Is D90 a Radiobiologically Sound Endpoint for Evaluating Permanent Seed Prostate Brachytherapy?

Wayne M. Butler, PhD[*, †], Gregory S. Merrick, MD*[*, †], and Kent E. Wallner, MD*[§]
[, †] Schiffler Cancer Center and Wheeling Jesuit University, Wheeling, WV; [§] Puget Sound Health Care System, Seattle, WA*

Purpose

The dosimetric quality parameter D90, which is the minimum percentage of the prescribed dose (mPD) covering 90% of the target volume, has been found to predict biochemical disease free status following permanent seed prostate brachytherapy. This study considers under what circumstances that single predictor may be inappropriate.

Materials and Methods

Model monotherapy implants were manually designed and optimized for a single 38.7 cm³ prostate and its associated 67.2 cm³ planning target volume (PTV). Each design was required to have a PTV D90 of 125.0% ± 0.02%, a V100 > 99.6% of the PTV, the urethral V150 ≤ 0.01% of the urethral volume, and the total volume covered by the prescription dose to be the same for each radionuclide within 0.03 cm³. The seed strengths used ranged from 0.5 to 1.0 U for I-125 and from 2.4 to 6.0 U for Pd-103. Tumor control probabilities (TCP) were derived from the dose volume histograms (DVHs) using commonly accepted values for radiobiological parameters in the linear quadratic formulation and assuming random microscopic spread of disease throughout the PTV.

1. Survival, S, calculated using the linear quadratic formulation of Wang and Li

$$S = e^{-(\alpha D_{eff} + \beta PD_{eff}^2 - \gamma T_{eff})}$$

α = linear component of cell kill

β = quadratic component of cell kill

$\gamma = \ln 2/T_{pot}$ (γ *is the tumor cell growth constant,* T_{pot} *is the tumor cell potential doubling time)*

$$T_{eff} = \frac{1}{\lambda}\ln\left(\frac{\gamma}{\alpha D_0 \lambda}\right)$$

$\lambda = ln\ 2/t½$, D_0 = *prescription dose*

$$D_{eff} = D_i\left(1 - e^{(1-\lambda T_{eff})}\right)$$

D_i is the total dose in the volume of interest

$$P = \frac{2\lambda}{(\mu - \lambda)}\left[\left(\frac{1}{2\lambda}\right)\left(1 - e^{-2\lambda T_{eff}}\right) - \left(\frac{1}{(\mu + \lambda)}\right)\left(1 - e^{-(\mu+\lambda)T_{eff}}\right)\right]$$

P is the protraction factor

μ is the tumor cell repair constant

$\mu = ln\ 2/t½_{rep}$

2. Tumor control probability, TCP

$$TCP = \prod_{i=1}^{n} e^{-Kv_iS_i}$$

K = number of tumor clonogens in the PTV

v_i = fractional volume of PTV at dose $D_{eff,I}$

S_i = survival fraction for volume v_i

3. Radiobiological parameters applied in calculating tumor control probability

Variable	Description, Units	^{125}I	^{103}Pd
α	linear component of cell kill, Gy^{-1}	0.15	0.15
β	quadratic component of cell kill, Gy^{-2}	0.05	0.05
γ	cell repopulation rate (T_{pot} = 42 d), d^{-1}	0.0165	0.0165
μ	cell repair constant (t½ = 1 h), d^{-1}	16.64	16.64
K	clonogen number	5×10^6	5×10^6
D_0	prescription dose, Gy	145	125
λ	radionuclide decay constant, d^{-1}	0.01167	0.04079
T_{eff}	effective treatment time, d	234.2	94.04
P	protraction factor	6.98×10^{-4}	2.44×10^{-3}

Results

To adequately cover the PTV, as many as 122 seeds were used for a low seed strength Pd-103 implant and as few as 52 seeds for a high seed strength I-125 implant. The mean dosimetric margin from the ultrasound prostate to the PTV was 4.2 mm and from the PTV to the 100% isodose line was 2.2 ± 0.01 mm for all plans. At constant D90 of 125.0% mPD, V150 varied from 52% to 59% of the PTV for I-125 and from 66% to 72% of the PTV for Pd-103 over the range of strengths studied. Although the PTV was completely covered by the prescribed dose in low strength implants, the poorer dosimetric conformality of high strength seeds caused a V100 of 98.6% volume for those implants. Accordingly, D100 was 102% versus 87% for low strength and high strength I-125 implants, respectively, and 103% versus 81% for low strength and high strength Pd-103 implants, respectively. This resulted in a TCP 22% lower for high strength I-125 seeds than for low strength seeds. A similar difference — 8% lower TCP for high strength over low strength — was seen for Pd-103 implants.

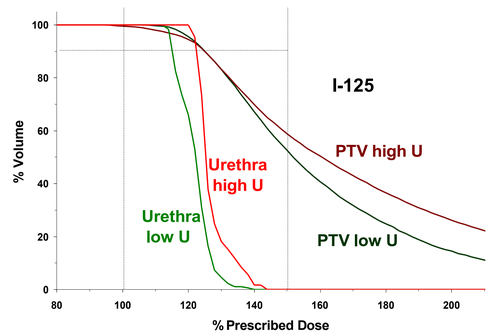
5. Monotherapy mean values

Parameter	^{125}I Low U seeds	^{125}I High U seeds	^{103}Pd Low U seeds	^{103}Pd High U seeds
Arithmetic mean (% mPD)	164	183	184	230
(Std. Dev. of mean)	*(47)*	*(81)*	*(66)*	*(140)*
Geometric mean (% mPD)	159	172	175	203
Harmonic mean (% mPD)	155	164	168	185

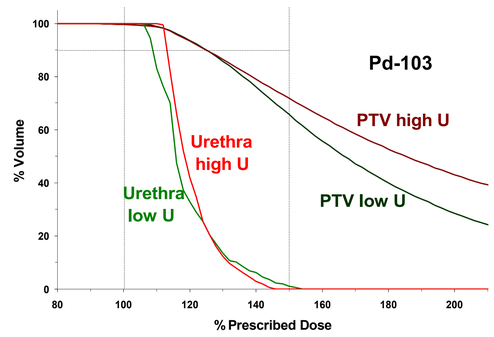
4. Treatment planning parameters for the 67.2 cm³ PTV *(38.7 cm³ prostate)*

Parameter	^{125}I Low U seeds	^{125}I High U seeds	^{103}Pd Low U seeds	^{103}Pd High U seeds
Seed strength (U)	0.47	1.11	2.4	6.2
Number of seeds	114	52	122	56
Total strength (U)	53.6	57.7	293	347
V_{100} (% PTV)	100	99.6	100	99.6
D_{90} (% mPD)	125.0	125.0	125.0	125.0
Urethra V_{150} (% volume)	0.0	0.0	0.2	0.0
Total vol. at mPD (cm³)	86.0	86.0	86.0	86.0
PTV margin to 100% (mm)	2.16	2.16	2.16	2.16

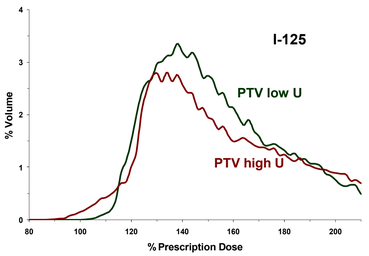
6. Dose volume histograms with the PTV D90 = 125.0% mPD for I-125



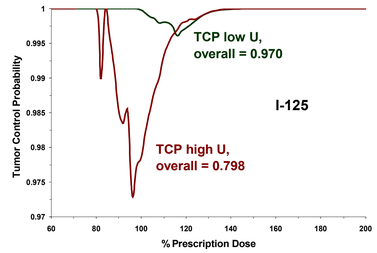
7. Dose volume histograms with the PTV D90 = 125.0% mPD for Pd-103



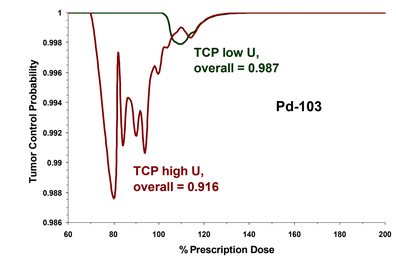
8. Differential DVHs for PTV using I-125



9. Tumor control probability for sub-volumes of the PTV using I-125



10. Tumor control probability for sub-volumes of the PTV using Pd-103



Conclusion

Through a single D90 point on a DVH plot, a large number of clinically feasible curves may be generated, but an implant that is dosimetrically hot by most common measures may not result in the best TCP. D90 therefore is inadequate as a single parameter to describe implant quality across institutions with different target coverage goals and choice of seed strength.