Using Task Group 137 to Prescribe and Report Dose

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AAPM Recommendations on Dose Prescription and Reporting Methods for Permanent Interstitial Brachytherapy for Prostate Cancer

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M. J. Rivard
Y. Yu
TG 137 Charge

- Review
  - Prescription
  - Reporting
  - Radiobiological models

- Consensus
  - Min requirements for prescription and reporting
    - Pre implant
    - Post implant

- Recommend
  - Optimal requirements for prescription and reporting
    - Pre implant
    - Post implant
Outline
Permanent Prostate Implants

• Impact of dose reporting based upon
  – Imaging modalities
  – Timing of imaging study
  – Treatment planning approaches
  – Interoperative planning strategies

• Biophysical models
  – BED
  – EUD
  – TCP
History Dose Prescription

- **Nomogram**

### Table 1. Nomogram for monotherapy (125 Gy) using NASI MED3633 $^{103}\text{Pd}$ seed

<table>
<thead>
<tr>
<th>Implant Volume (cc)</th>
<th>Average Dimension (cm)</th>
<th>Total Activity (U)</th>
<th>No. of Seeds (1.6 U/seed)</th>
<th>No. of Seeds (1.8 U/seed)</th>
<th>No. of Seeds (2.0 U/seed)</th>
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<td>55</td>
<td>3.8</td>
<td>245</td>
<td>154</td>
<td>137</td>
<td>123</td>
</tr>
</tbody>
</table>

Based on a modified peripheral loading

History Dose Reporting

$D_{99}$ – Dose to 99% of target
mPD – minimum Peripheral Dose

US PROSTATE DVH

- Best Fit
- 0.5 cm superior
- 1.0 cm superior
- 0.5 cm inferior
- 1.0 cm inferior

Implant too deep
Implant too shallow

Dose Gy

Volume %
Plan evaluation today

- **V100**
  - Vol that receives 100% of dose
  - 90% excellent implant

- **D90**
  - Dose to 90% of the volume
  - Prescribed dose
Today

- $D_{90}$ - Dose to 90% of target
- $V_{100}$ - Volume that receives Rx dose
• Dose calculation
• Imaging
Today

- $D_{90}$ – Dose to 90% of target
- $V_{100}$ – Volume that receives Rx dose
D90 issue

False Decrease D90

False Increase D90

CT Prostate

MR prostate
Impact of Imaging Modality on Dose Reporting

- Ultrasound Imaging
- CT Imaging
- MR Imaging
- Recommendations on Imaging modality
• Target delineation
## Imaging Modalities

<table>
<thead>
<tr>
<th></th>
<th>Plane films</th>
<th>CT</th>
<th>MRI</th>
<th>TRUS</th>
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<td>* Identification</td>
<td>++</td>
<td>+</td>
<td>-</td>
<td>--</td>
</tr>
<tr>
<td>* Localization</td>
<td>+</td>
<td>++</td>
<td>0</td>
<td>--</td>
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<td>Prostate Delineation</td>
<td>--</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Critical St Delineation</td>
<td>--</td>
<td>+</td>
<td>++</td>
<td>0</td>
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<tr>
<td>Comfort</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>--</td>
</tr>
<tr>
<td>Cost &amp; Convenience</td>
<td>++</td>
<td>-</td>
<td>--</td>
<td>+</td>
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</tbody>
</table>
Ultrasound

- Prostate
- Urethra
- Rectal wall
Ultrasound Apex / GUD Transition

- Prostate
- Apex
- GUD

Bulbourethral Gland

H shaped External sphincter
MRI Coronal vs. CT Coronal
MR Anatomy

- Prostate
- Urethra
- Rectal wall
- Corpus Cavernosum
- Pudendal Arteries
- Sphincter
- Neurovascular bundle
CT Prostate

• Apex – when do you stop
• Base – bladder neck obliteration
Intra - lumen bladder density-small gland
Bladder Neck Obliteration
MRI Coronal vs. CT Coronal
MRI Coronal vs. CT Coronal
CT Prostate – post implant

- Apex – when do you stop
- Base – bladder neck obliteration
- Seminal vesicles
- Rectal surface
## Variations without a Standard (Lee)

### Observer 1
- **Vol**: 39 cc
- **D90**: 142 Gy
- **V100**: 93%

### Observer 2
- **Vol**: 48 cc
- **D90**: 123 Gy
- **V100**: 86%

### Observer 3
- **Vol**: 32 cc
- **D90**: 155 Gy
- **V100**: 99%
Perils of CT contouring

McLaughlin et. al.
- Prostate
- Outer Rectum
- Inner Rectum – de-expansion 5 mm
- Urethra – Foley
- Penile Bulb
Why MR? EXPECT VARIATION
CT contouring / 6 national experts
CT contouring

Wide margin implants

Narayana et al.
Deviation from a Standard (6 experts)

MRI

Observer 1

Observer 2

36cc

34cc

38cc

Prostate Volume Agreement
Deviation from a Standard (6 experts)

MRI

Observer 1

Observer 2

148 Gy

153 Gy

143 Gy

D90 Agreement

✓
Deviation from a Standard (6 experts)

MRI

Observer 1

Observer 2

V100 Agreement
Prostate side view: Note labels on right. Prostate is not enlarged and does not extend into the bladder. Urethra opening from the bladder is open (yellow arrow). Sphincter is normal length and there is no bony restriction – note space between the bone and prostate (purple arrows)
normal prostate - normal appearance with light peripheral zone where tumors form and the dark central area called the transition zone – this enlarges with age
Multiparameter Imaging

- T2
- DCE
- DWI
Right side of the gland panel is normal prostate with clear PZ and TZ. On the left side (red) note the dark area that extends into the TZ and from front to back. This is tumor.
with contrast the area of concern on the left side of the panel is clearly seen, with a suggestion of extension beyond the gland (arrow).
Note the tumor on the left side of the panel (red) and possible extension beyond the capsule.
Imaging Recommendations

• CT – 2/3 mm cuts
• Prostate – mindful of pitfalls
• Rectum outer – 1 cm sup and inf
• Rectal wall - 0.5 cm contraction
• Urethra
  – Foley Day 0
  – Foley Optional later scans
• Penial Bulb
Imaging Guidelines MR

• T2 3 mm cuts (no rectal coil)
  – immediately before or after CT
  – Axial, coronal, sagittal

• Rectum – 1 cm above & below

• Bladder – axial MR

• Urethra – axial and Sag MR

• Register CT-MR around prostate only

• CT – seed positions
Impact of timing of imaging on dose reporting

- Prostate edema
- Source displacement with time
- Optimal timing for post implant dosimetry
- Recommendations on timing of imaging
Edema

- Needle insertion
- Bleeding – needle penetration
- General inflammation
Edema Model

- $V_0$
- $V_T$
- $V_{\text{max}}$

Volume vs. Time

- $T_0$
- $T_{\text{max}}$
- $T$

2016 AAPM Spring 49
Edema Model

? T max

? Different imaging modalities

? Prostate Volumes
Edema

US

CT1 80%

14d

CT2 150%

CT3 120%

1m

Narayana et. al.
Edema

McLaughlin et. al

CT 130%

MR 101%

US

14 d
MR edema

3 w

MR

Implant

3 w

MR 130%

Chung et. al
Edema Model

- Max – 1 day
- Longer to resolve than initial swelling
- Quick resolution - 2 weeks
- Slow resolution – 2 to 4 weeks
- $T_{1/2} \sim 10$ d (4 to 25 days)
Effect on post implant dosimetry

- Day 1 – edema large
  - underestimate dose
- Day 100 – edema resolved
  - overestimate dose
Edema Model

• Assumes seeds move with the prostate
  – Seeds inside the prostate

? Stranded seeds
By how much?

- Timing of imaging
- Magnitude of prostate swelling
- Rate of resolution
- Radioactive $T_{1/2}$

$\uparrow$ Short $T_{1/2}$ & low energy
Optimal time

- $^{131}$Cs 10±2 days
- $^{103}$Pd 16±2 days
- $^{125}$I 42±2 days
Recommendation Timing of imaging

• Pre-Implant prostate volume
• Implant day dosimetry
  – US immediate
  – CT/MR 2 to 4 h
• Post-Implant dosimetry
  – $^{131}$Cs 10±2 days
  – $^{103}$Pd 16±2 days
  – $^{125}$I 1 month±1 week
The optimal timing for post implant dosimetry is

1. Immediately following the implant
2. 2 weeks after the implant
3. 1 month after the implant
4. 10, 16 and 42 days for $^{131}$Cs, $^{103}$Pd, $^{125}$I respectively
5. No post implant dosimetry is required
The optimal timing for post implant dosimetry is

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Answer: 4
Reference: AAPM TG137, Nath et. al. 2009
Post implant prostate volume under- or overestimation is a result of:

1. The timing of dosimetry
2. Magnitude of preimplant prostate swelling
3. The rate of edema resolution
4. The radioactive decay half-life
5. All of the above
Post implant prostate volume under- or overestimation is a result of

1. The timing of dosimetry  [20%]
2. Magnitude of preimplant prostate swelling  [20%]
3. The rate of edema resolution  [20%]
4. The radioactive decay half-life  [20%]
5. All of the above  [20%]

Answer: 5
Reference: AAPM TG137, Nath et. al. 2009
Impact of treatment planning approaches on dose reporting

- Planning techniques
- Choice of isotope
- Choice of source strength
- Calculation Algorithm
- Dose indices for target and normal tissue
- Recommendations for planning and dose reporting
Peripheral loading?

Prostate, with error

Prostate + 0.5 cm margin, with error

Narayana et. al.
Loose seeds vs strands

- **Loose Seeds**
  - 😊 Expand with the prostate
  - 😞 Migrate to the lung

- **Strands**
  - 😊 No migration
  - 😞 May not track with the prostate
Seed Drop off

- Stranded preloaded
- Mick applicator
- Thin stranded seeds
- Preloaded cartridge
## Seed Drop off

<table>
<thead>
<tr>
<th></th>
<th>Rapid Strand</th>
<th>Mick applicator</th>
<th>Thin strand</th>
<th>Preloaded cartridge</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prostate V100 %</strong></td>
<td>96.5±2</td>
<td>93.2±5</td>
<td>93.4±4</td>
<td>94.1±3</td>
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<tr>
<td><strong>Prostate D90 Gy</strong></td>
<td>109±7</td>
<td>102±19</td>
<td>106±17</td>
<td>101±8</td>
</tr>
<tr>
<td><strong>Rec wall D1cc Gy</strong></td>
<td>95±18</td>
<td>70.4±8</td>
<td>70±23</td>
<td>73±11</td>
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<tr>
<td><strong>Rec wall D2cc Gy</strong></td>
<td>59±17</td>
<td>53±18</td>
<td>52±18</td>
<td>54±18</td>
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<tr>
<td><strong>Urethra D10 Gy</strong></td>
<td>156±25</td>
<td>163±36</td>
<td>164±21</td>
<td>158±31</td>
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</tbody>
</table>
Choice of Isotope

- $^{131}\text{Cs}$
- $^{103}\text{Pd}$
- $^{125}\text{I}$
- I-125 vs. Pd-103

![Graph comparing I-125 and Pd-103](image-url)
Seed Drop off

<table>
<thead>
<tr>
<th></th>
<th>Rapid Strand</th>
<th>Mick applicator</th>
<th>Thin strand</th>
<th>Preloaded cartridge</th>
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<td>Prostate V100%</td>
<td>96.5±2</td>
<td>93.2±5</td>
<td>93.4±4</td>
<td>94.1±3</td>
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<tr>
<td>Prostate D90 Gy</td>
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<td>102±19</td>
<td>106±17</td>
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<td>156±25</td>
<td>163±36</td>
<td>164±21</td>
<td>158±31</td>
</tr>
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</table>
Source strength?

*Prospective Randomized Trial*

- high vs. low mCi
- No sig diff

Narayana et. al
Recommendations

- GTV
- CTV – no posterior expansion
- PTV = CTV
- OAR
  - Urethra
  - Rectum
  - Penile bulb
Recommendations

• Dose clinical decision
  – $^{131}$Cs 115 Gy ? (100-125 Gy)
  – $^{103}$Pd  125 Gy
  – $^{125}$I  145 Gy
Recommendations Planning criteria

- **CTV**
  - $V_{100} > 95\% \text{ of } CTV$
  - $D_{90} > 100\% \text{ of } Rx$
  - $V_{150} < 50\% \text{ of } CTV$

- **Rectum D2cc < Rx dose**

- **Urethra**
  - $D_{10} < 150\% \text{ of } Rx$ dose
  - $D_{30} < 130\% \text{ of } Rx$ dose

- **Penile bulb - investigational**
Recommendations Dose Reporting

• DVH for target
  – Primary, D90, V100, V150
  – Secondary V200, V90, D100
• Urethra – D10
  – Secondary: D0.4cc, D30, D5
• Rectum – D2cc,
  – Secondary: D0.1 cc, V100
Primary dose parameters for prostate implant that should always be reported are:

<table>
<thead>
<tr>
<th>20%</th>
<th>1. $D_{90}$</th>
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<tbody>
<tr>
<td>20%</td>
<td>2. $V_{100}$</td>
</tr>
<tr>
<td>20%</td>
<td>3. $D_{90} &amp; V_{150}$</td>
</tr>
<tr>
<td>20%</td>
<td>4. $D_{90} V_{100} &amp; V_{150}$</td>
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<tr>
<td>20%</td>
<td>5. $D_{90} D_{100} V_{90} V_{100} &amp; V_{150}$</td>
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Primary dose parameters for prostate implant that should always be reported are

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<th>Percentage</th>
<th>Parameters</th>
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<td>20%</td>
<td>$V_{100}$</td>
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<tr>
<td>20%</td>
<td>$D_{90}$ &amp; $V_{150}$</td>
</tr>
<tr>
<td>20%</td>
<td>$D_{90}$ $V_{100}$ &amp; $V_{150}$</td>
</tr>
<tr>
<td>20%</td>
<td>$D_{90}$ $D_{100}$ $V_{90}$ $V_{100}$ &amp; $V_{150}$</td>
</tr>
</tbody>
</table>

Answer: 4
Reference: AAPM TG137, Nath et. al. 2009
Intraoperative treatment planning strategies

- Intraoperative preplanning
- Interactive planning
- Dynamic dose calculations
- Recommendations on Intraoperative planning and evaluation
Pre vs. OR planning

Pre

- 2 procedures
- Reproducible setup
- Time pressure
- # of seeds ordered

OR

- Target Volume
- Stress
Techniques

• Intraoperative
  – Creation of plan in OR just before the implant
  – Immediate execution

• Interactive
  – Stepwise refinement
  – Computerized dose calculations based on image feedback

• Dynamic
  – Calculations constantly updated using continuous deposited-seed-position feedback
Recommendations

• Enhanced implant quality

• Post implant dosimetry
  – Edema
  – Seed migration
Sector analysis

- Research setting
Biophysical Models

- BED for prostate implants
- EUD calculations
- TCP
- Recommendations for reporting radiobiological response
$$BED = D[1 + D/(\alpha / \beta)]$$
BED for inhomogeneous dose

\[
BED = -\frac{1}{\alpha} \ln\left(\sum_i \nu_i e^{-\alpha \cdot BED_i}\right)
\]

\[
D(T_{eff}) \cdot RE(T_{eff}) - \ln 2 \frac{T_{eff}}{\alpha T_p} = -\frac{1}{\alpha} \ln\left(\sum_i \nu_i e^{-\alpha \cdot BED_i}\right)
\]
Equivalent uniform EBRT dose

\[ EUD_d = \frac{-\ln\left(\sum_i \nu_i e^{-\alpha \cdot BED_i}\right)}{\alpha + \beta d - \gamma \ln 2 / (d \cdot T_p)} \]
TCP

\[ TCP(D) = \frac{1}{1 + (TCD_{50} / D)^k} \]

\[ TCP = \exp[-N_0 \exp(-\alpha \cdot BED)] \]
### Example

<table>
<thead>
<tr>
<th>Indices</th>
<th>$^{125}$I</th>
<th>$^{103}$Pd</th>
<th>$^{131}$Cs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose (Gy)</td>
<td>145.0</td>
<td>125.0</td>
<td>120.0</td>
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<tr>
<td>BED (Gy)</td>
<td>110.9</td>
<td>115.4</td>
<td>117.3</td>
</tr>
<tr>
<td>EUD (Gy)</td>
<td>69.7</td>
<td>72.6</td>
<td>73.8</td>
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<tr>
<td>TCP (%)</td>
<td>74.1</td>
<td>85.9</td>
<td>89.2</td>
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<tr>
<td>$T_{eff}$ (day)</td>
<td>235.3</td>
<td>93.9</td>
<td>60.8</td>
</tr>
</tbody>
</table>

**Calculated with:** $\alpha = 0.15$ Gy$^{-1}$, $\beta = 0.05$ Gy$^{-2}$, $\alpha/\beta = 3.0$ Gy, $T_p = 42$ days, repair half-life of 0.27 hour, and $N_0 = 5 \times 10^6$
Linear Quadratic Model

\[ ERD = Nd \left[ 1 + \frac{d}{\alpha/\beta} \right] \]

- N = \# fx
- D = dose/fx
- \( \alpha/\beta = 3\text{Gy} \)
Linear Quadratic Model

\[ ERD = NRt \left[ 1 + G \frac{Rt}{\alpha/\beta} \right] \]

- R = dose rate
- t = time
Linear Quadratic Model

\[ G_{LDR} = \frac{2}{\mu t} \left[ 1 - \frac{\left(1 - e^{-\mu t}\right)}{\mu t} \right] \]

- \( \mu = \) repair rate const

\[ ERD = N R_t \left[ 1 + G \frac{R_t}{\alpha/\beta} \right] \]
Linear Quadratic Model

\[
\text{ERD}_{\text{IMP}} = \frac{R}{\lambda} \left[ 1 + \frac{R}{(\mu + \lambda)\alpha/\beta} \right]
\]

- \( R \) = dose rate
- \( \lambda \) = decay constant
- \( \mu \) = repair rate constant
- \( \alpha/\beta \) = tissue specific parameter
Linear Quadratic Model

- **Beam**
  - \( d = 2 \text{ Gy/fx} \)
  - \( \alpha/\beta = 3\text{ Gy} \)

- **Brachy**
  - \( R = 4.4 \text{ cGy/h} \)
  - \( \lambda = 0.693/59.4 \text{ d}^{-1} \)
  - \( \alpha/\beta = 3\text{ Gy} \)
  - \( \mu = .4 \text{ h}^{-1} \)

\[
ERD = D_{eq} \left[ 1 + \frac{d}{\alpha/\beta} \right]
\]

\[
ERD = R / \lambda \left[ 1 + \frac{R}{(\mu + \lambda)\alpha/\beta} \right]
\]
Recommendations

• Adequate information
  – BED
  – EUD
  – TCP
  – Other
Recommendation

- Model parameters should be specified
- All parameters required to calculate the biodose should be specified
- Encourage vendors to provide models
What is the cause of most inconsistencies in dose reporting?

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>20%</td>
<td>1. Identification of source positions</td>
</tr>
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<td>20%</td>
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<tr>
<td>20%</td>
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</tr>
<tr>
<td>20%</td>
<td>4. Timing of the imaging study</td>
</tr>
<tr>
<td>20%</td>
<td>5. Type of isotope used</td>
</tr>
</tbody>
</table>
What is the cause of most inconsistencies in dose reporting?

1. Identification of source positions
2. Dose calculations
3. Target delineation
4. Timing of the imaging study
5. Type of isotope used

Answer: 3
Reference: AAPM TG137, Nath et. al. 2009