Conventional RT in Prostate Cancer

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Introduction

- Prostate cancer is one of the most common cancer in men and is a very high cause of mortality. It is the second leading cancer after Lung in USA

- Majority of new cases are non metastatic and 83% are confined to local or regional sites

Risk stratification

NCCN 2008

Low	Intermediate	High	very high
T1-T2a	T2b-c	T3a	T3b/T4 or N1)
GS 2 to 6	GS 7	GS 8-10	
PSA <10	PSA 10 - 20	PSA >20	

Indications for RT

- Definitive RT
  - Any risk .
  - Optional in low risk
  - Alternate to radical prostatectomy in intermediate and high risk.
- Adjuvant RT
- Salvage RT – local or biochemical recurrence following radical prostatectomy
- Palliative – bone/brain metastasis.
- Preoperative Radiotherapy?

(Phase I -Supiot et al , Radiotherapy Oncology 2008)

Volume for RT

- Prostate ± seminal vesicles
- LN irradiation
  - For all high risk cases
  - Optional for intermediate risk cases
  - No LN irradiation for Low risk cases
- Brachytherapy alone for low risk

Role of Pelvic RT?

Lymphatic drainage

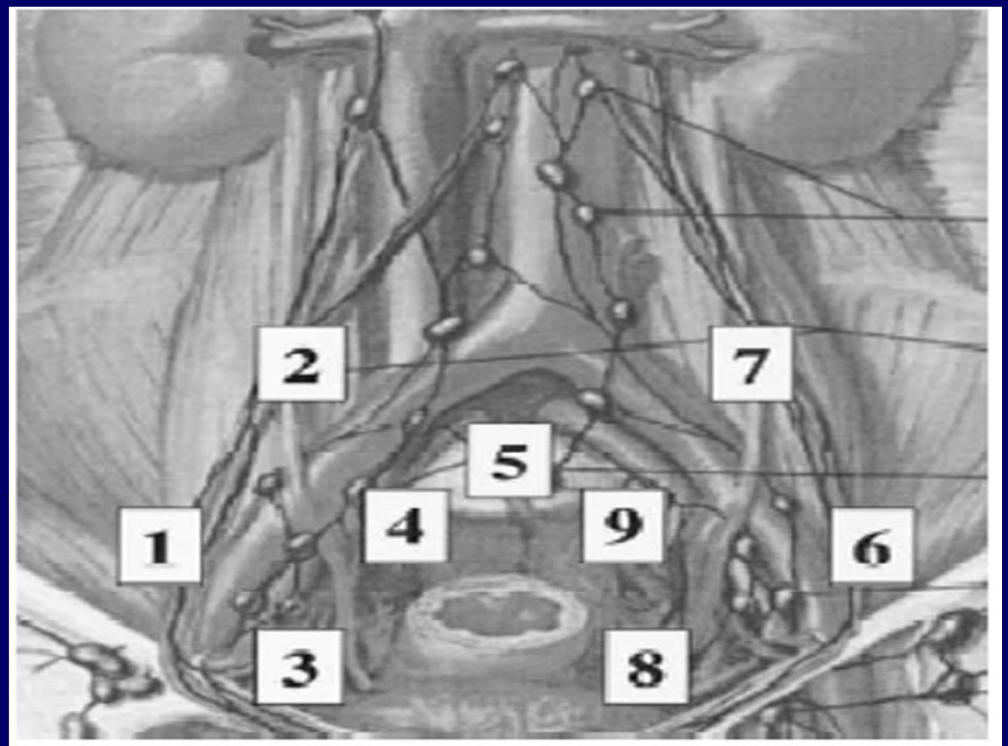

Figure 1. Distribution and localization of 9 selective fields for extended pelvic lymphadenectomy, including right external iliac (1), common iliac (2), obturator fossa (3) and internal iliac (4) lymph nodes, presacral lymph nodes (5), and left external iliac (6), common iliac (7), obturator fossa (8) and internal iliac (9) lymph nodes. (Reprinted with permission.[11])

Seminars in Radiation Oncology, Vol 13, No 2 (April), 2003: pp 109-120

Incidence of LN involvement

Table 1. Distribution of Node Metastasis in Clinically Localized Prostate Cancer

Nodal Sites	*Involved %*	*Single %*
#1 External iliac	60	0
#2 Obturator	53	20
#3 Presacral	53	7
#4 Presciatic	47	7
#5 Common iliac	27	0
#6 Hypogastric	14	0
#1 + 2 External iliac/obturator	86	NA
#3 + 4 Presacral/presciatic	80	NA

Portals must include external iliac, obturator, hypogastric and presacral

Seminars in Radiation Oncology, Vol 13, No 2 (April), 2003:

The "Partin tables" - developed by urologists Alan W. Partin, M.D., Ph.D., and Patrick C. Walsh, M.D. based on accumulated data from hundreds of patients treated for prostate cancer.

Based upon PSA, Gleason Score, and Clinical Staging, a probability is calculated for each of the following four:

Organ Confined Disease, **Extraprostatic Extension**, **Seminal Vesicle Invasion**, and **Lymph Node Invasion**

- Using Partin nomogram - Roach used a formula to predict LN involvement

Risk of LN involvement = (2/3)PSA + ([GS – 6] x10)

Whole Pelvic RT

- Factors favouring
  - High percentage harbour occult pelvic LN mets
  - If orderly spread from LN to distant sites - treating pelvis will have an impact on DFS and OS
  - Therapeutic sterilization of known sites of disease
- RTOG 85-31: in LA+positive pelvic nodes GS 7-10, def. RT+Adjuvant AS improves absolute survival from 39% to 49%
- RTOG 86-10: LA + +ve pelvic nodes GS 2-6, def.RT+goserelene2mths prior+flutamide during RT -12% improvement in DFS and LC compared to RT alone

Contd.,

- **RTOG 94-13:** combined androgen suppression (CAS) and whole-pelvic (WP) radiotherapy (RT) followed by a boost to the prostate improves progression-free survival (PFS) by 10% compared with CAS and prostate-only (PO) RT. (**Roach M 3rd**,et al 2003)

- Neoadjuvant HT + WPRT improves PFS in LA and High risk prostate cancer . No OS benefit (Lawton C A et al 2005)

Whole pelvic RT Contd.,

- RTOG 77-06 : no benefit in survival with WPRT in localised prostate cancer
- Preliminary results of GETUG 1 : pelvic irradiation was well tolerated but no improvement in PFS
- "Lack of benefit of pelvic radiation in prostate cancer patients with a high risk of positive pelvic lymph nodes treated with high-dose radiation.". Median f/u 4 yrs for all pts, 4.3 yrs for those high risk pts. For the high risk pts, there was no difference in clinical failure, CSS, or OS.(BF not asessed)

Contd.,

1.Roach M et al. J Clin Oncol. 2003 May 15;21(10):1904-11.).

2.Updated Analysis of RTOG 94-13." Lawton CA et al. IJROBP Volume 63, Supplement 1, 1 October 2005, Page S19.

3.Terence Roberts and Mack Roach III

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4.Is There a Role for Pelvic Irradiation in Localized Prostate Adenocarcinoma? Preliminary Results of GETUG-01." Pommier P et al. J Clin Oncol. 2007 Dec 1;25(34):5366-5373.

5. Lack of benefit of pelvic radiation in prostate cancer patients with a high risk of positive pelvic lymph nodes treated with high-dose radiation Vargas CE et al. Int J Radiat Oncol Biol Phys. 2005 Dec 1;63(5):1474-82.

✓Current standard : whole pelvic RT for patients with high risk of pelvic nodes. Dian Wang et al: Semin Radiat Oncol 18:35-40 2008

Evidence is lacking for using pelvic fields in intermediate- and high-risk PCA. Suggest randomized trial for T3/T4 and GS >=4+3

- In general 66-70 Gy /1.8-2Gy/Fr /5Fr/ week with conventional RT
- 45 – 50 gy whole pelvis + prostate boost up to 70.2 gy

- Based on stage –
  - T1a – 66-70 Gy
  - T1b,c – T2b – 70-72 Gy
  - T2c – 74 Gy

4 field	**4 yr DFS**
60 – 70 gy	54%
3DCRT	
67-77gy	71%
74-78gy	77%

Pollack A Zagars G K et al .IJROBP 53:1097-1105,2002

Adjuvant RT

- The rationale for treating patients at high risk for local recurrence with adjuvant radiation is well established for many tumor sites.
- Goal is to reduce the risk of local persistence of disease, thereby improving local control and the chance of remaining free of metastatic disease
- The general rule for adjuvant radiotherapy is that local control is improved by about 40% to 50%

postoperative radiation is a safe option in the patient at high risk for local recurrence based on adverse pathology or clinical features (eg,extensive extracapsular disease, positive margins, high volume Gleason score >7, and so on). Administration of an adequate dose of prostate bed radiation (ie, >64 Gy) in men with these adverse prognostic features appears to effectively reduce prostate-specific antigen (PSA) recurrence rates.

Richard K. Valicenti,et al :

Seminars in Radiation Oncology, Vol 13, No 2 (April), 2003: pp 130-140

Adjuvant RT contd.,

- The "Han tables" developed by urologists, Misop Han, M.D., Alan W. Partin, M.D., Ph.D., and Patrick C. Walsh, M.D., based on accumulated data from patients of prostate cancer treated at the James Buchanan Brady Urological Institute, Johns Hopkins Hospital.

the Han Tables correlate the three common factors known about prostate cancer, PSA level, Gleason score, and clinical stage (or pathological stage). the Han Tables are used to predict the probability of prostate cancer recurrence up to 10 years following surgery. Based on the result of the probability of recurrence, pts and their doctors can decide the best course of treatment after surgery.

- Based upon PSA, Gleason Score, and Clinical Stage, **recurrence probability is calculated at 3, 5, 7, and 10 years following surgery** (**preop model**)

- Based upon PSA, Surgical Gleason Score, and Pathological Stage, **recurrence probability is calculated at 3, 5, 7, and 10 years following surgery** (**postop model**)

Adjuvant RT

- adjuvant RT has not been shown to improve overall survival compared with active surveillance. Longer follow-up from completed RCTs is required to accurately assess this outcome. Adjuvant RT does, however, significantly improve bPFS and is not associated with excess severe late toxicity.

(Morgan SC et al,Radiother Oncol. 2008 May 21. [Epub)

Adjuvant RT

- PSA recurrence; 8.5% (4/47) for low risk patients and 44.8% (30/67) for high risk. Tumor progression was seen in no low risk patient and in 9% (6) with high risk.
- Immediate use of adjuvant treatment should be reserved for those patients with a high risk of recurrent disease

(**Lowe BA**, **Lieberman SF** , J Urol. 1997 Oct;158(4):1452-6)

- Patients with high-risk pathologic features, such as a positive margin or seminal vesicle involvement, have a 40% to 50% risk of developing biochemical failure at some point in the future. Because the morbidity of postoperative radiotherapy is relatively low, when pathologic high risk factors are present adjuvant radiotherapy should be considered.

Abramowitz MC, **Pollack A**. semin Radiat Oncol. 2008 Jan;18(1):15-22

Summary of Published Series Reporting Results of Adjuvant Radiation Therapy for T3N0M0 Prostate Cancer Compared With a Control Group

Author	*No. of Patients*	*Radiation Dose*	*Free of Progression*	*F/U (mo)*
Gibbons	23 23	None 49 – 72 gy	70 NED 95	94 57
Morgan	33 17	None 60 – 66 gy	64 bNED 94	11
Anscher	46 113	None 55 – 65 gy	60 68	10 yrs
Stein	91 24	None 55 – 60 gy	43 bNED 75	48
Schild	228 60	None 57 – 68 gy	40 b NED 57	32
Valecenti	36 36	None 59.4 – 70.2 gy	55 88	41

Ongoing phase III randomized trials

- the **Southwestern Oncology Group (SWOG) (protocol 9887/INT0086),** which recently completed its accrual and
- the **European Organization for Research and Treatment of Cancer (EORTC) (study 2291)**

  randomize patients after radical prostatectomy to observation or adjuvant radiation therapy to prostatic fossa

- **RTOG 96-01** is a randomized double-blind study in patients with pT2-T3 prostate cancer and/or positive surgical margins.With rising PSA between 0.2 ng/mL and 4 ng/mL are randomized to receive hormonal monotherapy (Casodex; AstraZeneca,Wilmington, DE, 150 mg daily) or a placebo for 2 years+prostatic fossa irradiation to a dose of 64.8 Gy.

- **RTOG P-0011** is a Randomized study to test whether the addition of androgen suppression to radiation therapy (63 to66 Gy) leads to better outcome than each used separately in high risk postprostatectomy pts

Salvage Radiotherapy

- low risk for disease progression (ie, PSA< 10 ng/mL, Gleason score 7, negative surgical margins) wait and watch policy provided salvage therapy is initiated early at the time of PSA relapse.
- High risk patients immediate adjuvant RT to prostatic fossa with/without HT(RTOG 85-31)
- GS≤7,Pre RT PSA ≤2ng/ml,+ve surg.margin or PSA DT >10 mths, high probabality of benefit from RT
- SV+LN+PSA DT<10 mths , lower probabality of benefit from RT

Role of RT in PSA failure after Radical Prostatectomy

- Eqarva et al - RT is useful only in a small set of pts. RT is in adequate to eradicate the residual disease

- Moul J W - RT likely to benefit in patients with
  1. no adverse pathology
  2. low PSA at recurrence
  3. recurrence after one year

Palliative RT

- Bone Metastases
- Brain Metastases
- Visceral Metastases

Dose – 30 Gy /10 Fr

Conventional RT with minimal margins preferred

- Current recommendations such as the NCCN advise 3DCRT +/- Brachytherapy or IMRT for prostate Ca

- What then is the role of conventional RT today?

Conventional External beam RT

- Treatment planning method wherein the prostate and other target tissues identified by the anatomy of surrounding structures(bony landmarks and contrast enhanced viscera
- First report of EBRT in curative treatment of Ca prostate

Radiotherapy in the conservative treatment of operable and locally inoperable carcinoma of the prostate. (**1967 Del Regato** JA., Radiology. 1967)

- Important to realize that many centers still do not have the facilities of LINAC / IMRT or 3DCRT.

- Brachytherapy needs experience and permanent implants are not practiced in many places in India.

No. of RT Centers : 214 (2006)

- Teletherapy Units : 363
- Cobalt-60 : 263
- Cesium-137 : 8
- Linac : 92

Conventional (2D) Technique

- Treatment fields are generally 6x6 cm to 11x11 cm "four-field box" determined by bony landmarks, and if necessary rectal contrast and foley catheter.
- For large fields, the superior border is set midway through the L5SI joint, inferior border at the level of ischial tuberosities, the lateral border 1.5-2.0cm lateral to the pelvic rim, the anterior border at the front edge of pubic symphisis, and the posterior border at the S2/S3 interspace.
- For small fields and boost, the superior border extends to the top of the acetabulum and lateraly to include 2/3 of the obturator foramen.

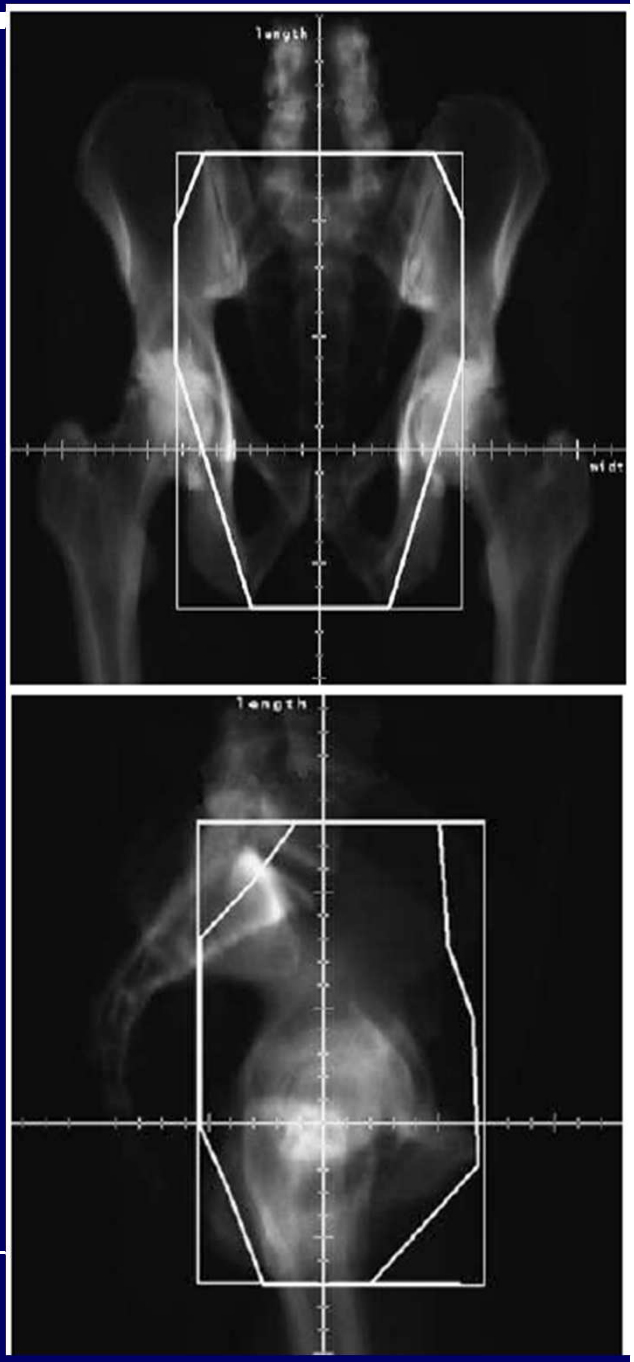
RT technique

Portals – 4 Field

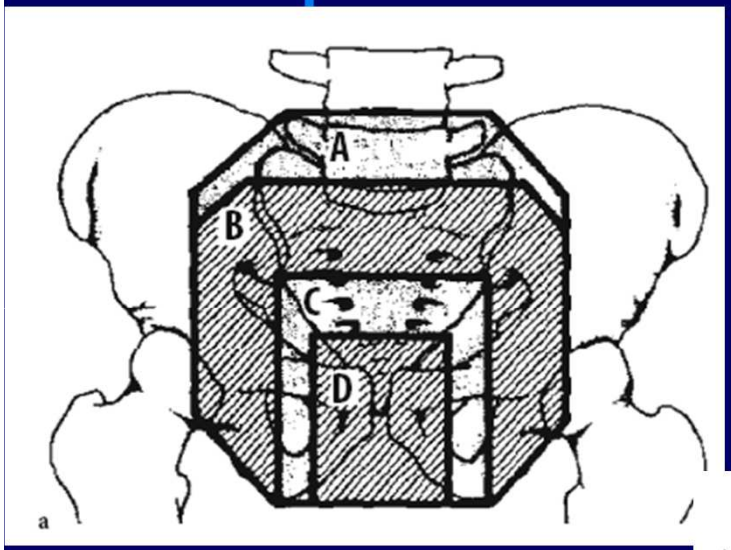
- Superior – L5- S1 Junction
- Inferior - 1 cm below the area in which the contrast narrows to a point on the urethrogram or lower border of ischial tuberosity
- Lateral - 1.5 -2 cm lateral to bony pelvis

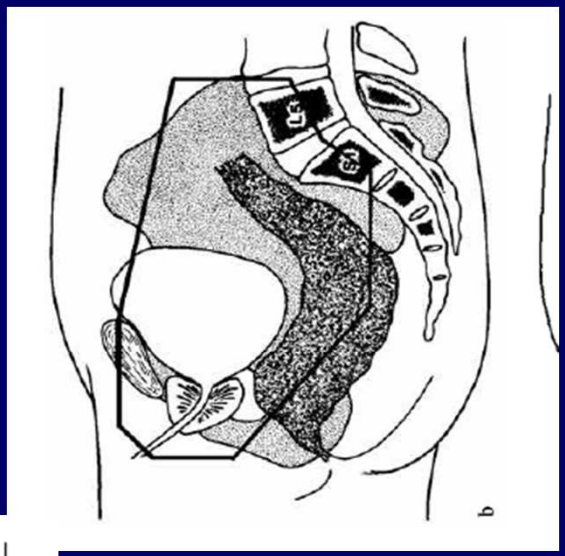
For lateral fields

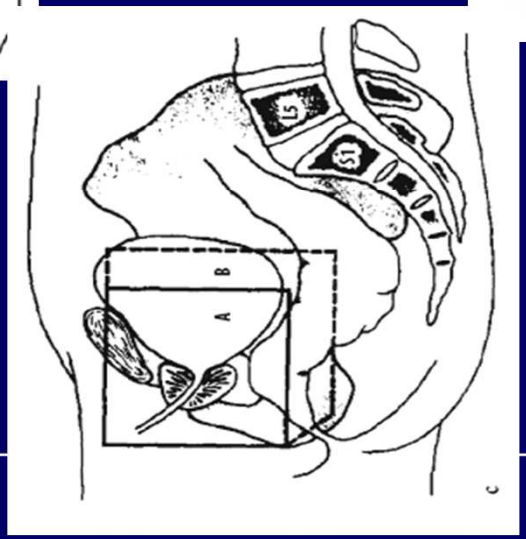
- Anterior - anterior portion of the pubic symphysis.
- Posterior- S2-3 interspace to include the upper presacral lymph nodes.



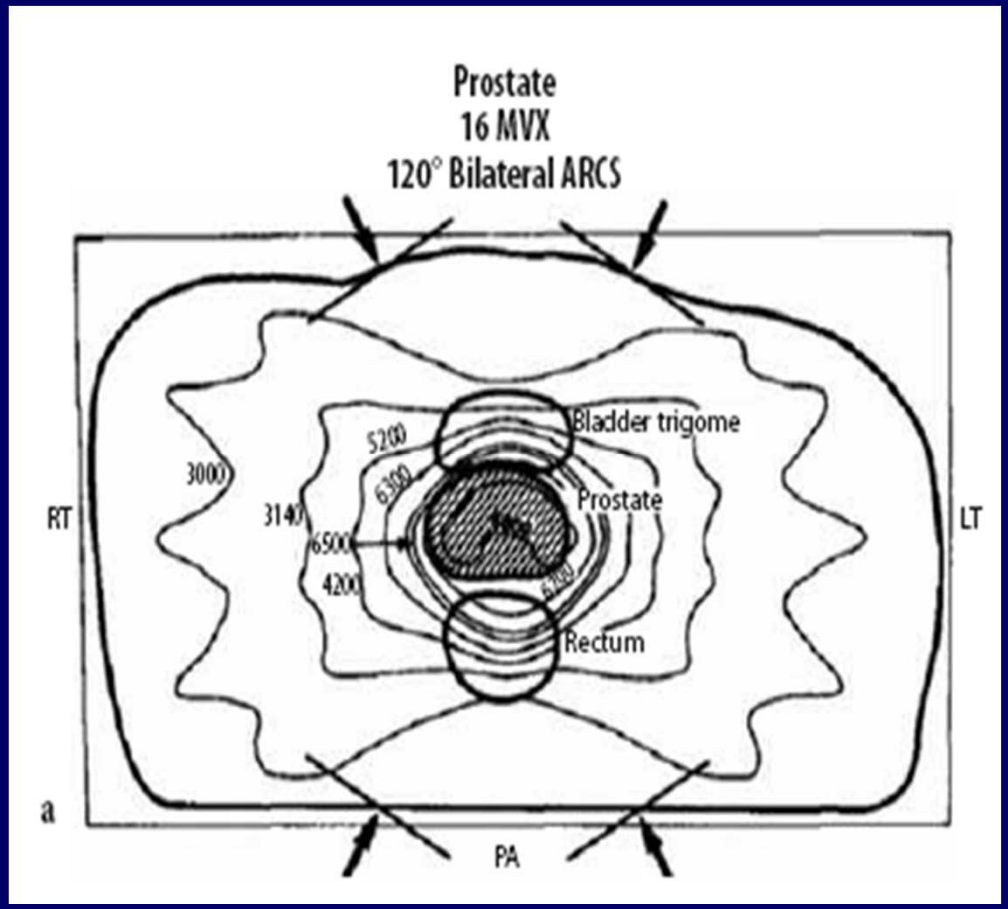
- Following 45- 50 Gy to the whole pelvis the prostate is boosted upto 70 Gy







- Other method of boost – rotational arc – bilateral 120° arc



- X ray simulation with retrograde urethrocystogram with contrast in the bulb of Folleys Catheter can be used for planning prostatic boost.

Conventional Vs 3DCRT

- In GS <4 ng/ml,T1b-c or T2 no statistically different DFS between conventional and conformal RT

(Perez CA et al, Clin Prostate Cancer. 2002 Sep;1(2):97-104)

- In T1,T2,PSA <10ng/ml, at 67.7gy same rate of control as with higher doses (Pollack et al)

Conventional RT

Advantages

- Time tested
- Easy to plan and execute
- Saves time especially in high volume centres
- Cost effective

Disadvantages

- More Normal tissue irradiated
- Dose escalation not possible
- Inferior results

Conformal RT

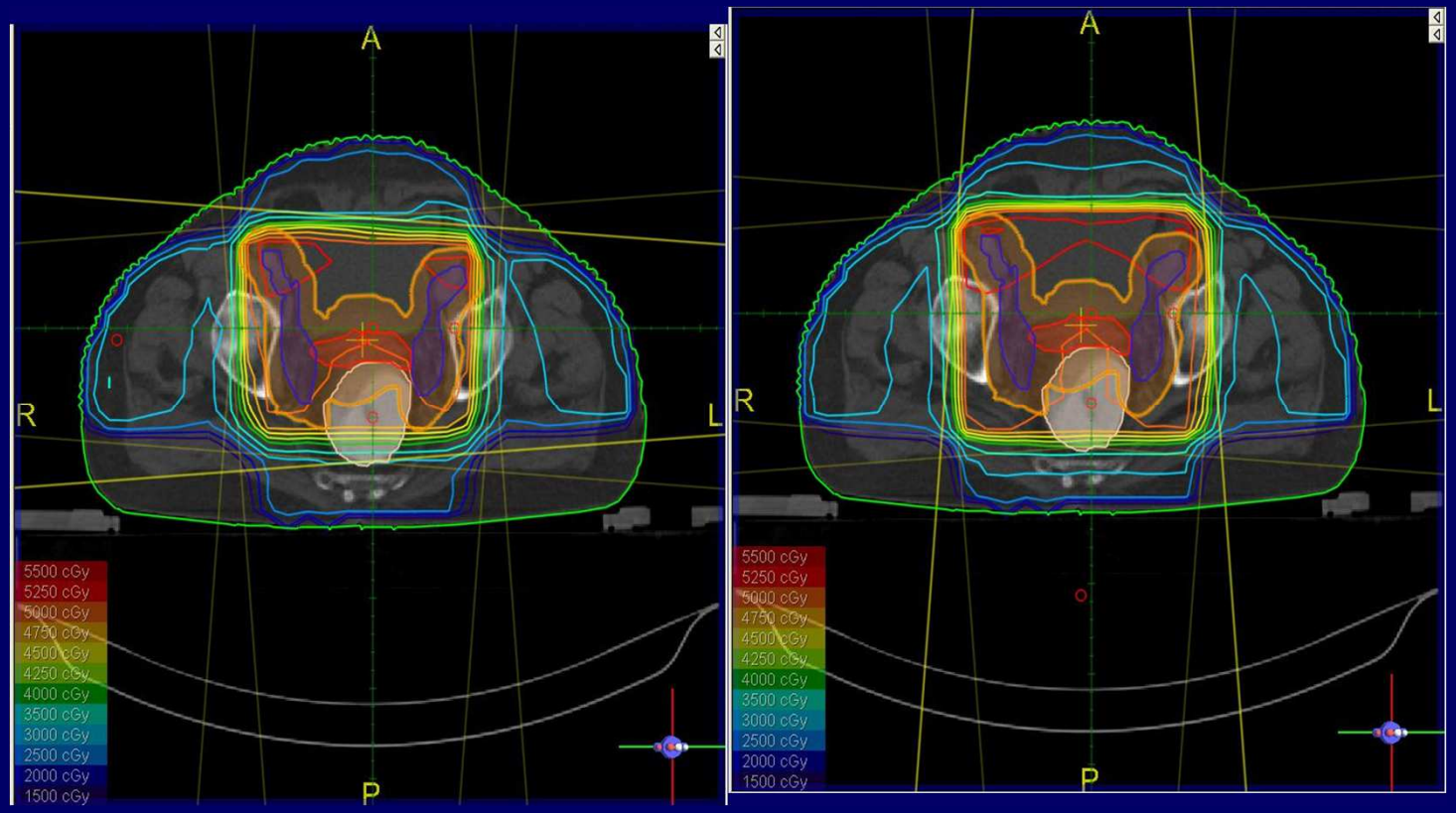
Advantages

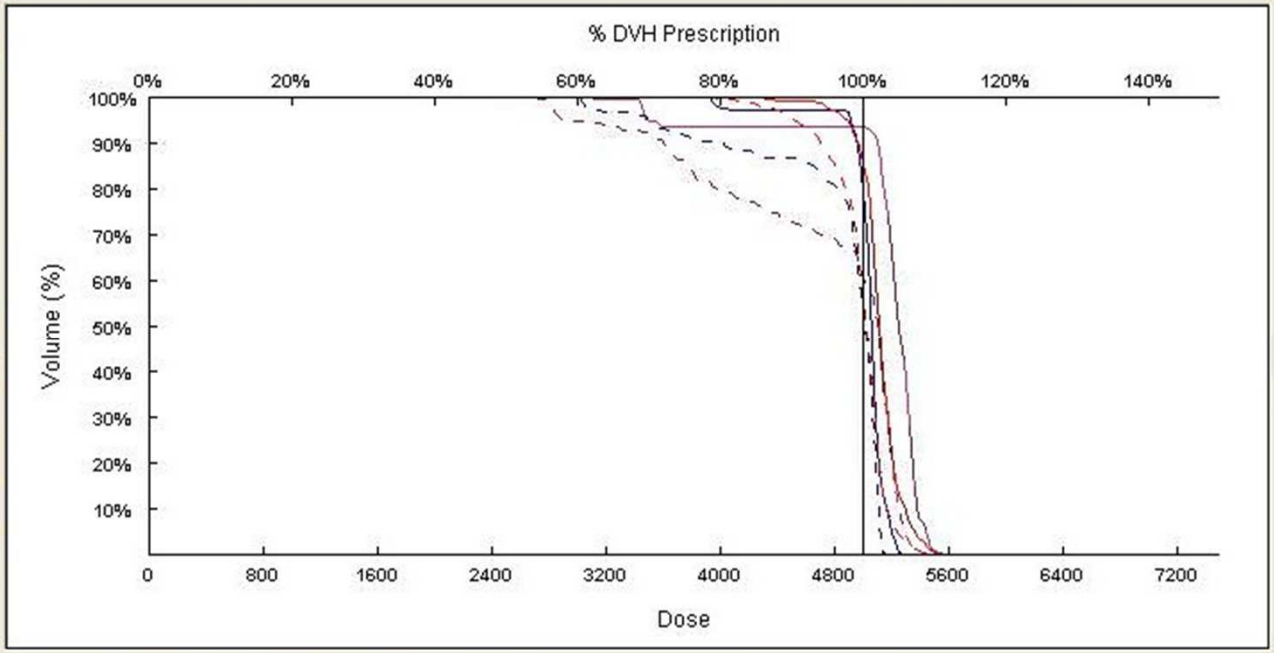
- Better sparing of normal tissue
- Dose escalation
- 3D planning
- BEV
- DVH

Disadvantages

- Interphysician variabililty in target delineation
- Chance of missing tumour due to close margins
- Longer planning time
- Good QA
- Steep learning curve

4field 2D vs 4 field 3DCRT





Show	Name	Type
☐	External	External
☐	right femur	Organ
☐	left femur	Organ
☒	bladder	Organ
☐	intestine	Organ
☒	rectum	Organ
☐	GTV	GTV
☐	CTV	CTV
☐	PTV NEW	CTV
☒	PTV NEW Margin	CTV

Histogram Mode
- (•) Integrated
- ( ) Differential

Histogram Background
- (•) White
- ( ) Black

DVH Prescription 5000.00 cGy

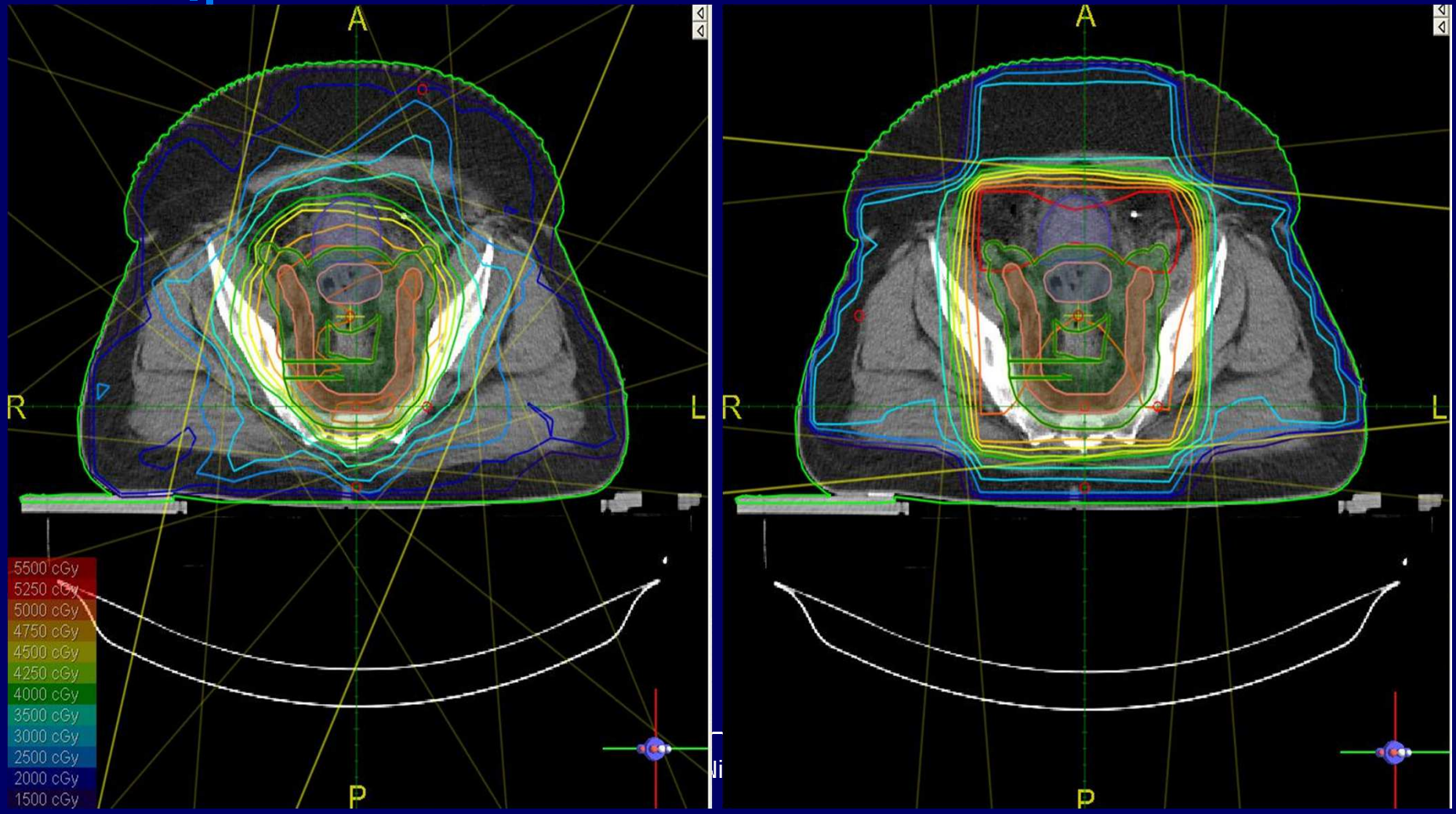
Dose Plot Max 7500.00 cGy

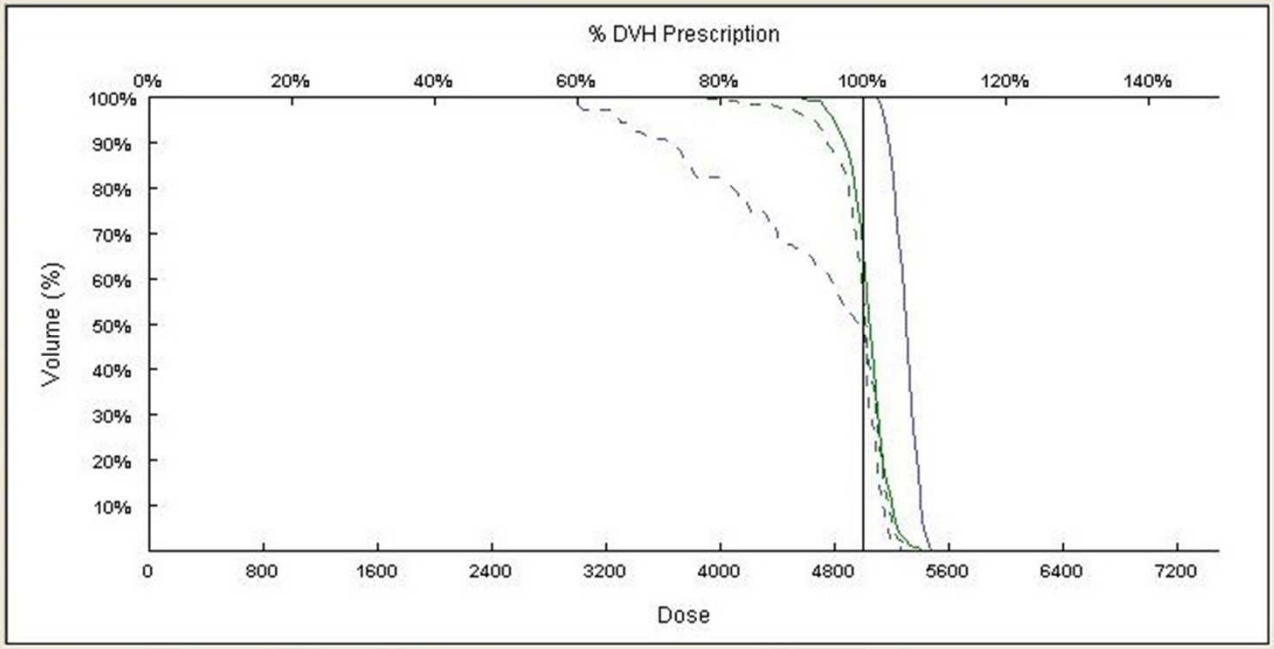
Dose Level 5000.00 cGy

Compare Plan: mlc

Name	Vol	DLV	DLV	D-X (cGy)			V-X (%)			Min	Max	Mean	Median	Modal	EUD	
	[cc]	[cc]	[%]	100	90	80	150	100	90	[cGy]	[cGy]	[cGy]	[cGy]	[cGy]	a	[cGy]
bladder (Cur)	166.4	155.7	93.6	3105.5	5085.9	5152.9	0.0	93.6	93.6	3092.4	5530.0	5134.9	5226.6	5309.8		–
bladder	166.4	98.9	59.5	2717.3	3586.6	3987.2	0.0	59.5	72.6	2712.5	5415.0	4707.6	5088.0	5115.7		–
rectum (Cur)	215.3	161.9	75.2	3937.3	4954.0	4964.7	0.0	75.2	97.4	3927.3	5244.8	5019.5	5032.6	5032.6		–
rectum	215.3	107.9	50.1	3022.3	4011.5	4809.8	0.0	50.1	86.9	2996.2	5137.3	4806.0	5004.8	5088.0		–
PTV NEW Margin (Cur)	957.8	806.6	84.2	4048.2	4944.7	5045.7	0.0	84.2	99.2	4037.9	5526.8	5100.4	5115.7	5060.3		–
PTV NEW Margin	957.8	504.2	52.6	3660.0	4705.9	4864.6	0.0	52.6	95.2	3638.6	5496.4	4963.5	5004.8	5004.8		–

7 field 3DCRT vs 4 field 2D





Show	Name	Type
☐	External	External
☐	gtv nODE	GTV
☐	gtv TUMOR	GTV
☒	BLADDER	Organ
☐	hip jOIN r	Organ
☐	hIP l	Organ
☐	INTESTINE	Organ
☐	GTN_NEW	GTV
☒	GTN_NEW Margin	GTV

Histogram Mode
- (•) Integrated
- ( ) Differential

Histogram Background
- (•) White
- ( ) Black

DVH Prescription 5000.00 cGy

Dose Plot Max 7500.00 cGy

Dose Level 5000.00 cGy

Compare Plan: "7 FIELD_1CM

Name	Vol	DLV	DLV	D-X (cGy)			V-X (%)			Min	Max	Mean	Median	Modal	EUD	
	[cc]	[cc]	[%]	100	90	80	150	100	90	[cGy]	[cGy]	[cGy]	[cGy]	[cGy]	a	[cGy]
BLADDER (Cur)	188.6	188.6	100.0	5112.0	5145.4	5220.0	0.0	100.0	100.0	5094.7	5451.9	5280.7	5297.6	5269.1		–
BLADDER	188.6	89.1	47.2	2941.5	3604.1	4066.7	0.0	47.2	67.6	2913.6	5242.5	4608.2	4983.5	5012.0		–
GTN_NEW Margin (Cur)	964.1	593.8	61.6	4512.3	4829.6	4920.9	0.0	61.6	99.8	4498.5	5375.2	5024.6	5040.6	5040.6		–
GTN_NEW Margin	964.1	501.2	52.0	3684.1	4715.8	4857.2	0.0	52.0	96.9	3660.8	5327.9	4971.8	5012.0	5012.0		–

Table 28.6. Comparison of mean dosimetric parameters for 3D conformal or standard bilateral arc rotation in carcinoma of prostate. *PTV* planning target volume, *ICRU* International Commission on Radiation Units and Measurements. (From PEREZ et al. 1997)

Parameter	Prostate irradiation only	
	3D conformal therapy	Standard therapy
No. of observations	87	87
Percentage of PTV receiving the prescribed dose or more	92.9±13.9	92.9±10.8
ICRU dose (Gy)	69.1±2.6	69.2±2.6
Minimum tumor dose (Gy	66.3±5.3	63.5±8.6
Mean tumor dose (Gy)	69.8±2.6	69.7±2.8
Maximum dose (Gy)	71.7±2.4	71.3±2.8
Percentage of volume rectum ≥65 Gy	33.7±15	62.7±21
Percentage of volume rectum ≥70 Gy	8.5±11.8	28.8±28.9
Percentage of volume bladder ≥65 Gy	22.3±12.5	50.5±22.8
Percentage of volume bladder ≥70 Gy	6.3±8.4	19.4±24.4

PEREZ et al. 1997

Toxicities

Toxicity	2D	3D
Chronic rectal (GII or >)	4%	0
Chronic GU (GII or >)	6%	0
Acute urinary	26%	40%
Acute GI	28%	26%
Erectile dysfunction		<7%

J M O'Sullivan et al,

Clinical Oncology (2000)12:217–221

G. Borghede, H. Hedelin / Radiotherapy and Oncology 43 (1997) 139–146

Contraindications to RT

- Prior Pelvic Rt
- Acute Inflammatory disease of Rectum
- Permanent indwelling Folley's Catheter

CONCLUSION

- Conventional RT is the standard of care in many centers in India
- It is time tested, easy to execute and less time consuming
- More cost effective
- If meticulously planned toxicity is comparable to 3DCRT
- Results slightly inferior to 3DCRT as dose escalation is not possible
- It provides the learning curve for the student

Thank you