Prostate brachytherapy

Canberra Prostate Support Group

July 2011

Prostate Brachytherapy

- Why brachytherapy?
- How do we do it?
- What are the results?
  - Ongoing Issues

Why brachytherapy?

- Radiation falls off with the inverse square of distance
- Anatomically the bladder and rectum are close to the prostate and limit dose
- Highest dose is required for larger lumps of tumour, and lower doses at the periphery
- As stage increases the risk of tumour spread outside the prostate increases

Staging determines which Treatment is Appropriate- TNM stage

- **Stage 1-** Ca confined to prostate
- **Stage 2a-** less than ½ one side
- **Stage 2b-** more than ½ one side
- **Stage 2c-** both sides of prostate
- **Stage 3a-** outside capsule
- **Stage 3b-** into seminal vesicles
- **Stage 4a-** into other organs
- **N1**-into lymph nodes,
- **M1** distant spread

Risk grouping

- D'Amico Criteria (USA)
- Low risk
- PSA <10, Gleason <7, Stage <T2c

- Intermediate Risk
- 1 risk factor
- PSA 10-15, Gleason >7, Stage > T2c

- High Risk
- > 2 risk factors and All PSA >15

- NCCN Criteria (British)
  Low Risk
- PSA <10, Gleason <7, Clinical Stage <T2c

- Intermediate Risk
- PSA 10-20, Gleason > 7, Stage >T2c

- High Risk
- >2 factors and all PSA > 20
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Rationale for HDR Prostate brachytherapy

- Dose escalation improves outcome in int risk and high risk CaP (Pollack, Zelefsky, Dearneley)
- Ultimate conformality in dose escalation
- Acceptable toxicity, reduces linac time
- Large dose/fraction radiobiologically better
- Shorter treatment time

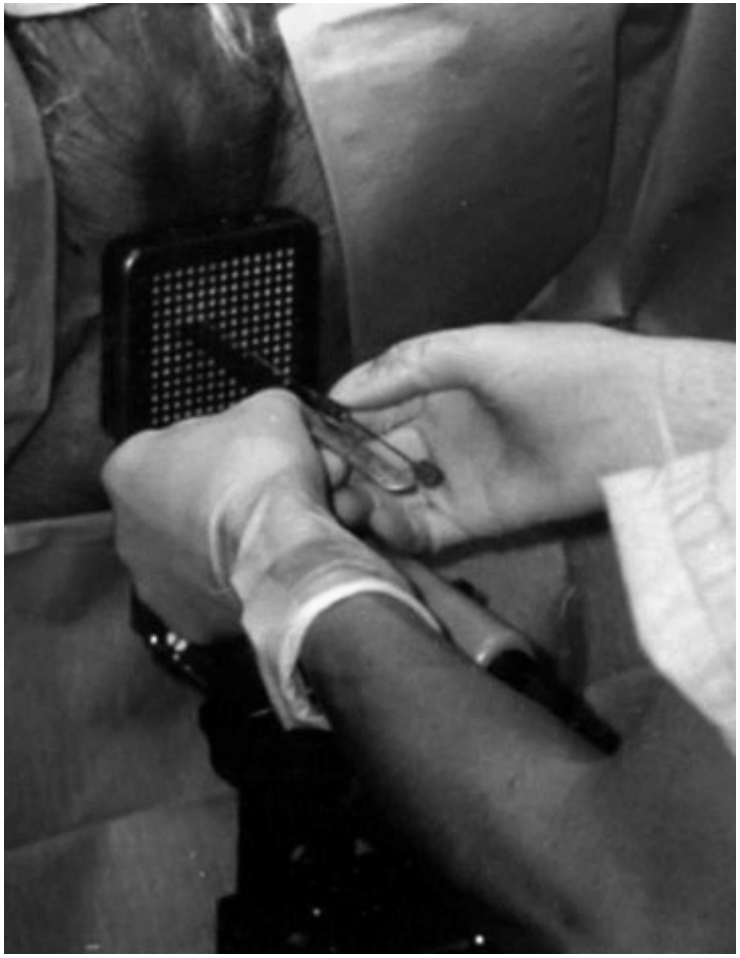
Dose escalation

- High dose (dose escalated) EBRT-conformal/IMRT
- EBRT with brachytherapy boost
- Brachytherapy with intraprostatic boost

BED for HDR CaP treatment

	BED(10)	BED(1.5)
86.4Gy/48#	102	190
50.4Gy/28# +	59.5	111
10Gy x 2	100	264
6Gy x 3	88.5	201
5Gy x 4	89.5	198
8.5Gy x 2	91	224
9.5Gy x 4	74	279

How do we do it?



Brachytherapy Eligibility

- Is it a Practical Treatment?
- Consent
- Pubic arch acceptable
- Able to hyperflex hips
- Life expectancy > 10 yrs
- Hip replacements *(poor CT visualisation,req MR)*
- Obesity

- Is Patient at Increased Risk of Complications?
- Anticoagulation
- TURP *(size of TURP defect)*
- AUA < 12, Flow rate > 12 (catheter risk)
- Chronic prostatitis

Preop

- Volume study –awake patient, bowel prep
- prostate volume, (ellipsoid + calculated)
- correlation with CT and MR volume QA
- echogenicity – Ca
- Pubic arch
- Anaesthetic assessment

Intraop

- Patient in stirrups
- Insertion of catheters –inder Xray and ultrasound guidance
- CT planning scan postop
- Bladder irrigation until no bleeding
- Treatment day of procedure and next day x 2
- Implant removed under sedation
- Catheter remains until bleeding settled
- Discharge home once passed urine and bowel motion

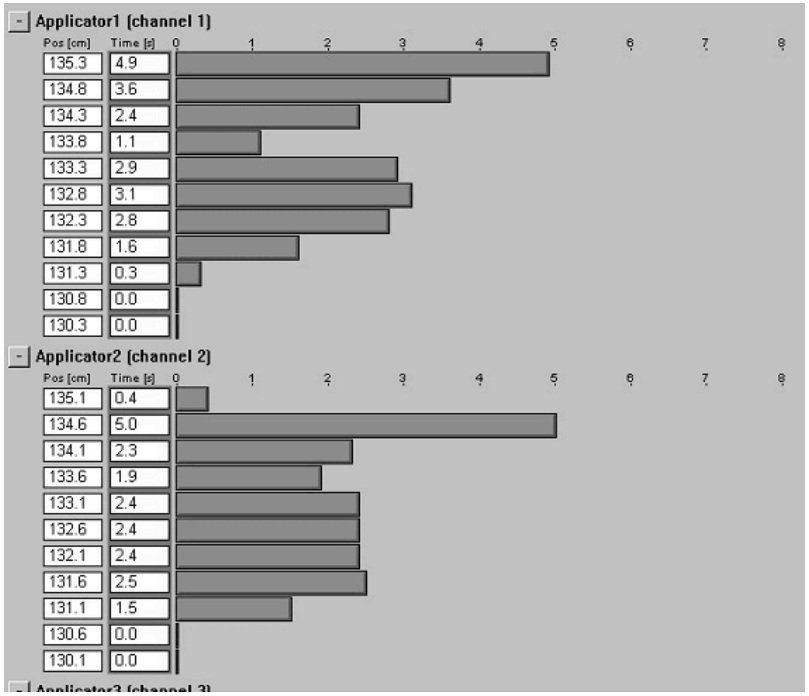
Post op

- Patient is not radioactive
- Low fibre diet to avoid bowel motions
- Pressure point cares
- Pain relief-endone
- No fluid in ends of catheters
- Treatments –replan before each
- Catheters removed under sedation
- Patient can be discharged once voided
- Country patients – bladder obstruction risk
- Followed by 46Gy EBRT

Post implant care

- Flomaxtra 0.4mg 1 month
- NSAID for 5-10 days
- Simple analgesia prn
- Norfloxacin 5 days (10 if diabetic)
- Hormones-continue if high risk
- Ural for dysuria (NSAID)
- Cranberry juice/tomatoes/orange juice acidity can exacerbate dysuria

HDR treatment



- The radiation distribution and dose is determined by which dwell positions the source stops at and the length of time it “dwells” there

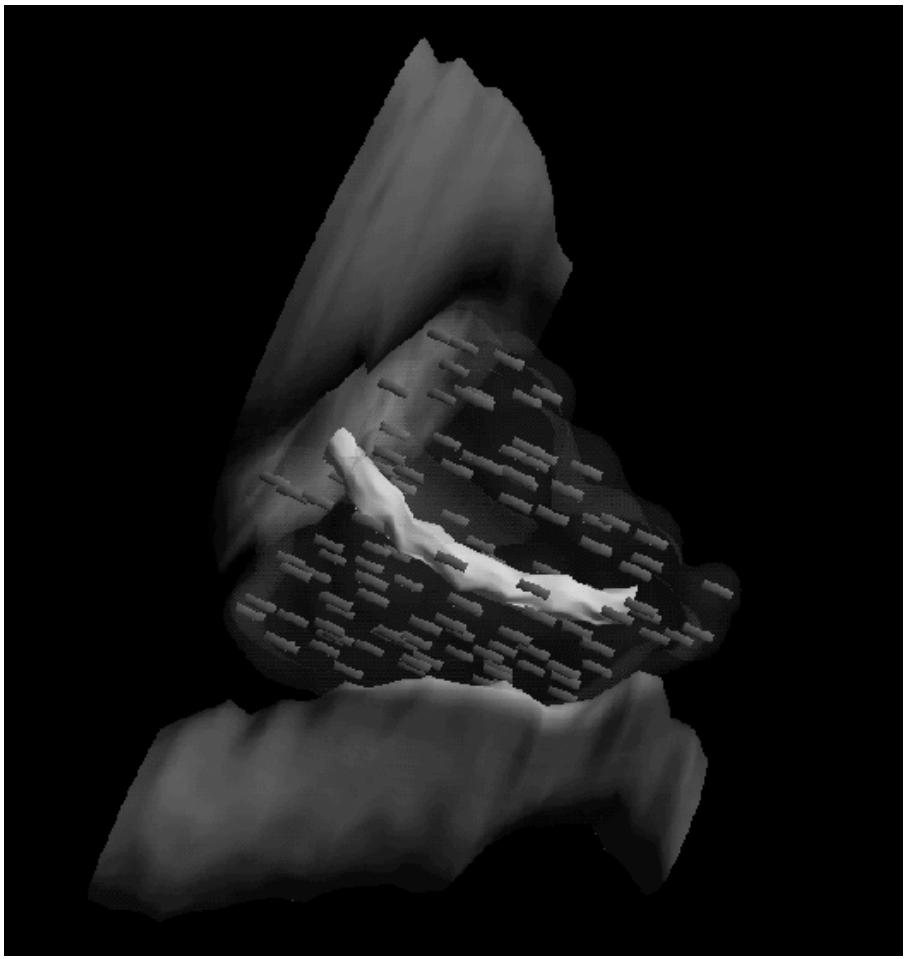
Acute toxicity HDR brachytherapy

- Periprocedural
- Pain, bleeding, urinary retention(10%)
- EBRT component
- Proctitis rare, dysuria, frequency, urgency
- Acute post RT symptoms
- Rectal symptoms settle early
- Uruinary symptoms take 6-12 months to settle

Long Term

- Stricture- 3-15%
- Impotence-
- Perineal nerve function
- Dysuria
- Bowels

Results



Results of treatment

- Warning:
- Problems with interpreting the data
  - Not all patient groups are equal
  - Differences in reporting data
  - No consensus on reporting dose

HDR Treatment Outcomes

Study	*No.*	*Median PSA*	*Median Fup*	*bNED(5)*
Mate 1998 (Seattle)	104	12.9	45mo	iPSA<20:84% iPSA>20:50%
Ealau (Seattle)	104	12.9	6.3yr	OAS5 83% OAS 10 77%
Kestin	161	9.9	2.5yr	83%
Borghede 1997	50	NR	45mo	84% (18 mo)1
Galalae 2002	144	12.15 mean25.6	8yr	69%(10yr) 74% (5yr)

HDR Late Toxicity

Study	*GI*	*GU*
Mate(1998)	2% G2	6.7% urethral stricture
Kestin (2000)	No G3	4% stricture
Galalae (2002)	4% G3 7% G2 10% G1	2% G3 cystitis 4%G2 12%G1
Borhegde (1997)	8% G2 proctitis No G3	12% G1-3 0 urethral strictures

TABLE 40.6.18 Biochemical Outcomes after Combined High-Dose-Rate (HDR) Brachytherapy and External-Beam Radiotherapy (EBRT)

Study (Reference) Series	*No. of Patients*	*Median Follow-Up (months)*	*Treatment Regimen*	*PSA Outcome According to Prognostic Risk Grouping*
Vargas et al. (205)	560	51	Median HDR, 23 Gy Median EBRT, 42 Gy	High risk with ADT, 84% High risk without ADT, 81%
Galalae et al. (200)	611	60	Seattle, 3-4 Gy × 4 Kiel, 9 Gy × 2 Beaumont, 5.5-11 Gy × 2	Low, 96% Intermediate, 88% High, 69%
Demanes et al. (201)	209	87	6 Gy × 4, HDR + 36 Gy EBRT	Low, 90% Intermediate, 87% High, 69%
Yamada et al. (203)	105	44	5.5-6.5 Gy × 3, HDR + 50.4 Gy IMRT	Low, 100% Intermediate, 98% High, 92%
Phan et al. (204)	309	59	8 Gy × 4, HDR 39.6-45 Gy EBRT	Low, 98% Intermediate, 90% High, 78%
Hoskin et al. (205)	109	30	8.5 Gy × 2, HDR 37.5 Gy EBRT	Low, 100% Intermediate, 90% High, 81%
Deger et al. (204)	442	60	10 Gy × 2 40 Gy EBRT	Low, 80% Intermediate, 65% High, 58%
Pellizon et al. (207)	119	41	4 Gy × 4-5, HDR 45 Gy EBRT	Low risk, 78% High risk, 76%

PSA, prostate-specific antigen; ADT, androgen deprivation therapy; IMRT, intensity-modulated radiation therapy.

TABLE 40.6.19 **Late Toxicity Outcomes after Combined High-Dose-Rate (HDR) Brachytherapy and External-Beam Radiotherapy**

Study (Reference) Series	*No. of Patients*	*Median Follow-Up (years)*	*Late Genitourinary Toxicity*	*Late Gastrointestinal Toxicity*
Galalae et al. (200)	144	8	Grade 2, 4% Grade 3, 2% Incontinence, 6% (8 of 9 had TURP before or after HDR)	Grade 2, 7% Grade 3, 4%
Deger et al. (202)	442	5	Grade 3, 9% (urethral strictures) Urinary incontinence, 2% Grade 4, 1%	—
Martinez et al. (211)	207	4.4	Grade 3, 8% (urethral strictures) Grade 4, 0	Grade 3, 0.5% Grade 4, 0.5%
Pellizon et al. (207)	119	3.4	Grade ≤2, 4.6% Grade 3-4, 0	Grade ≤2, 12% Grade 3-4, 0%
Yamada et al. (203)	105	4	Grade 2, 2% Grade 3, 2% (urethral strictures) Grade 4, 0	Grade 1-2, 7% Grade 3-4, 0%
Phan et al. (204)	309	5	Grade 2, 15% Grade 3, 4% (urethral strictures)	Grade 1-2, 4% Grade 4, <1%
Demanes et al. (201)	209	7.25	Grade 2, 8% Grade 3, 7% (urethral strictures) Grade 4, 1%	Grade 1-2, 2% Grade 3-4, 0

TURP, transurethral resection of the prostate.

LDR brachytherapy

- I-125 iodine seeds or Pd-103 palladium
- Theoretically Pd better as shorter half-life-no proven benefit *($t_{1/2}$64.2d vs 17d)*
- Implant technique very important as dosimetry "fixed" by seed position
- Controversy re dosimetry on day 1 or day 30
- 10% of patients have increased swelling at day 30 leading to poorer implant dosimetry
- Discharge same day after catheter removed
- 10% reinsertion of catheter

TABLE 40.6.16 Prostate-Specific Antigen (PSA) Relapse-Free Survival Outcomes for Low-Dose-Rate Brachytherapy

Study (Reference)	*No. of Patients*	*Median Follow-Up (years)*	*Treatment*	*5-Year Biochemical Outcome According to Risk Group*	*Comments*
Stock et al. (169)	1,377	4.2	MT/CMT	Low, 94% Intermediate, 89.5% High, 78%	Interactive real-time planning
Zelefsky et al. (153)	2,693	5.2	MT	Low, 82% Intermediate, 70% High, 48%	D90 ≥130 Gy 8 year PSA control, – 93% D90 <130 Gy 8-year PSA control, – 76%
Guedea et al. (170)	1,050	2.5	MT	Low, 93% Intermediate, 88% High, 80%	—
Khaksar et al. (171)	300	4	MT	Low, 96% Intermediate, 89% High, 93%	—
Zelefsky et al. (172)	367	5.3	MT	Low, 96% Intermediate, 89%	Real-time intraoperative planned implants
Sylvester et al. (173)	232	9.4	CMT	Low, 86% Intermediate, 80% Unfavorable, 68%	—
Potters et al. (155)	1,449	7	MT/CMT	Low, 89% Intermediate, 78% Unfavorable, 63%	—

MT, monotherapy; CMT, combined-modality therapy (implant + external beam); PSA, prostate-specific antigen.

TABLE 40.6.17 Late Toxicity Outcomes after Prostate Brachytherapy

Study (Reference)	*No. of Patients*	*Median Follow-Up (years)*	*Genitourinary*	*Gastrointestinal*
Stock et al. (169)	325 Incontinence, 1%	7	Grade 3, 2% (urethral stricture)	Grade ≤2, 24% Grade 3-4, 0%
Waterman and Dicker (188)	98	3		Grade 2, 10%
Merrick et al. (190)	1,186	4.3	Grade 3, 3.6% Urethral stricture	
Gelblum et al. (190,191)	825	4	Grade 3, 4.7% 17% post TURP developed incontinence	Grade 1, 9% Grade 2, 6.6% Grade 3, 0.5%
Bottomley et al.	667	2.5	Acute retention, 14.5% Late retention, 1% Urethritis @ 6 months, 13.5% Urethritis @ 24 months, 2.5%	Grade 4, <1%
Lee et al. (209) (RTOG 0019)	138	4	Late ≥ grade 3 GI/GU, 15% (combined-modality therapy)	
Shah et al. (159)	135	3.5		Diarrhea, 7.3% Urgency, 6.5% Bleeding, 7.3%
Keyes et al. (186)	805	3.3	AUR: IPSS 0-5, 8% IPSS 10-15, 15% IPSS >16, 21%	
Albert et al. (198)	201	2.8	Radiation-cystitis Monotherapy, 0% Combined-modality therapy, 5%	Grade 3 Monotherapy, 8% Combined-modality therapy, 30%
Zelefsky et al. (172)	367	5.2	Grade 2, 19% Grade 3, 4%	Grade 2, 7% Grade 3, 1%

LDR brachytherapy-toxicity

- Dysuria peaks at 6 weeks, gone in 75% by 3 months,95% gone by 6 months.
- 3% catheter dependence at 12 months
- Half of these removed over next 2 years, remaining ongoing intermittent catheterisation
- PSA bounce-up to 2 years post implant
- Prostatitis-increased dysuria and frequency, mostly sterile Rx NSAID, trial cipro fro 1/12

Ongoing Issues - Prediction of Stage

- Staging System-Risk Grouping
- Biopsies do not predict disease extent well
- Radiological tests do not adequately predict micrometastatic disease