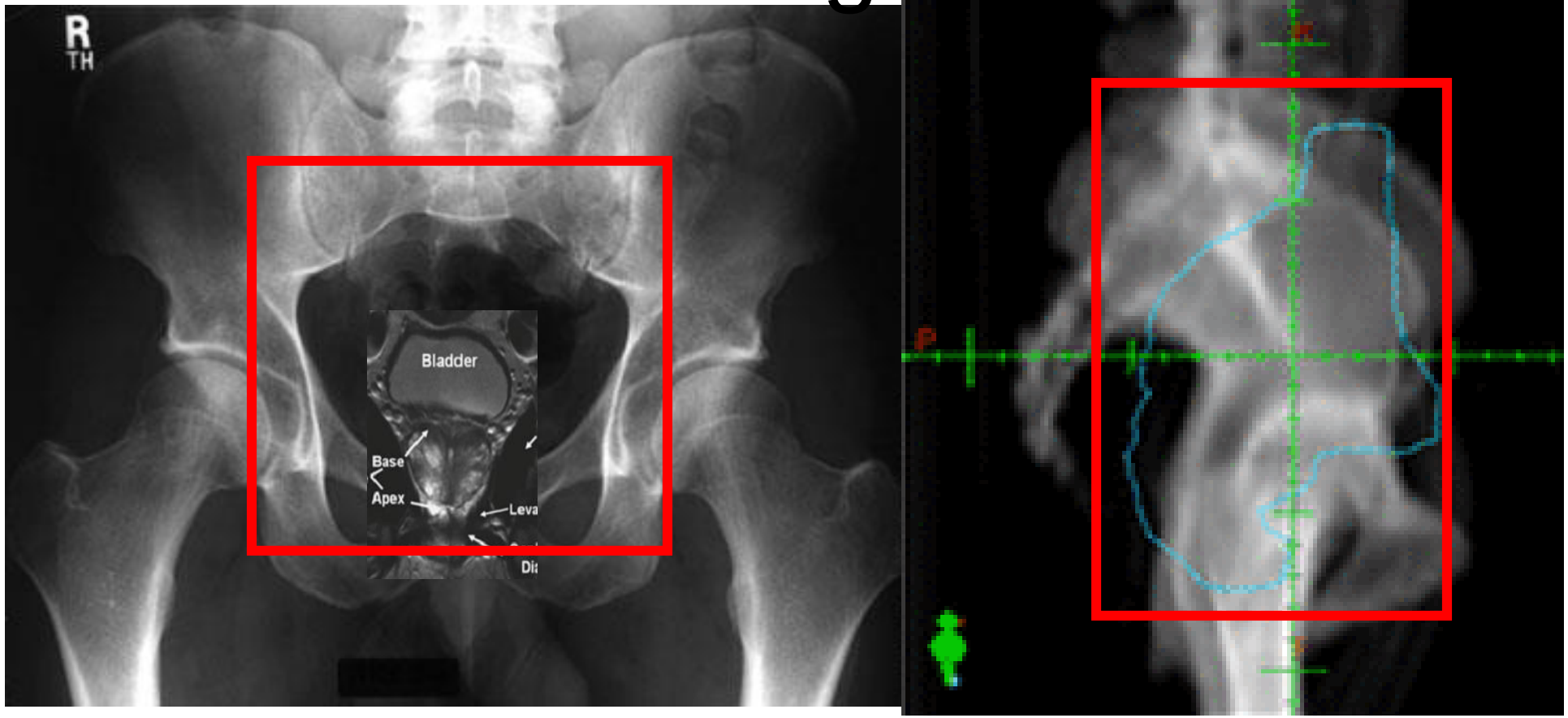
Role of Different Fractionation and 2 D Radiation Planning for Prostate Ca



SUN ICRO PG Webinar
30 July 2020

Prof Manoj Gupta
AIIMS Rishikesh

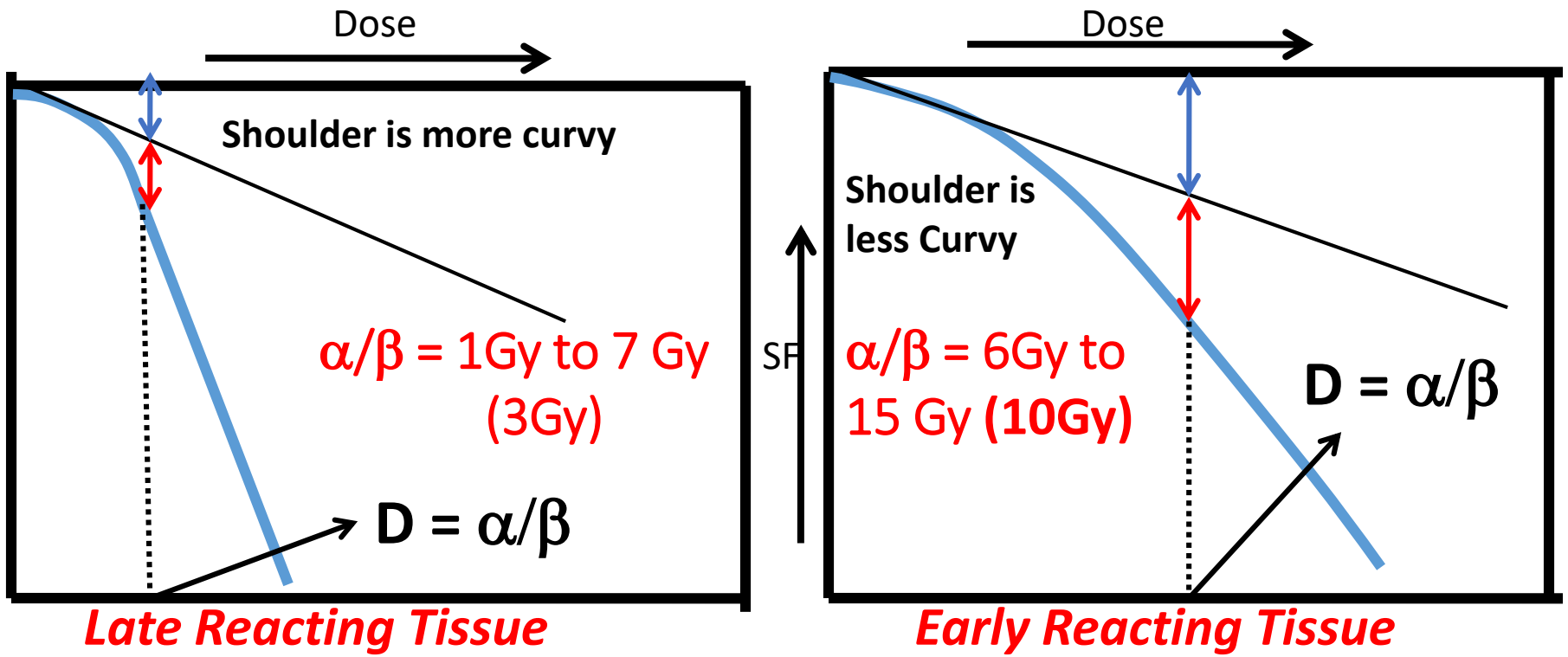
Radiation options for Ca Prostate

Conventional EBRT

Hypofractionation

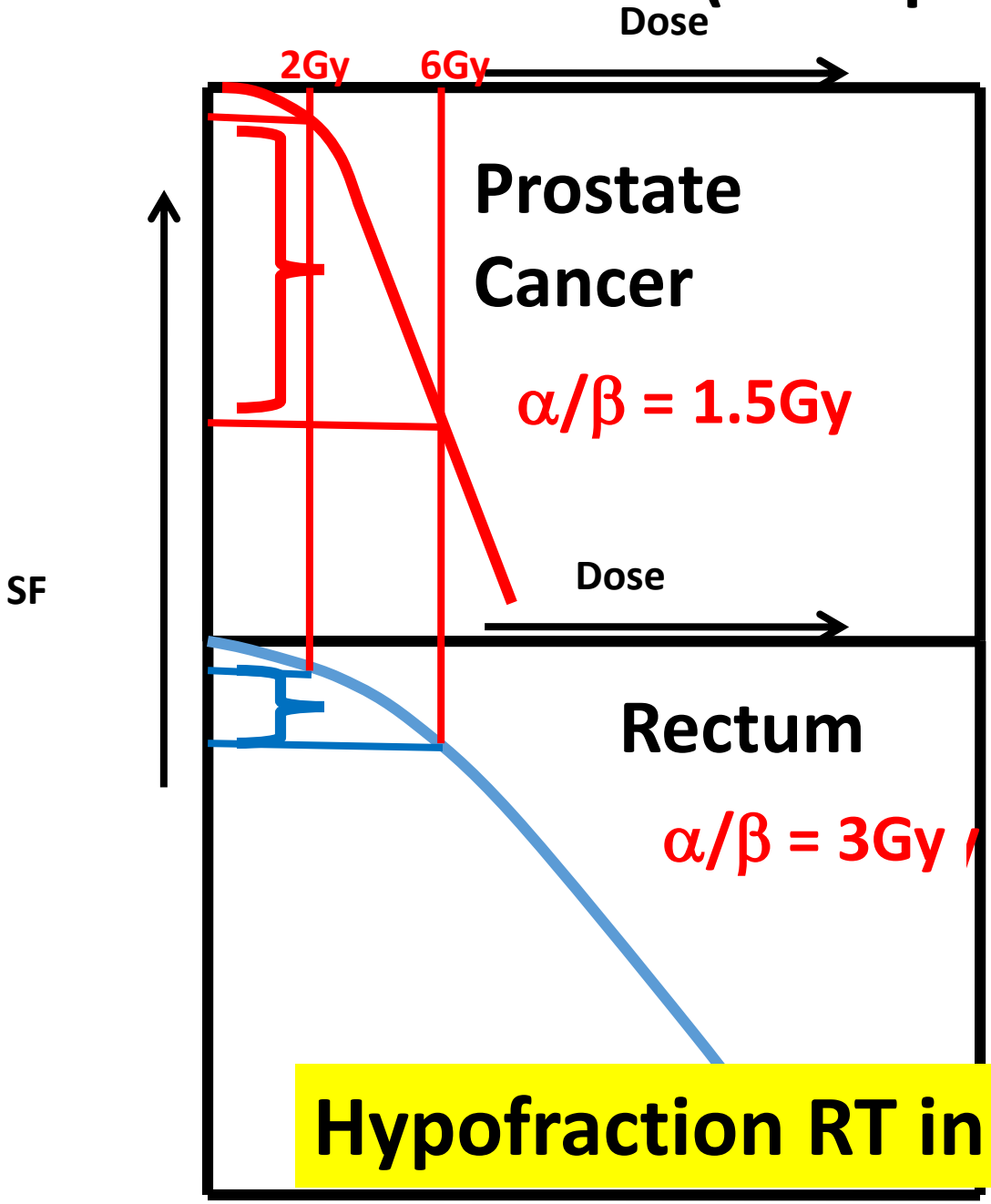
α/β Ratio defines "curviness" of survival curve

Based on α/β ratio, the body tissues have been divided into two category.



Malignant Tissue behave like early reacting tissue with average **α/β = 6Gy to 15 Gy (10Gy)**

Fraction size (Dose per fraction)



- Increase in dose per fraction damages the tissue with low α/β ratio more than Tissue with high α/β ratio.

- *We usually do not go more than 2 Gy per fraction*

Hypofraction RT in Prostate ca

Hypofractionation In Prostate Ca

- Two major approaches
  - Moderate hypofractionation
    2.5 – 3.5 Gy/#
  - Extreme hypofractionation/ Ultrahypofractionation
    > 5 Gy/#

Moderate hypofractionation

Moderate hypofractionation trials

Trial	Risk group	Arms	EQD2 (1.8)	Primary outcome	Result
CHHiP (n - 3216)	LR – 15% IR – 73% HR – 12%	1. 74Gy/37# (1065) 2. 60Gy/20# (1074) 3. 57Gy/19# (1077)	74 75.8 72	Biochem – clinical failure	1.Standard arm 2.Non inferior 3.Not non-inf
PROFIT (n- 1204)	IR	1. 78Gy/39# (598) 2. 60Gy/20# (407)	78 75.8	Biochem – clinical failure	1.Standard arm 2.Non inferior
RTOG 0415 (n – 1067)	LR	1. 73.8Gy/41# (542) 2. 70Gy/28# (550)	69.9 79.2	DFS	1.Standard arm 2.Non inferior
HYPRO (n – 800)	IR – 26% HR – 74%	1. 78Gy/39# (397) 2. 64.5Gy/19# (407)	78 88.2	RFS	1.Standard arm 2.Not superior

Acute Toxicity

Trial	Arms	EQD2 (10)	Peak acute toxicity (Grade II or more)			
			GU (%)	p value	GI (%)	p value
CHHiP (n - 3216)	1. 74Gy/37# (1065)	74	46	-	25	-
	2. 60Gy/20# (1074)	65	49	NS	38	S
	3. 57Gy/19# (1077)	61.8	46	NS	38	S
PROFIT (n- 1204)	1. 78Gy/39# (598)	78	27	-	10	-
	2. 60Gy/20# (407)	65	27	NS	16	S
RTOG 0415 (n – 1067)	1. 73.8Gy/41# (542)	72.6	24.7	-	9.7	-
	2. 70Gy/28# (550)	72.9	23.7	NS	9.9	NS
HYPRO (n – 800)	1. 78Gy/39# (397)	78	58	-	31	-
	2. 64.5Gy/19# (407)	72	61	NS	42	S
S – Significant; NS – Non significant						

Irrespective of the peak acute toxicity, the rates of acute toxicity at the end of 3 months were similar in all studies

Late Toxicity

Trial	Arms	EQD2 (3)	Late toxicity (Grade II or more)			
			GU (%)	p value	GI (%)	p value
CHHiP (n - 3216)	1. 74Gy/37# (1065)	74	9.1	-	13.7	-
	2. 60Gy/20# (1074)	72	11.7	NS	11.9	NS
	3. 57Gy/19# (1077)	68.4	6.6	NS	11.3	NS
PROFIT (n- 1204)	1. 78Gy/39# (598)	78	22.0	-	13.9	-
	2. 60Gy/20# (407)	72	22.2	NS	8.9	**S**
RTOG 0415 (n – 1067)	1. 73.8Gy/41# (542)	70.8	20.5	-	11.4	-
	2. 70Gy/28# (550)	77	26.2	S	18.3	S
HYPRO (n – 800)	1. 78Gy/39# (397)	78	39.0	-	17.7	-
	2. 64.5Gy/19# (407)	82.5	41.3	NS*	21.9	NS*

* Non-inferiority could not be confirmed; S – Significant; NS – Non significant

No Significant difference

Comments

- Pelvic LN stations were not treated
- Outcomes compared in these trials are imperfect surrogates for meaningful oncologic outcomes (Overall survival)
- Long term data will give a clearer picture to frame guidelines

Extreme hypofractionation (Ultrahypofractionation)

Extreme hypofractionation trials

Trial	Risk group	Arms	EQD2 (1.8)	Primary outcome	Result
HYPO–RT–PC (n - 1200)	IR – 89% HR – 11%	1. 78Gy/39# (591) 2. 42.7Gy/7# (589)	78 88.8	Biochem – clinical failure	1.Standard arm **2.Non inferior**
Munsuru et al (n- 582)	LR	1. 76Gy/38# (66) 2. 35Gy/5# (84)	76 81.1	6yr Bioch – clinical failure	Not reported
Katz et al. (n – 515)	LR – 63% IR – 30% HR – 7%	35 – 36.25 Gy/5# (515)	81.1 – 86.3	8yr DFS	1.93.6% 2.84.3% 3.65.0%
Loblaw et al. (n – 602)	LR	1. 74 – 79.8Gy/37 – 42# (40) 2. 35Gy/5# (40)	74 – 78 81.1	6yr bFFS	1.Standard arm **2.Better sig**

Acute Toxicity

Trial	Arms	EQD2 (10)	Peak acute toxicity (Grade II or more)			
			GU (%)	p value	GI (%)	p value
HYPO–RT–PC (n - 1200)	1. 78Gy/39# (591) 2. 42.7Gy/7# (589)	78 57.3	23 28	- NS	6 8	- NS
Munsuru et al (n- 582)	1. 76Gy/38# (66) 2. 35Gy/5# (84)	76 49.6	NR	-	NR	-
Katz et al. (n – 515)	35 – 36.25 Gy/5# (515)	49.6 – 52.1	0	-	0	-
Loblaw et al. (n – 602)	1. 74 – 79.8Gy/37 – 42# (40) 2. 35Gy/5# (40)	74 – 79 49.6	- 0	-	- 1	-
S – Significant; NS – Non significant						

Late Toxicity

Trial	Arms	EQD2 (3)	Cumulative late toxicity (Gr. II or more)			
			GU (%)	p value	GI (%)	p value
HYPO–RT–PC (n - 1200)	1. 78Gy/39# (591) 2. 42.7Gy/7# (589)	78 77.7	18 17	- NS	10 10	- NS
Munsuru et al. (n- 582)	1. 76Gy/38# (66) 2. 35Gy/5# (84)	76 70	19.7 **12**	- **S**	7.6 **4.8**	- **S**
Katz et al. (n – 515)	35 – 36.25 Gy/5# (515)	70 74.3	0	-	1.7	-
Loblaw et al. (n – 602)	1. 74 – 79.8Gy/37 – 42# (40) 2. 35Gy/5# (40)	74 – 78 70	- 1	-	- 1	-

- Only RCT; data is for 5 year followup

S – Significant; NS – Non significant

ASTRO/ ASCO/ AUA guidelines

ASTRO/ ASCO/ AUA guidelines

- Risk classification used is the D'amico risk classification

Score	Stage	Gleason grade	PSA (ng/mL)
0	T1, T2a	≤ 6	< 10
1	T2b	7	10 – 20
4	T2c, T3, T4	≥ 8	> 20

Total score	Risk class
0	Low
≤ 3	Intermediate
> 3	High

Moderate hypofractionation Take Home

- In men with LR and IR prostate cancer with or without radiation to the seminal vesicles,
- In men with HR prostate cancer, moderate hypofractionation should be offered if pelvic nodes are planned to be excluded.
- Acute and Late toxicities are comparable to conventional RT.
- Discuss the limited follow-up beyond five years for most of existing RCTs.

Moderate hypofractionation Take Home

- Regimens suggested:
  - 60Gy delivered in 20 fractions of 3Gy
  - 70Gy delivered in 28 fractions of 2.5Gy

  One optimal regimen cannot be determined since fractionation schemes have not been compared head to head

- Efficacy of moderately hypofractionated EBRT regimens does not appear to be impacted by
  - patient age, -- comorbidity,
  - anatomy, -- urinary function

Ultrahypofractionation Take Home

- In men with LR and IR prostate cancer ultrahypofractionation may be offered
- In men with HR prostate cancer, ultrahypofractionation should **not** be offered due to insufficient data

- The recommendations apply to
  - prostate volume < 100 cc
  - Mild to moderate urinary symptoms at baseline (IPSS < 20)

Ultrahypofractionation Take Home

- Regimens suggested:
  - 3500 to 3625 cGy in 5 fractions of 700 to 725 cGy

    may be offered to low- and intermediate-risk patients with prostate sizes less than 100 cm3.

- Five-fraction doses above 3625 cGy to the planning target volume is not suggested due to risk of late toxicity

- Five-fraction prostate ultrahypofractionation using consecutive daily treatments is **not** suggested due to potential increased risk of late urinary and rectal toxicity

2D Radiation Planning

General Considerations

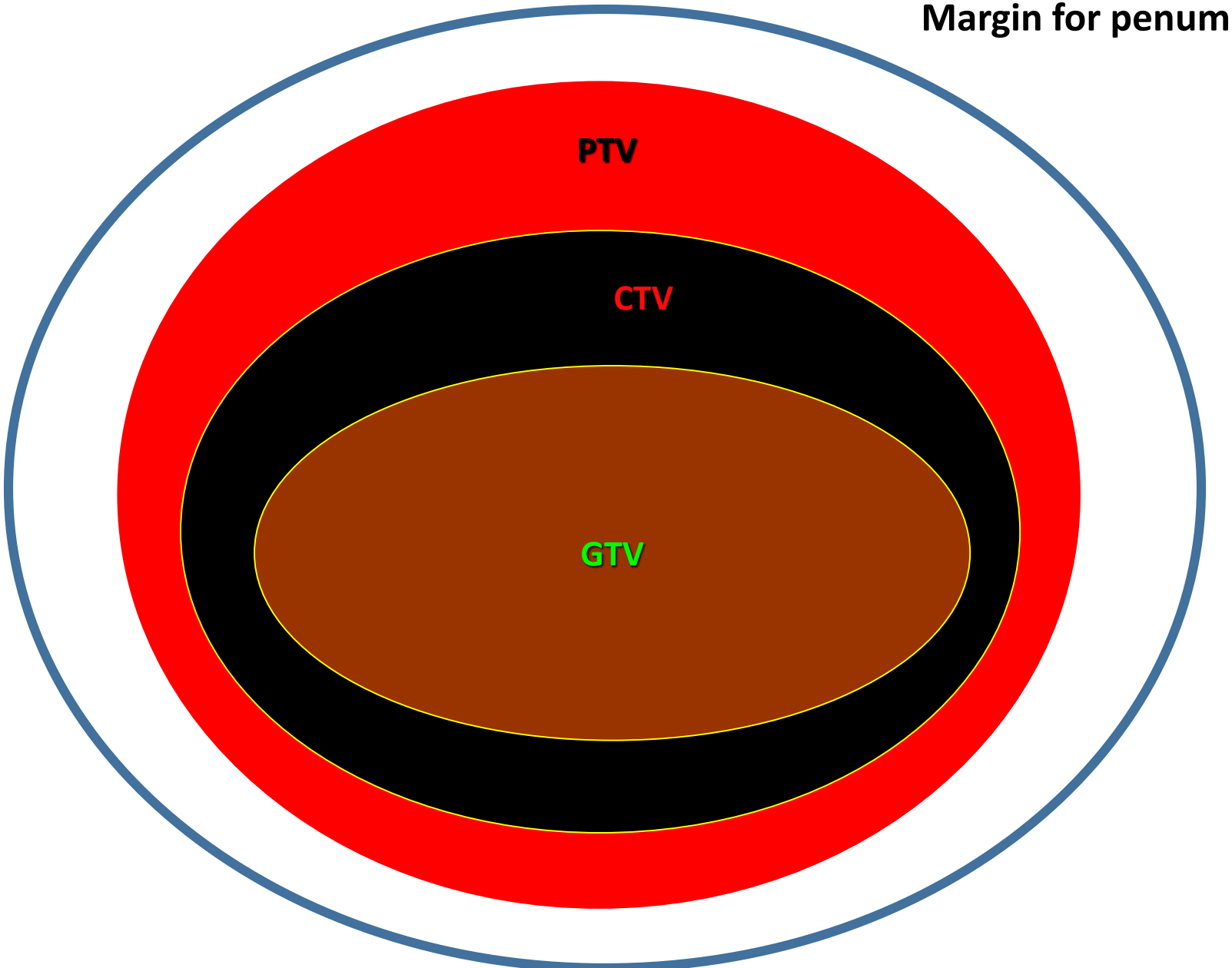
Position **Supine** **More comfortable**

Immobilization

Immobilization

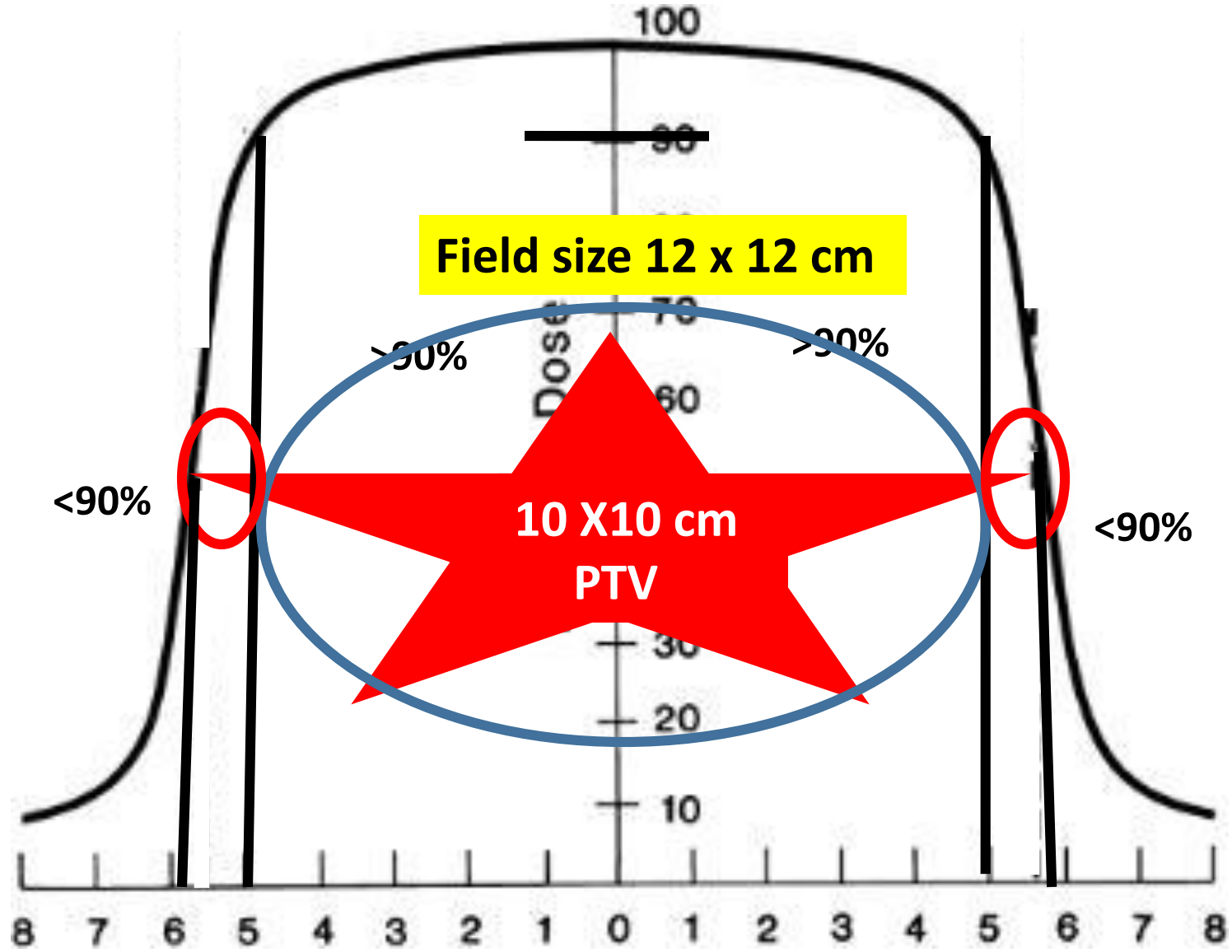
Position of the feet should be fixed and reproducible. Change in the foot position also change the relative position of the bony references points used to set the isocenter.

Margins for Radiotherapy Planning



Margin for dose fall off at edges (Penumbra)

1 cm margin is given for cobalt **0.7cm margin for LA**



Take Home

- In 2D planning margins for penumbra is to be added at the time of defining the radiation portals by radiation oncologis.

- In image based planning Radiation Oncologist define up to PTV and margins for penumbra is to be added by medical physicist during dose calculation.

2D Radiotherapy Planning

- **We need to define four borders.**
- ***AP:PA Portal***
  - Cranial Border
  - Caudal Border
  - Two Lateral Borders
- ***Lateral Portal***
  - Cranial Borders
  - Caudal Borders

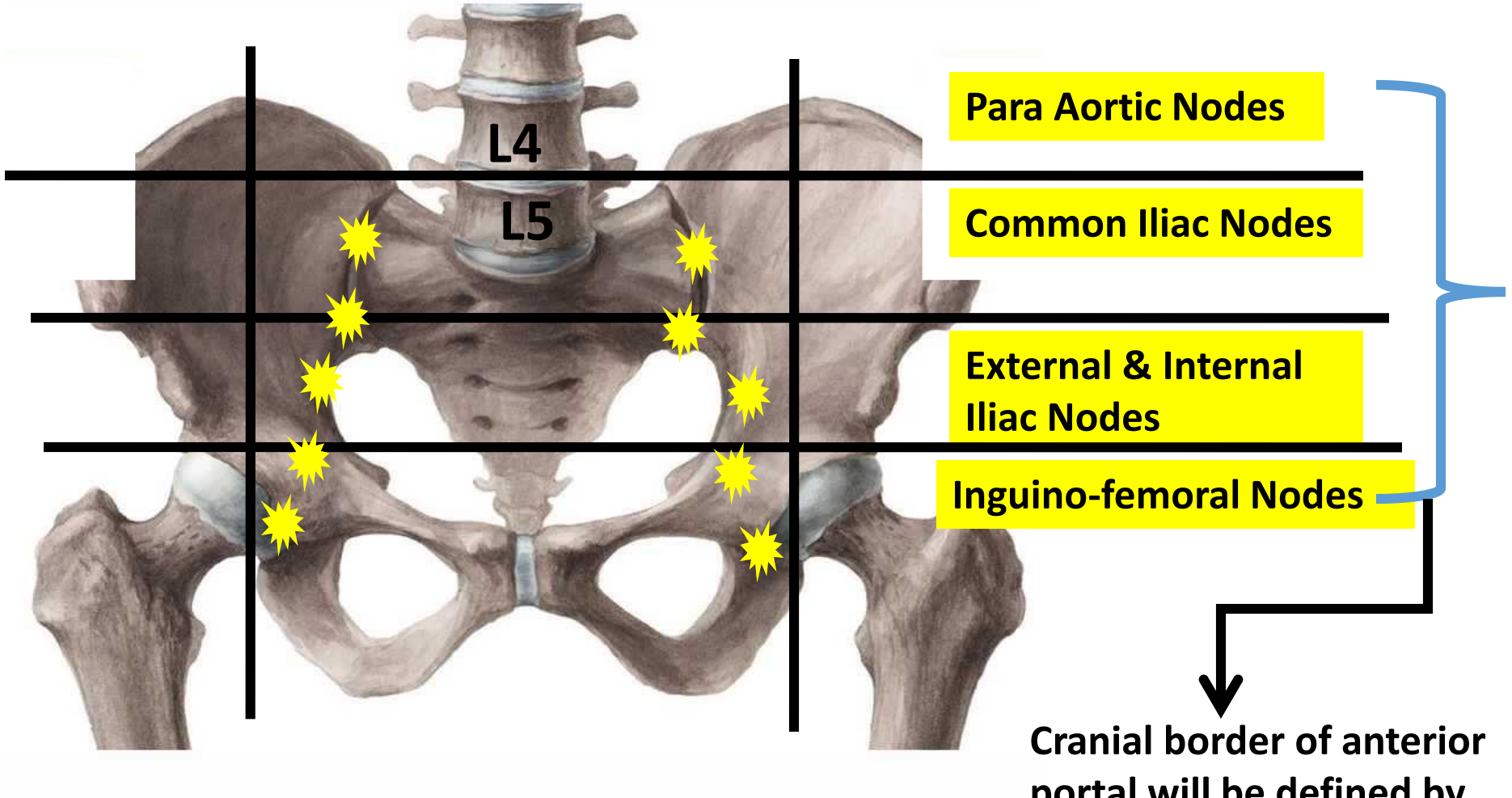
  } **Usually same as in AP:PA portals**
  - Anterior borders
  - Posterior Borders

2D Radiotherapy Planning

- **Borders are defined by**
  - Primary disease
  - Potential sites of regional disease mainly by metastasis in regional lymph nodes.
    - *Microscopic*
    - *Gross*

All the borders are defined in respect of bony land marks

AP:PA Portals: Location of Lymph Nodes



Lateral border of Ant portal will be defined by location of Ext iliac nodes.

Cranial border of anterior portal will be defined by level of nodes to be treated

AP:PA Portals

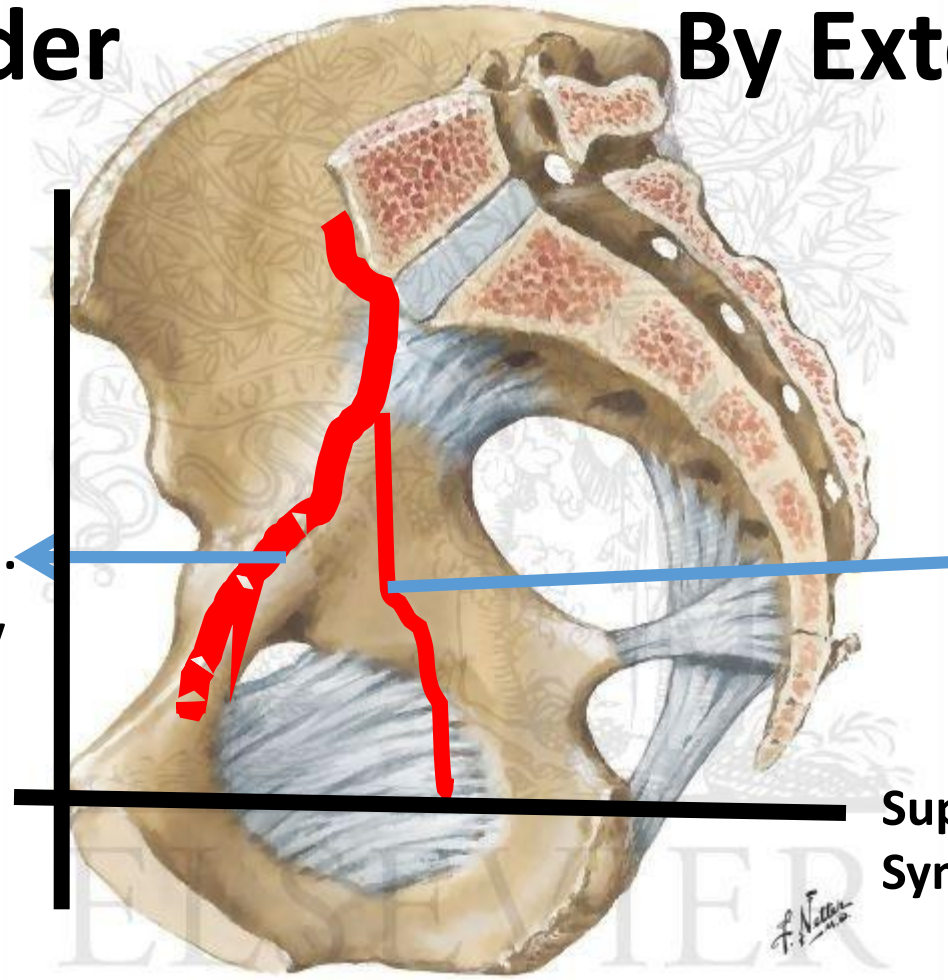
Lower border will be defined by extent of gross disease

Lower Border
OR
Caudal Border

Lateral Portals

Anterior Border

By Extent of Ext Iliac Node OR Primary Disease



External Iliac a.
Goes anteriorly

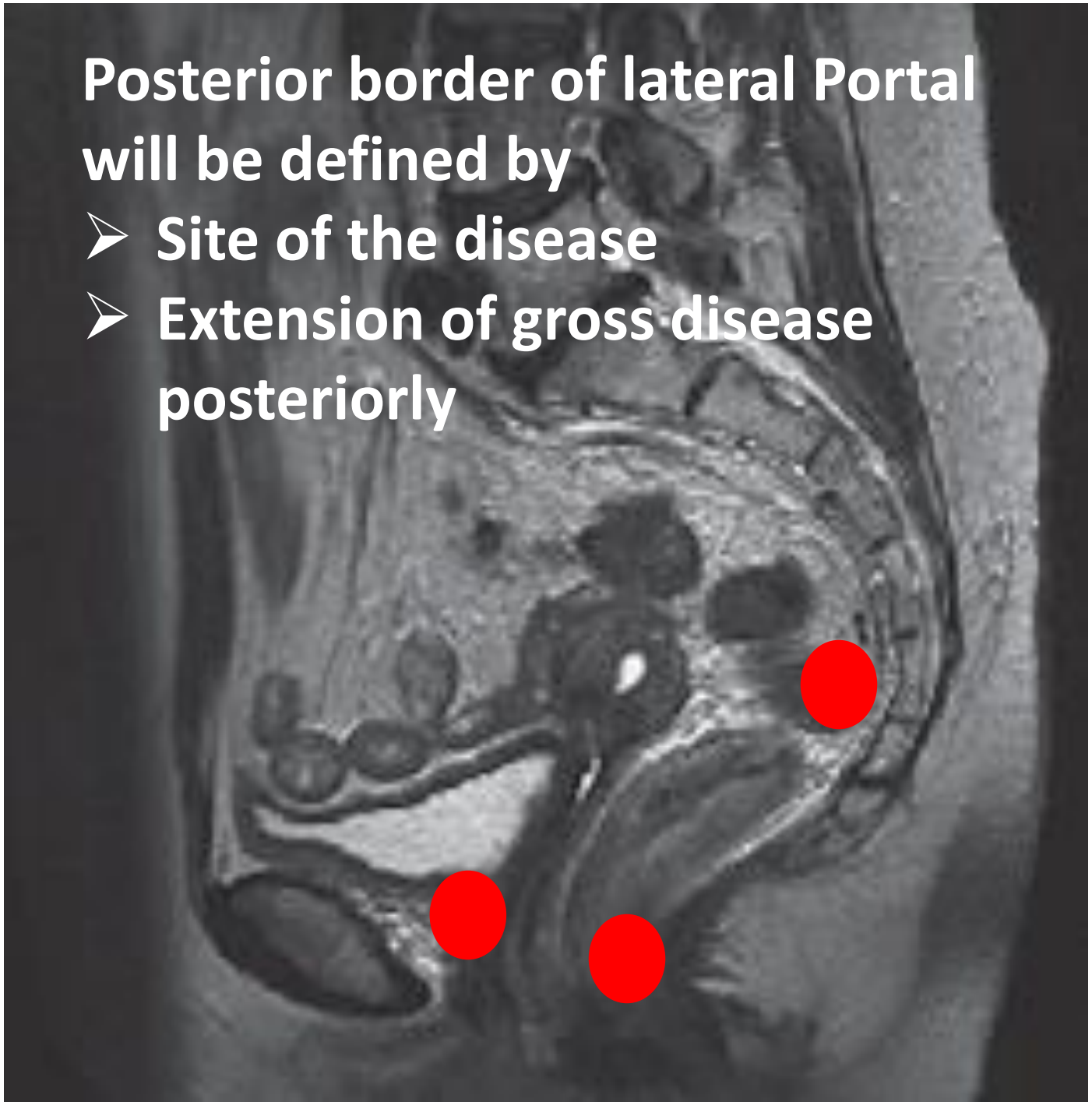
Internal Iliac a.
Goes Posteriorly

Superior border of Pubic Symphysis

Anterior border of lateral portal will be defined by location of ext iliac nodes

Caudal extent of obturator nodes

Lateral Portals



Take Home

- ***AP:PA Portal***
  - Upper border and Lateral Borders are defined by level and location of the lymph nodes to be treated.
  - Lower border is defined by the extension of primary disease
- ***Lateral Portal***
  - Anterior border is defined by location of the external iliac nodes
  - Posterior border is defined by site and size of the primary disease

Targets

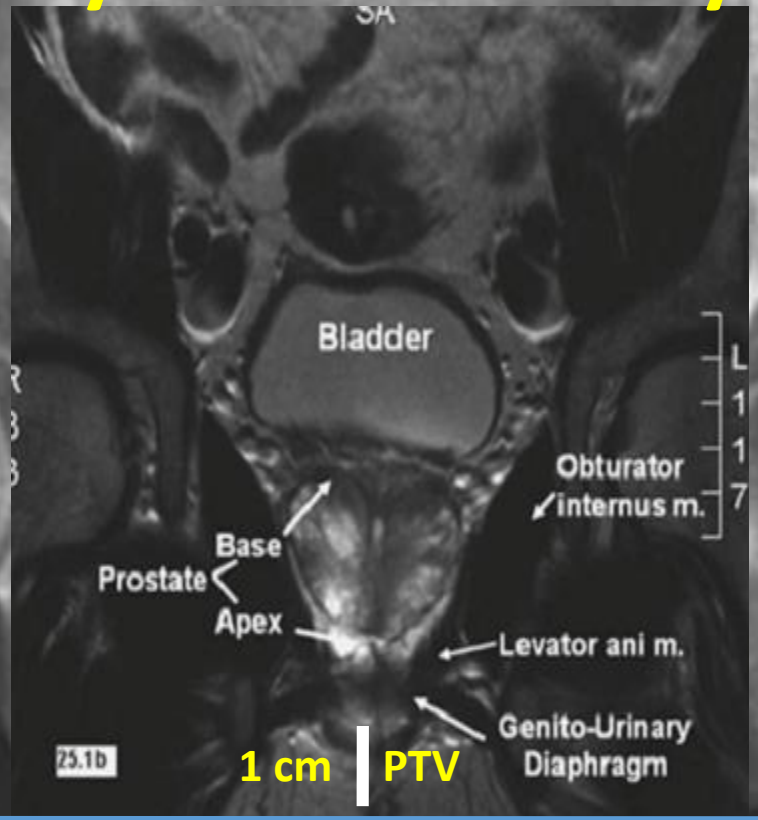
- **Primary**
  - Prostate
  - Seminal vesicle
- **Nodes**
  - External Iliac
  - Obturator
  - Internal Iliac
  - Pre sacral

General Considerations

- **Position** Supine
- **Portals** Four
- AP:PA and two lateral
- **Dose:-**
  - Whole Pelvis→ 45 Gy/25fx/5weeks
  - Boost→ 20 Gy/10fx/2weeks

Lower border of the field

How to identify Genito-Urinary diaphragm

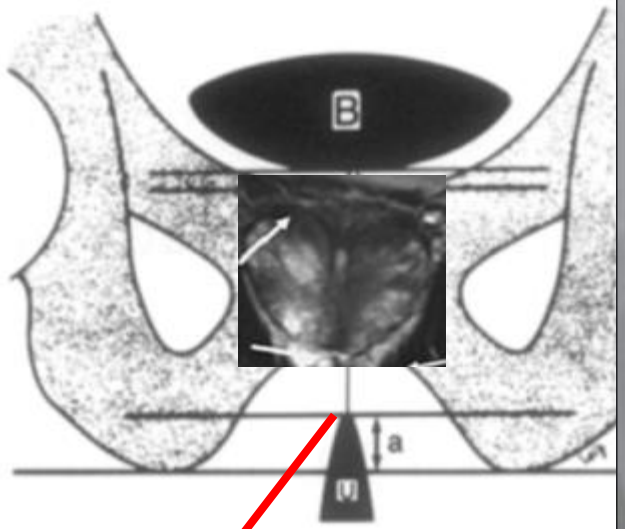


1 cm | PTV

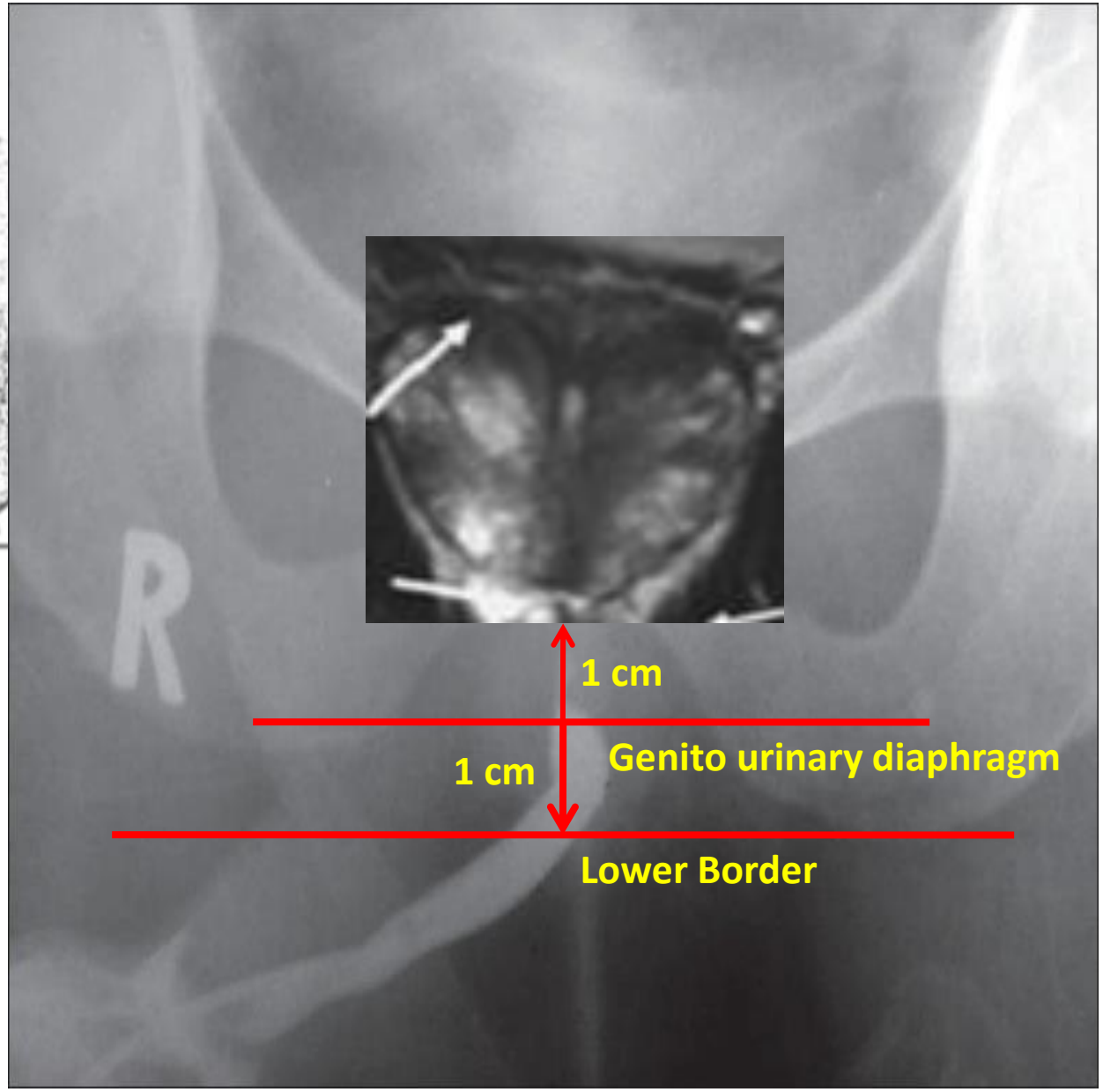
1 cm | Penumbra

1 cm below genito-urinary diaphragm

Retrograde Uretherography



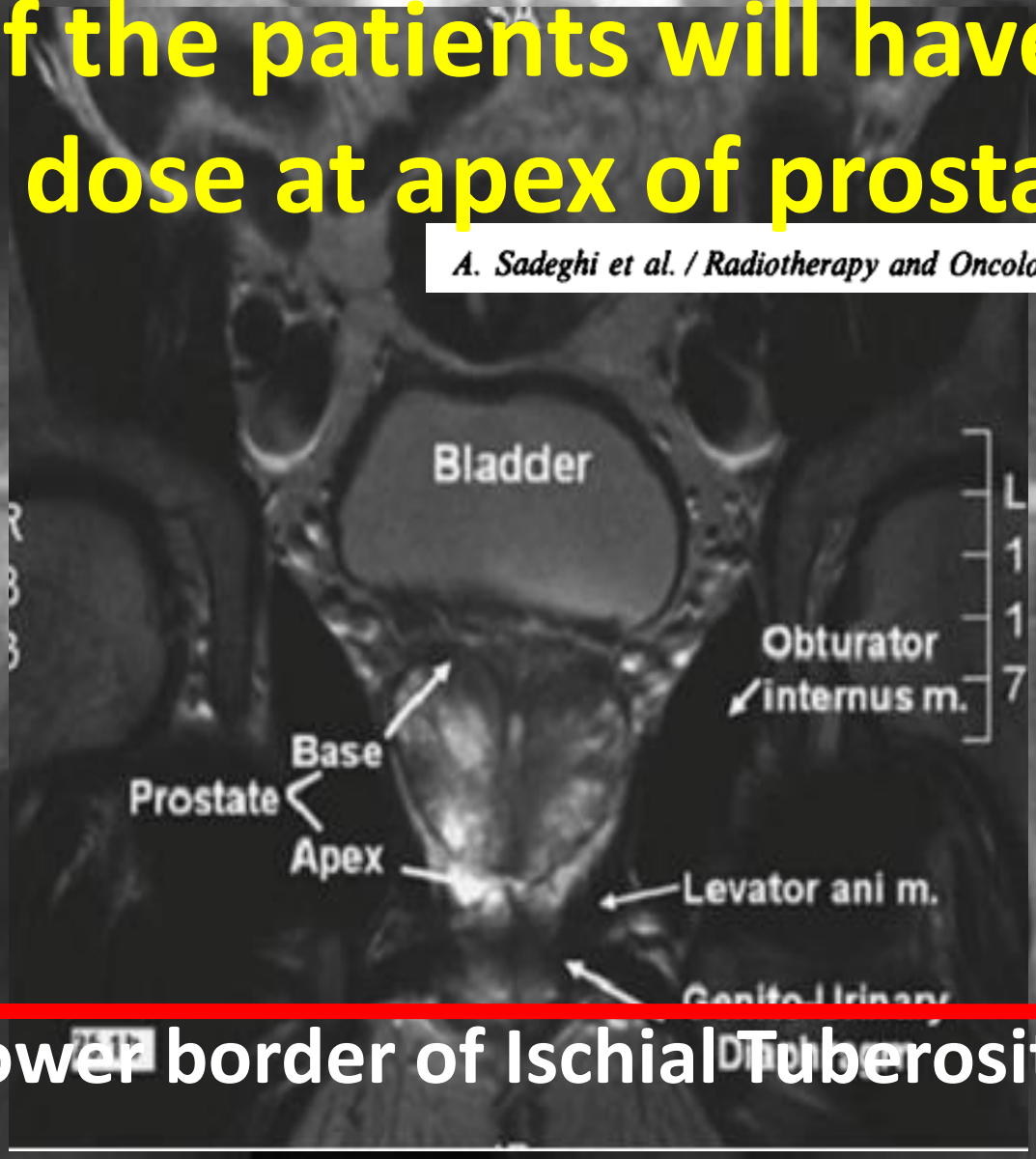
Apex of the opacified cone represents the position of Genito-urinary diaphragm



Lower border of the field

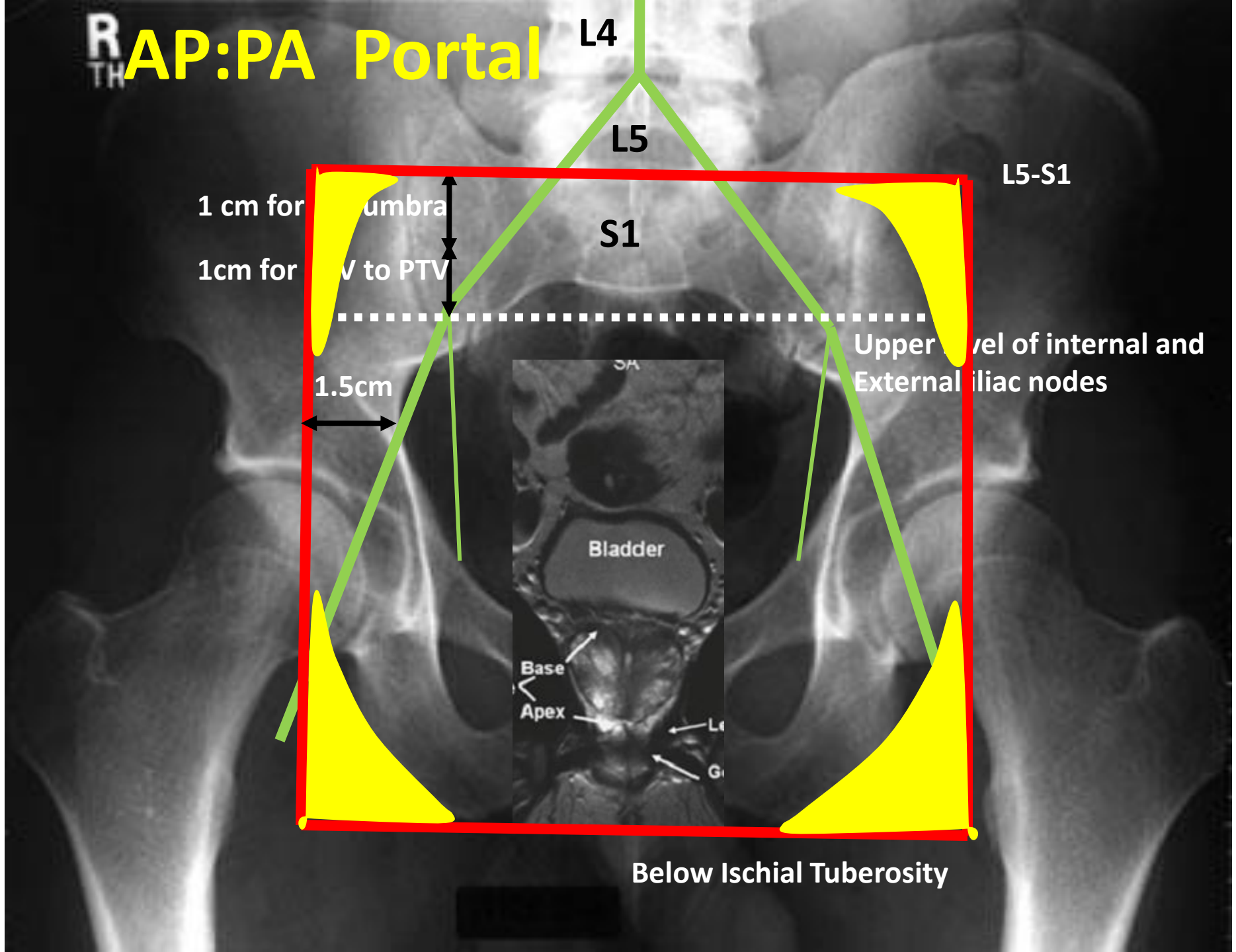
10% of the patients will have under dose at apex of prostate

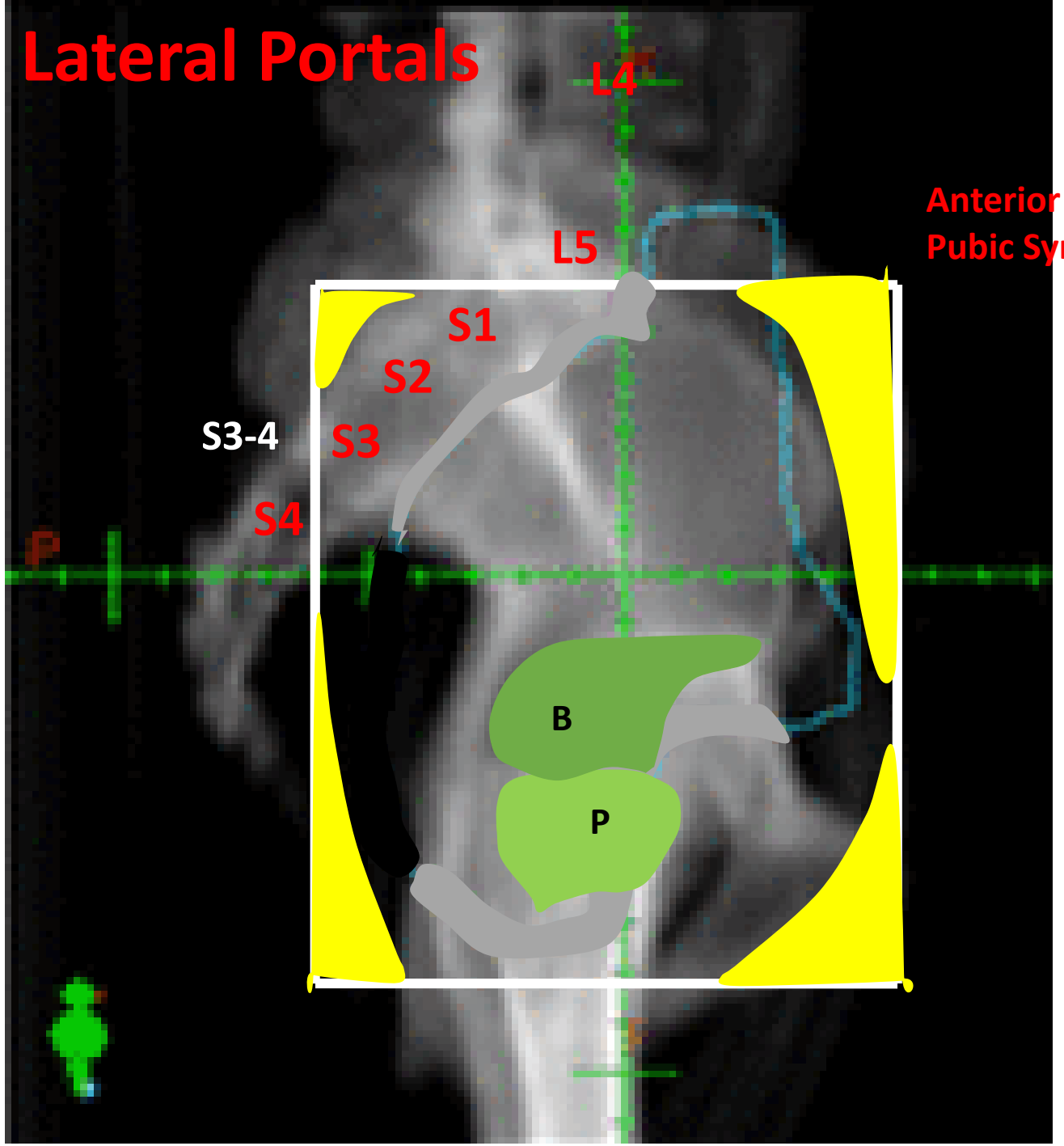
A. Sadeghi et al. / Radiotherapy and Oncology 38 (1996) 215–222

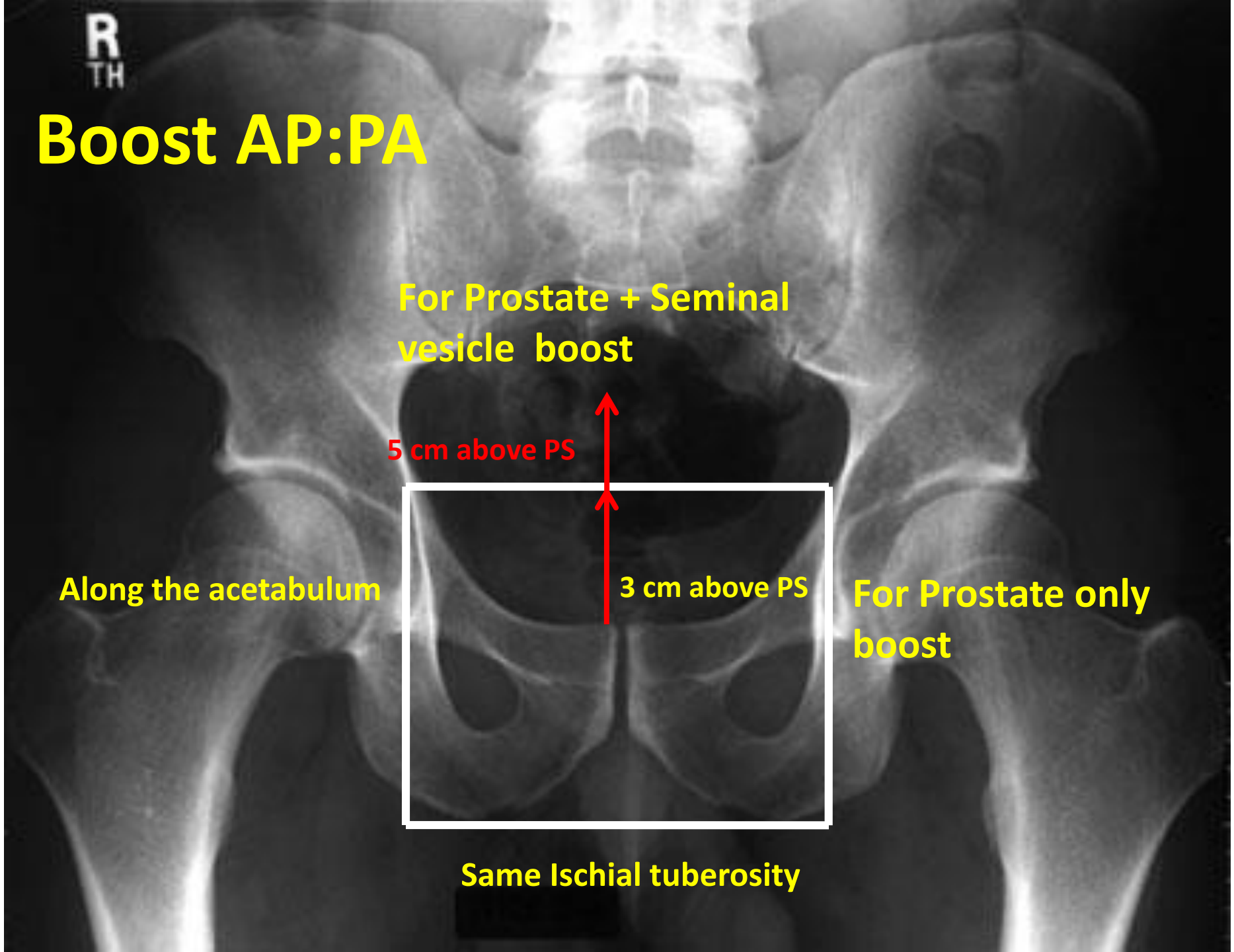


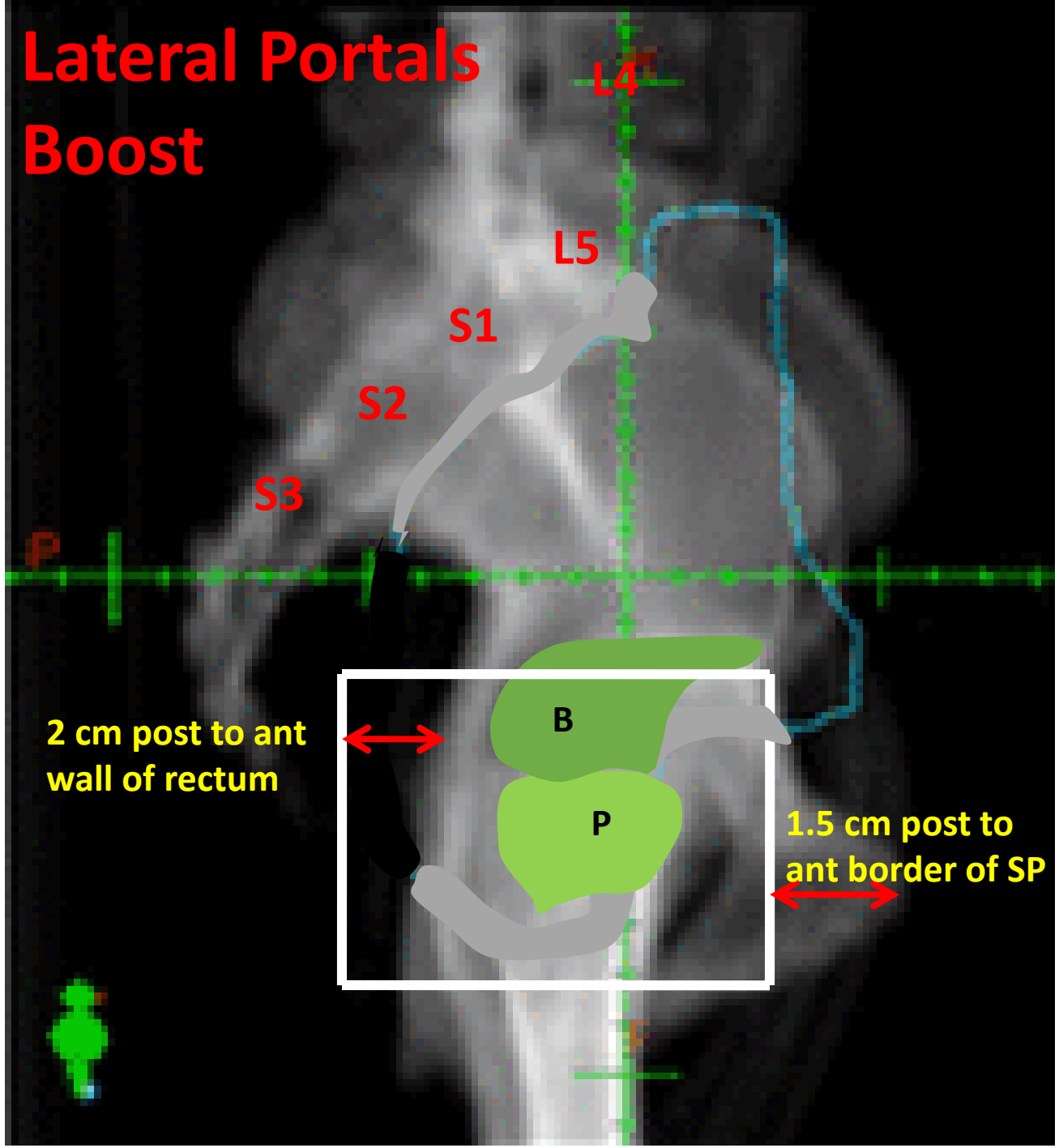
Lower border of Ischial Tuberosity

AP:PA Portal


L4
L5
L5-S1
S1
1 cm for umbra
1cm for V to PTV
1.5cm
Upper vel of internal and
External iliac nodes
Bladder
Base
Apex
Below Ischial Tuberosity


Lateral Portals
L4
L5
S1
S2
S3-4
S3
S4
P
B
P
Anterior border of
Pubic Symphisis


R
TH
Boost AP:PA
For Prostate + Seminal vesicle boost
5 cm above PS
3 cm above PS
Along the acetabulum
For Prostate only boost
Same Ischial tuberosity


Lateral Portals
Boost
L4
L5
S1
S2
S3
P
B
P
2 cm post to ant
wall of rectum
1.5 cm post to
ant border of SP

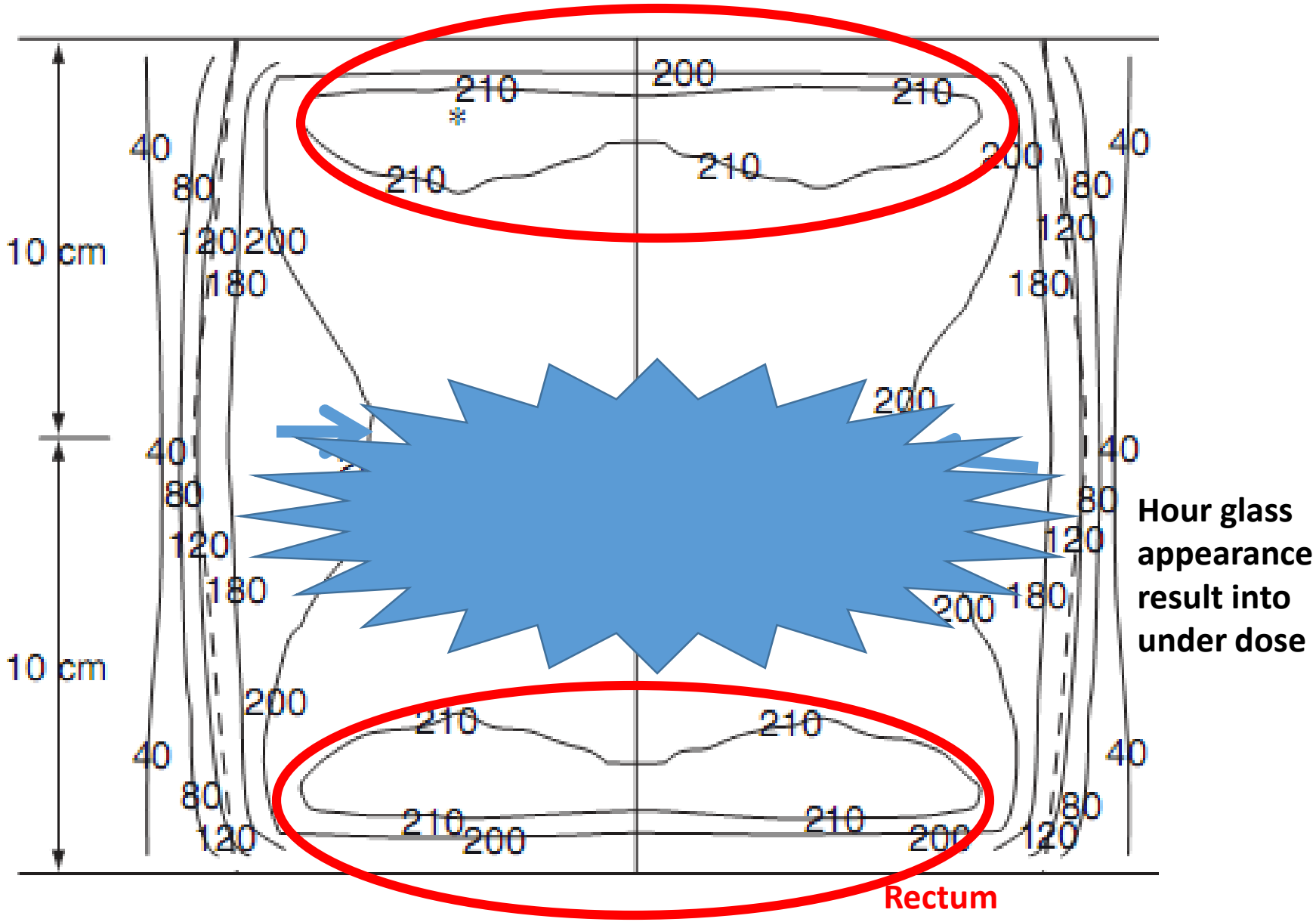
Dosimetric Issues

Two Field AP/PA

Four Field Box technique

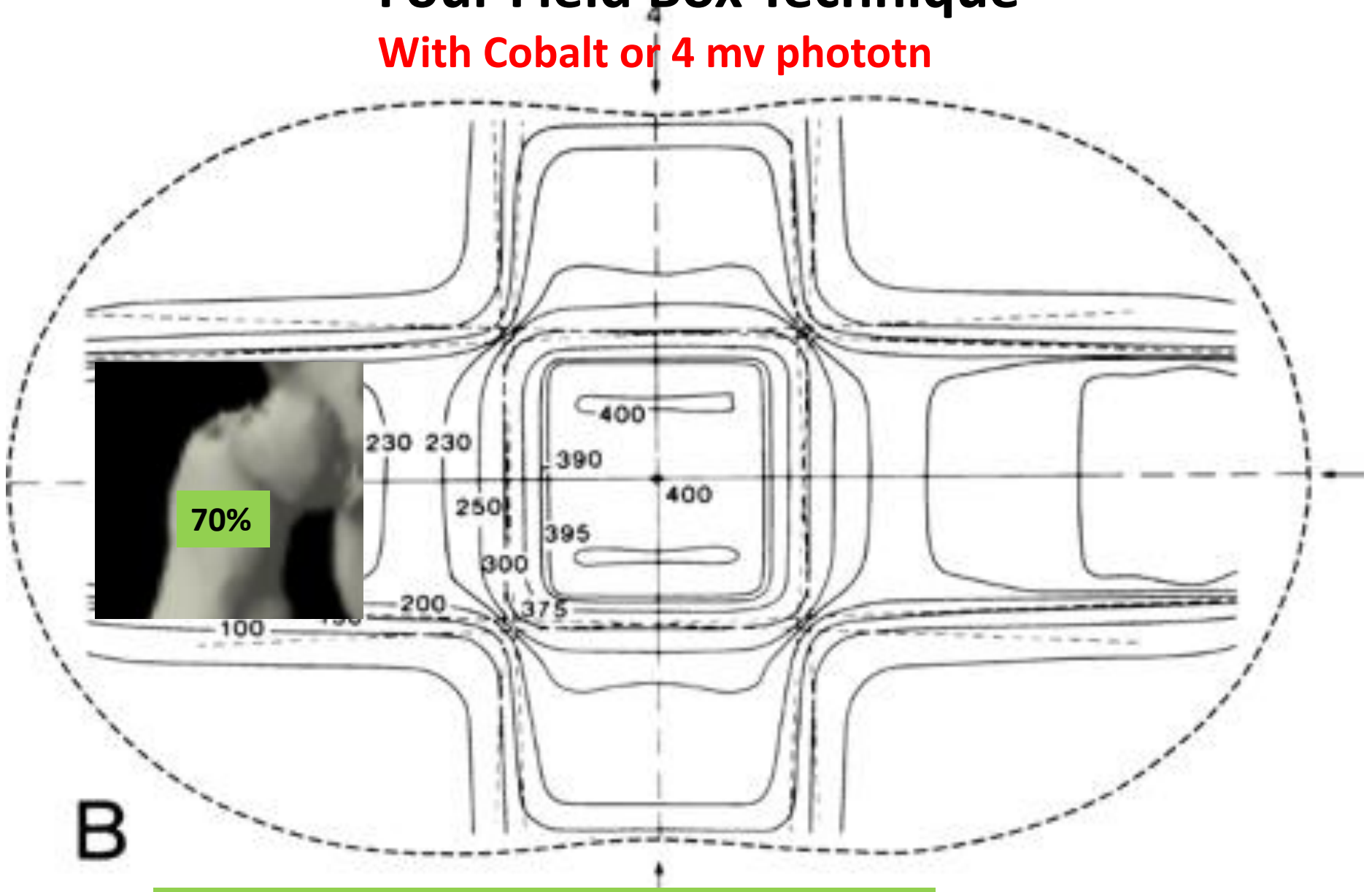
AP/PA with separation more than 18cm

Peripheral organs get higher doses like subcutaneous tissue and bladder



Four Field Box Technique

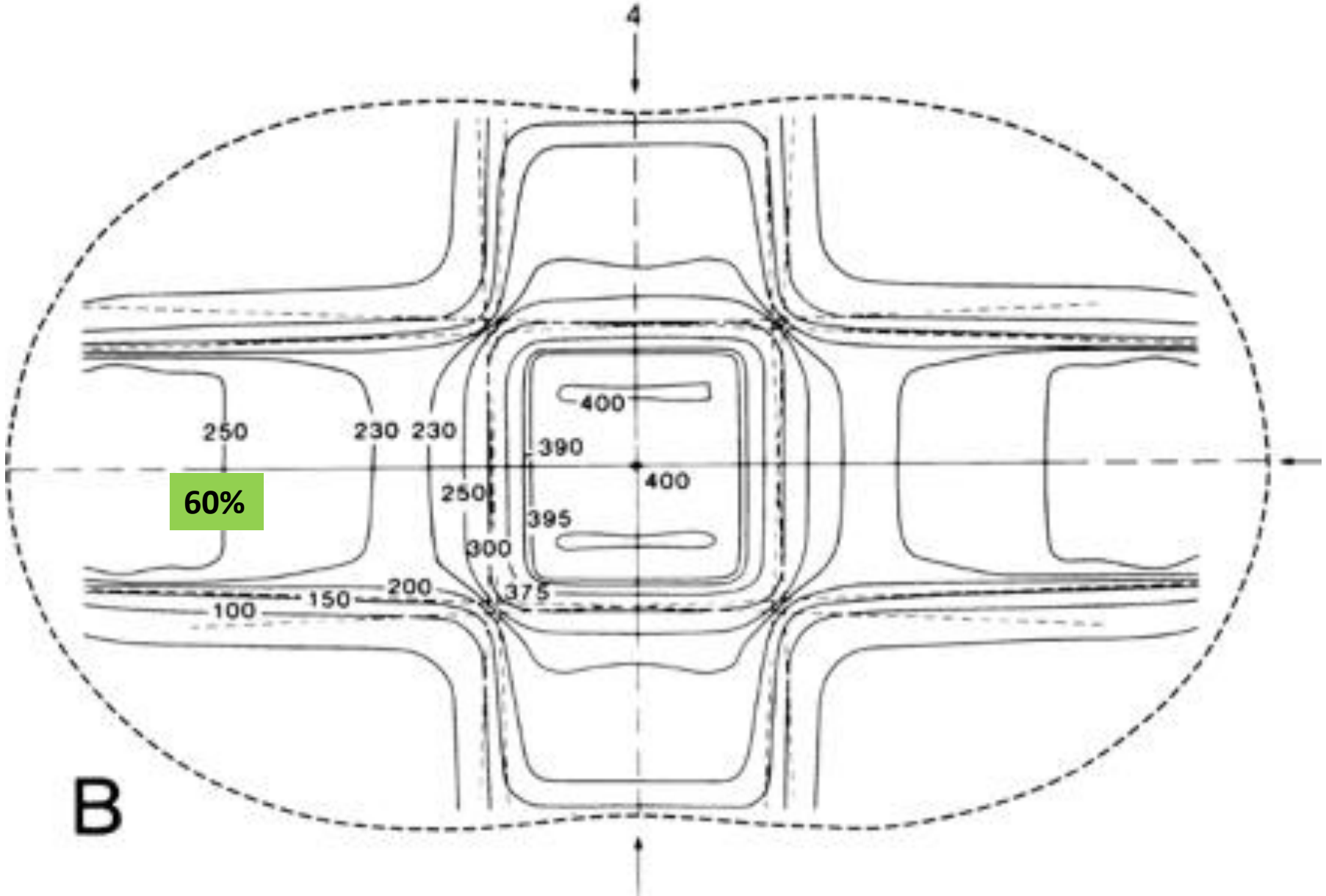
With Cobalt or 4 mv phototn



Head and Neck of the femur will receive high doses

Four Field Box Technique

High Energy photon 15 mv



Four Field Box Technique

With Cobalt or 4 mv phototn