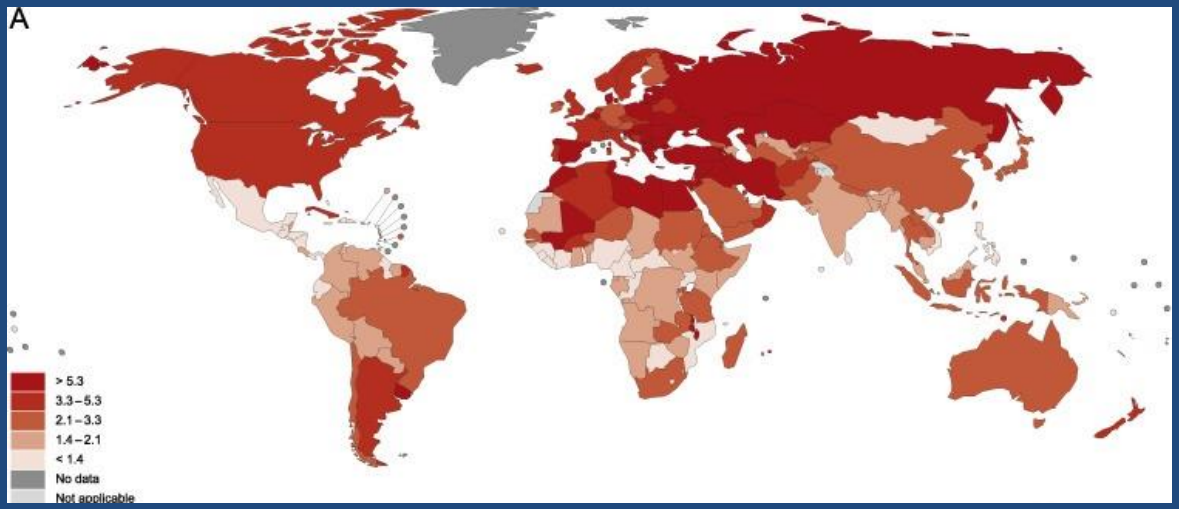
Bladder Cancer

Daniel Gorovets, M.D.
Department of Radiation Oncology
Spring 2025

Etiology and Epidemiology

- 6th most common cancer worldwide



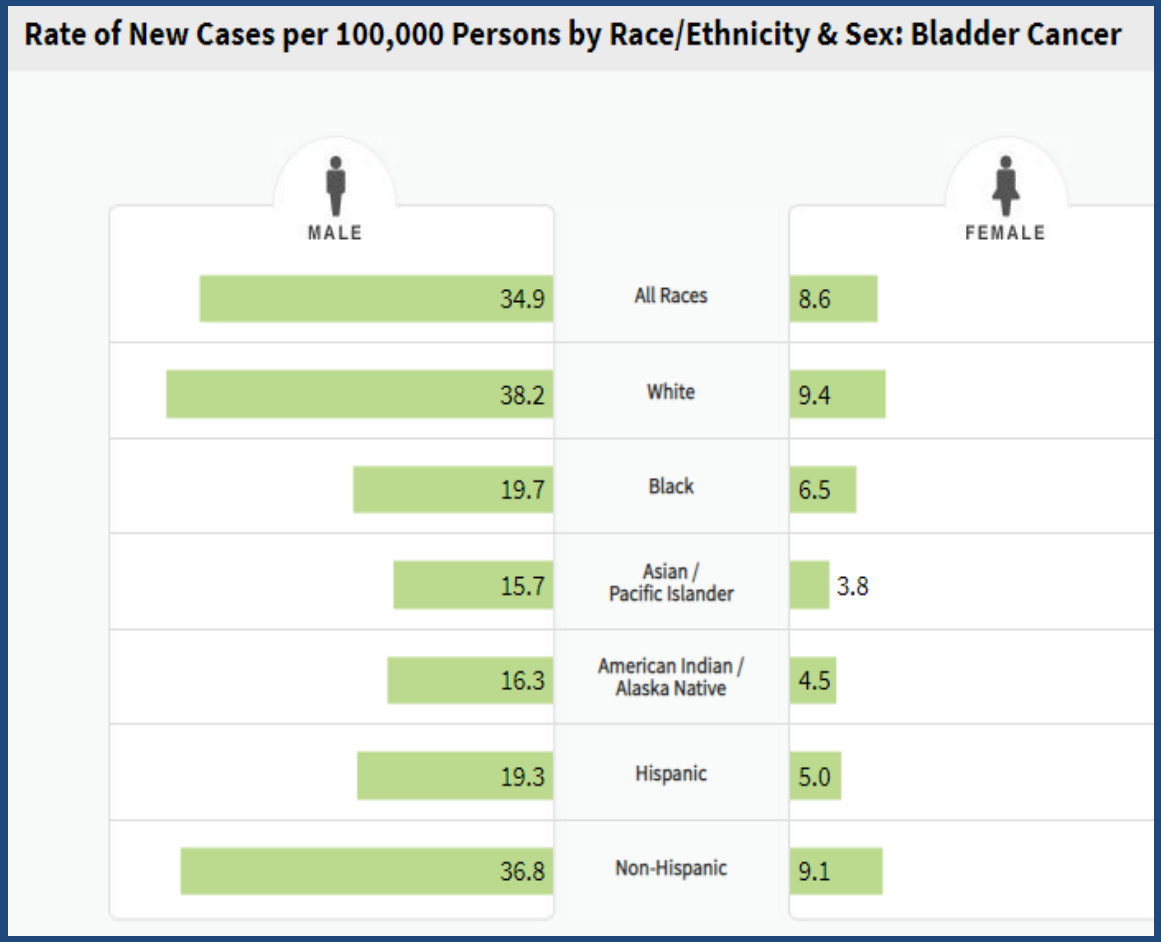
Antoni et al Eur Urol 2017

- Highest frequencies in Europe and N. America
- US:
  - 81,400 estimated new cases in 2020 (4.5% of all new cancer cases)
  - 17,980 estimated deaths
  - Highest incidence in Northeast (lowest in Hawaii and Utah)!

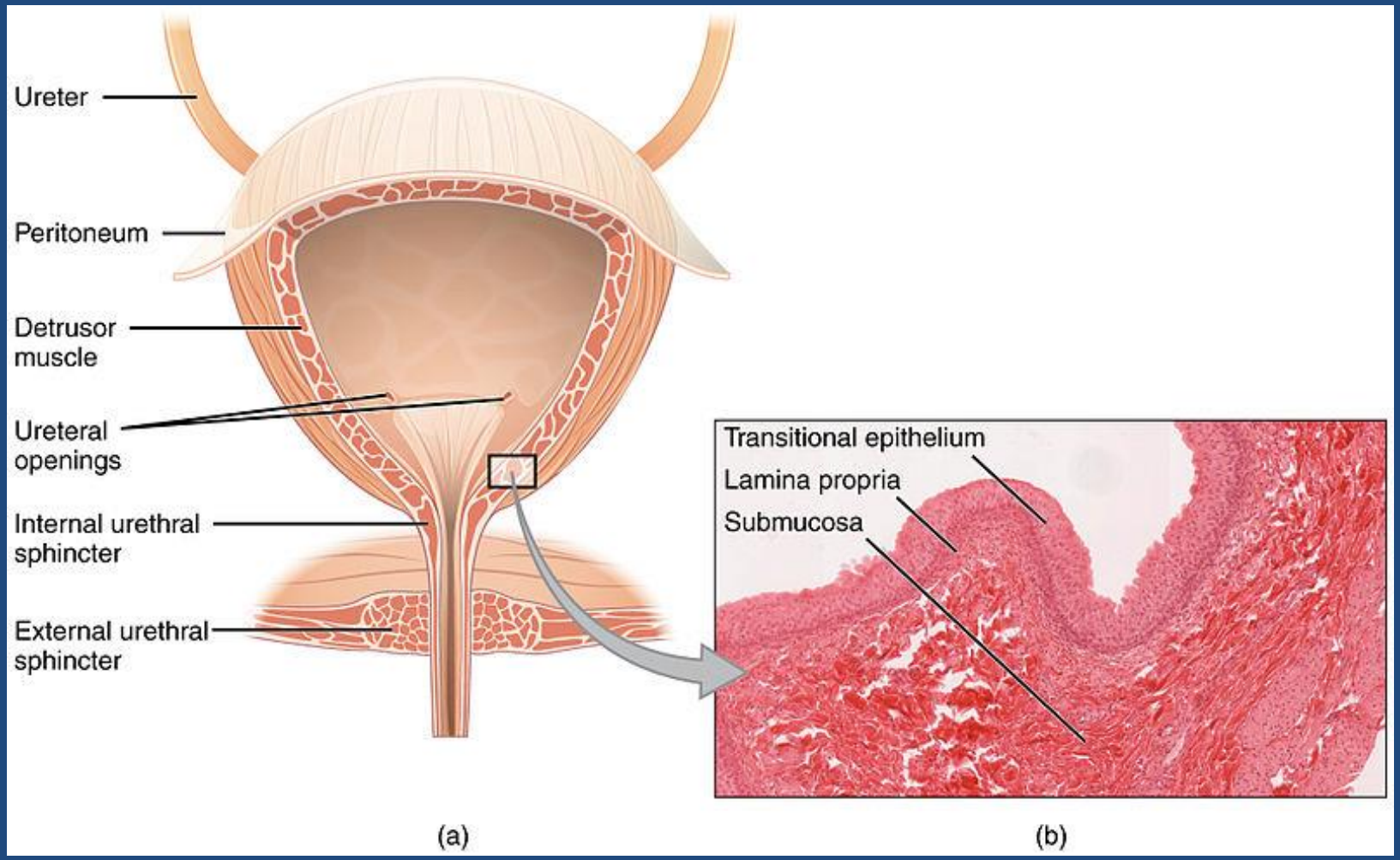
Epidemiology

- Male:Female 3:1
- White: Black 2:1

- Avg age= 73 (90% >55)



SEER 2013-2017, age adjusted


Ureter
Peritoneum
Detrusor muscle
Ureteral openings
Internal urethral sphincter
External urethral sphincter
Transitional epithelium
Lamina propria
Submucosa
(a)
(b)

Risk Factors

- Tobacco smoking
  - Single most important risk factor
  - 60 known carcinogens in tobacco smoke
  - 3-4 fold higher risk of bladder cancer smoker vs never smoker
  - Extent of smoking correlates to cancer stage
  - Smoking cessation decreases but does not eliminate risk



Risk Factors

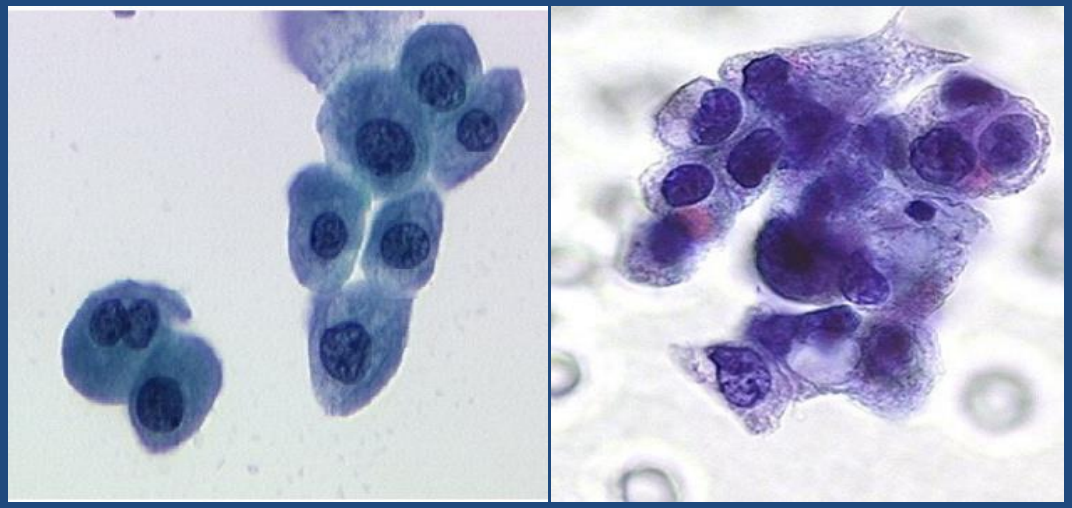
- Chronic irritation (S. haematobium, chronic cath etc)
- Congenital anomalies (extrophy, urachal remnant)
- Antineoplastic agents
  - Radiation therapy- 1.5-4 fold- latency 5-10yrs
  - cyclophosphamide- acrolein inactivated by MESNA
- Occupational chemical exposure
  - polycyclic aromatic hydrocarbons (PAH)- paint, plastics, leather, rubber, metal workers, miners, firefighters
  - diesel exhaust- trucking
  - Hair dye- hairdressers, barbers (not personal users ☺)
- Drinking water
  - Chlorination byproducts (trihalomethanes)
  - arsenic contamination
- History of upper tract cancers
- Genetic (family history, Cowden disease (PTEN), Lynch Syndrome)
- HPV

Clinical presentation

- Gross, painless hematuria most common
  - Intermittent
  - Throughout micturition
- Irritative voiding symptoms (dysuria, frequency, urgency)
- Pain
  - Flank- could indicate hydronephrosis
  - Suprapubic- perivesical invasion or urine retention
  - Rectal/perineal- local invasion
  - Bone- metastases
- Constitutional
  - weight loss
  - appetite changes
  - fatigue

Diagnosis/workup

- Urinalysis/cytology
  - Need “clean catch” specimen
  - 20% false negative rate
  - 1-12% false positive (<u>better for high grade</u>)
    - Inflammation
    - Prior chemotherapy or radiation



Normal Malignant

Imaging

- CT urogram with chest
- MR urogram

- Bone scan
  - If symptomatic or elevated Alkaline phosphatase

CT urogram



-Primary tumor
-LN involvement
-Upper tract disease







MR urogram

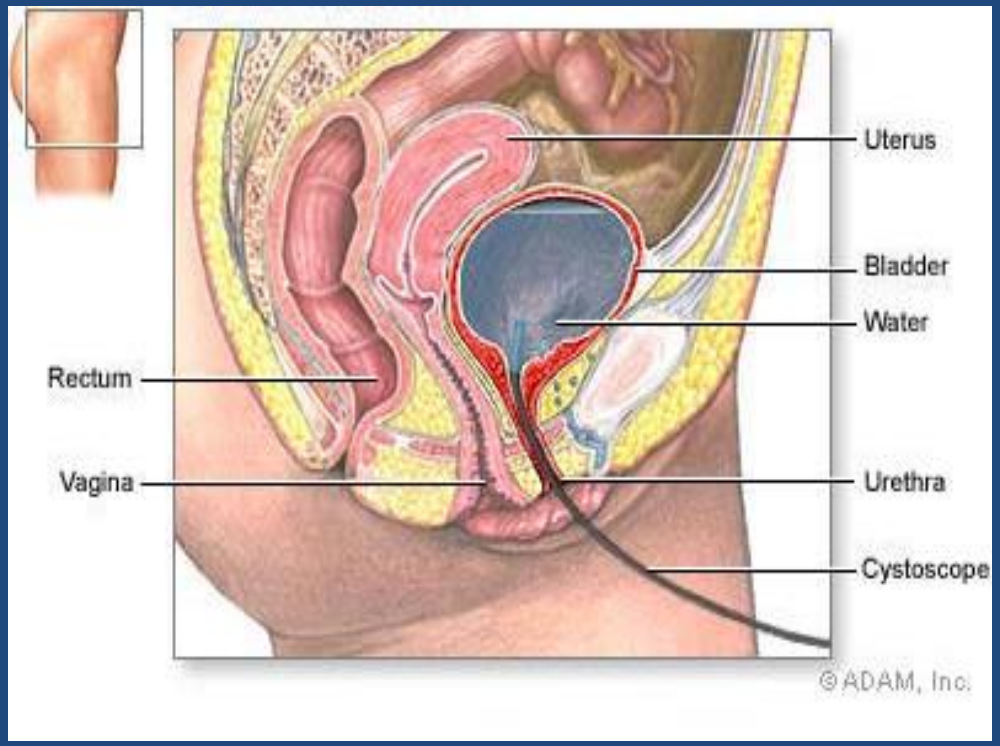


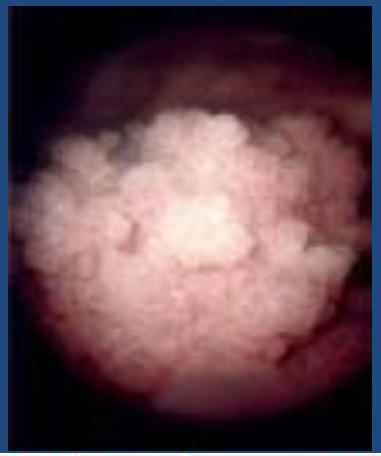


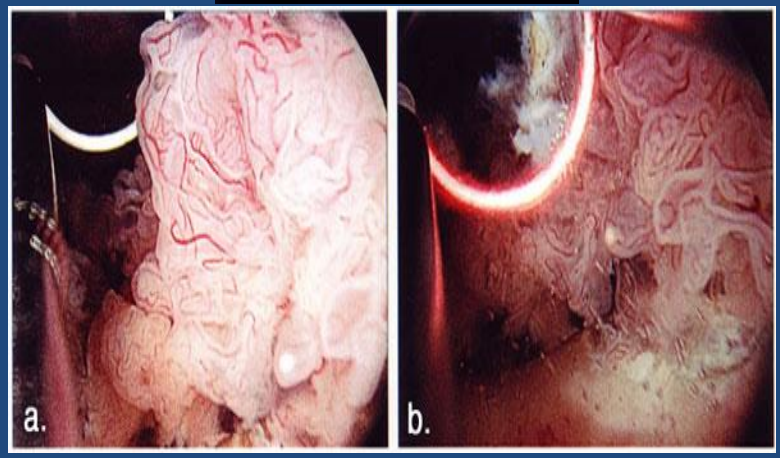
Better tissue plane delineation
Non-nephrotoxic contrast agent

Less efficient
Not as widely used

- **Cystourethroscopy**
  - Bimanual exam under anesthesia
  - Urine obtained for cytology
  - TURBT of visible tumors
  - Biopsy of grossly uninvolved walls (“field cancerization”)
  - Biopsy of prostatic urethra
  - Bladder mapping- note size, #, location







Histology

- ***Urothelial (Transitional) cell carcinoma* (90%)**
  - Squamous differentiation
  - Glandular differentiation
  - Nested
  - Microcystic
  - Micropapillary
  - Lymphoepithelioma-like
  - Lymphoma-like and plasmacytoid
  - Sarcomatoid
- ***Squamous cell carcinoma***
- ***Adenocarcinoma***
  - Nonurachal
  - Urachal
- ***Small Cell***

- ***Other:***
  - Sarcoma
  - pheochromocytoma
  - Lymphoma
  - carcinoid

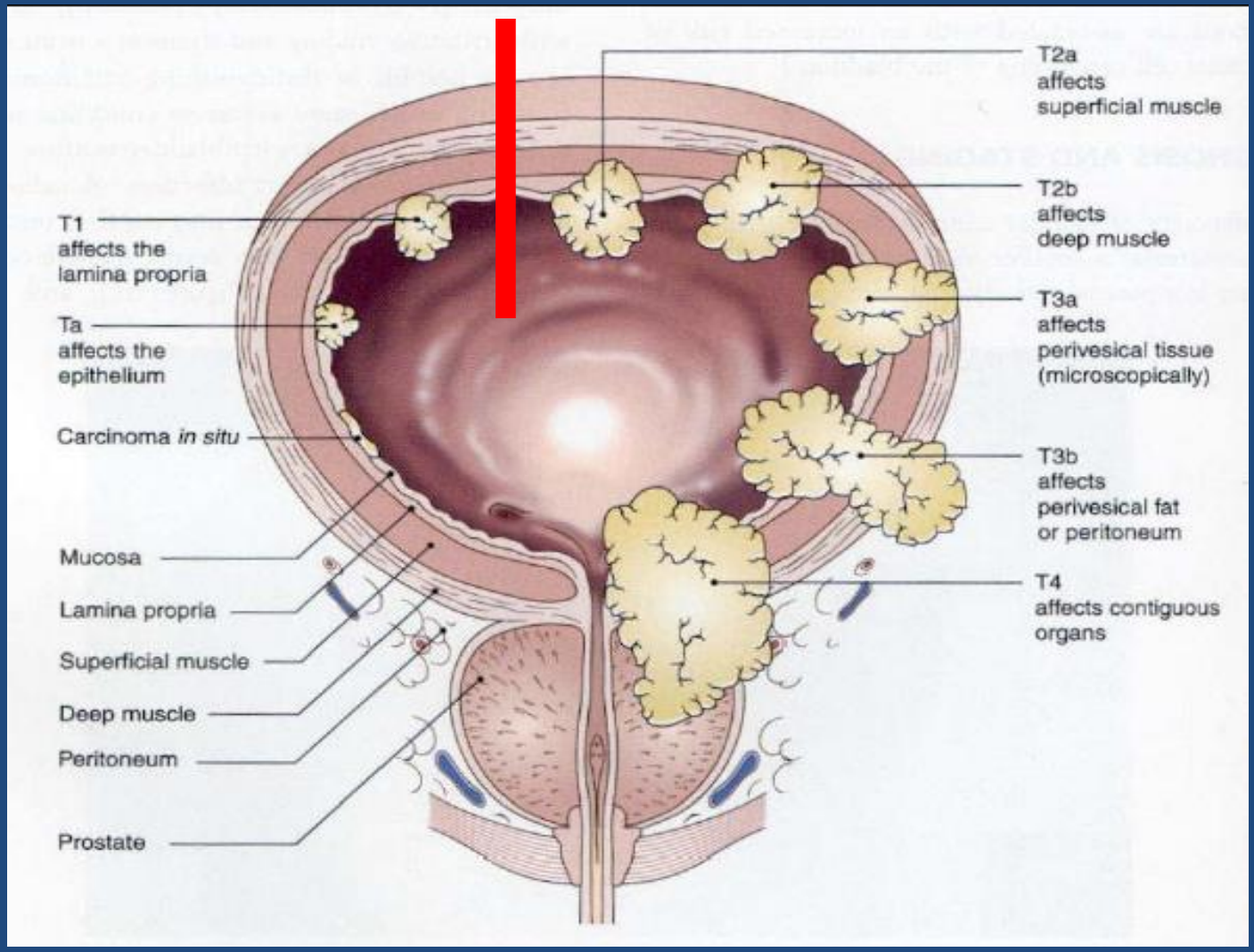
Natural history

- ***Local invasion***
  - Majority with superficial disease will recur
  - 60% develop invasive disease within 5 years

- ***Lymphatic spread***
  - 25-60% of patients with muscle-invasive disease
    - 25-30% T2-T3a
    - 50-60% T3b-4
  - 5% with superficial disease
- ***Hematogenous spread***
  - 5-20% of patients
  - Most common: liver, lung, bone

AJCC Staging

- ***Primary tumor* (T)**



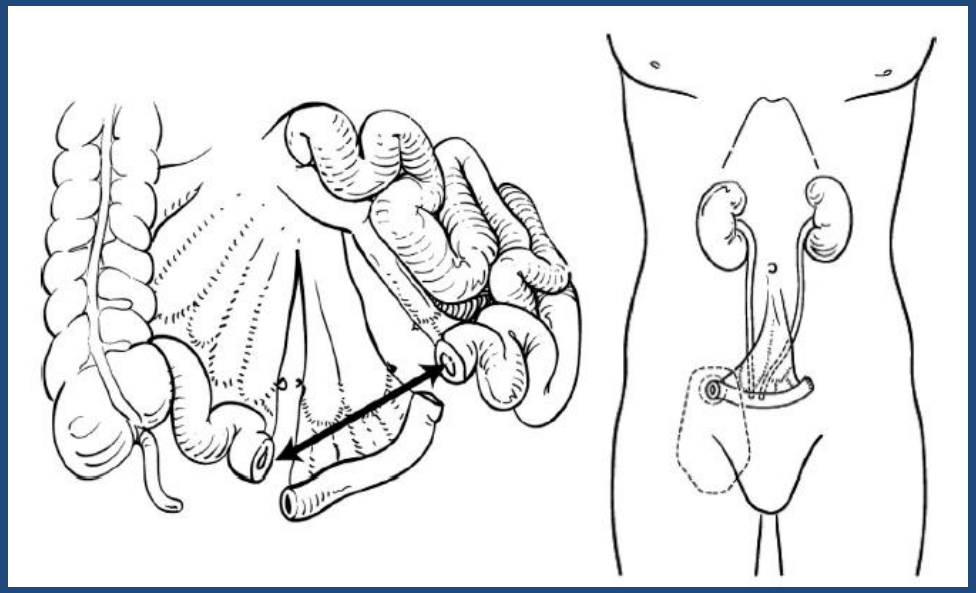
Treatment options for MIBC

- Radical cystectomy + pelvic node dissection
  - +/- chemotherapy (gemcitabine/cisplatin)

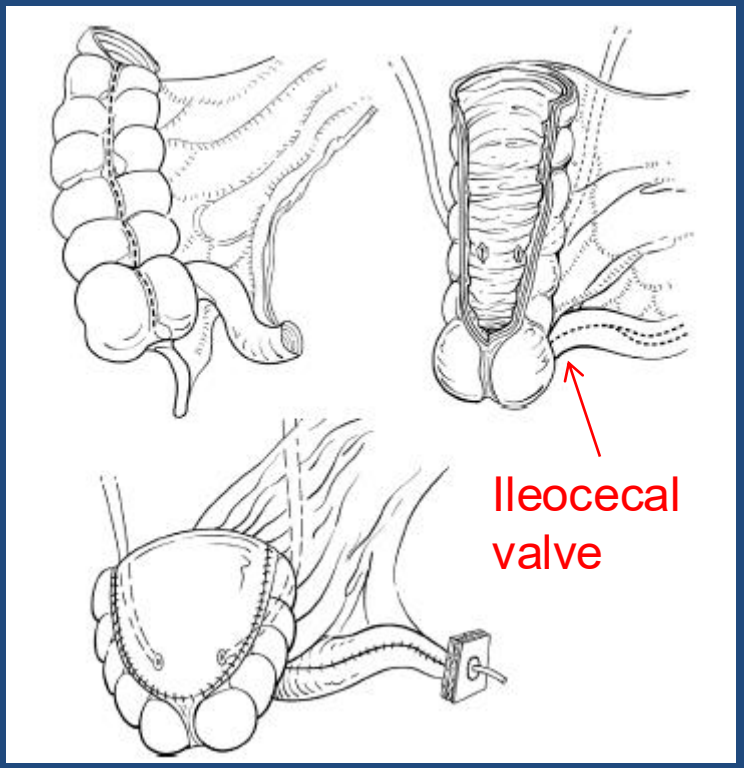
- External beam radiation therapy + concurrent low dose chemotherapy

Radical Cystectomy/PLND

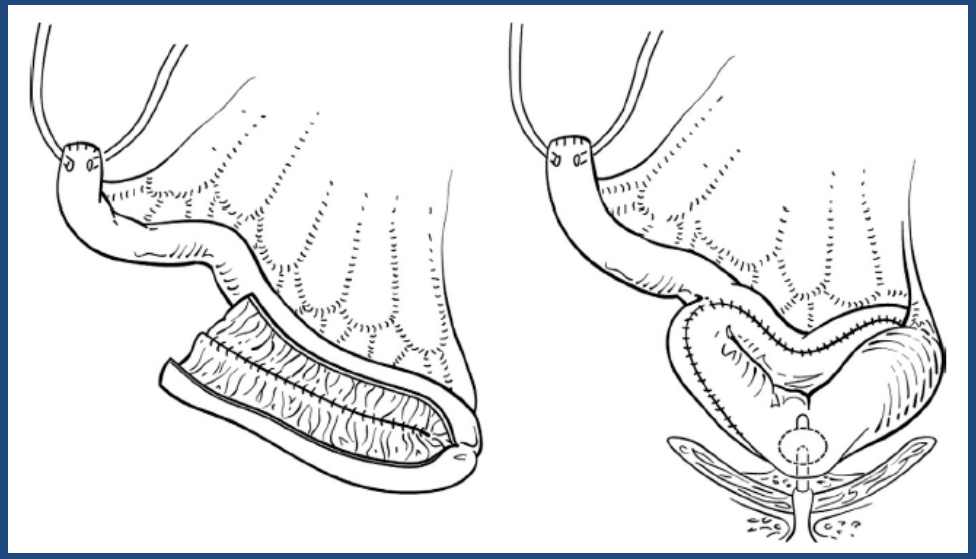
- Male
  - Bladder, perivesical fat, distal ureters
  - Prostate, seminal vesicles, proximal vas deferens
- Female
  - Bladder, perivesical fat, distal ureters
  - Uterus, ovaries, fallopian tubes, anterior vaginal wall
  - Proximal urethra
- Pelvic lymph nodes below aortic bifurcation
  - at least 10 to 14 LNs should be removed
  - Standard=b/l external iliac, obturator, internal iliac (hypogastric), and common iliac chains
  - Extended= plus paracaval, interaortocaval, para-aortic, and presacral nodes



Incontinent stoma (Ileal conduit)



Continent stoma (Indiana pouch)



Orthotopic Neobladder

Chemoradiation for bladder cancer

- Optimally involves maximal transurethral resection of visible disease
- Survival benefit shown for concurrent chemotherapy (James et al BC2001 NEJM 2012)
- Variation in treatment volumes and techniques across institutions
- Requires dedicated multidisciplinary team (urologist, medical oncologist, radiation oncologist)

Simulation

- Supine
- Thermoplastic mold
- Oral contrast- for small bowel visualization
- IV contrast- may help identify vessels

  *use with caution in patients with ↓renal function

Conventional radiation therapy

Initial fields

- Bilateral pelvic lymph nodes
- Bladder + gross tumor (GTV)
- Proximal urethra

39.6-45 Gy

1.8-2.0 Gy/d

EMPTY BLADDER

boost

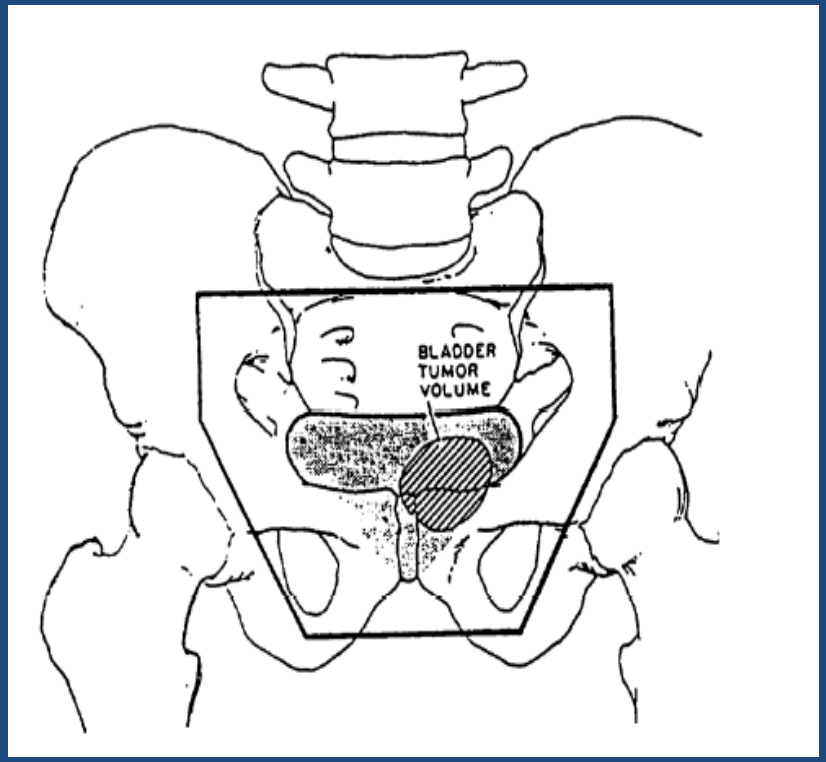
GTV + margin

12-21.6 Gy

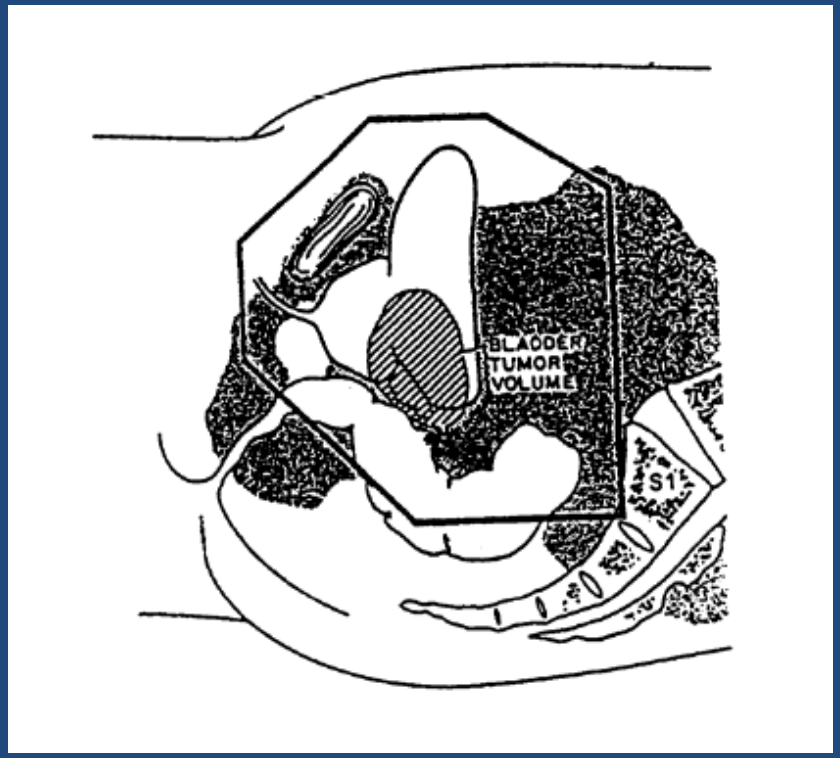
total dose= 64- 66.6Gy

FULL BLADDER

Classic radiation therapy fields

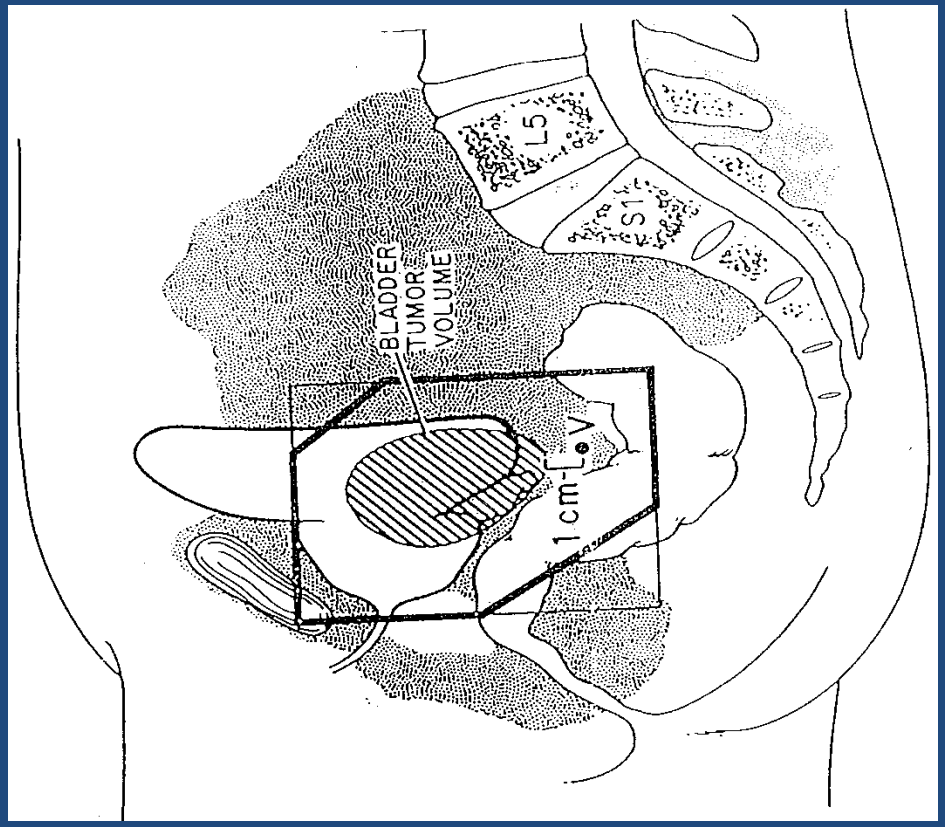


ANTERIOR/POSTERIOR

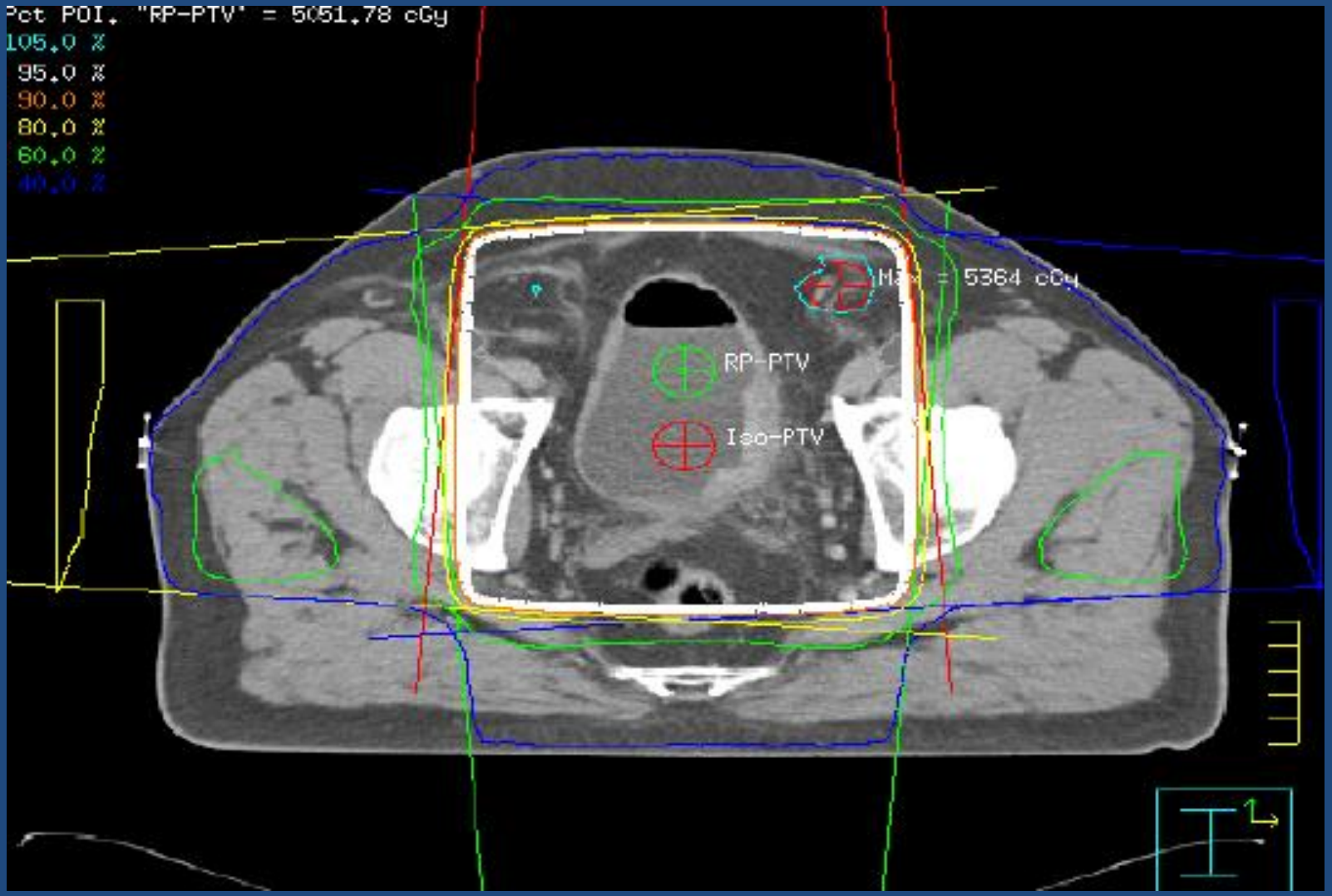


LATERALS

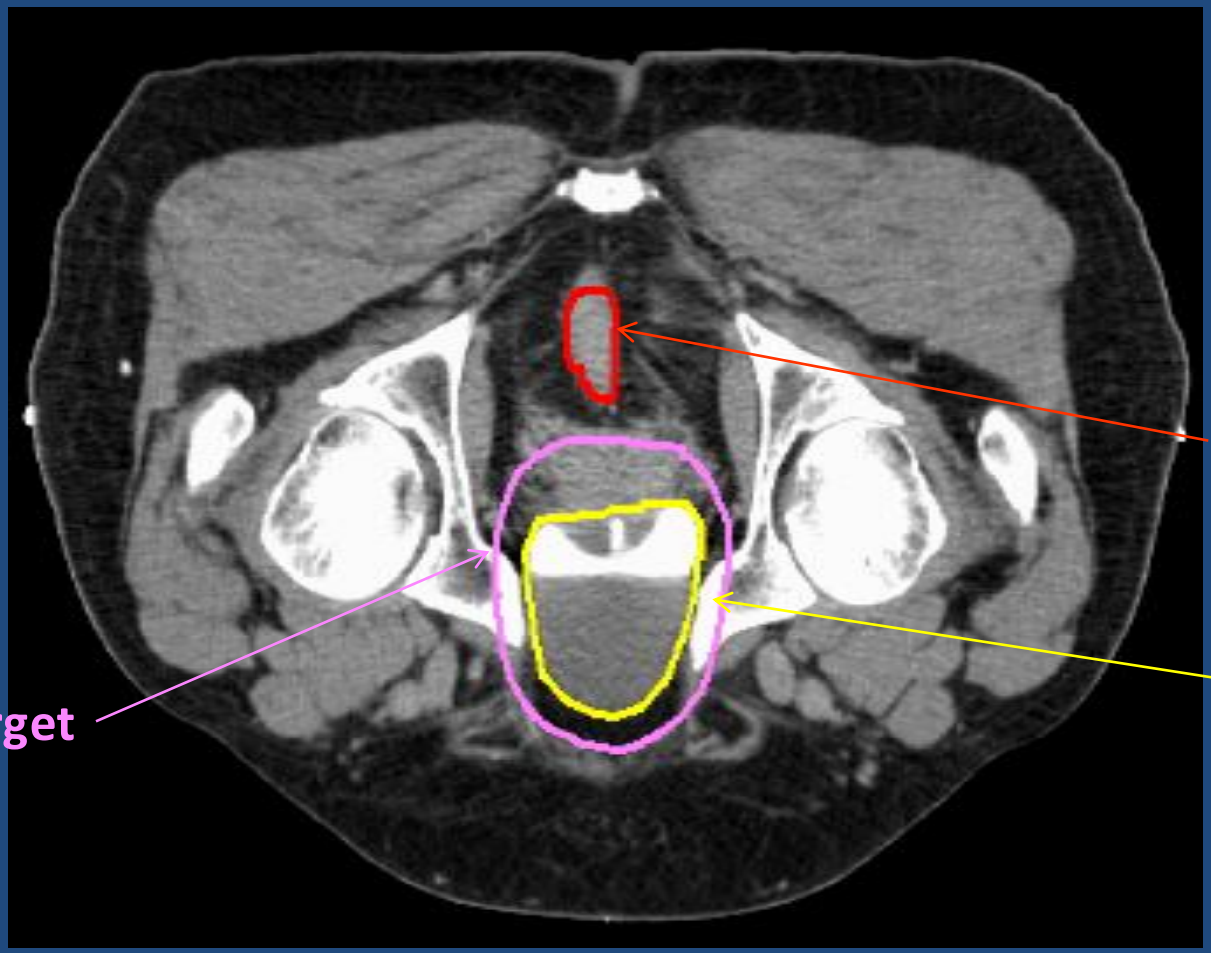
Boost fields



LATERALS


Pct POI, "RP-PTV" = 5051.78 cGy
105.0 %
95.0 %
90.0 %
80.0 %
60.0 %
40.0 %
RP-PTV
Iso-PTV

3D conformal radiation therapy



from Dr. H. Sandler

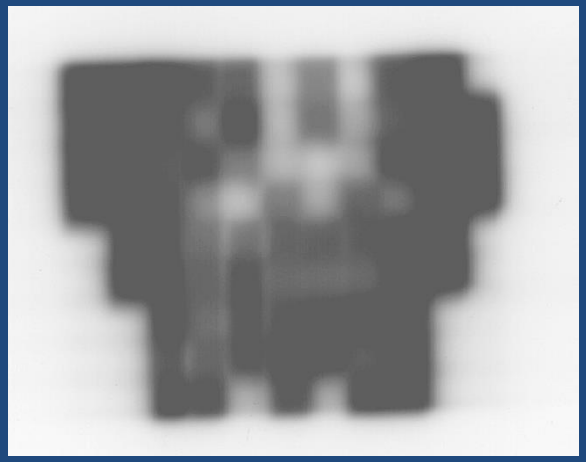
Can we do better?

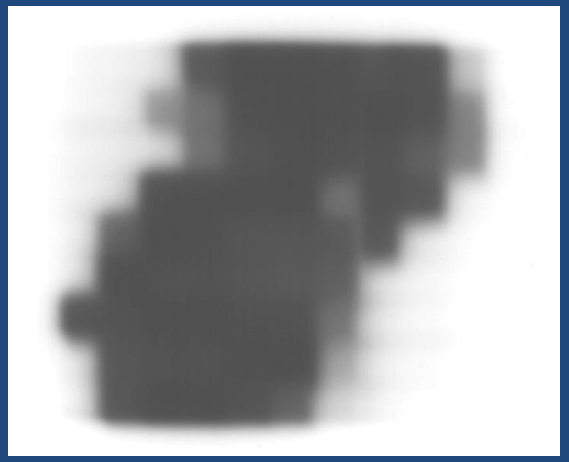
- IMRT
  - Patient-specific treatment planning
    - Uses CT-based planning allowing 3D organ definition
    - Variable beam intensity based on patient-specific parameters

      Not one beam for everyone!
  - design based on “inverse planning”
    - Dose to target defined
    - Constraints placed on normal tissue
  - dose escalation while minimizing toxicity?

meaning…?

- Better control over dose shaping
- Higher dose to target with less to normal tissue





- Dose escalation feasible
- Reduction of margins?

But the bladder moves…

- With respiration
- With bladder filling/emptying
- With rectal filling/emptying

- With day to day set up variations
- With bladder volume changes during RT

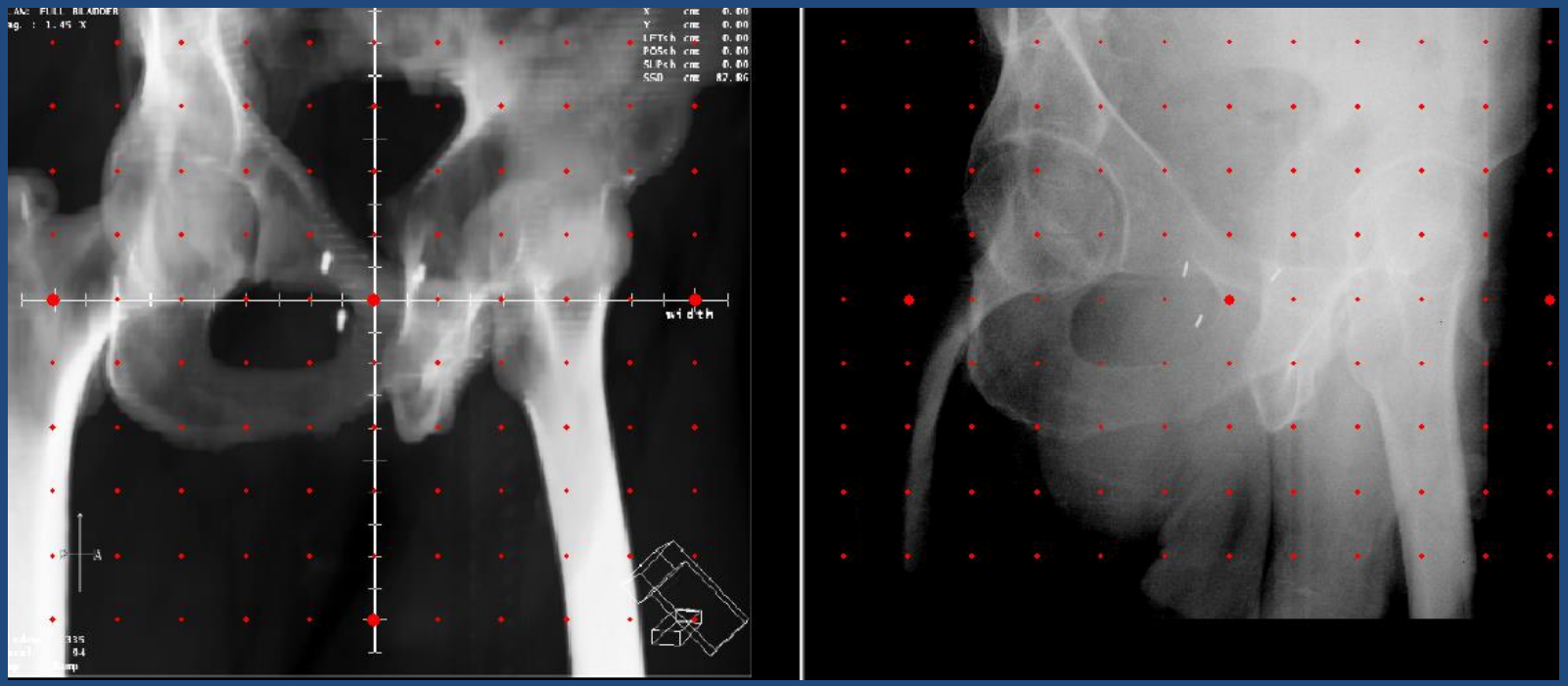
- Requires 1.5-2cm margins = lots of bowel irradiated
- Most significant in the superior direction
  - Important for dome lesions- may be out of field!

- Must know where tumor is
  - Detailed bladder map
  - Pre-TURBT imaging

CRITICAL!!

….but still only an estimate

Borrowing from prostate cancer treatment



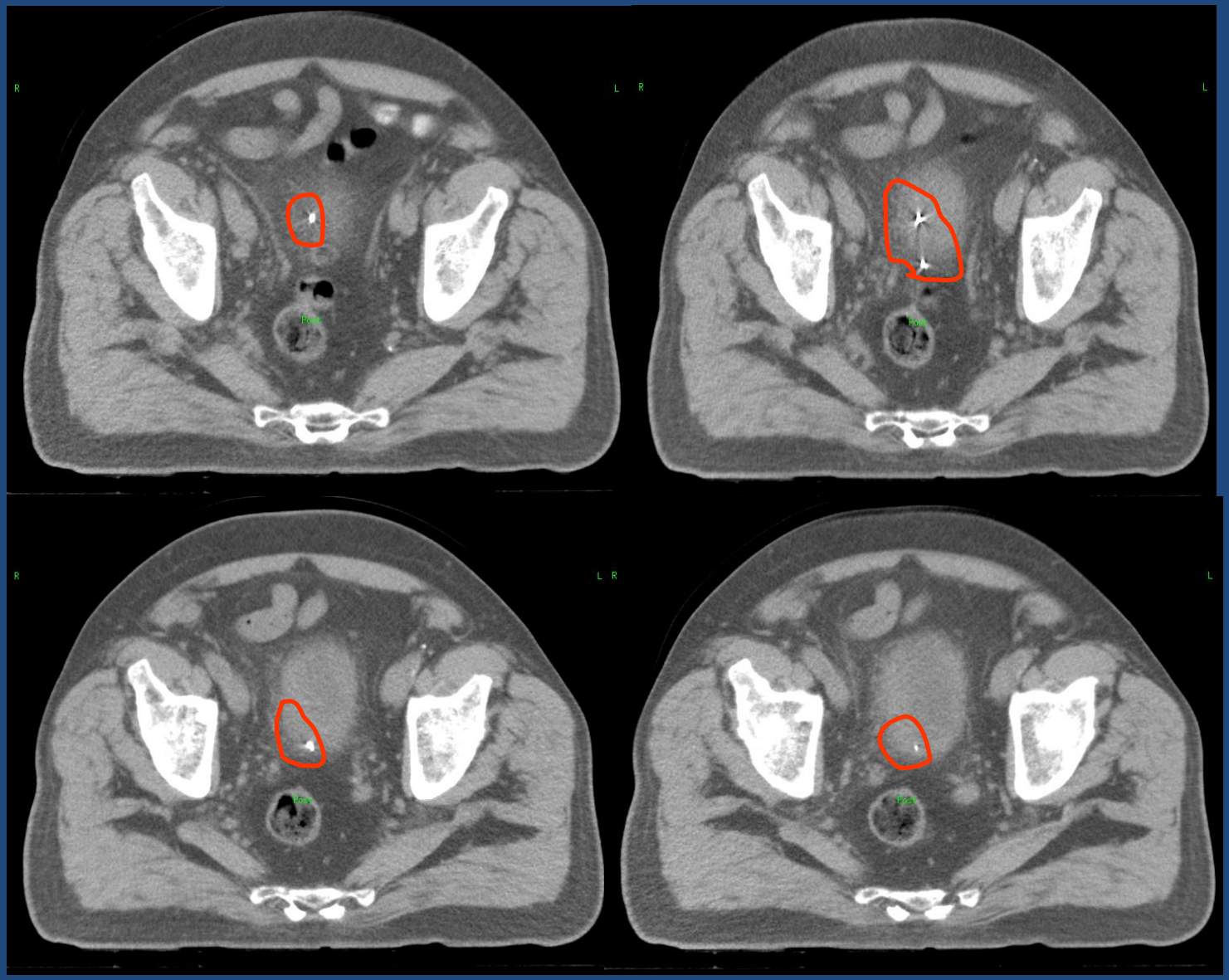
DRR **Portal image**

Fiducials for bladder cancer

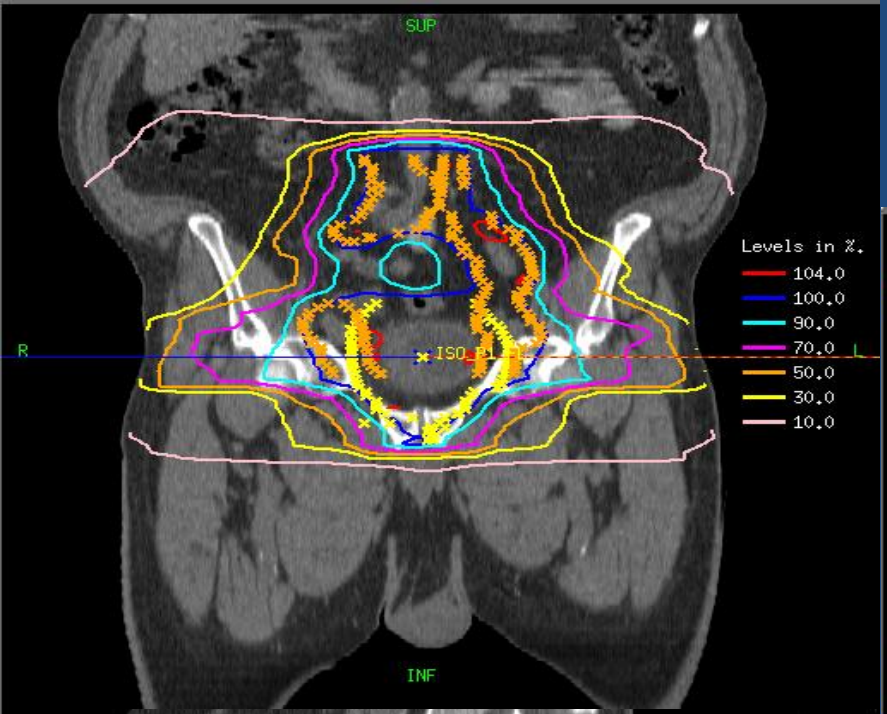
- Feasible with no significant toxicity
- High seed drop out rate due to motion of the bladder
- Flexible fiducial marker may be more stable (Visicoil®)

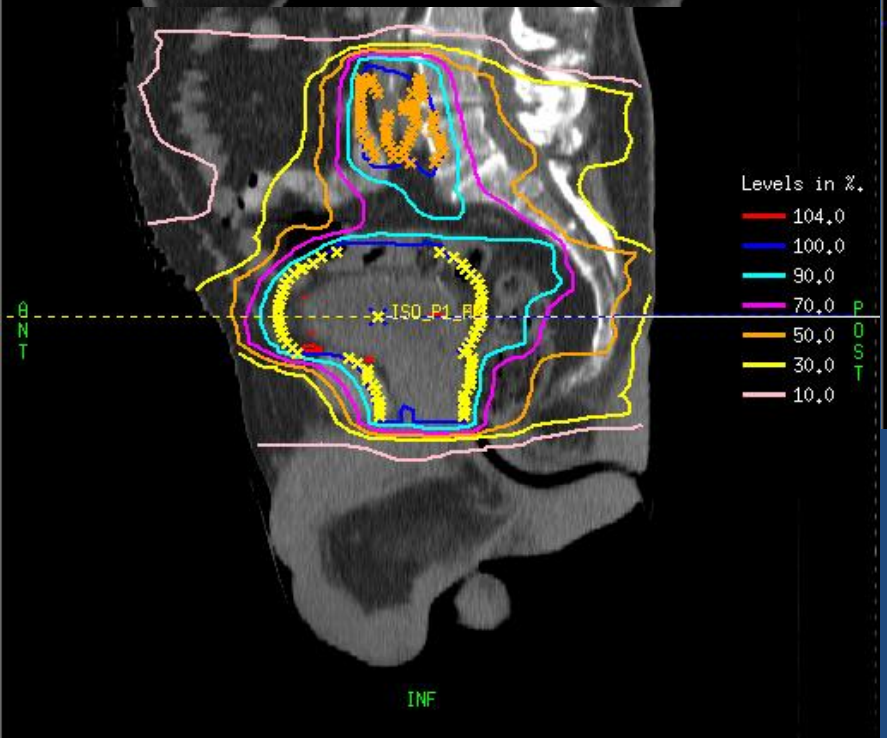


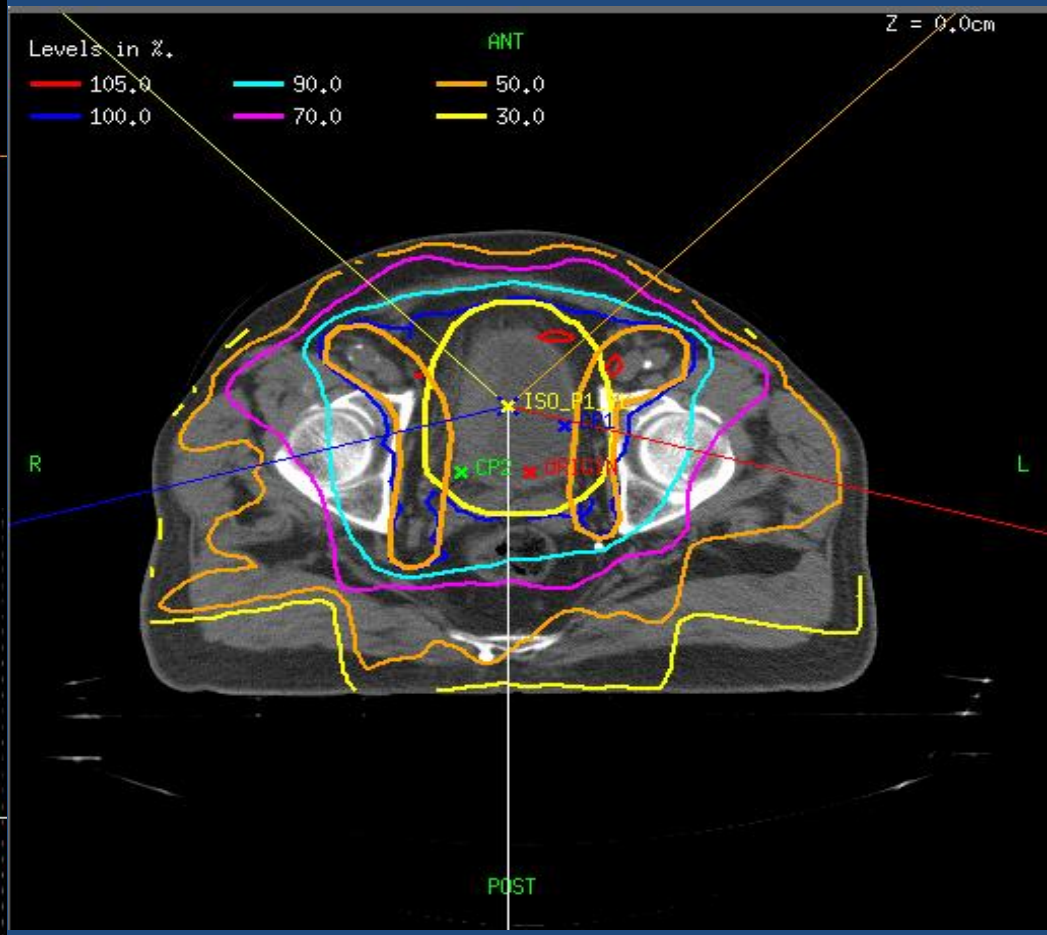
- IMRT
  - May allow dose escalation while reducing bowel dose and toxicity
  - Must know where bladder/tumor are
    - Respiration
    - Bladder and rectal filling
    - Fiducial markers
  - Investigational


R
L
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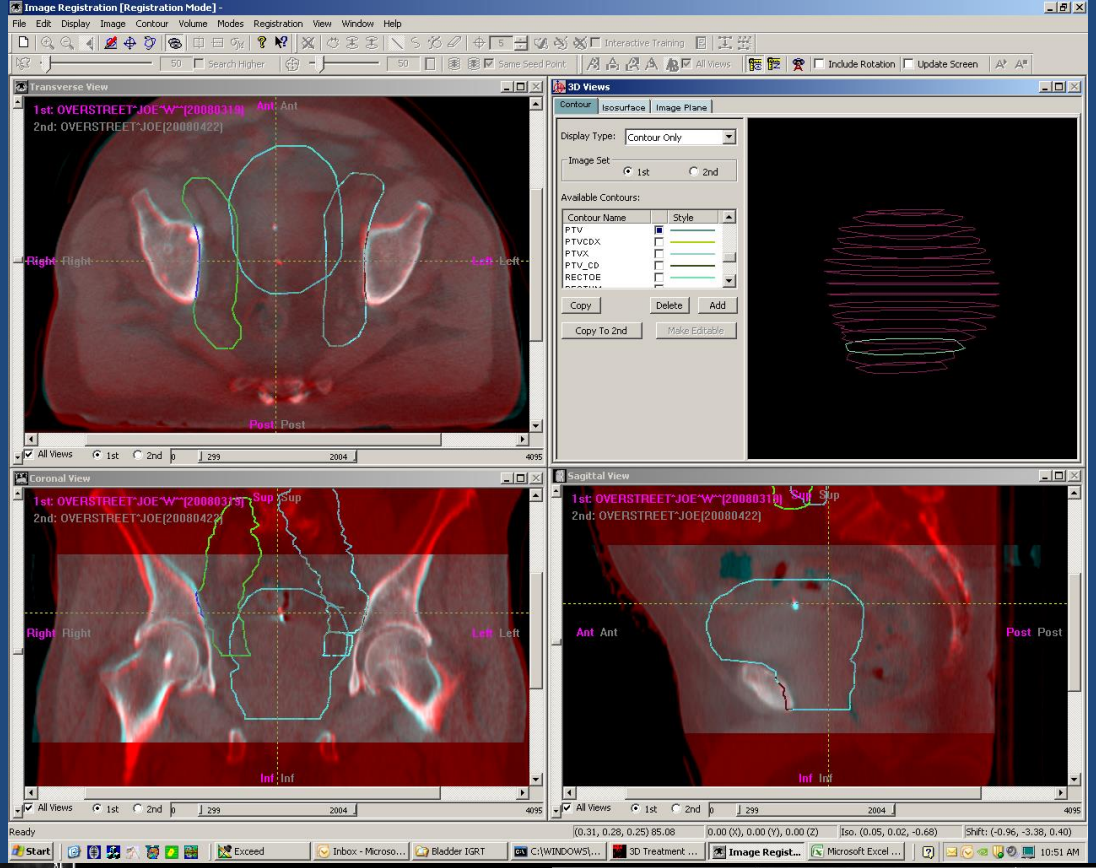
Initial plan treating bilateral pelvic lymphatics (extended field)



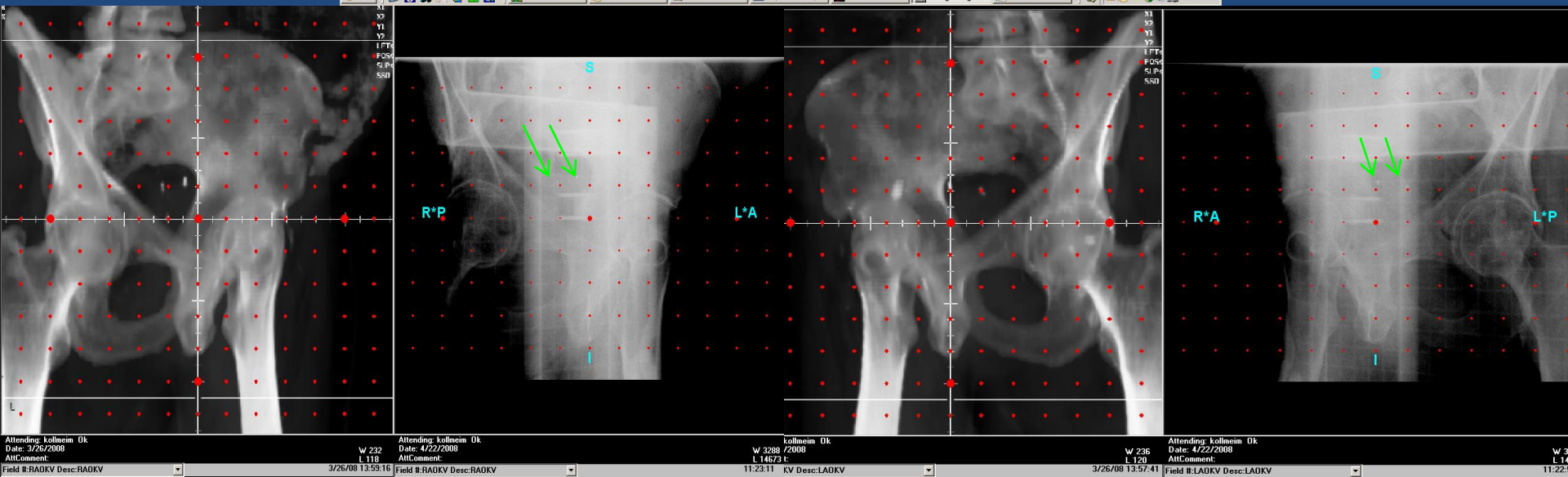




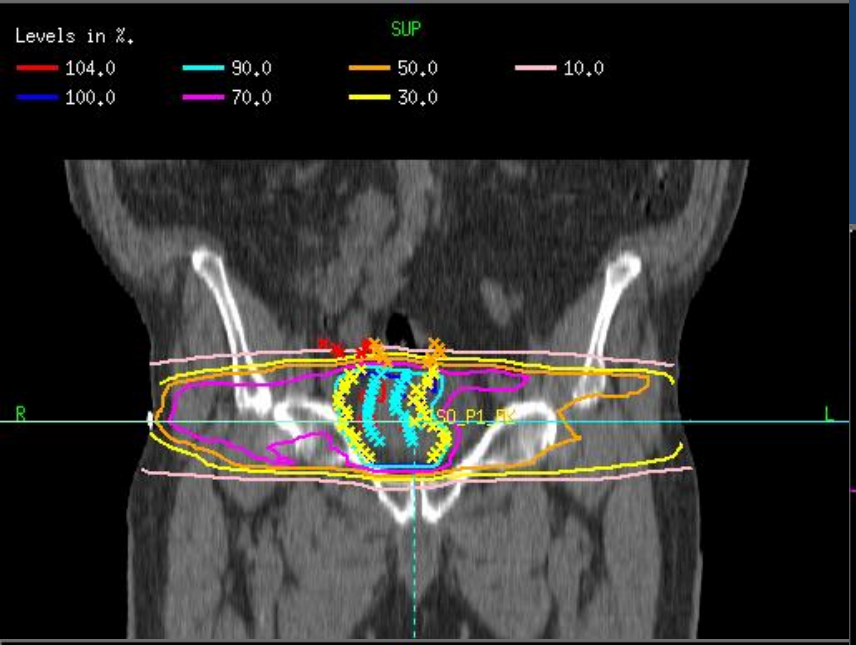
Cone beam

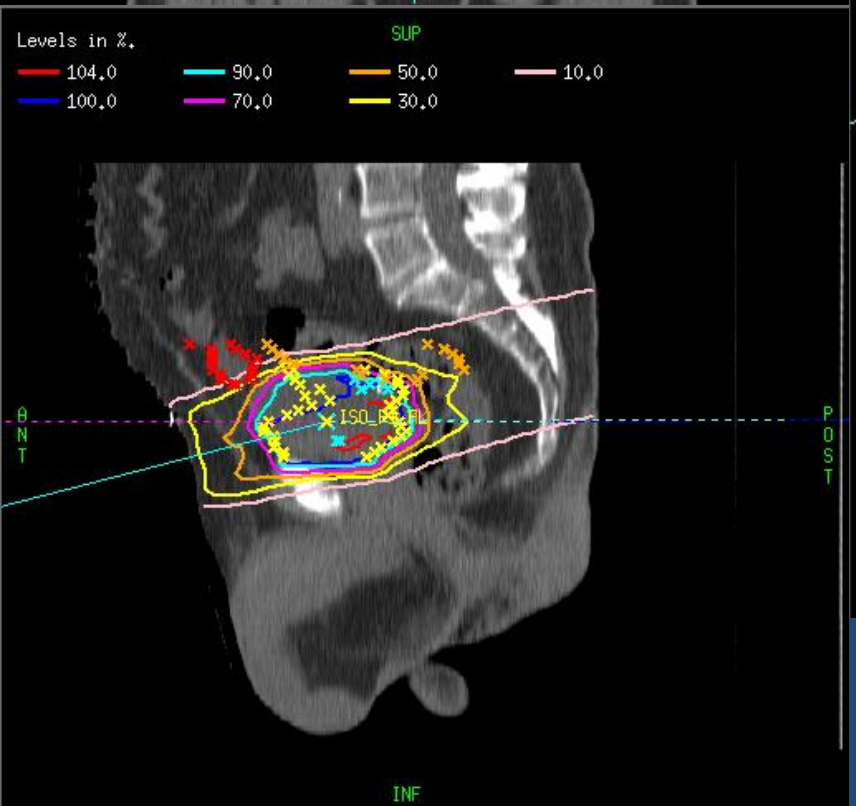


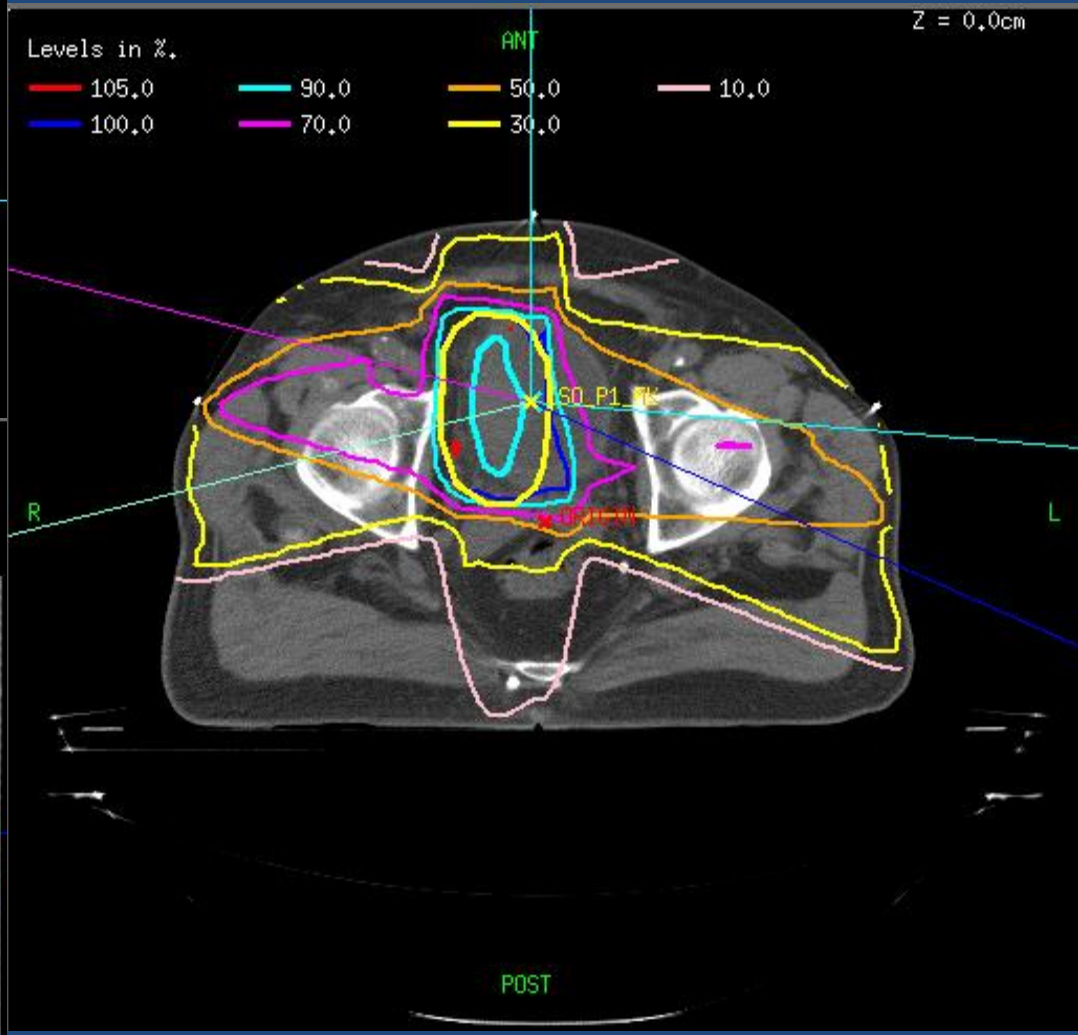
2D kv daily



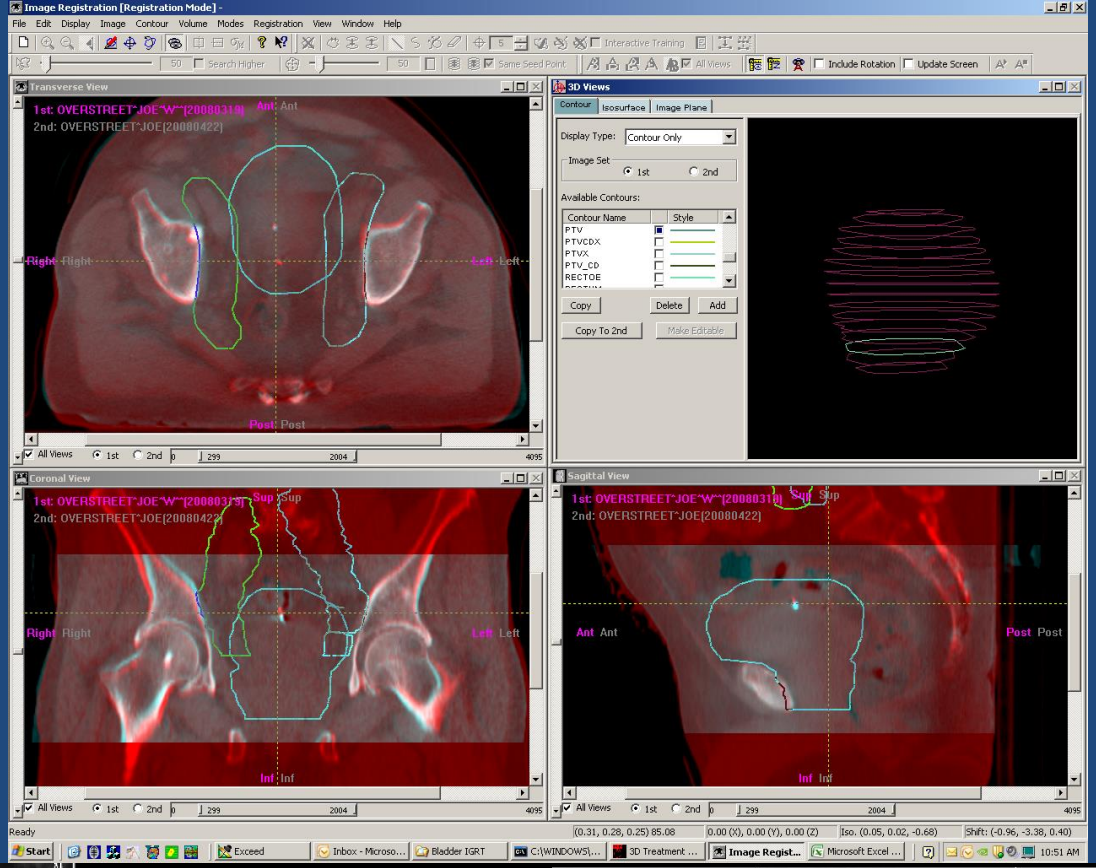
Cone down plan



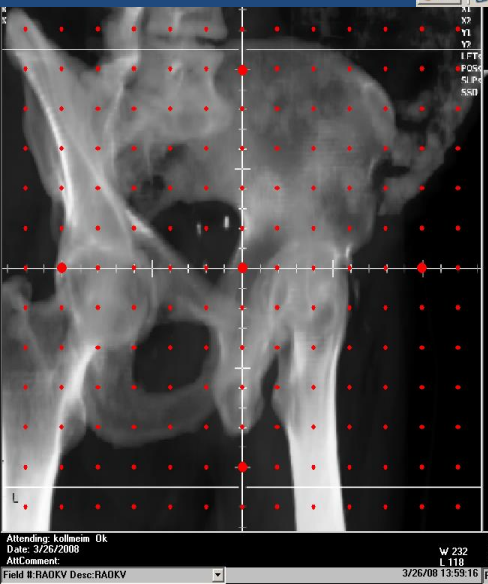


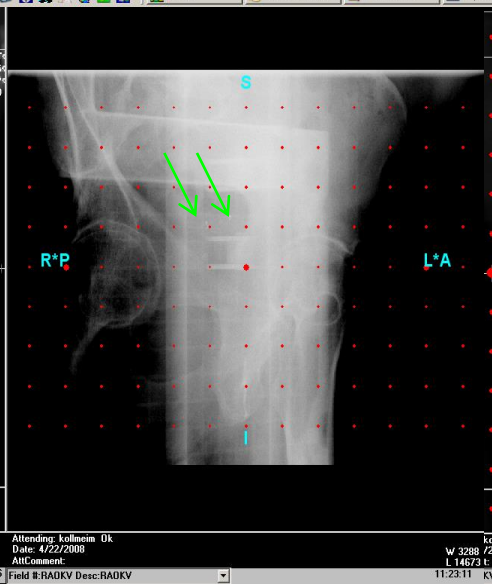


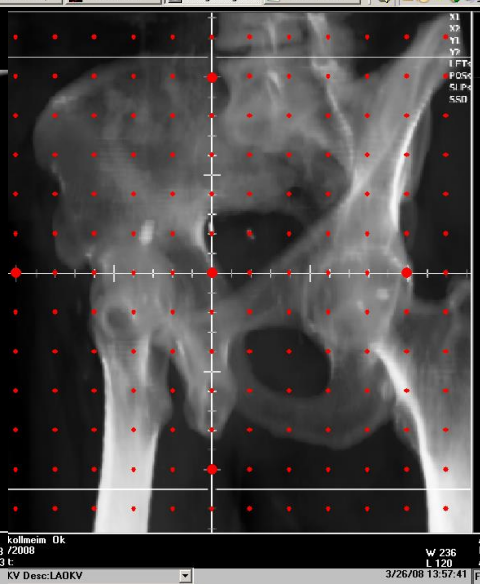
Cone beam

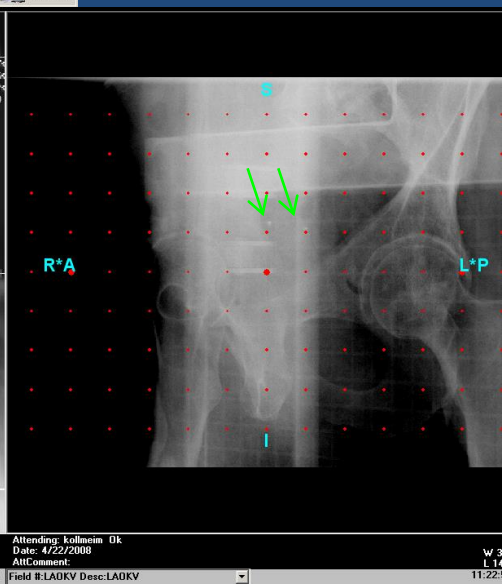


2D kv daily



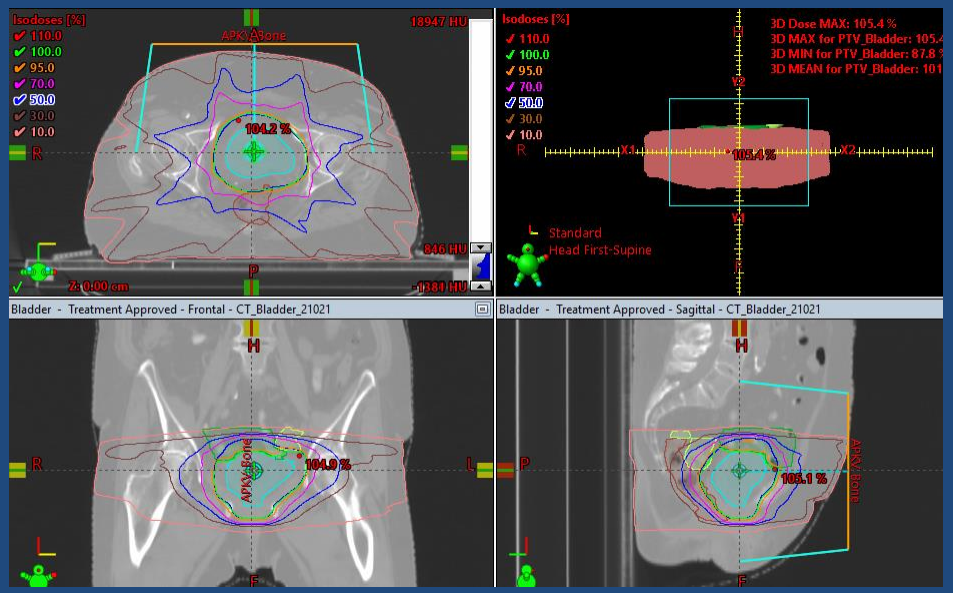






Moderate hypofractionation

- 55Gy in 20 fractions
- Treatment to whole bladder/urethra
- Empty bladder
- CBCT daily
- +/-fiducial markers



- Useful for:
  - Elderly patients
  - Patients with multifocal disease
  - Patients with gross disease in bladder

Multidisciplinary Approach

- Organ preservation with combined modality therapy is feasible and tolerable
- Survival outcomes do not appear compromised by attempts at organ preservation
- Requires coordination of multidisciplinary team for optimal therapy… and motivated patient
- Modern image-guided approaches may improve outcomes and reduce toxicity