical control and QOL

- Groupe d'Etude des Tumeurs Uro-Génitales (GETUG-17)
  - French
  - Hormonal therapy for 6 months
  - Primary endpoint EFS (including biochemical)
Long-Term Outcomes After High-Dose SRT
Goenka et al; IJROBP 2012

- N=285 (95% had $\geq$66 Gy and 72% $\geq$ 70 Gy)
- Median PSA before SRT 0.4 ng/ml
- 7 yr PSARFS: 37% and DMFS: 77%; LFFS: 94%
- On MVA: preRT PSA $>$0.4, -SM, VI, GS $>$7, SVI and no ADT predicted BF
- PSADT $<$ 3 months predictor of DM on MVA
Long-Term Outcomes After High-Dose SRT

Goenka et al; IJROBP 2012
Long-Term Outcomes After High-Dose SRT
Goenka et al; IJROBP 2012
Salvage RT

Factors:
- Pre-RT PSA
- Surgical margin
- PSA doubling time
- Gleason score
- Interval to PSA failure
- Pre-prostatectomy PSA
- SVI
<table>
<thead>
<tr>
<th>Localized Disease Favored</th>
<th>Systemic Disease Favored</th>
</tr>
</thead>
<tbody>
<tr>
<td>Margins positive</td>
<td>Margins negative</td>
</tr>
<tr>
<td>pT2</td>
<td>pT3 (ECE+ or SV+)</td>
</tr>
<tr>
<td>pGS ≤7</td>
<td>pGS ≥8</td>
</tr>
<tr>
<td>PSADT &gt;12 mo</td>
<td>PSADT &lt;6 mo</td>
</tr>
<tr>
<td>Undetectable PSA postop achieved</td>
<td>Detectable first postop PSA</td>
</tr>
<tr>
<td>No PNI/LVI</td>
<td>PNI/LVI</td>
</tr>
<tr>
<td>PSA at salvage</td>
<td>PSA at salvage</td>
</tr>
<tr>
<td>RT &lt;1 ng/mL</td>
<td>RT &gt;1 ng/mL</td>
</tr>
<tr>
<td>Time to detectable PSA &gt;1 y</td>
<td>Time to detectable PSA &lt;6 mo</td>
</tr>
</tbody>
</table>

Abbreviations: ECE, extracapsular extension; LVI, lymphovascular invasion; pGS, pathologic Gleason score; PNI, perineural invasion; PSA, prostate-specific antigen; PSADT, PSA doubling time; SV, seminal vesicle.
Timing of Salvage RT: Review

- King et al, Red Journal 2012
  - Based on 41 studies and 5597 patients
  - PSA level before salvage RT and RT dose: significant and independent factors for RFS after SRT
  - Better tumor control with lower PSA and higher dose of SRT
  - PSA ≤0.2 before SRT, RFS 64%
  - Therefore early SRT maybe an equivalent strategy to ART (Caution: not based on RCT)
Timing of Salvage RT: Review

2.6% loss of RFS per incremental 0.1 ng/mL PSA

Spearmen p<0.0001
Model fit p<0.0001

Relapse Free Survival (%) vs Median PSA pre-Salvage RT (ng/mL)
Timing of Salvage RT: Review

2% gain in RFS per incremental Gy

Spearman p=0.0052
Model fit p=0.0005
ART vs SRT

- Matched control analysis:
  - AIMRT 144 and SIMRT 134 matched according to preop PSA, GS, pTstage
  - Median Dose: 74 Gy and 76 Gy respectively
  - 3 yr bRFS: 90% vs 65%
  - Early SIMRT vs late SIMRT (86% vs 46%)
  - No diff in ESIMRT (PSA <0.5) vs AIMRT
• Clinical Investigation

• **Genomic Prostate Cancer Classifier Predicts Biochemical Failure and Metastases in Patients After Postoperative Radiation Therapy**
  
  Red Journal Vol. 89, 2014

• GC predicted BF and mets after post-RP RT. Lower GC may benefit from delayed RT; needs prospective validation
• GC uses a whole transcriptome microarray assay from formalin-fixed paraffin embedded PCa specimens; this signature was developed and validated as a predictor for clinical mets after RP
RT Techniques

- RT target based on sites of relapse:
  - Anastomosis (posterior more common), bladder neck and retrovesical space
  - Prostate bed includes bladder neck, NV bundles and periprostatic tissues including clips, remnants of SVs, inferiorly top of penile bulb, laterally medial aspect of OI muscle, posteriorly rectal wall
  - ?pelvic nodes
# Site of Bx proven relapse after RP

*Radiother Oncol* 2007

## Table 1

<table>
<thead>
<tr>
<th>Location of the local relapses in the prostatic bed after radical prostatectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients</strong></td>
</tr>
</tbody>
</table>
| Silverman [38] | 31 | Clinically detected or PSA rising, biopsy confirmed | 31 | Posterior: 16  
Anterior: 9  
Combination: 6  
-- |
| Connolly [10] | 61 | PSA rising biopsy confirmed | 42 | Posterior: 26  
Anterior: 5  
Lateral: 11  
Retrovesical: 8  
Bladder neck: 10  
Combination: 1 |
| Leventis [24] | 31 | Clinically detected or PSA rising, biopsy confirmed | 17 | Retrovesical: 2  
Bladder neck: 7  
Combination: 5 |
| Sella [36] | 39 | MRI detected (15/39 biopsy confirmed) | 12 | Retrovesical: 17  
Residual SV: 9  
Combination: 1 |
| **Total** | 162 | | 102 (63%) | Retrovesical: 27 (17%)  
Bladder neck: 17 (10%)  
Other: 16 (10%) |
Sites of local recurrence

Radiother Oncol 2007
Contouring for PORT

Radiother Oncol 2007
RT Delivery to prostate bed

- Daily reproducibility: stable internal anatomy
  - Comfortably full bladder
  - Diet to minimize rectal gas
  - Daily CBCT with feedback instructions to patient

- Rectal balloon; cumbersome and uncomfortable
- Retrograde urethrogram X

- Adaptive RT: ultimate solution
The boundaries for the planning target volume (PTV) should be: abutting the proximal penile bulb inferiorly, inclusive of seminal vesicle remnants superiorly, hugging the symphysis anteriorly, encroaching into the levator ani and obturator internus muscles laterally, and inclusive of the anterior rectal wall posteriorly. Finally, a generous inclusion within the PTV of regions with demonstrated pathologically involved margins should be made. The Radiotherapy Oncology Group (RTOG) has published consensus guidelines for the definition of the clinical target volume in the postoperative setting, which include a corresponding online computed tomography (CT) atlas.11
Ongoing SRT Trials

• Who, When, Where, and How: Salvage Prostate Cancer With Radiotherapy
  • Ongoing trials that aim to shed light on the benefits of adjuvant vs salvage radiotherapy include the RADICALS (Radiotherapy and Androgen Deprivation in Combination After Local Surgery), GETUG (Groupe d'Étude des Tumeurs Uro-Génitales)-17, and RAVES (Radiotherapy Adjuvant Versus Early Salvage following radical prostatectomy) studies
  • Is SRT equal to ART if initiated early
RADICALS

- MRC and NCIC conducted trial
  - RT & AD in combination after local surgery
  - Two random.: RT timing and HT duration
  - QOL: sexual, urinary and bowel function after PORT and AD (different durations)
  - Retrospective data shows advantage for STAD with salvage RT
RADICALS

RADICALS – RT timing randomisation: Immediate RT vs salvage RT post-operatively

Post-operative uncertainty about the need for immediate RT

RT timing RANDOMISATION

Immediate RT & Salvage RT Policy (RT for PSA failure)

RADICALS - hormone duration randomisation: Use of hormones with post-operative RT

Patient for post-operative RT (either immediate or salvage RT)

Hormone duration RANDOMISATION

Radiotherapy Alone & Radiotherapy + 6 months hormone therapy & Radiotherapy + 2 years hormone therapy

Fig. 1 — The RADICALS trial has two separate randomisations. Patients may take part in one or both.
Fig. 2. — Overall trial design.
Ongoing trials

- RTOG 0534: A PHASE III TRIAL OF SHORT TERM ANDROGEN DEPRIVATION WITH PELVIC LYMPH NODE OR PROSTATE BED ONLY RADIOTHERAPY (SUPPORT) IN PROSTATE CANCER PATIENTS WITH A RISING PSA AFTER RADICAL PROSTATECTOMY
A Phase III Trial of Short Term Androgen Deprivation with Pelvic Lymph Node or Prostate Bed Only Radiotherapy (SUPPORT) in Prostate Cancer Patients with a Rising PSA After Radical Prostatectomy

SCHEMA (1/8/09) (3/24/10)

<table>
<thead>
<tr>
<th>SV Involvement</th>
<th>S</th>
<th>T</th>
<th>R</th>
<th>P</th>
<th>I</th>
<th>F</th>
<th>Y</th>
<th>E</th>
<th>M</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. No</td>
<td>2. Yes</td>
<td>Prostatectomy Gleason Score</td>
<td>N</td>
<td>A</td>
<td>D</td>
<td>O</td>
<td>Arm 1: PBRT Alone</td>
<td>PBRT 64.8-70.2 Gy</td>
<td>Arm 2: PBRT + NC-STAD</td>
<td>PBRT 64.8-70.2 Gy + NC-STAD for 4-6 months, beginning 2 months before RT</td>
</tr>
</tbody>
</table>

SV = seminal vesicle; RT = radiotherapy; PBRT = prostate bed RT; PLNRT = pelvic lymph node RT; NC-STAD = neoadjuvant and concurrent short term androgen deprivation

NOTE: It is mandatory the treating physician determine the radiation therapy technique (3D-CRT vs. IMRT) to be used prior to the site registering the patient. See pre-registration requirements in Section 5.1. See details of radiation therapy and hormone therapy in Sections 6.0 and 7.0.

Patient Population: (See Section 3.0 for Eligibility) (3/31/09) (3/24/10)

Lymph node negative adenocarcinoma of the prostate treated with radical prostatectomy
Post-radical prostatectomy PSA of ≥ 0.1 - < 2.0 ng/mL; pathologic T3N0/Nx disease or pathologic T2N0/Nx disease, with or without a positive prostatectomy surgical margin; Gleason ≤ 9
<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Eligibility</th>
<th>Arms</th>
<th>RT Dose</th>
<th>ADT</th>
<th>Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>RADICALS: RT and ADT In Combo After Local Surgery MRC-UK</td>
<td>No path criteria, PSA cutoff 0.1</td>
<td>ART vs eSRT, PSA cutoff 0.1</td>
<td>66 Gy PB or WP</td>
<td>ADT: none vs 6 mo vs 2 years LHRH or bicalutamide, 150 mg</td>
<td>PCSS</td>
</tr>
<tr>
<td>RAVES: RT Adj. Vs Early Salvage Trans- Tasman (TROG)</td>
<td>pT3 or M+</td>
<td>ART vs eSRT, PSA cutoff 0.2</td>
<td>64 Gy</td>
<td>No ADT</td>
<td>bPFS</td>
</tr>
<tr>
<td>GETUG-17 French Urology Study Group</td>
<td>pT3 or M+</td>
<td>ART vs eSRT, PSA cutoff 0.2</td>
<td>64 Gy</td>
<td>ADT 6 mo LHRH</td>
<td>bPFS</td>
</tr>
<tr>
<td>Trial Name</td>
<td>Eligibility</td>
<td>Arms</td>
<td>RT Dose</td>
<td>ADT</td>
<td>End Point</td>
</tr>
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<td>------------</td>
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<tr>
<td>GETUG-16</td>
<td>pT2-4, PSA up to 20</td>
<td>RT alone vs RT w/ADT</td>
<td>66 Gy</td>
<td>ADT 6 mo LHRH</td>
<td>bPFS</td>
</tr>
<tr>
<td>RTOG 96-01</td>
<td>pT3 or M+, PSA &gt;0.2</td>
<td>RT alone vs RT w/ADT</td>
<td>64.8 Gy to PB</td>
<td>ADT 2 y bicalutamide 150 mg</td>
<td>OS</td>
</tr>
<tr>
<td>RTOG 05-34</td>
<td>pT3 or M+, PSA 0.1-2</td>
<td>RT to PB ± ADT vs RT</td>
<td>64.8-70.2 Gy to PB, to WP w/ADT</td>
<td>ADT 4-6 mo LHRH and bicalutamide</td>
<td>bPFS</td>
</tr>
</tbody>
</table>
Case Scenario

A 62-year-old gentleman s/p robotic assisted laparoscopic prostatectomy, with pGS 4 + 3, pT3aN0 with focally positive margin at apex, postop PSA at 3 months <0.01 ng/mL, and initial prostate-specific antigen (iPSA) was 12. He still has moderate stress urinary incontinence but has preserved erectile function.
A 58-year-old gentleman s/p robotic assisted laparoscopic prostatectomy, with pGS 3 + 4, pT2cNx, perineural invasion +, negative margins but described as pathologically close, and pre-op PSA 7. Postop PSA initially undetectable, but at 12 months postop, it was 0.05 ng/ml; at 15 months, it was 0.07; and at 18 months, it was 0.08. He has no urinary incontinence and has preserved erectile function.
A 70-year-old gentleman s/p radical retropubic prostatectomy, with pGS 4 + 4, pT3bN0, positive margins, postop PSA at 2 and 4 months was 0.08 and 0.12 ng/mL, respectively, and initial PSA was 4. Preop imaging was negative.
Conclusions

• Adjuvant RT should be considered for patients with high risk pathologic factors following RP
• Reduced morbidity with the use of contemporary techniques such as IMRT and IGRT
• When indicated, salvage RT should be considered at the earliest