PROSTATE CANCER BRACHYTHERAPY

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Risk categorization

Very Low Risk	T1c GS≤6 PSA <10ng/ml <3 Bx core +ve with ≤6 Cancer in each core PSA Density < 0.15ng/mL/g
Low Risk	T1-T2 GS≤6 PSA <10ng/ml
Intermediate Risk	T2b –T2c or GS 7 or PSA 10-20 ng/mL
High Risk	T3a or GS 8-10 or PSA >20ng/mL
Very High Risk	T3b-T4 or Primary Gleason Pattern>5 or >4core with GS8-10
Metastatic	any T,N1 or any T, any N, M1 disease

NCCN 2016

Prostate cancer : Treatment Outlook

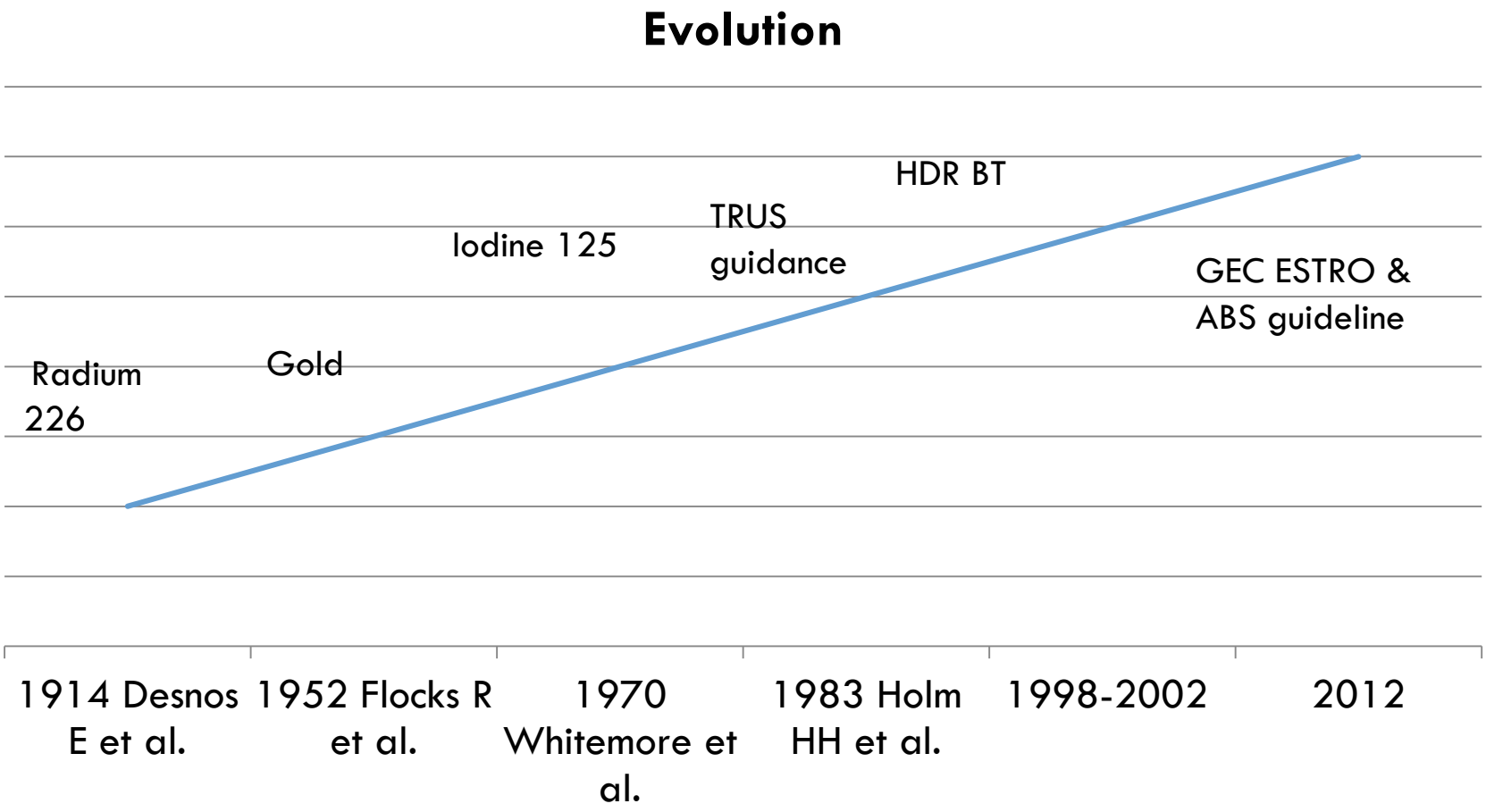
TABLE 66.1 RECOMMENDATIONS OF PELVIC RADIOTHERAPY AND HORMONES

	Low Risk	*Favorable Intermediate Risk*	*Unfavorable Intermediate Risk*	*High Risk*
Radiotherapy Androgen suppression therapy	PORT Not indicated	PORT Neoadjuvant (2 mo) Concurrent	WPRT Neoadjuvant (2 mo) Concurrent ± Adjuvant (2 mo)	WPRT Neoadjuvant (2 mo) Concurrent Adjuvant (24–36 mo)

PORT, prostate-only radiotherapy; WPRT, whole-pelvic radiotherapy.

Perez 6th Edn p1319

Role Of Brachytherapy



Why Brachytherapy?

- Escalation of Biological Effective Dose to much higher extent than External Beam RT (IMRT)

  Higher cure rate.
- Minimizing RT dose to nearby critical organ.
- Encompasses Prostate motion better than External RT.
- Overall Treatment time lesser than usual 8weeks time for dose escalated External RT.

Role of Brachytherapy

- BT Mono-therapy:

  Low Risk group

  Favorable Intermediate group

  (Low volume disease/Predominant pattern3/one adverse feature)

- Brachytherapy Boost (after/before EBRT):

  Unfavorable Intermediate group

  High risk group

- Recurrence

Types of Brachytherapy used

- Low Dose Rate Brachytherapy (LDR BT)

  Permanent Prostate BT (PPB)

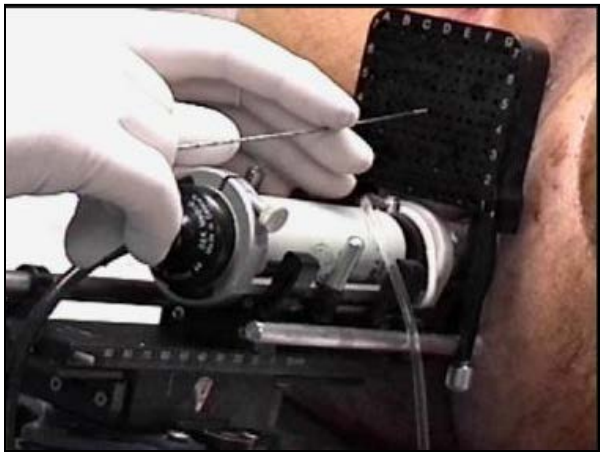
Isotope	T 1/2	Mean Energy	Seed strength
Iodine 125	60days	27keV	0.3-0.6 mCi
Palladium 103	17days	21 keV	1.2-2.2 mCi
Cesium 131	9.7days	30.4 keV	2.5-3.9 mCi

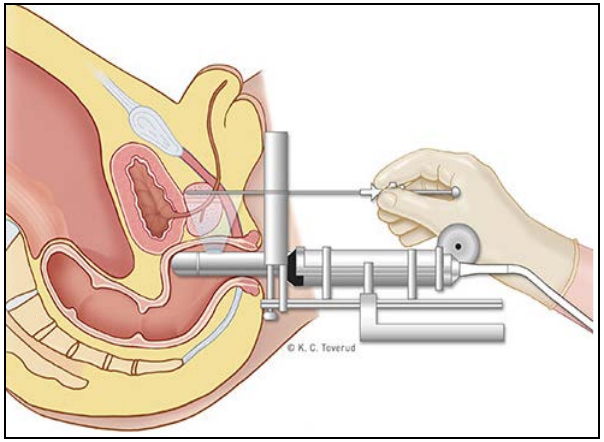
Type	Dose rate (Gy/h)
LDR	0.4-2
HDR	>12

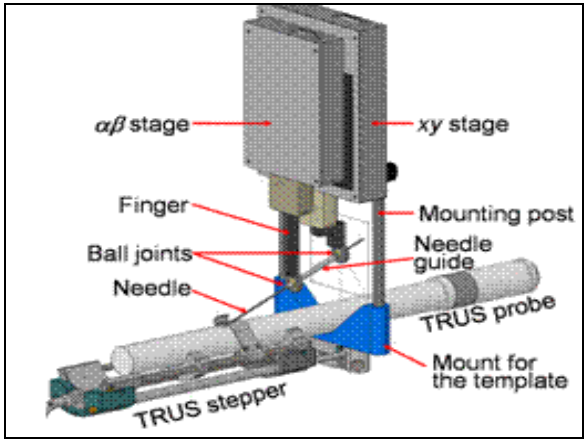
- High Dose Rate Brachytherapy (HDR BT)

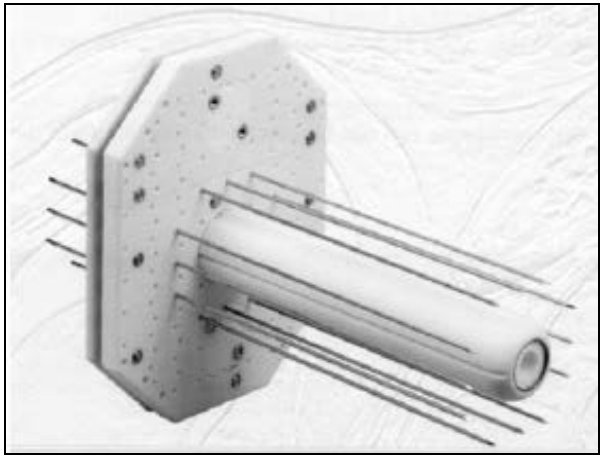
Isotope	T 1/2	Mean Energy	T-AKR (μGy.m2/GBq.h)
Iridium 192	73.8days	0.38MeV	108
Cobalt 60	5.26years	1.25MeV	308

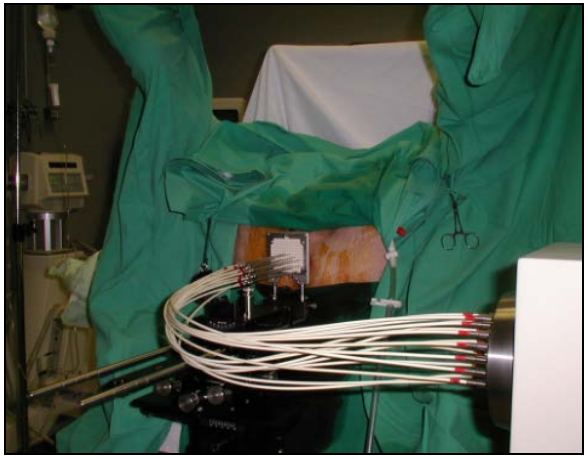
Prostate BT applicators











Permanent Prostate Brachytherapy

Patient evaluation and work up:

HP with GS

Pre Treatment PSA

DRE to access Clinical “T”

Prostate Volume (TRUS)

Access tolerability of patient for extended dorsal lithotomy position

Pre anesthetic check up

Contraindications of PPB

Absolute	Relative
Limited life expectancy	IPSS>20
Ataxia Telangiectasia	Prior Pelvic RT
High Operative Risk	Volume>60cc
Absence of Rectum	Large median lobes
Large TURP defect	Inflammatory Bowel Disease

PPB Procedure

Pre Implant Planning

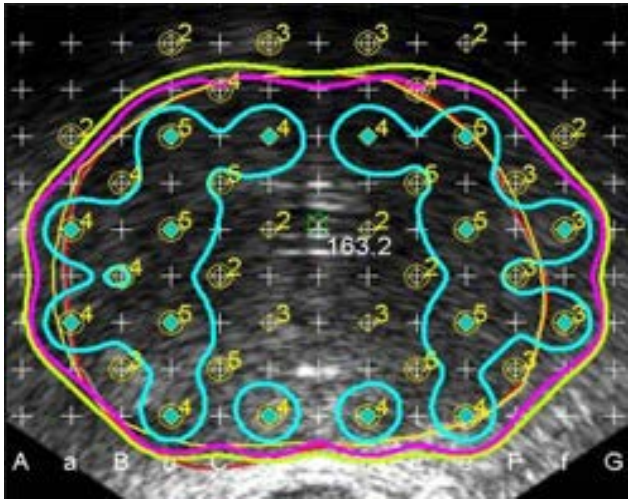
Imaging

(MRI > TRUS> CECT)

Target volume determination

Virtual planning

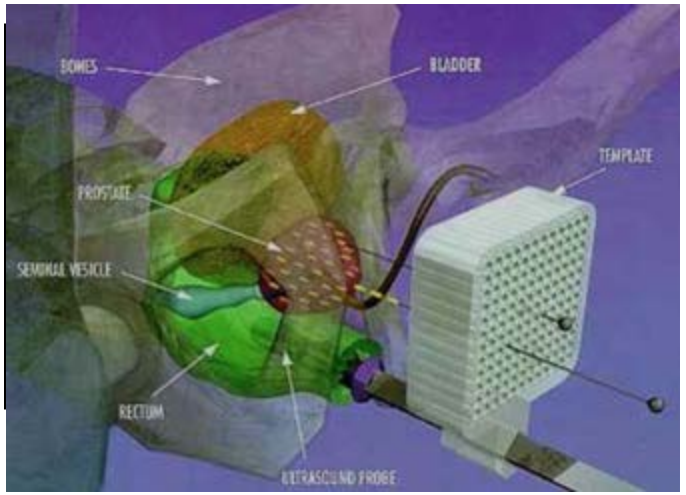
Mapping of seed positions in template

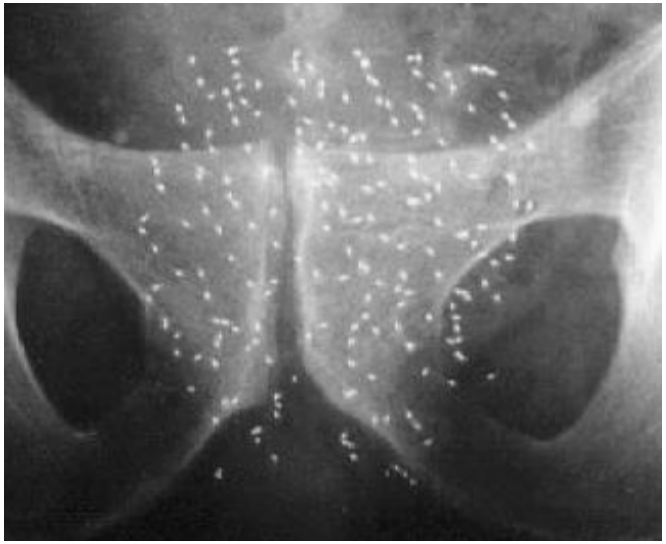


PPB procedure

Implantation Procedure

- Trans-perineal seed implantation
- TRUS and template guidance
- Seed positions as per preplanning sketch





PPB dose to Planning Target Volume

Iodine 125

- Mono therapy

  140-160Gy
- Combined

  EBRT: 41.4-50.4Gy

  1.8Gy/per day

  BT: 108-110Gy

Palladium 103

- Mono therapy

  110-125Gy
- Combined

  EBRT: 41.4-50.4Gy

  1.8Gy/per day

  BT: 90-100 Gy

BJ Devis et al. Brachytherapy 2012

Post implant Care

Post operative care

- Check cystoscopy
- Analgesic
- Antibiotic
- Antispasmodic
- Tamsulosin
- CT scan at week 6
- Emergency care

Radiation Protection

- No mandatory precaution
- Avoid contact with children and pregnant women
- Normal sexual life

PPB Results : Mono-therapy

Researcher	n	Follow up (Years)	Early Risk	Intermediate Risk	High Risk	Remarks
Sylevester et al. 2011	215	15	86%	80%%	62	PSARFS
Taira et al. 2011	1656	7	98.6%	-	-	7yr OS 77.5%
Zelefsky et al. (Multi Inst) 2007	2693	8	82%	80%	48%	PSA RFS
Stone et al. 2011	2111	12	88%	-	-	PSARFS
Zelefsky et al. 2012	1446	5	98%	95%	-	PSARFS
Potter et al. 2011	1449	12	89%	-	-	PSARFS

PPB results : Boost (with EBRT)

Authors	n	Follow up (years)	Intermediate Risk	High Risk	Remarks
Sylvester et al. 2007	232	15	80%	68%	PSA RFS
RTOG P - 0019	130	4	86%	-	PSA RFS
McMaster University	104	8.2	24%	-	Prostate biopsy rate

High Dose Rate Brachytherapy (HDR BT)

High Dose Rate BT

- **Advantages:**
- Radiobiological advantage
- Image guided accurate needles placement
- Individualized source position and optimization facility.
- Rapid delivery nullifies the influence of organ motion.
- Cost effective.
- Better radiation protection for personnel.

High Dose Rate BT

- **Disadvantages:**
- Fractionated radiation
- Increased work load per patient
- Logistic issues (TRUS guidance)
- Quality assurance

HDR BT : Results

Published outcome data for temporary high-dose-rate brachytherapy (HDR) with external beam radiotherapy in prostate cancer (most recent data cited where recurrent publications from the same group).

First author	Patient numbers	HDR dose	bRFS (%)				G3/4 toxicity (%)
			Low	Inter	High		
Borghede 1997	50	10 Gy × 2		84%		45 mo	10:GI 12:GU
Degar 2002	230	9–10 Gy × 2	100%	70%	65%	40 mo	12.2: GU
Pellizon 2003	209	4–6 Gy × 4	91%	90%	89%	64 mo	
Hiratsuka 2004							
Chiang 2004							
Astrom 2005							
Martinez 2005							
Yamada 2006							
Vargas 2006							
Chin 2006							
Phan 2007							
Chen 2007							
Kalkner 2007							
Sato 2008	53	7.5 Gy × 2	100%		43%	61 mo	
Demanes 2009	209	5.5–6 Gy × 4	90%	87%	69%	84 mo	8:GU
Zwahlen 2010	196	4–5 Gy × 4	94% (includes 3DCRT alone group also)	83%	76%	65 mo	7:GU 3:GI
Wilder 2010	284	5.5 Gy × 4	100%	100%	93%	66 mo	7:GU
Morton 2011	125	15 Gy × 1		97.9%		45 mo	1:GU
Kaprealian 2012	165	6 Gy × 3	92%	79%	89%	105 mo	2:GU
		9.5 Gy × 2	95%	81%	77%	43 mo	1:GU

HDR BT as Boost with EBRT is effective dose escalation strategy with good bRFS, Local Control and Survival

Hoskin PJ . Radiotherapy and Oncology 2013

HDR BT + EBRT : Patient selection

Inclusion criteria

- Stages T1b–T3b
- Any Gleason score
- Any PSA level

Exclusion criteria

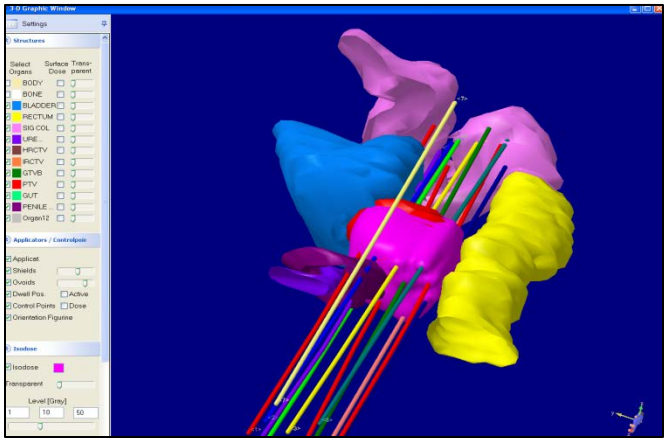
- TURP within 3–6 months
- Maximum urinary flow rate (Qmax) <10 ml/s
- IPSS > 20
- Pubic arch interference
- Lithotomy position or anaesthesia not possible
- Rectal fistula

GEC- ESTRO 2013 guideline

Requirement for HDR BT

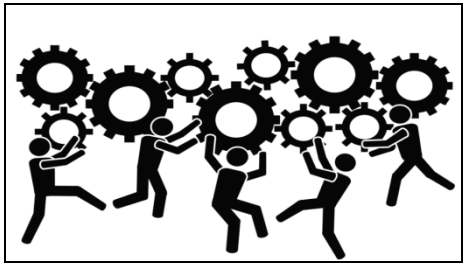
OT and Brachytherapy Suit with Anesthesia support

Remote after loader



Modern Planning system

Prostate Template



The Team Effort

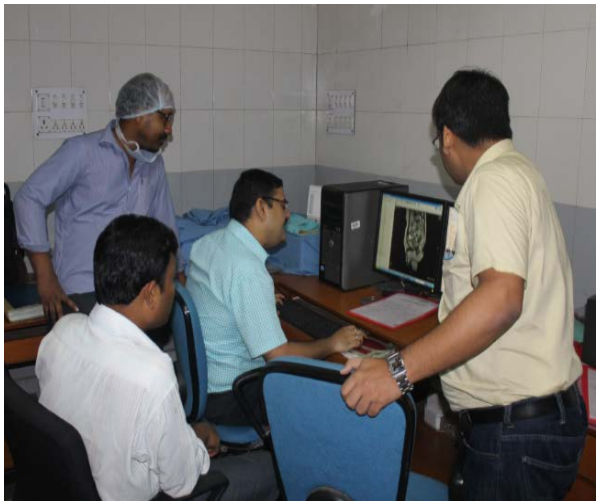
Steps of HDR BT

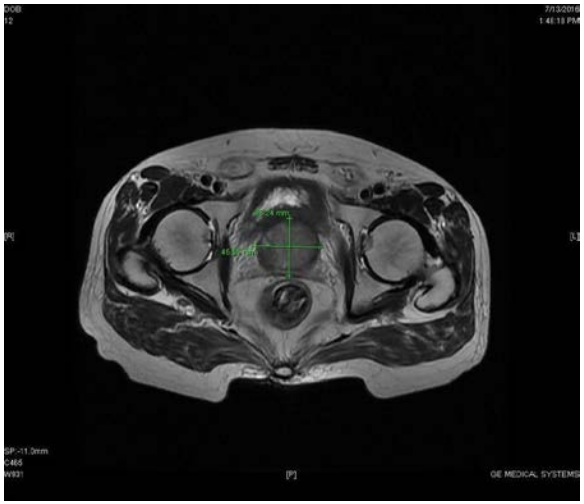
- Patient preparation
- Pre BT MRI
- Pre Planning
- Anesthesia (Spinal)
- Procedure
- Imaging
- Planning
- Evaluation
- Treatment
- Post Radiation Care

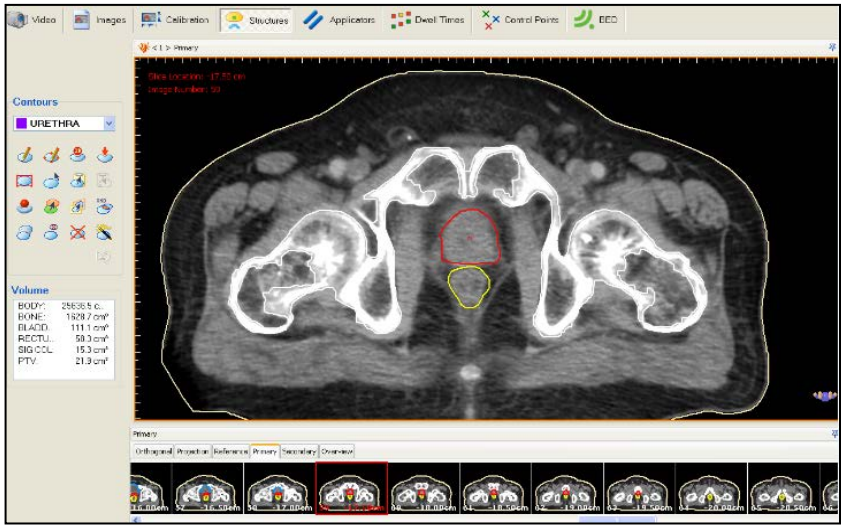
Pre Procedure works

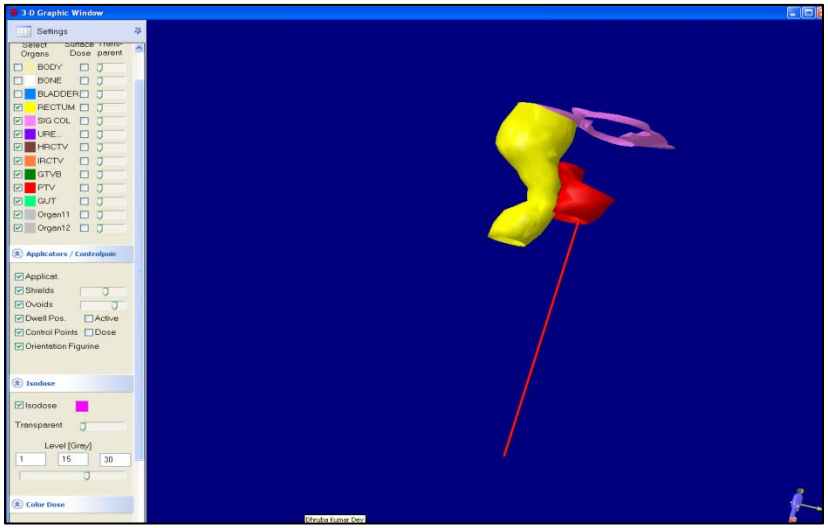
- **Patient Preparation**
- PAC Check up
- Pelvic MRI
- Bowel Preparation

Pre planning



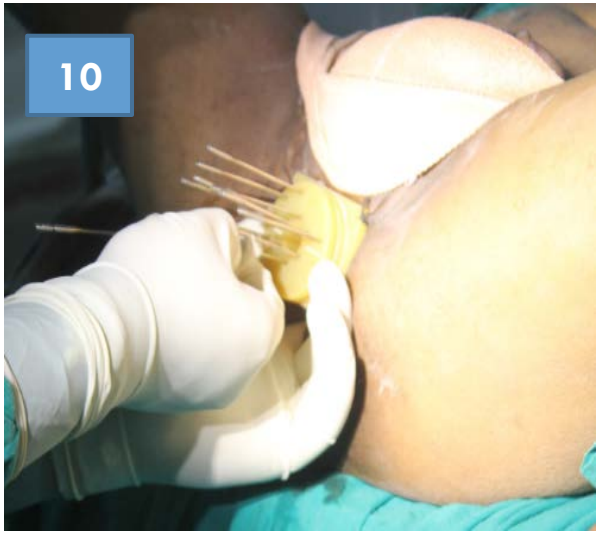


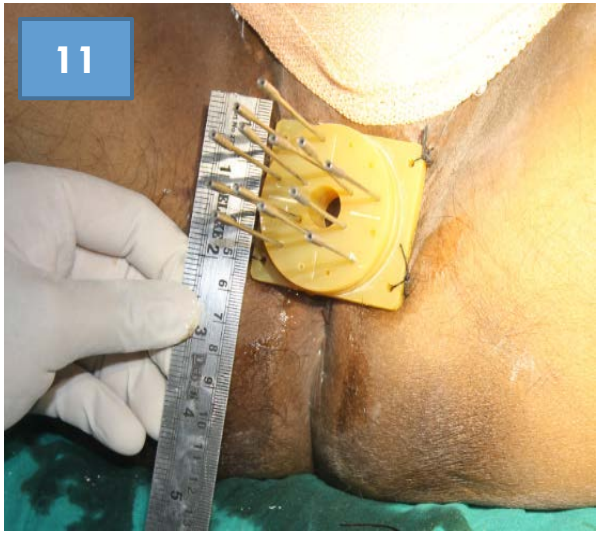




Application

Application





Imaging

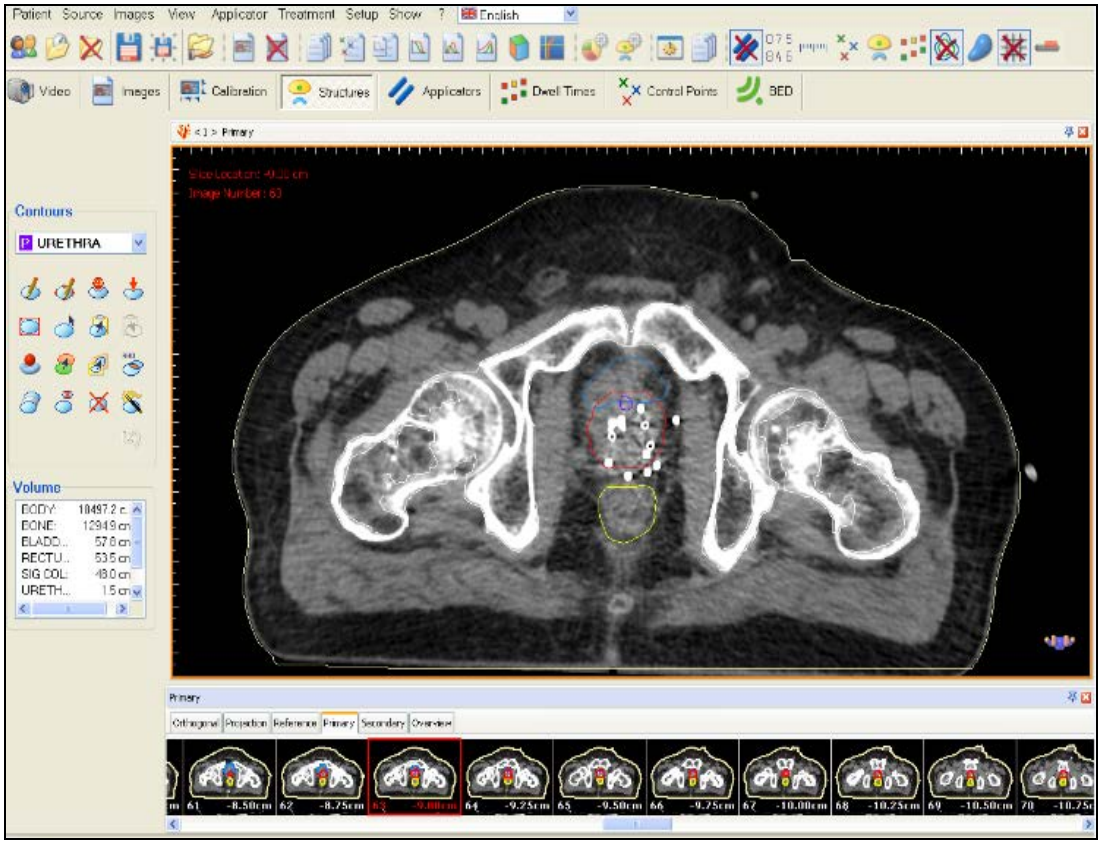
- CT or MR images obtained following recovery from anesthetics.
- CT Slice thickness ≤ 3mm
- MRI:
- T2 : Optimal anatomical definition
- T1: Accurate catheter reconstruction
- Image fusion may maximize image accuracy

Contouring

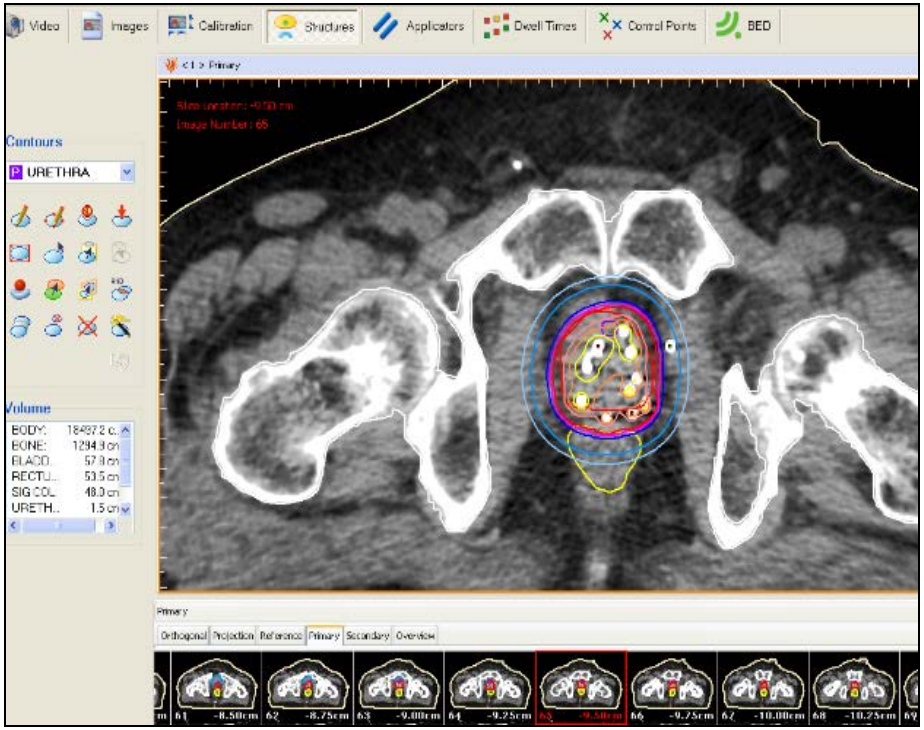
Contouring :

- **Target:**
- Clinical Target Volume
- **Organ At Risk:**
- Urinary Bladder
- Rectum
- Sigmoid Colon
- Urethra
- Penile Bulb

Clinical Target Volume (CTV):
Prostate + extra prostatic extension + SV
3mm margin to cover macroscopic spread



Planning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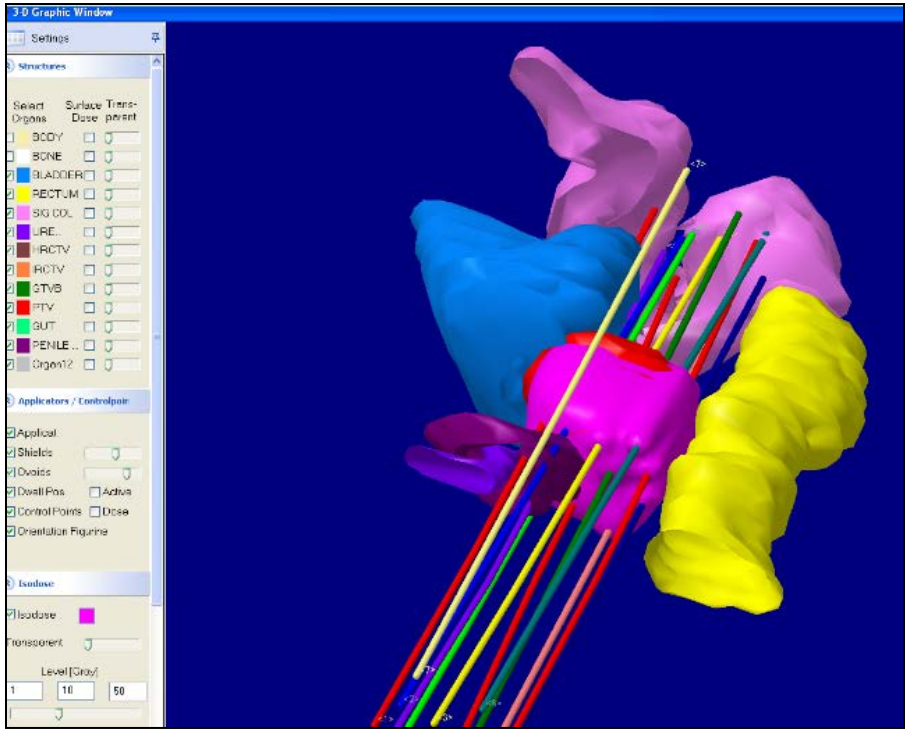
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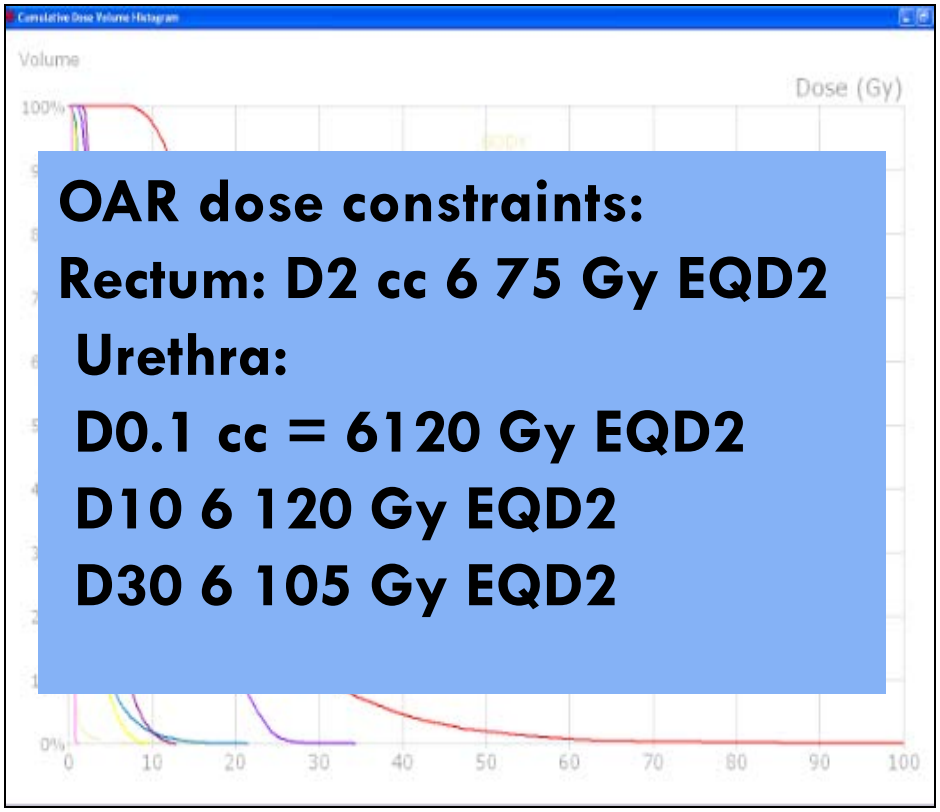
Plan evaluation

Dose reporting

- External beam dose
- Implant technique; number of catheters;
- CTV: D90, V100, V150, V200
- PTV (if defined): D90, V100, V150, V200
- Organs at risk:
- a. Rectum: D2 cc, D0.1 cc
- b. Urethra: D0.1 cc, D10, D30

Dose Volume Histogram Parameters



OAR dose constraints:

Rectum: D2 cc 6 75 Gy EQD2

Urethra:

D0.1 cc = 6120 Gy EQD2

D10 6 120 Gy EQD2

D30 6 105 Gy EQD2

Dose: Planning aim dose

EBRT + HDR BT

- EBRT dose : 45-50Gy
- BT Dose:
  15 Gy in 3 #
  11–22 Gy in 2 #
  12–15 Gy in 1#

Golden Rule

D90 > Planning aim (100%)
PTV V100 ≥ 95%

HDR BT Mono-therapy

- 34 Gy in 4 #
- 36–38 Gy in 4 #
- 31.5 Gy in 3 #
- 26 Gy in 2 #

HDR BT in recurrence

- 36 Gy in 6 fractions
- 21 Gy in 3 fractions

GEC ESTRO guideline 2013

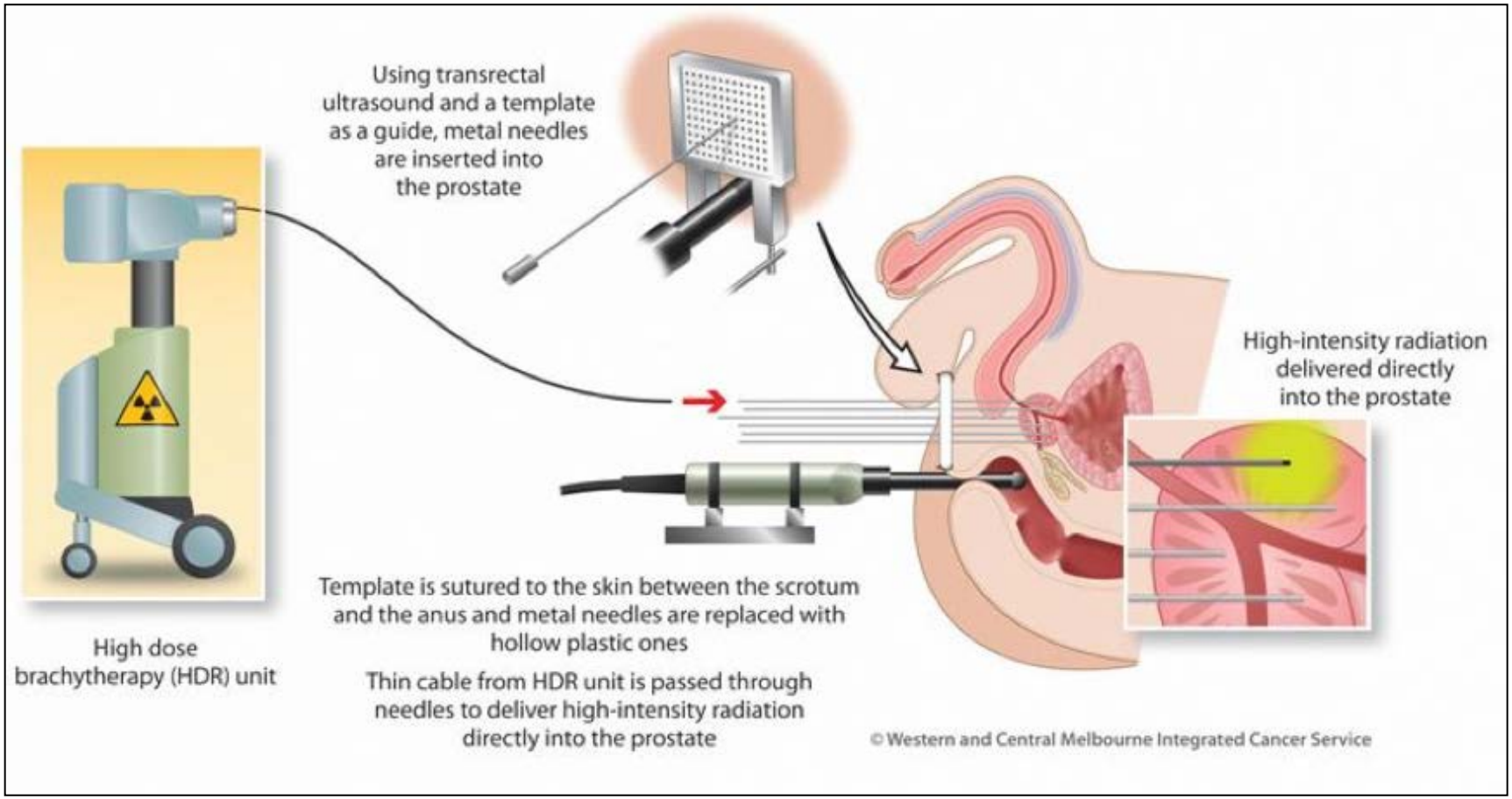
Dose fractionation evidences

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%

Y Yamada et al. Brachytherapy 2012

Treatment


Using transrectal ultrasound and a template as a guide, metal needles are inserted into the prostate
High-intensity radiation delivered directly into the prostate
High dose brachytherapy (HDR) unit
Template is sutured to the skin between the scrotum and the anus and metal needles are replaced with hollow plastic ones
Thin cable from HDR unit is passed through needles to deliver high-intensity radiation directly into the prostate
© Western and Central Melbourne Integrated Cancer Service

HDR BT

- **Post Implant care**
- Analgesia : Epidural preferred
- If multiple fraction : give 2# < 24hrs

  > 2# repeat implantation
- Antispasmodic
- Antibiotic
- Bladder irrigation if needed
- Check catheter displacement

Follow up

- 4-6monthly for first 2years
- Annually >2 years

To do list:

- DRE
- Serum PSA
- Other investigations as per clinical need
- Evaluate GU/rectal/Sexual toxicities

Toxicity

Genitourinary

- Acute :
- Reversible urgency and frequency
- Acute urinary retention (<5%)

- Late:
- Urinary stricture (<15%)
- Prolonged urinary incontinence (Rare)

Toxicity

Grade 3 late GU complications

Author	*N*	Followup (mo)	Dose	Type of treatment	Comments
Astrom (60)	214	48	10Gyx2	Boost	13 patients experienced urethral strictures
Demanes (17)	209	86	5.5 Gy–6.0Gyx4	Boost	6.7% late Grade 3 and 1% Grade 4 GU toxicity (TUR related)
Hsu (7)	112	30	9.5Gyx2	Boost	Less than 3% Grade 3 toxicity at 18 mo
Phan (49)	309	59	6Gyx4	Boost	4% late Grade 3 GU
Deger (50)	442	60	9–10 Gyx2	Boost	9% late Grade 3 GU toxicity
Martinez (77)	207	66	5.5–11Gyx2	Boost	8% late Grade 3 GU toxicity
Sullivan (52)	425	41	4–5Gyx46.5 Gyx3	Boost	8% late Grade 3 GU toxicity
Zwahlen (73)	587	66	5Gyx4–6Gyx3	Boost	7% late Grade 3 GU toxicity
Demanes (57)	298	62	7Gyx6 9.5Gyx4	Mono	3% late Grade 3 GU toxicity
Ghilizan (51)	173	17	12–13.5Gyx2	Mono	1% late GU Grade 3 toxicity
Hoskin (78)	197	37	8.5Gyx4 9Gyx4 10.5Gyx3 13Gyx2	Mono	3–7% strictures

GU = genitourinary; TUR = transurethral resection.

Yamada Y et al Brachytherapy 2012

Toxicity

Rectal toxicity

- Acute :
- Proctitis
- Transient urgency and frequency

- Late:
- Rectal telangeictasia (4-11%)
- Rectal Ulcer (<2%)
- Rectal fistula (<1%)

Sexual

- Erectile dysfunction

  (40% cases)

  Reversible

  (PD 5 Inhibitors)

Study	Treatment	Number of Patients	Follow-up (Month)	Erectile Dysfunction Incidence (%)
Stock et al.	BRT	65	18	21
Zelefsky et al.	BRT	221	48	29
Merrick et al.	BRT	209	40	61 at 6 yr

Perez and Brady 2013