

Extracapsular Radiation Dose Annulus Correlates with Biochemical Control in Low-risk Prostate Brachytherapy Patients: Results of a Prospective Randomized Trial

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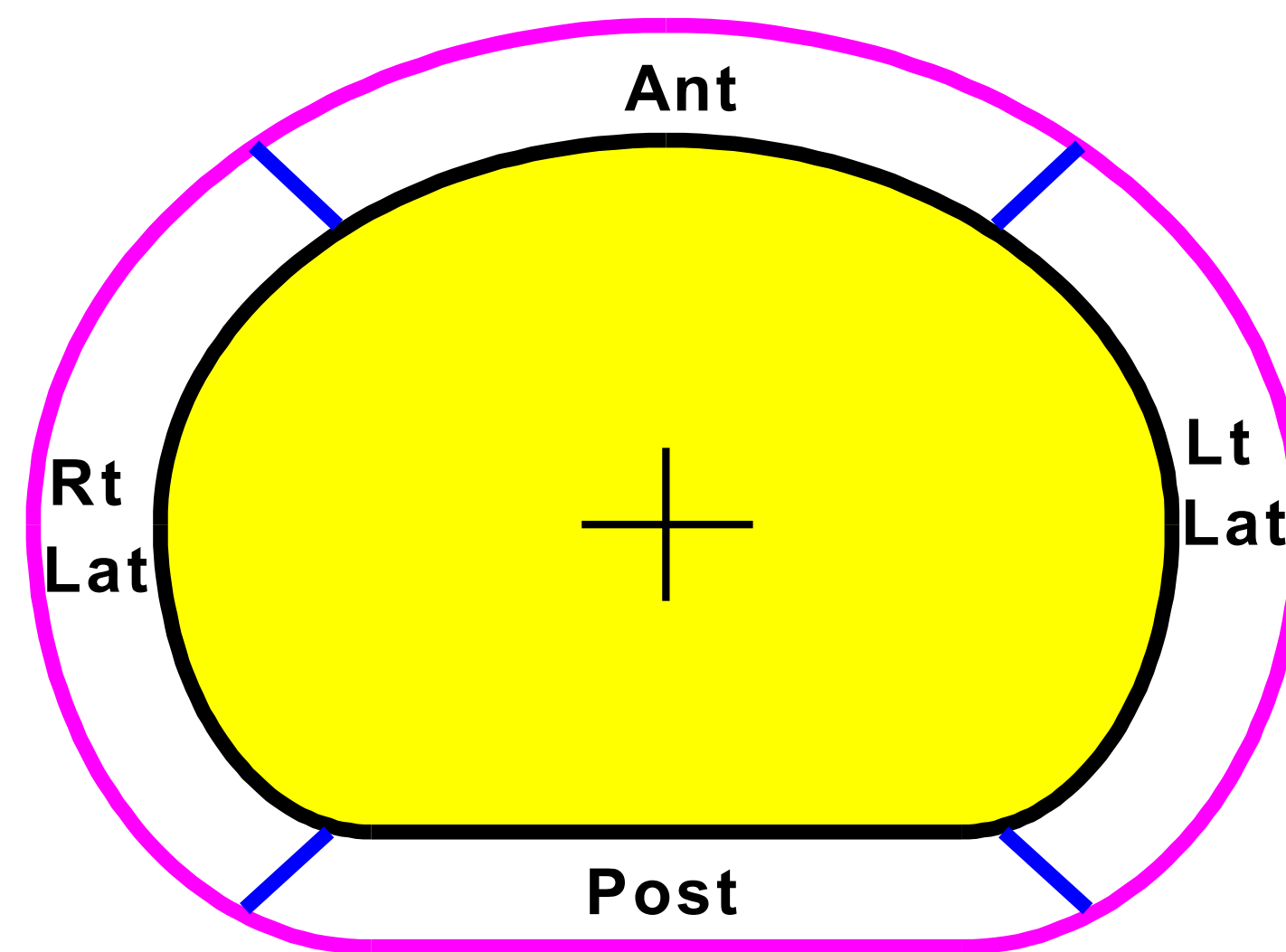
Purpose

Recent studies have suggested that extracapsular brachytherapy treatment margins correlate with biochemical control. It is likely that volumetric geographic dosimetric parameters will be more robust than selected radial measurements. Accordingly, we evaluated extracapsular volumetric dosimetric parameters in low-risk patients.

Materials and Methods

Two hundred sixty-three low-risk prostate cancer patients randomized to Pd-103 versus I-125 were implanted with a brachytherapy target volume consisting of the prostate with a 5 mm periprostatic margin. The median follow-up was 4.2 years. All patients were implanted at least 3 years prior to analysis. Within 2 hours of implantation, an axial CT was obtained for post-implant dosimetry. A 5 mm 3-dimensional periprostatic annulus was constructed around the prostate and evaluated in its entirety and in 90° segments. Prostate and annular dosimetric parameters consisted of V100/150/200 and D90. Biochemical progression-free survival (bPFS) was defined as a PSA ≤ 0.50 ng/mL after nadir.

Transverse view of the prostate and annulus segments.



The annular volume was created by adding a 0.5 cm margin around the TRUS prostate anteriorly, posteriorly, laterally, superiorly and inferiorly.

Results

The Pd-103 and I-125 arms were well-matched in terms of clinical, biochemical and pathologic presentation. Six-year bPFS was 96.8% vs. 99.2% for I-125 vs. Pd-103 ($p = 0.149$). The most recent median post-treatment PSA was < 0.04 ng/mL for both isotopes. No significant differences in post-operative annular doses were discerned between bPFS and failed patients.

Clinical, treatment, and dosimetric parameters of the study population stratified by radionuclide

Continuous Variables	Radionuclide I-125 (n = 127)		Radionuclide Pd-103 (n = 136)		p^*	All Patients (n = 263)	
	Mean ± SD	Median	Mean ± SD	Median		Mean ± SD	Median
Age at implant (years)	64.4 ± 7.2	65.0	65.1 ± 6.6	66.0	0.397	64.8 ± 6.9	65.0
Follow-up (months)	52.6 ± 11.4	53.0	52.0 ± 11.4	52.0	0.687	52.3 ± 11.4	53.0
Pre-treatment PSA (ng/mL)	6.4 ± 1.7	6.0	6.7 ± 1.9	6.4	0.136	6.6 ± 1.8	6.1
Gleason score	5.9 ± 0.3	6.0	6.0 ± 0.3	6.0	0.179	6.0 ± 0.3	6.0
% positive biopsies [§]	22.5 ± 13.4	16.7	23.8 ± 17.2	16.7	0.591	23.2 ± 15.5	16.7
US volume (cm ³)	34.4 ± 11.0	33.2	34.4 ± 9.5	35.1	0.964	34.4 ± 10.3	34.1
Planning volume (cm ³)	54.4 ± 22.5	59.0	56.0 ± 22.8	62.7	0.583	55.2 ± 22.6	61.0
Prostate V ₁₀₀ (% volume)	97.4 ± 3.9	99.0	93.3 ± 8.0	96.0	< 0.001	95.3 ± 6.7	98.0
V ₁₅₀ (% volume)	75.4 ± 13.7	79.0	66.7 ± 15.3	68.0	< 0.001	70.8 ± 15.2	72.0
V ₂₀₀ (% volume)	39.7 ± 14.2	39.0	36.9 ± 12.8	36.0	0.088	38.3 ± 13.6	37.0
D ₉₀ (% mPD)	131.9 ± 20.2	131.9	116.6 ± 23.7	114.9	< 0.001	124.0 ± 23.3	125.3
Last PSA (ng/mL) for disease free pts.	0.1 ± 0.2	<0.04	0.1 ± 0.2	<0.04	0.737	0.1 ± 0.2	<0.04
Categorical Variables	Count (%)	Count (%)	p^{\ddagger}	Count (%)			
Perineal invasion [§]	4 (5.1)	9 (10.2)	0.259	13 (7.8)			

* - p values calculated by t-test
 \ddagger - p values determined by 2-sided Fisher's Exact Chi-squared
 \S - Wheeling patients only (n = 163)

Post-implant annulus dosimetry stratified by radionuclide

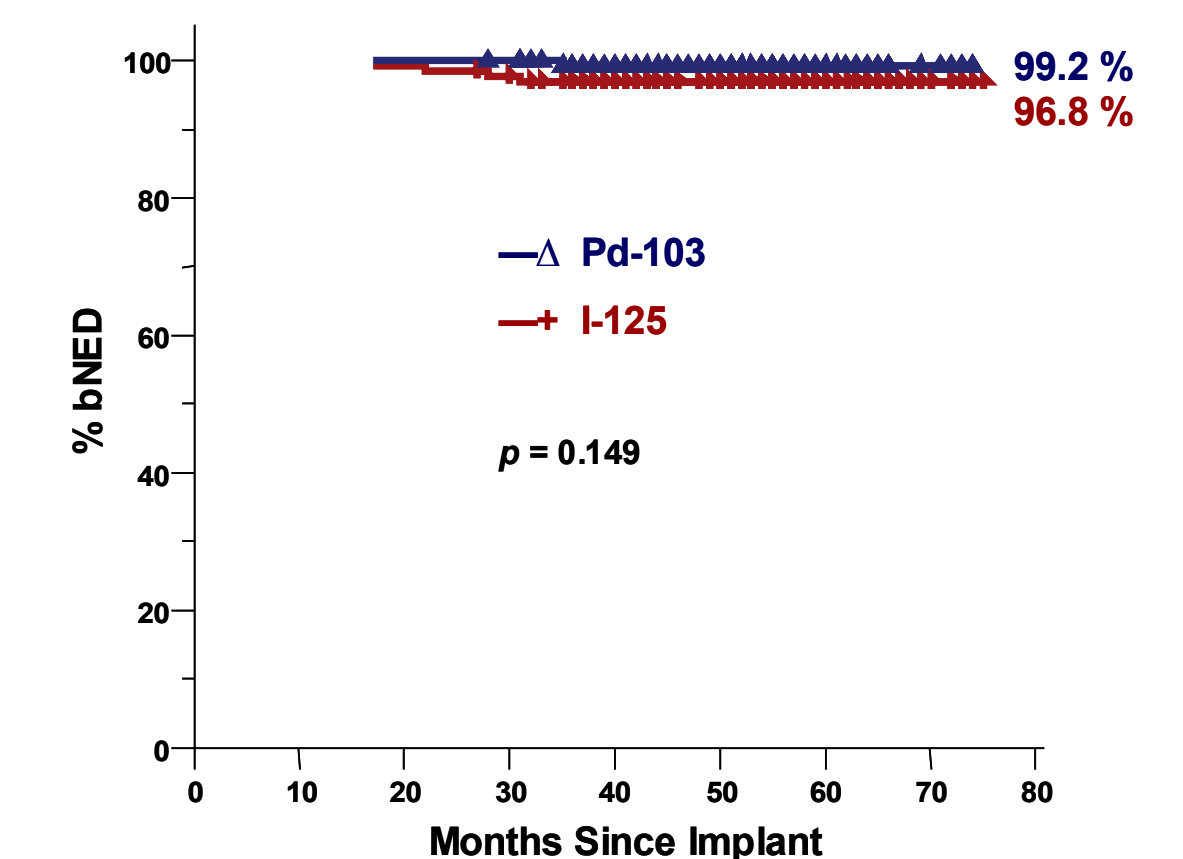
Structure	Parameter*	I-125 (n = 127)	Pd-103 (n = 136)	p^{\ddagger}	All Patients (n = 263)	
		Mean ± SD	Mean ± SD		Mean ± SD	Median
Anterior Annulus	V100	59.3 ± 23.3	53.4 ± 27.6	0.064	56.2 ± 26.7	62.0
	V150	21.6 ± 14.7	24.7 ± 16.5	0.103	23.2 ± 15.7	22.0
	V200	7.9 ± 7.3	10.9 ± 8.1	0.002	9.5 ± 7.8	8.0
	D90	76.8 ± 17.5	67.2 ± 24.9	< 0.001	71.8 ± 22.2	75.0
Left Lateral Annulus	V100	88.1 ± 16.0	78.9 ± 25.0	< 0.001	83.3 ± 21.6	94.0
	V150	60.7 ± 21.3	55.0 ± 25.5	0.055	57.8 ± 23.7	63.0
	V200	33.9 ± 16.9	31.5 ± 17.9	0.280	32.7 ± 17.5	32.0
	D90	109.9 ± 28.5	98.8 ± 36.0	0.006	104.2 ± 33.0	109.4
Right Lateral Annulus	V100	85.7 ± 18.4	77.6 ± 26.3	0.004	81.5 ± 23.1	93.0
	V150	57.0 ± 23.7	54.8 ± 26.7	0.481	55.8 ± 25.3	64.0
	V200	30.9 ± 17.5	32.1 ± 19.5	0.621	31.5 ± 18.5	31.0
	D90	107.4 ± 28.2	98.2 ± 38.0	0.027	102.6 ± 33.9	109.6
Posterior Annulus	V100	78.5 ± 21.6	61.8 ± 26.7	< 0.001	70.0 ± 25.8	78.0
	V150	34.1 ± 18.4	28.0 ± 16.4	0.005	30.9 ± 17.6	31.0
	V200	13.6 ± 12.1	11.8 ± 8.0	0.146	12.7 ± 10.2	11.0
	D90	94.4 ± 23.9	74.7 ± 26.3	< 0.001	84.2 ± 27.0	89.1
Superior Annulus	V100	77.1 ± 20.5	70.8 ± 26.4	0.031	73.8 ± 23.9	81.0
	V150	41.8 ± 19.1	45.3 ± 25.3	0.208	43.6 ± 22.5	44.0
	V200	19.2 ± 12.5	24.5 ± 17.8	0.006	22.0 ± 15.7	18.0
	D90	91.1 ± 22.9	84.0 ± 34.7	0.052	87.4 ± 29.8	87.5
Inferior Annulus	V100	85.3 ± 20.9	68.1 ± 28.0	< 0.001	76.4 ± 26.2	86.0
	V150	49.4 ± 27.1	38.4 ± 23.6	< 0.001	43.7 ± 5.9	40.0
	V200	22.4 ± 16.9	19.5 ± 15.3	0.150	20.9 ± 16.1	17.0
	D90	109.3 ± 29.6	85.1 ± 33.1	< 0.001	96.8 ± 33.7	97.1
Total Annulus	V100	80.3 ± 15.0	70.4 ± 22.5	< 0.001	75.2 ± 19.9	83.0
	V150	46.6 ± 14.8	43.3 ± 18.9	0.120	44.9 ± 17.1	48.0
	V200	23.4 ± 10.1	23.4 ± 11.7	0.989	23.4 ± 10.9	23.0
	D90	90.8 ± 20.2	78.0 ± 27.6	< 0.001	84.2 ± 25.1	90.0

* - V_{xx} parameters are in terms of % volume; D90 is in terms of % prescribed dose
 \ddagger - p values calculated by t-test, significant differences < 0.05 in bold

Post-implant annulus dosimetry stratified by biochemical failure status

Structure	Parameter*	bPFS (n = 244)	Failure (n = 5)	p^{\ddagger}
		Mean ± SD	Mean ± SD	
Prostate	V100	95.5 ± 6.6	96.0 ± 2.9	0.718
	V150	71.0 ± 14.9	77.4 ± 14.1	0.371
	V200	38.2 ± 13.3	46.2 ± 15.5	0.316
	D90	124.4 ± 23.0	131.5 ± 23.3	0.536
Anterior Annulus	V100	57.2 ± 25.2	36.8 ± 36.2	0.277
	V150	23.5 ± 15.6	16.6 ± 21.7	0.517
	V200	9.6 ± 7.7	7.0 ± 8.7	0.550
	D90	72.8 ± 21.9	60.9 ± 29.3	0.416
Left Lateral Annulus	V100	84.3 ± 21.0	79.8 ± 11.8	0.448
	V150	58.8 ± 23.0	44.8 ± 27.3	0.316
	V200	33.2 ± 17.0	26.4 ± 23.9	0.561
	D90	105.4 ± 32.5	100.4 ± 33.1	0.753
Right Lateral Annulus	V100	82.7 ± 22.3	72.6 ± 16.5	0.244
	V150	57.1 ± 24.7	42.0 ± 32.0	0.351
	V200	32.2 ± 18.0	26.4 ± 32.4	0.708
	D90	104.2 ± 33.0	96.0 ± 51.9	0.766
Posterior Annulus	V100	70.7 ± 25.4	79.8 ± 15.7	0.268
	V150	31.4 ± 17.6	41.4 ± 18.0	0.283
	V200	12.8 ± 10.3	20.8 ± 8.6	0.104
	D90	85.2 ± 26.9	92.1 ± 11.1	0.246
Superior Annulus	V100	74.6 ± 23.6	85.2 ± 9.5	0.316
	V150	44.2 ± 22.5	54.8 ± 21.0	0.325
	V200	22.2 ± 15.6	32.4 ± 21.1	0.341
	D90	88.3 ± 29.5	101.7 ± 32.3	0.409
Inferior Annulus	V100	77.1 ± 25.3	62.6 ± 44.9	0.212
	V150	43.7 ± 26.3	37.4 ± 38.3	0.733
	V200	20.5 ± 15.2	19.8 ± 24.7	0.953
	D90	97.0 ± 32.5	89.9 ± 42.7	0.728
Total Annulus	V100	76.2 ± 19.4	71.2 ± 15.3	0.514
	V150	45.7 ± 16.8	41.0 ± 21.9	0.657
	V200	23.8 ± 10.8	23.0 ± 17.9	0.927

Kaplan-Meier curve of patients with biochemical control stratified by isotope.



There were four failures in the I-125 arm and one failure in the Pd-103 arm. The p-value was determined by the log rank test.

Conclusion

A post-implant 5 mm, three-dimensional periprostatic annulus provides substantial information regarding dosimetric coverage. However, with a median follow up of 4.2 years, such volumetric and geographic parameters have not proven useful in predicting biochemical outcome in low risk patients.