Conventional RT in Prostate Cancer

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Introduction

- Prostate cancer is one of the most common cancer in men and is a very high cause of mortality. It is the second leading cancer after Lung in USA.

- Majority of new cases are non metastatic and 83% are confined to local or regional sites.
Risk stratification

NCCN 2008

- **Low**
  - T1-T2a
  - GS 2 to 6
  - PSA <10

- **Intermediate**
  - T2b-c
  - GS 7
  - PSA 10 - 20

- **High**
  - T3a
  - GS 8-10
  - PSA >20

- **very high**
  - T3b/T4 or N1)
Indications for RT

- **Definitive RT**
  - Any risk.
  - Optional in low risk.
  - Alternate to radical prostatectomy in intermediate and high risk.

- **Adjuvant RT**

- **Salvage RT** – local or biochemical recurrence following radical prostatectomy

- **Palliative** – bone/brain metastasis.

- **Preoperative Radiotherapy?**

  (Phase I - Supiot et al, Radiotherapy Oncology 2008)
Volume for RT

- Prostate ± seminal vesicles

- LN irradiation
  - For all high risk cases
  - Optional for intermediate risk cases
  - No LN irradiation for Low risk cases

- Brachytherapy alone for low risk
Role of Pelvic RT?
Figure 1. Distribution and localization of 9 selective fields for extended pelvic lymphadenectomy, including right external iliac (1), common iliac (2), obturator fossa (3) and internal iliac (4) lymph nodes, presacral lymph nodes (5), and left external iliac (6), common iliac (7), obturator fossa (8) and internal iliac (9) lymph nodes. (Reprinted with permission.)
Incidence of LN involvement

Portals must include external iliac, obturator, hypogastric and presacral
The "Partin tables" - developed by urologists Alan W. Partin, M.D., Ph.D., and Patrick C. Walsh, M.D. based on accumulated data from hundreds of patients treated for prostate cancer.

Based upon PSA, Gleason Score, and Clinical Staging, a probability is calculated for each of the following four:

**Organ Confined Disease, Extraprostatic Extension, Seminal Vesicle Invasion, and Lymph Node Invasion**
Using Partin nomogram - Roach used a formula to predict LN involvement

Risk of LN involvement = \((2/3)\text{PSA} + (\text{GS} - 6) \times 10\)
Factors favouring
- High percentage harbour occult pelvic LN mets
- If orderly spread from LN to distant sites - treating pelvis will have an impact on DFS and OS
- Therapeutic sterilization of known sites of disease

RTOG 85-31: in LA+positive pelvic nodes GS 7-10, def. RT+Adjuvant AS improves absolute survival from 39% to 49%

RTOG 86-10: LA + +ve pelvic nodes GS 2-6, def.RT+goserelene2mths prior+flutamide during RT -12% improvement in DFS and LC compared to RT alone
Contd.,

- **RTOG 94-13**: combined androgen suppression (CAS) and whole-pelvic (WP) radiotherapy (RT) followed by a boost to the prostate improves progression-free survival (PFS) by 10% compared with CAS and prostate-only (PO) RT. ([Roach M 3rd](#), et al 2003)

- Neoadjuvant HT + WPRT improves PFS in LA and High risk prostate cancer. No OS benefit ([Lawton C A et al](#) 2005)
Whole pelvic RT Contd.,

- RTOG 77-06: no benefit in survival with WPRT in localised prostate cancer

- Preliminary results of GETUG 1: pelvic irradiation was well tolerated but no improvement in PFS

- "Lack of benefit of pelvic radiation in prostate cancer patients with a high risk of positive pelvic lymph nodes treated with high-dose radiation.". Median f/u 4 yrs for all pts, 4.3 yrs for those high-risk pts. For the high-risk pts, there was no difference in clinical failure, CSS, or OS. (BF not assessed)
3. Terence Roberts and Mack Roach III
   Seminars in Radiation Oncology, Vol 13, No 2 (April), 2003
4. Is There a Role for Pelvic Irradiation in Localized Prostate Adenocarcinoma?


 Evidence is lacking for using pelvic fields in intermediate- and high-risk PCA. Suggest randomized trial for T3/T4 and GS \( \geq 4+3 \).
☐ In general 66-70 Gy /1.8-2Gy/Fr /5Fr/ week with conventional RT
☐ 45 – 50 gy whole pelvis + prostate boost up to 70.2 gy

☐ Based on stage –
  ☐ T1a – 66-70 Gy
  ☐ T1b,c – T2b – 70-72 Gy
  ☐ T2c – 74 Gy
<table>
<thead>
<tr>
<th>4 field</th>
<th>4 yr DFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>60 – 70 gy</td>
<td>54%</td>
</tr>
<tr>
<td>3DCRT</td>
<td></td>
</tr>
<tr>
<td>67-77gy</td>
<td>71%</td>
</tr>
<tr>
<td>74-78gy</td>
<td>77%</td>
</tr>
</tbody>
</table>

Pollack A Zagars G K et al. IJROBP 53:1097-1105, 2002
Adjuvant RT

- The rationale for treating patients at high risk for local recurrence with adjuvant radiation is well established for many tumor sites.

- Goal is to reduce the risk of local persistence of disease, thereby improving local control and the chance of remaining free of metastatic disease.

- The general rule for adjuvant radiotherapy is that local control is improved by about 40% to 50%.
postoperative radiation is a safe option in the patient at high risk for local recurrence based on adverse pathology or clinical features (e.g., extensive extracapsular disease, positive margins, high volume Gleason score >7, and so on). Administration of an adequate dose of prostate bed radiation (i.e., >64 Gy) in men with these adverse prognostic features appears to effectively reduce prostate-specific antigen (PSA) recurrence rates.

Richard K. Valicenti, et al:

Seminars in Radiation Oncology, Vol 13, No 2 (April), 2003: pp 130-140
Adjuvant RT contd.,

- The "Han tables" developed by urologists, Misop Han, M.D., Alan W. Partin, M.D., Ph.D., and Patrick C. Walsh, M.D., based on accumulated data from patients of prostate cancer treated at the James Buchanan Brady Urological Institute, Johns Hopkins Hospital.

- The Han Tables correlate the three common factors known about prostate cancer, PSA level, Gleason score, and clinical stage (or pathological stage). The Han Tables are used to predict the probability of prostate cancer recurrence up to 10 years following surgery. Based on the result of the probability of recurrence, pts and their doctors can decide the best course of treatment after surgery.

  - Based upon PSA, Gleason Score, and Clinical Stage, recurrence probability is calculated at 3, 5, 7, and 10 years following surgery (preop model)

  - Based upon PSA, Surgical Gleason Score, and Pathological Stage, recurrence probability is calculated at 3, 5, 7, and 10 years following surgery (postop model)
Adjuvant RT

- adjuvant RT has not been shown to improve overall survival compared with active surveillance. Longer follow-up from completed RCTs is required to accurately assess this outcome. Adjuvant RT does, however, significantly improve bPFS and is not associated with excess severe late toxicity.

(Morgan SC et al, Radiother Oncol. 2008 May 21. [Epub])
PSA recurrence; 8.5% (4/47) for low risk patients and 44.8% (30/67) for high risk. Tumor progression was seen in no low risk patient and in 9% (6) with high risk.

Immediate use of adjuvant treatment should be reserved for those patients with a high risk of recurrent disease

Patients with high-risk pathologic features, such as a positive margin or seminal vesicle involvement, have a 40% to 50% risk of developing biochemical failure at some point in the future. Because the morbidity of postoperative radiotherapy is relatively low, when pathologic high risk factors are present adjuvant radiotherapy should be considered.

Summary of Published Series Reporting Results of Adjuvant Radiation Therapy for T3N0M0 Prostate Cancer Compared With a Control Group

<table>
<thead>
<tr>
<th>Author</th>
<th>No. of Patients</th>
<th>Radiation Dose</th>
<th>Free of Progression</th>
<th>F/U (mo)</th>
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<tr>
<td>Gibbons</td>
<td>23</td>
<td>None 49 – 72 gy</td>
<td>70 NED 95</td>
<td>94 57</td>
</tr>
<tr>
<td>Morgan</td>
<td>33</td>
<td>None 60 – 66 gy</td>
<td>64 bNED 94</td>
<td>11</td>
</tr>
<tr>
<td>Anscher</td>
<td>46</td>
<td>None 55 – 65 gy</td>
<td>60 68</td>
<td>10 yrs</td>
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<tr>
<td>Stein</td>
<td>91</td>
<td>None 55 – 60 gy</td>
<td>43 bNED 75</td>
<td>48</td>
</tr>
<tr>
<td>Schild</td>
<td>228</td>
<td>None 57 – 68 gy</td>
<td>40 b NED 57</td>
<td>32</td>
</tr>
<tr>
<td>Valecenti</td>
<td>36</td>
<td>None</td>
<td>55</td>
<td>41</td>
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14/08/2013
Ongoing phase III randomized trials

- **Southwestern Oncology Group (SWOG) (protocol 9887/INT0086)**, which recently completed its accrual and
- **European Organization for Research and Treatment of Cancer (EORTC) (study 2291)**
  randomize patients after radical prostatectomy to observation or adjuvant radiation therapy to prostatic fossa

- **RTOG 96-01** is a randomized double-blind study in patients with pT2-T3 prostate cancer and/or positive surgical margins. With rising PSA between 0.2 ng/mL and 4 ng/mL are randomized to receive hormonal monotherapy (Casodex; AstraZeneca, Wilmington, DE, 150 mg daily) or a placebo for 2 years+prostatic fossa irradiation to a dose of 64.8 Gy.

- **RTOG P-0011** is a Randomized study to test whether the addition of androgen suppression to radiation therapy (63 to 66 Gy) leads to better outcome than each used separately in high risk postprostatectomy pts
Salvage Radiotherapy

- Low risk for disease progression (ie, PSA < 10 ng/mL, Gleason score 7, negative surgical margins) wait and watch policy provided salvage therapy is initiated early at the time of PSA relapse.
- High risk patients: immediate adjuvant RT to prostatic fossa with/without HT (RTOG 85-31)
  - GS ≤ 7, Pre RT PSA ≤ 2 ng/ml, +ve surg. margin or PSA DT > 10 mths, high probability of benefit from RT
  - SV+LN+PSA DT < 10 mths, lower probability of benefit from RT
Role of RT in PSA failure after Radical Prostatectomy

- Eqarva et al - RT is useful only in a small set of pts. RT is in adequate to eradicate the residual disease

- Moul J W - RT likely to benefit in patients with
  1. no adverse pathology
  2. low PSA at recurrence
  3. recurrence after one year
Palliative RT

- Bone Metastases
- Brain Metastases
- Visceral Metastases

Dose – 30 Gy /10 Fr

Conventional RT with minimal margins preferred
Current recommendations such as the NCCN advise 3DCRT +/- Brachytherapy or IMRT for prostate Ca

What then is the role of conventional RT today?
Conventional External beam RT

Treatment planning method wherein the prostate and other target tissues identified by the anatomy of surrounding structures (bony landmarks and contrast enhanced viscera)

First report of EBRT in curative treatment of Ca prostate

Important to realize that many centers still do not have the facilities of LINAC / IMRT or 3DCRT.

Brachytherapy needs experience and permanent implants are not practiced in many places in India.
No. of RT Centers : 214 (2006)

- Teletherapy Units : 363
- Cobalt-60 : 263
- Cesium-137 : 8
- Linac : 92
Conventional (2D) Technique

Treatment fields are generally 6x6 cm to 11x11 cm "four-field box" determined by bony landmarks, and if necessary rectal contrast and foley catheter.

For large fields, the superior border is set midway through the L5SI joint, inferior border at the level of ischial tuberosities, the lateral border 1.5-2.0cm lateral to the pelvic rim, the anterior border at the front edge of pubic symphisis, and the posterior border at the S2/S3 interspace.

For small fields and boost, the superior border extends to the top of the acetabulum and lateraly to include 2/3 of the obturator foramen.
RT technique

Portals – 4 Field

- **Superior** – L5- S1 Junction
- **Inferior** - 1 cm below the area in which the contrast narrows to a point on the urethrogram or lower border of ischial tuberosity
- **Lateral** - 1.5 -2 cm lateral to bony pelvis
  
  For lateral fields
  - **Anterior** - anterior portion of the pubic symphysis.
  - **Posterior**- S2-3 interspace to include the upper presacral lymph nodes.
Following 45-50 Gy to the whole pelvis the prostate is boosted up to 70 Gy.
Other method of boost – rotational arc – bilateral 120° arc
X ray simulation with retrograde urethrocystogram with contrast in the bulb of Folley's Catheter can be used for planning prostatic boost.
Conventional Vs 3DCRT

- In GS <4 ng/ml, T1b-c or T2 no statistically different DFS between conventional and conformal RT
  (Perez CA et al, Clin Prostate Cancer. 2002 Sep;1(2):97-104)
- In T1, T2, PSA <10ng/ml, at 67.7gy same rate of control as with higher doses (Pollack et al)

14/08/2013
Dr. Nirmala
Conventional RT

Advantages
- Time tested
- Easy to plan and execute
- Saves time especially in high volume centres
- Cost effective

Disadvantages
- More Normal tissue irradiated
- Dose escalation not possible
- Inferior results
Conformal RT

**Advantages**

- Better sparing of normal tissue
- Dose escalation
- 3D planning
- BEV
- DVH

**Disadvantages**

- Interphysician variability in target delineation
- Chance of missing tumour due to close margins
- Longer planning time
- Good QA
- Steep learning curve
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<tr>
<td>bladder [Cur]</td>
<td>166.4</td>
<td>155.7</td>
<td>93.6</td>
<td>3105.5</td>
<td>5085.9</td>
<td>5152.9</td>
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<td>rectum [Cur]</td>
<td>215.3</td>
<td>161.9</td>
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<td>3937.3</td>
<td>4954.0</td>
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<td>rectum</td>
<td>215.3</td>
<td>107.9</td>
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<td>957.8</td>
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<td>4048.2</td>
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<td>84.2</td>
<td>99.2</td>
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<td>5526.8</td>
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<td>PTV NEW Margin</td>
<td>957.8</td>
<td>504.2</td>
<td>52.6</td>
<td>3660.0</td>
<td>4705.9</td>
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<td>52.6</td>
<td>95.2</td>
<td>3638.6</td>
<td>5496.4</td>
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<tr>
<td>Name</td>
<td>Vol</td>
<td>DLV</td>
<td>DLV</td>
<td>D-X (cGy)</td>
<td>V-X (%)</td>
<td>Min</td>
<td>Max</td>
<td>Mean</td>
<td>Median</td>
<td>Modal</td>
<td>EUD</td>
</tr>
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<tr>
<td>BLADDER [Cur]</td>
<td>188.6</td>
<td>89.1</td>
<td>47.2</td>
<td>2941.5</td>
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<td>188.6</td>
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<td>52.0</td>
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<td>52.0</td>
<td>96.9</td>
<td>3660.8</td>
<td>5327.9</td>
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</tbody>
</table>
Table 28.6. Comparison of mean dosimetric parameters for 3D conformal or standard bilateral arc rotation in carcinoma of prostate. PTV planning target volume, ICRU International Commission on Radiation Units and Measurements. (From Perez et al. 1997)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Prostate irradiation only</th>
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<tbody>
<tr>
<td></td>
<td>3D conformal therapy</td>
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<tr>
<td>No. of observations</td>
<td>87</td>
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<tr>
<td>Percentage of PTV receiving the prescribed dose or more</td>
<td>92.9±13.9</td>
</tr>
<tr>
<td>ICRU dose (Gy)</td>
<td>69.1±2.6</td>
</tr>
<tr>
<td>Minimum tumor dose (Gy)</td>
<td>66.3±5.3</td>
</tr>
<tr>
<td>Mean tumor dose (Gy)</td>
<td>69.8±2.6</td>
</tr>
<tr>
<td><strong>Maximum dose (Gy)</strong></td>
<td><strong>71.7±2.4</strong></td>
</tr>
<tr>
<td>Percentage of volume rectum ≥65 Gy</td>
<td>33.7±15</td>
</tr>
<tr>
<td>Percentage of volume rectum ≥70 Gy</td>
<td>8.5±11.8</td>
</tr>
<tr>
<td>Percentage of volume bladder ≥65 Gy</td>
<td>22.3±12.5</td>
</tr>
<tr>
<td>Percentage of volume bladder ≥70 Gy</td>
<td>6.3±8.4</td>
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</table>

Perez et al. 1997
## Toxicities

<table>
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<tr>
<th>Toxicity</th>
<th>2D</th>
<th>3D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic rectal (GII or &gt;)</td>
<td>4%</td>
<td>0</td>
</tr>
<tr>
<td>Chronic GU (GII or &gt;)</td>
<td>6%</td>
<td>0</td>
</tr>
<tr>
<td>Acute urinary</td>
<td>26%</td>
<td>40%</td>
</tr>
<tr>
<td>Acute Gl</td>
<td>28%</td>
<td>26%</td>
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<tr>
<td>Erectile dysfunction</td>
<td>&lt;7%</td>
<td></td>
</tr>
</tbody>
</table>
Contraindications to RT

- Prior Pelvic Rt
- Acute Inflammatory disease of Rectum
- Permanent indwelling Folley’s Catheter
CONCLUSION

- Conventional RT is the standard of care in many centers in India
- It is time tested, easy to execute and less time consuming
- More cost effective
- If meticulously planned toxicity is comparable to 3DCRT
- Results slightly inferior to 3DCRT as dose escalation is not possible
- It provides the learning curve for the student