A modest decrease in testosterone has been reported after conventional dose 3D-conformal RT with no change in testosterone reported after low-dose rate brachytherapy (LDR) or proton therapy. We investigated whether dose-escalated intensity modulated radiation therapy (IMRT) and LDR are associated with a change in testosterone and if any association exists between testosterone and BCF.

PURPOSE
A modest decrease in testosterone has been reported after conventional dose 3D-conformal RT with no change in testosterone reported after low-dose rate brachytherapy (LDR) or proton therapy. We investigated whether dose-escalated intensity modulated radiation therapy (IMRT) and LDR are associated with a change in testosterone and if any association exists between testosterone and BCF.

METHODS
- Single-institution, retrospective analysis
- Treatment years: 2002-2008
- Mean follow-up: 49 months (4-105)
- BCF was defined as PSA Nadir + 2.0 ng/ml
- Patient Inclusion:
  - Low or Intermediate Risk Prostate Cancer
  - PSA < 20 or Gleason Score ≤7
  - Treated w/ IMRT or LDR
  - ≥ 3 post-RT testosterone levels
- Patient exclusion:
  - Androgen deprivation therapy
  - 1st Testosterone >12mo post RT

Data Analysis:
- Testosterone normalized for comparison
- Endpoints were assessed by:
  - Wilcoxon signed rank test was used to assess change in normalized testosterone at 3, 9, 15 and 21 mos post-RT
  - Cox proportional hazards modeling (MVA) was used for inferences about initial change in testosterone and BCF

RESULTS

Table 1: Select Patient Characteristics (n=259)

<table>
<thead>
<tr>
<th>T stage</th>
<th>N(%)</th>
<th>Drop &gt;100</th>
<th>Drop 0-100</th>
<th>Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1b</td>
<td>1 (0.4)</td>
<td>66 (47-79)</td>
<td>68 (42-84)</td>
<td>66 (51-82)</td>
</tr>
<tr>
<td>T1c</td>
<td>204 (78.8)</td>
<td>200 (77.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2a</td>
<td>38 (14.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2b</td>
<td>8 (3.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2c</td>
<td>8 (3.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gleason Score</th>
<th>Drop &gt;100</th>
<th>Drop 0-100</th>
<th>Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-6</td>
<td>200 (77.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>59 (22.8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Actuarial 5 yr FFBCF:
  - Intermediate Risk: 81%
  - Low Risk: 96% (p=0.001)
- Significant predictors of BCF:
  - Intermediate Risk (HR 3.5, p=0.02)
  - Decrease in testosterone (continuous) after RT (p=0.039)
  - Most significant in pts with >100ng/dl initial decrease in testosterone (HR 6.02, p=0.04) (Figure 1).
- MVA containing age, initial testosterone, and drop in testosterone >100ng/dL(p<0.0001)

Table 2: Median Change in Testosterone Post-RT (ng/dL)

<table>
<thead>
<tr>
<th>3 Mos</th>
<th>9 mos</th>
<th>15mos</th>
<th>21mos</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMRT</td>
<td>-45 (p=0.004)</td>
<td>-42 (p&lt;0.001)</td>
<td>-33 (p=0.003)</td>
</tr>
<tr>
<td>LDR</td>
<td>-24 (p=0.084)</td>
<td>-24 (p=0.048)</td>
<td>-24 (p=0.055)</td>
</tr>
</tbody>
</table>

CONCLUSIONS
- IMRT and LDR were both associated with a post-RT decrease in testosterone.
- An initial decrease in testosterone after RT was associated with an increased risk of BCF, most significant in the low risk population with a >100 ng/dL testosterone decrease.
- These findings warrant further examination in larger, prospective datasets, but may afford a new avenue for risk stratification following RT.