Brachytherapy in Carcinoma Prostate

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Magnitude of the problem

- Prostate cancer relatively uncommon
- Life expectancy : 65 yrs
- Low awareness
- No PSA screening

Incidence

- Third commonest cancer in most PBCRs
- Incidence is rising : ?apparent ?real
- AAR: 7.1 per lakh population
- Majority present in locally advanced/metastatic stages
- Sizeable number of patients do come in early stages

Brachytherapy for Carcinoma Prostate

- As monotherapy : for low risk patients
- As Boost : for intermediate and high risk pts
- As salvage therapy : for recurrent cases

Why Brachytherapy ?

- Conformal treatment
- Short course therapy
- Excellent local control
- Better quality of life
- Preservation of sexual function
- Cost effective

Types of Brachytherapy

- High dose Rate (HDR) Brachytherapy
- Low dose Rate (LDR) Brachytherapy or Seed Brachytherapy

HDR Brachytherapy: Indications

Monotherapy

- Low- and intermediate risk

Boost (combined with EBRT)

- any T with N0 M0
- any PSA
- any Gleason-Score

HDR Brachytherapy: Absolute contraindications

1. Preexisting rectal fistula,
2. Medically unsuited for anesthesia, and
3. No proof of malignancy.

Patient Preparation

Spinal anesthesia

Lithotomy position

Foley catheter

Procedure

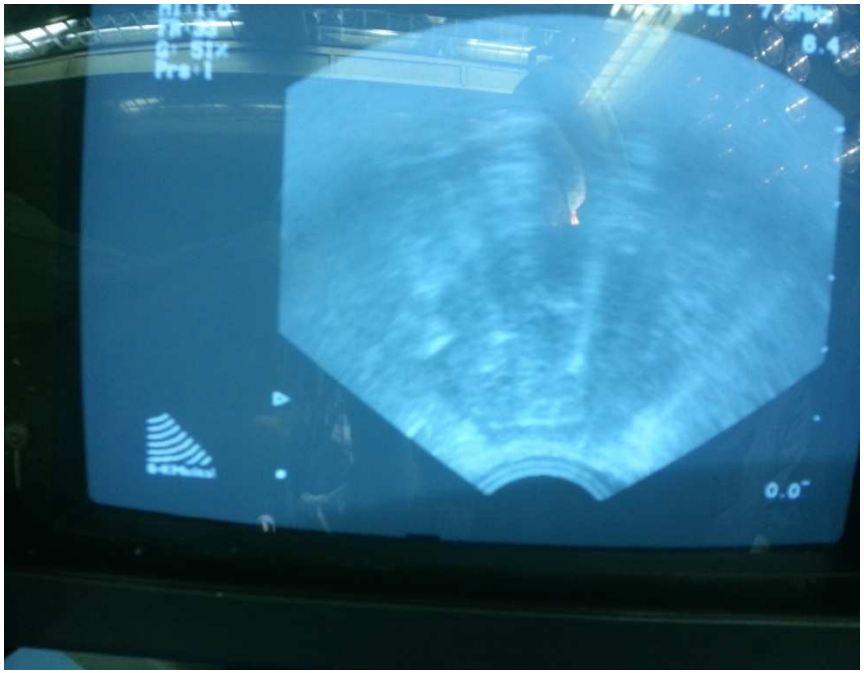
Let the Foley's be high up to avoid balloon rupture

LP Needle to Decide the Position of Template

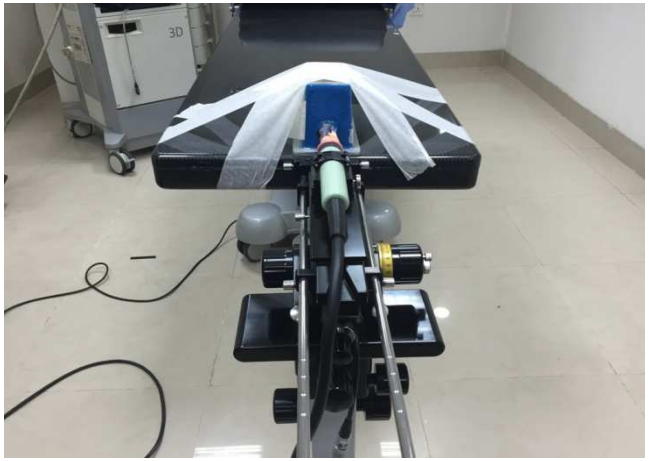
TRUS Imaging

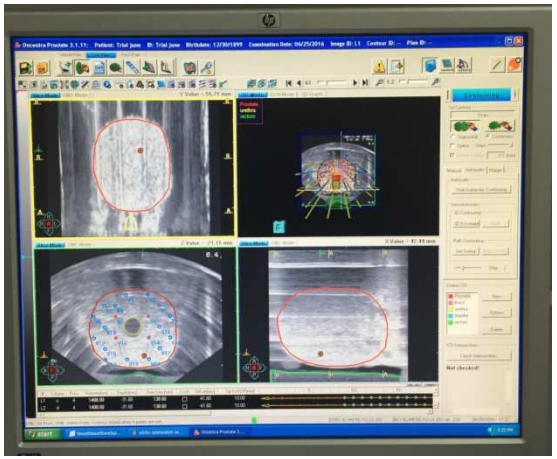
Fixation of probe and template on the stepper

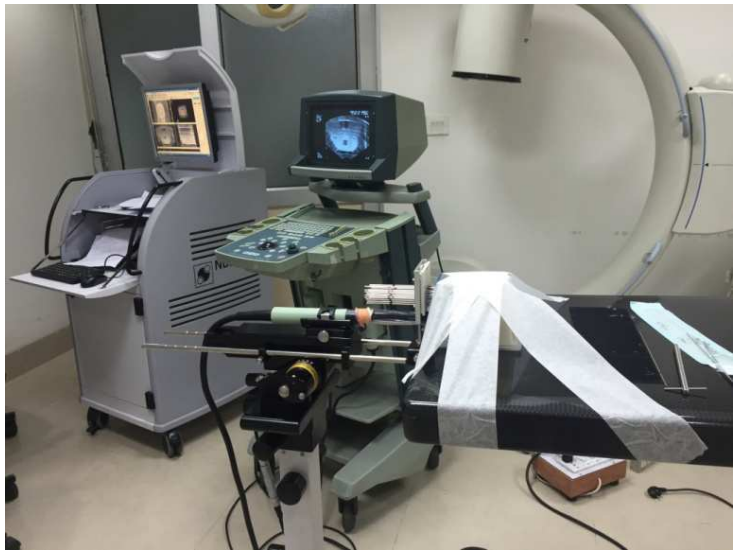
Needle insertion using USG guidance

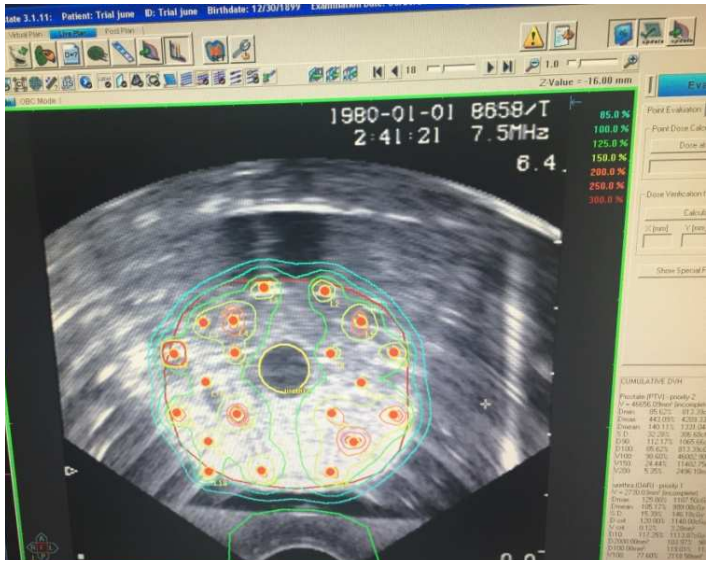


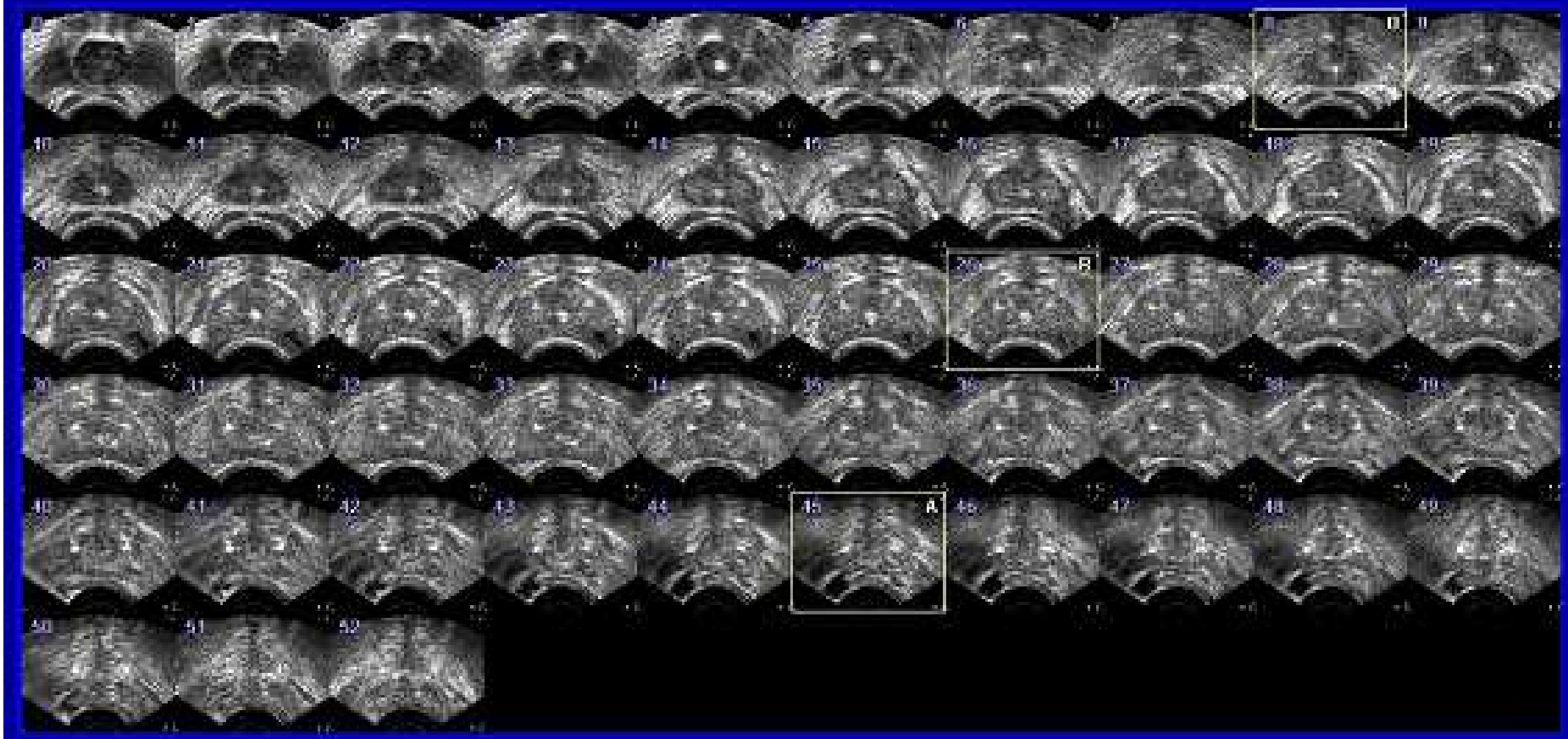
Phantom Trials to Streamline Workflow Logistics



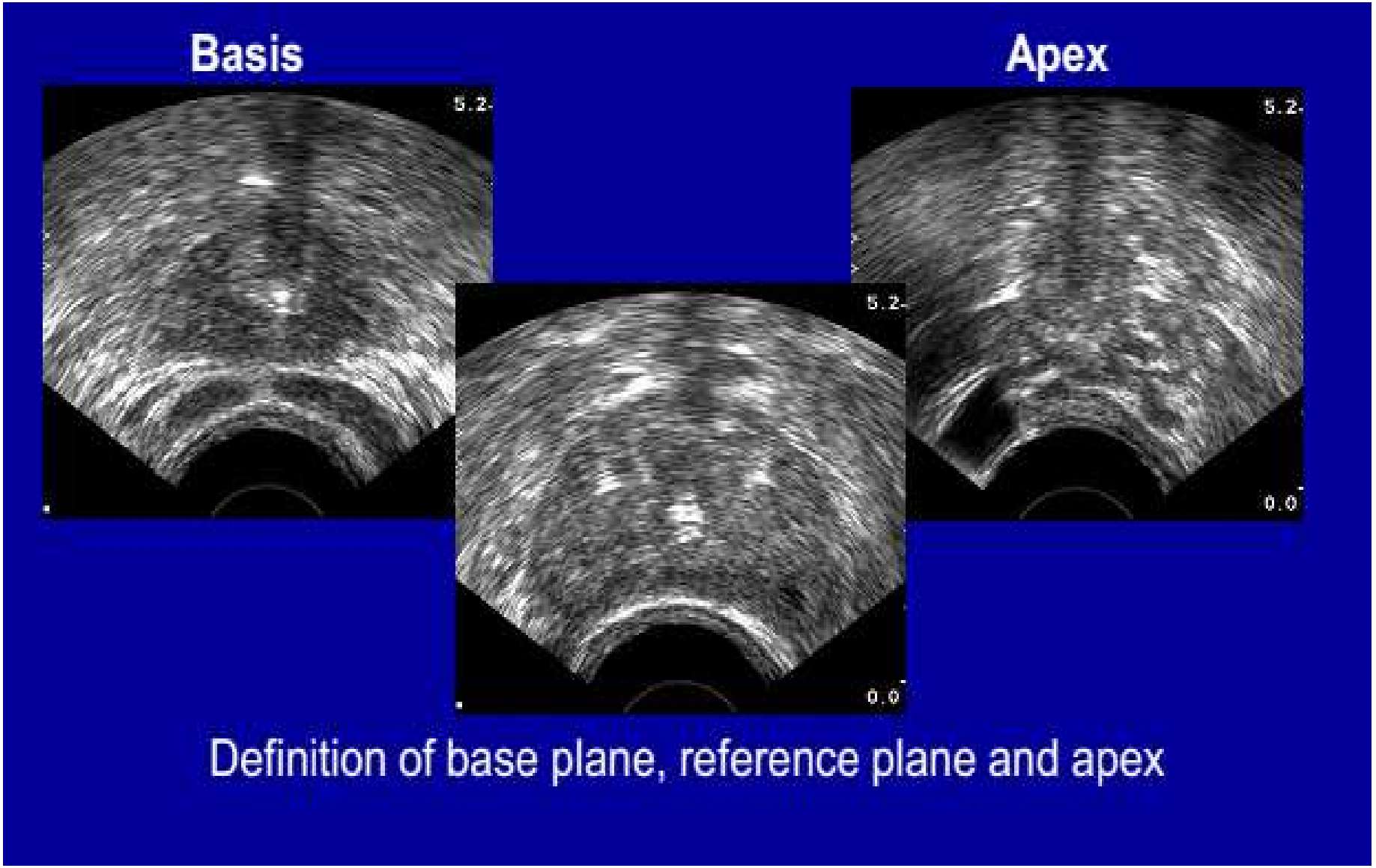








Continuous TRUS-image-recording with online transfer to the real-time planning system

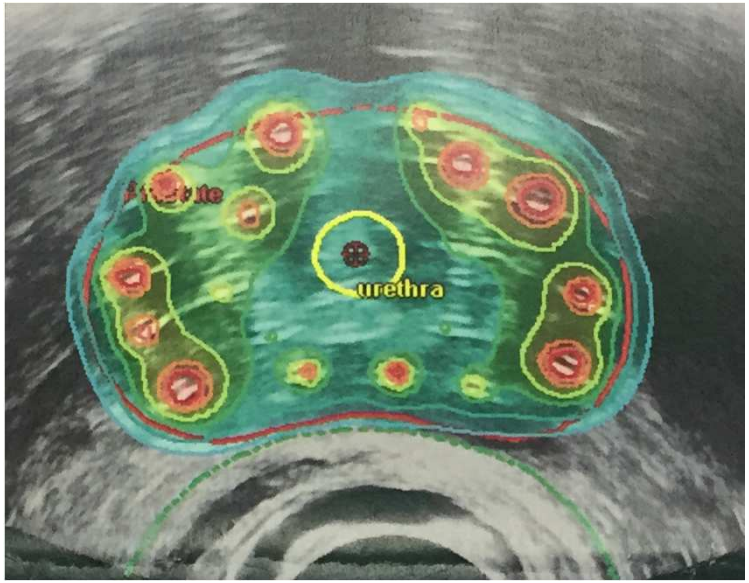


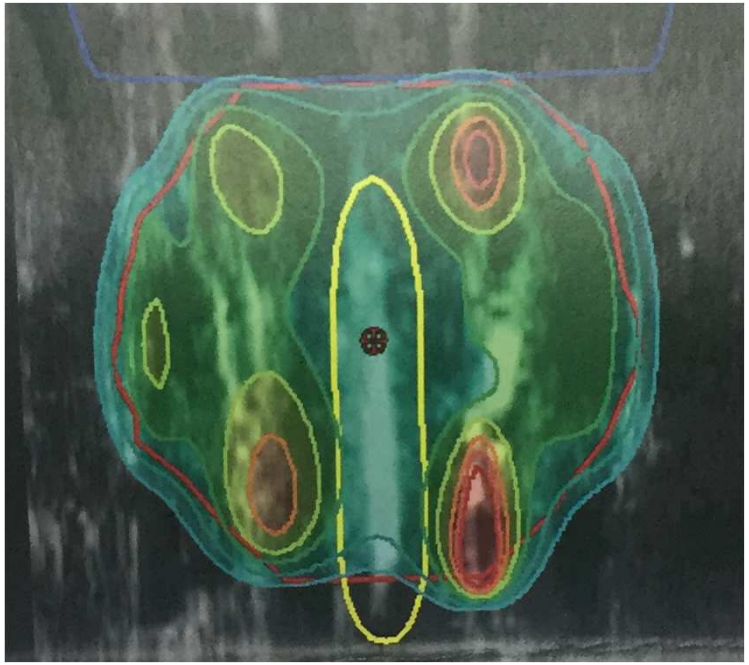
Definition of base plane, reference plane and apex

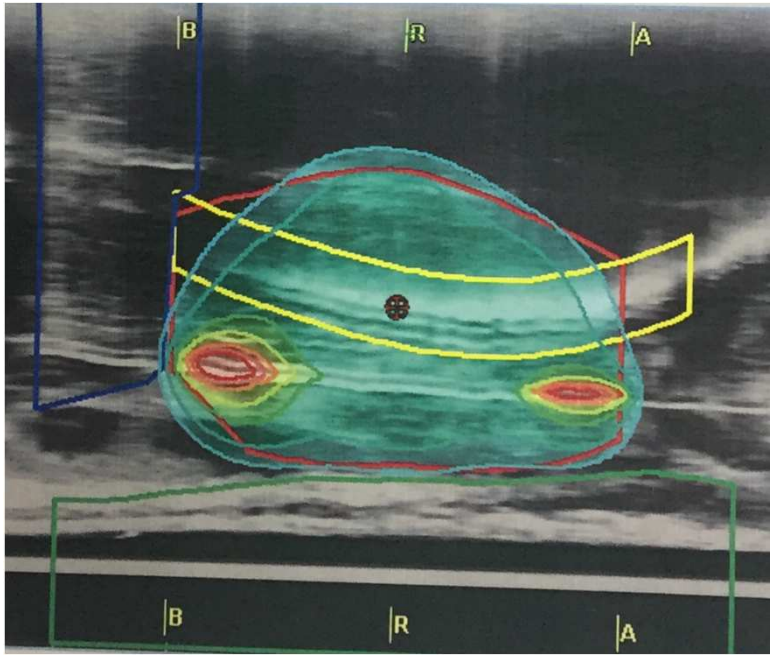
Prostate Steps contd..

- Needle insertion as per preplan
- Repeat 3D USG with Urethral contrast
- Catheter reconstruction and contouring
- Final plan and evaluation
- Connect for treatment
- Implant removal
- Bladder irrigation for hemostasis

Dosimetry







Pre-implant & Post Implant Care

- Antibiotic on the morning of implant
- Complete bowel preparation with PEGLEC the day prior
- Part preparation
- Post procedure Anti inflammatory, antibiotics & alpha blockers
- Bladder irrigation with normal saline till hematuria subsides
- Foleys out the next day

Current dose fractionation schedules

Institution	Dose fractionation	Bladder	Urethra	Rectum
MSKCC	Boost 7Gyx3 Mono 9.5Gyx4 Salvage 8Gyx4		<120% prescription	$D_{2\ cc} < 70\%$
UCSF	Boost 15Gyx1 Mono 10.5Gyx3 Salvage 8Gyx4*	$V_{75} < 1$ cc	$V_{125} < 1$ cc, $V_{150} = 0$ cc *(dose tunnel whenever possible)	$V_{75} < 1$ cc
WBH	Boost 10.5Gyx2 Mono 4 × 9.5 Gy (historical) 12–13.5Gyx2 (current) Salvage 7Gyx4 combined with hyperthermia	No constraint (intra-op TRUS-based dosi)	$V_{100} < 90\%$ of prescription $V_{115} < 1\%$ of prescription	$V_{75} < 1\%$ of prescription
TCC	Boost 6Gyx2 ×2 implants	<80% of Rx	<125% of prescription	<80% of Rx to outer wall
GW	Boost 6.5Gyx3 Mono two sessions of 6.5Gyx3	<100% prescription	<110% prescription	mucosa <60%, outer wall <100%
Toronto	Boost 15Gyx1	n/a	$D_{10} < 118\%$ Max < 125%	$V_{80} < 0.5$ cc
UCLA-CET	Boost 6Gyx4 Mono7.25Gyx6	90–100% wall 80% balloon	120% combo 105% any TUR 110% mono	Rectal wall 80% Rectal wall 80–85%

Initial Results of HDR Brachytherapy in Prostate Cancer: AIIMS Experience

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Combined HDR Brachytherapy and External Beam Radiotherapy Vs External Beam Radiotherapy Alone By IMRT in Localized Prostate Cancer; Interim Analysis of Acute Genitourinary and Gastrointestinal Toxicity and Biological Dose Volume Parameters From a Prospective Randomized Control Trial

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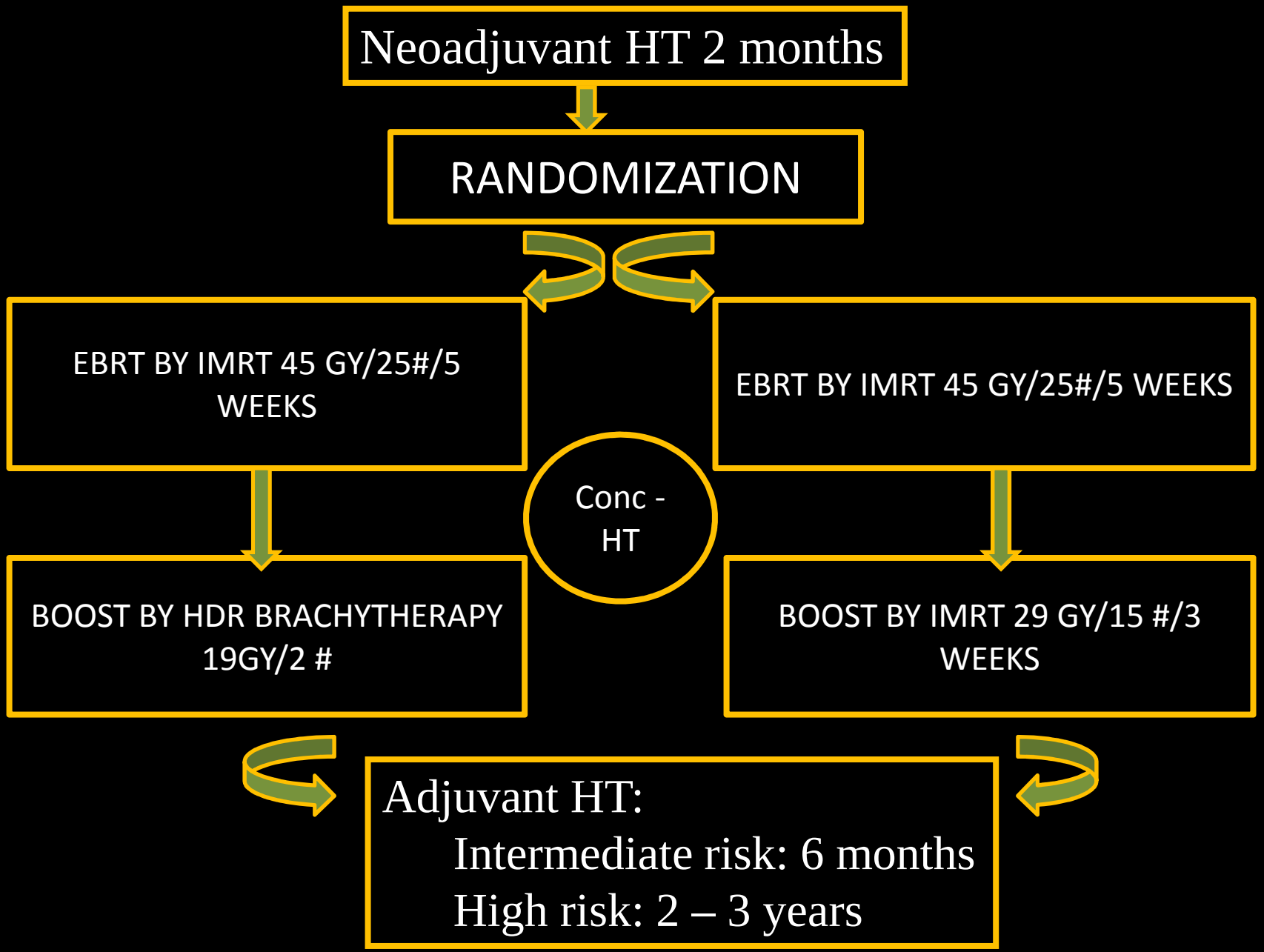
AIMS & OBJECTIVES

1.Feasibility of combining Brachytherapy boost after EBRT (IMRT)

2. To compare dosimetric parameters for PTV between IMRT & Brachytherapy arm

3. To compare dosimetric parameters for OAR (bladder & rectum)

Treatment schema



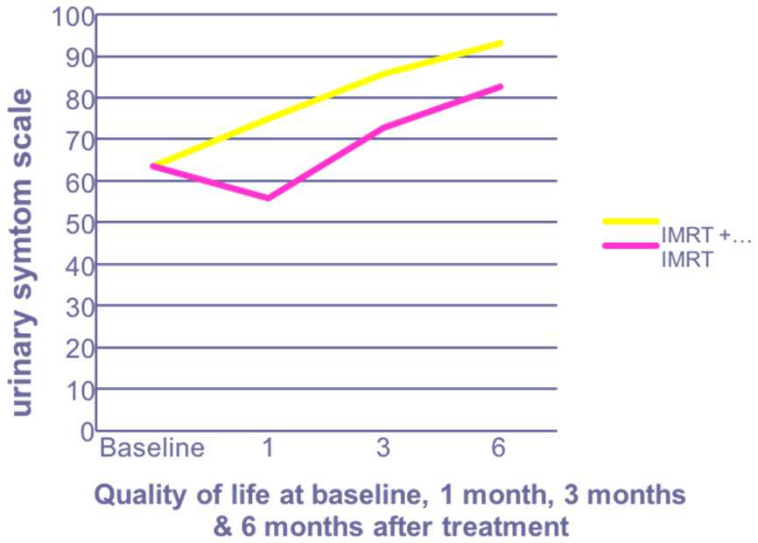
RESULTS

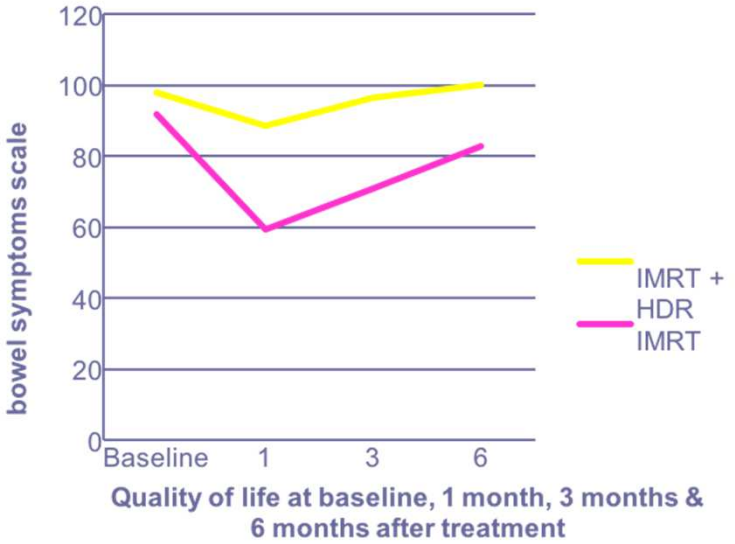
- Total: 30 patients: Median follow up: 8.5 months
- Median age: 68 years: Stage distribution:T2b -T3b
- Median Gleason: 7 (Range 6-8)
- Mean S.PSA :34.9ng/ml
- Intermediate risk – 9 (30%) High risk – 21 (70%)
- The median prostate volume: 49.2mL(26.2-63.5)
- The major symptoms of acute GU toxicity were dysuria, increase in urinary frequency or nocturia
- The major symptoms of acute GI toxicity were diarrhea and tenesmus

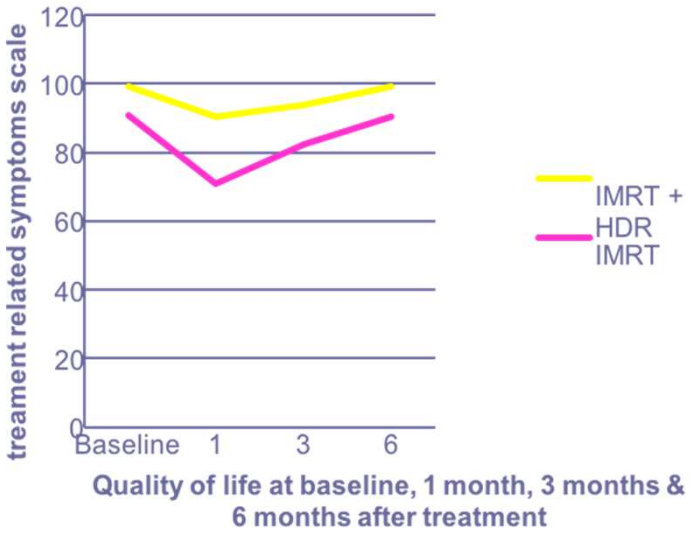
BOOST PHASE	BRACHY ARM	IMRT ARM	p
EQD2 for 95% of PTV (a/b: 1.5Gy)	45.7Gy	28.4Gy	0.001
EQD2 for Dmean to PTV (a/b: 1.5Gy)	46.5Gy	29.3Gy	0.001
EQD2 for Dmean of Rectum	7.4Gy	13.5Gy	0.001
EQD2 for 33% of Rectum	6.8Gy	17.4Gy	0.001
EQD2 for Dmean of Bladder	5.4Gy	12.8Gy	0.001
EQD2 for 1cc of Bladder	16.7Gy	27.9Gy	0.001

Toxicity	Symptoms	Arm 1 (%)	Arm 2 (%)	P
Acute genitourinary ≥ grade 2	Dysuria	33	40	0.591
	Frequency	40	46	0.279
	Hematuria	6	0	0.264
Acute gastrointestinal ≥ grade 2	Diarrhea	20	33	0.137
	Tenesmus	6	13	0.345
Any late genitourinary ≥ grade 2		33	46	0.280
Any late gastrointestinal ≥ grade 2		6	20	0.139

QLQ PR-25 subscales (differences between arms)	Mean difference (Arm 1*)	Mean difference (Arm 2#)	P
Urinary scale 1 month	11.3	-7.8	0.072
Urinary scale 3 months	22	9.1	0.157
Urinary scale 6 months	29.4	19.1	0.121
Bowel scale 1 month	-9.5	-32.6	0.001
Bowel scale 3 months	-1.4	-21	0.005
Bowel scale 6 months	2.1	-8.9	0.018
Treatment related scale 1 month	-8.5	-19.9	0.160
Treatment related scale 3 months	-5.2	-8.3	0.580
Treatment related scale 6 months	20	-20	0.941
Sexual scale 1 month	4.4	8.2	0.196
Sexual scale 3 months	10.2	11.8	0.818
Sexual scale 6 months	11.9	15.2	0.556


urinary symtom scale
100
90
80
70
60
50
40
30
20
10
0
Baseline
1
3
6
IMRT +…
IMRT
Quality of life at baseline, 1 month, 3 months & 6 months after treatment


bowel symptoms scale
120
100
80
60
40
20
0
Baseline
1
3
6
IMRT +
HDR
IMRT
Quality of life at baseline, 1 month, 3 months & 6 months after treatment


treament related symptoms scale
120
100
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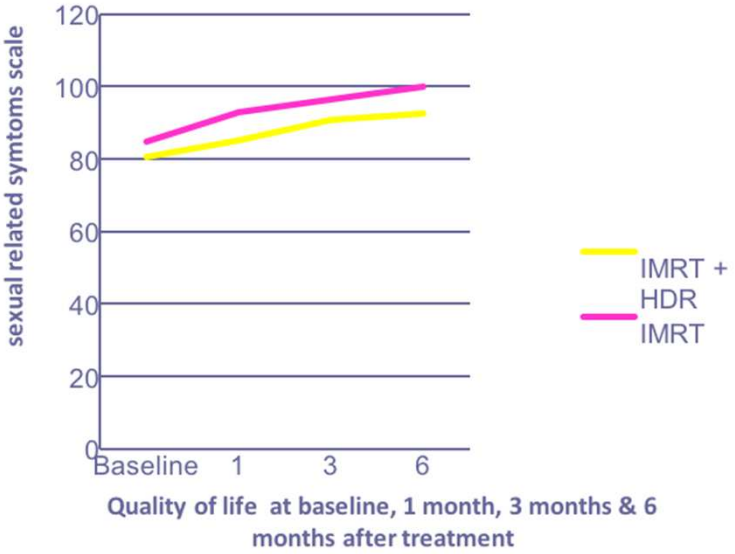
20
0
Baseline
1
3
6
IMRT +
HDR
IMRT
Quality of life at baseline, 1 month, 3 months & 6 months after treatment


sexual related symtoms scale
120
100
80
60
40
20
0
Baseline
1
3
6
IMRT +
HDR
IMRT
Quality of life at baseline, 1 month, 3 months & 6 months after treatment

Study Conclusion

- HDR BT produced a more conformal plan & provides higher mean dose to prostate
- Doses to the OAR are lower than IMRT
- Brachytherapy is effective in achieving dose escalation
- No difference in bladder & bowel toxicity
- QOL (bowel symptom scale) better in brachytherapy
- Longer follow-up is needed to evaluate the efficacy

Seed Brachytherapy in Carcinoma Prostate

Permanent prostate implant

- Mainly monotherapy
- May be used as boost
- Salvage of recurrent tumors

Brief history

- 1917: Young HH used Radium-226 implants thru bladder, urethra, rectum

- 1970s: Whitmore and Hilaris, retropubic implantation of I-125

- 1980s: Holm and Pederson, transrectal ultrasonography guided I-125 implantation

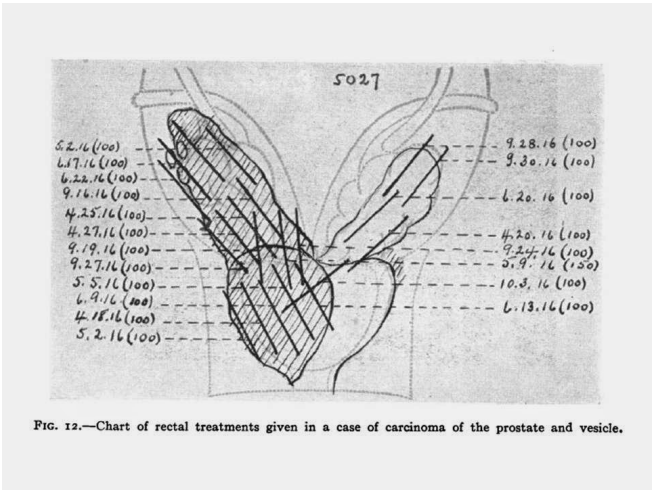


FIG. 12.—Chart of rectal treatments given in a case of carcinoma of the prostate and vesicle.

Patient selection

I-125/Pb-103 Mono-therapy:

- cT1 ~ T2b
- PSA < 10
- GS: 2 - 6
- T1-T2 / GS < 7 / PSA < 10,

ELSEVIER

Brachytherapy 11 (2012) 6–19

BRACHYTHERAPY

American Brachytherapy Society consensus guidelines for transrectal ultrasound-guided permanent prostate brachytherapy

Brian J. Davis[1,*], Eric M. Horwitz[2], W. Robert Lee[3], Juanita M. Crook[4], Richard G. Stock[5], Gregory S. Merrick[6], Wayne M. Butler[6], Peter D. Grimm[7], Nelson N. Stone[8], Louis Potters[9], Anthony L. Zietman[10], Michael J. Zelefsky[11]

Suggested treatment schema for low-, intermediate-, and high-risk disease for PPB

Risk group per NCCN	Brachytherapy alone?	Combined with EBRT?	Combined with androgen deprivation?
Low	Yes	Not favored	Not favored
Intermediate	Optional	Optional	Optional
High	No	Yes	Favored

Relative contraindications

- Severe urinary irritative/obstructive symptomatology
- Extensive TURP defect
- Substantial median lobe hyperplasia
- Prostate dimensions larger than the grid (>60 mm in width & >50mm in height)
- Severe pubic arch interference
- Gross seminal vesicle involvement
- Prior pelvic radiotherapy
- Inflammatory bowel disease
- Pathologic involvement of pelvic lymph nodes

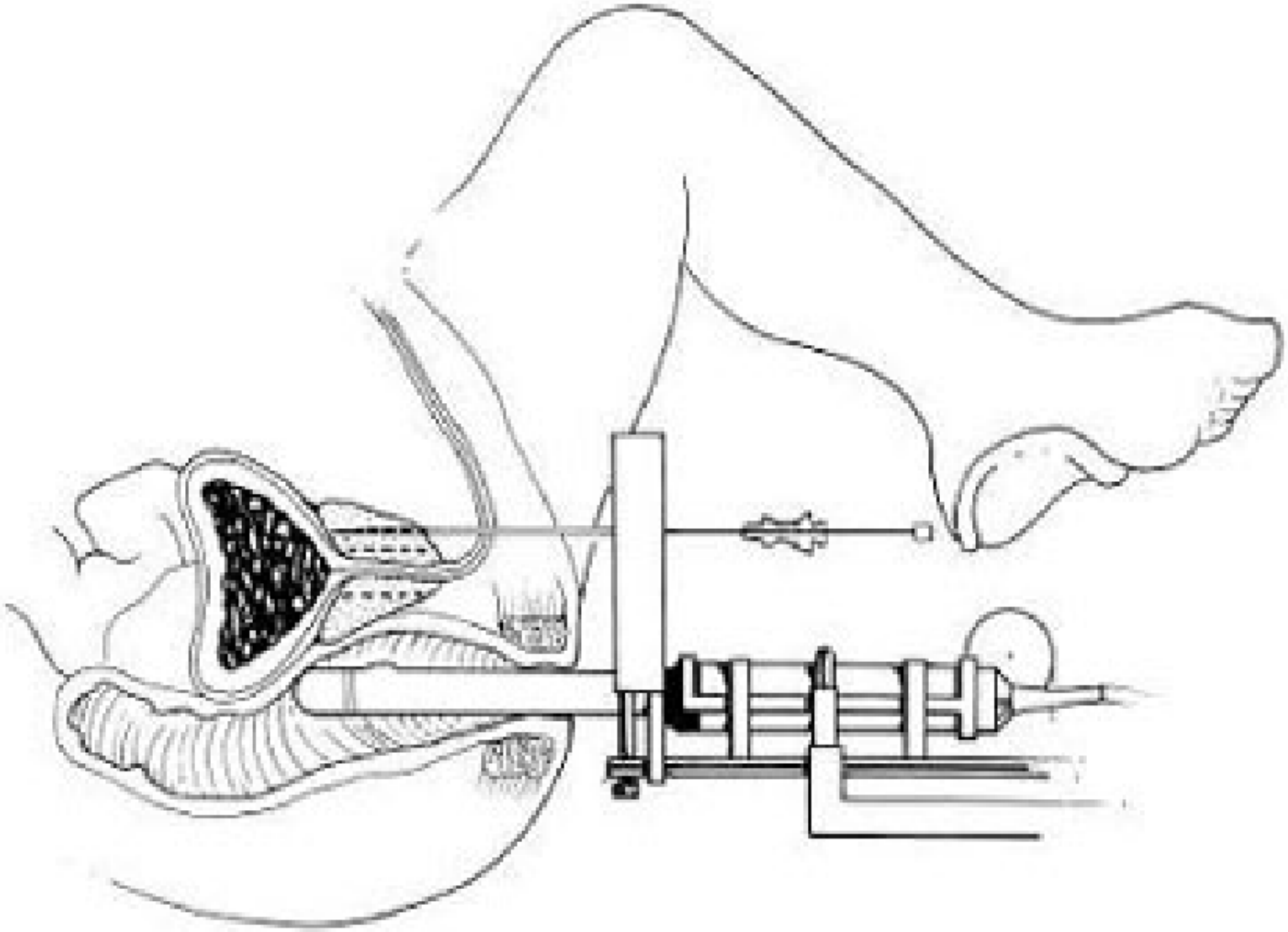
Absolute contraindications to TRUS-guided PPB
Limited life expectancy
Unacceptable operative risks
Distant metastases
Absence of rectum such that TRUS guidance is precluded
Large TURP defects, which preclude seed placement and acceptable radiation dosimetry
Ataxia telangiectasia

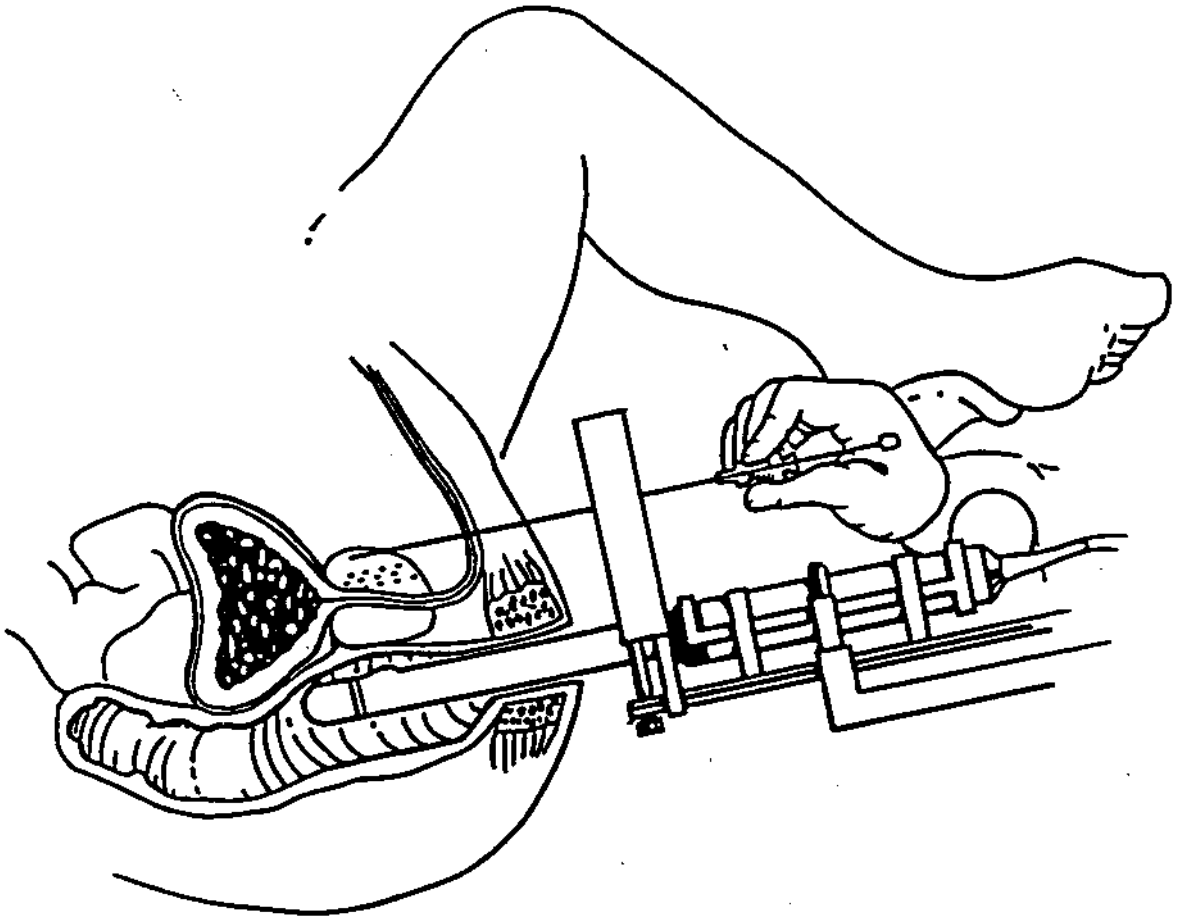
Radionuclides for permanent prostate brachytherapy

Radionuclide	Half-life (d)	Average energy (keV)	Year introduced	Typical monotherapy seed strength	
				(mCi)	(U)
^{125}I	59.4	28.4	1965	0.3–0.6	0.4–0.8
^{103}Pd	17.0	20.7	1986	1.1–2.2	1.4–2.8
^{131}Cs	9.7	30.4	2004	2.5–3.9	1.6–2.5

Prescription doses to the planning target volume	
^{125}I	
Monotherapy	140–160 Gy
Combination	
EBRT	41.4–50.4 Gy (1.8 Gy/d[a])
PPB dose	108–110 Gy
^{103}Pd	
Monotherapy	110–125 Gy
Combination	
EBRT	41.4–50.4 Gy (1.8 Gy/d[a])
PPB dose	90–100 Gy

Implant procedure





STEPS:

Planning-TRUS guided volume study—computer preplan

Brachytherapy procedure-TRUS guided trans perineal needle-..

peripheral loading..

seeds placed along the tract from base to apex.

Post implant evaluation-by CT scan

Prostate: D_{90} (in Gy and percent)

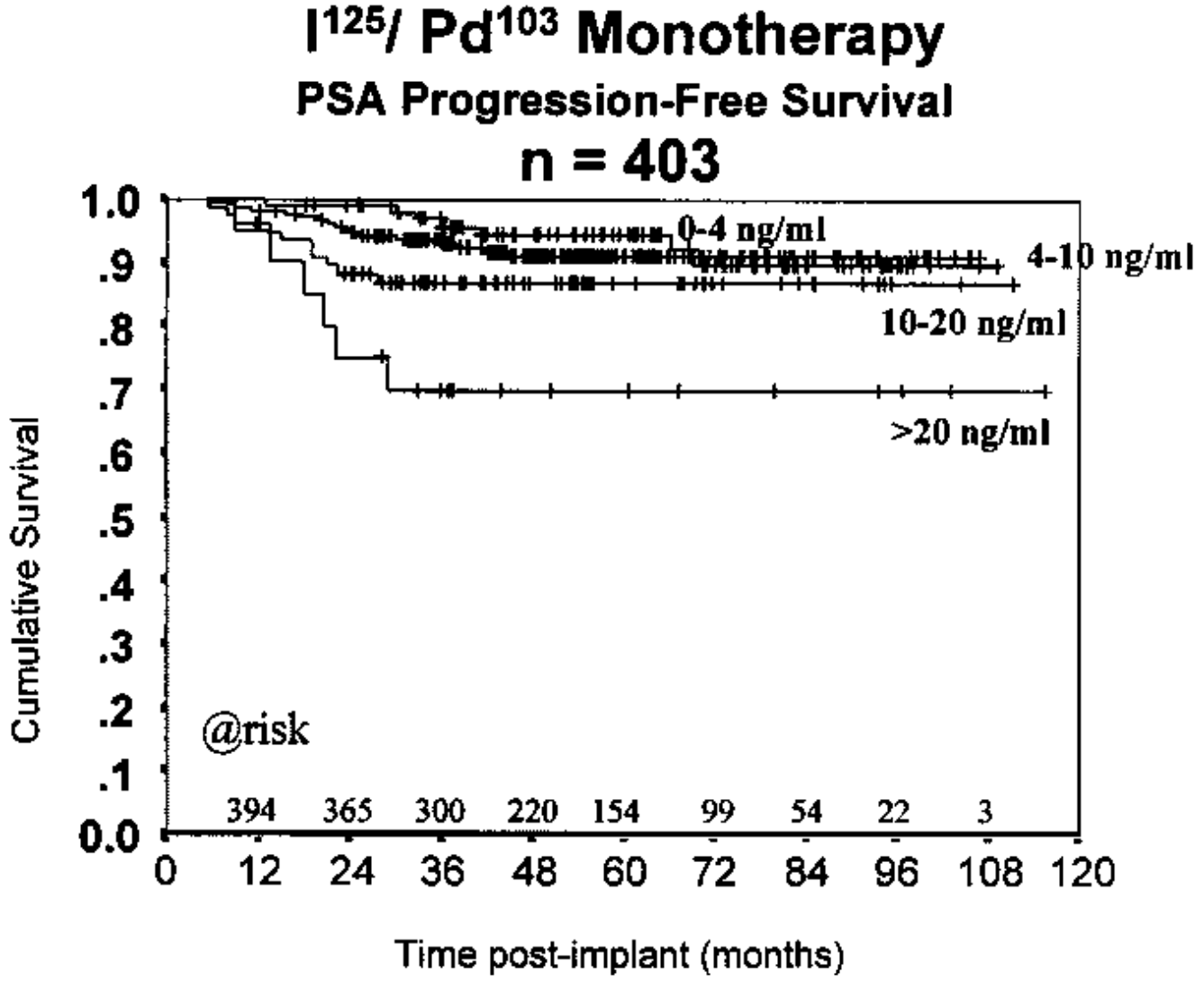
V_{100} and V_{150} (in percent)

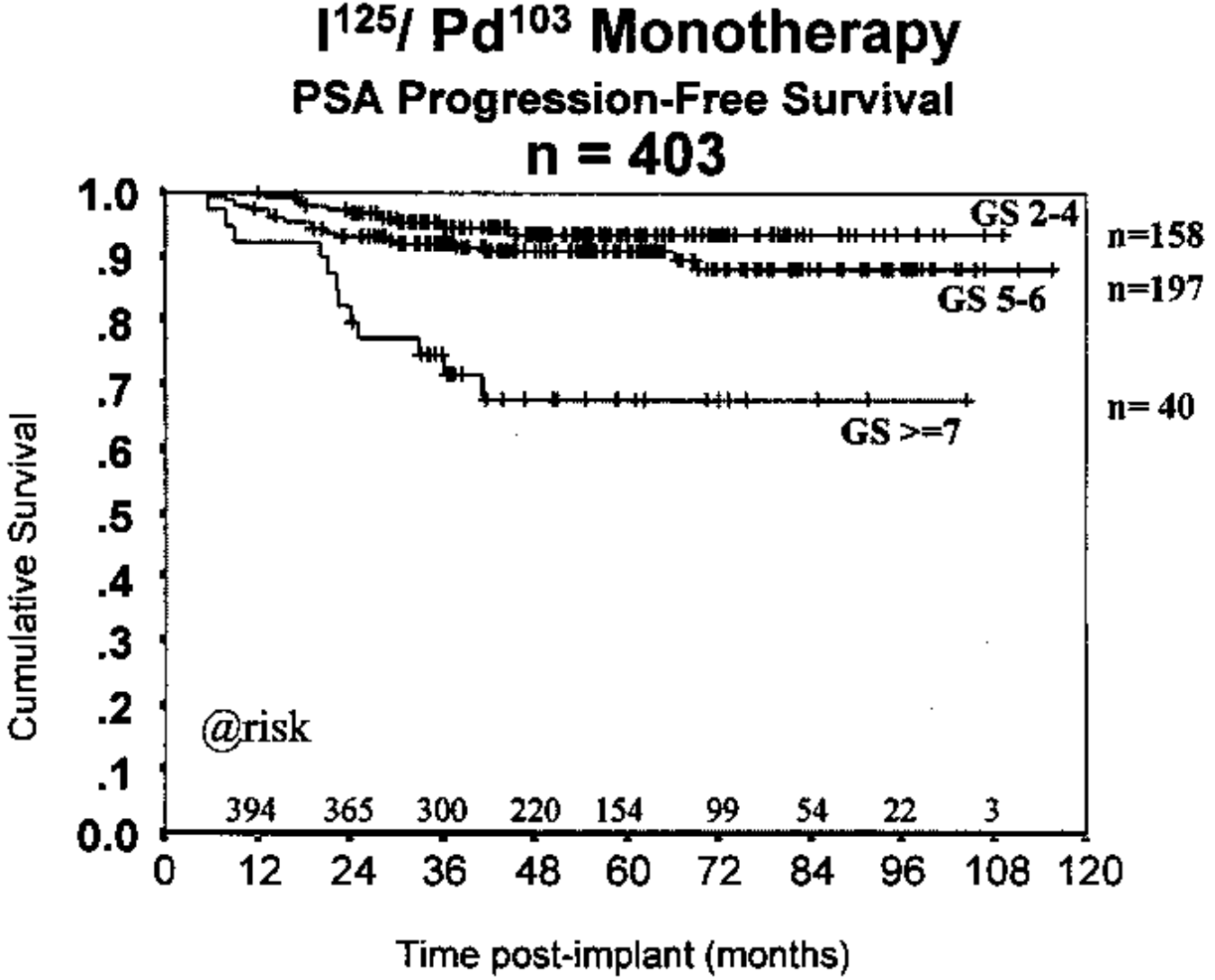
Urethra: UV_{150} (in volume)

UV_5, UV_{30} (percent)

Rectum: RV_{100} (in volume)

Aim to keep UV5<150% and UV30<125% in the preplan

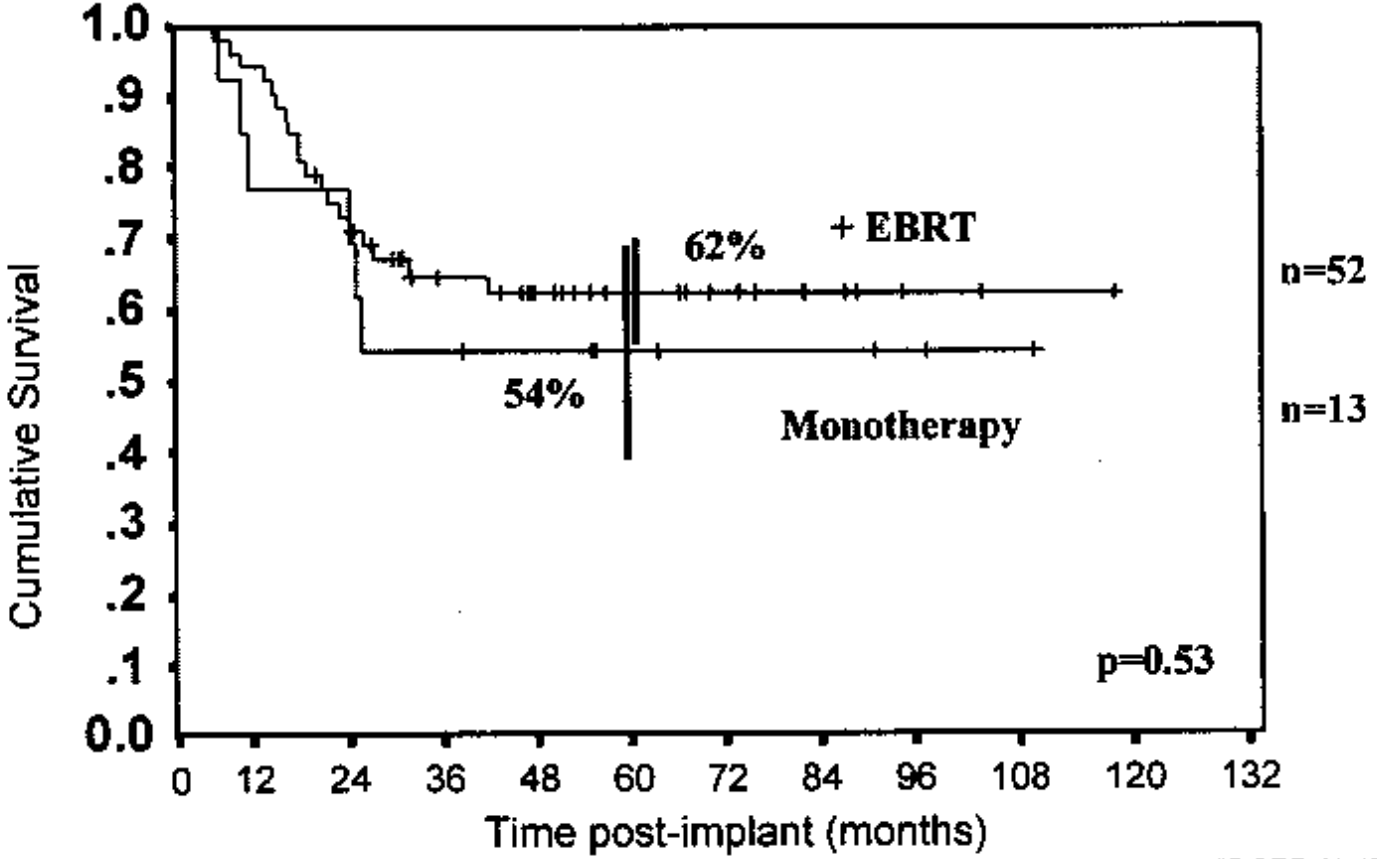

I125/ Pd103 Monotherapy
PSA Progression-Free Survival
n = 403
1.0
.9
.8
.7
.6
.5
.4
.3
.2
.1
0.0
Cumulative Survival
0-4 ng/ml
4-10 ng/ml
10-20 ng/ml
>20 ng/ml
@risk
394 365 300 220 154 99 54 22 3
0 12 24 36 48 60 72 84 96 108 120
Time post-implant (months)


I125/ Pd103 Monotherapy
PSA Progression-Free Survival
n = 403
1.0
.9
.8
.7
.6
.5
.4
.3
.2
.1
0.0
Cumulative Survival
GS 2-4
n=158
GS 5-6
n=197
GS >=7
n= 40
@risk
394 365 300 220 154 99 54 22 3
0 12 24 36 48 60 72 84 96 108 120
Time post-implant (months)

I^{125}/ Pd^{103} Implant ± EBRT

PFS: "Unfavorable Risk Group"*

cT3 or GS >6 or iPSA >10: (2+ factors)



*Zelefsky, Leibel, et al. IJROBP 41:491-500, 1998.

Acute Symptoms

- Dysuria (often)
- Hematuria (common)
- Perineal hematoma (significant < 3 %)
- Obstruction (5-12%)
- Perineal Pain (< 5%)
- Diarrhea (< 10%)

Delayed Complications

- Chronic cystitis (3-7 %)
- Incontinence (1% for non-TURP, 25-42% for TURP)
- Rectal ulceration (< 1 %)
- Urethral necrosis (< 1 %)
- Erectile dysfunction (> 70y/o, 20-25%; < 70y/o, 10-15%)

Conclusion

- Brachytherapy is an important treatment for carcinoma prostate
- Can be used for monotherapy for low risk patients and boost for intermediate/high risk patients
- Provides excellent local control
- Preservation of sexual function