3D-CRT
Carcinoma Prostate

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3D-CRT in Ca Prostate

- Introduction
- Advantages in Ca-Prostate
- Steps of 3D-CRT in Ca Prostate
  - Patient Positioning
  - Immobilization
  - Planning Imaging
  - Target Volume Delineation
  - Computerized Planning
  - Plan Evaluation
  - Plan Implementation
  - Quality Assurance
- Clinical Outcome studies
- Conclusion
3D-CRT in Ca Prostate

**Introduction**

- Multi Leaf Collimators
  - Planning CT Scan/ MRI
  - Computerized Plan
    - 3 Dimensional Dose Evaluation
    - Dose Volume Histogram (DVH)
3D-CRT in Ca Prostate

**Introduction**

- The radiation beam is shaped to include a 3-dimensional anatomic configuration of the organ sparing adjacent normal tissue (BEV)
3D-CRT in Ca Prostate

Introduction

- This technique allows for more precise delivery of therapy to the target volume
3D-CRT in Ca Prostate

Advantages

- Relative immobility of the organ (typically <1 cm)
- Allows higher doses of radiation to the prostate without significant toxicity to the rectum and bladder
- Favorable dose-response relationships because of the ability to escalate the dose with less concern over the toxicity to normal tissue
- Fast treatment planning and delivery due to computer assistance
Steps of 3D-CRT in Ca Prostate

Patient positioning - Supine

- Supine position with knee support is standard

- Advantages
  - Ease of daily setup for the patient and staff
  - The ability to fuse treatment-planning images with previously obtained diagnostic images (i.e., MRI)
Steps of 3D-CRT in Ca Prostate

Patient positioning - *Prone*

- Prone position is being used in some institutes

- Advantage-
  - Relative sparing of small bowel from the radiation portals
Steps of 3D-CRT in Ca Prostate

Immobilization

- **External**
  - Thermoplastic Mask (Aquaplast, Orfit)
  - Vacuum shaping bags (Vac Lock)

- **Internal**
  - Rectal balloon
Steps of 3D-CRT in Ca Prostate Planning Imaging – CT Scan

- Advantages
  - Widely available
  - Density data is used for dose computing

- Disadvantages
  - Prostate apex is not well defined
Steps of 3D-CRT in Ca Prostate Planning Imaging – MRI Scan

- **Advantages**
  - Prostate apex is well defined, tumor volume delineation is more precise

- **Disadvantages**
  - Can’t use MRI images for dose computing
  - Fusion of MRI with CT may not be perfect
Steps of 3D-CRT in Ca Prostate Planning Imaging – PET-CT Scan

- **Limitations**
  - Minimal or no uptake of FDG in prostate – due to lipid metabolism
  - Not widely available

- **Advantages**
  - Precise tumor vol delineation in FDG avid disease (e.g. involved LN)
Steps of 3D-CRT in Ca Prostate
Target Volume Delineation

- CTV and PTV are identified on each relevant axial CT slice

- Normal structures outlined on each CT slice:
  - bladder wall, rectum, small bowel, & bony structures
Guidelines for primary radiotherapy of patients with prostate cancer

Dirk Boehmer\textsuperscript{a,*}, Philippe Maingon\textsuperscript{b}, Philip Poortmans\textsuperscript{c}, Marie-Hélène Baron\textsuperscript{d}, Raymond Miralbell\textsuperscript{e}, Vincent Remouchamps\textsuperscript{f}, Christopher Scrase\textsuperscript{g}, Alberto Bossi\textsuperscript{h}, Michel Bolla\textsuperscript{i}, on behalf of the EORTC radiation oncology group

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Steps of 3D-CRT in Ca Prostate
CTV- Prostate alone

- In EBRT, whole prostate constitutes CTV

- Low risk of Seminal vesicle invasion or Extra-capsular Invasion
  - Low risk patients with <50% positive biopsies
  - Intermediate risk pts with <17% positive biopsies
CTV- Prostate alone
Steps of 3D-CRT in Ca Prostate

CTV- Prostate + Seminal Vesicles

- Increased levels of capsular invasion is associated with increased risk of SVI or LN metastasis

- Perineural invasion is associated with Extracapsular Extension as well as high Gleason Score

- In intermediate risk pts, 1cm of seminal vesicles may be included in CTV

- In high risk pts, 2cm of seminal vesicles may be included in CTV
Steps of 3D-CRT in Ca Prostate
CTV- Prostate + 5mm margin

- In patients with intermediate and high risk prostate ca additional margin of 5mm of periprostatic tissue should encompass CTV
CTV- Prostate + Seminal Vesicles
CTV- Prostate + 5mm margin
Steps of 3D-CRT in Ca Prostate

PTV = CTV + margin

**TABLE 1**

Summary of target definitions and dose prescriptions for prostate IMRT

<table>
<thead>
<tr>
<th>Study</th>
<th>GTV</th>
<th>CTV</th>
<th>PTV</th>
<th>Prescription (TD/FS) in Gy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zelefsky et al</td>
<td>NS</td>
<td>P + SV</td>
<td>CTV + 1.0 cm UE</td>
<td>PTV: 81/1.8, ≥ 90% to receive ≥ 70</td>
</tr>
<tr>
<td>81-Gy plan</td>
<td></td>
<td></td>
<td>(0.6 cm posterior)</td>
<td></td>
</tr>
<tr>
<td>86.4-Gy plan</td>
<td>NS</td>
<td>P + SV</td>
<td>CTV + 1.0 cm UE</td>
<td>PTV: 86.4/1.8, ≥ 85% to receive ≥ 86.4</td>
</tr>
<tr>
<td>Ezzell et al</td>
<td>NS</td>
<td>P + SV</td>
<td>CTV + 1.0 cm UE</td>
<td>75.6/1.8 to ≥ 95% CTV</td>
</tr>
<tr>
<td>Jani et al</td>
<td>P + SV</td>
<td>CTV1 = GTV1</td>
<td>PTV1 = CTV1 + 1.0 cm UE</td>
<td>PTV1: 50/2</td>
</tr>
<tr>
<td>Phase I</td>
<td></td>
<td></td>
<td>(0.6 cm posterior)</td>
<td></td>
</tr>
<tr>
<td>Phase II</td>
<td>P</td>
<td>CTV2 = GTV2</td>
<td>PTV2 = CTV2 + 1.0 cm UE</td>
<td>PTV2: 24/2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.6 cm posterior)</td>
<td></td>
</tr>
<tr>
<td>Sethi et al</td>
<td>NS</td>
<td>NS</td>
<td>PTV1 = (P + SV) + 1.0 cm UE</td>
<td>PTV1: 55.8/1.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PTV2 = (P) + 1.0 cm UE</td>
<td>PTV2: 18/1.8, 25.2/1.8, or 34.2/1.8*</td>
</tr>
<tr>
<td>Teh et al*</td>
<td>NS</td>
<td>Prostatic fossa and periprostatic tissues</td>
<td>CTV + 0.5 cm UE</td>
<td>PTV: 60-66/2 to 86% line</td>
</tr>
</tbody>
</table>

CTV = clinical tumor volume; FS = fraction size; GTV = gross tumor volume; NS = not specified; P = prostate; PTV = planned treatment volume; SV = seminal vesicles; TD = total dose; UE = uniform expansion.

*Dose escalation (total dose, 73.8, 81, or 90 Gy)

† Subjects were studied postprostatectomy.
3D-CRT in Ca Prostate Target Vol Delineation

- The target volume and normal structures are digitally reconstructed in 3 dimensions and displayed with the beam's eye view (BEV) technique.
Steps of 3D-CRT in Ca Prostate Computerized Planning

- Fixation of Isocenter
- Selection of Beam angles
- Shielding of OARs (Organ at risk) with help of Beam’s Eye View (BEV)
- Dose Calculation
3D-CRT in Ca Prostate – 4 Fields
3D-CRT in Ca Prostate – 6 Fields
3D-CRT in Ca Prostate – 8 Fields
Steps of 3D-CRT in Ca Prostate
Plan Evaluation

- Isodose distribution in each CT Slice

- 3D Volumetric isodose evaluation
  - Dose-volume Histogram (DVH)
  - Sagital and Coronal image reconstruction
Steps of 3D-CRT in Ca Prostate
Plan Evaluation

- PTV Coverage
  - 95% isodose line

- Sparing of Normal Organs
  - Bladder – Post wall
  - Rectum – Ant wall
Cumulative Dose Volume Histogram

4 field 3D CRT

<table>
<thead>
<tr>
<th>V(CC)</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>External</td>
<td>16683.8</td>
<td>0.0</td>
<td>7049.0</td>
<td>913.0</td>
</tr>
<tr>
<td>CTV_Prostate</td>
<td>62.1</td>
<td>6882.0</td>
<td>7048.0</td>
<td>6959.3</td>
</tr>
<tr>
<td>PTV_Prostate</td>
<td>322.2</td>
<td>5263.0</td>
<td>7060.0</td>
<td>6911.5</td>
</tr>
<tr>
<td>OAR-Rectum</td>
<td>94.0</td>
<td>2686.0</td>
<td>6981.0</td>
<td>5523.7</td>
</tr>
<tr>
<td>OAR-Bladder</td>
<td>169.9</td>
<td>3743.0</td>
<td>7021.0</td>
<td>5672.4</td>
</tr>
<tr>
<td>A</td>
<td>31.3</td>
<td>6391.0</td>
<td>6981.0</td>
<td>6786.5</td>
</tr>
<tr>
<td>Copy of OAR-Bladder</td>
<td>54.6</td>
<td>6858.0</td>
<td>7028.0</td>
<td>6953.2</td>
</tr>
<tr>
<td>Copy of OAR-Rectum</td>
<td>54.1</td>
<td>3575.0</td>
<td>6815.0</td>
<td>5119.1</td>
</tr>
<tr>
<td>OAR-Bladder1</td>
<td>113.4</td>
<td>3740.0</td>
<td>6985.0</td>
<td>5155.2</td>
</tr>
<tr>
<td>DLC P</td>
<td>35.6</td>
<td>1895.0</td>
<td>3724.0</td>
<td>3258.6</td>
</tr>
</tbody>
</table>

#random points=1000 Volume min/max: 2.00 cc
Cumulative Dose Volume Histogram

Eight field 3D CRT

Steps of 3D-CRT in Ca Prostate
Plan Evaluation

- Rectal Wall 30% - 75.6 Gy
- Small bowel Dmax ≤ 50 Gy
- Large bowel Dmax ≤ 60 Gy
# Steps of 3D-CRT in Ca Prostate

## Plan Evaluation

## Dose Constraint

<table>
<thead>
<tr>
<th></th>
<th>Rectum</th>
<th>Bladder</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Zelefsky</td>
<td>&lt; 30% &gt; 75 Gy</td>
<td>&lt; 53% &gt; 47 Gy</td>
</tr>
<tr>
<td></td>
<td>&lt; 53% &gt; 47 Gy</td>
<td>&lt; 53% &gt; 47 Gy</td>
</tr>
<tr>
<td>2. Ezzell</td>
<td>&lt; 10% &gt; 75 Gy</td>
<td>&lt; 30 % &gt; 70 Gy</td>
</tr>
<tr>
<td></td>
<td>&lt; 30 % &gt; 70 Gy</td>
<td>Dmax &lt; 81</td>
</tr>
<tr>
<td>3. Sethi</td>
<td>&lt; 30% &gt; 65 Gy</td>
<td>&lt; 30% &gt; 65 Gy</td>
</tr>
</tbody>
</table>
Steps of 3D-CRT in Ca Prostate Plan Implementation

- Simulation
- Comparison of Simulator film with DRR (Digitally reconstructed radiograph)
- Transfer of Computer Plan to treatment machine
- Remote controlled treatment delivery
Steps of 3D-CRT in Ca Prostate

Quality Assurance

- Comparison of port film with Simulator film and DRR image
- EPID (Electronic portal imaging device) imaging with correction of set-up errors
Table 2. Principles of Radiotherapy, According to the National Comprehensive Cancer Network.

<table>
<thead>
<tr>
<th>Three-dimensional conformal or intensity-modulated radiotherapy techniques should be used.</th>
</tr>
</thead>
</table>

Doses of 70 to 75 Gy in 35 to 41 fractions to the prostate (with or without inclusion of the seminal vesicles for part of the therapy) appear to be appropriate for patients with low-risk cancers, whereas for patients with intermediate- or high-risk disease, doses of 75 to 80 Gy appear to provide improved disease control as assessed on serum PSA testing.

Patients with high- or very-high-risk cancers are candidates for radiotherapy to the pelvic lymph nodes with neoadjuvant or adjuvant androgen-suppression therapy, or both.

If target margins are reduced, such as for the administration of doses greater than 75 Gy, extra attention to daily image guidance, with the use of techniques such as implanted markers, transabdominal ultrasonography, or endorectal balloon, is indicated.
3D-CRT in Ca Prostate Clinical Outcome Studies

Table 11: Summary of results in recent three-dimensional conformal radiation therapy (3D-CRT) series

<table>
<thead>
<tr>
<th>Series</th>
<th>Patients Description</th>
<th>Biochemical freedom from failure (prostate-specific antigen &lt; 1 ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roach et al., 1996 (13)</td>
<td>501 T1-T2</td>
<td>90% 4-year</td>
</tr>
<tr>
<td></td>
<td>IPSA &lt; 4 ng/mL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IPSA 4-10 ng/mL</td>
<td>60% 4-year</td>
</tr>
<tr>
<td></td>
<td>IPSA 10-20 ng/mL</td>
<td>35% 4-year</td>
</tr>
<tr>
<td></td>
<td>IPSA &gt; 20 ng/mL</td>
<td>30% 4-year</td>
</tr>
<tr>
<td>Zelefsky et al., 1998 (28)</td>
<td>213 T1-T2 (leuprolide and flutamide given 3 months before 3D-CRT)</td>
<td>93% 5-year</td>
</tr>
<tr>
<td></td>
<td>IPSA ≤ 10 ng/mL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IPSA &gt; 10 ≤ 20 ng/mL</td>
<td>60% 5-year</td>
</tr>
<tr>
<td></td>
<td>IPSA &gt; 20 ng/mL</td>
<td>40% 5-year</td>
</tr>
<tr>
<td>Anderson et al., 1998 (29)</td>
<td>172 T1-T2a,b; Gleason score 2-6; no PNI</td>
<td>91%* 5-year</td>
</tr>
<tr>
<td></td>
<td>94 T2c-T3 or Gleason score 7-10 or PNI</td>
<td>74%* 5-year</td>
</tr>
</tbody>
</table>

IPSA = initial PSA; PNI = perineural invasion.
* p = 0.0024 (definition of failure was PSA ≥ 1.5 ng/mL and two consecutive rises).
Ca Prostate Dose Escalation 3D-CRT

- 743 pts, Phase I Study
- Radiation dose
  - increased from 64.8 to 81 Gy in increments of 5.4 Gy
- Evaluation
  - PSA ≤ 1ng/ml
  - Prostate biopsy after 2.5 yrs
- Results
  - 75.6-81 Gy - 90% achieved PSA <1ng/ml
  - 70.2 Gy – 76% achieved PSA <1ng/ml
  - 64.8 Gy – 56% achieved PSA <1ng/ml

5 yr actuarial PSA relapse free survival for favourable gr, intermediate gr and unfavourable gr was 85%, 65% and 35%

Zelefsky, IJROBP 1998
Ca Prostate - 3D-CRT Vs Std RT

- 3D CRT
  - 312 pts
  - T1b-c-T2
  - 68-74 Gy

- Standard RT
  - 135 pts
  - T1b-c-T2
  - 68-70 Gy

- GS <4  No chemical disease free survival difference
- GS 5-7  5 yr Survival 83% Vs 59%

- PSA <10  chemical disease free survival rate 80% Vs 72%
- PSA 10-20  survival rate 71% Vs 43%
- PSA >20  survival rate 59% Vs 16%

- Bladder toxicity (Moderate dysuria)  2-5% Vs 6-9%
- Rectal toxicity  Diarrhea  3-5% Vs 8-19
  Rectal bleeding  1% Vs 7%

Perez, Clin Prost Cancer 2002
Ca Prostate- Dose Escalation 3D-CRT

- 1473 pts
- Dose was increased from 60 to 80.4 Gy

“For intermediate-risk pts, each 1-Gy increment in total radiation dose was associated with a highly significant 8% reduction in the probability of failure

(hazard ratio = 0.92, p = 0.005)”

Symon, IJROBP 2003
Ca Prostate- Dose Escalation 3D-CRT

- 1325 pts from 9 institutes
- Radiation dose
  - 1061 pts <72 Gy, 15% of pts had high-risk disease
  - 564 pts >72 Gy, 22% of pts had high-risk disease
- The 5-year PSA-DFS estimates for <72 Gy vs. > or =72 Gy were 63% vs. 69%, respectively (p = 0.046).

“Higher than conventional RT were associated with improved PSA-DFS when controlled for the influence of pretreatment PSA levels, biopsy GS, and clinical T stage”

Kupelian, IJROBP 2005
Ca Prostate Dose Escalation 3D-CRT

- 839 pts
- Radiotherapy (RT) dose
  - < 72 Gy,
  - 72 to 75.9 Gy
  - >=76 Gy

“RT dose escalation to 76 Gy or greater improved patient outcome for all prognostic groups except those at the favorable and unfavorable extremes.”

Pollack, J Urol 2004
### Early Ca Prostate
Sequelae with diff treatment modalities

<table>
<thead>
<tr>
<th>MODALITY</th>
<th>RECTAL TOXICITY</th>
<th>INCONTINENCE</th>
<th>IMPOTENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>SURGERY</td>
<td>1% (Catalona et al 1999). 1.1% (Guillonneau 1999)</td>
<td>80% (.post surgery)</td>
<td>66% (neve spring)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6% (.late; 1 year later)</td>
<td>75% (standard RP)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>53% (Schwartz et al 2002)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>25% ((Guillonneau 1999) (6 months).</td>
<td></td>
</tr>
<tr>
<td>CEBRT</td>
<td>29.6% (Scwartz et al 2002). 14% (Storey et al 2000).</td>
<td>19.2% (Scharwz et al 2002).</td>
<td>45% (Robinson et al 2002).</td>
</tr>
<tr>
<td></td>
<td>15% (Dearnaley et al 1999).</td>
<td>20% (Storey et al 2000).</td>
<td>50% (Bagshawet al 1988).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10% (Lawton et al 1991).</td>
<td>35% (Schroder et l 2000).</td>
</tr>
<tr>
<td>3D-CRT</td>
<td>21% (Storey et al 2000). 5% (Dearnaley et al 1999).</td>
<td>9% (Storey et al 2000).</td>
<td>40% (Robinson et al 2002)</td>
</tr>
<tr>
<td>BRACHYTHERAPY</td>
<td>1% (Koutrouvelis et al 2003). 1% (Kang et al 2002).</td>
<td>1% (Koutrouvelis et al 2003).</td>
<td>24% (Robinson etal).</td>
</tr>
<tr>
<td></td>
<td>2% (Syed et al 2001) 3% ( Schroder et al 2000).</td>
<td>2% (Syed et al 2001)</td>
<td>7% (Nag S. 1985).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3% (Schroder et al 2000).</td>
<td></td>
</tr>
</tbody>
</table>
3D-CRT in Ca Prostate

Conclusions

- 3D-CRT has definite advantages over conventional EBRT in Prostate Cancer

- 3D-CRT allows sparing of normal tissues (i.e. rectum and bladder) to a greater extent resulting in significant reduction in short-term and long-term toxicities

- 3D-CRT allows higher doses of radiation to the prostate resulting in improved outcome, especially in intermediate-risk group pts

- 3D-CRT allows fast treatment planning and delivery due to computer assistance
3D-CRT in Ca Prostate

Conclusions contd..

- RT dose to Prostate should be **70-75 Gy in low-risk pts and 75-80 Gy in intermediate and high-risk pts** are appropriate for tumor control.

- RT dose to Pelvic LN should be **45 Gy for elective LN radiation and 55-60 Gy for involved LN in pts with high-risk group**.
Changing beam **shapes**!

Does it really make a difference?
Changing beam shapes!

‘No Ext beam regimen is superior to another In reduction of mortality rates’

Results from 18 RCT and 473 observation studies

I am still going strong!

“3D-CRT could still be used to deliver effective doses in prostate”
Many Thanks

Dr. Vijay Anand Reddy P
MD, DNB, (RO), Med Onc (ESMO)
Director
Apollo Cancer Hospital, Hyd
Thank You!
Summary

- Dose escalation possible
- Good dose conformity to PTV
- Better sparing of normal structures
- Cost effective!
- 3D CRT is still the standard of care
<table>
<thead>
<tr>
<th>MODALITY</th>
<th>Disease Free Survival (10 Years)</th>
<th>Overall survival (10 Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3D-CRT</td>
<td>73% (3 years  Geinizet aal 2002). 78%(3 years , Dearnaley et al 1999).</td>
<td></td>
</tr>
</tbody>
</table>
Then and Now

Conv RT

3D CRT

A sketch of a simple 3-beam conformal radiotherapy geometry.

IMRT

Some images and diagrams illustrating different radiation therapy techniques.