3D-CRT
Carcinoma Prostate

Dr. Vijay Anand P. Reddy
Director
Apollo Cancer Institute, Hyderabad

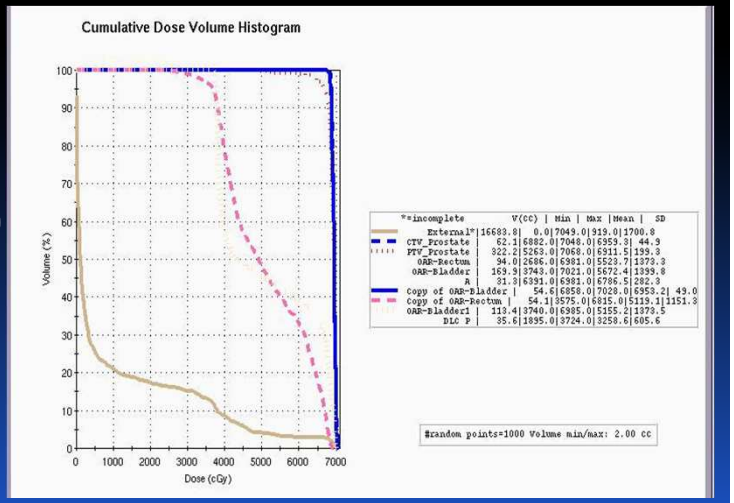
3D-CRT in Ca Prostate

- Introduction
- Advantages in Ca-Prostate
- Steps of 3D-CRT in Ca Prostate
  - Patient Positioning
  - Immobilization
  - Planning Imaging
  - Target Volume Delineation
  - Computerized Planning
  - Plan Evaluation
  - Plan Implementation
  - Quality Assurance
- Clinical Outcome studies
- Conclusion

3D-CRT in Ca Prostate

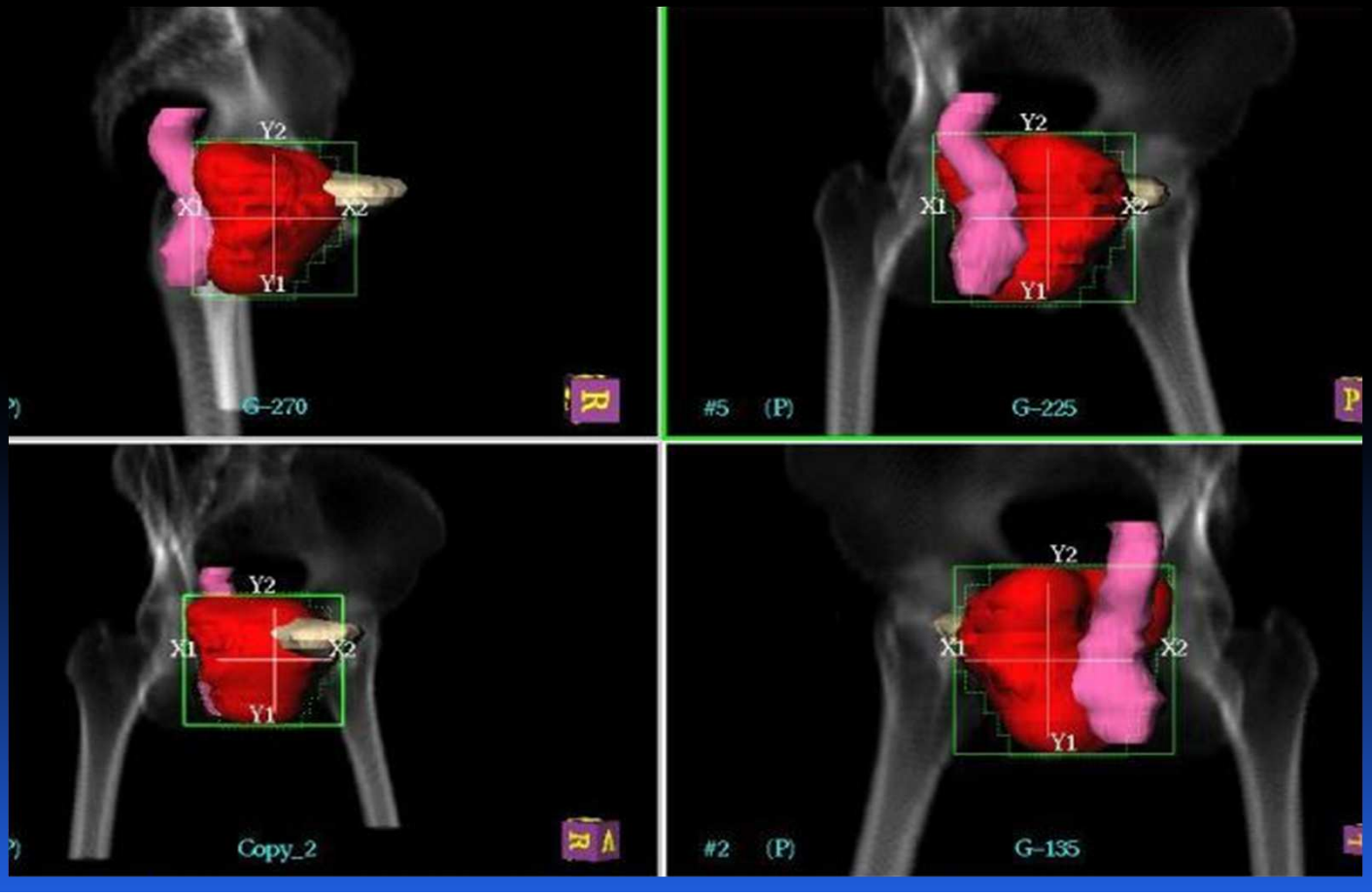
Introduction

- ✓ Multi Leaf Collimators
- Planning CT Scan/ MRI
- Computerized Plan
  - 3 Dimensional Dose Evaluation
  - Dose Volume Histogram (DVH)



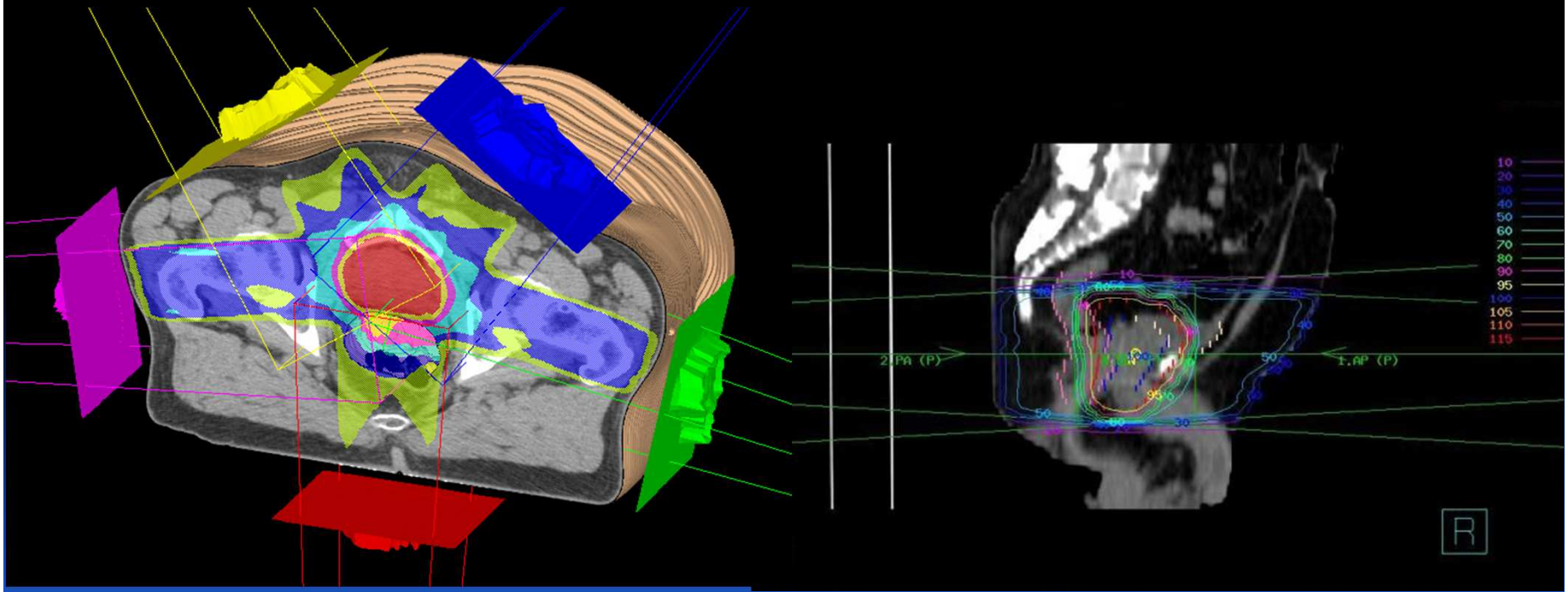
3D-CRT in Ca Prostate
Introduction

- The radiation beam is shaped to include a 3-dimensional anatomic configuration of the organ sparing adjacent normal tissue (BEV)



3D-CRT in Ca Prostate
Introduction

- This technique allows for more precise delivery of therapy to the target volume



3D-CRT in Ca Prostate

Advantages

- Relative immobility of the organ (typically <1 cm)
- Allows higher doses of radiation to the prostate without significant toxicity to the rectum and bladder
- Favorable dose-response relationships because of the ability to escalate the dose with less concern over the toxicity to normal tissue
- Fast treatment planning and delivery due to computer assistance

Steps of 3D-CRT in Ca Prostate

Patient positioning - Supine

- Supine position with knee support is standard

- Advantages
  - Ease of daily setup for the patient and staff
  - The ability to fuse treatment-planning images with previously obtained diagnostic images (i.e., MRI)

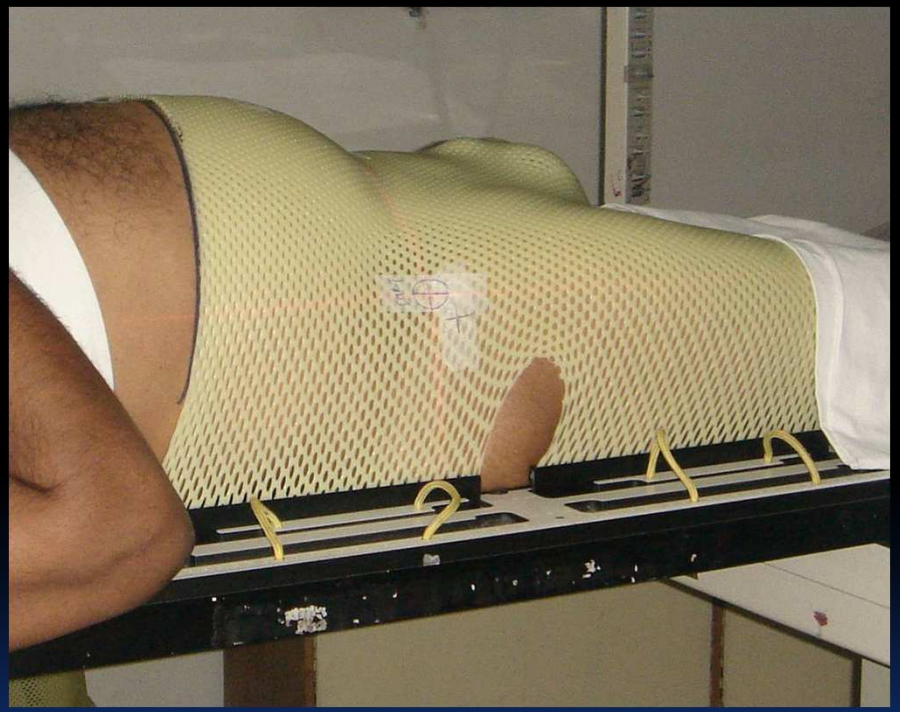
Steps of 3D-CRT in Ca Prostate

Patient positioning - *Prone*

- Prone position is being used in some institutes

- Advantage-
  - Relative sparing of small bowel from the radiation portals

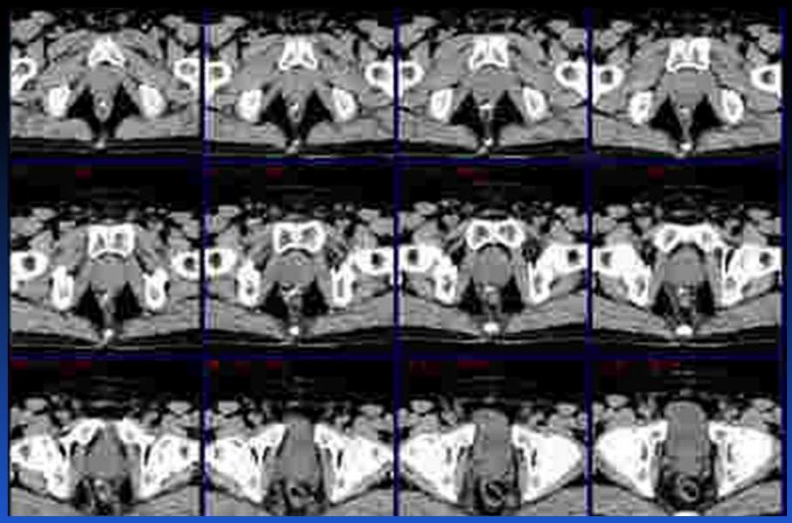
Steps of 3D-CRT in Ca Prostate
Immobilization



- External
  - Thermoplastic Mask (Aquaplast, Orfit)
  - Vacuum shaping bags (Vac Lock)
- Internal
  - Rectal balloon

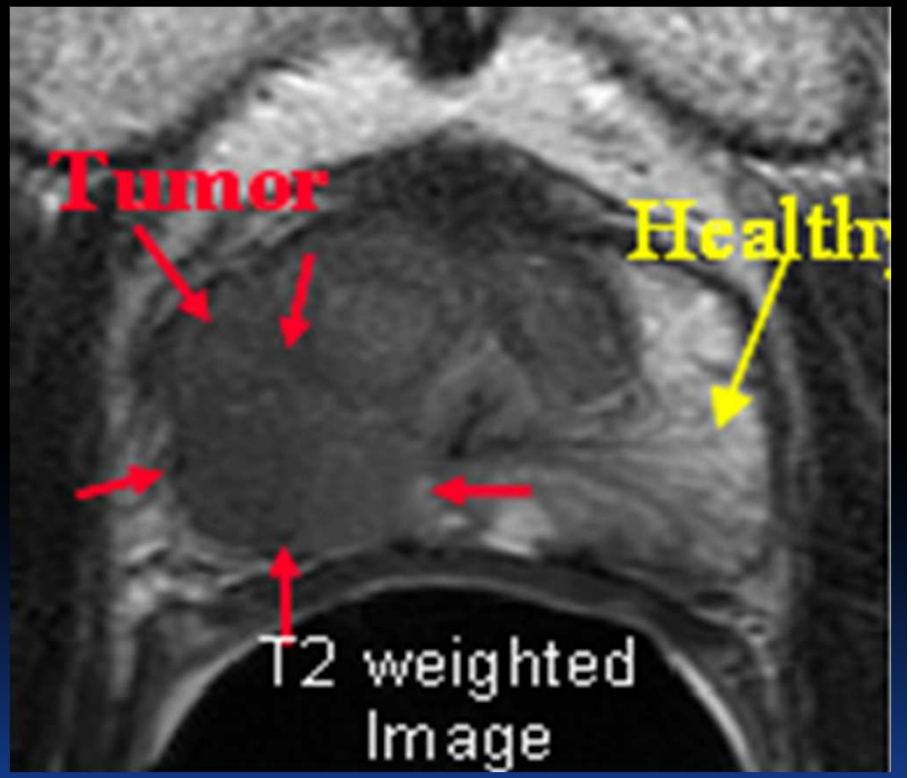
Steps of 3D-CRT in Ca Prostate
Planning Imaging – CT Scan

- Advantages
  - Widely available
  - Density data is used for dose computing
- Disadvantages
  - Prostate apex is not well defined



Steps of 3D-CRT in Ca Prostate
Planning Imaging – MRI Scan

- Advantages
  - Prostate apex is well defined, tumor volume delineation is more precise
- Disadvantages
  - Can’t use MRI images for dose computing
  - Fusion of MRI with CT may not be perfect



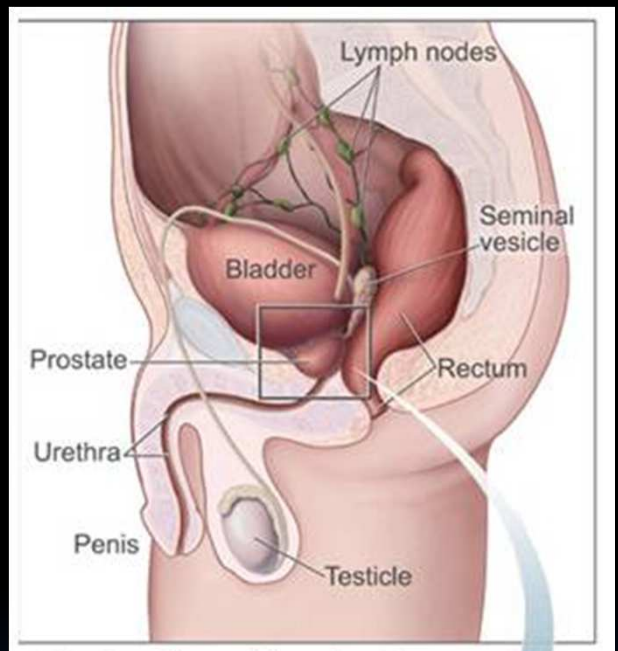
Steps of 3D-CRT in Ca Prostate
Planning Imaging – PET-CT Scan

- Limitations
  - Minimal or no uptake of FDG in prostate – due to lipid metabolism
  - Not widely available
- Advantages
  - Precise tumor vol delineation in FDG avid disease (e.g. involved LN)

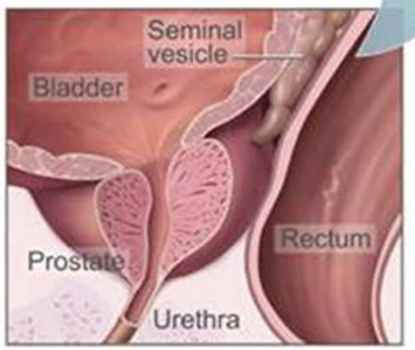
Steps of 3D-CRT in Ca Prostate

Target Volume Delineation

- CTV and PTV are identified on each relevant axial CT slice
- Normal structures outlined on each CT slice :
  - bladder wall, rectum, small bowel, & bony structures



This shows the prostate and nearby organs.



This shows the inside of the prostate, urethra, rectum, and bladder.

3D-CRT in Ca Prostate
Guidelines

Radiotherapy and Oncology 79 (2006) 259-269
www.thegreenjournal.com

Radioth & Oncol 2006

Guidelines

Guidelines for primary radiotherapy of patients with prostate cancer

Dirk Boehmer[a,*], Philippe Maingon[b], Philip Poortmans[c], Marie-Hélène Baron[d], Raymond Miralbell[e], Vincent Remouchamps[f], Christopher Scrase[g], Alberto Bossi[h], Michel Bolla[i], on behalf of the EORTC radiation oncology group

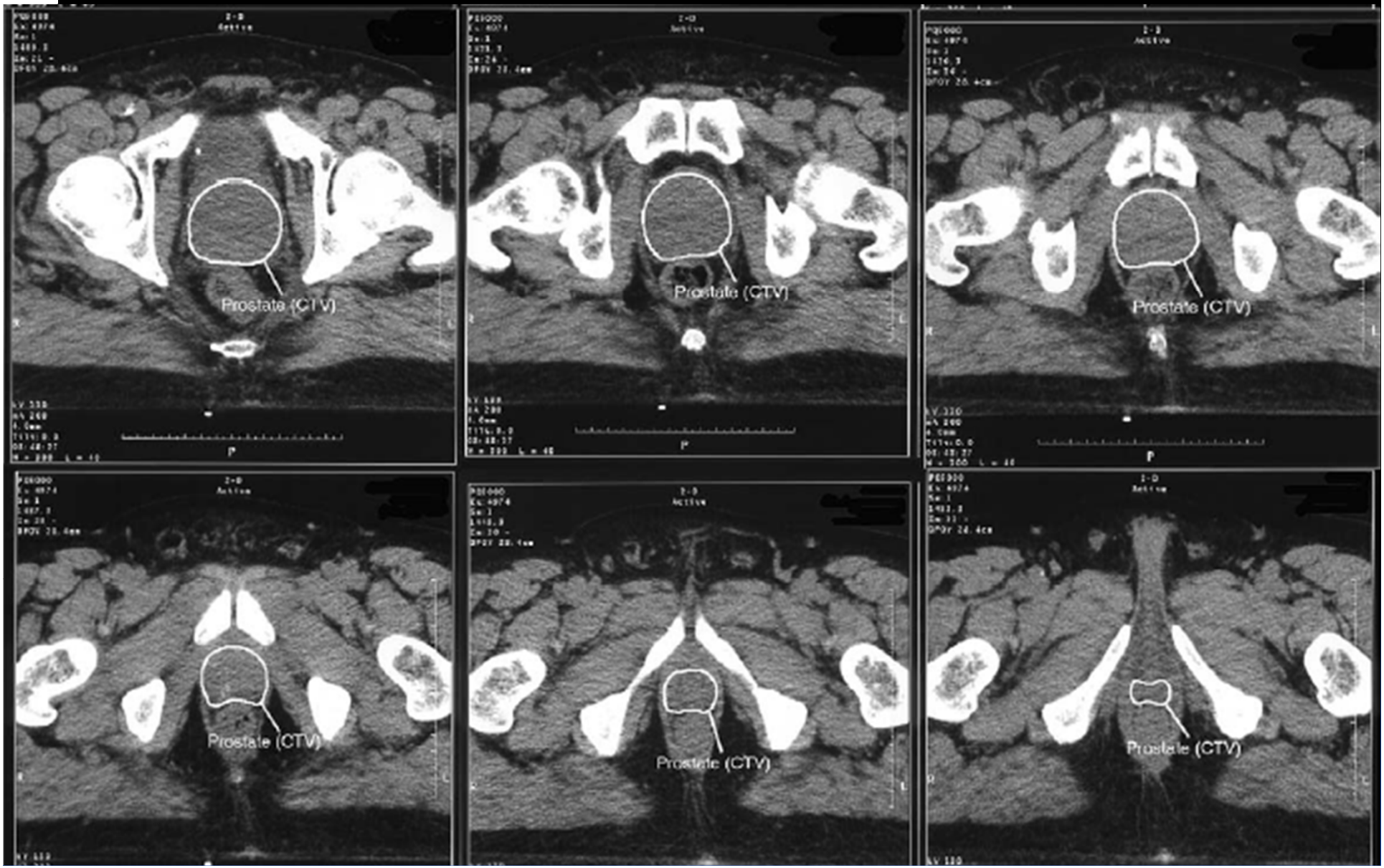
[a]*Klinik f. Strahlentherapie, Universitätsmedizin Berlin, Charité Campus Mitte, Berlin, Germany,* [b]*Unité de Radiothérapie, Centre Georges-François-Leclerc, Dijon Cedex, France,* [c]*Dr B. Verbeeten Institute, LA Tilburg, The Netherlands,* [d]*Service de Radiothérapie C.H., Régional et Universitaire Hôpital Jean Minjoz, Besancon Cedex, France,* [e]*Division de Radiooncologie, Hòpitaux Universitaires, Geneva, Switzerland,* [f]*Clinique & Maternité Ste. Elisabeth, Service d'Oncologie, Radiothérapie et Médecine Nucléaire, Namur, Belgium,* [g]*Ipswich Hospital NHS Trust, England, UK,* [h]*Department of Radiotherapy, UZ Gasthuisberg, Leuven, Belgium,* [i]*C.H. Régional et Universitaire Hôpital, Grenoble Cedex, France*

Steps of 3D-CRT in Ca Prostate

CTV- Prostate alone

- In EBRT, whole prostate constitutes CTV
- Low risk of Seminal vesicle invasion or Extra-capsular Invasion
  - Low risk patients with <50% positive biopsies
  - Intermediate risk pts with <17% positive biopsies

CTV- Prostate alone



Steps of 3D-CRT in Ca Prostate

CTV- Prostate + Seminal Vesicles

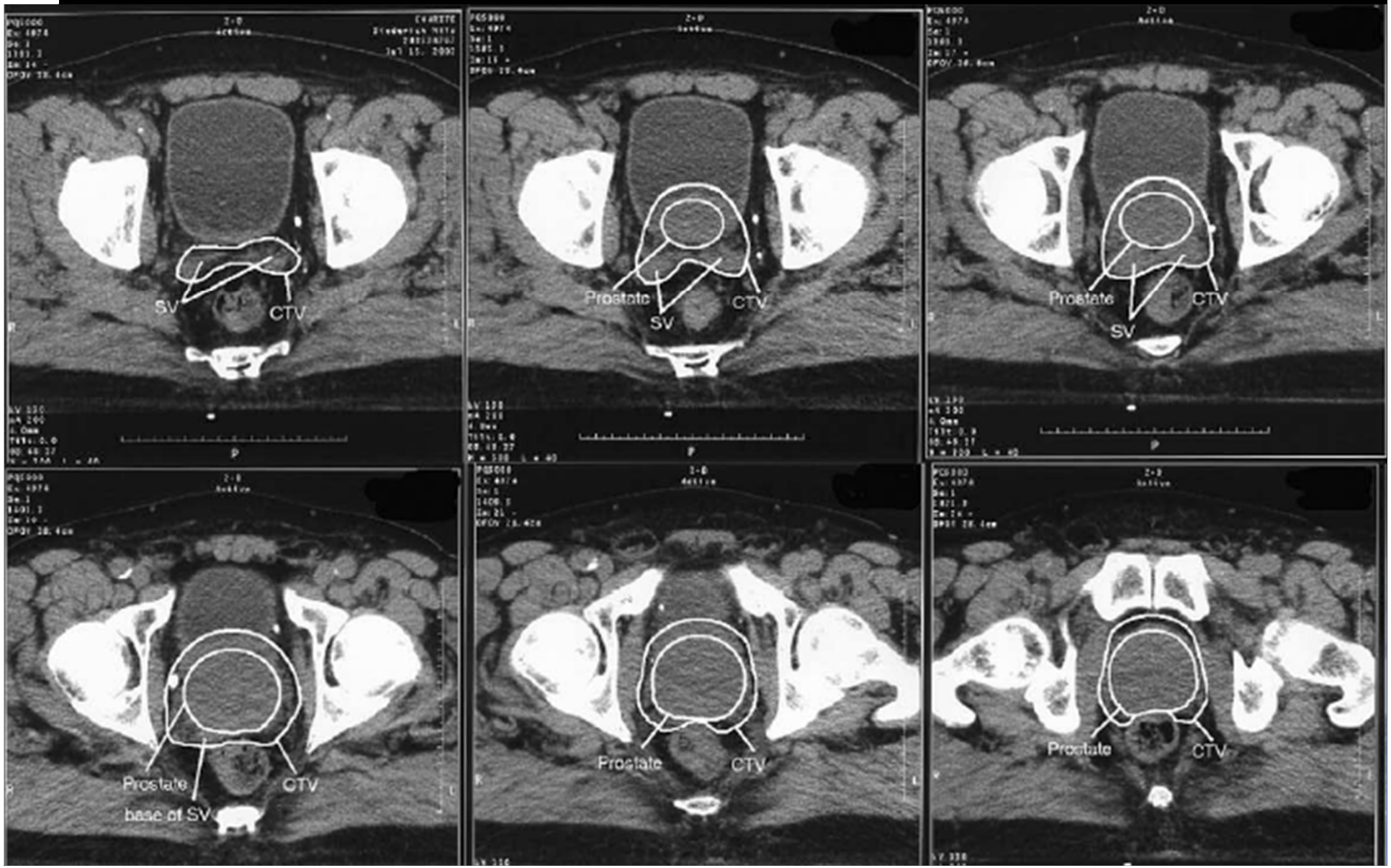
- Increased levels of capsular invasion is associated with increased risk of SVI or LN metastasis
- Perineural invasion is associated with Extracapsular Extension as well as high Gleason Score
- In intermediate risk pts, 1cm of seminal vesicles may be included in CTV
- In high risk pts, 2cm of seminal vesicles may be included in CTV

Steps of 3D-CRT in Ca Prostate

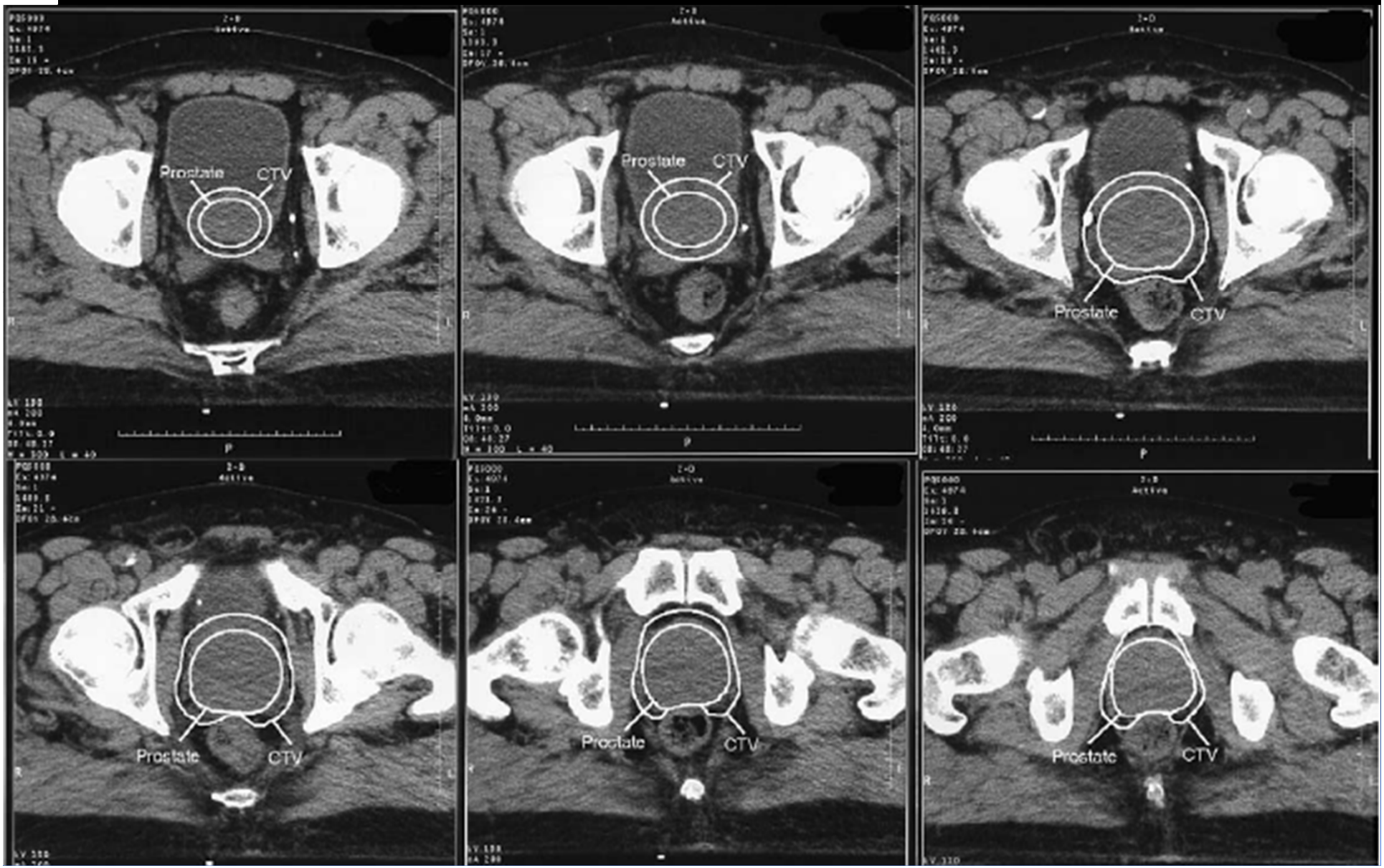
CTV- Prostate + 5mm margin

- In patients with intermediate and high risk prostate ca additional margin of 5mm of periprostatic tissue should encompass CTV

CTV- Prostate + Seminal Vesicles



CTV- Prostate + 5mm margin



Steps of 3D-CRT in Ca Prostate
PTV= CTV+ margin

TABLE 1

Summary of target definitions and dose prescriptions for prostate IMRT

Study	GTV	CTV	PTV	Prescription (TD/FS) in Gy
Zelefsky et al[11]				
81-Gy plan	NS	P + SV	CTV + 1.0 cm UE (0.6 cm posterior)	PTV: 81/1.8 ≥ 90% to receive ≥ 70
86.4-Gy plan	NS	P + SV	CTV + 1.0 cm UE (0.6 cm posterior)	PTV: 86.4/1.8 ≥ 85% to receive ≥ 86.4
Ezzell et al[18]	NS	P + SV	CTV + 1.0 cm UE	75.6/1.8 to ≥ 95% CTV
Jani et al[12]				
Phase I	P + SV	CTV1 = GTV1	PTV1 = CTV1 + 1.0 cm UE	PTV1: 50/2
Phase II	P	CTV2 = GTV2	PTV2 = CTV2 + 1.0 cm UE (0.6 cm posterior)	PTV2: 24/2
Sethi et al[19]	NS	NS	PTV1 = (P + SV) + 1.0 cm UE PTV2 = (P) + 1.0 cm UE	PTV1: 55.8/1.8 PTV2: 18/1.8, 25.2/1.8, or 34.2/1.8*
Teh et al[20†]	NS	Prostatic fossa and periprostatic tissues	CTV + 0.5 cm UE	PTV: 60-66/2 to 86% line

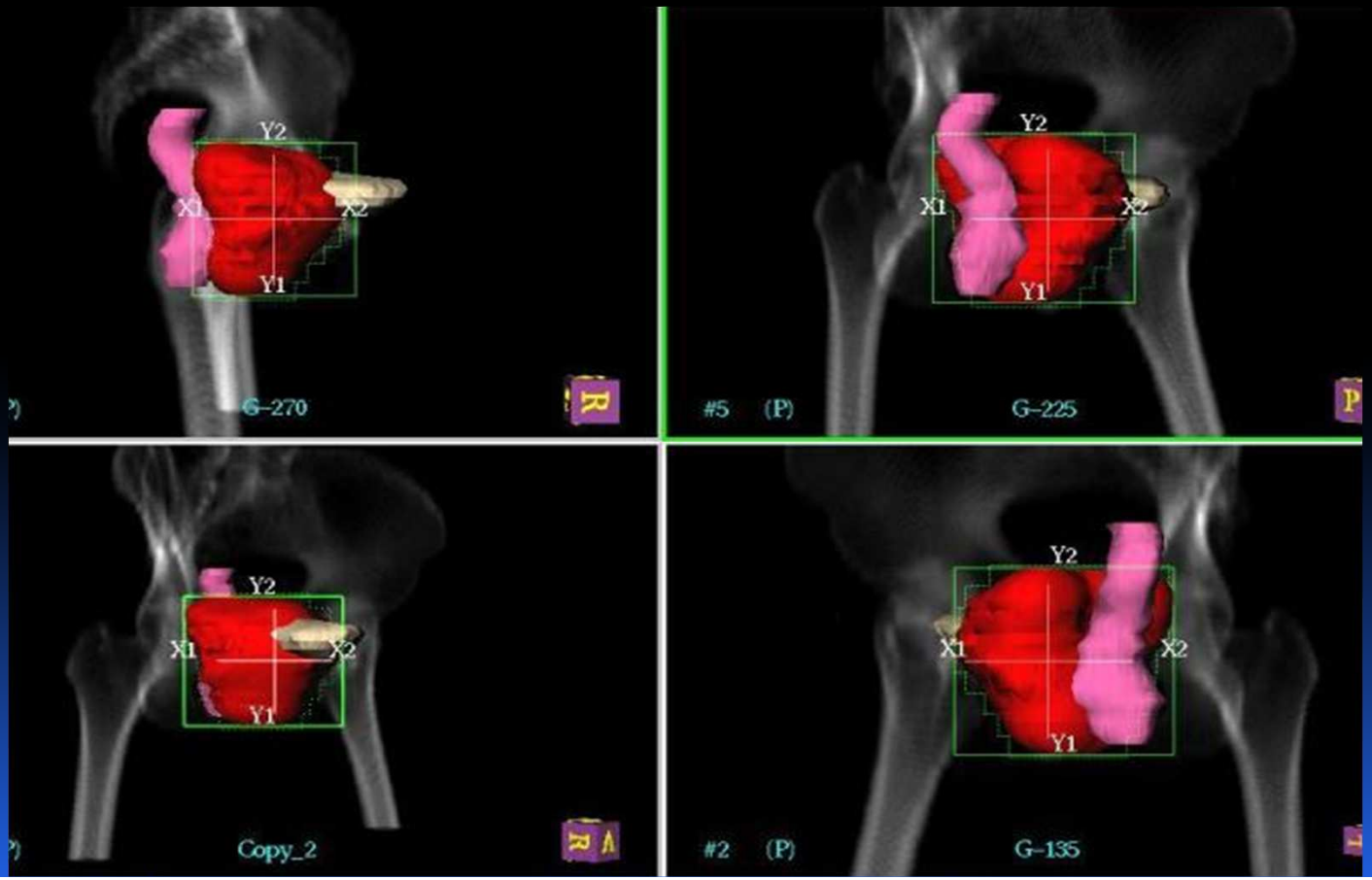
CTV = clinical tumor volume; FS = fraction size; GTV = gross tumor volume; NS = not specified; P = prostate; PTV = planned treatment volume; SV = seminal vesicles; TD = total dose; UE = uniform expansion

*Dose escalation (total dose, 73.8, 81, or 90 Gy)

† Subjects were studied postprostatectomy.

3D-CRT in Ca Prostate Target Vol Delineation

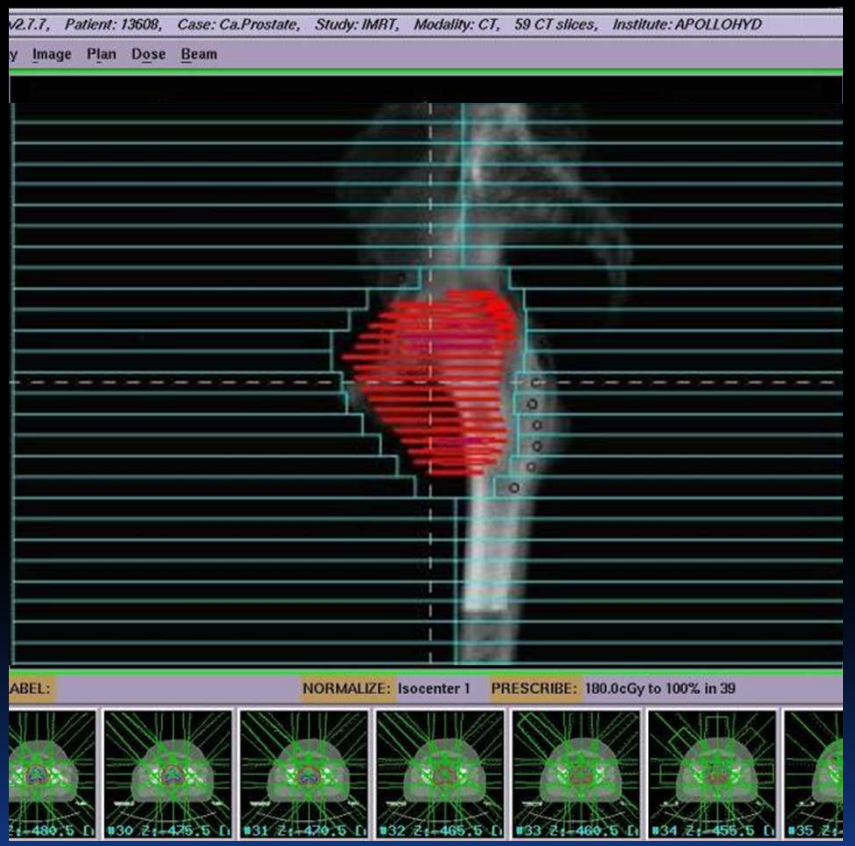
- The target volume and normal structures are digitally reconstructed in 3 dimensions and displayed with the beam's eye view (BEV) technique



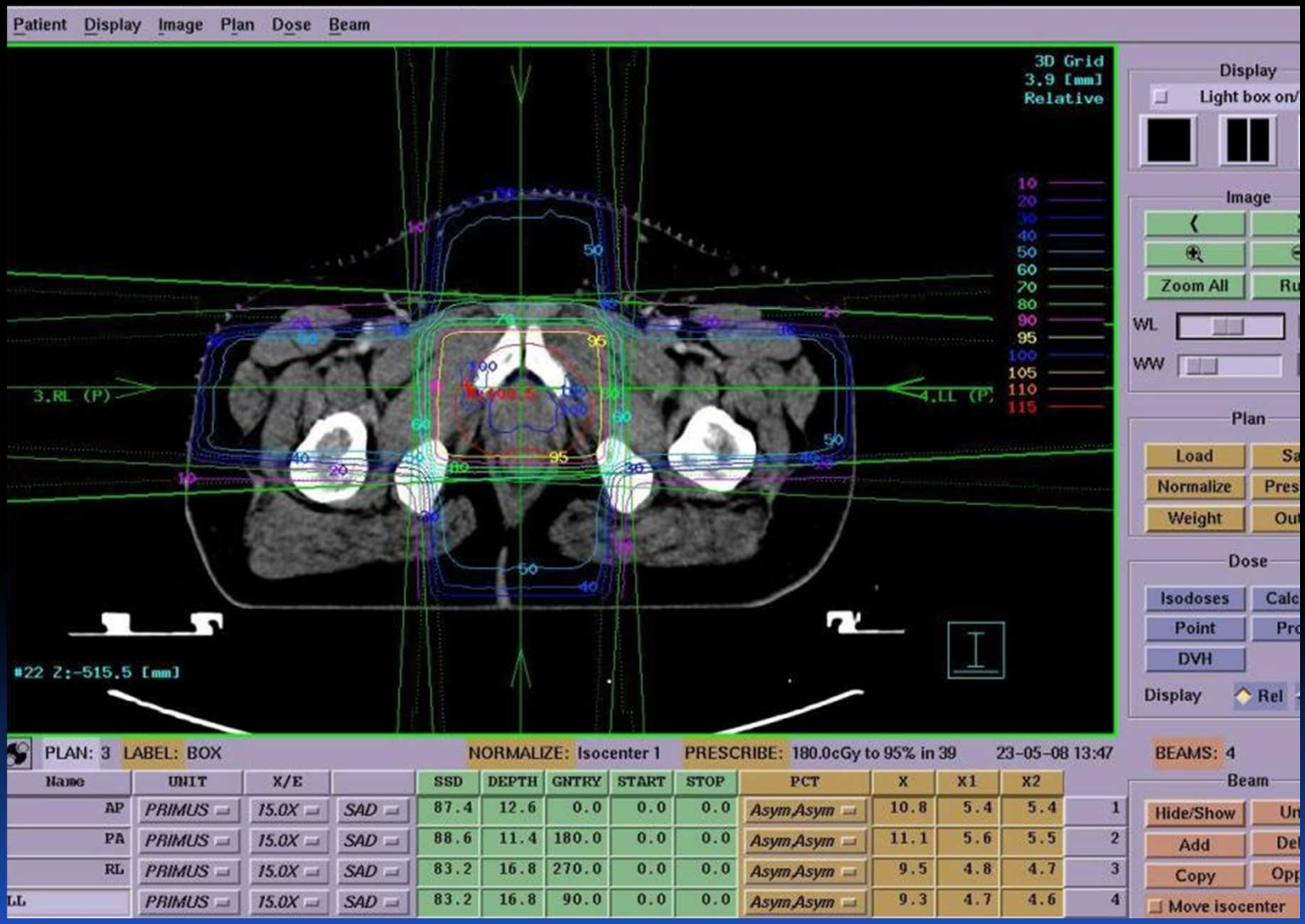
Steps of 3D-CRT in Ca Prostate

Computerized Planning

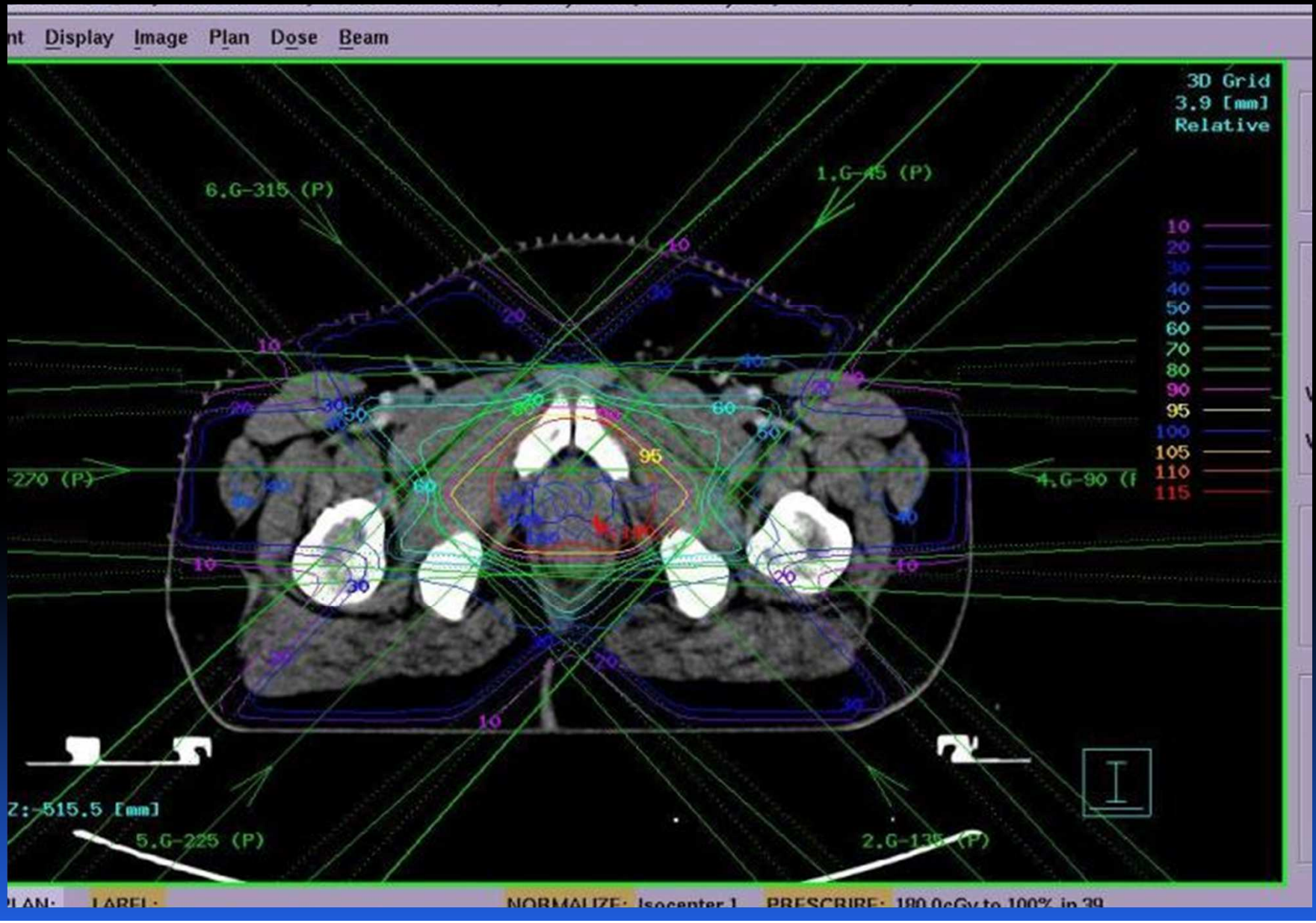
- Fixation of Isocenter
- Selection of Beam angles
- Shielding of OARs (Organ at risk) with help of Beam's Eye View (BEV)
- Dose Calculation



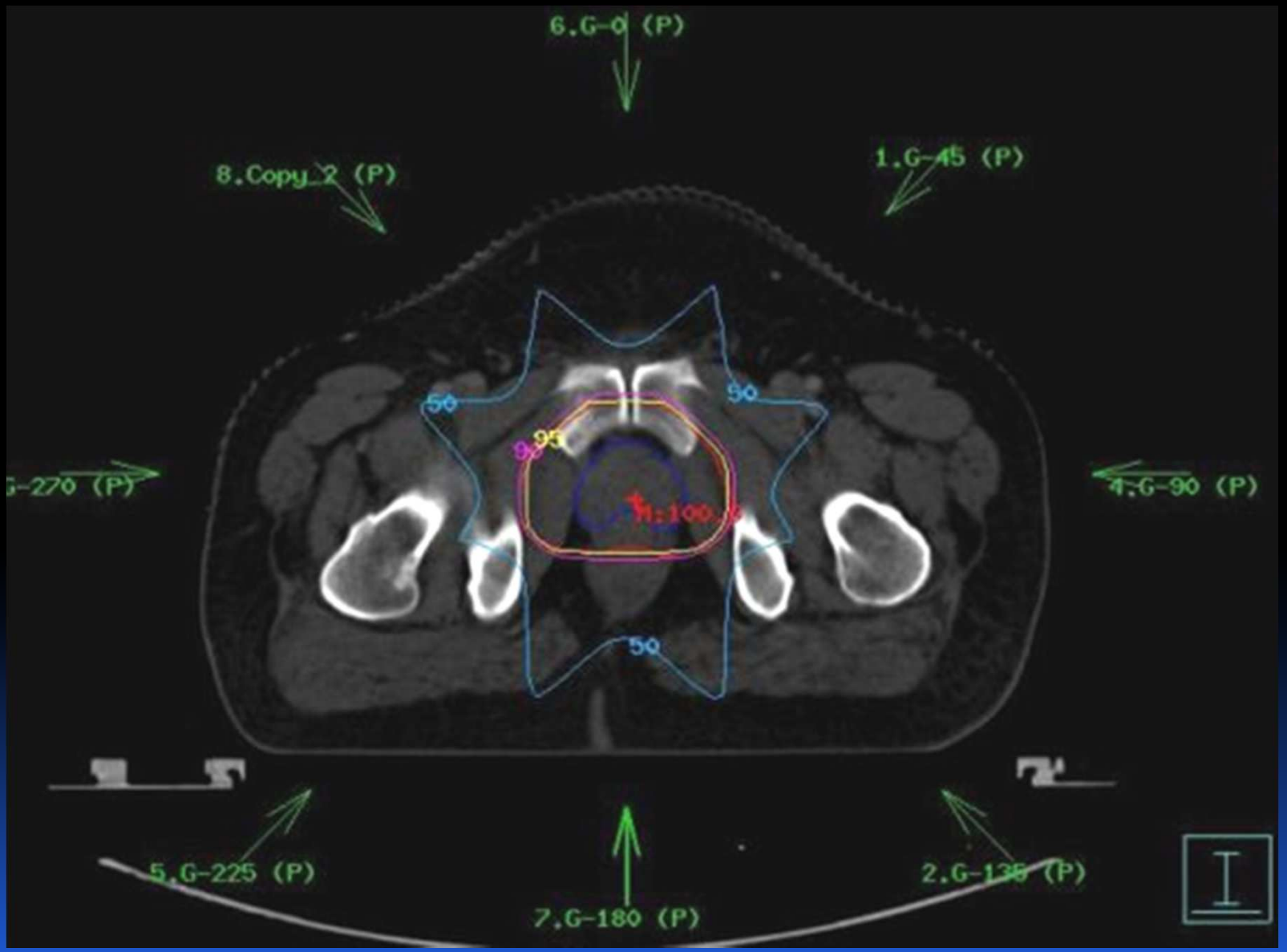
3D-CRT in Ca Prostate – 4 Fields



3D-CRT in Ca Prostate – 6 Fields



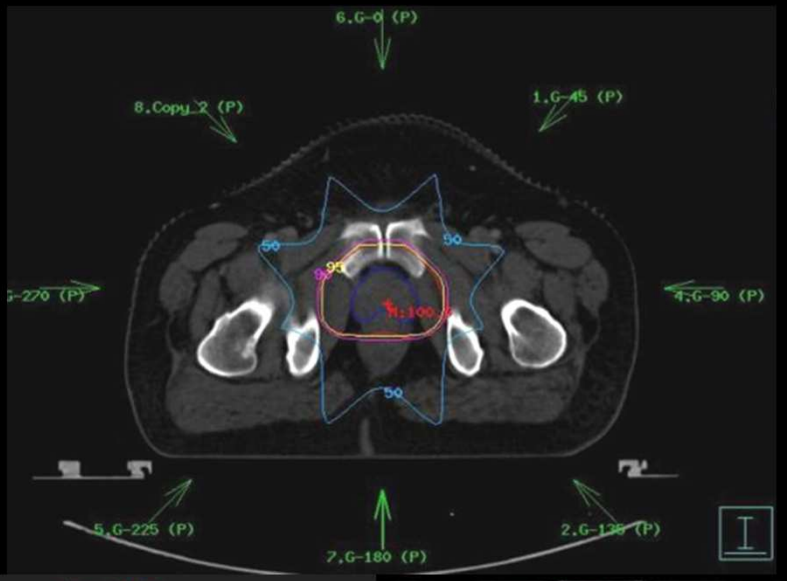
3D-CRT in Ca Prostate – 8 Fields

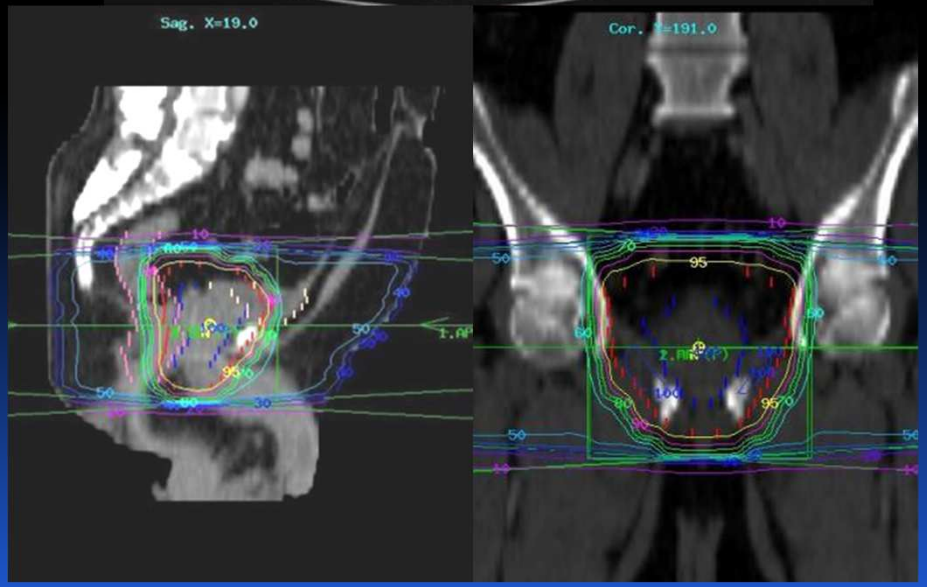


Steps of 3D-CRT in Ca Prostate

Plan Evaluation

- Isodose distribution in each CT Slice
- 3D Volumetric isodose evaluation
  - Dose-volume Histogram (DVH)
  - Sagital and Coronal image reconstruction

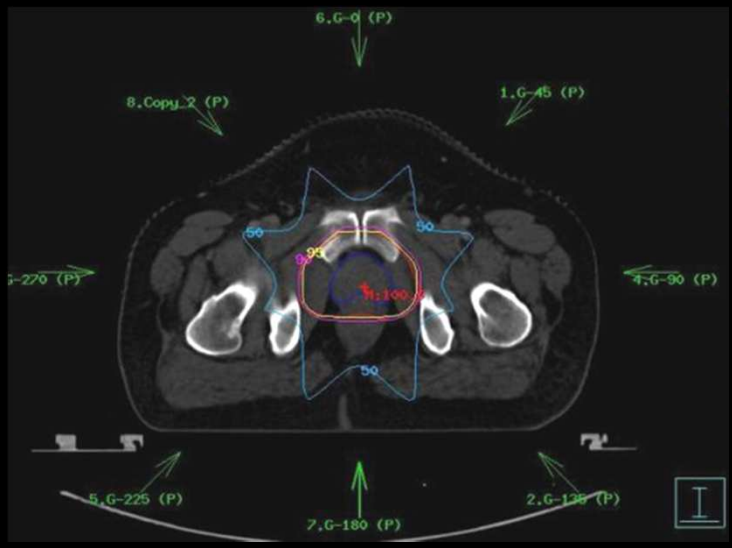


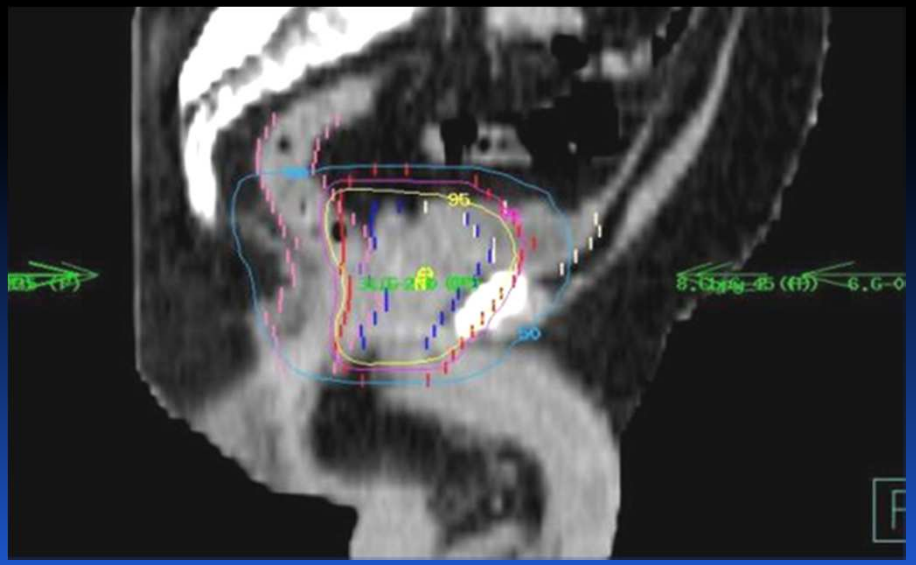


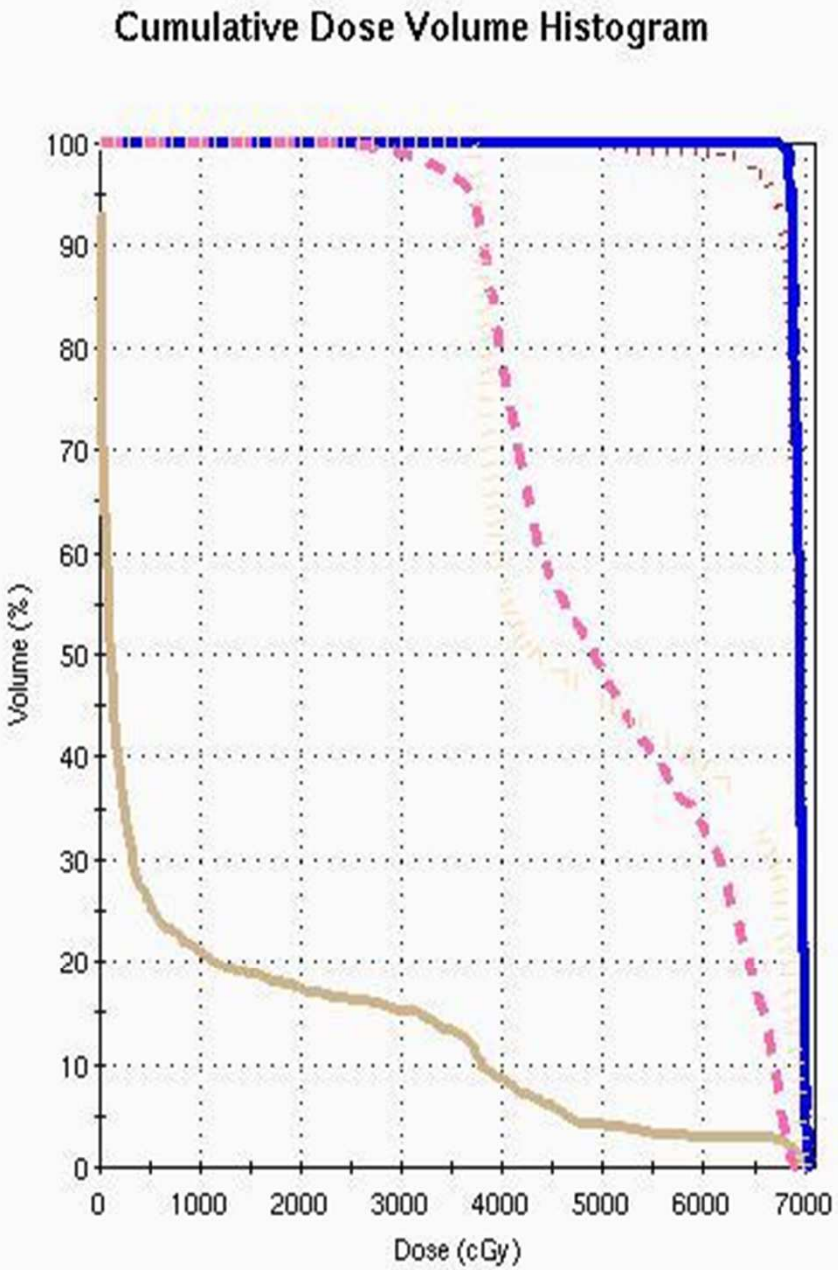
Steps of 3D-CRT in Ca Prostate

Plan Evaluation

- PTV Coverage
  - 95% isodose line
- Sparing of Normal Organs
  - Bladder – Post wall
  - Rectum – Ant wall



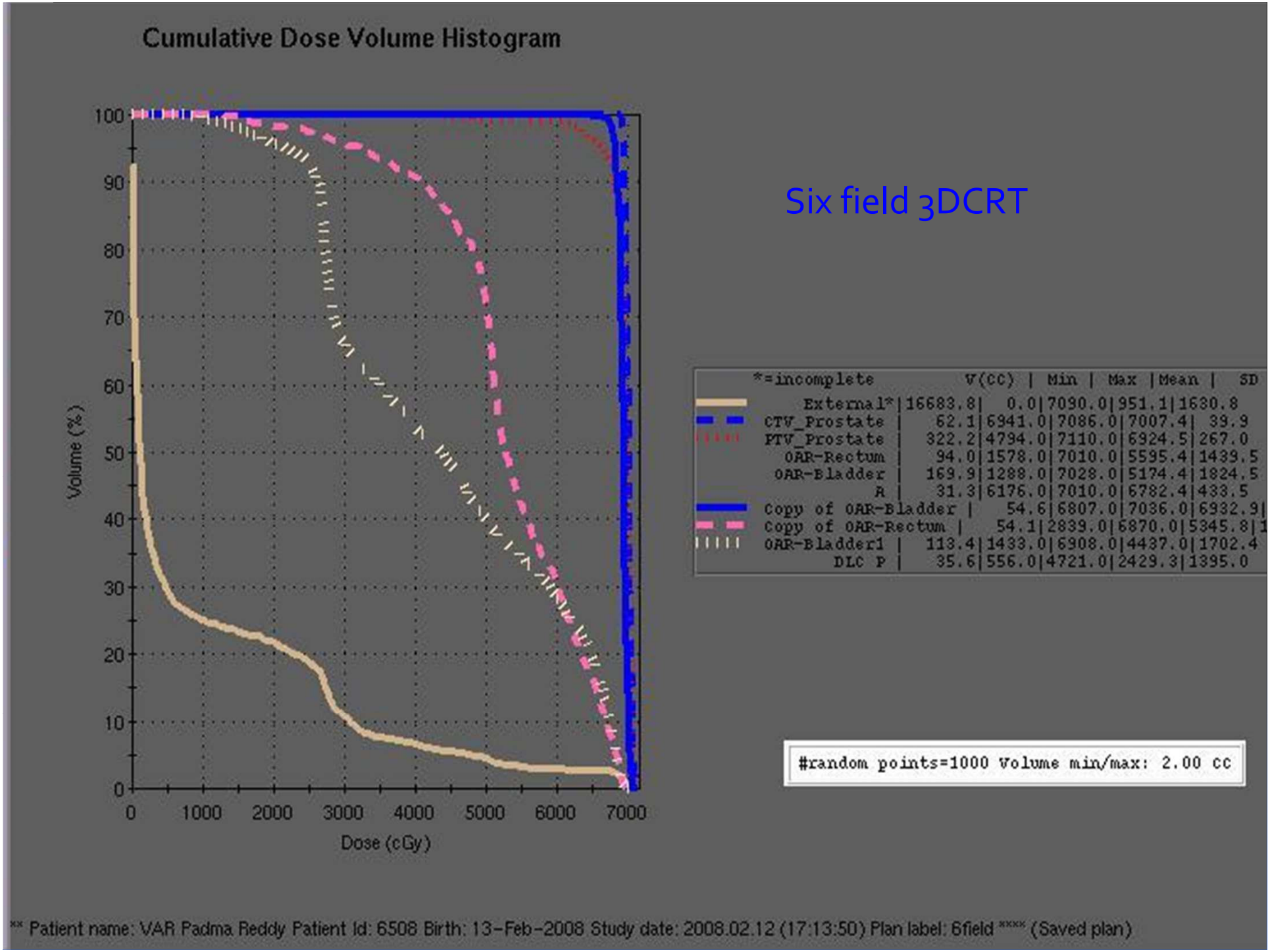




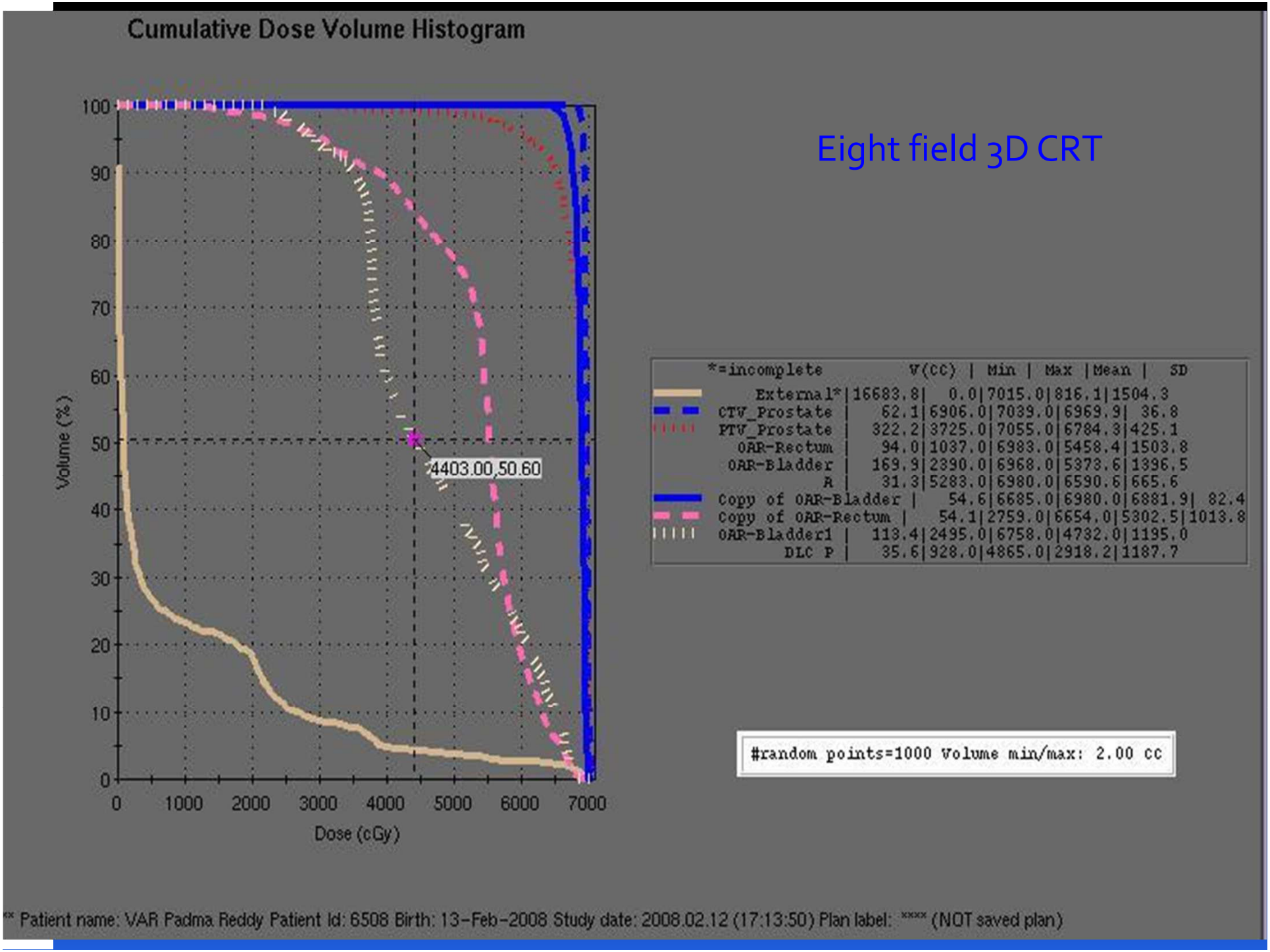
4 field 3D CRT

*=incomplete	V(cc)	Min	Max	Mean	SD
External*	16683.8	0.0	7049.0	919.0	1700.8
CTV_Prostate	62.1	6882.0	7048.0	6959.3	44.9
PTV_Prostate	322.2	5263.0	7068.0	6911.5	199.3
OAR-Rectum	94.0	2686.0	6981.0	5523.7	1373.3
OAR-Bladder	169.9	3743.0	7021.0	5672.4	1399.8
A	31.3	6391.0	6981.0	6786.5	282.3
Copy of OAR-Bladder	54.6	6858.0	7028.0	6953.2	49.0
Copy of OAR-Rectum	54.1	3575.0	6815.0	5119.1	1151.3
OAR-Bladder1	113.4	3740.0	6985.0	5155.2	1373.5
DLC P	35.6	1895.0	3724.0	3258.6	605.6

#random points=1000 Volume min/max: 2.00 cc


Cumulative Dose Volume Histogram
Volume (%)
Dose (cGy)
0
10
20
30
40
50
60
70
80
90
100
0
1000
2000
3000
4000
5000
6000
7000
Six field 3DCRT
*=incomplete V(CC) | Min | Max |Mean | SD
External* |16683.8| 0.0|7090.0|951.1|1630.8
CTV_Prostate | 62.1|6941.0|7086.0|7007.4| 39.9
PTV_Prostate | 322.2|4794.0|7110.0|6924.5|267.0
OAR-Rectum | 94.0|1578.0|7010.0|5595.4|1439.5
OAR-Bladder | 169.9|1288.0|7028.0|5174.4|1824.5
R | 31.3|6176.0|7010.0|6782.4|433.5
Copy of OAR-Bladder | 54.6|6807.0|7036.0|6932.9|
Copy of OAR-Rectum | 54.1|2839.0|6870.0|5345.8|1
OAR-Bladder1 | 113.4|1433.0|6908.0|4437.0|1702.4
DLC P | 35.6|556.0|4721.0|2429.3|1395.0
#random points=1000 Volume min/max: 2.00 cc
** Patient name: VAR Padma Reddy Patient Id: 6508 Birth: 13-Feb-2008 Study date: 2008.02.12 (17:13:50) Plan label: 6field **** (Saved plan)

Eight field 3D CRT



Steps of 3D-CRT in Ca Prostate

Plan Evaluation

- Rectal Wall 30% - 75.6 Gy
- Small bowel Dmax $\leq$ 50 Gy
- Large bowel Dmax $\leq$ 60 Gy

Steps of 3D-CRT in Ca Prostate
Plan Evaluation

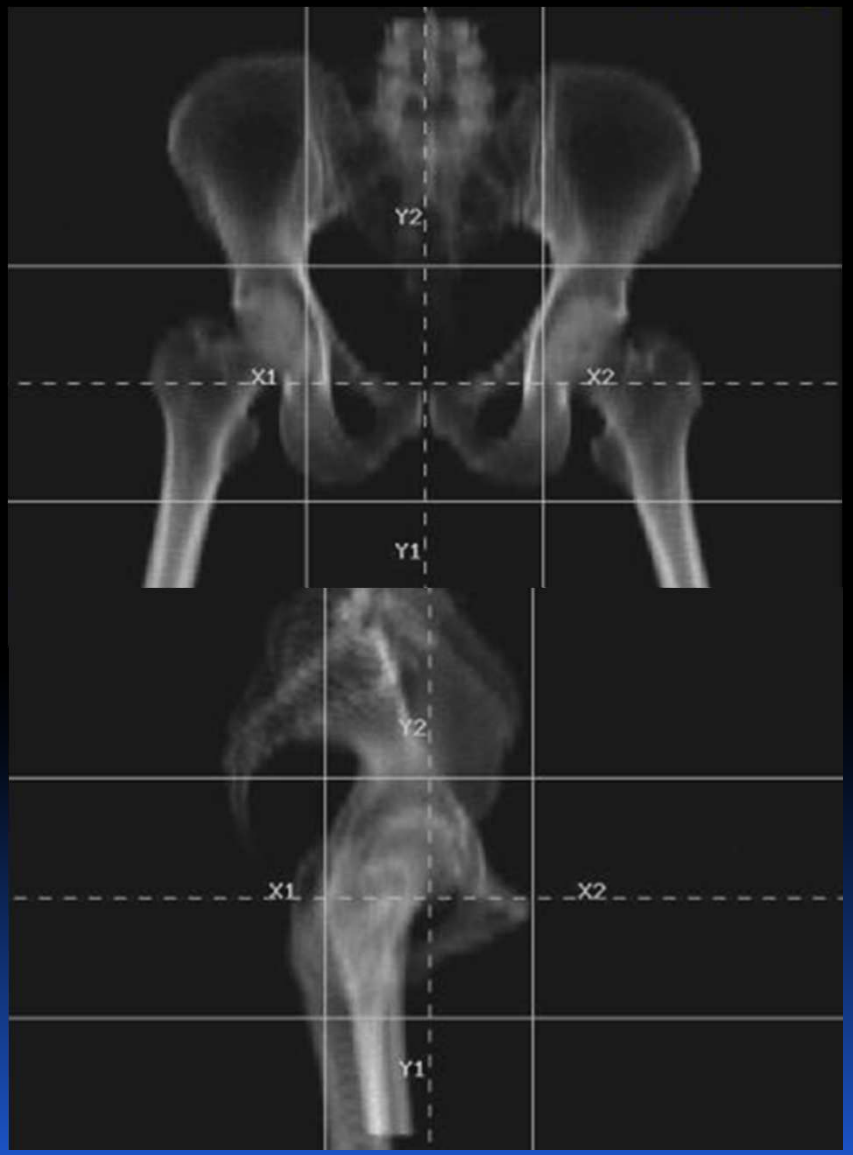
Dose Constraint

	Rectum	Bladder
1. Zelefsky	< 30% > 75 Gy	
	< 53% > 47 Gy	< 53% > 47 Gy
2. Ezzell	< 10% > 75 Gy	
	< 30 % > 70 Gy	
	Dmax < 81	< 30% > 75 Gy
3. Sethi	< 30% > 65 Gy	< 30% > 65 Gy

Steps of 3D-CRT in Ca Prostate

Plan Implementation

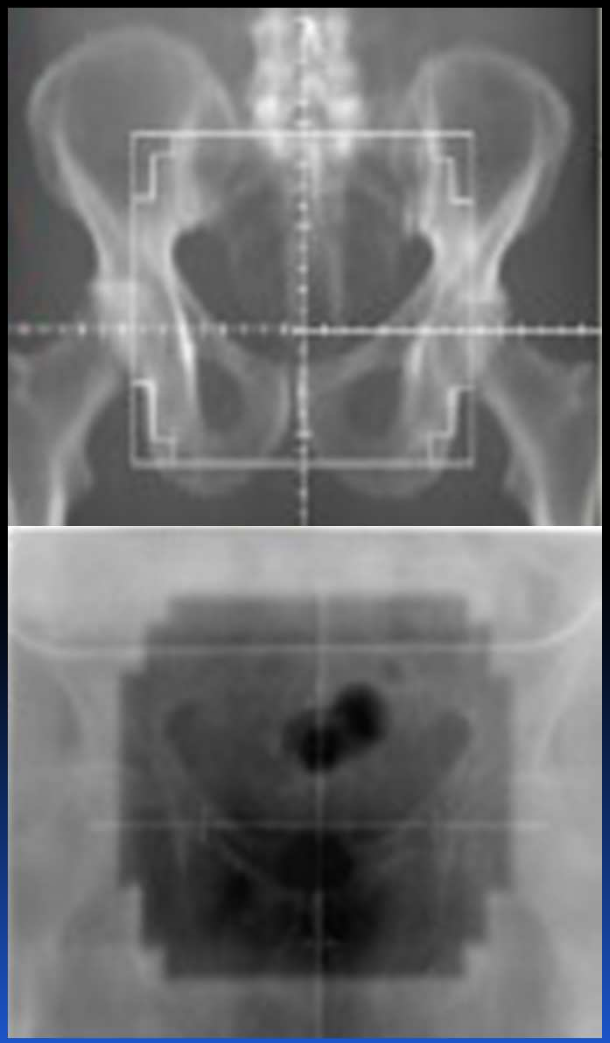
- Simulation
- Comparison of Simulator film with DRR (Digitally reconstructed radiograph)
- Transfer of Computer Plan to treatment machine
- Remote controlled treatment delivery



Steps of 3D-CRT in Ca Prostate
Quality Assurance

- Comparison of port film with Simulator film and DRR image

- EPID (Electronic portal imaging device) imaging with correction of set-up errors



3D-CRT in Ca Prostate
Dose Recommendations

The NEW ENGLAND JOURNAL of MEDICINE

NEJM, 2006

Table 2. Principles of Radiotherapy, According to the National Comprehensive Cancer Network.

Three-dimensional conformal or intensity-modulated radiotherapy techniques should be used.

Doses of 70 to 75 Gy in 35 to 41 fractions to the prostate (with or without inclusion of the seminal vesicles for part of the therapy) appear to be appropriate for patients with low-risk cancers, whereas for patients with intermediate- or high-risk disease, doses of 75 to 80 Gy appear to provide improved disease control as assessed on serum PSA testing.

Patients with high- or very-high-risk cancers are candidates for radiotherapy to the pelvic lymph nodes with neoadjuvant or adjuvant androgen-suppression therapy, or both.

If target margins are reduced, such as for the administration of doses greater than 75 Gy, extra attention to daily image guidance, with the use of techniques such as implanted markers, transabdominal ultrasonography, or endorectal balloon, is indicated.

3D-CRT in Ca Prostate
Clinical Outcome Studies

Table 11: Summary of results in recent three-dimensional conformal radiation therapy (3D-CRT) series

Series	Patients	Biochemical freedom from failure (prostate-specific antigen < 1 ng/mL)
Roach et al., 1996 (13)	501 T1-T2	
	IPSA < 4 ng/mL	90% 4-year
	IPSA 4-10 ng/mL	60% 4-year
	IPSA 10-20 ng/mL	35% 4-year
	IPSA > 20 ng/mL	30% 4-year
Zelefsky et al., 1998 (28)	213 T1-T2 (leuprolide and flutamide given 3 months before 3D-CRT)	
	IPSA ≤ 10 ng/mL	93% 5-year
	IPSA > 10 ≤ 20 ng/mL	60% 5-year
	IPSA > 20 ng/mL	40% 5-year
Anderson et al., 1998 (29)	172 T1-T2a,b; Gleason score 2-6; no PNI	91%* 5-year
	94 T2c-T3 or Gleason score 7-10 or PNI	74%* 5-year

IPSA = initial PSA; PNI = perineural invasion.
* p = 0.0024 (definition of failure was PSA ≥ 1.5 ng/mL and two consecutive rises).

Ca Prostate Dose Escalation 3D-CRT

- 743 pts, Phase I Study
- Radiation dose
  - increased from 64.8 to 81 Gy in increments of 5.4 Gy
- Evaluation
  - PSA </= 1ng/ml
  - Prostate biopsy after 2.5 yrs
- Results
  - 75.6-81 Gy - 90% achieved PSA <1ng/ml
  - 70.2 GY – 76% achieved PSA <1ng/ml
  - 64.8 Gy – 56% achieved PSA <1ng/ml

5 yr actuarial PSA relapse free survival for favourable gr, intemediate gr and unfavourable gr was 85%, 65% and 35%

Zelefsky, IJROBP 1998

Ca Prostate- 3D-CRT Vs Std RT

- 3D CRT
  - 312 pts
  - T1b-c-T2
  - 68-74 Gy
- Standard RT
  - 135 pts
  - T1b-c-T2
  - 68-70 Gy

- GS <4 No chemical disease free survival difference
- GS 5-7 5 yr Survival 83% Vs 59%

- PSA <10 chemical disease free survival rate 80% Vs 72%
- PSA 10-20 survival rate 71% Vs 43%
- PSA >20 survival rate 59% Vs 16%

- Bladder toxicity (Moderate dysuria) 2-5% Vs 6-9%
- Rectal toxicity Diarrhea 3-5% Vs 8-19
  Rectal bleeding 1% Vs 7%

Perez, Clin Prost Cancer 2002

Ca Prostate- Dose Escalation 3D-CRT

- 1473 pts
- Dose was increased from 60 to 80.4 Gy

> "For intermediate-risk pts, each 1-Gy increment in total radiation dose was associated with a highly significant 8% reduction in the probability of failure
>
> (hazard ratio = 0.92, p = 0.005)"

Symon, IJROBP 2003

Ca Prostate- Dose Escalation 3D-CRT

- 1325 pts from 9 institutes
- Radiation dose
  - 1061 pts <72 Gy, 15% of pts had high-risk disease
  - 564 pts >72 Gy, 22% of pts had high-risk disease
- The 5-year PSA-DFS estimates for <72 Gy vs. > or =72 Gy were 63% vs. 69%, respectively (p = 0.046).

"Higher than conventional RT were associated with improved PSA-DFS when controlled for the influence of pretreatment PSA levels, biopsy GS, and clinical T stage"

Kupelian, IJROBP 2005

Ca Prostate
Dose Escalation 3D-CRT

- 839 pts
- Radiotherapy (RT) dose
  - < 72 Gy,
  - 72 to 75.9 Gy
  - >/=76 Gy

"RT dose escalation to 76 Gy or greater improved patient outcome for all prognostic groups except those at the favorable and unfavorable extremes. "

Pollack, J Urol 2004

Early Ca Prostate
Sequelae with diff treatment modalities

MODALITY	RECTAL TOXICITY	INCONTINENCE	IMPOTENCE
SURGERY	1%(Catalona et al 1999). 1.1% (Guillonneau 1999)	80%(.post surgery) 6%(.late ; 1 year later) Schaefffer et al 1998). 53%(Schwartz et al 2002) 25%((Guillonneau 1999) (6 months).	66%(neve spring) 75%%(standard RP) Robinson et al (2002).
CEBRT	29.6%(Scwartz et al 2002). 14%(Storey et al 2000). 15% (Dearnaley et al 1999).	19.2%(Scharwz et al 2002). 20%(Storey et al 2000). 10%(Lawton et al 1991).	45%(Robinson et al 2002). 50%((Bagshawet al 1988). 35%(Schroder et l 2000).
3D-CRT	21%(Storey et al 2000). 5%((Dearnaley et al 1999).	9%(Strorey et al 2000).	40%(Robinson et al 2002)
BRACHYTHERAPY	1%(Koutrouvelis et al 2003). 1%(Kang et al 2002). 2% (Syed et al 2001 3%(Schroder et al 2000).	1% (Koutrouvelis et al 2003). 2%(Syed et al 2001) 3%(Sharkey et al(1998). 3%(Schroder et al 2000).	24%(Robinson etal). 7%(Nag S. 1985). 10% (Sharkey et al(1998).

3D-CRT in Ca Prostate

Conclusions

- 3D-CRT has definite advantages over conventional EBRT in Prostate Cancer
- 3D-CRT allows sparing of normal tissues (i.e. rectum and bladder) to a greater extent resulting in significant reduction in short-term and long-term toxicites
- 3D-CRT allows higher doses of radiation to the prostate resulting in improved outcome, especially in intermediate-risk group pts
- 3D-CRT allows fast treatment planning and delivery due to computer assistance

3D-CRT in Ca Prostate
Conclusions contd..

- RT dose to Prostate should be 70-75 Gy in low-risk pts and 75-80 Gy in intermediate and high-risk pts are appropriate for tumor control
- RT dose to Pelvic LN should be 45 Gy for elective LN radiation and 55-60 Gy for involved LN in pts with high-risk group.

*Changing beam **shapes!***

CEBRT

3D CRT

IMRT

IGRT

Does it really make a difference?

*Changing beam **shapes!***

'No Ext beam regimen is superior to another

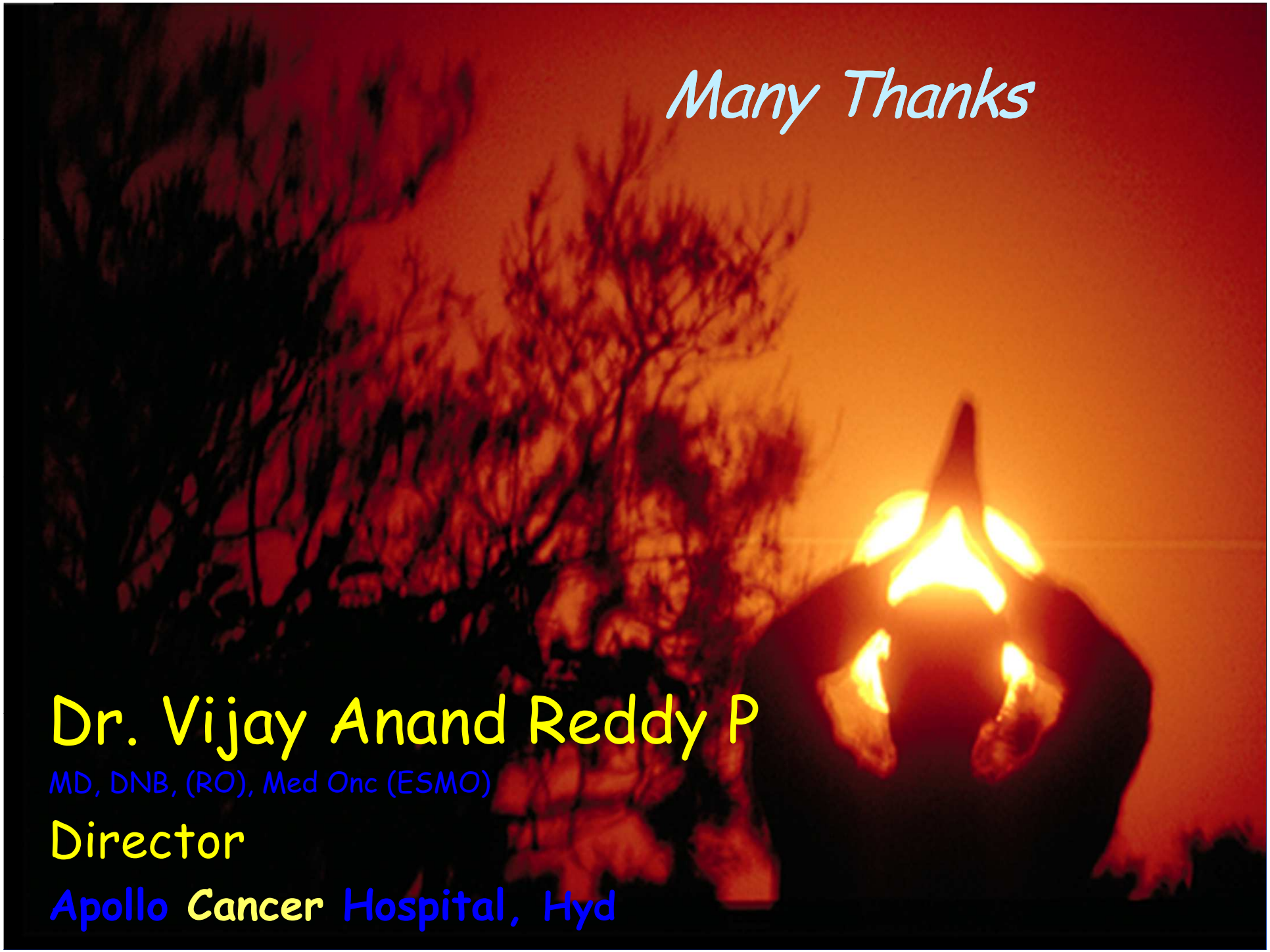
In reduction of mortality rates'

Results from 18 RCT and 473 observation studies

Ann Intern Med. 2008; 148:435-448

I am still going strong!

"3D-CRT could still be used to deliver effective doses in prostate "


Many Thanks
Dr. Vijay Anand Reddy P
MD, DNB, (RO), Med Onc (ESMO)
Director
Apollo Cancer Hospital, Hyd

Thank You!

Summary

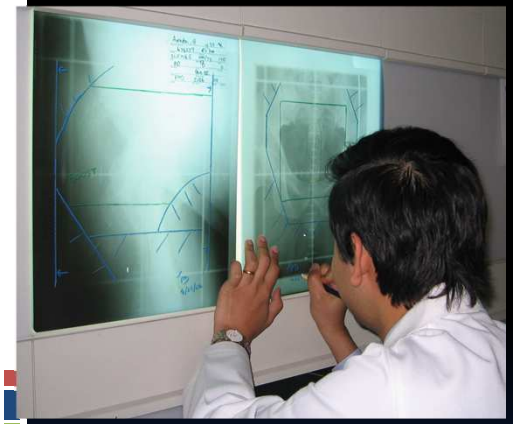
- Dose escalation possible
- Good dose conformity to PTV
- Better sparing of normal structures
- Cost effective !
- 3D CRT is still the standard of care

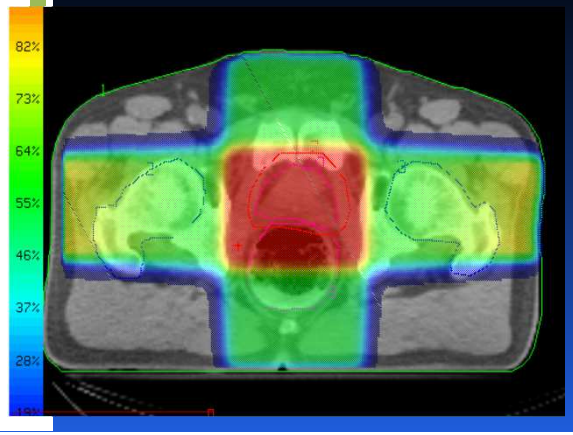
Early Ca Prostate
Survival with diff treatment modalities

MODALITY	**Disease Free Survival** (10 Years)	**Overall survival** (10 Years)
SURGERY	82% **Sciarra** et al (2003) 72%(Han et al 2003) 88%(**D'Amico** et al 2002)	76%(Do LV et al 2002). 75%((Hanks 1988) 78%(Lu, Yao , 1997).
CEBRT	78%(**D'Amico** et al 2002) 78%(**Nguyen** et al 2002). 76%(**Zimmermann 2001)**	68% (**Hahn** et al 1996). 69%(Hank 1988). 65%(Lee et al 1994). 63%(Lu, Yao , 1997). 69%(Gray et al 2000).
3D-CRT	73% (3 years Geinizet aal 2002). 78%(3 years , Dearnaley et al 1999).	
BRACHYTHERAPY	77% Ragde et al 2001 96%(Koutrouvelis et al 2003) 80%(5 years Nag S. 1985).	66%(Stamey et al 2000).
EBRT+BOOST BRACHYTHERAPY	**78%Puthawala et al (2001)**	79%(Stamey et al 2000).

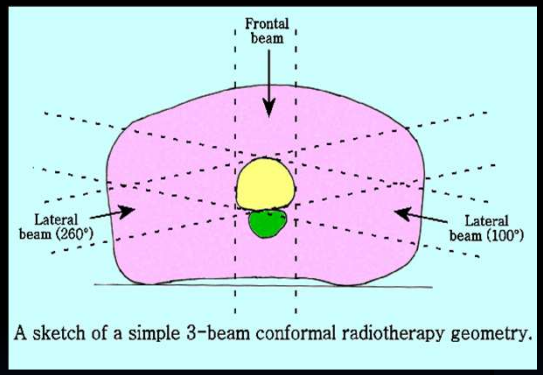
Then and Now

Conv RT

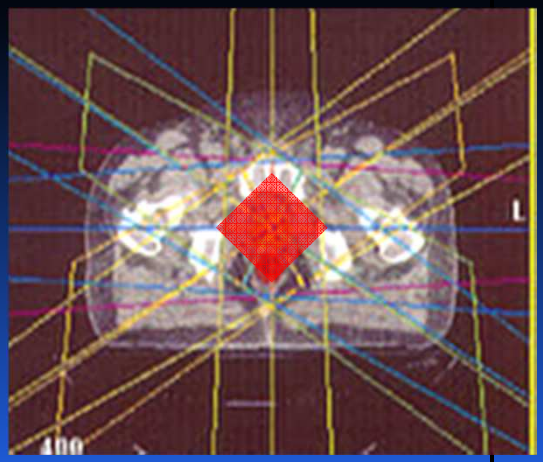




3D CRT



A sketch of a simple 3-beam conformal radiotherapy geometry.



IMRT