

# PTCOG 54: Proton Therapy for GU Cancer



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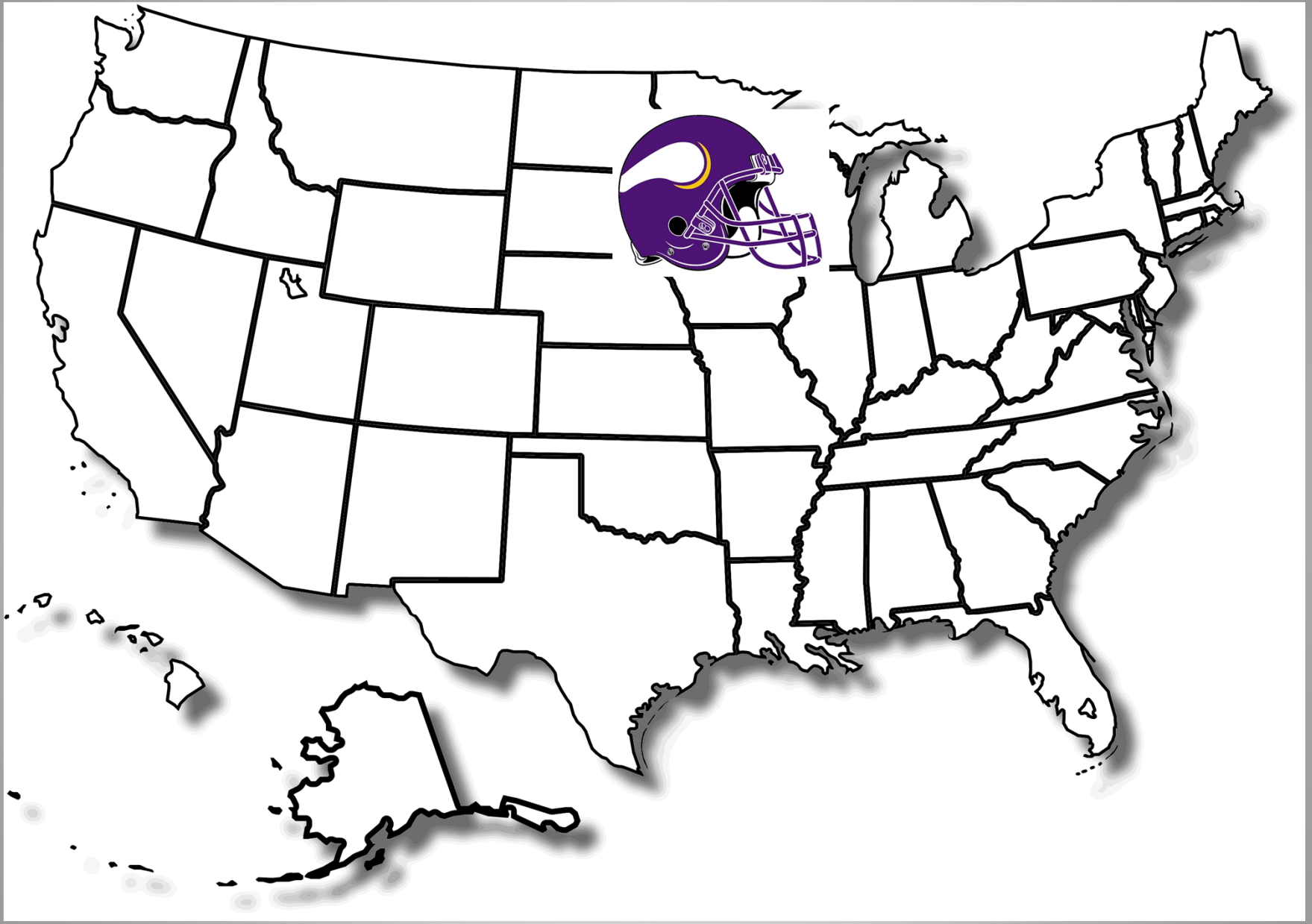




Irving

Houston





# Disclosures

- No relevant financial disclosures
- This presentation will not discuss off-label or investigational treatments

- **PROSTATE CANCER**

- Control organ motion/ radiologic path length
- Be accurate with CTV delineation
- Pencil beam for high-risk, nodes, postop

- **SEMINOMA**

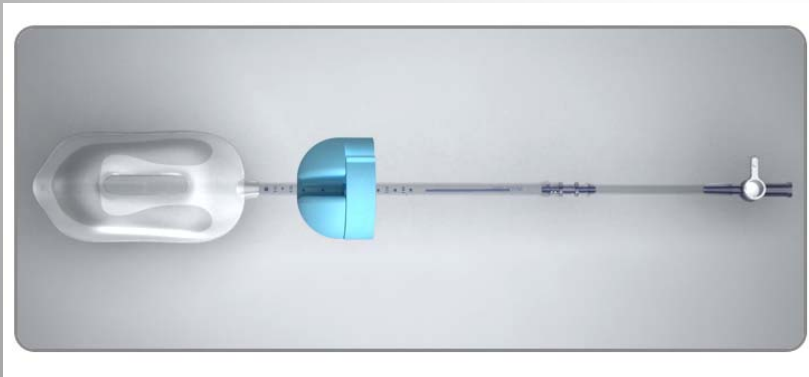
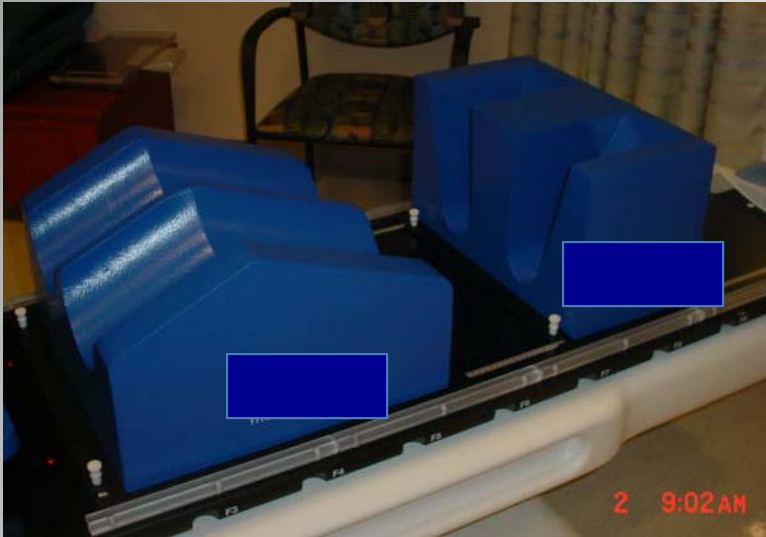
- Primary role for Stage I & II
- Define CTV nodal volumes + margins

- **BLADDER**

- Intent? (e.g. bladder preservation vs. non-operative)
- Concurrent chemotherapy
- Avoid treating whole bladder to full dose

# Prostate cancer proton therapy

- Low risk  
Prostate only (PSPT)  
78 GyE (2GyE) PTV...>80 GyE CTV  
72 GyE (2.4 GyE)  
55.5 GyE (3.7 GyE) on clinical trial
- Intermediate risk  
Prostate & “proximal” SV  
PSPT or SSPT  
HT x 4-6 months for select pts  
(2 mos TAB then leuprolide alone)
- High risk & T3  
Prostate & most of SV (SSPT)  
(Select pts LN)  
HT x 2 years



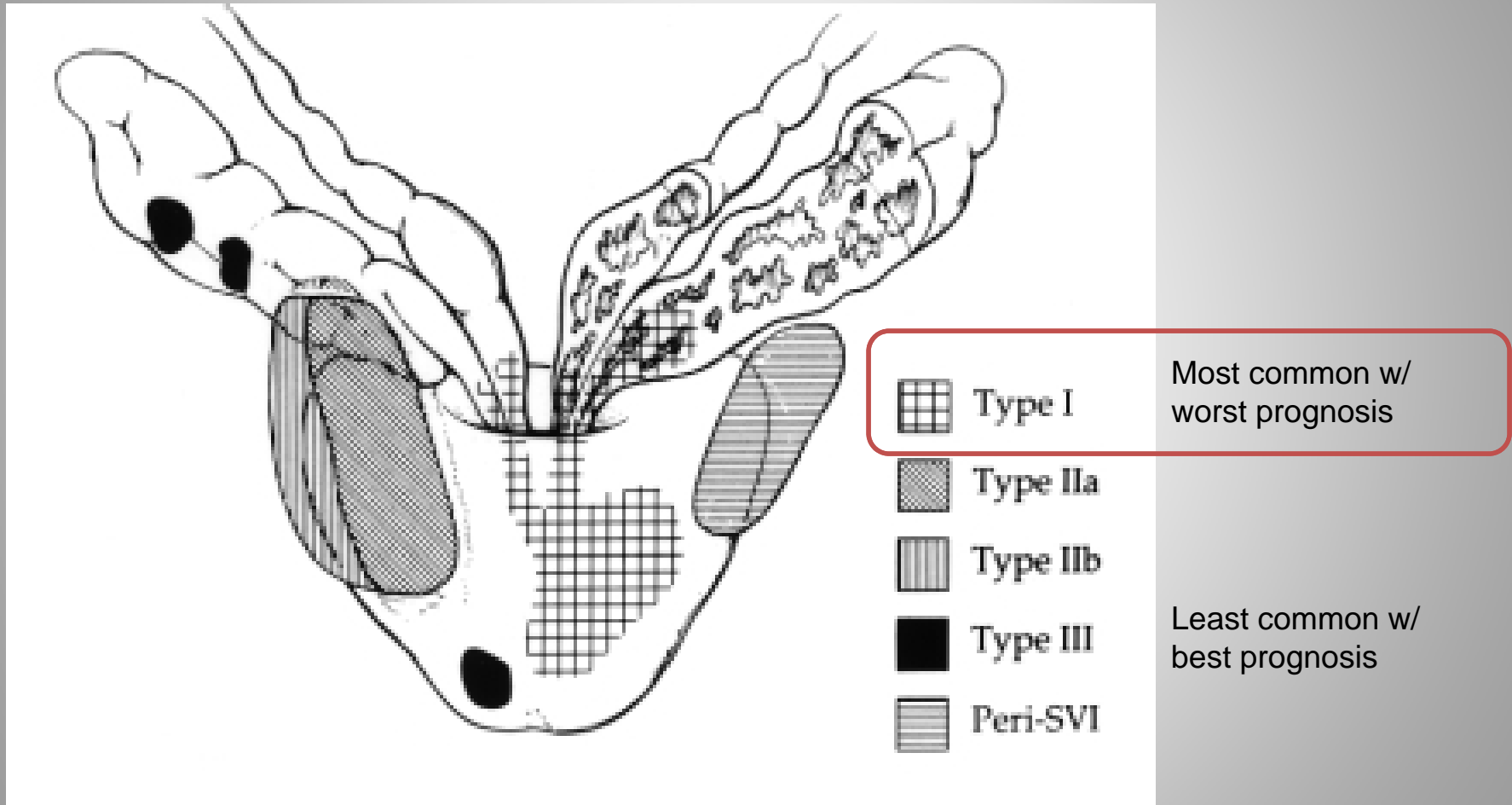
# Proton technique for Prostate Ca

- Supine
- ER Balloon w/ water (2 sizes: 80cc vs. 60cc) for most pts
- Bony and fiducial alignment
- 2-fields every day (opposed laterals)
  
- CTV = Prostate +/- portion of SV
  
- 2 CGE x 39 = 78 CGE to “PTV”
- Mean CTV dose ~81 CGE
  
- 2.4 CGE x 30 = 72 CGE to “PTV”



# Types of seminal vesicle invasion:

Type I direct invasion most common & worst prognosis

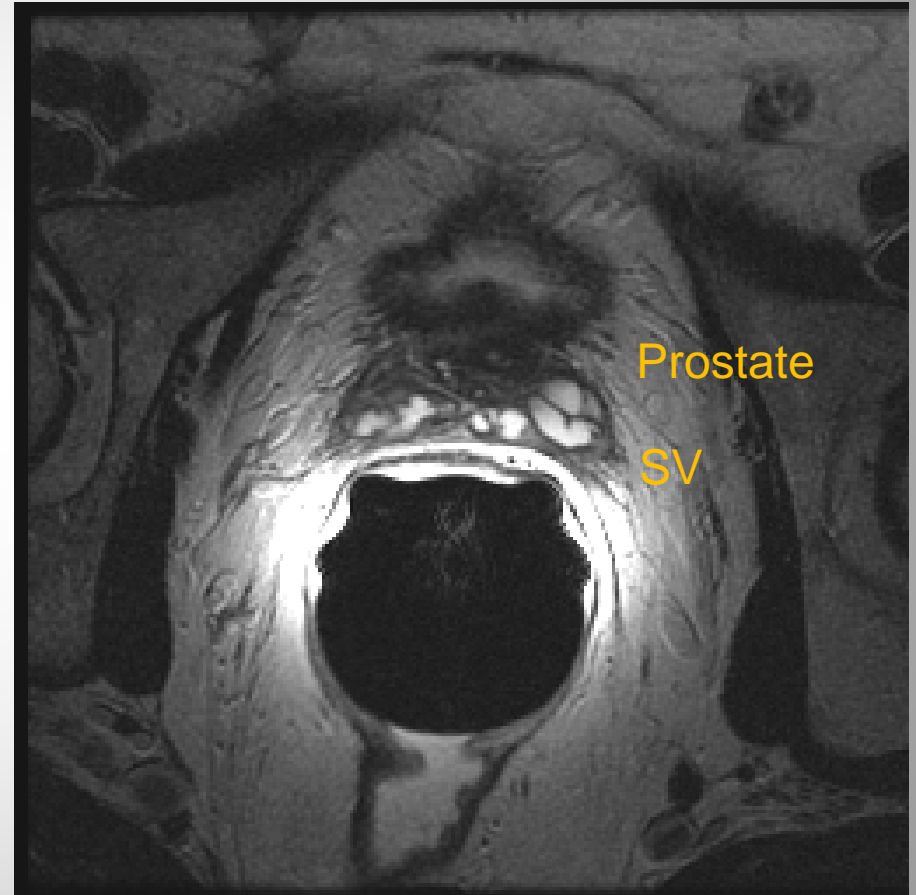
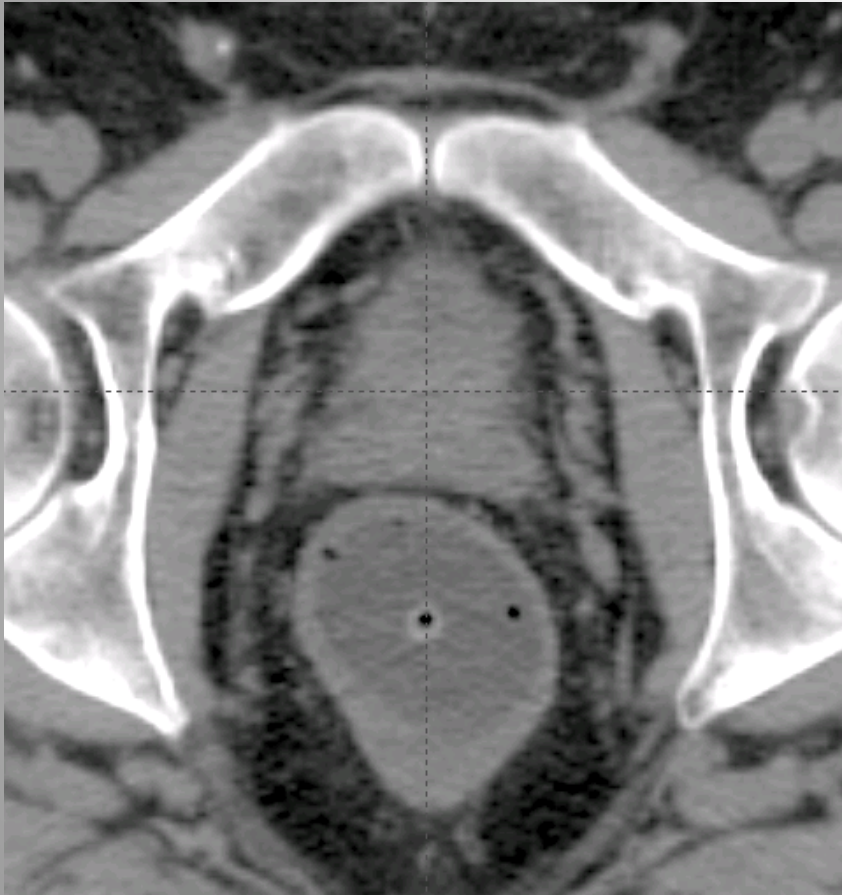


# Estimating risk of SVI

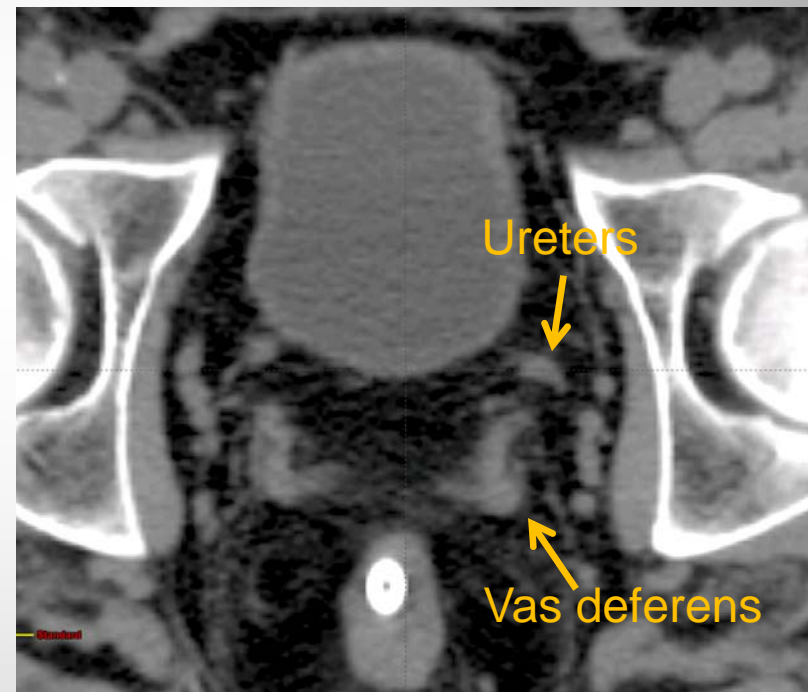
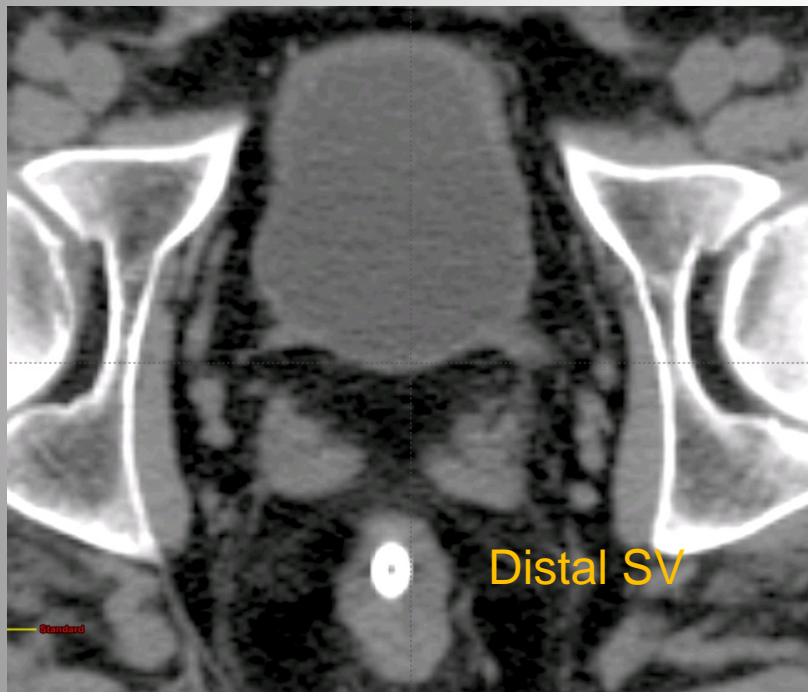
- SVI is rare in modern era (~5%) for T1-2
- Risk based stratification (pT3b may be >30% in higher risk patients)
- Gleason score, PSA, T-stage, % (+) biopsies, MRI findings
  
- Updated Partin tables
- Kattan nomogram

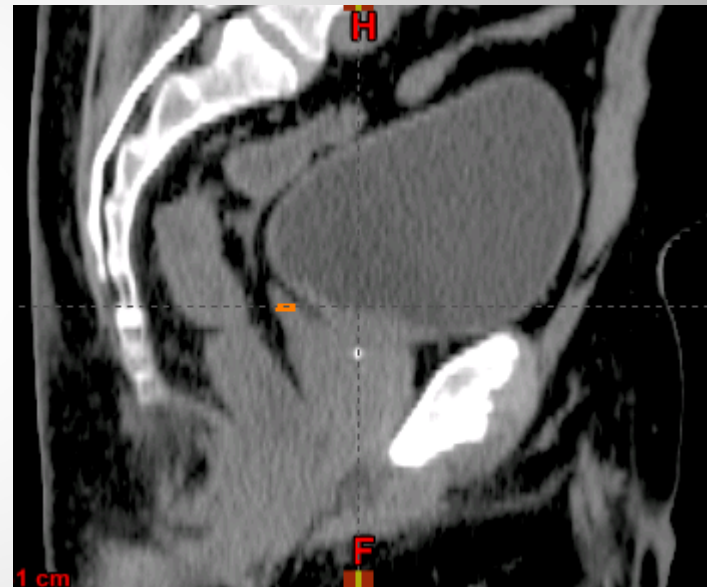
# CT vs. MRI

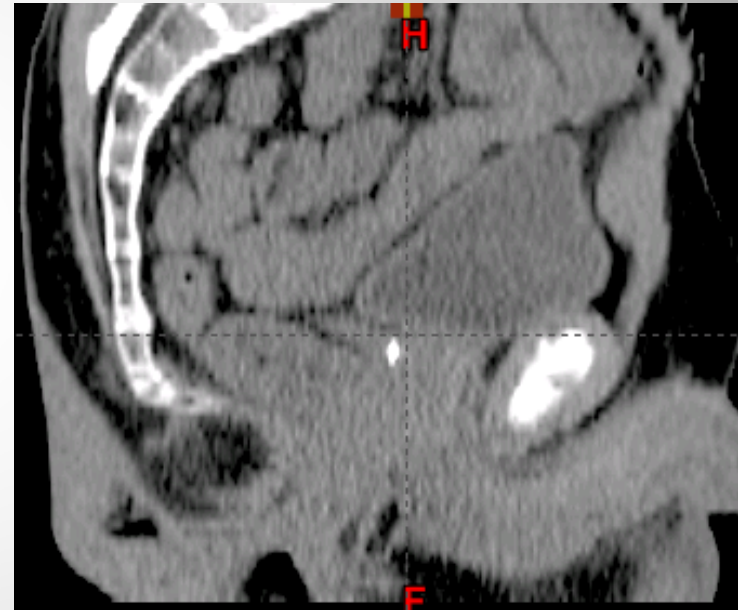
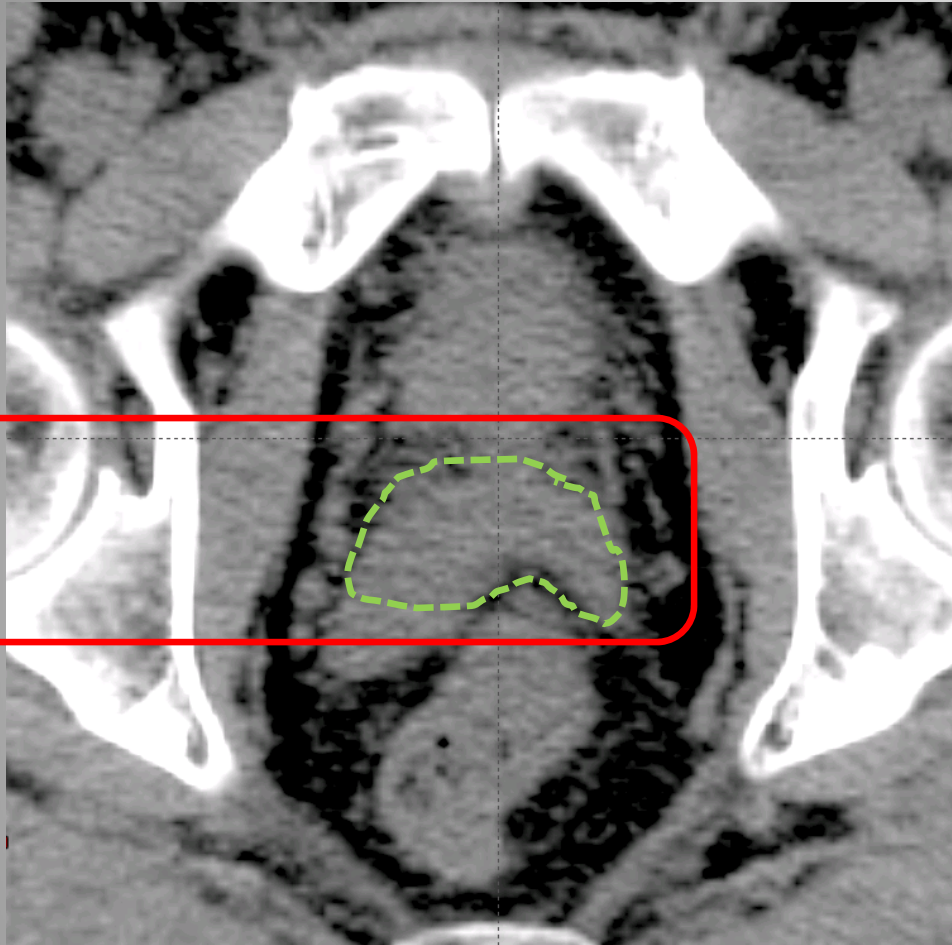
This has implications for SV length



# Distal SV vs. Something else







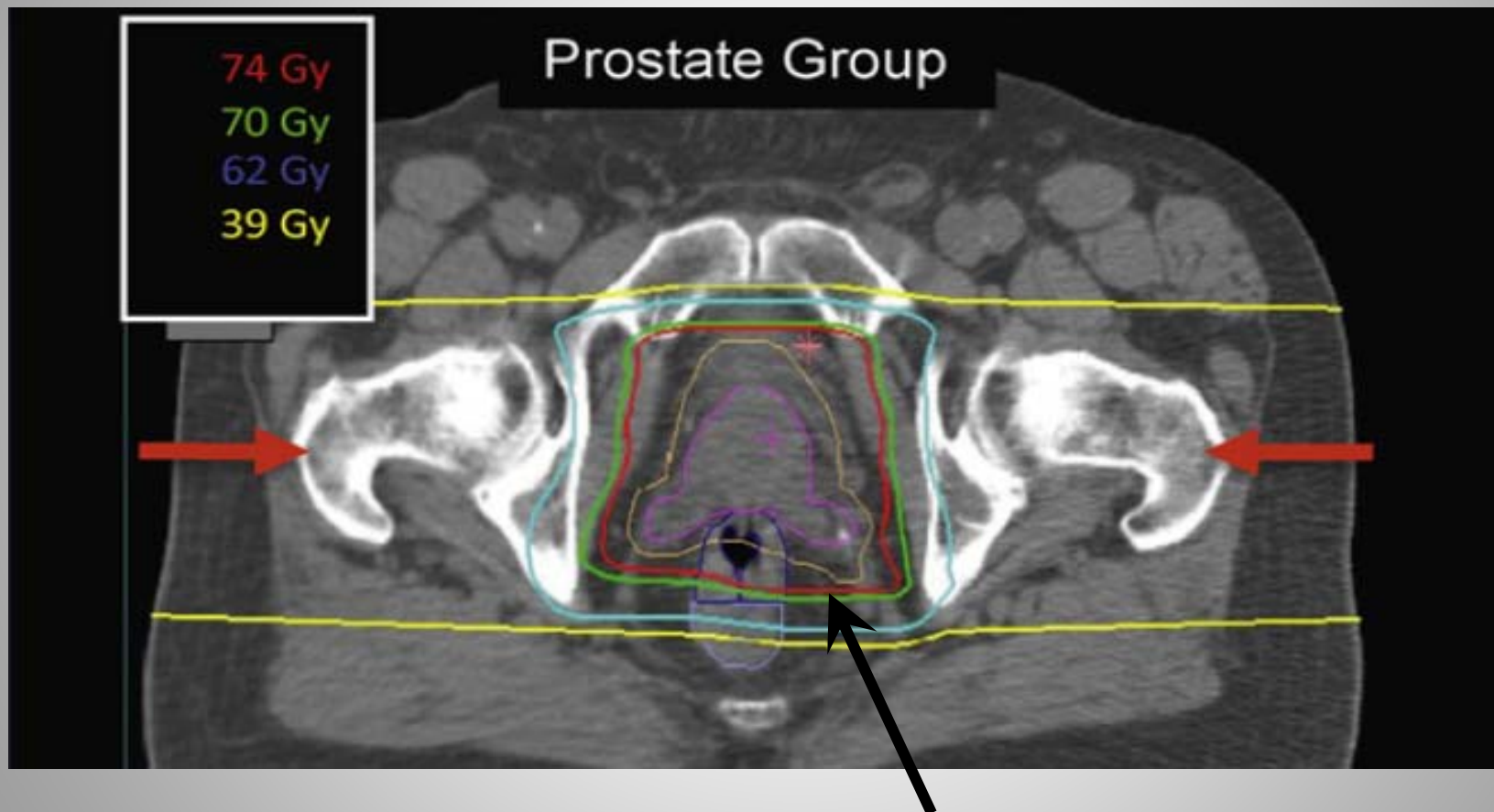
OPTIONS:

Decrease CTV...Not just superiorly but also laterally (remember type I SVI)

Decrease dose...Total dose or just SV followed by prostate boost

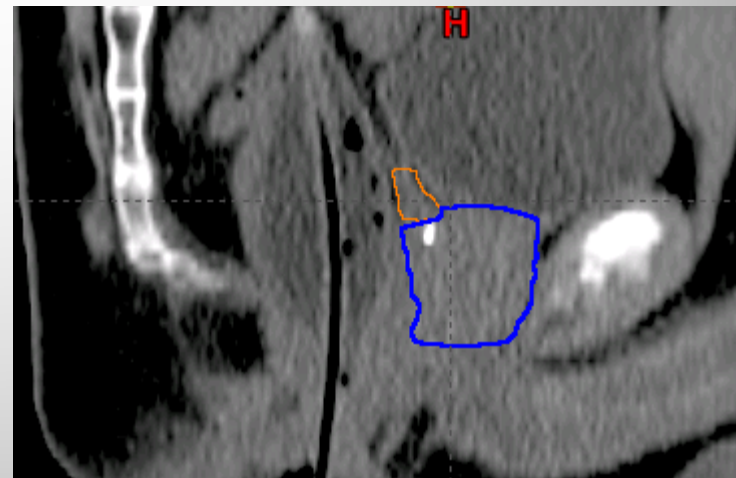
ERB...Does not always work....sometimes still have "droopy" SV

AVOID this regardless of how the  
rectal DVH looks



Half the rectum is getting 74Gy!!

# ERB may help geometry





# Planning parameters

## Right & left lateral beams (daily)

Improved conformality

Potentially more forgiving and robust

- Geometrically and biologically (RBE)

Trade off is patient throughout & inter-fraction motion

78 CGE (2 CGE/fxn) or 72 CGE (2.4 CGE) to CTV + margin

Usually prescribe to 98-96% isodose line

# Proximal and Distal Margins for passive-scattered planning

Setup uncertainty  $\leq 5\text{mm}$

Distal margin =  
 $(0.035 \times \text{distal CTV radiological depth}) + (3\text{mm})^*$

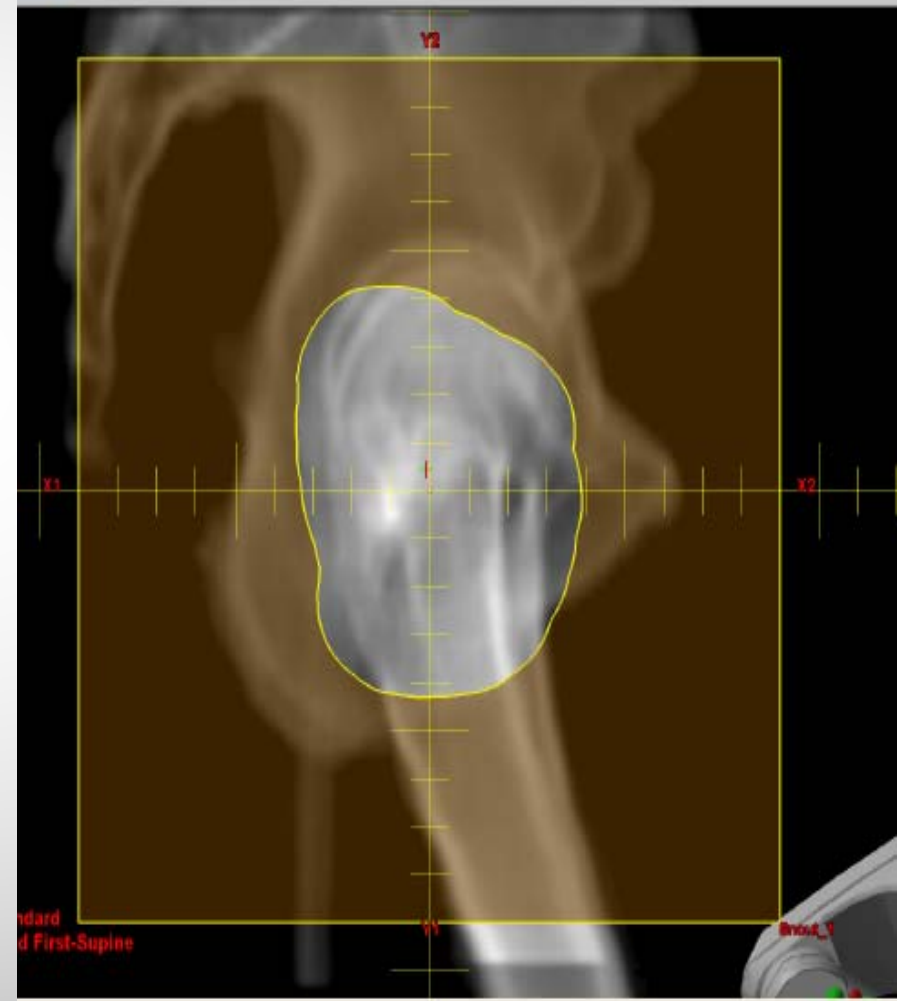
Proximal margin = same ( $\sim 1\text{cm}$ )

Smear  $\sim 0.8\text{-}0.9\text{ cm}$

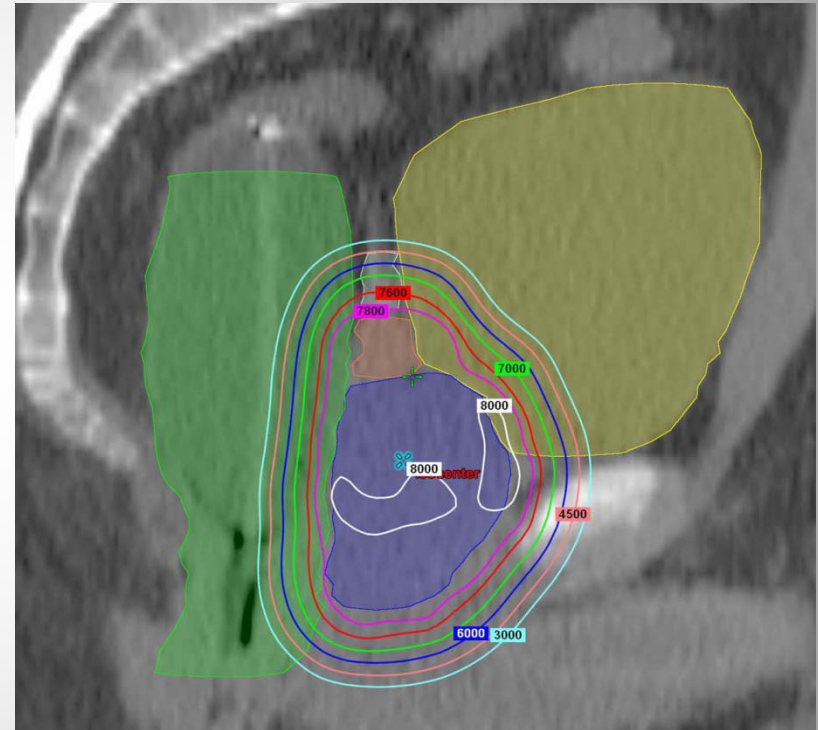
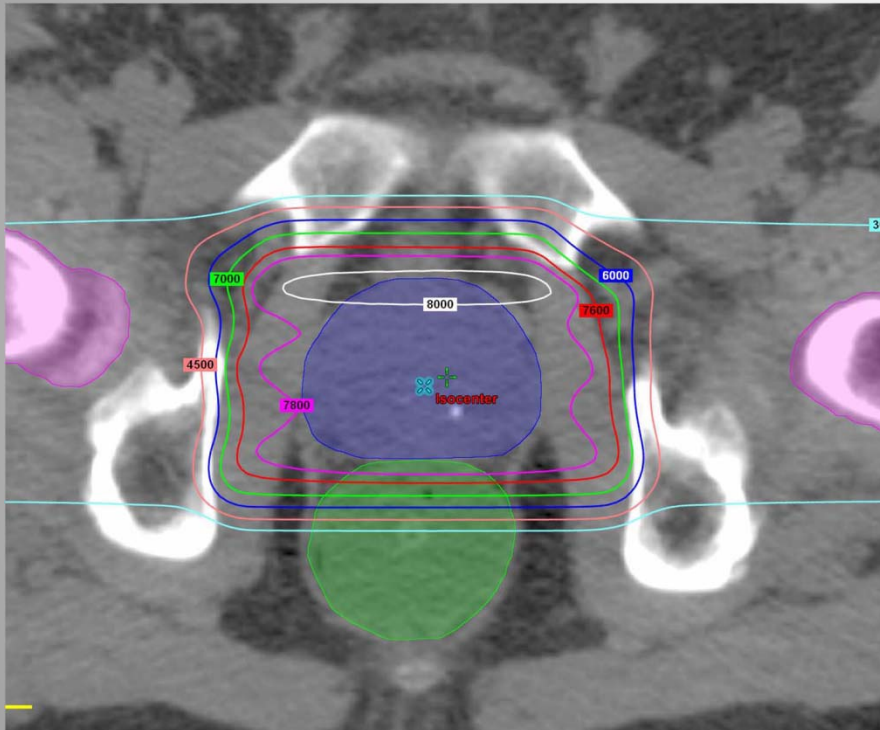
\*Beam range uncertainty

# Lateral Margin

- LM = setup uncertainty + penumbra
- Setup uncertainty = 0.5cm
- 225-250 MeV beam penumbra (95-50%) = 1.0-1.2cm
- LM = 1.2-1.7 cm
- Tighter posteriorly

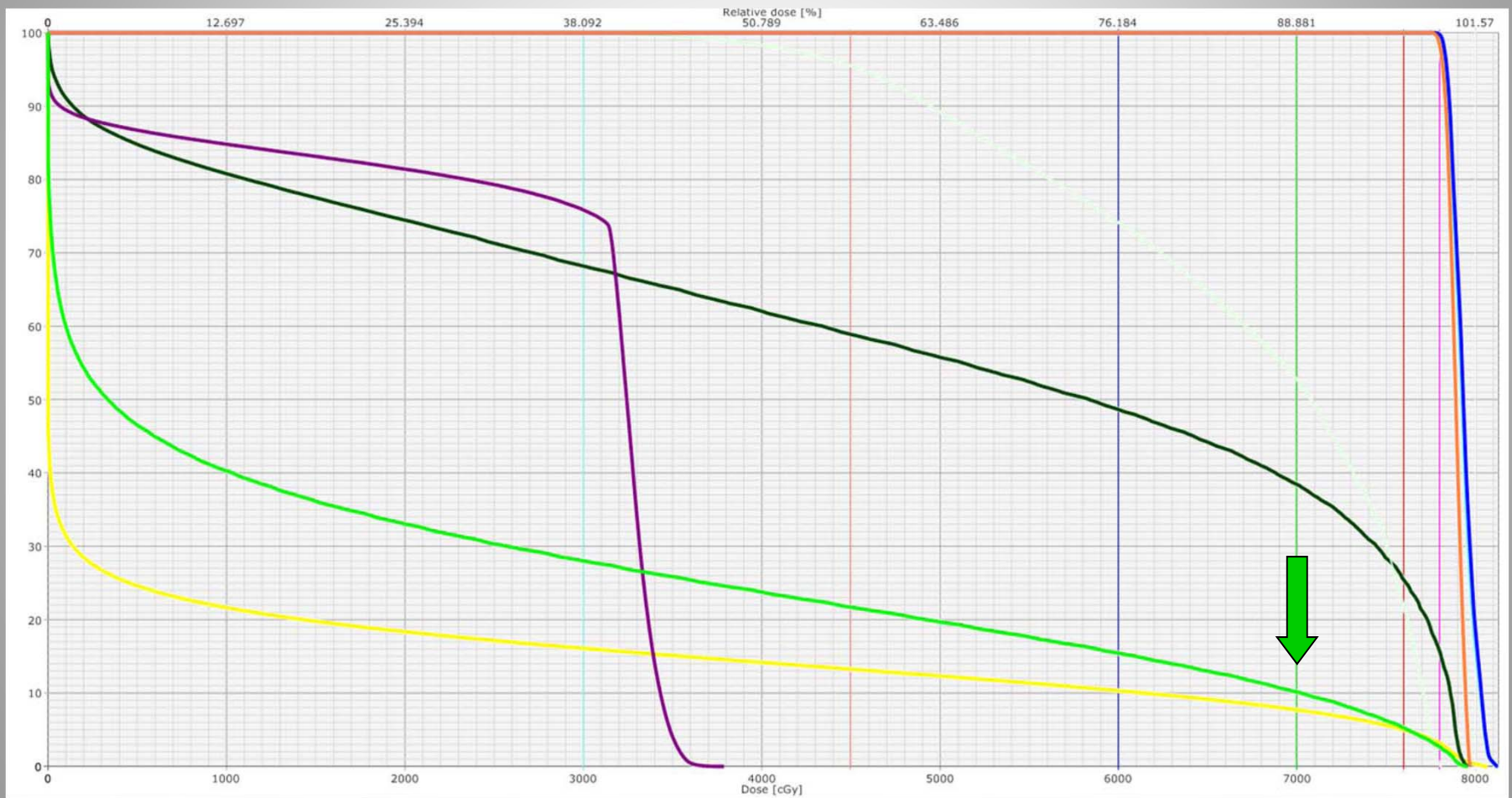


# Two opposed lateral beams

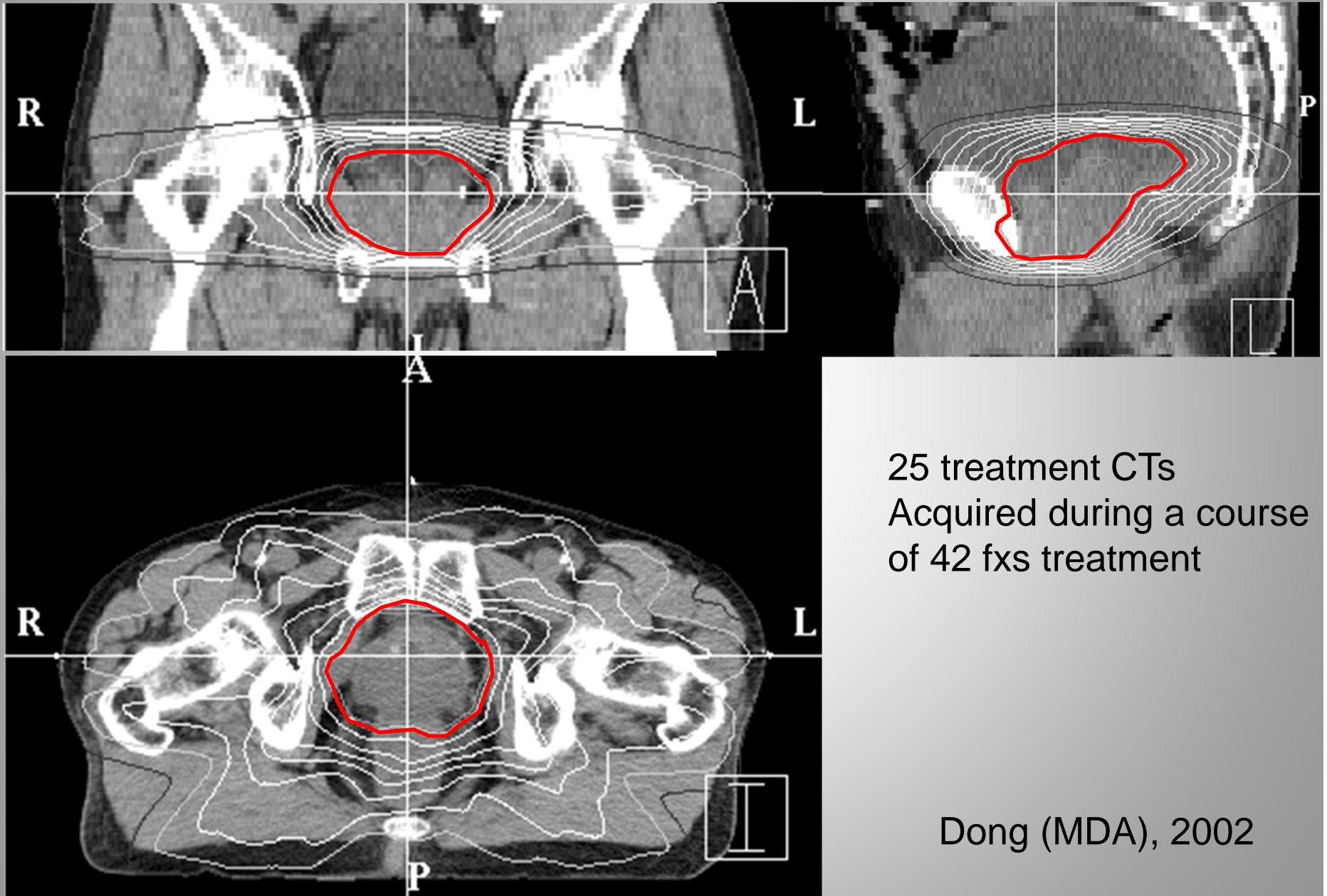


Rectal DVH V70 <12%

Anterior rectal wall V70 <40%



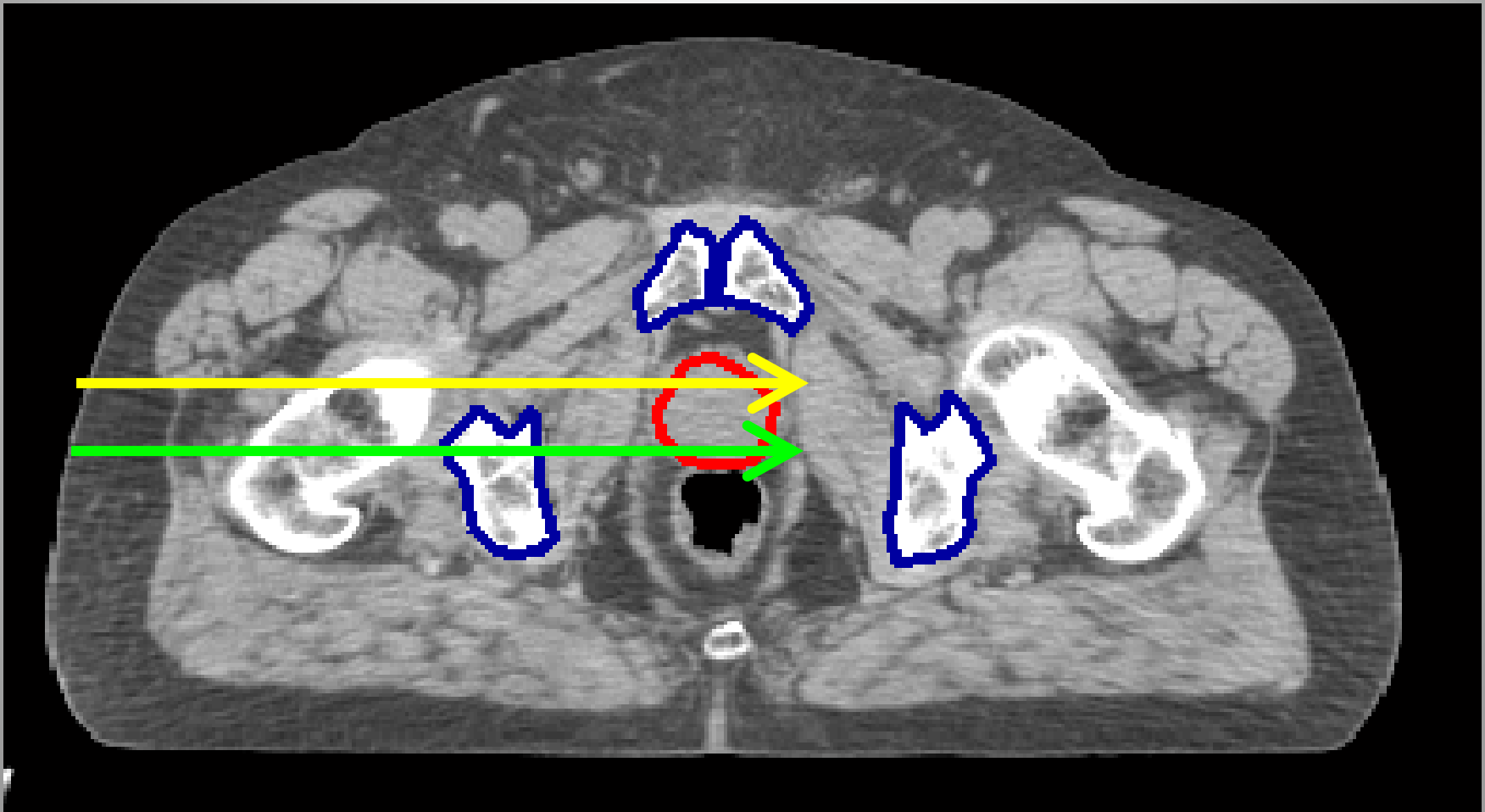
# Dancing prostate & hips using vacuum bag



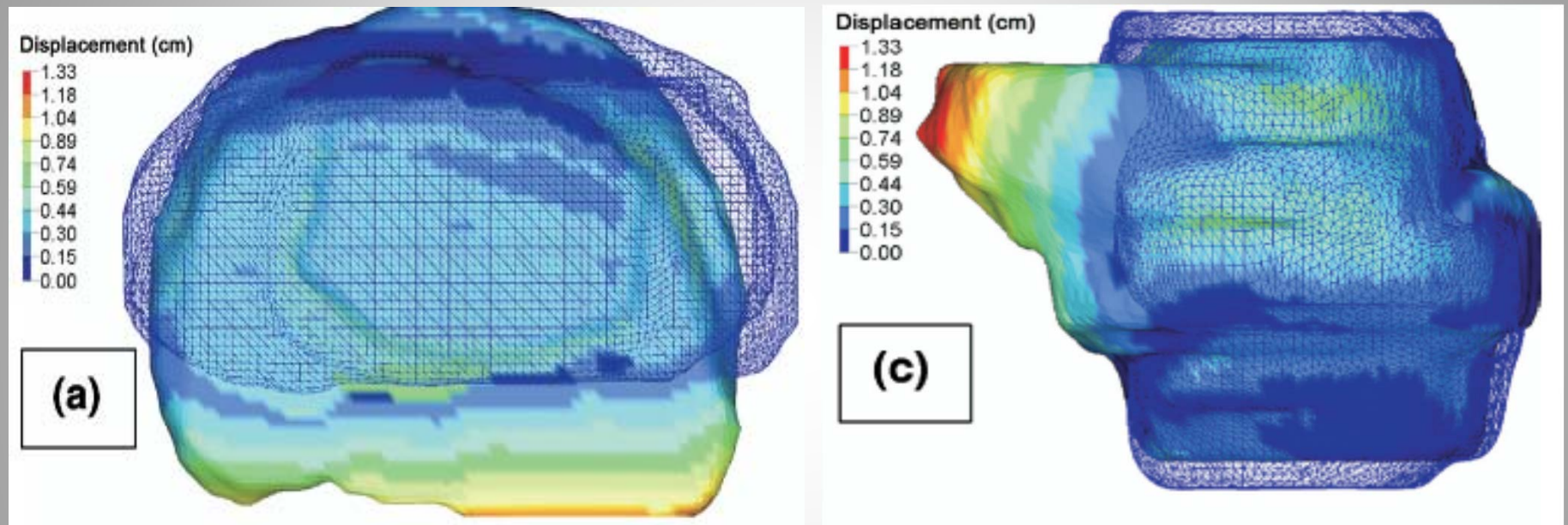
25 treatment CTs  
Acquired during a course  
of 42 fxs treatment

Dong (MDA), 2002

Range depends on radiologic path length



# Fiducials vs. MRI show residual errors

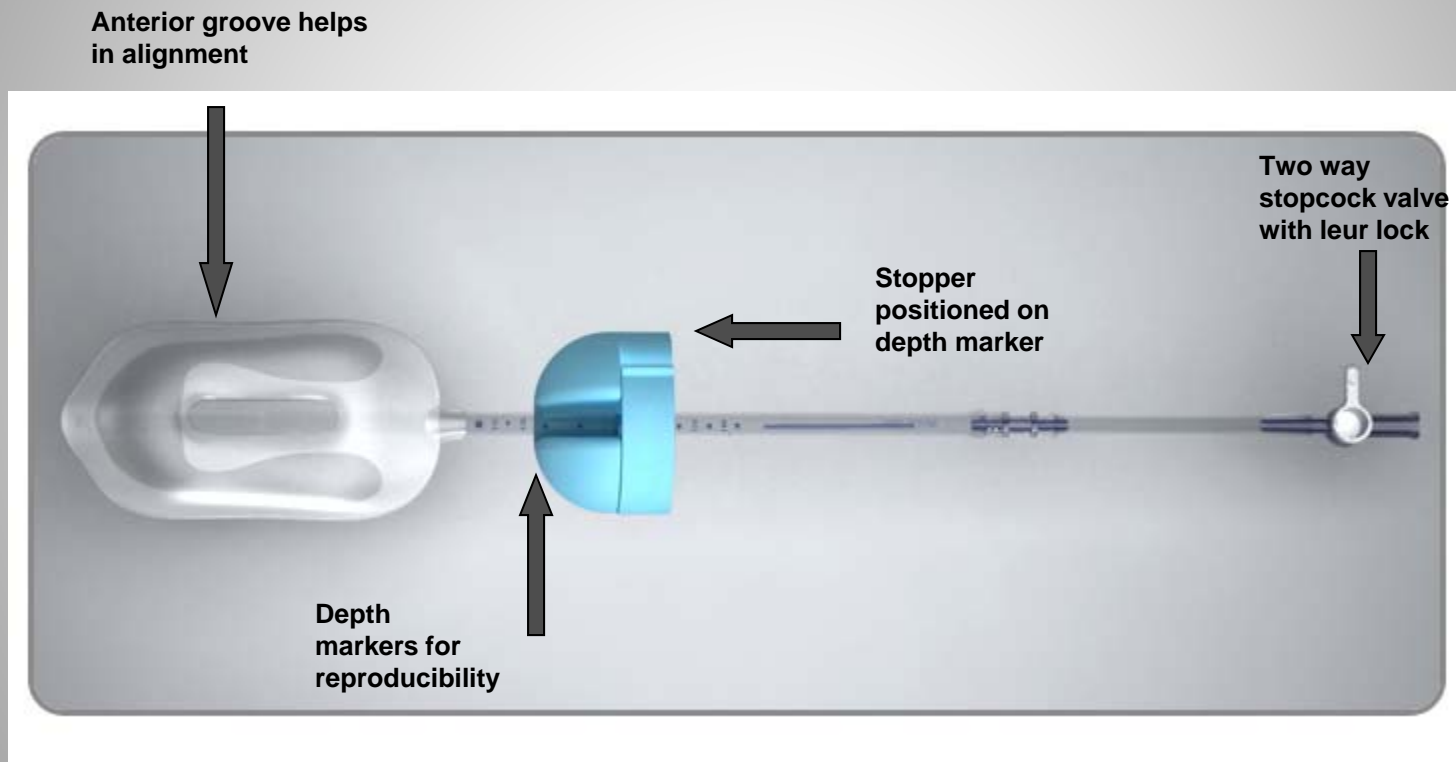


Max prostate deformations after translational matching of fiducials: 6mm x-direction, 13mm in y, 7mm in z

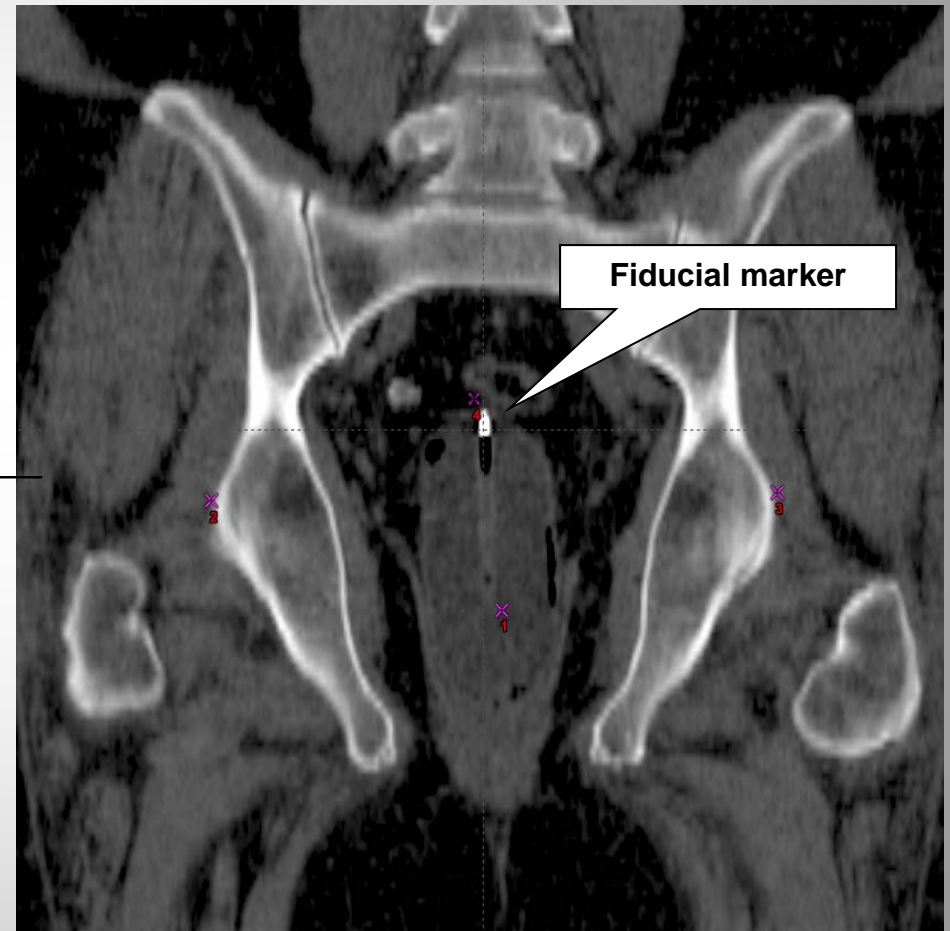
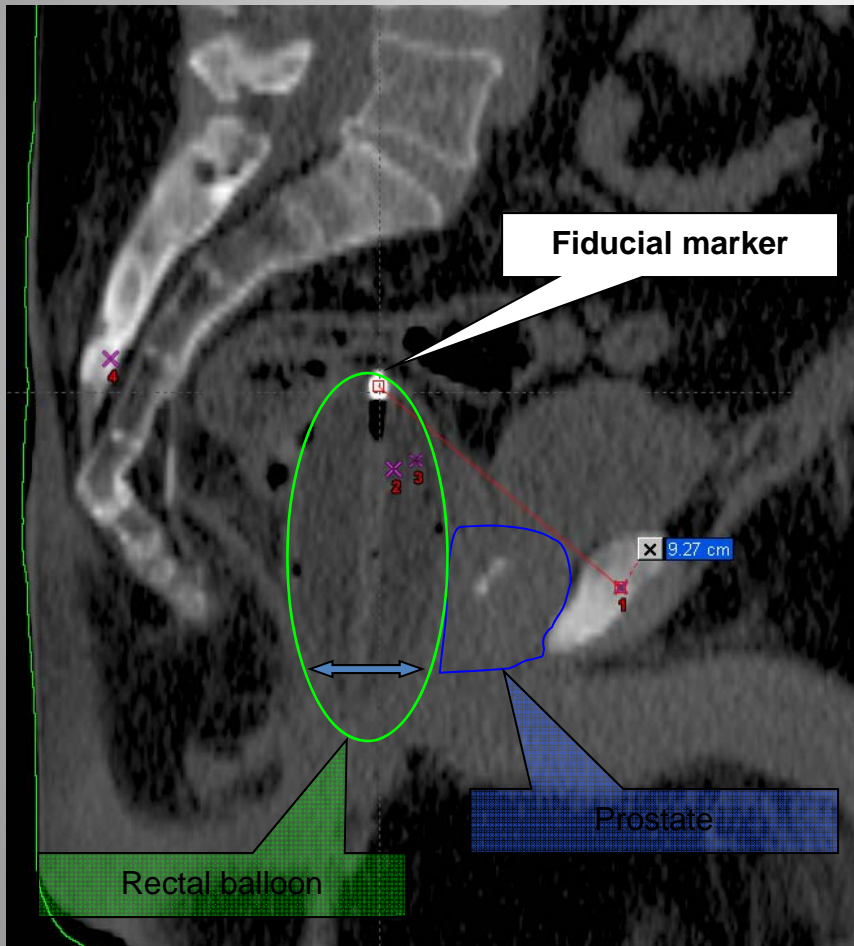
[Nichol et al. IJROBP 67, 2007]



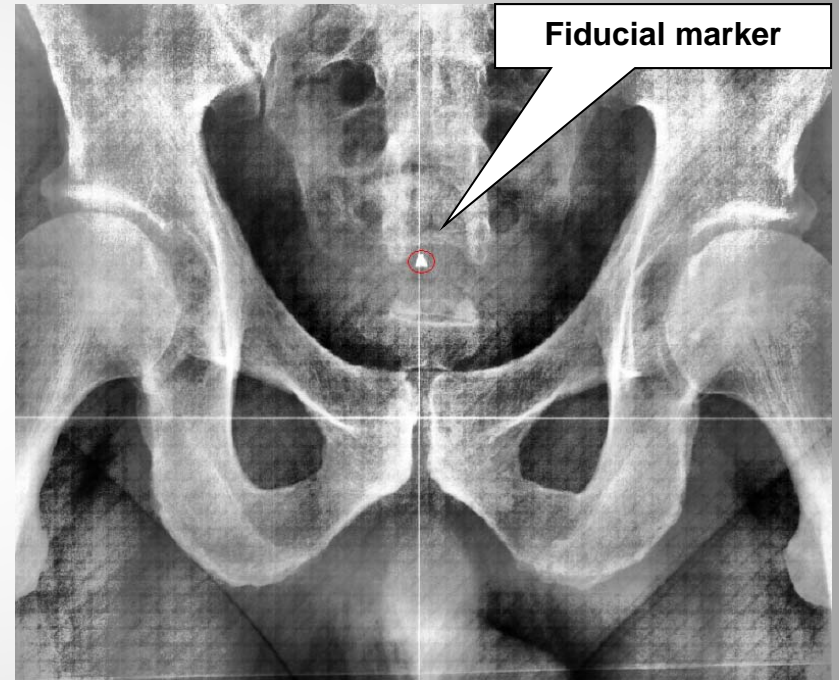
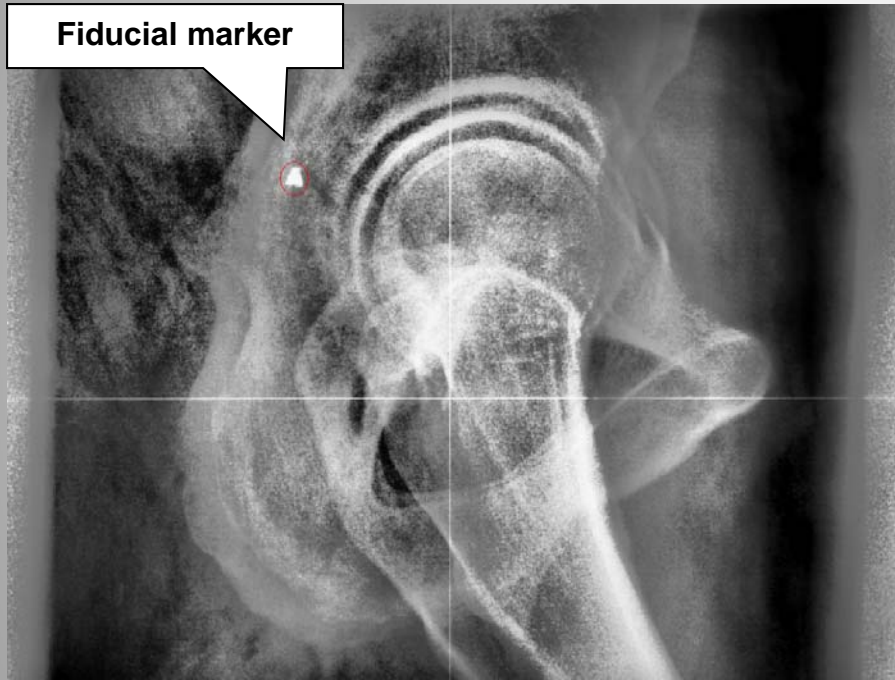
# Gas-release double-ported ERB



# Sagittal and Coronal



# Check ERB depth of insertion daily



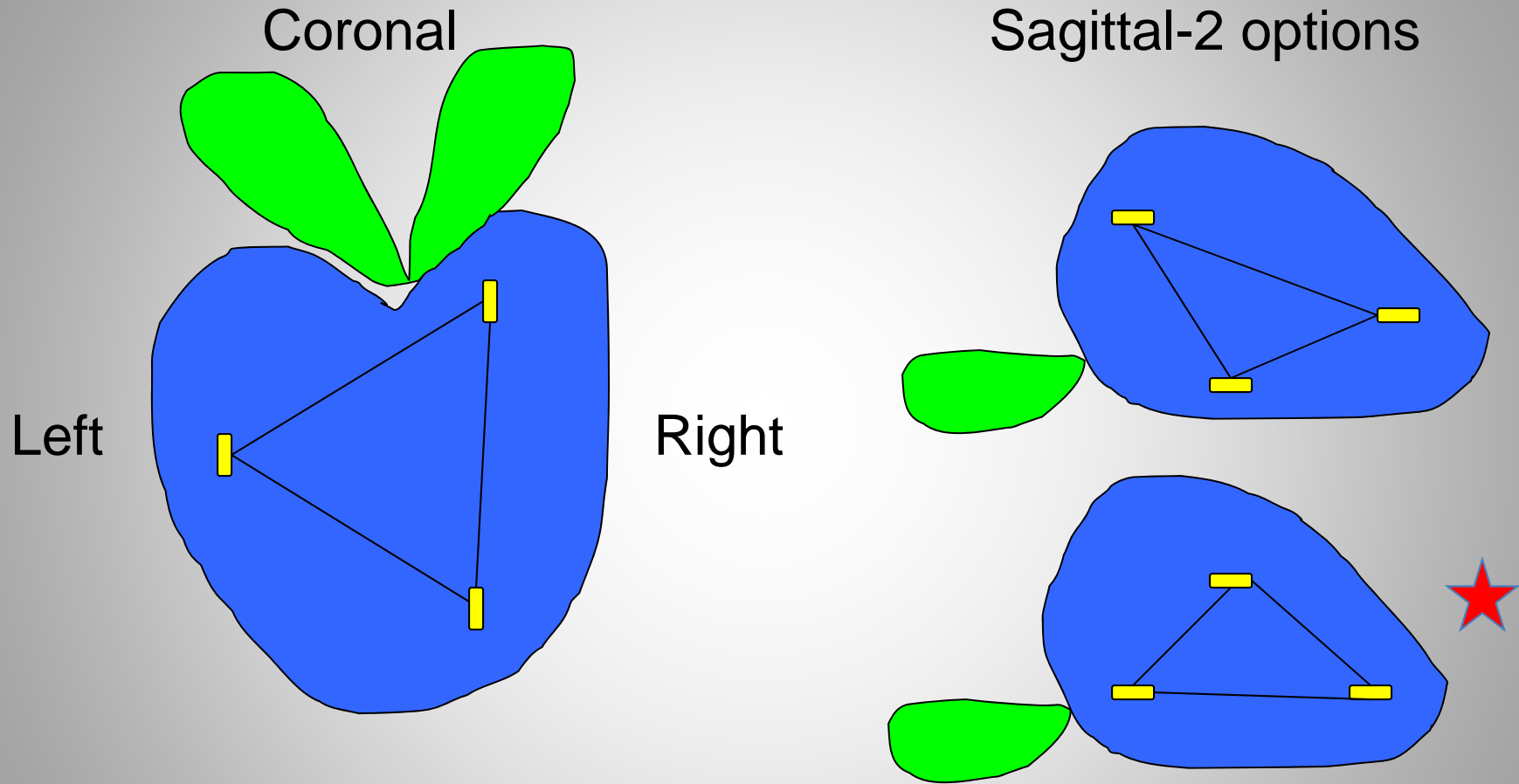
# Fiducial markers



# Fiducial markers for protons

- Increases accuracy and faster than bony alignment
- Use lowest density material that is visible on kV imaging
- Implant markers  $\geq$  4-5 days before sim if possible
  - If  $<$  4 days, consider verification CT 1<sup>st</sup> week of Rx
  - Two markers (base-apex) w/ ERB probably sufficient
  - Do NOT orient long axis of markers parallel to beam path
  - Do NOT overlap markers along beam path
- ***Investigate & correct large shifts between markers and/or bone!***

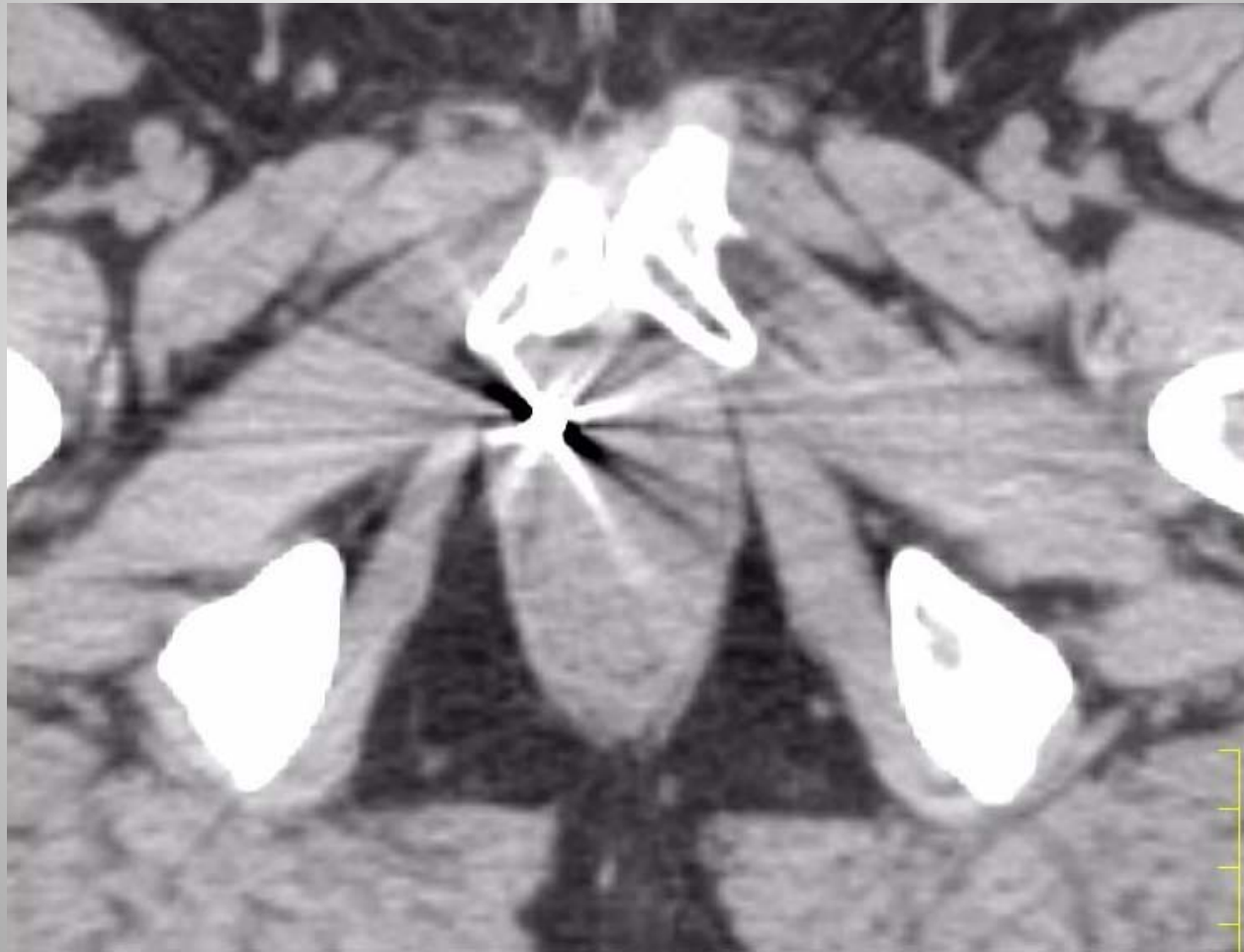
Fiducial markers should form a triangle in each dimension around the isocenter if possible



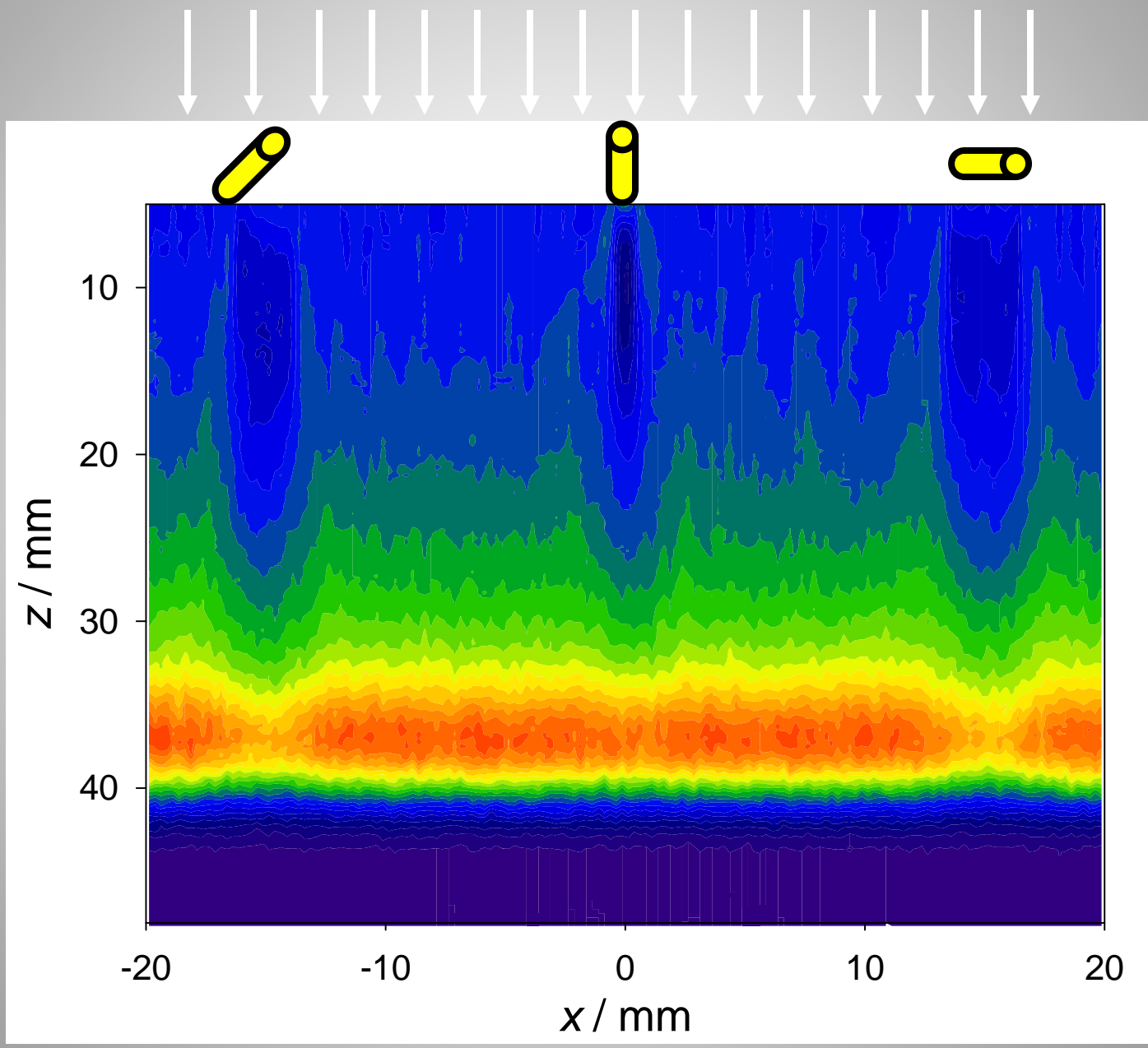
Fiducial markers should be >2mm away from prostate capsule, urethra, SV.

# Gold fiducial:

CT numbers, Volume, Dose shadowing



# Newhauser et al: Dose Perturbations from Au Cylinders



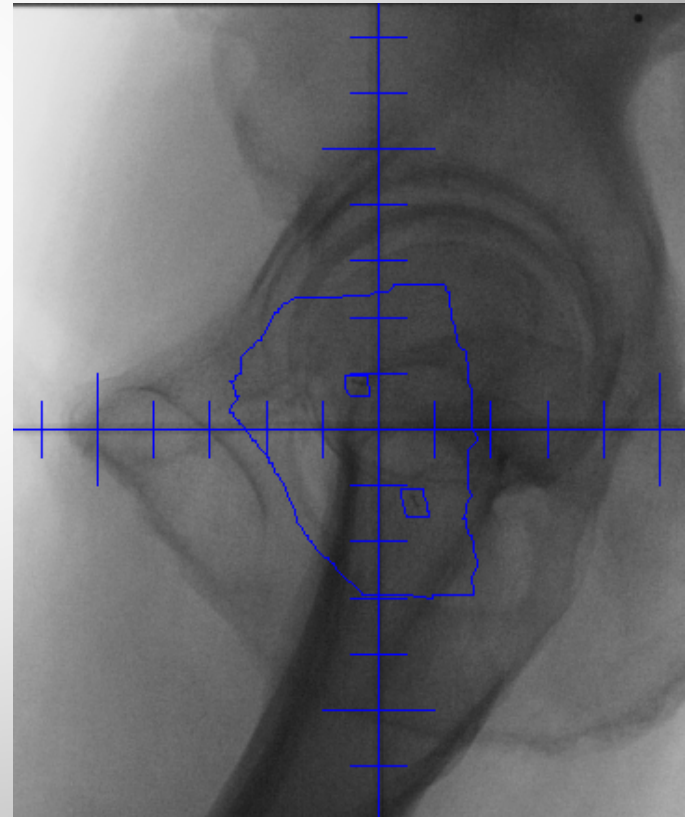
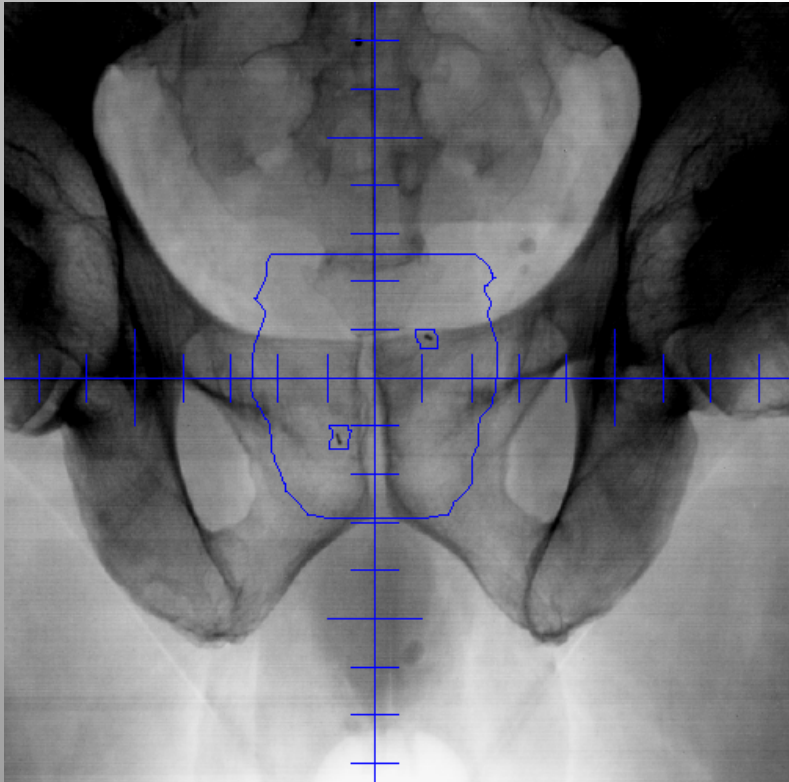


# Calcification vs. Carbon-coated ZrO<sub>2</sub>



# IGRT carbon-coated $ZrO_2$

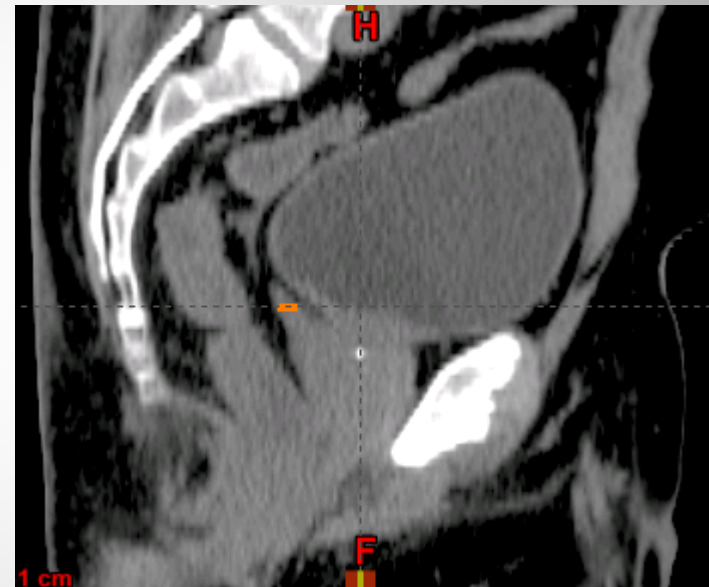
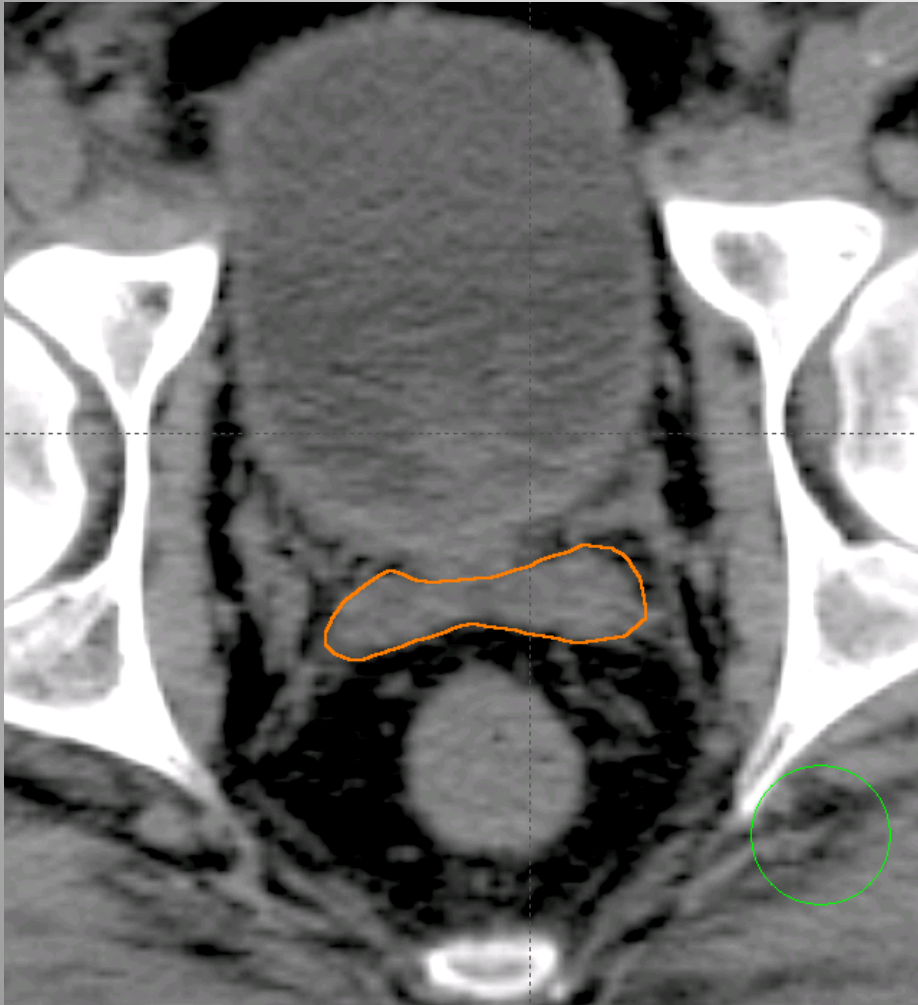
May need to collimate kV imager for better visibility



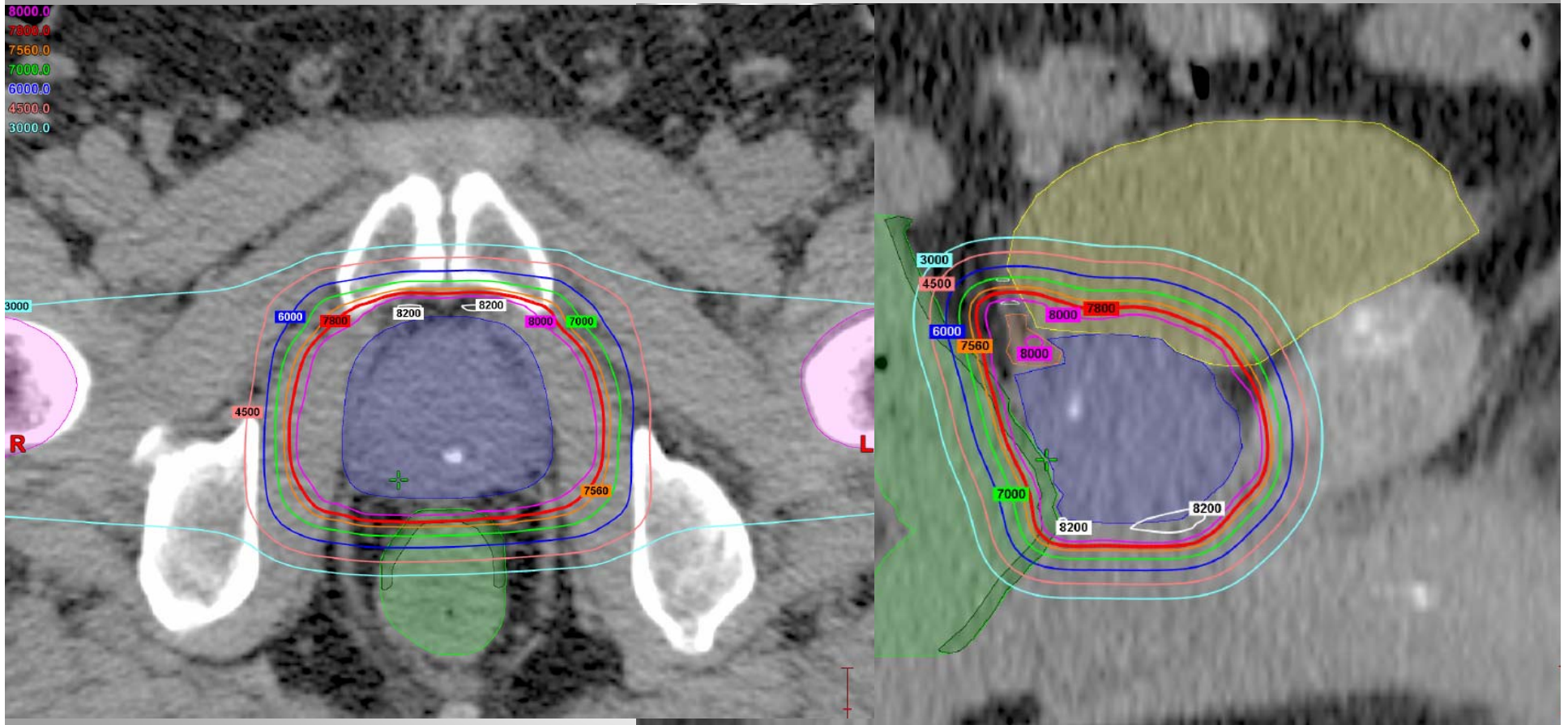
Translational shifts < 6mm and rotational shifts <5° do  
NOT significantly impact CTV coverage

- UF-Vargas et al. IJROBP 71, 2008
- NCC Korea-Yoon et al. IJROBP 71, 2008
- MDACC- Sejpal et al. IJROBP 2010

Some men may not require ERB



# Treating without ERB w/ fiducials

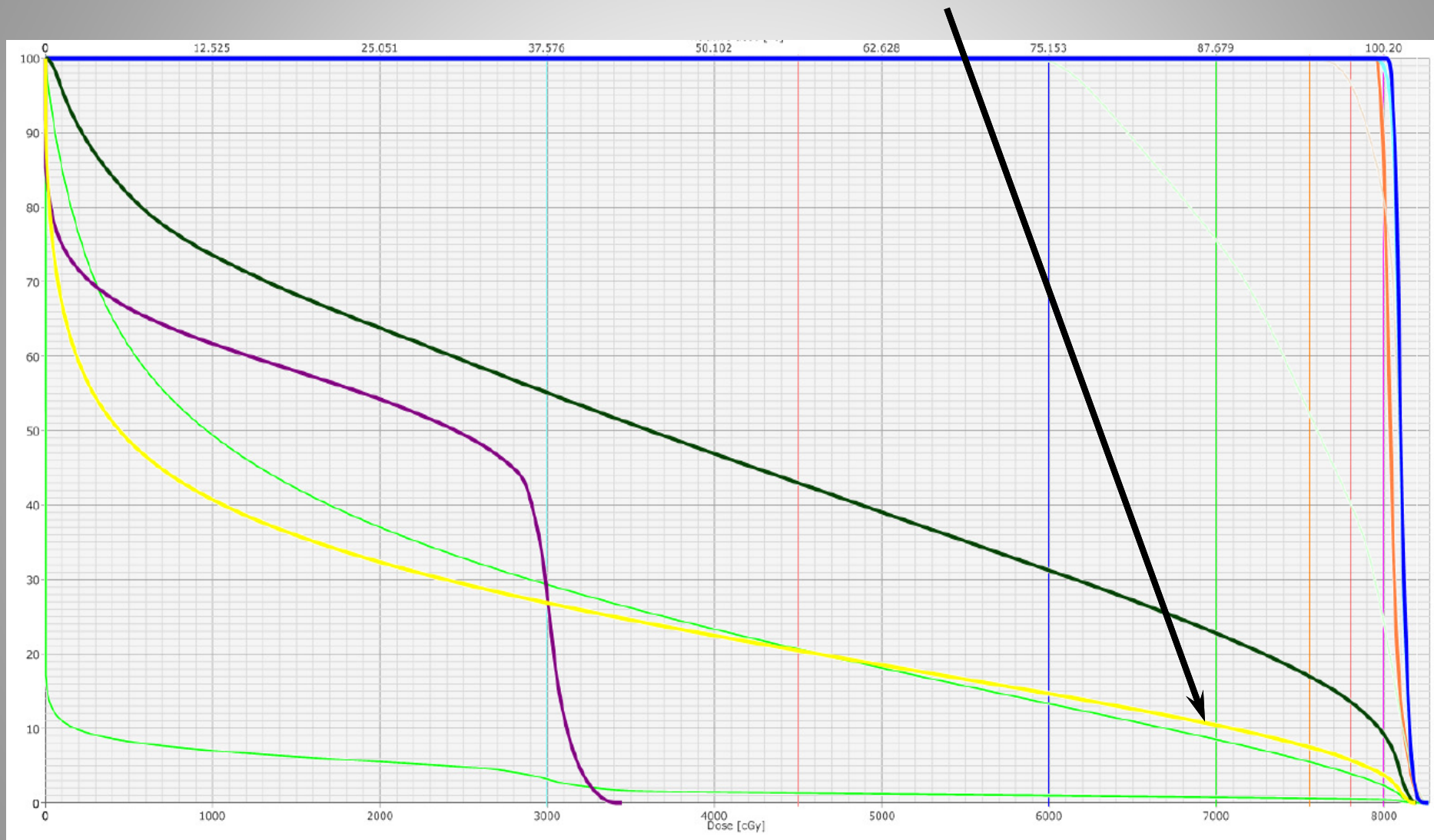


Patient anatomy: Posterior angulation of rectum, peri-prostatic/rectal fat

Patient compliance on rectal emptying (intervene if rectal gas on kV imaging)

# Treating without ERB DVH

Rectal V70 = 8% (light green)

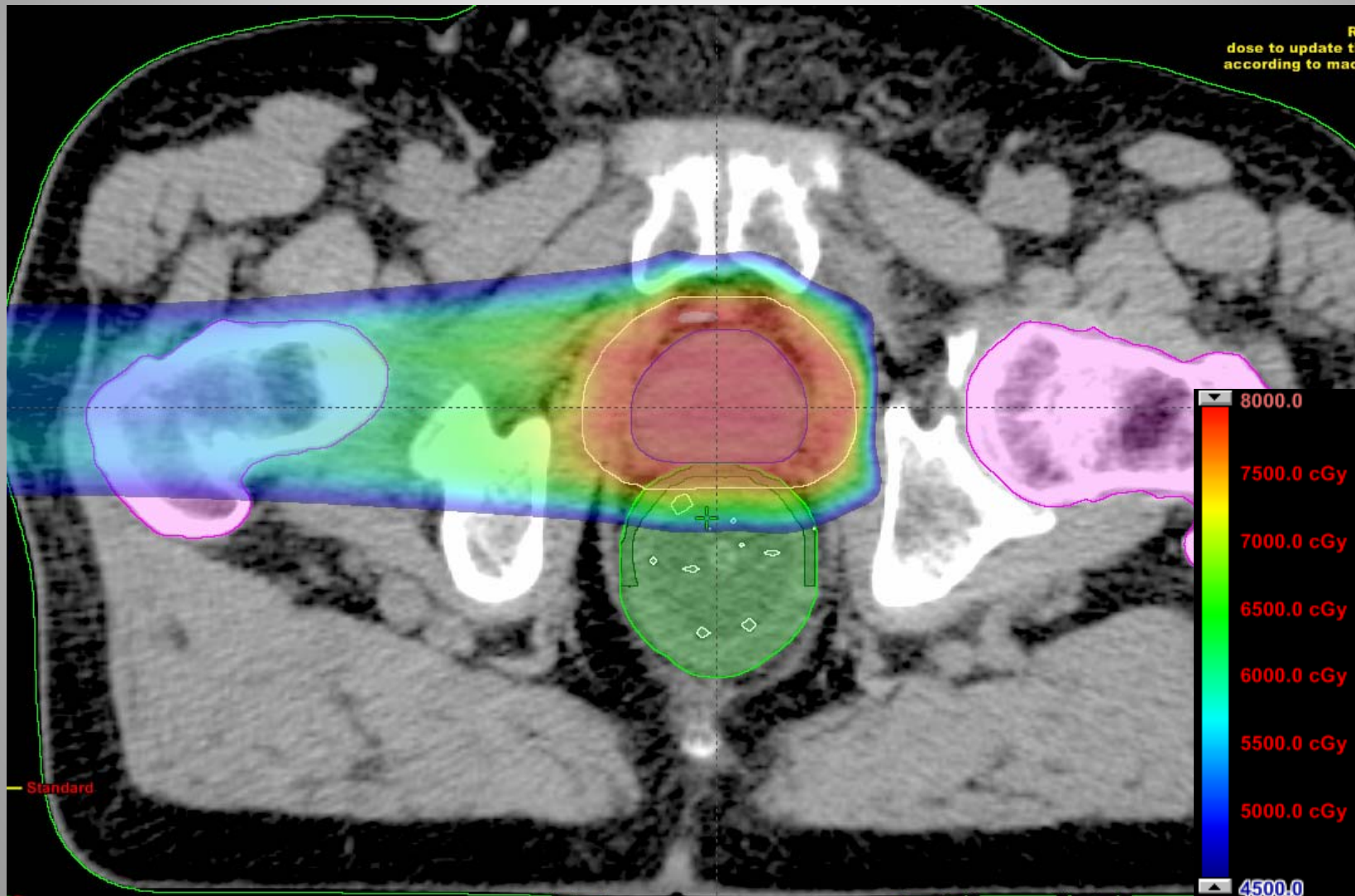


# Rank order for proton use in prostate Ca

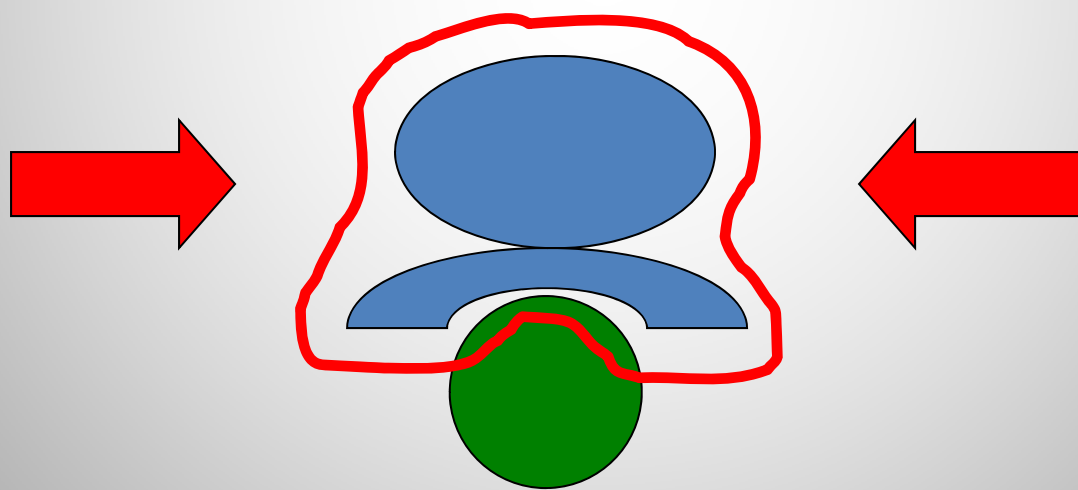
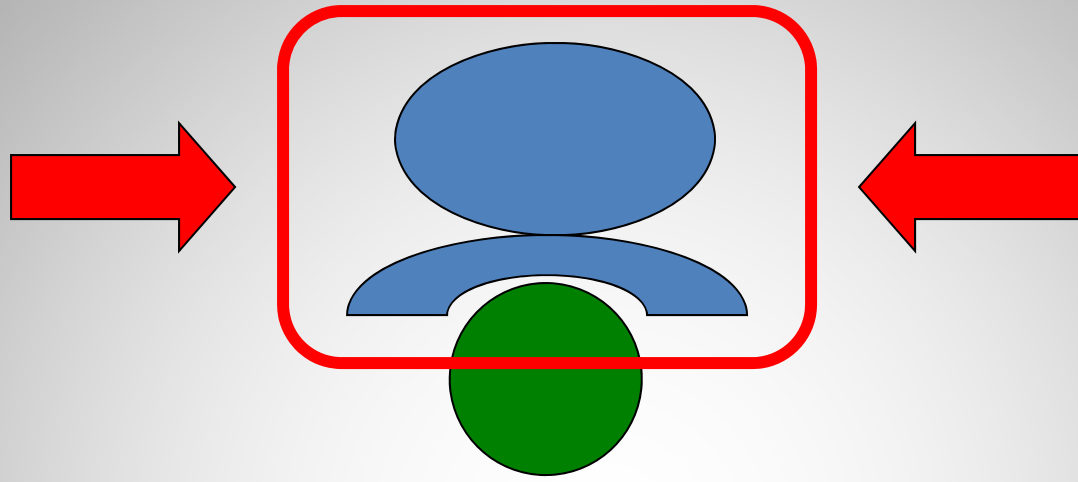
1. Passive scattered
2. Spot-scanning-SFUD: Each field **comprehensively** covers target
3. Spot-scanning w/ constraints: SFUD w/ more inverse planning
4. Multi-field optimized intensity modulated proton therapy (MFO-IMPT): Most conformal but most complicated

# SINGLE SSPT w/ SFUD

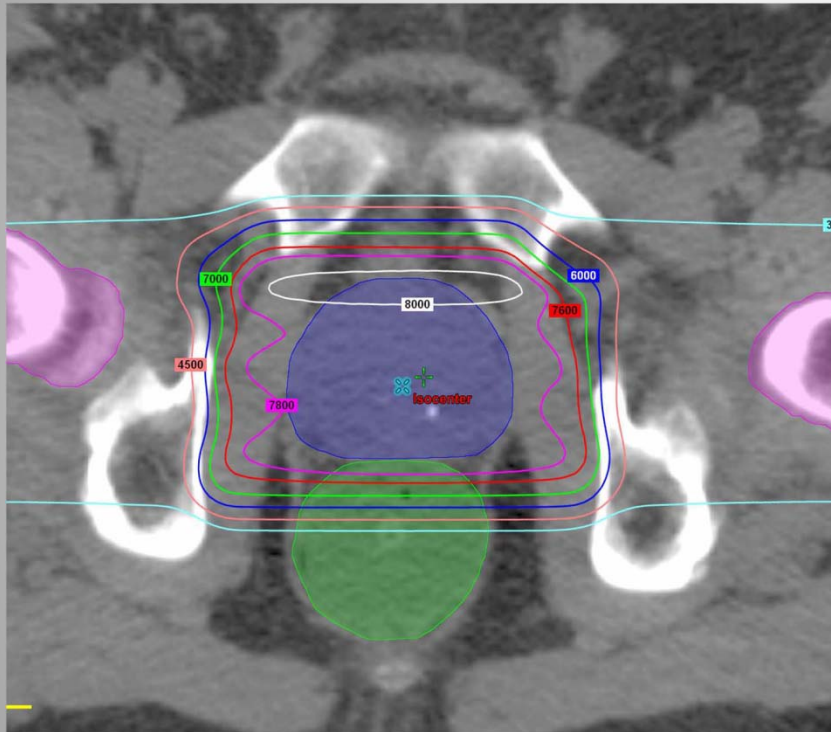
Single field comprehensively covers target



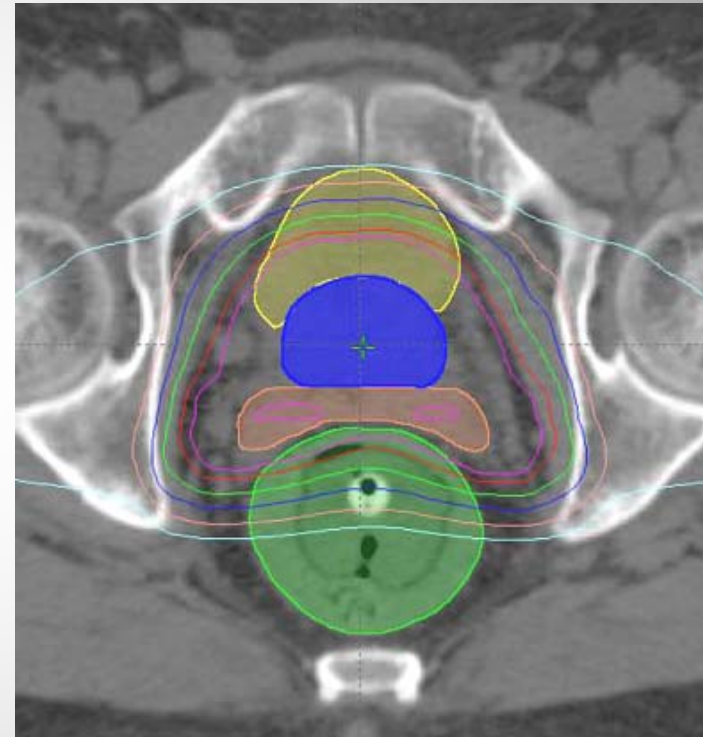




# Two opposed lateral fields

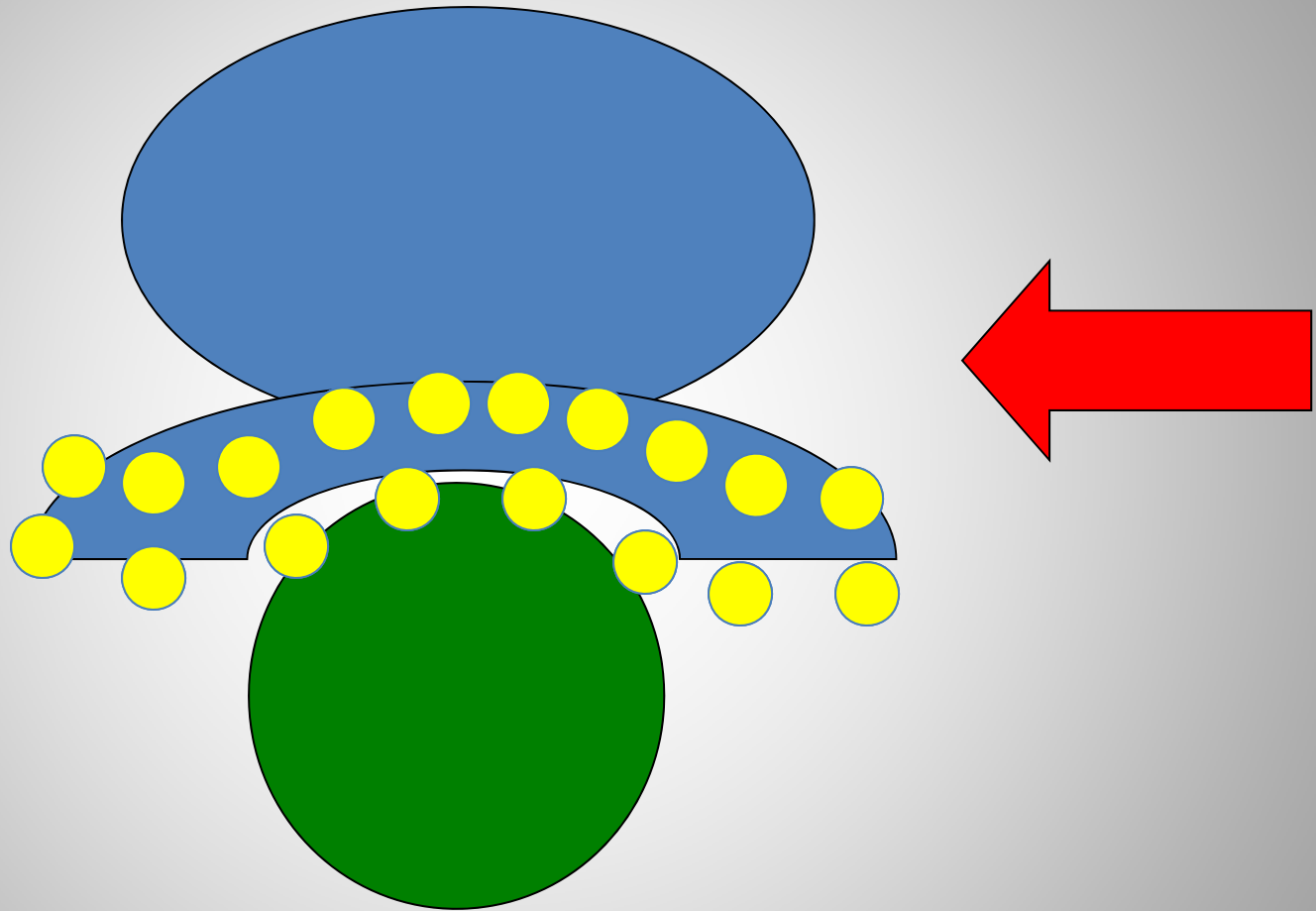


Passive

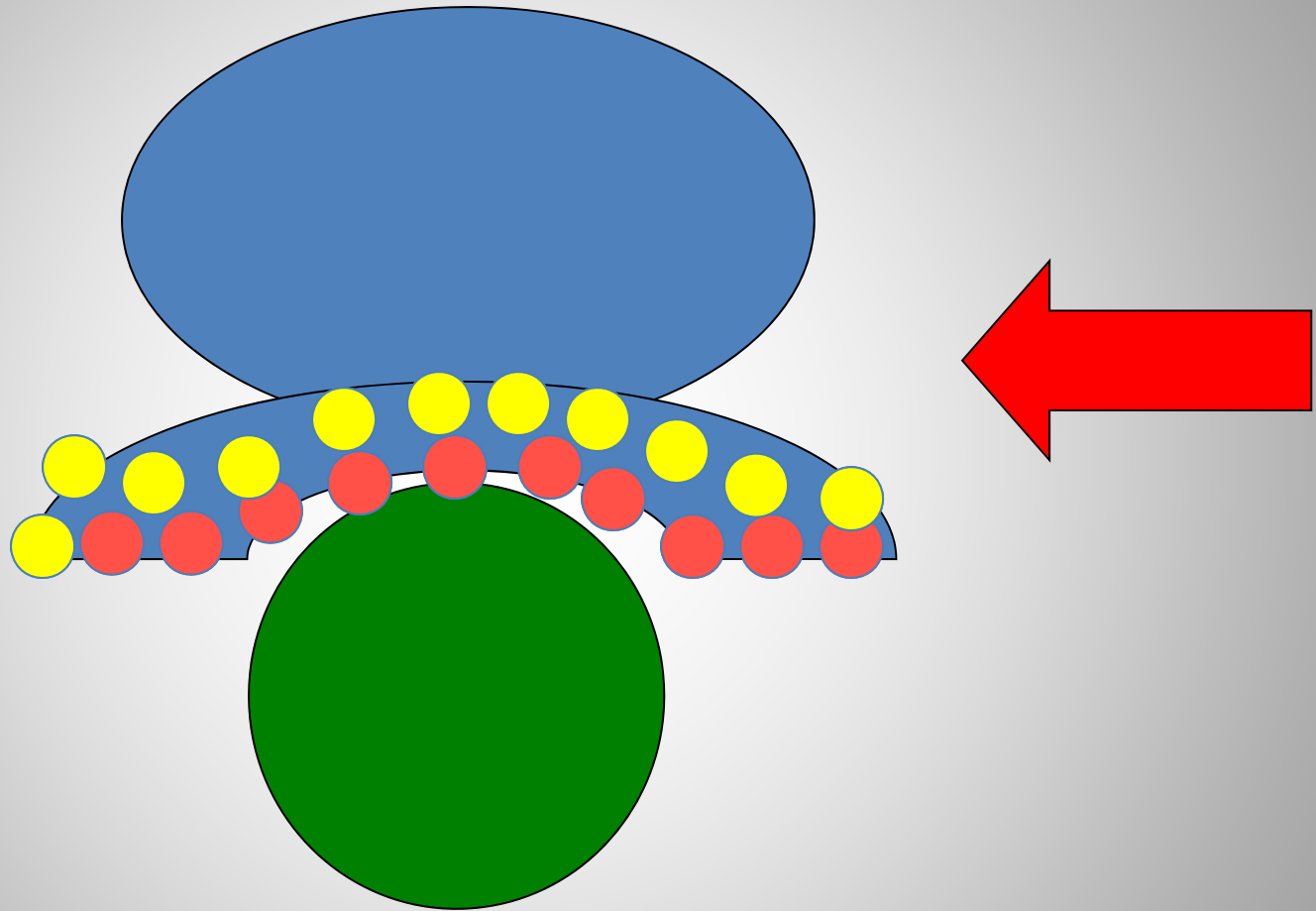


Spot-scanning (SFUD)

Some spots may be outside STV



# SFUD w/ some constraints



# SFUD for prostate cancer

- Typically for more advanced disease or challenging anatomy
- Cannot use classical distal & proximal margin formulas
- Use expanded volume to guide treatment planning:

## Scanning Target Volume (STV)

Considers setup and range uncertainty

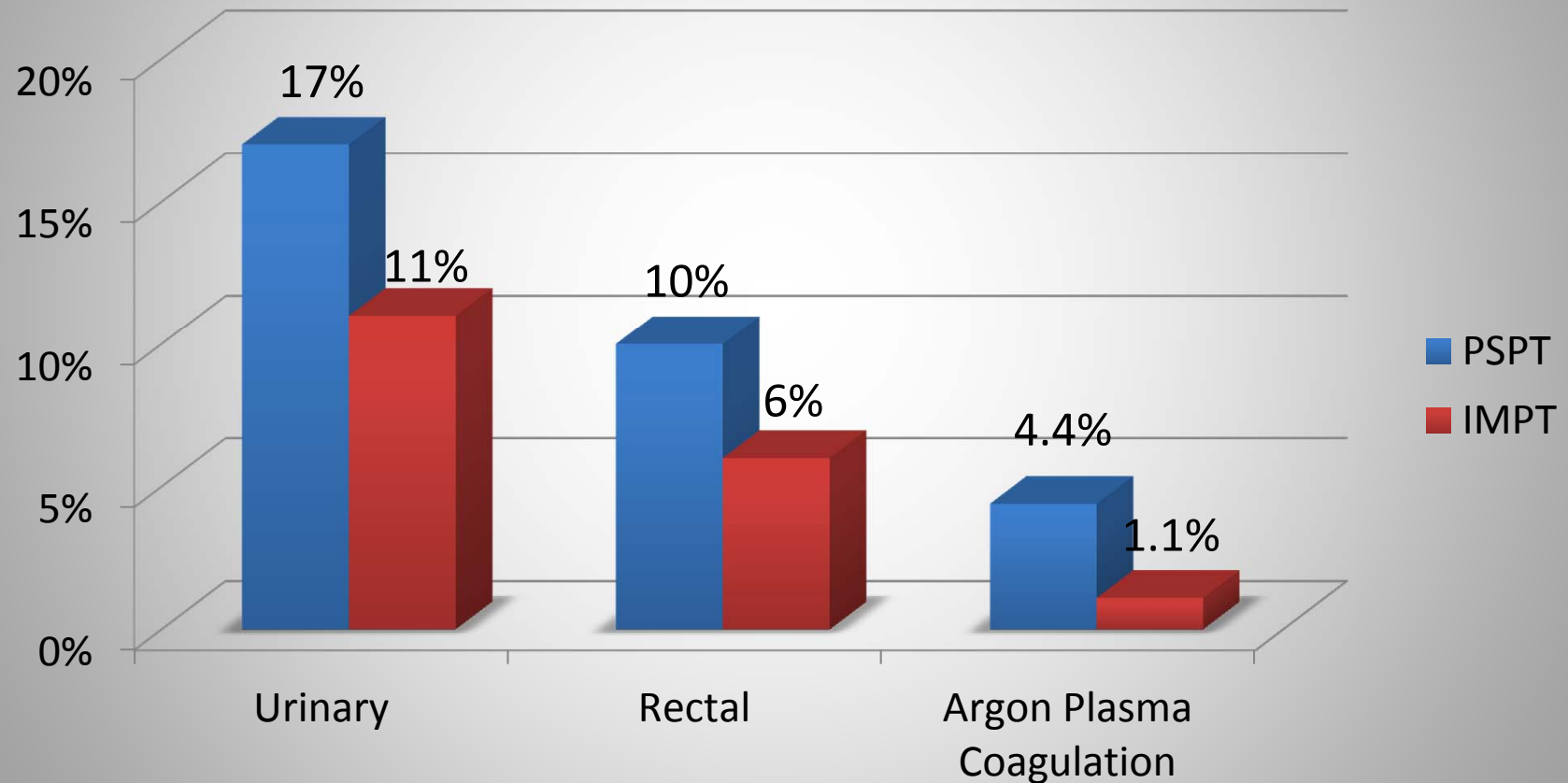
Proximal & Distal margin 12mm

Anterior 6mm, Sup-Inf 5mm, Posterior 4mm

- >96% STV and 100% CTV covered by prescription
- Typically prescribe to 97-98% isodose line
- If plan too heterogenous, consider increasing STV margins and prescribing to lower isodose

# Late Toxicity

## PSPT vs IMPT (SFUD)

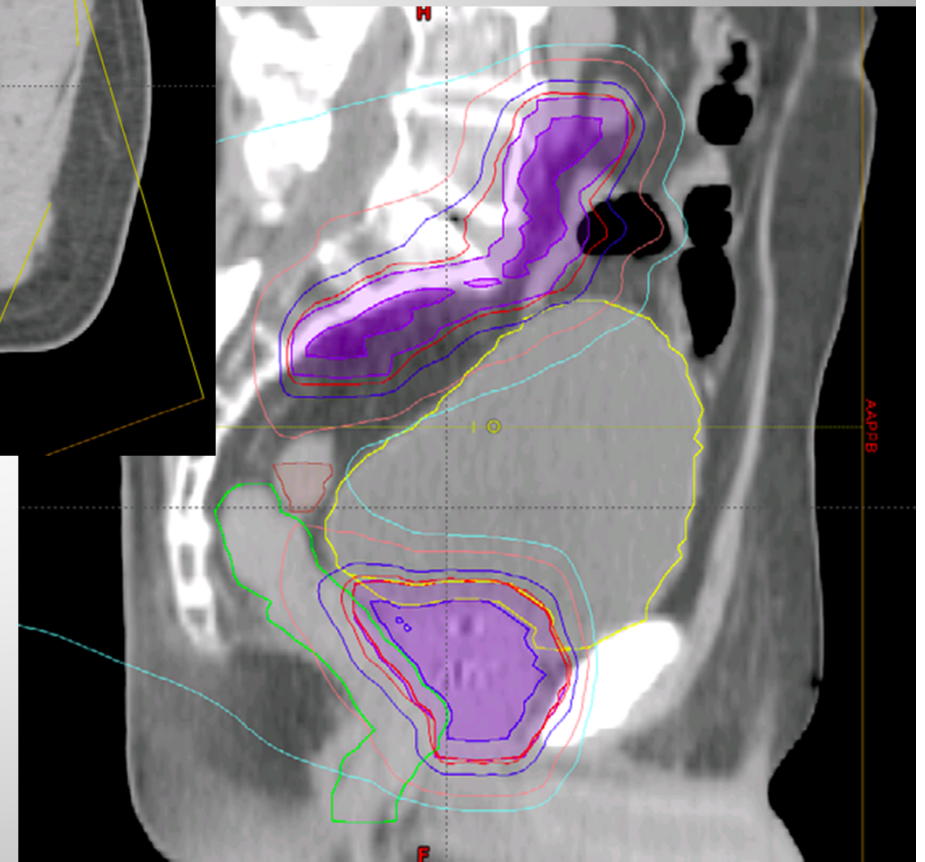
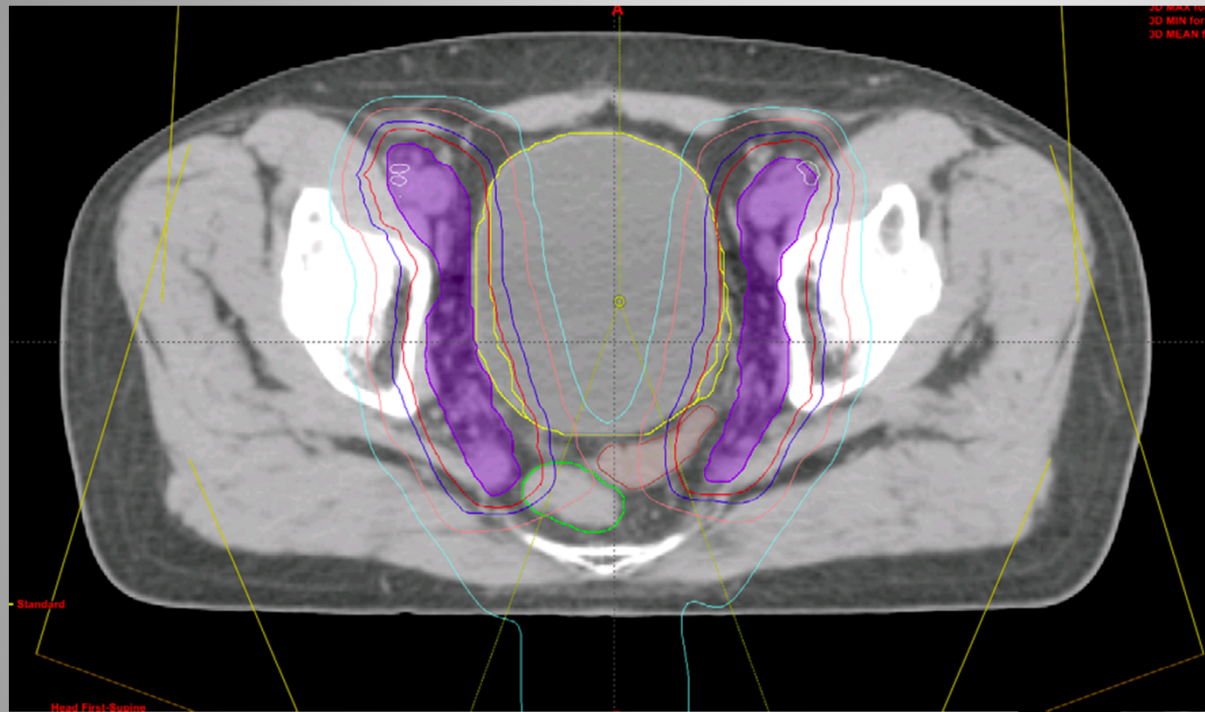


THIS IS BETTER THAN CURRENT PROSPECTIVE IMRT RESULTS

# Treating pelvic lymph nodes

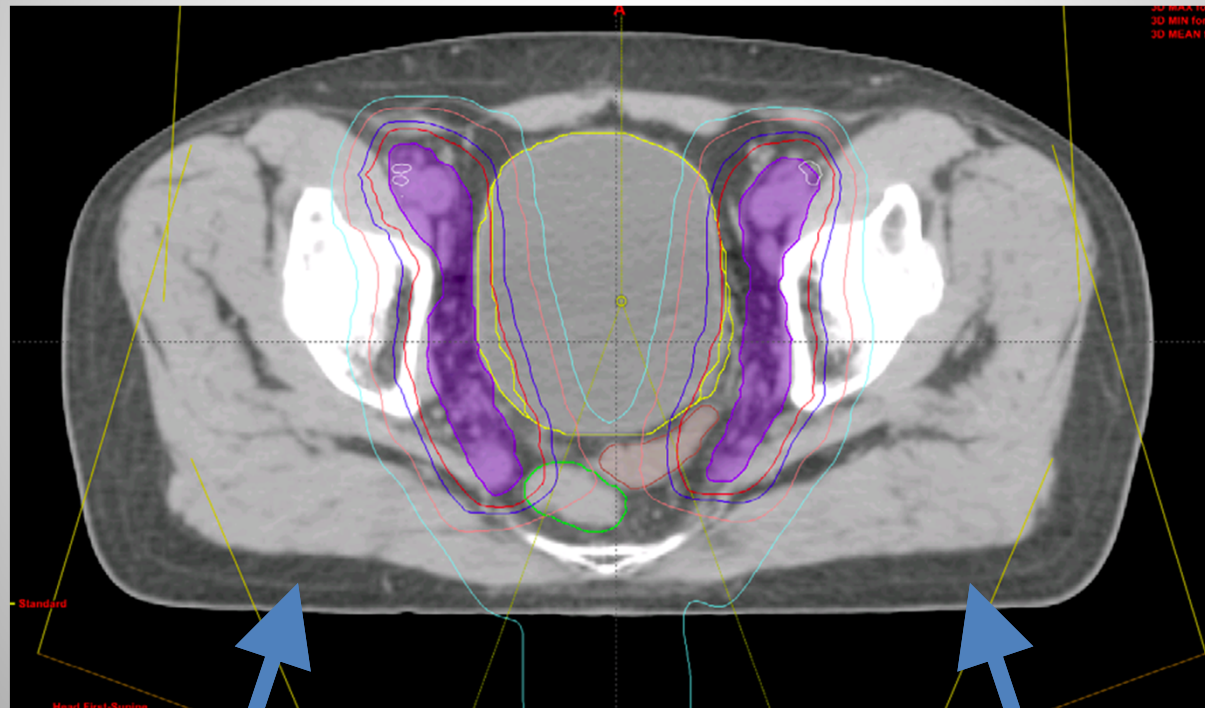
- Make sure you actually need to treat pelvic nodes
- Use adequate CTV (e.g. RTOG atlas)
- Spot scanning helps (conformal, faster)
- Choose beam arrangements that minimize radiologic path lengths and setup variability
- Construct STV accordingly
- Boost prostate w/ laterals
- Align to prostate...Do NOT under-dose prostate

# Treating pelvic lymph nodes w/ protons

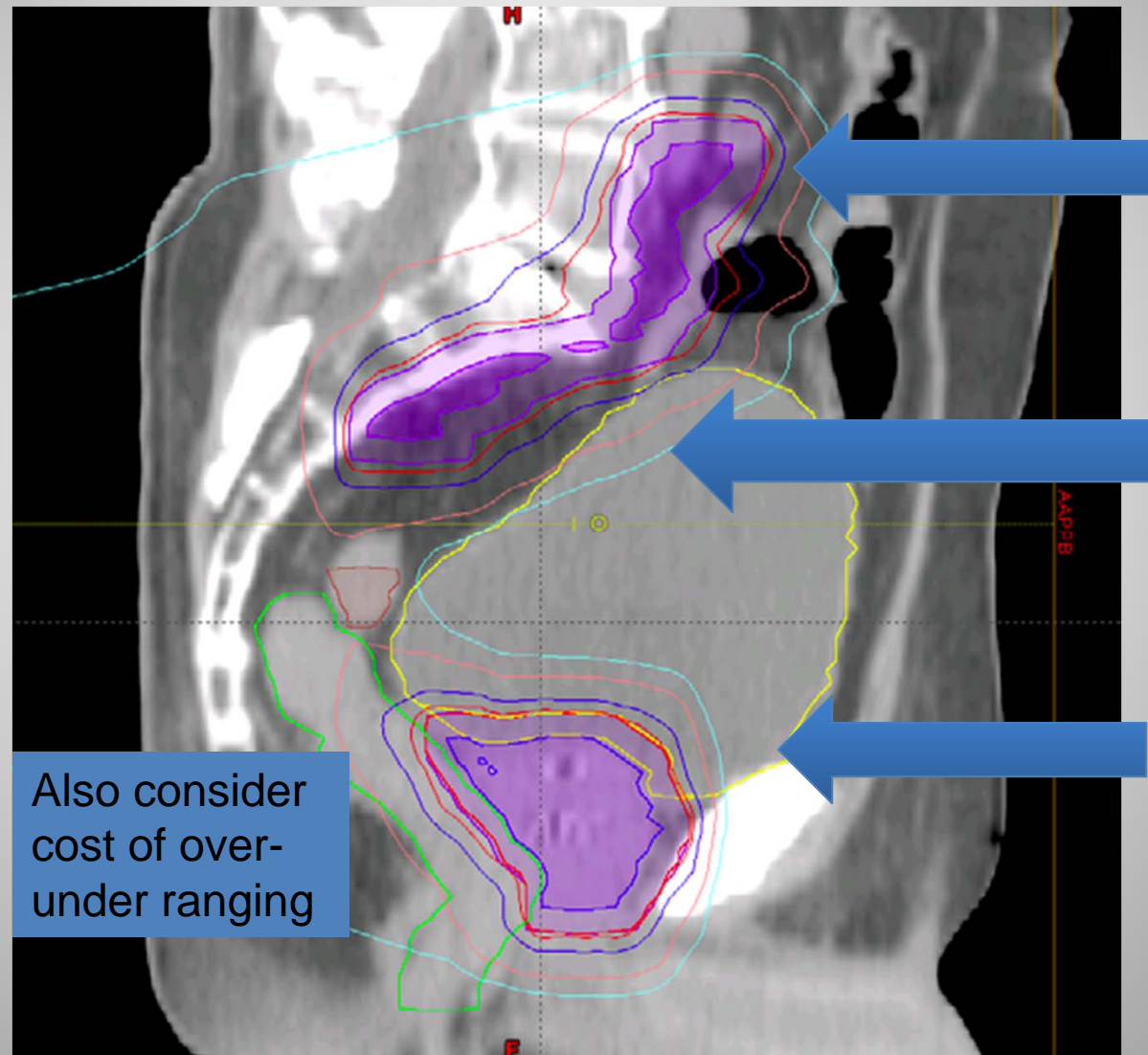




One option is 3 field technique  
AP and two Posterior obliques  
(Robust but slightly higher rectal dose)

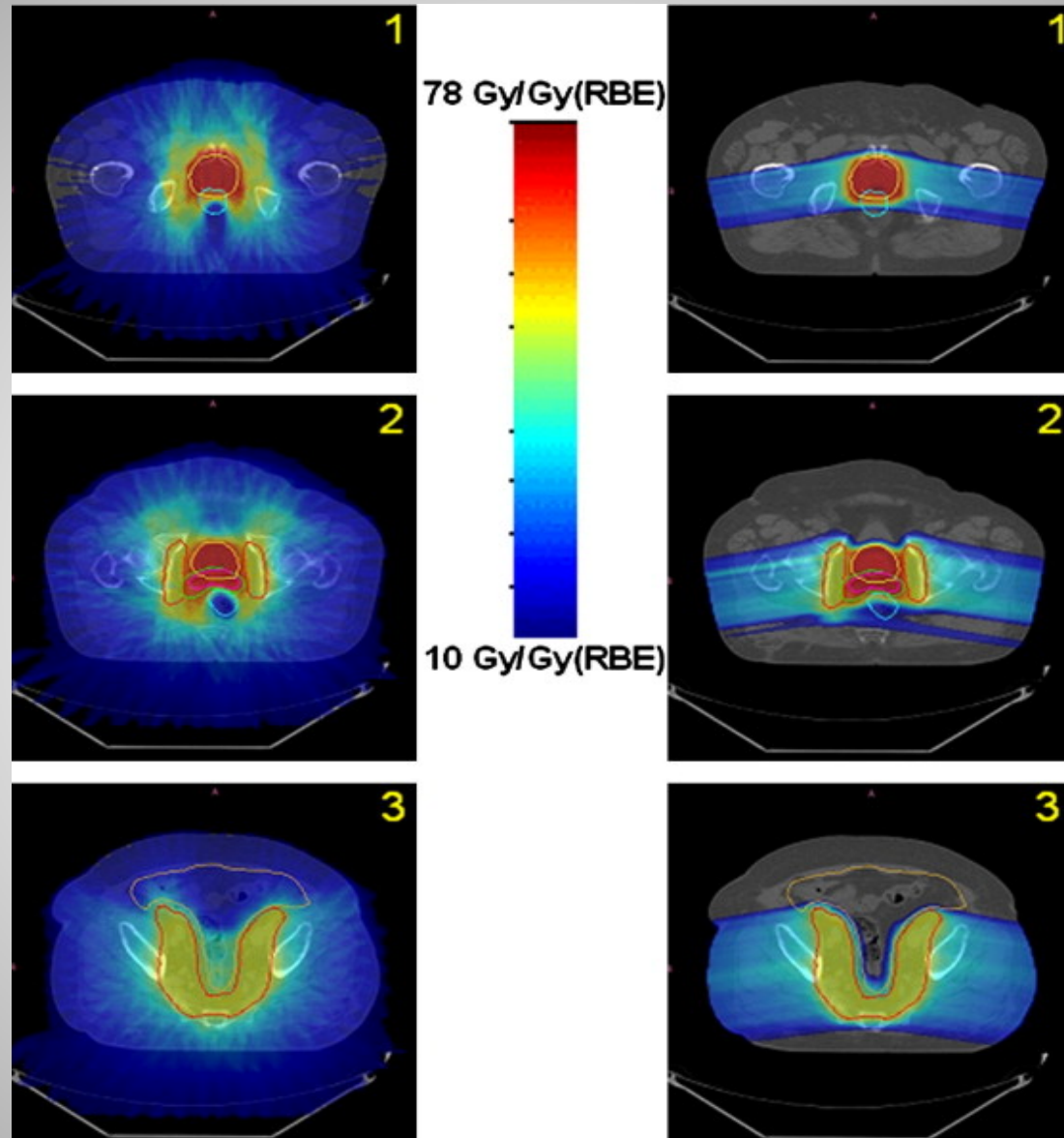


Radiologic path length and setup is variable  
Therefore STV expansion is variable

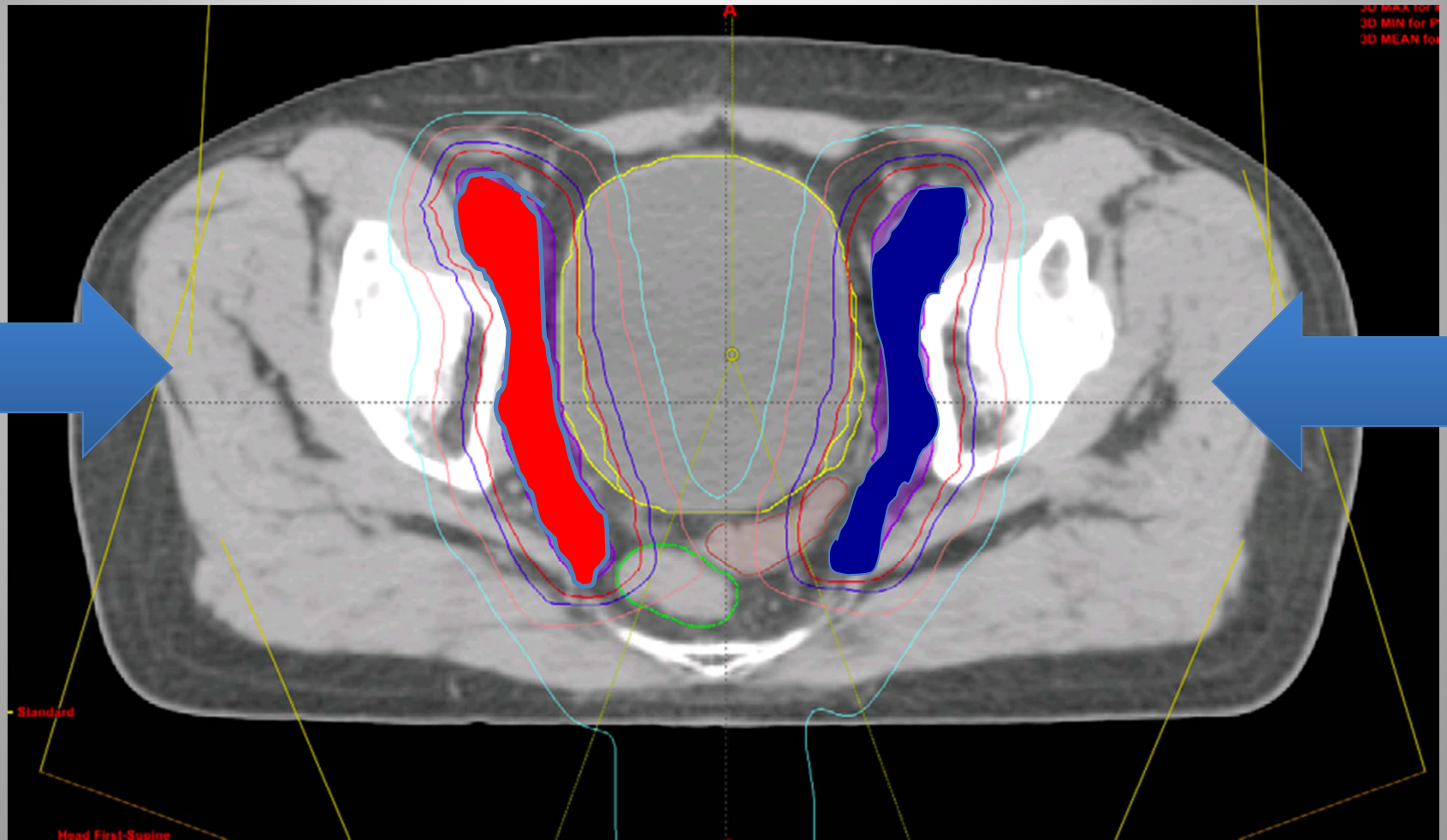


# TomorX

# IMPT

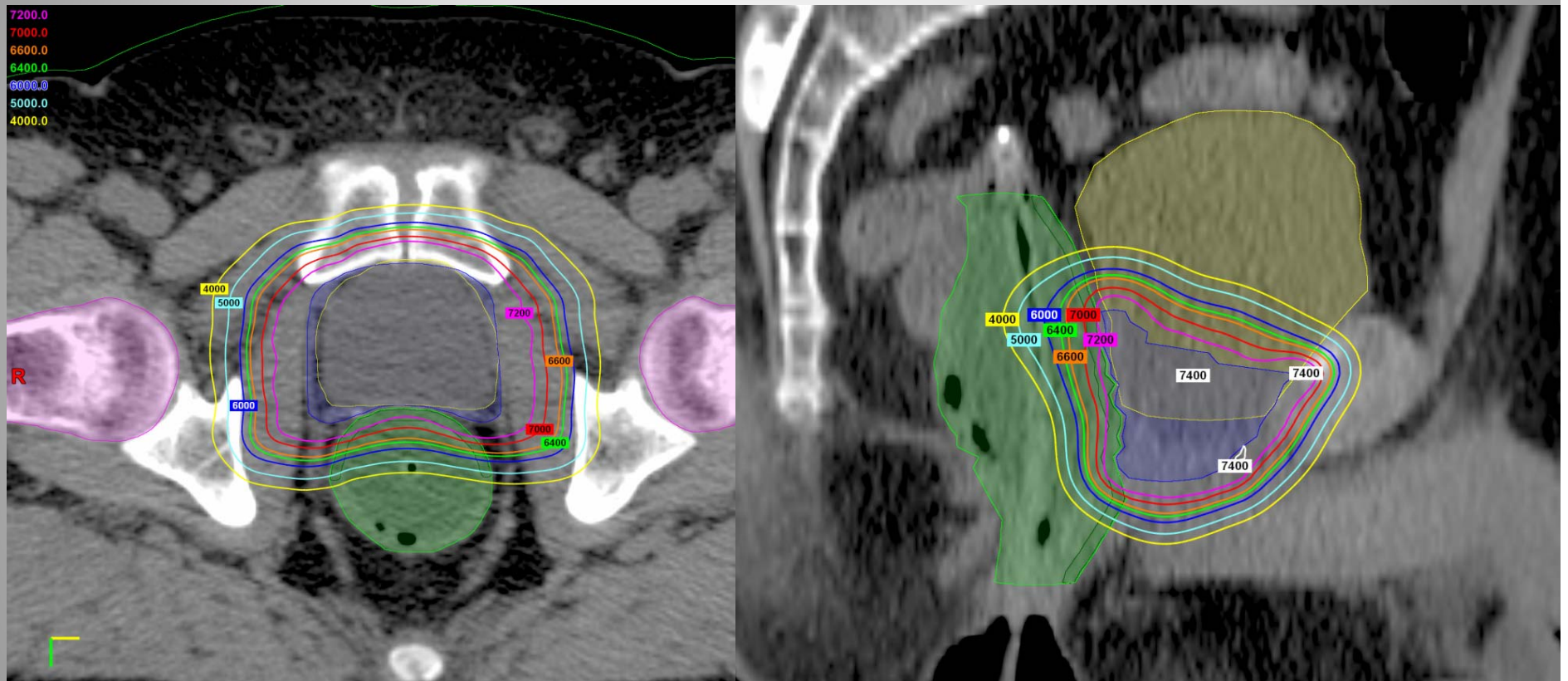


For laterals, depending upon range and TPS may have to split Rt & Lt nodal targets



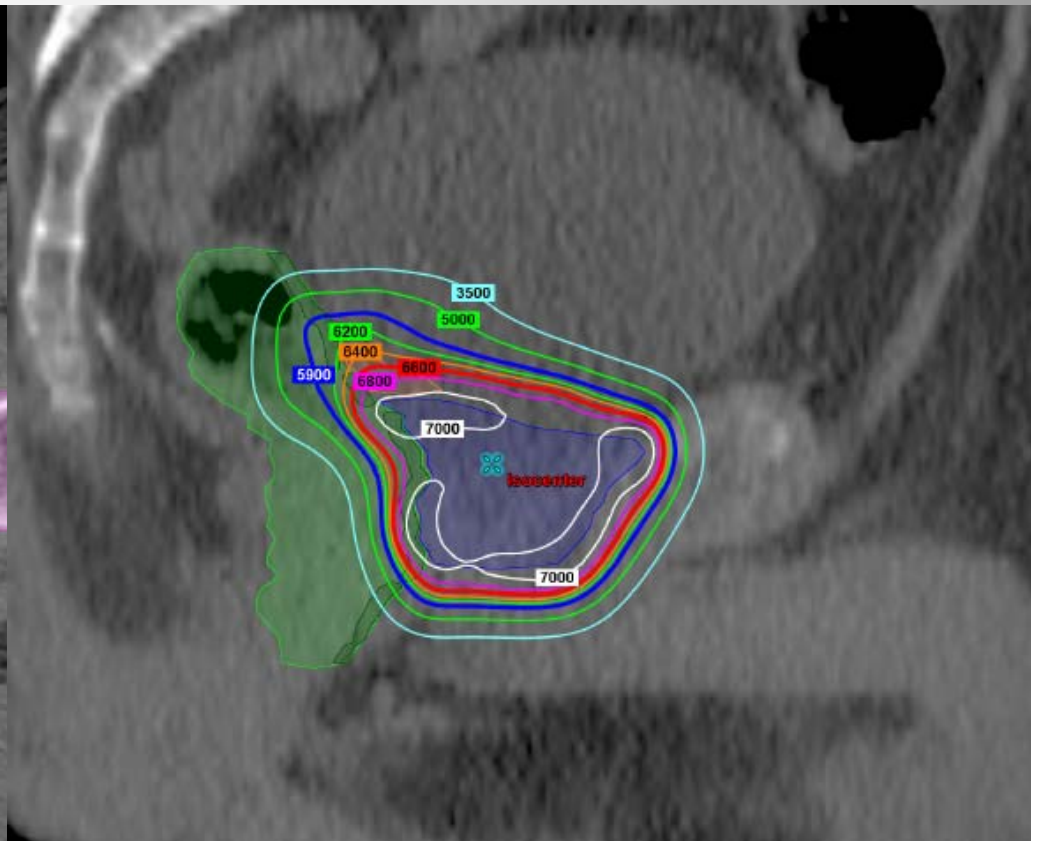
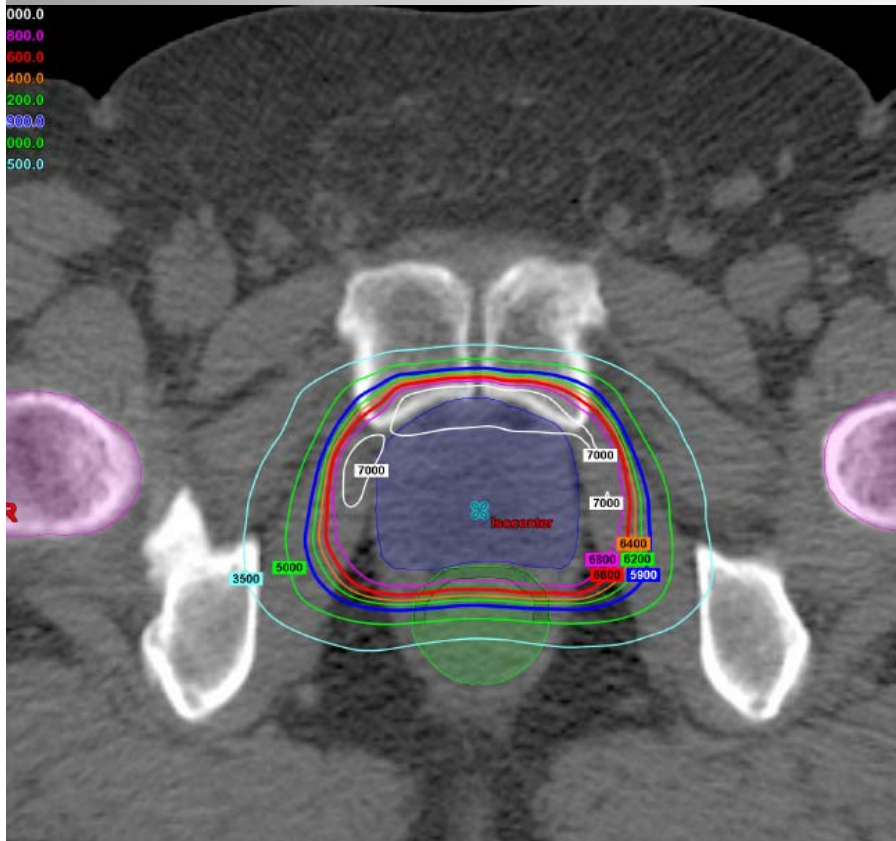
# Postop w/ SFUD

## Especially after Robotic-assisted LRP\*



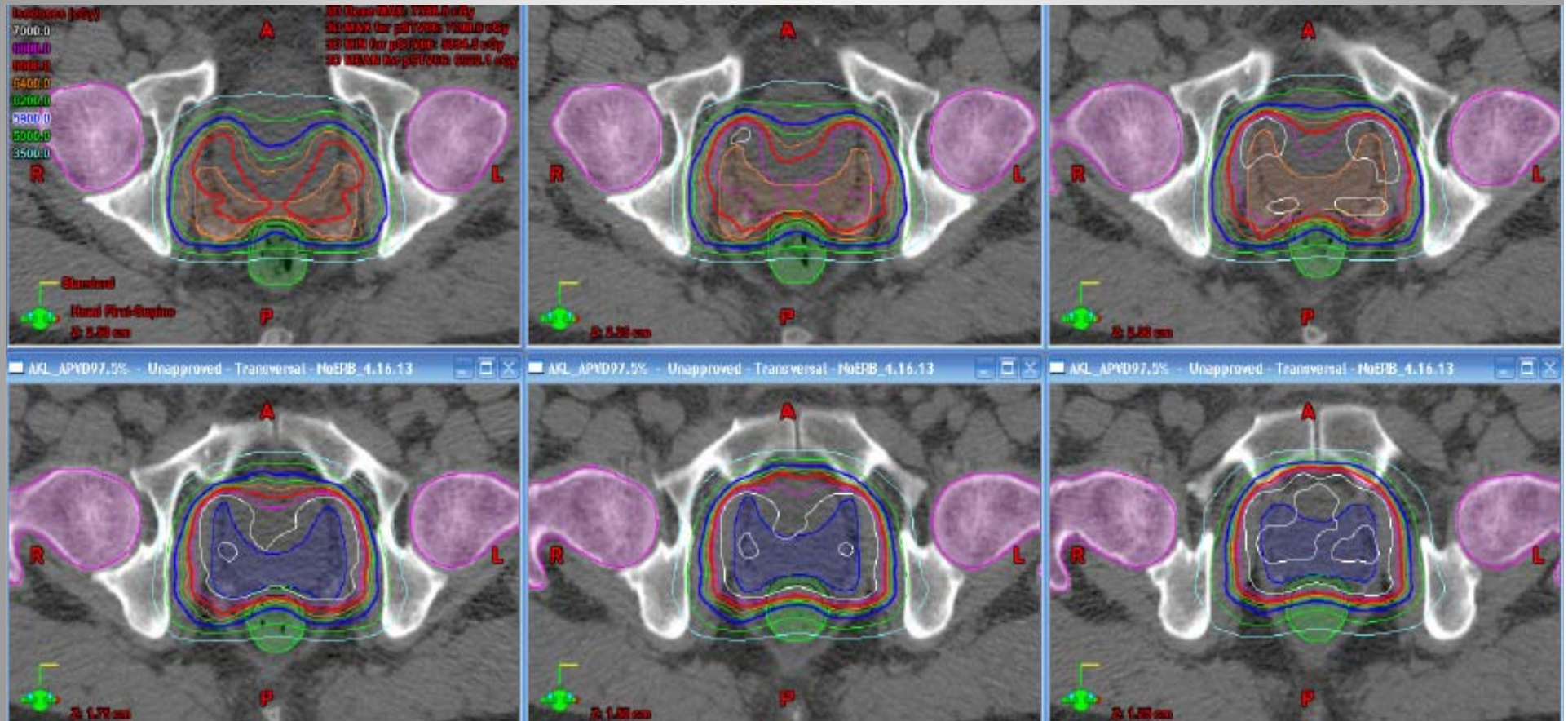
\*RALRP tends to use plastic surgical clips

# Postop w/ no ERB



# Concomitant boost w/ SFUD:

Postop 66 GyE (red) to Prostate bed  
SV beds concurrently 60 GyE (blue)



# Take home points

- Higher radiation doses yield higher PSA control rates
- Do not use too tight of a margin
- Proactively position the patient and target
  - Minimize inter- and intra-fraction variation
- Opposed lateral beams are relatively forgiving
- Do not treat more of seminal vesicles than needed



# **Radiation therapy for seminoma**

# Role of RT

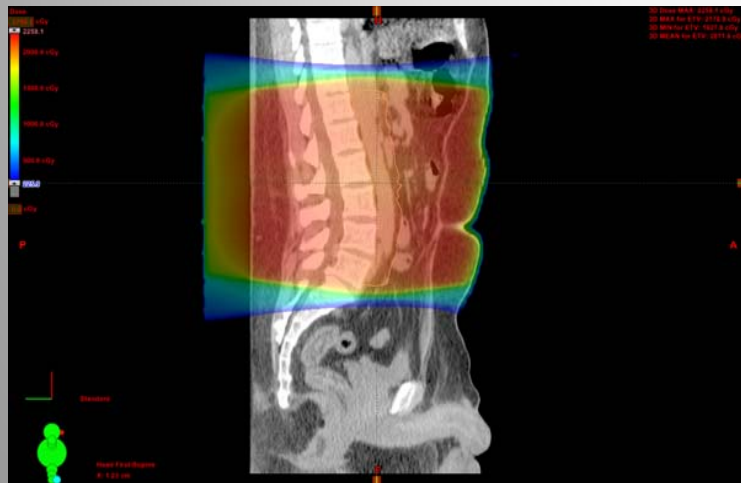
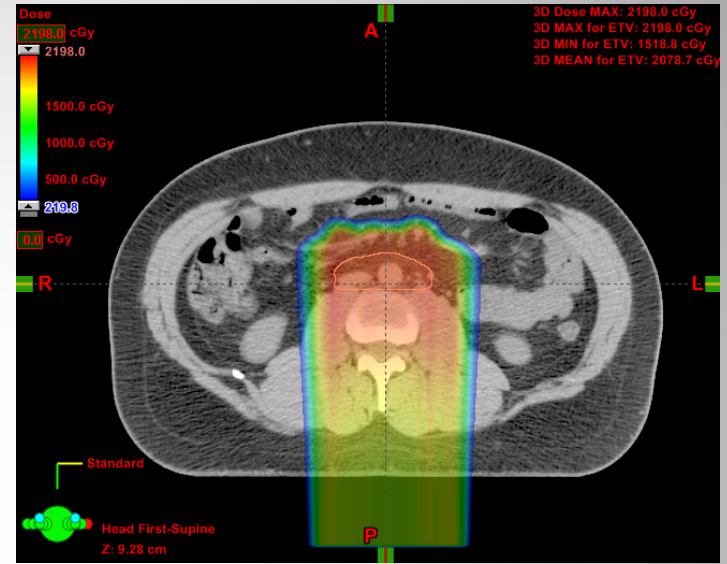
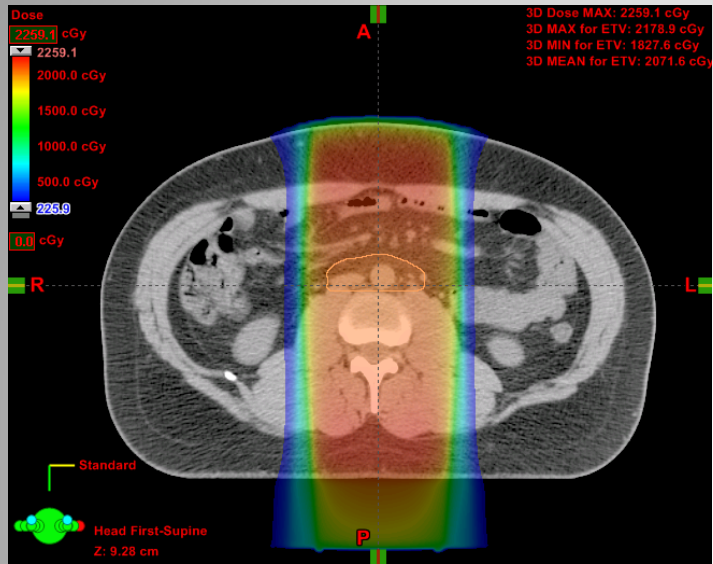
- Adjuvant for stage I (para-aortics LN)
- Adjuvant for stage II (para-aortics + pelvis)
  
- Consolidative post-chemo
- Salvage after chemo
- Palliative
  
- **Define CTV (not just vessels) and margins**

# Therapy after orchiectomy

- Stage I
  - XRT (20 Gy) from ~T12-L5 (inclusive)
  - Observation (size, rete testis+, age)
  - Carboplatin
- Stage II
  - XRT (20Gy → 6-8 Gy boost)
  - Chemotherapy for bulky disease >5cm

# AP/PA X-rays

# PA Protons



## MDACC recommendations for stage IIA/B

- PA + Pelvic (inferior border @ acetabulum)
  - PA field: T12-L5 inclusive (include thoracic duct)
- 20 Gy to elective sites
- Boost gross disease w/ additional 6-8 Gy
- I try to use protons instead of x-rays

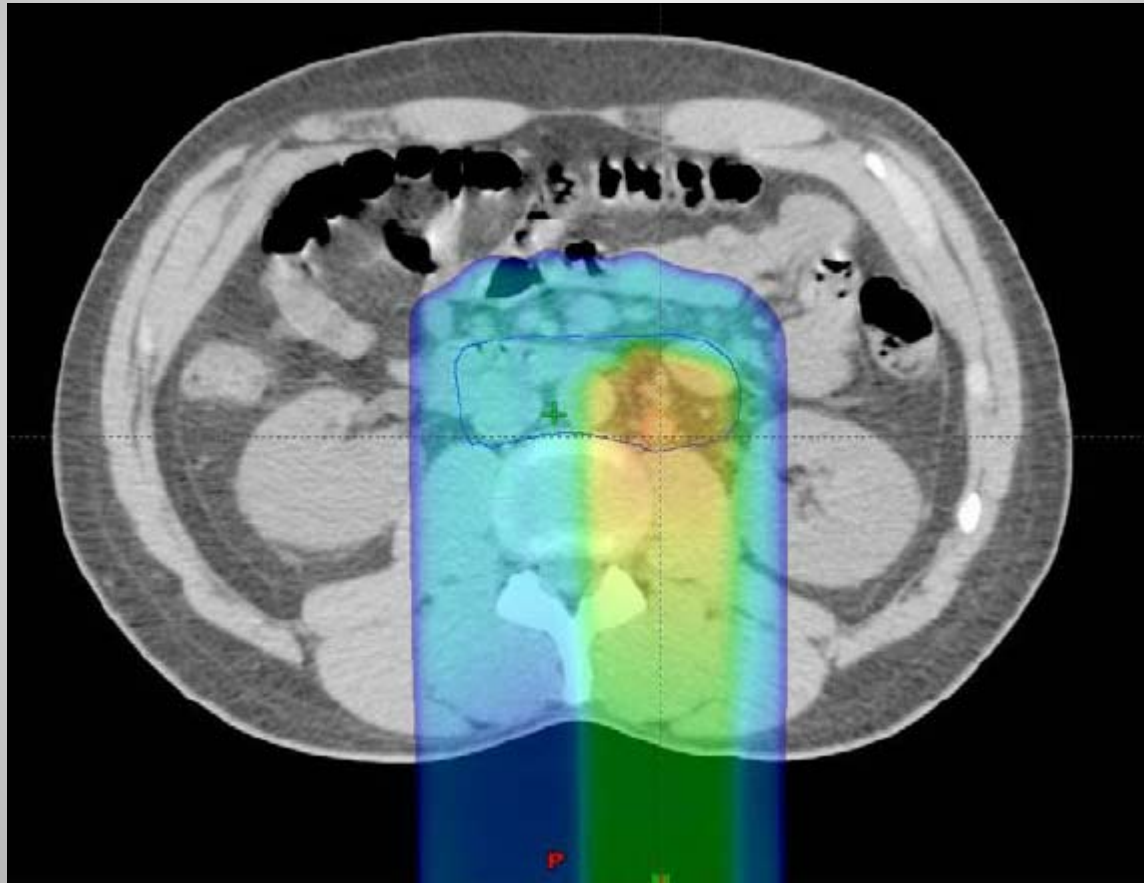
# RT field for CS IIA/B seminoma

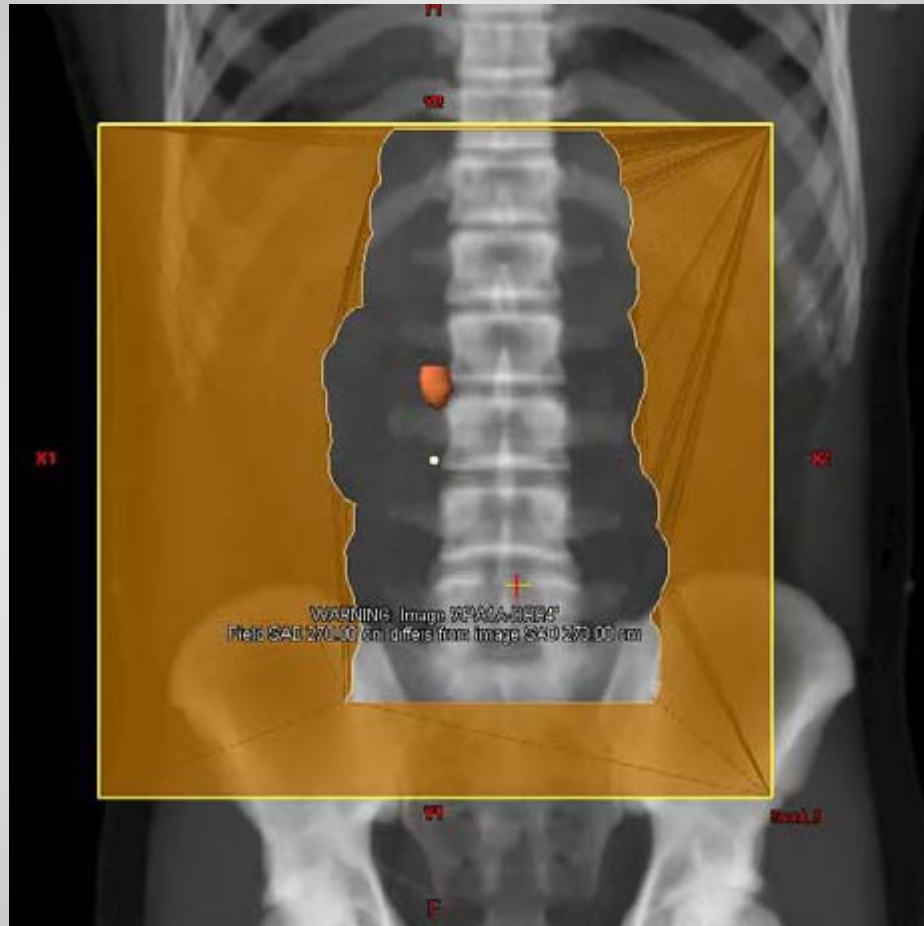


Inferior border  
used to be mid-  
obturator foramen  
until Classen et al.  
J Clin Oncol  
2003;21

\*\*Int J Radiat Oncol Biol Phys 83(4); 2012

# Posterior field for PA nodes

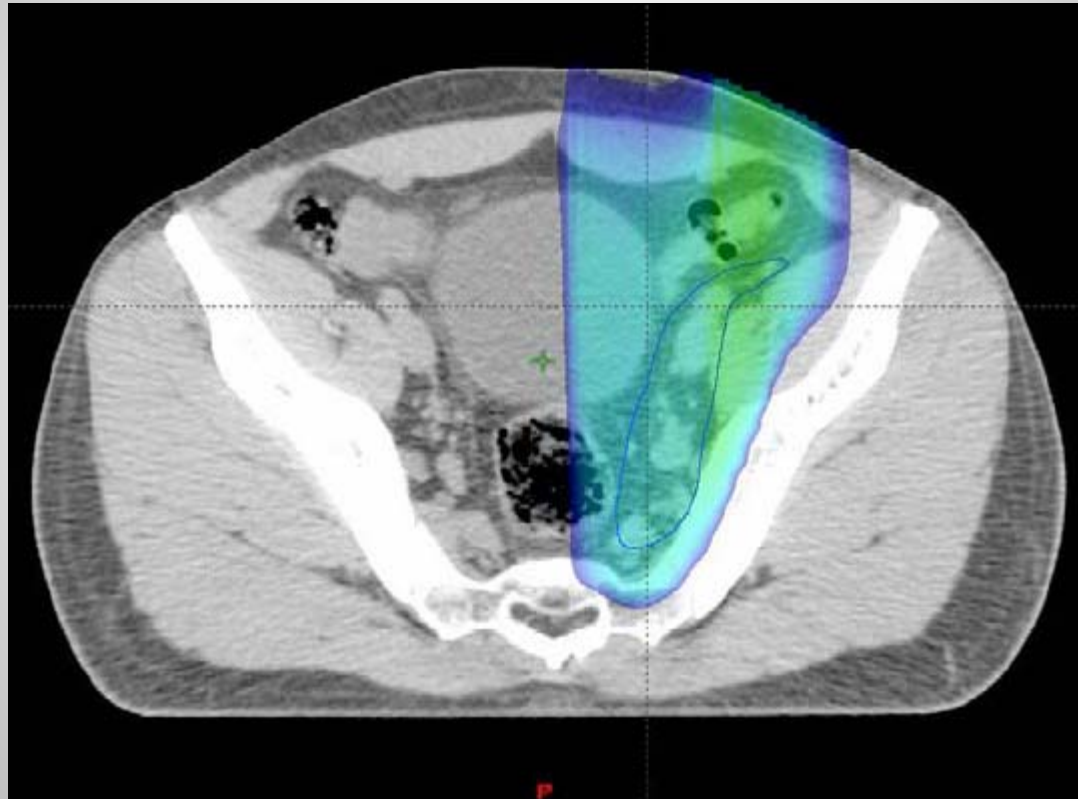


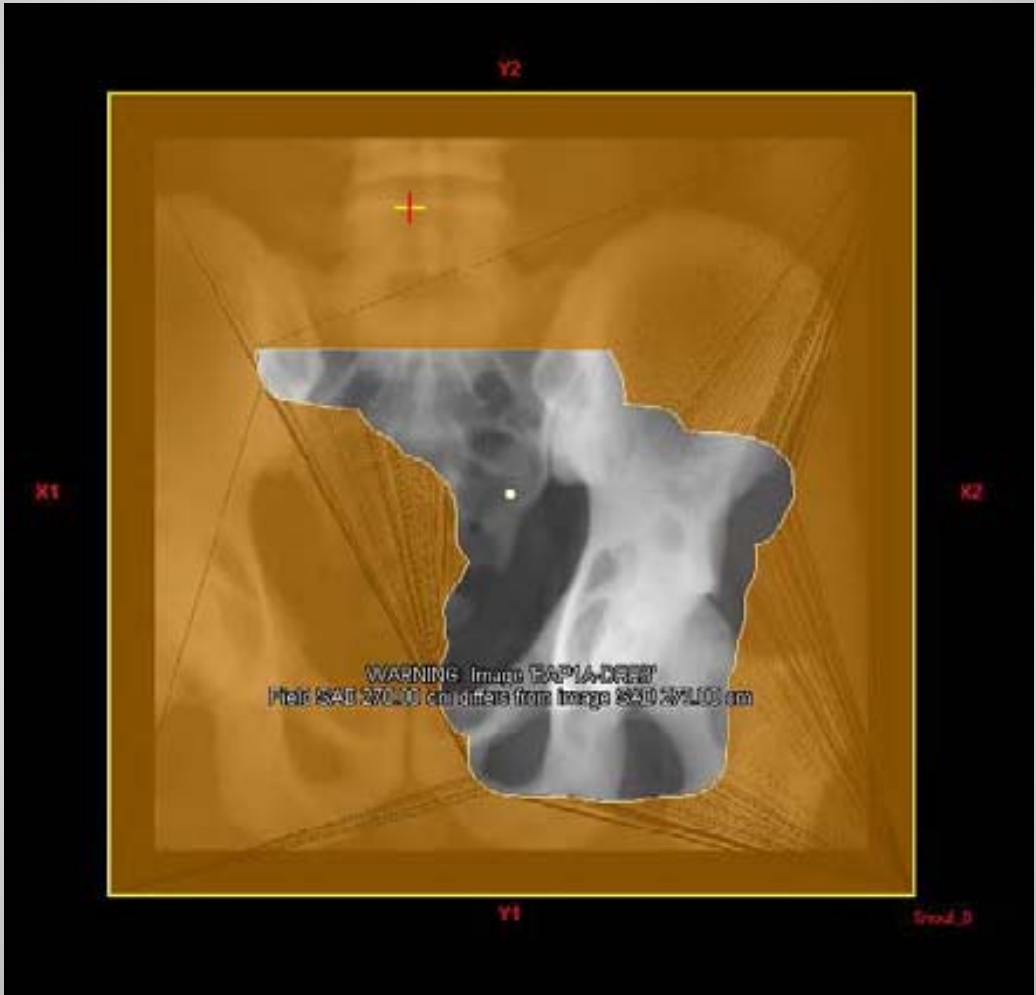




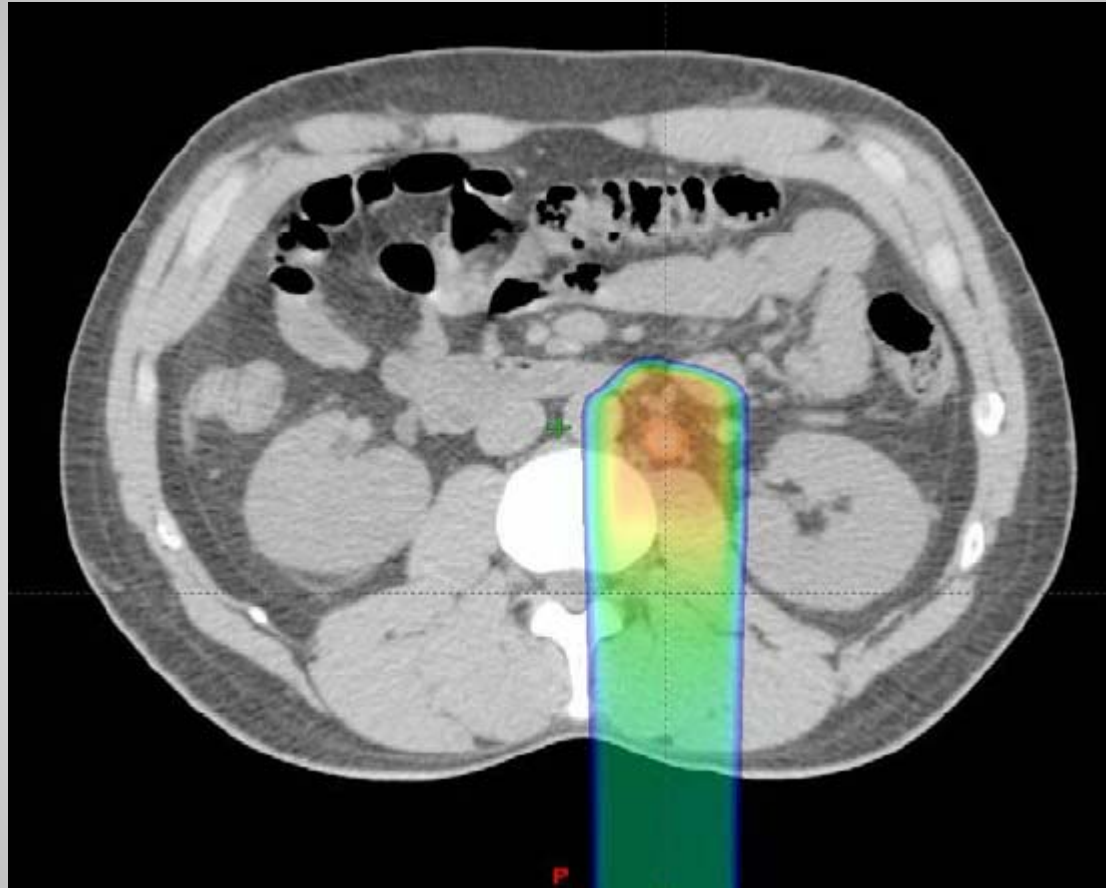
# AP field for pelvic nodes

Usually one junction shift w/ para-aortic field



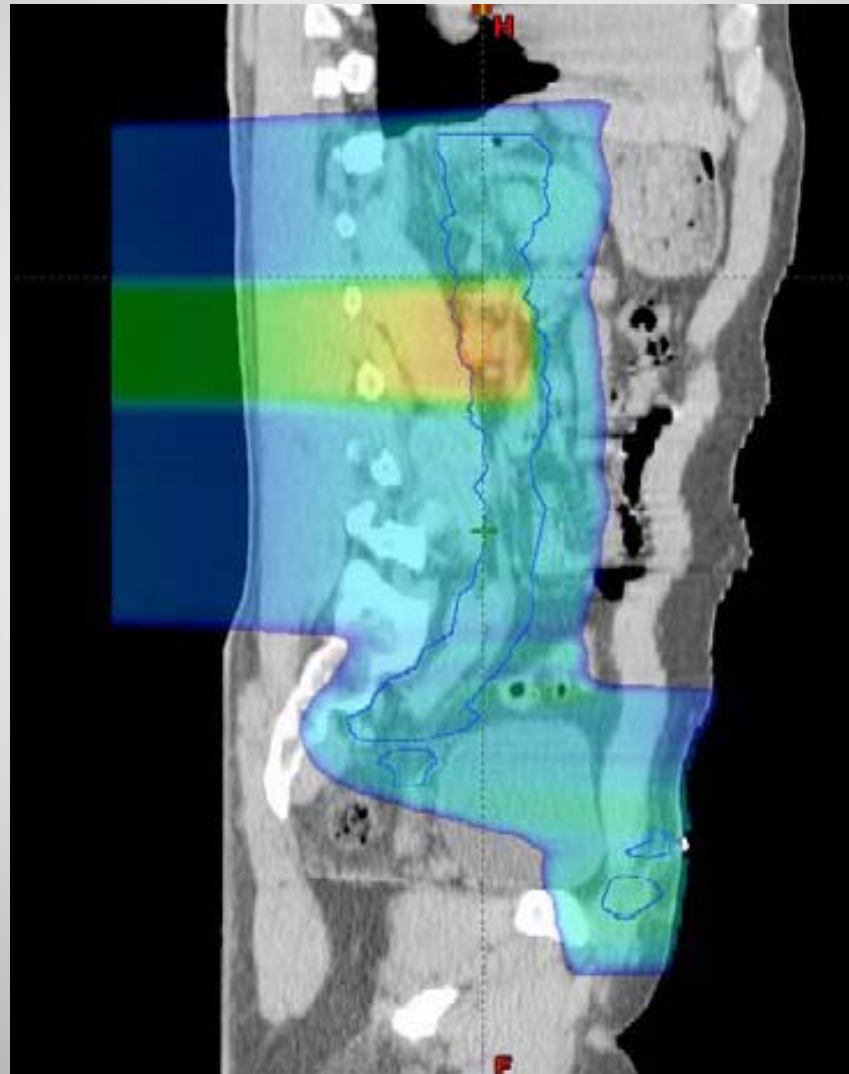


# Boost





# Composite plan



# Protons for Bladder Cancer

- In U.S., mostly transitional cell carcinoma
- Cystectomy +/- chemoRx most common Rx
  - Cystectomy is a big operation!
  - Overall survival similar to Chemo-RT
- Define intent of therapy
  - Bladder preservation
  - Non-surgical candidate
  - Palliative

# Protons for Bladder Cancer

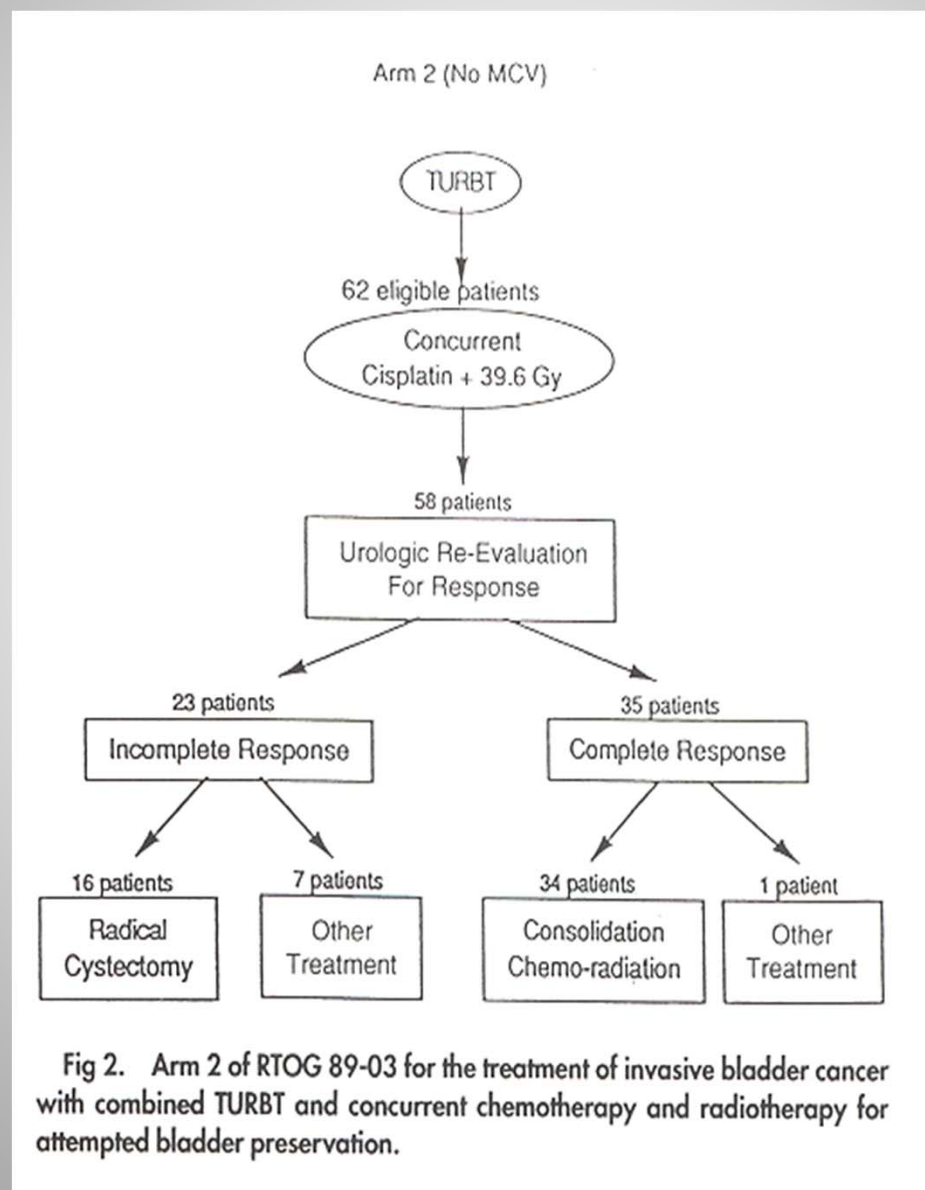
- Defining target
- Primary advantage may be to spare normal bladder tissue for boost
- Daily bladder filling/position needs to be verified
- Potential role of volumetric imaging

# Radiation for muscle invasive

- T<sub>a</sub> non-invasive papillary tumor
- T<sub>is</sub> In-situ ca (flat tumor, may extend)
- T<sub>1</sub> Sub-epithelial connective tissue
- T<sub>2a</sub> Inner half of muscle layer
- T<sub>2b</sub> Outer half (deep muscle)
- T<sub>3a,b</sub> Perivesical fat (micro, macro)
- T<sub>4a,b</sub> Other adjacent structures



# RTOG 89-03: Bladder preservation 64.8 Gy + cisplatin



Maximal TURBT  
w/ Bladder map



CDDP + RT  
**Low pelvis 39.6 Gy**



After 4 weeks..  
Evaluate response  
EUA, Cysto + bx,  
Cytology



If CR, then CDDP +  
**25.2Gy tumor**

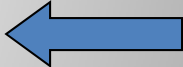


If <CR, then  
cystectomy



# Long-term MGH experience

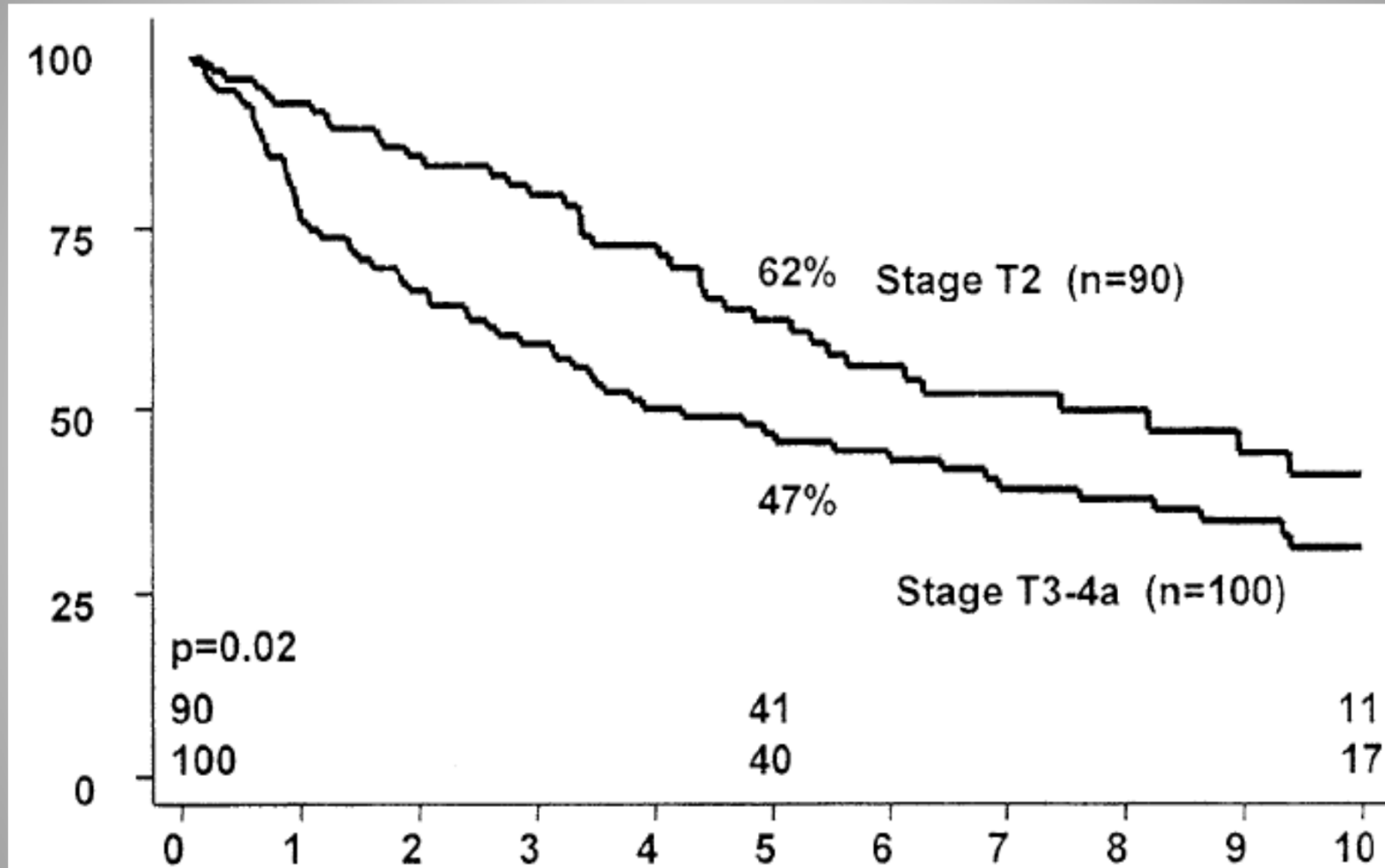
## [Urology 2002]

	<u>5 year</u>	<u>10 year</u>	
Actuarial OS	54%	36%	
DSS	63%	59%	
DSS w/ bladder	T2 57% T3-4 35%	T2 50% T3-4 24%	

Pelvic failure rate 8.4%

Not all relapses are muscle invasive!

## Overall survival: T2 better than T3-4



# Mid treatment re-evaluation for bladder preservation

- After ~40 Gy and 4 week break
- Examine under anesthesia
- Cystoscopy w/ tumor-site biopsy
- Urinary cytology
  
- If any of the above is positive, then cystectomy (unless non-CIS  $\leq$  T1 disease)

# Erlangen protocol

- Higher RT dose (45-50Gy) prior to re-evaluation
- Concurrent CDDP +/- 5-FU
- Dose depends upon level of TURBT
  - 45-50 Gy to slightly larger pelvic field
  - Immediate boost to entire bladder
  - **54Gy** for R0, **59.6Gy** for R1/2
  - Re-evaluation after 4-6 weeks
- Theoretical advantages to either technique
- Overall results similar

# Traditional XRT technique

- Target is bladder w/ true pelvic LN's
- 4 field with higher energy preferred
- Small pelvic field (40-50Gy)
- Boost field (64-70Gy)
- Bladder mapping & examine under anesthesia

**CYSTOSCOPY REPORT FORM**

PATIENT NAME \_\_\_\_\_ UNIT # \_\_\_\_\_

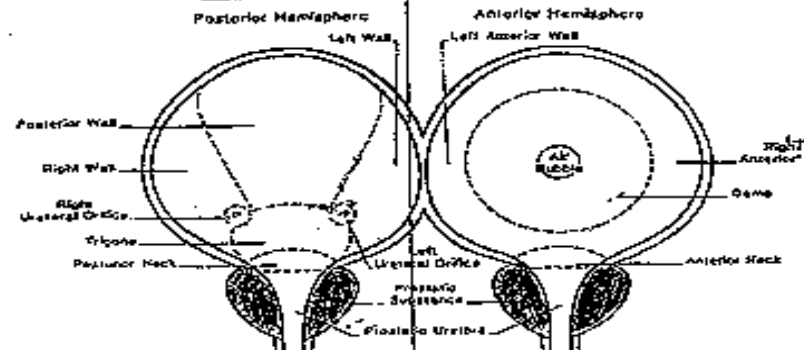
CYSTOSCOPY DATE \_\_\_/\_\_\_/\_\_\_ SURGEON \_\_\_\_\_

Specify location/origin of primary (at cysto or TURB) \_\_\_\_\_

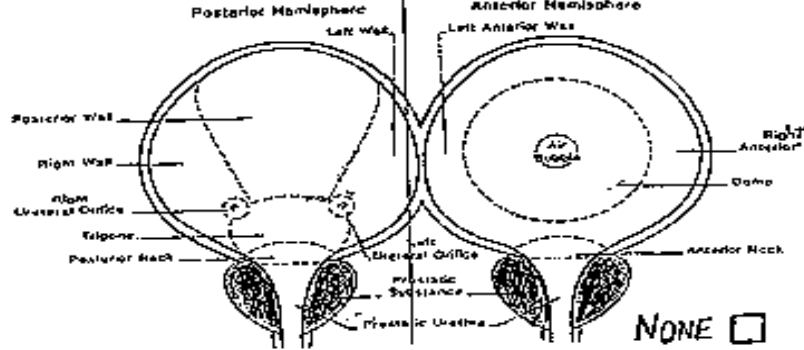
- Visibly complete TURB? Yes \_\_\_ No \_\_\_
- Palpable mass or induration persists after TURB? Yes \_\_\_ No \_\_\_
- Initial largest tumor (diameter): ≤1 cm \_\_\_ 1.1-2.9 cm \_\_\_ 3-4.9 cm \_\_\_ ≥5 cm \_\_\_
- Does tumor invade prostate or vagina? Yes \_\_\_ No \_\_\_
- Is tumor fixed to pelvic/abdominal wall? Yes \_\_\_ No \_\_\_

PLEASE COMPLETE THE FOLLOWING TWO DIAGRAMS:

**A. TUMOR LOCATION BEFORE TURB**



**B. POST-TURB: IF MACROSCOPIC TUMOR REMAINS AT END OF PROCEDURE, INDICATE ITS LOCATION. IF NOT, CHECK "NONE."**

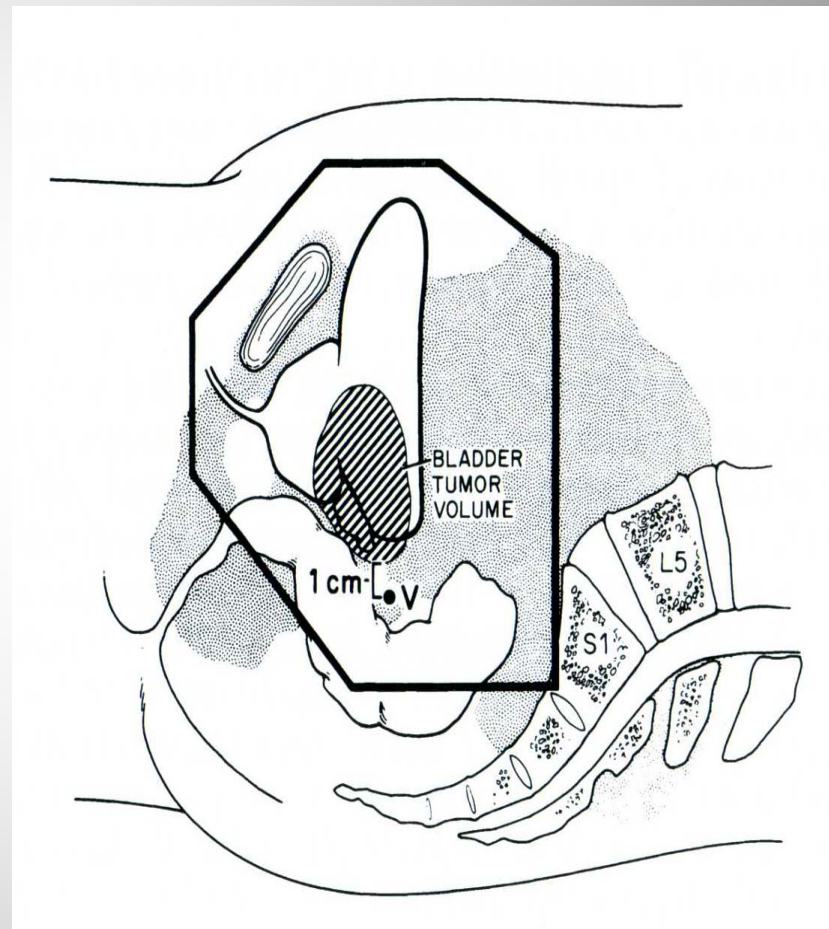
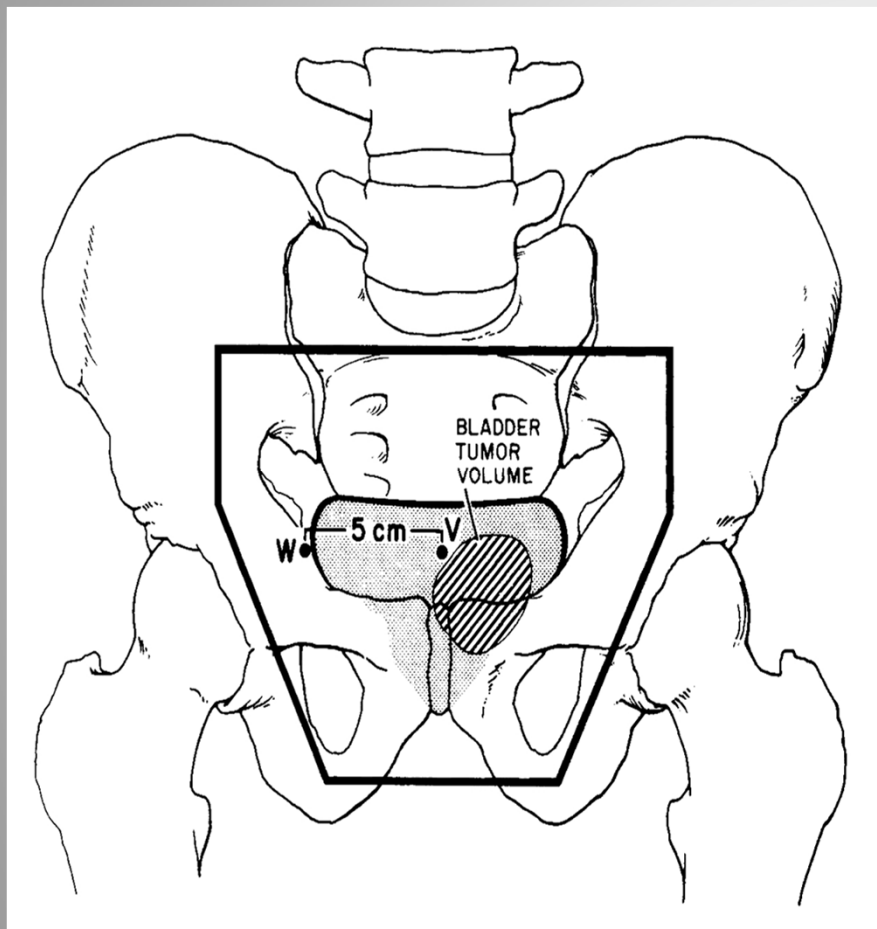




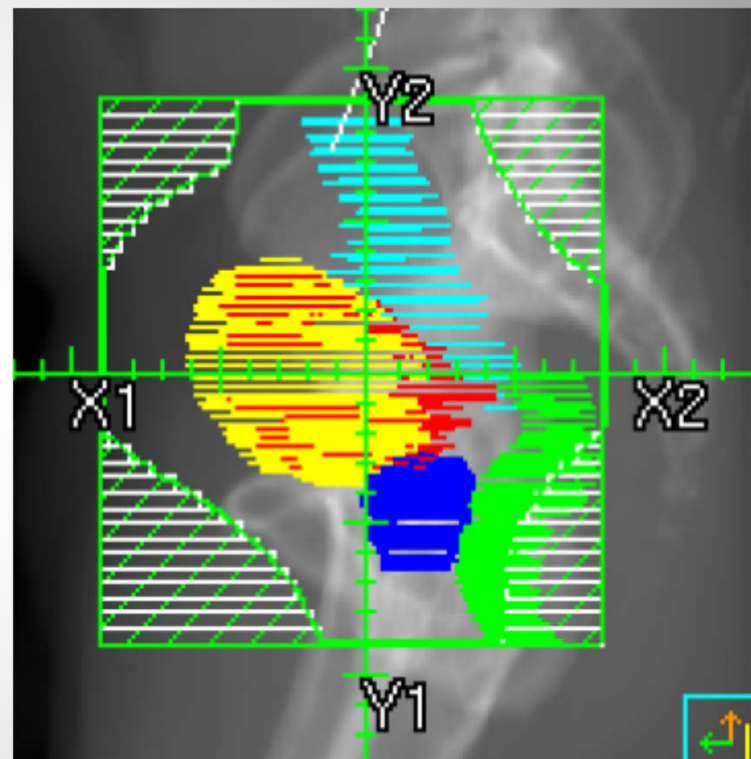
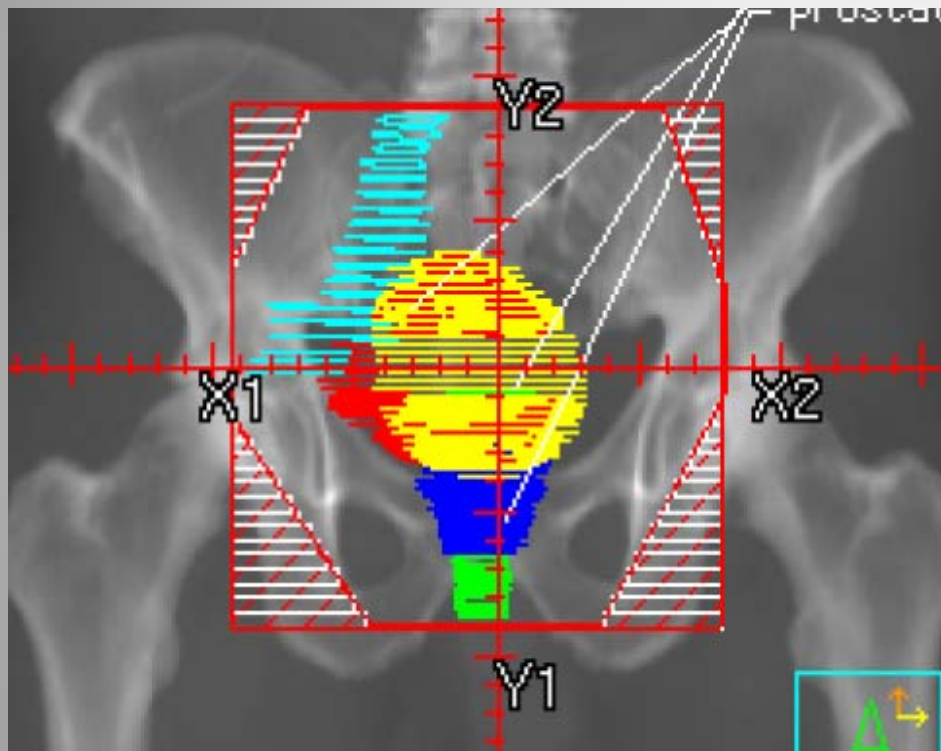
# Small pelvic fields-AP/PA

- Target is tumor, bladder, proximal urethra (male entire prostatic urethra) and first LN's (nodes below bifurcation of int-ext iliacs)
- Superior                      Mid-SI (S2-S3 junction)\*
- Inferior                        Bottom obturator foramen
- Lateral                         1.0 cm (1.5) on pelvic brim  
Block femoral heads

# MGH/RTOG Pelvic fields



\*Spare small bowel for urinary diversion/reconstruction



# UK BC 2001 trial

(James et al. NEJM 2012; 366)

- N=T2-4a bladder Ca (various histologies)
- Phase III 2x2 factorial design:

RT vs. RT + 5-FU/MMC

***Whole bladder RT (+ 1.5 cm) vs. Bladder tumor (+2cm)***

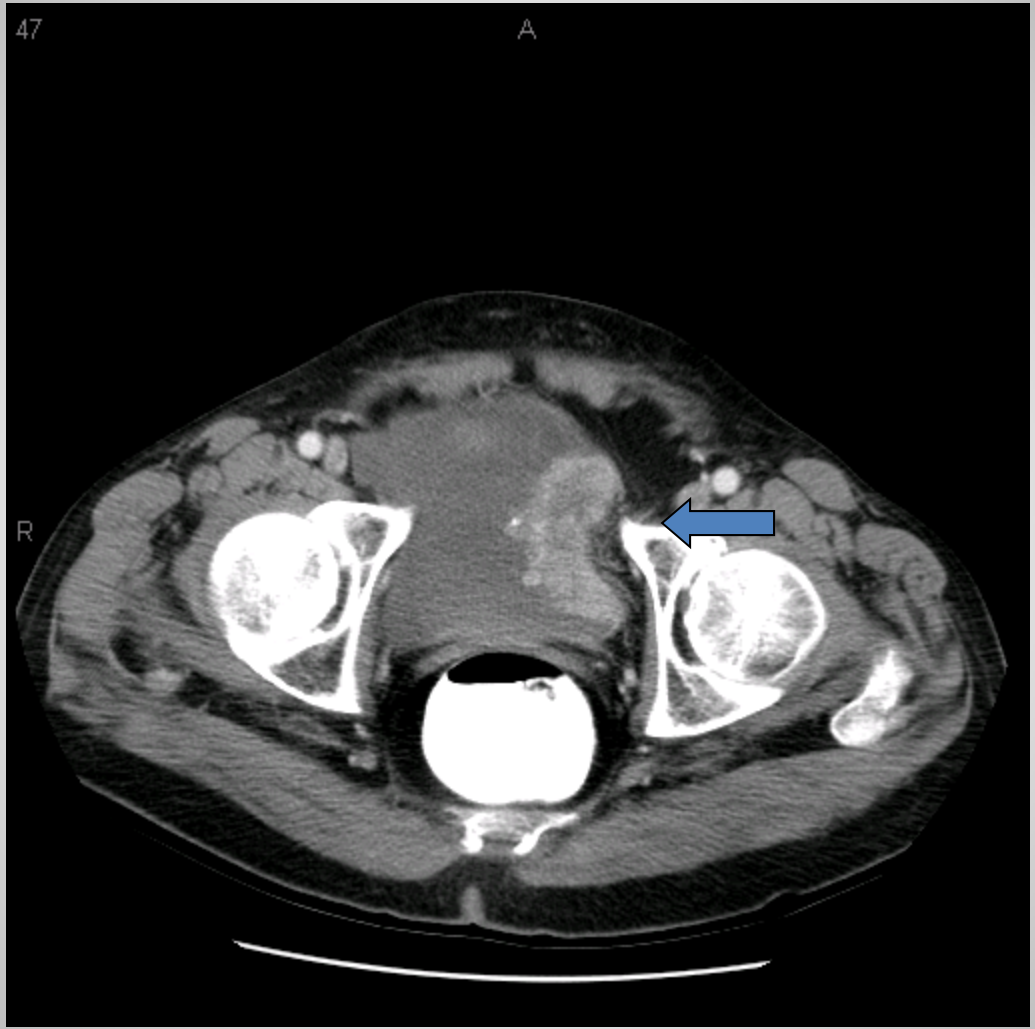
- RT dose either 55 Gy (20 fx) or 64 Gy (32 fx)
- No mid-Rx re-evaluation
- Primary endpoint was Loco-regional DFS
- RT + 5-FU/MMC did better than RT alone

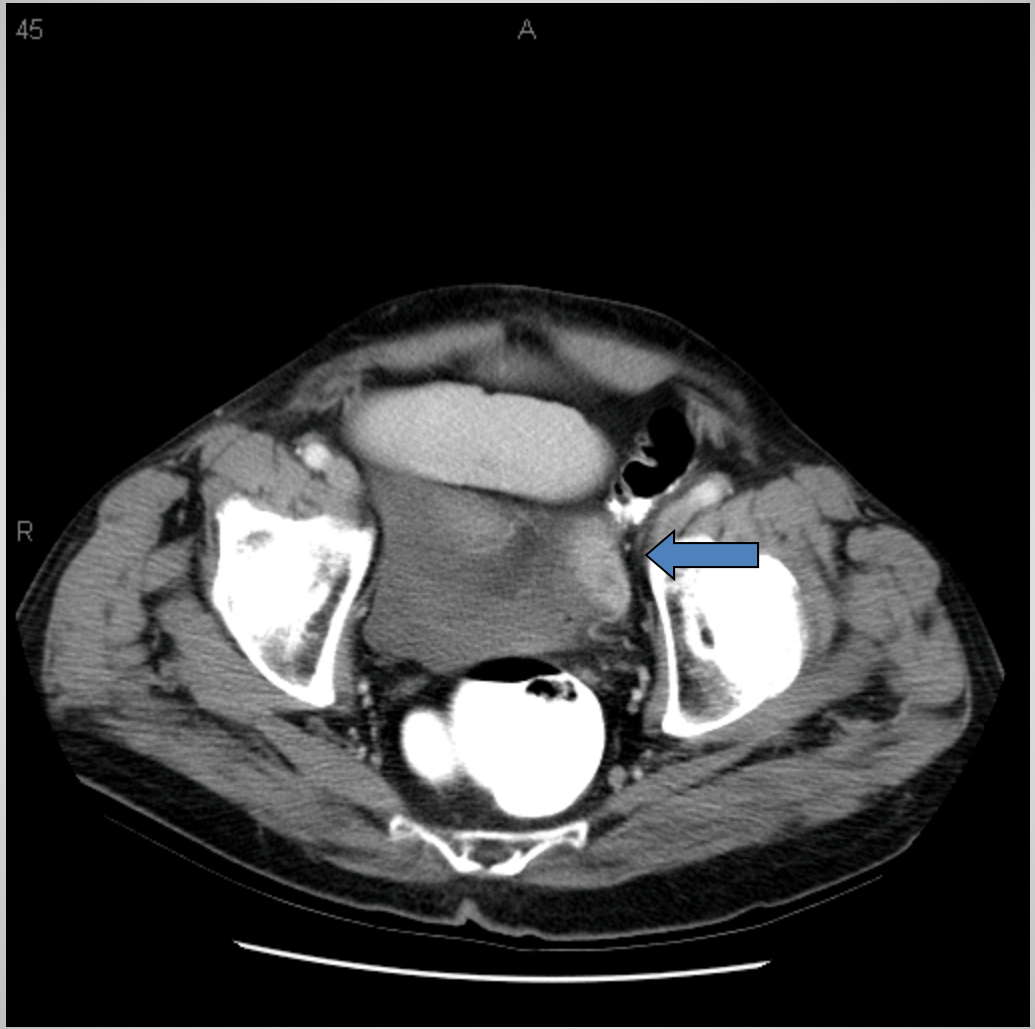
# Empty vs. Full bladder?

- Depends...
- Empty bladder allows for slightly smaller field & likely more reproducible but at potential cost of treating more small bowel
- Full bladder may be better for boost to spare some bladder mucosa

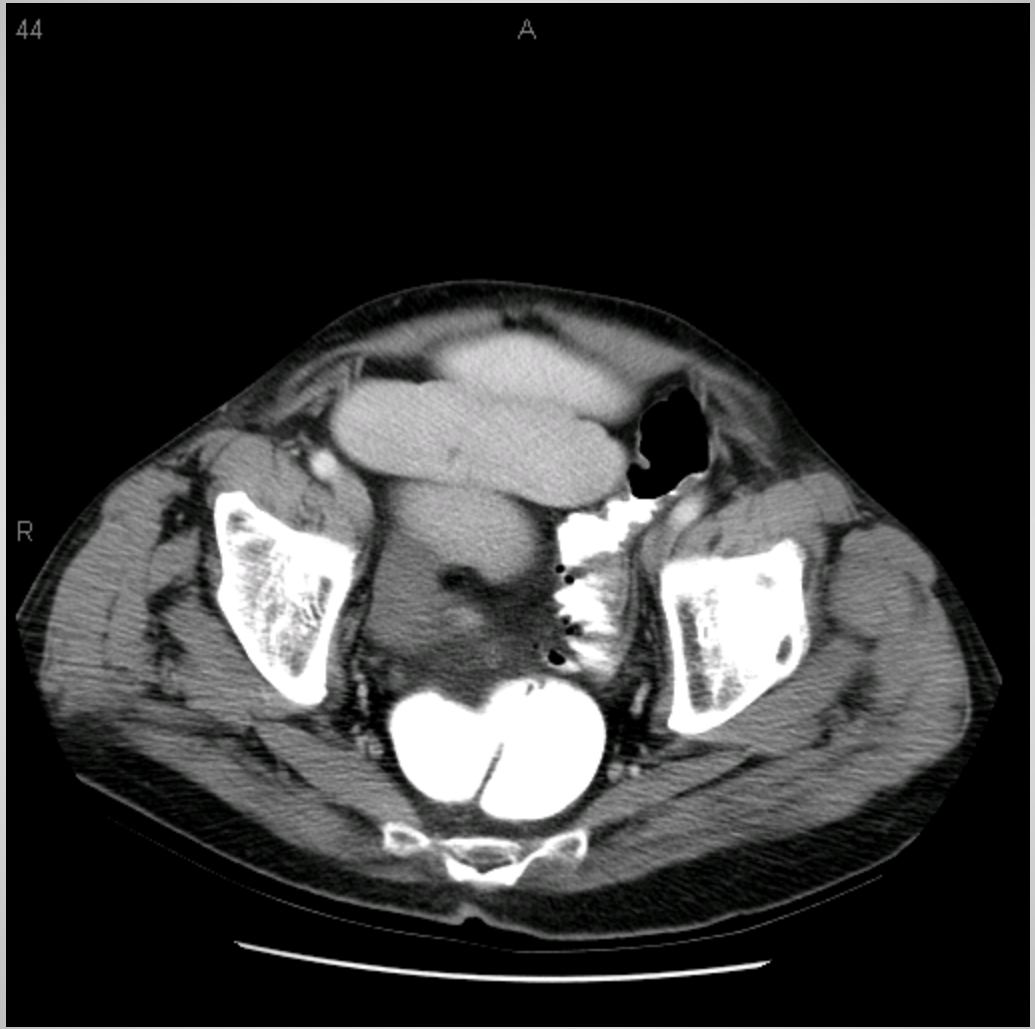
# Location of tumor matters

- Good
  - Bladder neck
  - Lateral
  - Posterior
  - Anterior
- Bad
  - Dome
  - Anything near small bowel





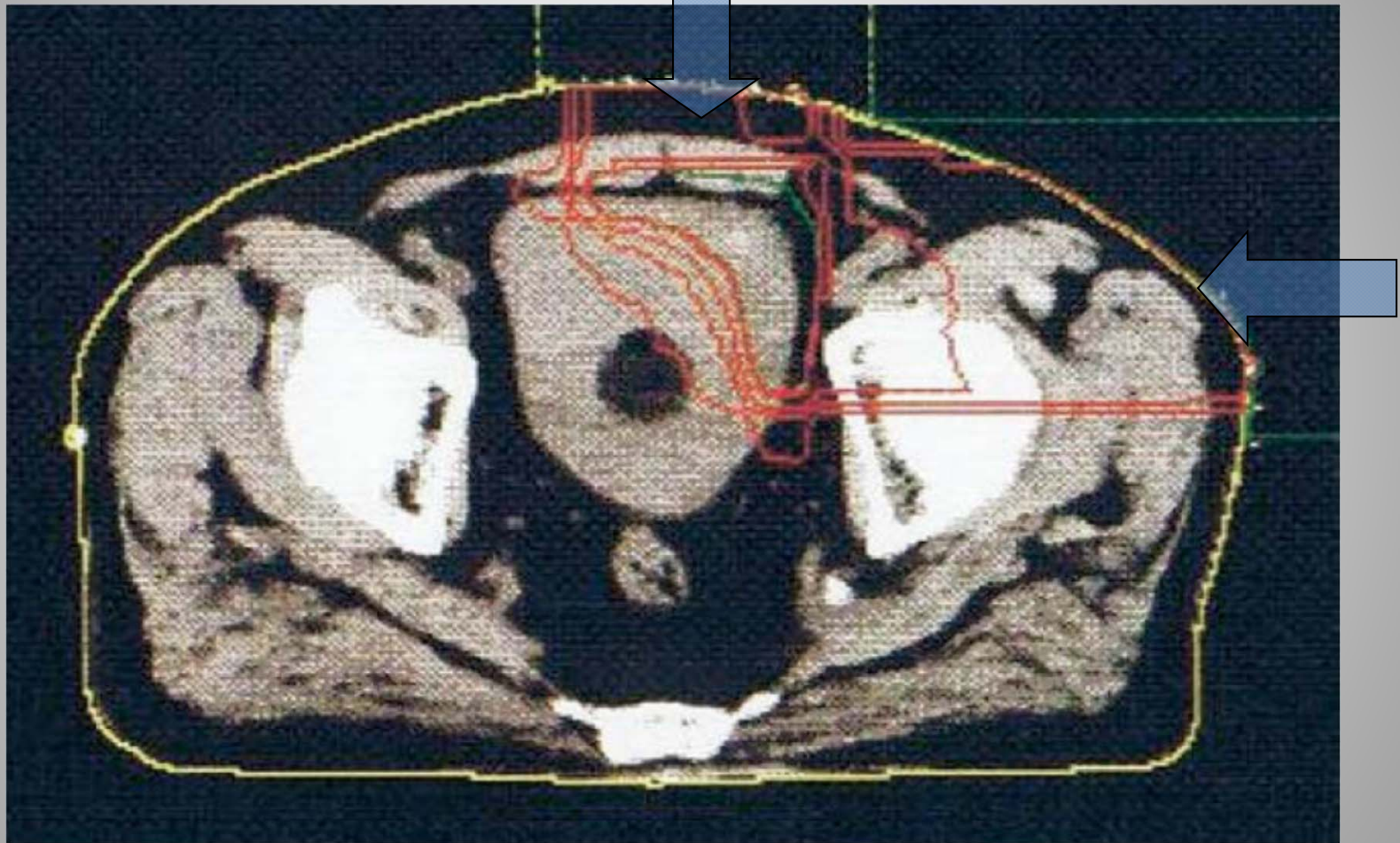




# Proton beam therapy for invasive bladder cancer...M. Hata et al.

- N=25 patients with TCC, T2-3 N0M0
  - TURBT
  - RT + intra-arterial MTX and CDDP
  - Re-evaluation w/ cysto + TURBT
  - IF CR, then proton boost
- 23/25 patients went onto proton boost
- 5y OS 60%      DFS 50%      CSS 80%

# Proton bladder boost (AP and Lt lateral)



Int J Radiat Biol Phys 64, 2006

# Bladder preservation

- GOOD Candidates

- Unifocal w/ no CIS
- < 5cm
- Complete TURBT
- Lower T (T2-3a)
- No hydronephrosis
- Complete response
- 2 hour bladder
- Will come for FU

- “BAD” Candidates

- Multifocal or CIS
- Incomplete TURBT
- T3b-4
- Hydronephrosis
- Incomplete response
- Tumors on dome are challenging

**THANK YOU**

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[TexasCenterForProtonTherapy.com](http://TexasCenterForProtonTherapy.com)