Role of Different Fractionation and 2 D Radiation Planning for Prostate Ca

SUN ICRO PG Webinar
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Radiation options for Ca Prostate

Conventional EBRT

Hypofractionation
**\(\alpha/\beta\) Ratio** defines “curviness” of survival curve

Based on \(\alpha/\beta\) ratio, the body tissues have been divided into two categories.

**Late Reacting Tissue**

- \(\alpha/\beta = 1\text{ Gy to 7 Gy (3Gy)}\)
- \(D = \alpha/\beta\)

**Early Reacting Tissue**

- \(\alpha/\beta = 6\text{ Gy to 15 Gy (10Gy)}\)

Malignant Tissue behave like early reacting tissue with average \(\alpha/\beta = 6\text{ Gy to 15 Gy (10Gy)}\)
Increase in dose per fraction damages the tissue with low $\alpha/\beta$ ratio more than tissue with high $\alpha/\beta$ ratio.

We usually do not go more than 2 Gy per fraction.
Hypofractionation In Prostate Ca

• Two major approaches

  • Moderate hypofractionation
    2.5 – 3.5 Gy/#

  • Extreme hypofractionation/ Ultrahypofractionation
    > 5 Gy/#
Moderate hypofractionation
## Moderate hypofractionation trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Risk group</th>
<th>Arms</th>
<th>EQD2 (1.8)</th>
<th>Primary outcome</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHHiP</td>
<td>LR – 15%</td>
<td>1. 74Gy/37# (1065)</td>
<td>74</td>
<td>Biochem – clinical failure</td>
<td>1. Standard arm</td>
</tr>
<tr>
<td></td>
<td>IR – 73%</td>
<td>2. 60Gy/20# (1074)</td>
<td>75.8</td>
<td></td>
<td>2. Non inferior</td>
</tr>
<tr>
<td></td>
<td>HR – 12%</td>
<td>3. 57Gy/19# (1077)</td>
<td>72</td>
<td></td>
<td>3. Not non-inf</td>
</tr>
<tr>
<td>PROFIT</td>
<td>IR</td>
<td>1. 78Gy/39# (598)</td>
<td>78</td>
<td>Biochem – clinical failure</td>
<td>1. Standard arm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. 60Gy/20# (407)</td>
<td>75.8</td>
<td></td>
<td>2. Non inferior</td>
</tr>
<tr>
<td>RTOG 0415</td>
<td>LR</td>
<td>1. 73.8Gy/41# (542)</td>
<td>69.9</td>
<td>DFS</td>
<td>1. Standard arm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. 70Gy/28# (550)</td>
<td>79.2</td>
<td></td>
<td>2. Non inferior</td>
</tr>
<tr>
<td>HYPRO</td>
<td>IR – 26%</td>
<td>1. 78Gy/39# (397)</td>
<td>78</td>
<td>RFS</td>
<td>1. Standard arm</td>
</tr>
<tr>
<td></td>
<td>HR – 74%</td>
<td>2. 64.5Gy/19# (407)</td>
<td>88.2</td>
<td></td>
<td>2. Not superior</td>
</tr>
<tr>
<td>Trial</td>
<td>Arms</td>
<td>EQD2 (10)</td>
<td>Peak acute toxicity (Grade II or more)</td>
<td>GU (%)</td>
<td>p value</td>
</tr>
<tr>
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</tr>
<tr>
<td><strong>CHHiP</strong> (n - 3216)</td>
<td>1. 74Gy/37# (1065)</td>
<td>74</td>
<td>46</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. 60Gy/20# (1074)</td>
<td>65</td>
<td>49</td>
<td>NS</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>3. 57Gy/19# (1077)</td>
<td>61.8</td>
<td>46</td>
<td>NS</td>
<td>S</td>
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<tr>
<td><strong>PROFIT</strong> (n- 1204)</td>
<td>1. 78Gy/39# (598)</td>
<td>78</td>
<td>27</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. 60Gy/20# (407)</td>
<td>65</td>
<td>27</td>
<td>NS</td>
<td>S</td>
</tr>
<tr>
<td><strong>RTOG 0415</strong> (n – 1067)</td>
<td>1. 73.8Gy/41# (542)</td>
<td>72.6</td>
<td>24.7</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. 70Gy/28# (550)</td>
<td>72.9</td>
<td>23.7</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td><strong>HYPRO</strong> (n – 800)</td>
<td>1. 78Gy/39# (397)</td>
<td>78</td>
<td>58</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. 64.5Gy/19# (407)</td>
<td>72</td>
<td>61</td>
<td>NS</td>
<td>S</td>
</tr>
</tbody>
</table>

S – Significant; NS – Non significant

Irrespective of the peak acute toxicity, the rates of acute toxicity at the end of 3 months were similar in all studies.
## Late Toxicity

<table>
<thead>
<tr>
<th>Trial</th>
<th>Arms</th>
<th>EQD2 (3)</th>
<th>Late toxicity (Grade II or more)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>GU (%)</td>
<td>p value</td>
<td>GI (%)</td>
<td>p value</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHHiP</td>
<td>1. 74Gy/37# (1065)</td>
<td>74</td>
<td>9.1</td>
<td>-</td>
<td>13.7</td>
</tr>
<tr>
<td>(n - 3216)</td>
<td>2. 60Gy/20# (1074)</td>
<td>72</td>
<td>11.7</td>
<td>NS</td>
<td>11.9</td>
</tr>
<tr>
<td></td>
<td>3. 57Gy/19# (1077)</td>
<td>68.4</td>
<td>6.6</td>
<td>NS</td>
<td>11.3</td>
</tr>
<tr>
<td>PROFIT</td>
<td>1. 78Gy/39# (598)</td>
<td>78</td>
<td>22.0</td>
<td>-</td>
<td>13.9</td>
</tr>
<tr>
<td>(n- 1204)</td>
<td>2. 60Gy/20# (407)</td>
<td>72</td>
<td>22.2</td>
<td>NS</td>
<td>8.9</td>
</tr>
<tr>
<td>RTOG 0415</td>
<td>1. 73.8Gy/41# (542)</td>
<td>70.8</td>
<td>20.5</td>
<td>-</td>
<td>11.4</td>
</tr>
<tr>
<td>(n – 1067)</td>
<td>2. 70Gy/28# (550)</td>
<td>77</td>
<td>26.2</td>
<td>S</td>
<td>18.3</td>
</tr>
<tr>
<td>HYPRO</td>
<td>1. 78Gy/39# (397)</td>
<td>78</td>
<td>39.0</td>
<td>-</td>
<td>17.7</td>
</tr>
<tr>
<td>(n – 800)</td>
<td>2. 64.5Gy/19# (407)</td>
<td>82.5</td>
<td>41.3</td>
<td>NS*</td>
<td>21.9</td>
</tr>
</tbody>
</table>

* Non-inferiority could not be confirmed; S – Significant; NS – Non significant

No Significant difference
Comments

• Pelvic LN stations were not treated

• Outcomes compared in these trials are imperfect surrogates for meaningful oncologic outcomes (Overall survival)

• Long term data will give a clearer picture to frame guidelines
Extreme hypofractionation (Ultrahypofractionation)
## Extreme hypofractionation trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Risk group</th>
<th>Arms</th>
<th>EQD2 (1.8)</th>
<th>Primary outcome</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR – 11%</td>
<td>2. 42.7Gy/7# (589)</td>
<td>88.8</td>
<td></td>
<td>2. Non inferior</td>
</tr>
<tr>
<td>Munsuru et al (n- 582)</td>
<td>LR</td>
<td>1. 76Gy/38# (66)</td>
<td>76</td>
<td>6yr Bioch – clinical failure</td>
<td>Not reported</td>
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<tr>
<td></td>
<td></td>
<td>2. 35Gy/5# (84)</td>
<td>81.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Katz et al. (n – 515)</td>
<td>LR – 63%</td>
<td>35 – 36.25 Gy/5# (515)</td>
<td>81.1 – 86.3</td>
<td>8yr DFS</td>
<td>1.93.6%</td>
</tr>
<tr>
<td></td>
<td>IR – 30%</td>
<td></td>
<td></td>
<td></td>
<td>2. 84.3%</td>
</tr>
<tr>
<td></td>
<td>HR – 7%</td>
<td></td>
<td></td>
<td></td>
<td>3.65.0%</td>
</tr>
<tr>
<td>Loblaw et al. (n – 602)</td>
<td>LR</td>
<td>1. 74 – 79.8Gy/37 – 42# (40)</td>
<td>74 – 78</td>
<td>6yr bFFS</td>
<td>1.Standard arm</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>81.1</td>
<td></td>
<td>2. Better sig</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. 35Gy/5# (40)</td>
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</tr>
</tbody>
</table>
## Acute Toxicity

<table>
<thead>
<tr>
<th>Trial</th>
<th>Arms</th>
<th>EQD2 (10)</th>
<th>Peak acute toxicity (Grade II or more)</th>
<th>GU (%)</th>
<th>p value</th>
<th>GI (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HYPO–RT–PC</strong> (n - 1200)</td>
<td>1. 78Gy/39# (591)</td>
<td>78</td>
<td>23</td>
<td>-</td>
<td>-</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2. 42.7Gy/7# (589)</td>
<td>57.3</td>
<td>28</td>
<td>NS</td>
<td>8</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td><strong>Munsuru et al</strong> (n- 582)</td>
<td>1. 76Gy/38# (66)</td>
<td>76</td>
<td>NR</td>
<td>-</td>
<td>NR</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. 35Gy/5# (84)</td>
<td>49.6</td>
<td></td>
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<tr>
<td><strong>Katz et al.</strong> (n – 515)</td>
<td>35 – 36.25 Gy/5# (515)</td>
<td>49.6 – 52.1</td>
<td>0</td>
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</tr>
<tr>
<td><strong>Loblaw et al.</strong> (n – 602)</td>
<td>1. 74 – 79.8Gy/37 – 42# (40)</td>
<td>74 – 79</td>
<td>-</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>2. 35Gy/5# (40)</td>
<td>49.6</td>
<td>0</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td></td>
</tr>
</tbody>
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*S – Significant; NS – Non significant*
## Late Toxicity

<table>
<thead>
<tr>
<th>Trial</th>
<th>Arms</th>
<th>EQD2 (3)</th>
<th>Cumulative late toxicity (Gr. II or more)</th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>HYPO–RT–PC</td>
<td>1. 78Gy/39# (591)</td>
<td>78</td>
<td>18</td>
<td>-</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2. 42.7Gy/7# (589)</td>
<td>77.7</td>
<td>17</td>
<td>NS</td>
<td>10</td>
<td>NS</td>
</tr>
<tr>
<td>Munsuru et al.</td>
<td>1. 76Gy/38# (66)</td>
<td>76</td>
<td>19.7</td>
<td>-</td>
<td>7.6</td>
<td>-</td>
</tr>
<tr>
<td>(n=582)</td>
<td>2. 35Gy/5# (84)</td>
<td>70</td>
<td>12</td>
<td>S</td>
<td>4.8</td>
<td>S</td>
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<tr>
<td>Katz et al.</td>
<td>35 – 36.25 Gy/5# (515)</td>
<td>70</td>
<td>0</td>
<td>-</td>
<td>1.7</td>
<td>-</td>
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<tr>
<td>(n=515)</td>
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<tr>
<td></td>
<td>2. 35Gy/5# (40)</td>
<td>70</td>
<td>1</td>
<td>-</td>
<td>1</td>
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</tr>
</tbody>
</table>

- Only RCT; data is for 5 year followup
S – Significant; NS – Non significant
ASTRO/ ASCO/ AUA guidelines
ASTRO/ ASCO/ AUA guidelines

- Risk classification used is the D’amico risk classification

<table>
<thead>
<tr>
<th>Score</th>
<th>Stage</th>
<th>Gleason grade</th>
<th>PSA (ng/mL)</th>
<th>Total score</th>
<th>Risk class</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>T1, T2a</td>
<td>≤ 6</td>
<td>&lt; 10</td>
<td>0</td>
<td>Low</td>
</tr>
<tr>
<td>1</td>
<td>T2b</td>
<td>7</td>
<td>10 – 20</td>
<td>≤ 3</td>
<td>Intermediate</td>
</tr>
<tr>
<td>4</td>
<td>T2c, T3, T4</td>
<td>≥ 8</td>
<td>&gt; 20</td>
<td>&gt; 3</td>
<td>High</td>
</tr>
</tbody>
</table>
• In men with LR and IR prostate cancer with or without radiation to the seminal vesicles,
• In men with HR prostate cancer, moderate hypofractionation should be offered if pelvic nodes are planned to be excluded.
• Acute and Late toxicities are comparable to conventional RT.
• Discuss the limited follow-up beyond five years for most of existing RCTs.
Regimens suggested:
- 60Gy delivered in 20 fractions of 3Gy
- 70Gy delivered in 28 fractions of 2.5Gy

One optimal regimen cannot be determined since fractionation schemes have not been compared head to head.

Efficacy of moderately hypofractionated EBRT regimens does not appear to be impacted by
- patient age,
- comorbidity,
- anatomy,
- urinary function
In men with LR and IR prostate cancer ultrahypofractionation may be offered.

In men with HR prostate cancer, ultrahypofractionation should not be offered due to insufficient data.

The recommendations apply to:
- prostate volume < 100 cc
- Mild to moderate urinary symptoms at baseline (IPSS < 20)
• Regimens suggested:
  – 3500 to 3625 cGy in 5 fractions of 700 to 725 cGy may be offered to low- and intermediate-risk patients with prostate sizes less than 100 cm³.

• Five-fraction doses above 3625 cGy to the planning target volume is not suggested due to risk of late toxicity.

• Five-fraction prostate ultrahypofractionation using consecutive daily treatments is not suggested due to potential increased risk of late urinary and rectal toxicity.
2D Radiation Planning
General Considerations

Position

Supine

More comfortable
Immobilization

VAC-LOK

Knee support will make the lower back of the patient relax when lying down on a rigid treatment couch.
Immobilization

Position of the feet should be fixed and reproducible. Change in the foot position also change the relative position of the bony references points used to set the isocenter.
Margins for Radiotherapy Planning

Margin for penumbra

PTV

CTV

GTV
Margin for dose fall off at edges (Penumbra)

1 cm margin is given for cobalt

0.7 cm margin for LA

Field size 12 x 12 cm

10 X10 cm

PTV
Take Home

• In 2D planning margins for penumbra is to be added at the time of defining the radiation portals by radiation oncologist.

• In image based planning Radiation Oncologist define up to PTV and margins for penumbra is to be added by medical physicist during dose calculation.
2D Radiotherapy Planning

• **We need to define four borders.**

• **AP:PA Portal**
  • Cranial Border
  • Caudal Border
  • Two Lateral Borders

• **Lateral Portal**
  • Cranial Borders
  • Caudal Borders
  • Anterior borders
  • Posterior Borders

  Usually same as in AP:PA portals
2D Radiotherapy Planning

• **Borders are defined by**
  - Primary disease
  - Potential sites of regional disease mainly by metastasis in regional lymph nodes.
    - Microscopic
    - Gross

---

All the borders are defined in respect of bony landmarks
AP:PA Portals: Location of Lymph Nodes

Lateral border of Ant portal will be defined by location of Ext iliac nodes.

- Para Aortic Nodes
- Common Iliac Nodes
- External & Internal Iliac Nodes
- Inguino-femoral Nodes

Cranial border of anterior portal will be defined by level of nodes to be treated.
Lower Border OR Caudal Border

Lower border will be defined by extent of gross disease.
Lateral Portals

Anterior Border

By Extent of Ext Iliac Nodes

OR

Primary Disease

External Iliac a.
Goes anteriorly

Internal Iliac a.
Goes posteriorly

Anterior border of lateral portal will be defined by location of ext iliac nodes

Superior border of Pubic Symphysis

Caudal extent of obturator nodes
Posterior border of lateral Portal will be defined by:

- Site of the disease
- Extension of gross disease posteriorly
Take Home

• **AP:PA Portal**
  - Upper border and Lateral Borders are defined by level and location of the lymph nodes to be treated.
  - Lower border is defined by the extension of primary disease

• **Lateral Portal**
  - Anterior border is defined by location of the external iliac nodes
  - Posterior border is defined by site and size of the primary disease
Targets

• **Primary**
  - Prostate
  - Seminal vesicle

• **Nodes**
  - External Iliac
  - Obturator
  - Internal Iliac
  - Pre sacral
General Considerations

- **Position**          Supine
- **Portals**          Four
- **AP:PA and two lateral**

**Dose:**
- Whole Pelvis $\rightarrow$ 45 Gy/25fx/5weeks
- Boost $\rightarrow$ 20 Gy/10fx/2weeks
Lower border of the field

How to identify Genito-Urinary diaphragm

1 cm PTV

1 cm Penumbra

1 cm below genito-urinary diaphragm
Retrograde Uretherography

Apex of the opacified cone represents the position of Genito-urinary diaphragm.
Lower border of the field
10% of the patients will have under dose at apex of prostate

A. Sadeghi et al. / Radiotherapy and Oncology 38 (1996) 215–222
1 cm for CTV to PTV

1.5 cm for penumbra

Upper level of internal and external iliac nodes

Below Ischial Tuberosity

AP:PA Portal
Boost AP:PA

For Prostate + Seminal vesicle boost

Along the acetabulum

3 cm above PS

For Prostate only boost

Same Ischial tuberosity

5 cm above PS
Lateral Portals Boost

2 cm post to ant wall of rectum

1.5 cm post to ant border of SP
Dosimetric Issues

Two Field AP/PA

Four Field Box technique
AP/PA with separation more than 18cm

Peripheral organs get higher doses like subcutaneous tissue and bladder.

Hour glass appearance result into under dose.
Four Field Box Technique
With Cobalt or 4 mv photon

Head and Neck of the femur will receive high doses
Four Field Box Technique

High Energy photon 15 mv
Four Field Box Technique
With Cobalt or 4 mv photon

Give high weightage from AP/PA field (60% and 40%)