

CESIUM-131 PERMANENT PROSTATE BRACHYTHERTHERY: AN INITIAL REPORT

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INTRODUCTION

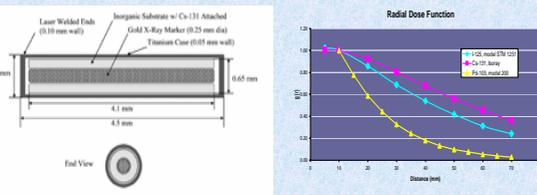
The use of brachytherapy as the sole modality of treatment for early-stage prostate cancer has gained popularity over the past decade due to the advent of the transrectal ultrasound-guided technique and the favorable reports of imaged-based brachytherapy with isotopes Iodine-125 (I-125) and Palladium 103 (Pd-103).¹⁻⁸ The primary difference between these two isotopes is the half-life, approximately 60 days for I-125 and 17 days for Pd-103. To date, there is no evidence of superiority of one isotope over the other, and in fact, Cha et al.⁹ recently compared their I-125 and Pd-103 experience using a matched-pair analysis and were unable to demonstrate any statistically significant difference in PSA outcomes or morbidity among all patients with Gleason scores between 2 and 8.

Cs-131 is a relatively new encapsulated isotope that has been FDA approved for use in brachytherapy.¹⁰ It is a particularly attractive isotope due to its energy which is similar to I-125 (29 KeV), but a substantially shorter half-life of 9.7 days. There are recent radiobiological data that suggest that isotopes of shorter half-lives may be more effective in the treatment of prostate cancer, particularly if the α/β ratio is lower for prostate tissue than the previously thought 5-10.¹¹ It may in fact be much lower, in the 1-3 range. These values of α/β are comparable to, if not lower than, late-responding normal tissues which would strengthen the argument for shorter lived radionuclides.

In addition to the potential advantages in terms of cellular lethality, a shorter acting isotope may have advantages in terms of morbidity. With a half-life of 9.7 days, and a presumed effective life of 4-5 half-lives, Cs-131 has spent meaningful dose by 39-48 days as opposed to 68-85 days for Pd-103, and 240-300 days for I-125. Theoretically then, any side effects which are dose or dose rate related would be expected to dissipate much faster with Cs-131 relative to the other isotopes.

PURPOSE

This is the first report of the clinical implementation of this isotope at multiple institutions following the same protocol in the treatment of organ confined prostate cancer.



MATERIALS AND METHODS

Radiobiological equations were derived which justify the prescription dose and the choice of isotope strength to match current design criteria. Empirical validation and adjustment of source strength was based upon replacement of ¹²⁵I sources with ¹³¹Cs sources in 42 recently performed patient plans.^{13,14} In addition, to date, 43 patients have undergone ¹³¹Cs prostate brachytherapy at five different institutions following the same treatment protocol with centralized dosimetric review. Day-0 post-implant dosimetry from these 43 patients was analyzed, and compared to day-0 dosimetry on 31 consecutive patients receiving ¹²⁵I implants within the same time period at one of the participating institutions (Texas Cancer Clinic).

Dale L-Q Model¹²

Salient Characteristics:
 • Total dose delivered.
 • Initial dose-rate.
 • Radionuclide half-life.
 • Dose-rate effect in tumour and normal tissue.
 • Sub-lethal damage tissue repair constants (μ values).
 • Fractionation sensitivities (α/β ratios) of tumour and normal tissue, which also are determinants of sensitivity to changes in dose-rate.
 • Tumour repopulation during treatment (K factors).
 • Relative Biological Effectiveness (RBE) values associated with the radionuclides emitted by the radionuclides.

Assumptions:

• The α/β value for late-responding tissue has been fixed throughout at 3Gy.
 • The α/β value for prostate tumour has been taken to be 10, 7, 5, 2.5 or 1.5Gy. Current evidence suggests a likelihood that this tumour possesses a value in the approximate range 1-4Gy [6-10].
 • The tissue repair constant for late-responding tissue has been fixed throughout at 0.5h⁻¹, corresponding to a repair half-time of 1.4h [11, 12].
 • The tissue repair constant for tumour has been taken to be 0.5h⁻¹ or 1.4h⁻¹, respectively corresponding to repair half-times of 1.4h and 0.5h [11, 12].
 • The average tumour doubling time has been fixed at 66days [13].
 • It is assumed that there is no repopulation of normal tissue during treatment.
 • The tumour radiosensitivity (α value) has been fixed at 0.1Gy⁻¹, corresponding to a radio-resistive tumour [13].
 • The RBE of I-125 seeds are assumed to be 1.0 or 1.45 [14-16].
 • The RBE of Pd-103 seeds are assumed to be 1.0 or 1.75 [14-16].
 • The RBE of Cs-131 is not known. Values of 1.0 or 1.45 (similar to that determined for I-125) are assumed here. It is assumed that tumour and normal tissues each receive the dose prescribed.

Conclusions:

• Cs-131 implants (even at the highest considered dose of 120 Gy) produce lower normal tissue BEDs than 145Gy of I-125.
 • Matched tumour effects are achievable with prescribed Cs-131 doses in the approximate range 105-120 Gy, depending on the assumed parameters.
 • Volume effects, alongside the likelihood that α/β for prostate tumour may well be lower than the value of 5Gy assumed in the calculations...
 • Prescribed Cs-131 doses of 100 Gy would appear to be reasonable.

RESULTS

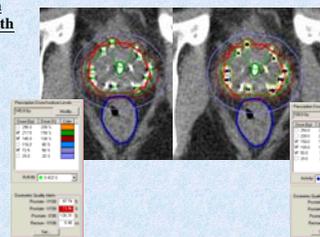
Results of the empirical validation suggested the use of 1.8 U sources to achieve equivalent prostate coverage and a slightly higher surface dose to the rectum and urethra of + 0.4%, +0.21 cm², and +0.08 cm², for the V100, R100, and U150, respectively, when converting from I-125 to Cs-131 for the 42 treatment plans. There was sufficient dosimetric data to compare prostate seed implants performed per protocol on 43 patients versus the 31 consecutive I-125 implants performed during the same period. Prostate coverage was comparable on Day 0 (V100: Cs-93.8%, I-94.0%; D90: Cs-105%, I-109%). Implant uniformity was better for 131Cs with V150 = 44.5% versus 57.3% for 125I. Average urethral doses (U150, Cs-0.04 cm³, I-0.19 cm³) and average rectal doses (R100, Cs-0.25 cm³, I-0.47 cm³) were lower for Cs. I-PS scores peaked at 2 weeks and urinary QOL scores returned to near baseline in approximately 2 months.

Plan Substitution Results

I-125 (4.3 U) \Leftrightarrow Cs-131 (1.8 U)

Direct Plan Substitution
I-125 (0.43 U) replaced with
Cs-131 (1.80 U)
(n = 42)

	¹²⁵ I	¹³¹ Cs
V ₁₀₀ (%)	96.6	97.0
V ₁₅₀ (%)	68.0	67.7
U ₁₅₀ (cm ³)	3.0	1.5
U ₂₀₀ (cm ³)	0.6	0.1
R ₁₀₀ (cm ³)	4.2	3.8
R ₁₅₀ (cm ³)	0.8	0.7



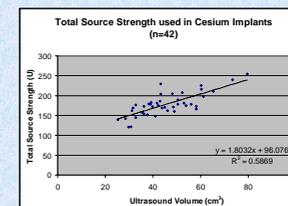
¹³¹Cs implants compared to ¹²⁵I implants

Characteristic	¹²⁵ Iodine	¹³¹ Cesium
Energy	28 keV	29 keV
Half-life	59.4 days	9.7 days
Rx Dose	145 Gy	100 Gy
Initial Dose Rate	7 cGy/hr	30 cGy/hr
Source Strength	0.43 U = 0.34 mCi	1.8 U = 2.8 mCi

Implant Series Results

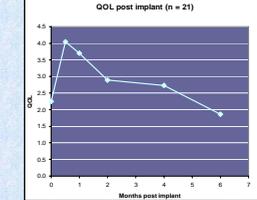
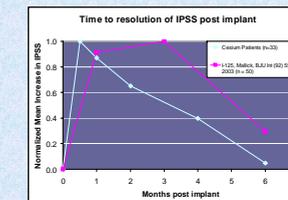
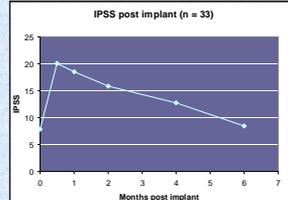
Series Dosimetric Characteristics, n = 42

Characteristic	Avg \pm StDev	Range
Prostate Volume post implant (cm ³)	45.5 \pm 12	25 - 79
Total Sources	97.5 \pm 17	65 - 142
Source Strength per Seed (U)	1.83 \pm 0.10	1.6 - 2.1
Prostate V ₁₀₀ (%)	93.8 \pm 4.2	81.4 - 99.3
D ₉₀ (Gy)	108 \pm 8	87 - 129
Urethra V ₁₅₀ (cm ³)	.037 \pm 0.05	0.0 - 0.20
Rectum V ₁₀₀ (cm ³)	0.25 \pm 0.37	0.0 - 1.6



Implant Dosimetry Results ¹²⁵I (n = 30) versus ¹³¹Cs (n = 42)

	¹²⁵ I	¹³¹ Cs
V ₁₀₀ (%)	94.0	93.8
V ₁₅₀ (%)	57.3	44.5
U ₁₅₀ (cm ³)	0.19	0.04
U ₂₀₀ (cm ³)	0.02	0.00
R ₁₀₀ (cm ³)	0.47	0.25
R ₁₅₀ (cm ³)	0.02	0.01



CONCLUSIONS

Our initial experience using Cs-131 in prostate brachytherapy suggests that a prescription dose of 100 Gy using a 1.8 U source strength will result in very similar monotherapeutic dosimetric coverage and improved dose uniformity relative to I-125, with reduced doses to critical structures, provided some slight modifications to the treatment plan are made. Cs-131 prostate implants using these parameters have been well tolerated to date, with minimal to moderate early urinary symptoms that resolve relatively rapidly, within approximately 4-8 weeks.

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