BLADDER SPARING THERAPIES FOR UROTHELIAL CANCER: A RADIATION ONCOLOGIST'S PERSPECTIVE

MINNESOTA SOCIETY OF CLINICAL ONCOLOGY

2024 SPRING CONFERENCE, 04/24/2024

OUTLINE

- Introduction
- Workup, Staging
- Definitive Management Options
- Bladder Preservation Principles
- Cases and Controversies
- Future Directions

INTRODUCTION

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- Adjunct Assistant Professor of Radiation Oncology at the University of Minnesota
- Residency: Mayo Clinic in Jacksonville, FL
- Medical School: Florida State University COM
- Undergraduate: University of South Florida
- Hobbies: Spending time with my wife and our rottweiler rescue, golf, Jaguars football

DISCLAIMER

- I AM A FEDERAL EMPLOYEE AT THE MINNEAPOLIS VETERANS AFFAIRS HEALTH CARE SYSTEM IN THE RADIATION ONCOLOGY DEPARTMENT AS A STAFF PHYSICIAN SERVING THOSE WHO HAVE SERVED.
- I AM ATTENDING THIS CONFERENCE AND SPEAKING TO YOU TODAY AS AN INDIVIDUAL, SEPARATE FROM MY VA APPOINTMENT.
- ALL DISCUSSION, COMMENTS, VIEWS, AND EXPRESSION ARE THAT OF MY OWN.
- THE INFORMATION SHARED DOES NOT REFLECT THE VIEWS OR STANCES OF THE VA OR THE US GOVERNMENT.
- I HAVE NO FINANCIAL DISCLOSURES TO REPORT

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WORK UP[1]

- H&P
- Cystoscopy, EAU, +/- Cytology
- CBC, Renal Profile, Alkaline Phosphatase
- Abdomen/Pelvis Imaging
- TURBT
- Chest Imaging
- Bone Imaging
- Smoking Cessation

STAGING[2]

- Ta: Non-invasive papillary
- Tis: Urothelial carcinoma in situ
- T1: lamina propria invasion
- T2: Muscularis propria Invasion
- T3: Peri-vesicular tissue invasion
- T4: Extra-vesicular organ invasion, pelvic wall involvement

- N1: single true pelvis node
- N2: Multiple true pelvis Nodes
- N3: common iliac node(s)

- M1a: retroperitoneal node(s)beyond iliacs
- M1b: distant metastasis

MIBC WORK UP CONTINUED

- **CYSTO/BIOSPY/TURBT**[1]
  - ENSURE ADEQUATE DEPTH OF SAMPLE TO CONFIRM T-STAGE
  - CAREFULLY REVIEW TUMOR LOCATION, SIZE, MULTIFOCALITY, EXTENT OF RESECTION
- **CT UROGRAM** HELPS IDENTIFY EXTRAVESICULAR DISEASE, ADENOPATHY, FIELD CANCERIZATION, AND/OR SYNCHRONOUS UPPER TRACT PRIMARIES
- **MRI > CT** FOR PRIMARY SITE SOFT TISSUE DELINEATION AND T-STAGING[3]
- **NUC MED BONE SCAN** IS INDICATED IF ALK PHOS ELEVATED OR BONE PAIN[1]
- **PET CT** IS BECOMING MORE ROUTINE WITH EMERGING DATA, RECOMMENDED PER A.C.R.[4,5]

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MIBC MANAGEMENT OPTIONS

- Neoadjuvant chemotherapy followed by radical cystectomy[6,7]
- Definitive Chemoradiation[8,9,10]
  - Non-Surgical Candidates (~**60%** of patients due to comorbidities)[11,12]
  - Patients that decline cystectomy, i.e. desire organ preservation

- Non-Category 1 treatment options
  - Neoadjuvant chemotherapy followed by partial cystectomy[1]
  - Radiation therapy alone[10]
  - TURBT alone[13]

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  - TURBT alone[13]

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- Introduction
- Workup, Staging
- Definitive Management Options
- **Bladder Preservation Principles**
  - ***Ideal patients***
  - ***Outcomes***
  - ***treatment planning pearls***
- Cases and Controversies
- Future Directions

"IDEAL" BLADDER PRESERVATION CANDIDATE[14,15]

- Functional bladder
- Solitary Tumor measuring < 5 cm
  - No carcinoma in situ
- T2 disease
  - no extravesicular spread or pelvic organ/side wall invasion
- Complete TURBT
- Absence of Hydronephrosis
- cisplatin based chemotherapy candidate
- No prior pelvis radiation
- No active inflammatory bowel disease
- Anticipated patient compliance with cystoscopy follow ups

"REAL WORLD" BLADDER PRESERVATION CANDIDATE[14,15]

- Non-operative candidate s/p maximal safe TURBT with ….

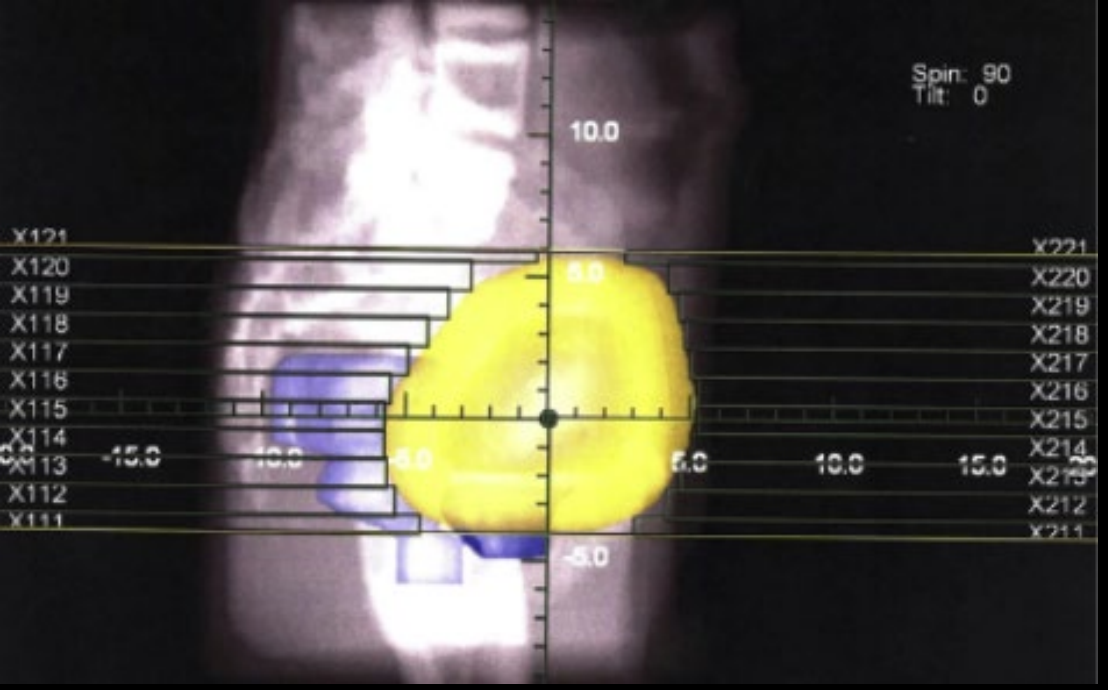
- No distant mets
- No prior pelvis radiation
- No active inflammatory bowel disease

CHEMORADIATION 5-YEAR OUTCOMES[8-10,16]

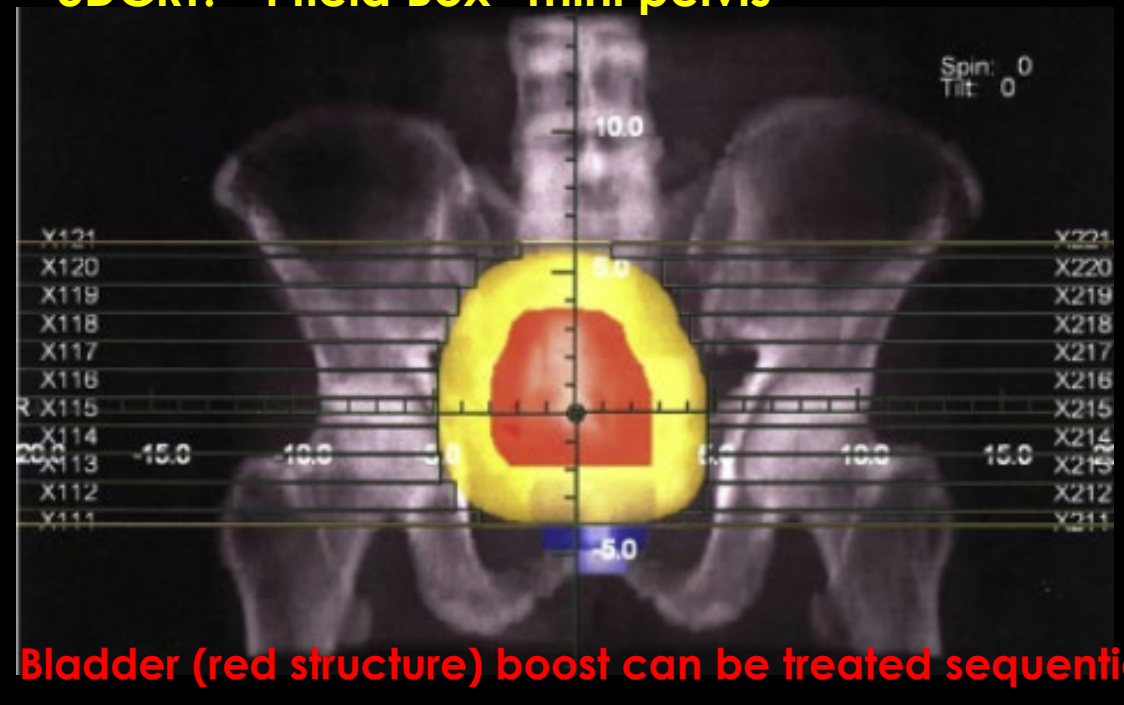
- Overall Survival: **48-57%**
- Distant Metastasis Rate: **~35%**
- Disease Free Survival: ~65%
  - Pelvic Nodal Failure: **~5%**
  - Muscle-Invasive local failure rate: **10-15%**
  - Non-Muscle Invasive (Ta, Tis) local failure rate: 15-36%
- Grade 3+ toxicity: GU 22-31%, Rectal: 3-6%
- Salvage Cystectomy rate: 10-15%

CHEMORADIATION VOCABULARY/DEFINITIONS

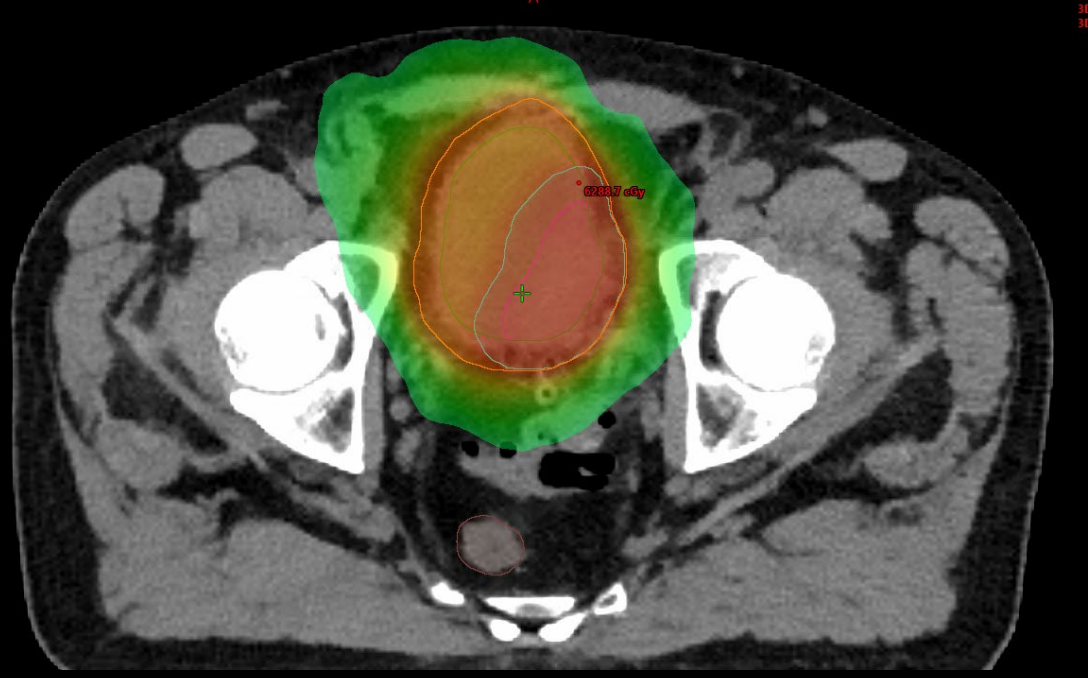
- Gray: absorbed dose of radiation
- Fraction(s): delivery of a dose of radiation
- **Conventional Fractionation:** Treatment at 1.8-2 Gy per Day (6-7 weeks of treatment)
- **Hypofractionation:** > 2 Gy per day (4 weeks of treatment)
- Stereotactic Body Radiation ("SBRT"): >>2 Gy per day, ≤5 fxn, ablative intent (*N/A to talk*)
- Split course: intentional gap in a radiation course (*no longer offered routinely*)
- **"Mini"/True Pelvis:** internal + external iliac, obturator, presacral, peri-vesicular LN field
- Standard Pelvis: Common iliac + Mini-pelvis field
- **3D Conformal Radiation Therapy**: standard/basic 3 to 4 field "box" of radiation
- **Intensity Modulated Radiation Therapy (IMRT):** advanced treatment planning, delivery technique
- Volumetric Modulated Arc Therapy (VMAT): rotational IMRT delivery
- Sequential Boost: giving additional dose after a primary course (mini-Pelvis → bladder boost)
- Simultaneous Boost: Given additional dose during a single course ("dose painting" boost)



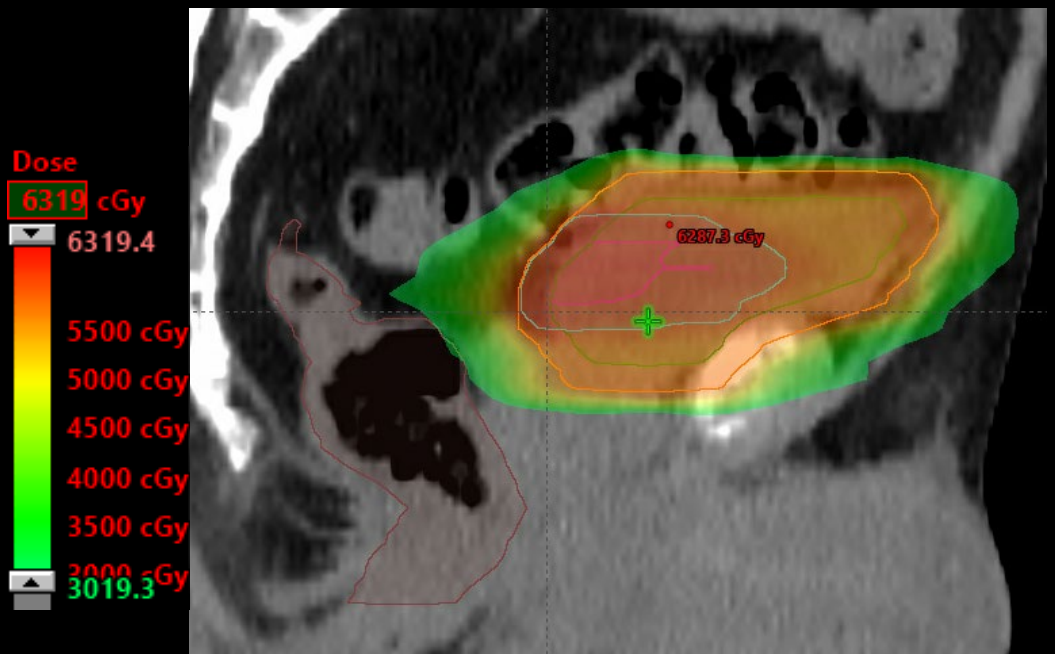
3DCRT: "4 field Box" mini pelvis[17]



Bladder (red structure) boost can be treated sequentially



IMRT: bladder only field with "Dose painted" tumor boost



Trimodality Therapy for Muscle-Invasive Bladder Cancer: Recent Advances and Unanswered Questions

Di Maria Jiang[1] · Peter Chung[2] · Girish S. Kulkarni[3] · Srikala S. Sridhar[4]

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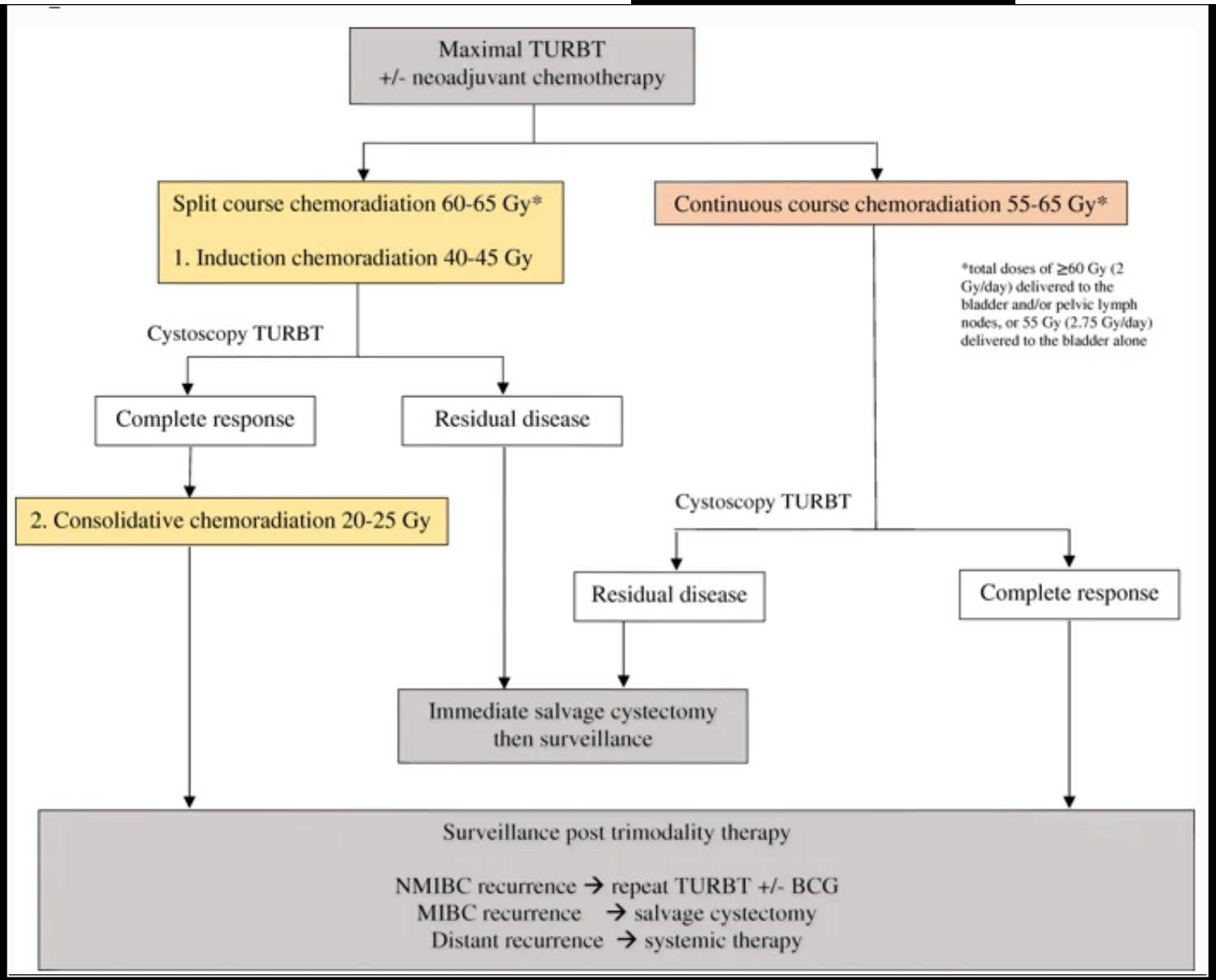
Current Oncology Reports (2020) 22: 14
https://doi.org/10.1007/s11912-020-0880-5



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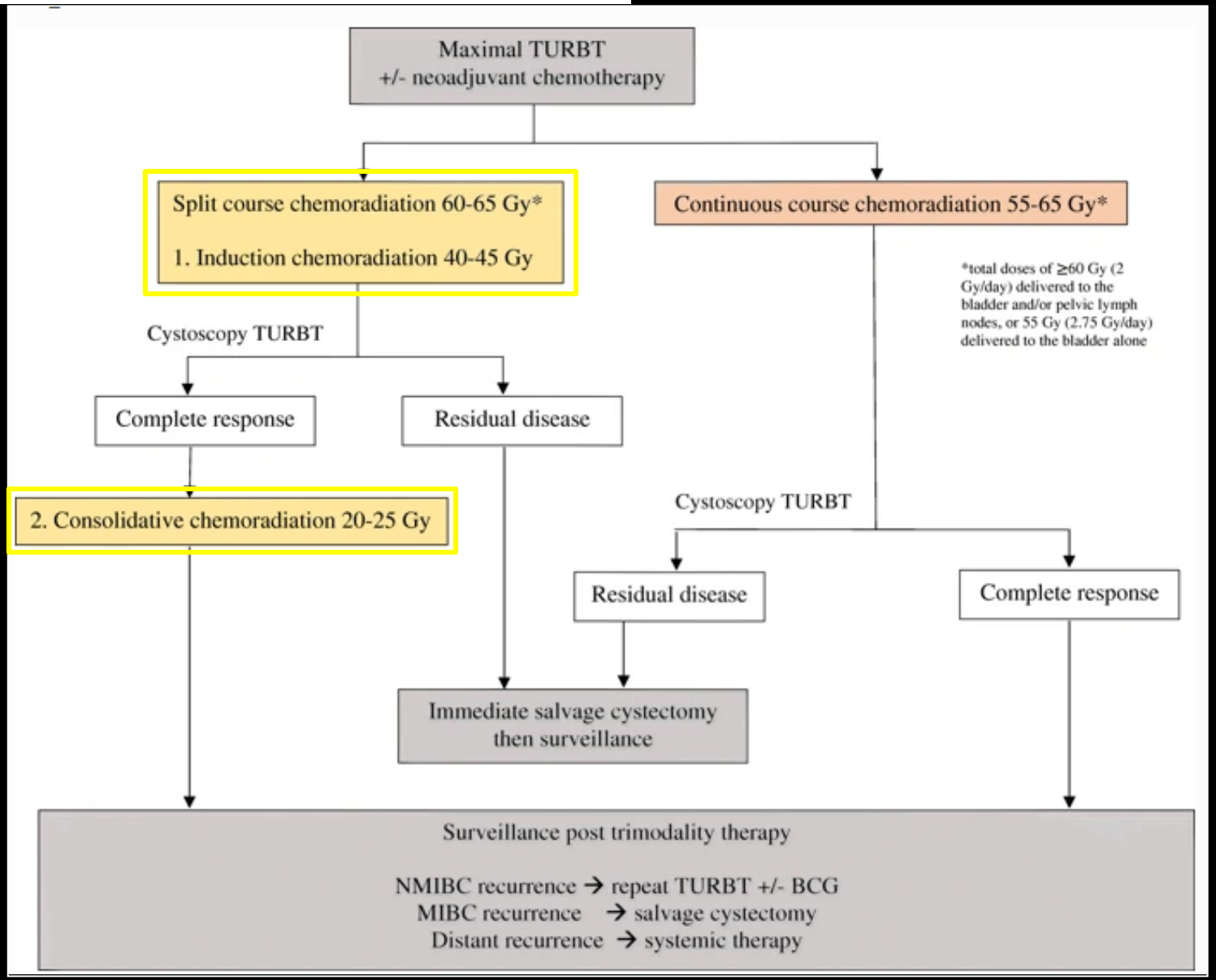
Most chemoRT patients are not operative candidates[11,12,18]

Thus, mid-treatment break for cysto eval does not change management



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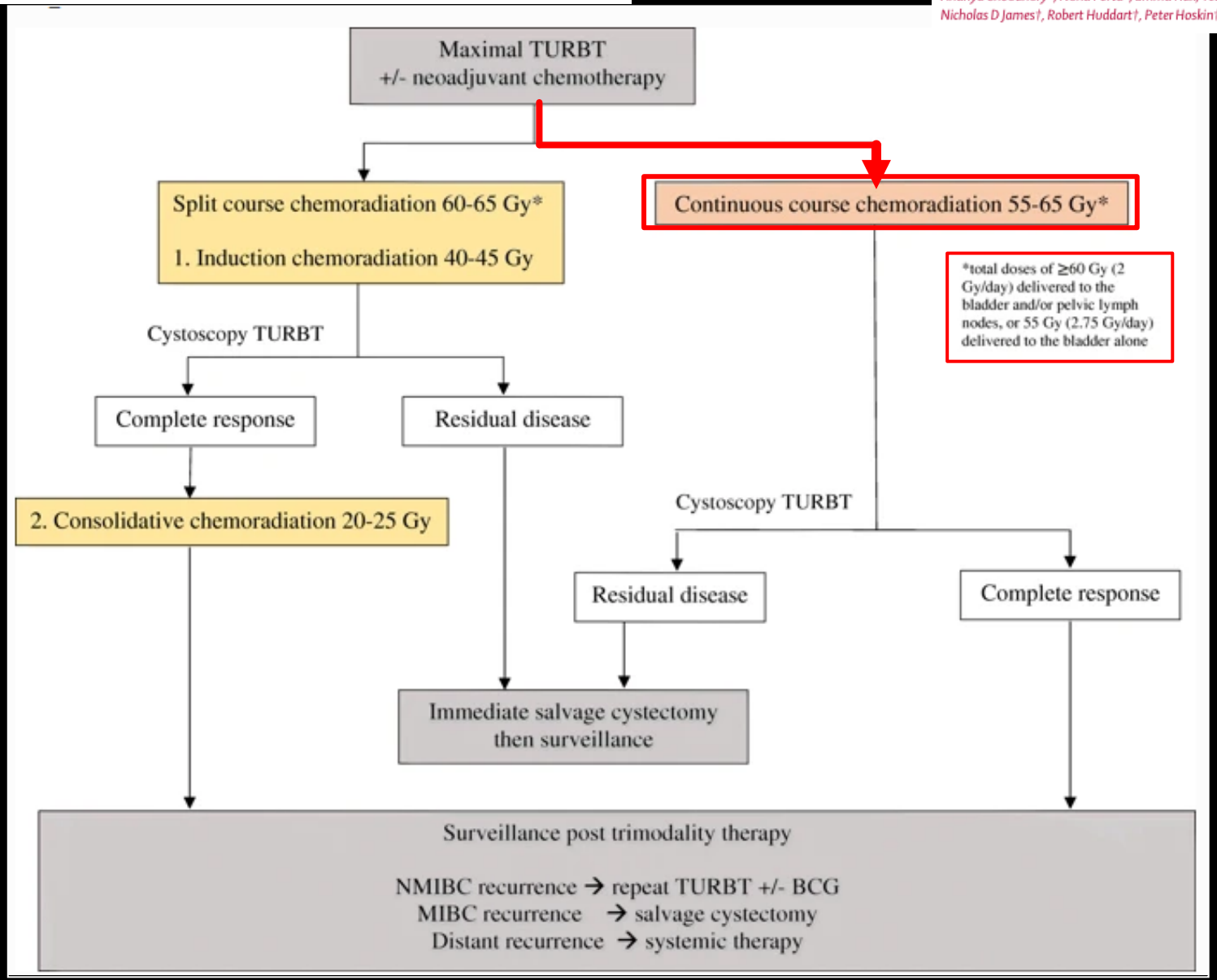
Hypofractionated radiotherapy in locally advanced bladder cancer: an individual patient data meta-analysis of the BC2001 and BCON trials

Lancet Oncol 2021; 22: 246–55

Ananya Choudhury, Nuria Porta*, Emma Hall, Yee Pei Song, Ruth Owen, Ranald MacKay, Catharine M L West, Rebecca Lewis, Syed A Hussain, Nicholas D James†, Robert Huddart†, Peter Hoskin†, on behalf of the BC2001 and BCON investigators*



Meta-Analysis data favors hypofractionation (2.75 Gy/day x4 weeks)[16]

→ Improved local regional control

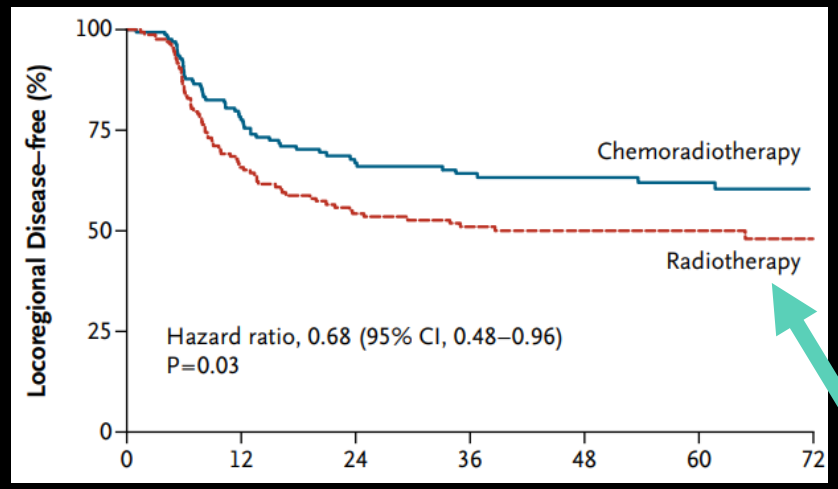
→ No difference in high grade GU or rectal toxicity

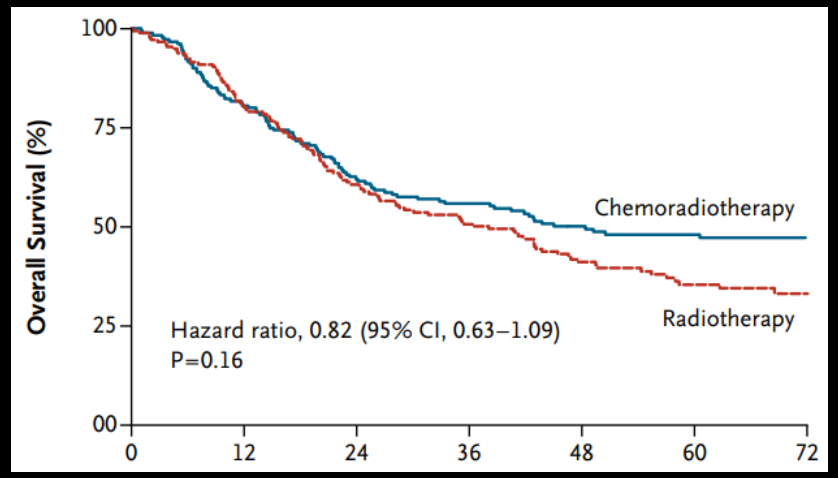
Radiotherapy with or without Chemotherapy in Muscle-Invasive Bladder Cancer

The NEW ENGLAND JOURNAL of MEDICINE
N ENGL J MED 366;16 NEJM.ORG APRIL 19, 2012

"UK Data"[10]

- PHASE III RCT, 360 PTS MIBC → RT +/- 5 FU/MMC
- 55 GY IN 20 FXN OR 64 GY IN 32 FXN ALLOWED
- 82% T2. ONLY 55% HAD COMPLETE TURBT

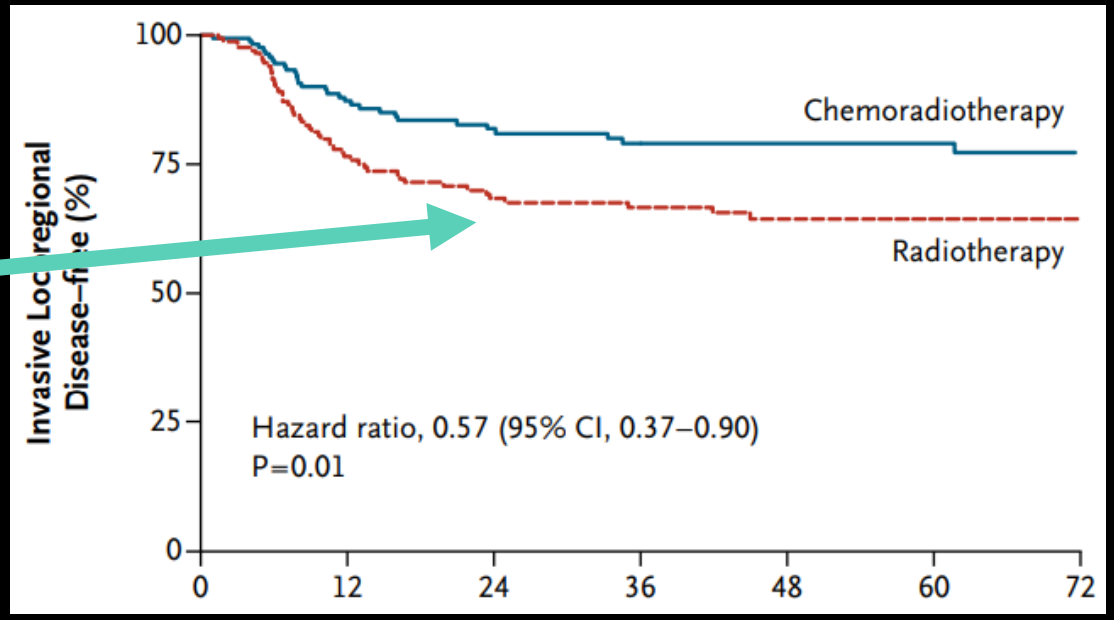




ChemoRT superior BUT … RT ALONE can offer very meaningful disease control

Chemoradiation Specific 5 year Data

- OS - 48%
- MIBC LR Rate 10%
- Non-MIBC LR Rate15%
- Salvage Cystectomy rate 11%
- G3+ Late GU toxicity - 22%
- Only 5% had Nodal relapse



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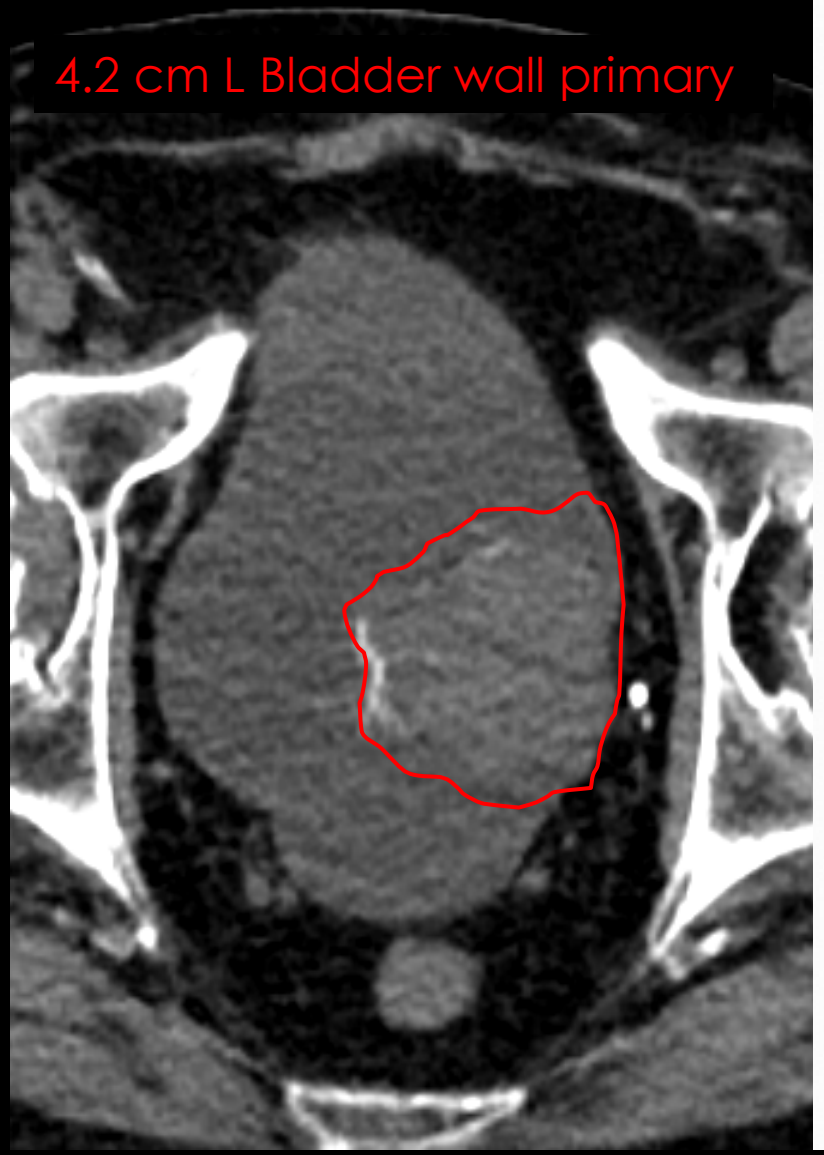
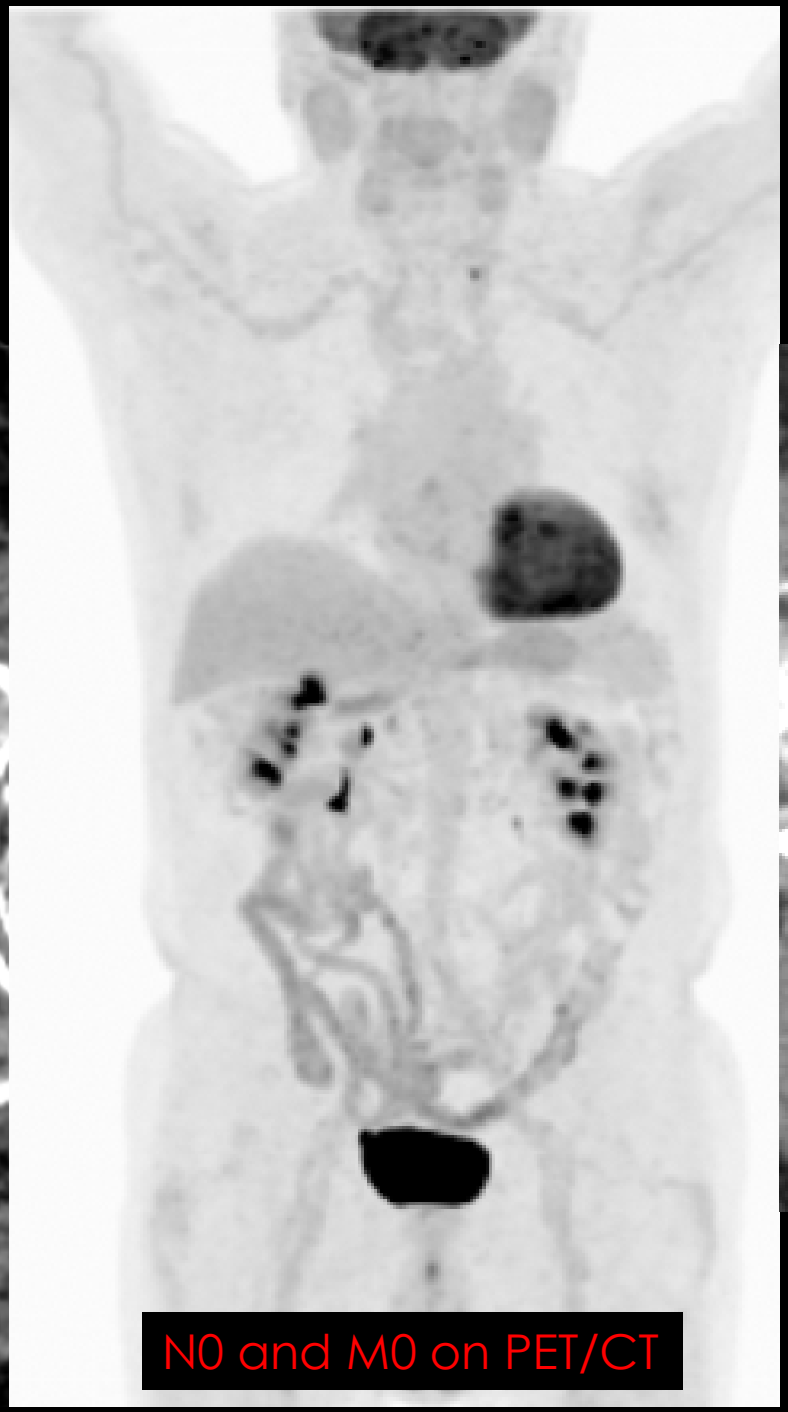
CASE 1

- 89 year old with mild cognitive impairment, CKD, HTN, hypothyroidism, and BPH.
- Prandial dyspepsia and poor PO intake resulted in CT Abd/Pelvis which incidentally identified at 4.2 cm left bladder wall mass. Denied hematuria. Had stable chronic BPH symptoms with slow protracted urinary voiding and incomplete emptying.
- Maximal safe TURBT was completed with final pathology showing high grade urothelial carcinoma with muscularis propria invasion. No Tis. No LVSI.
- PET/CT showed no evidence of LNs or distant mets.
- Stage II, T2 N0 M0, G3, 4.2 cm unifocal primary.
- Given age, comorbidities, frailty, ECOG 2 he was deemed a poor cystectomy candidate.
- Creatine 1.4 made him a poor cisplatin based chemo candidate.

CASE 1

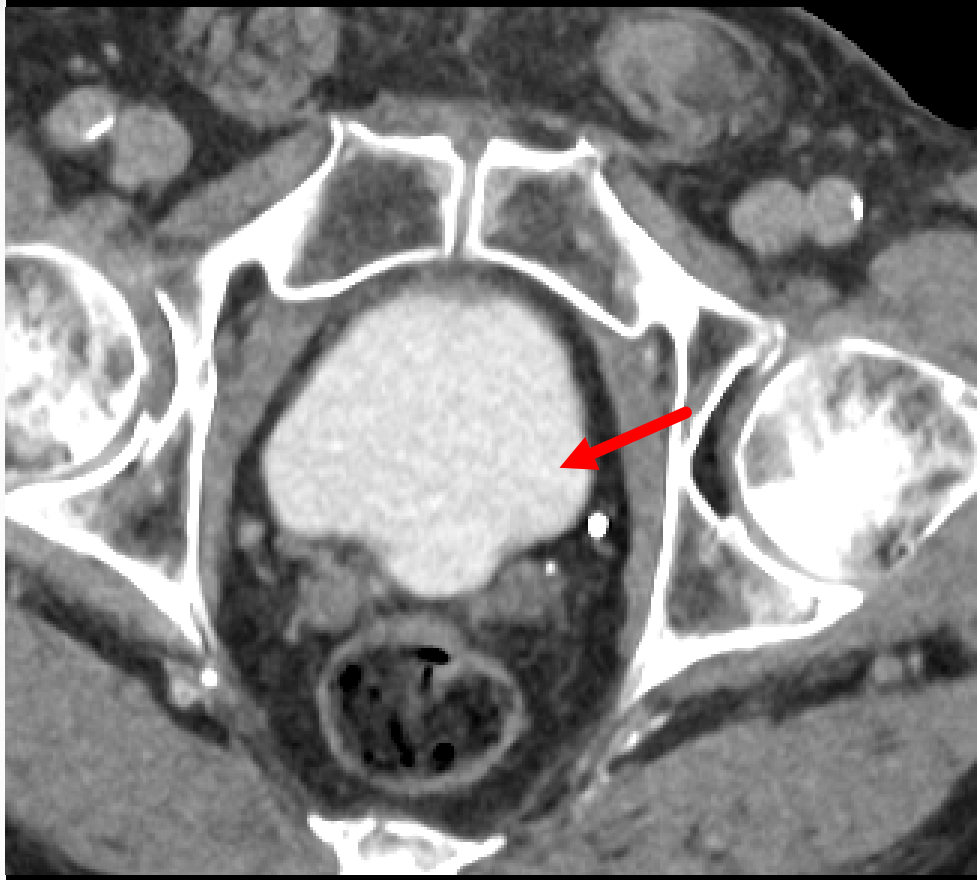
4.2 cm L Bladder wall primary





N0 and M0 on PET/CT

Excellent TURBT result



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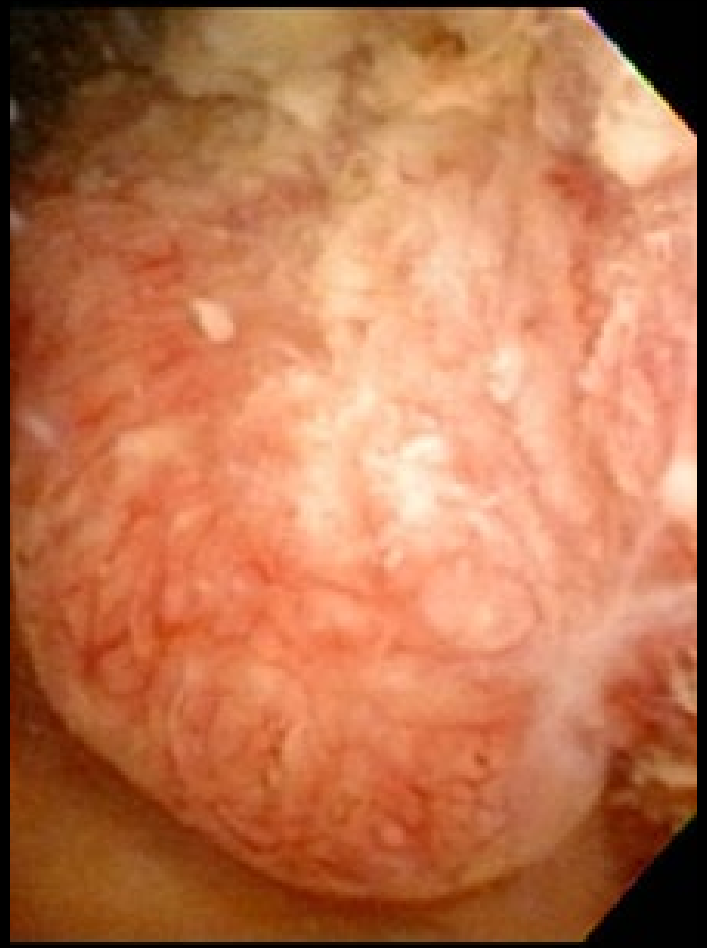
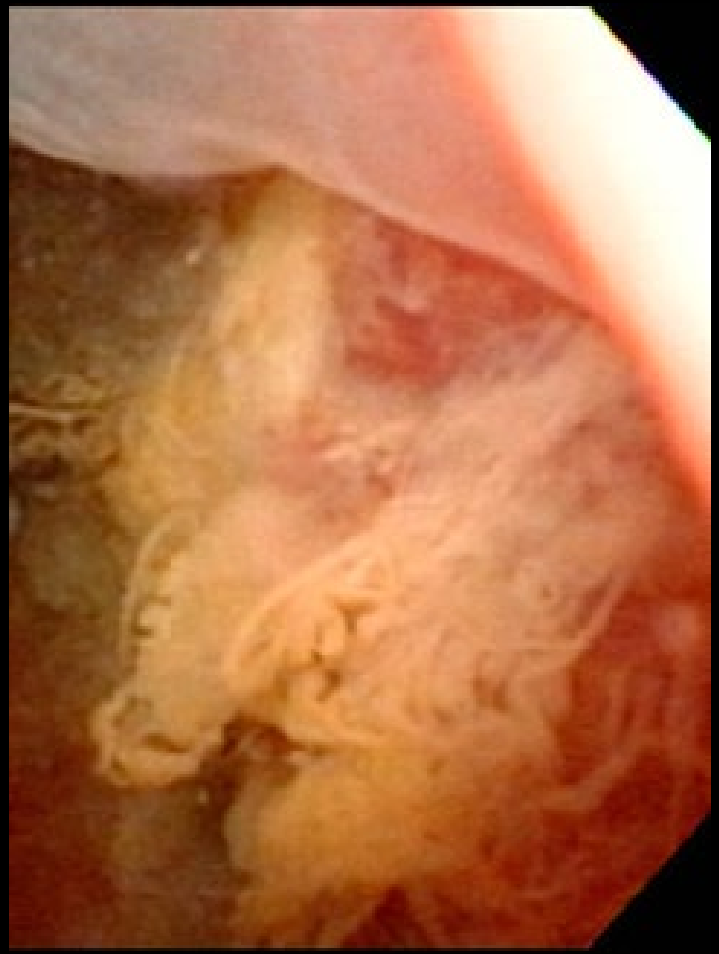
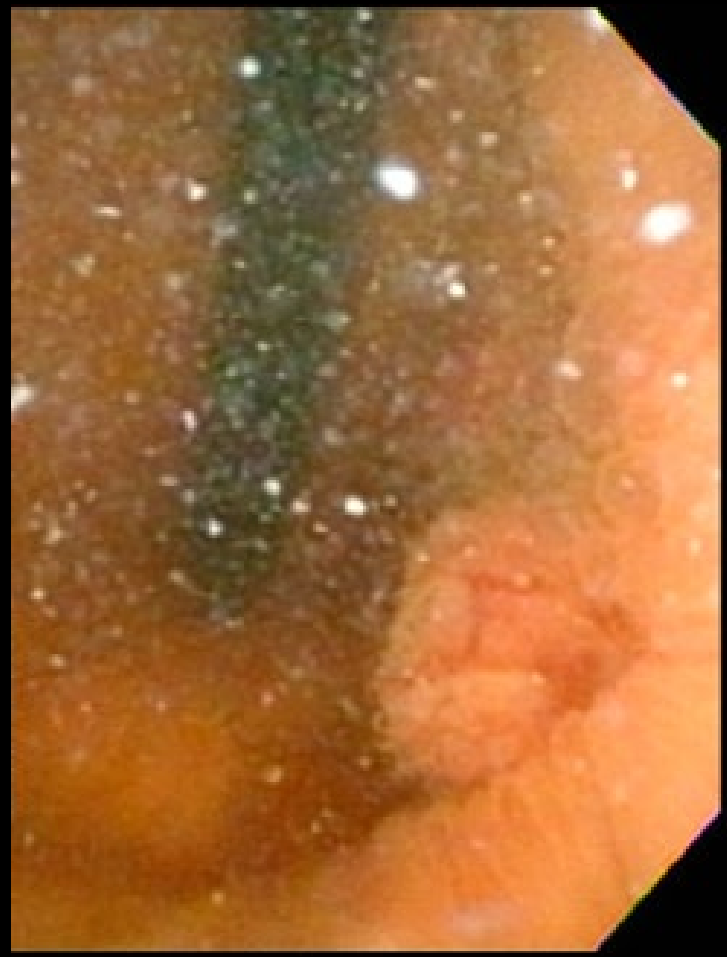


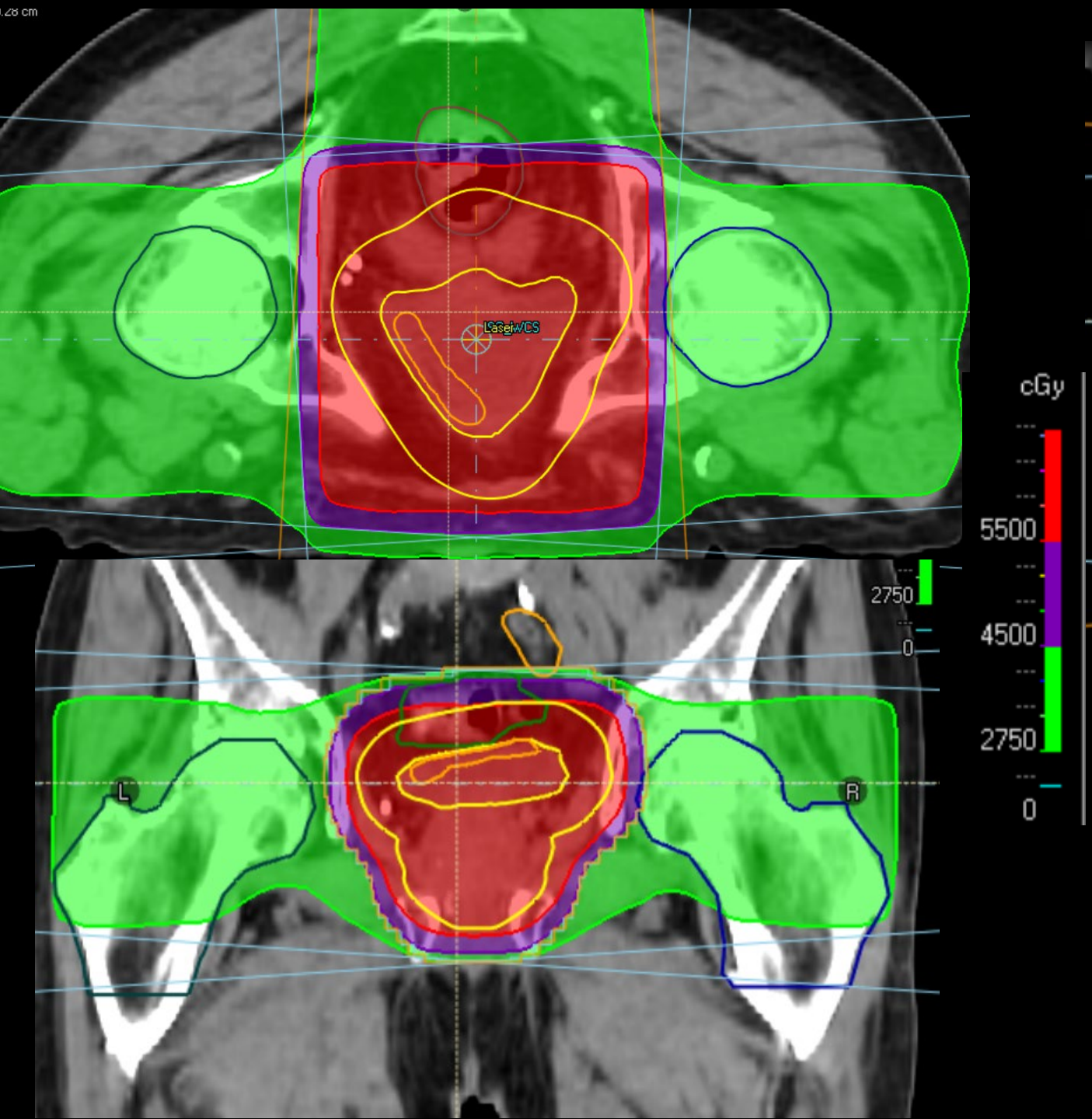


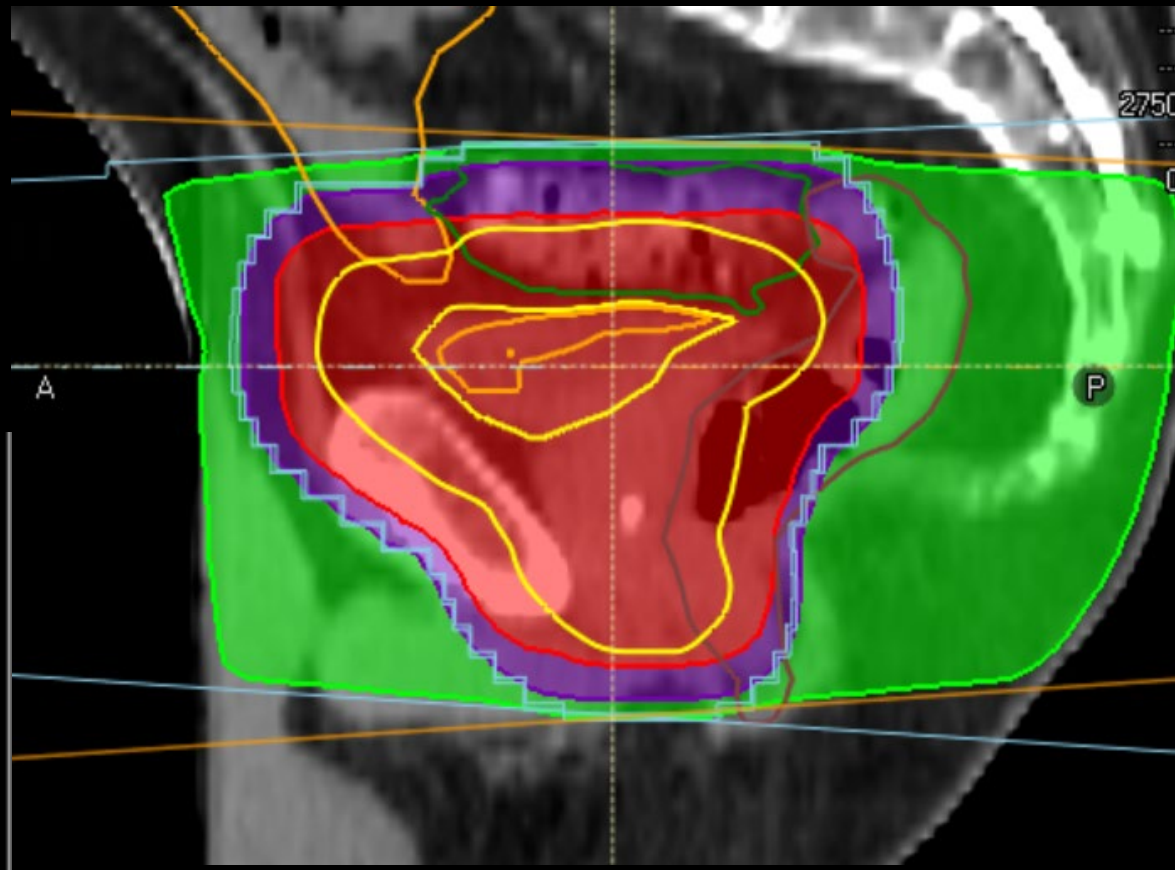


Maximal safe TURBT (before → mid-resection → after)

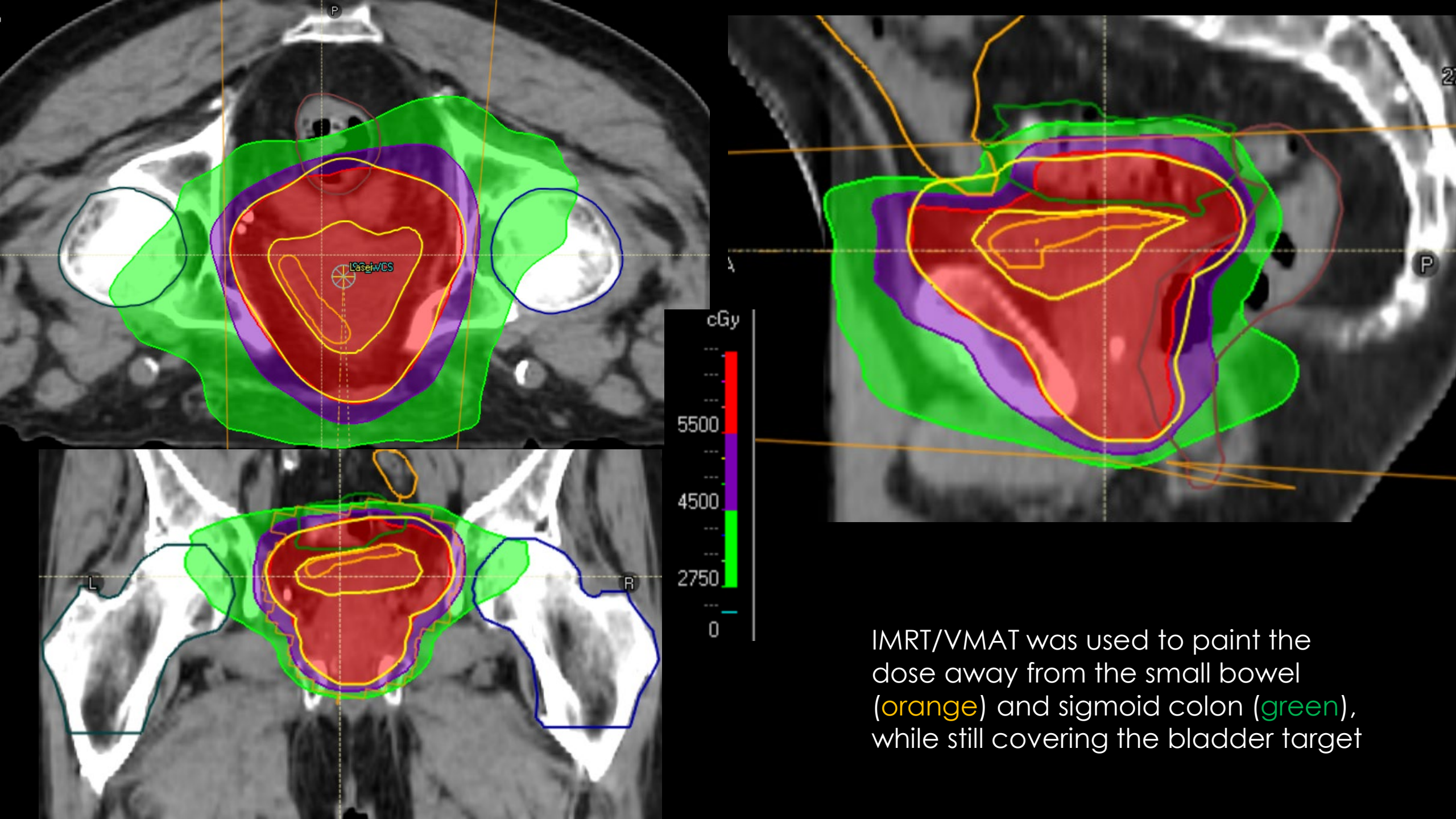
CASE 1

- Discussed curative vs palliative intent approach with patient and family
- Ultimately, he was treated with curative intent hypofractionated bladder only radiation with concurrent chemotherapy
  - 55 Gy in 20 fractions using IMRT
  - concurrent 5-FU and MMC

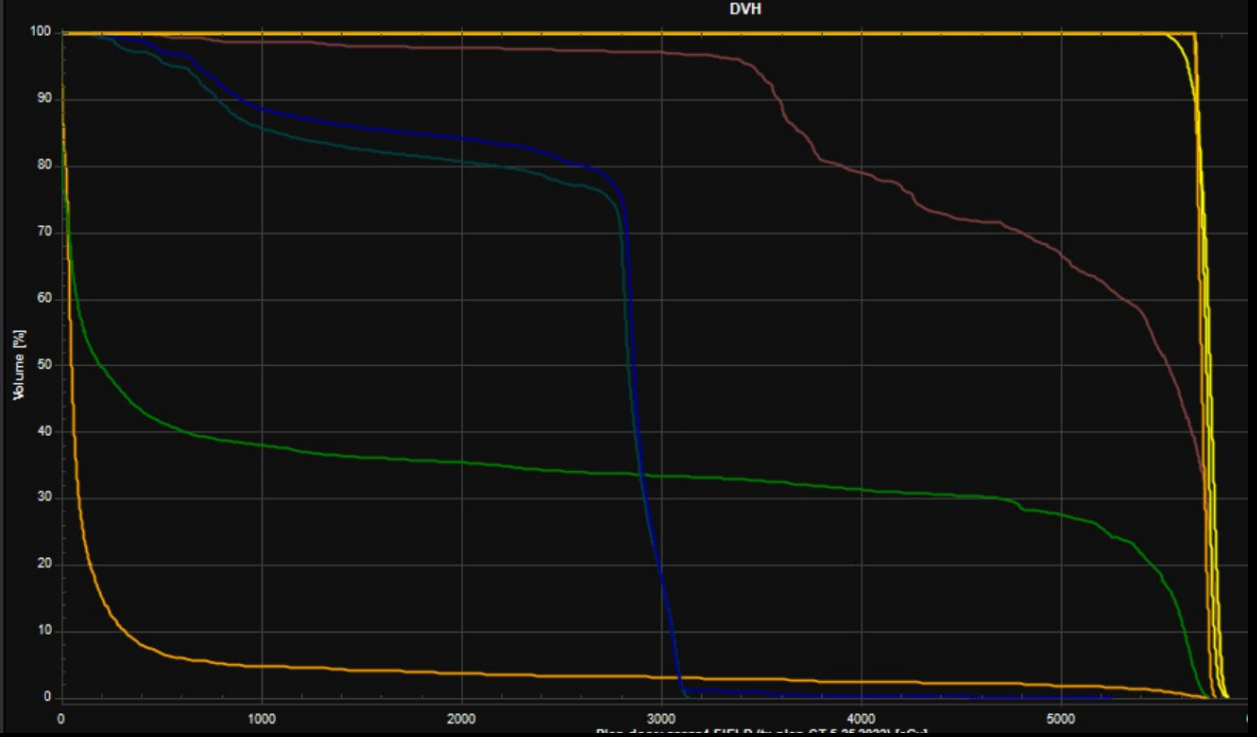




Dose to small bowel (orange) and sigmoid colon (green) too high with "4 field box"



IMRT/VMAT was used to paint the dose away from the small bowel (orange) and sigmoid colon (green), while still covering the bladder target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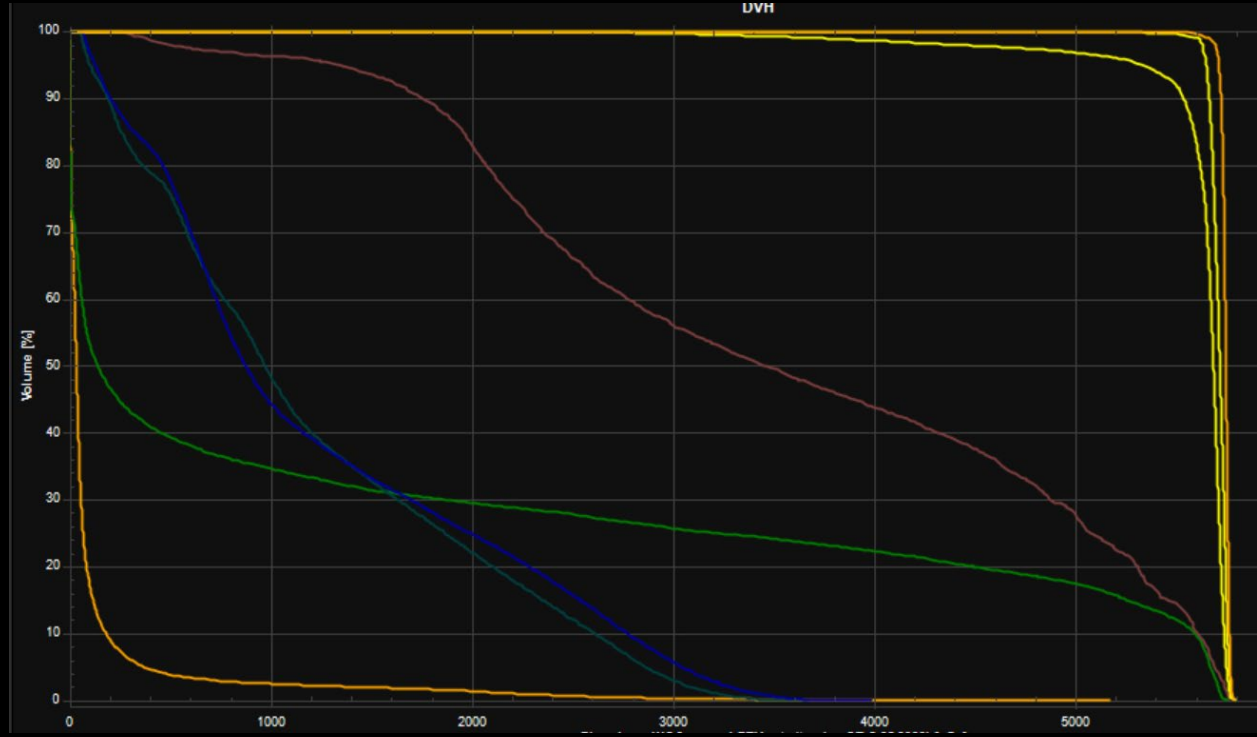
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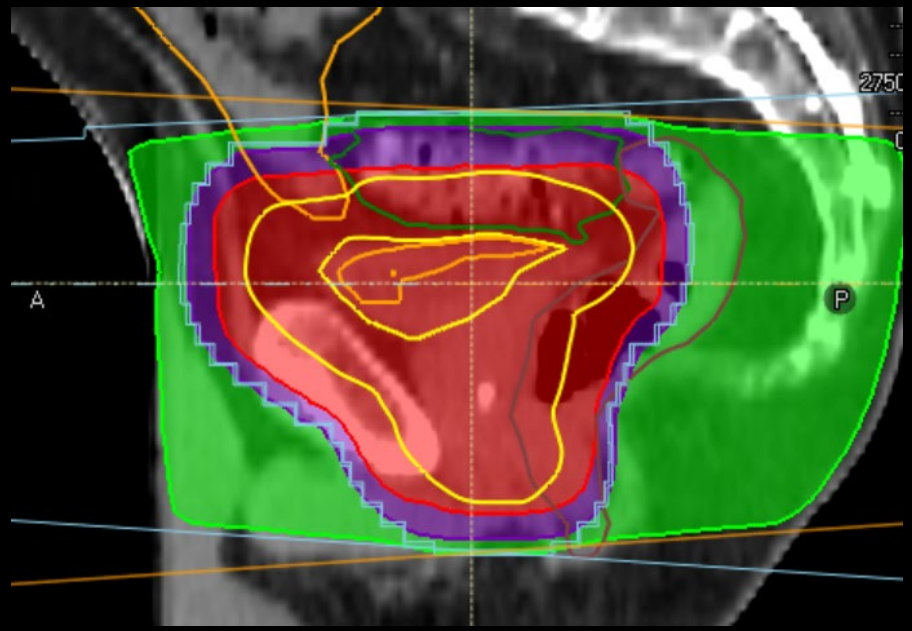
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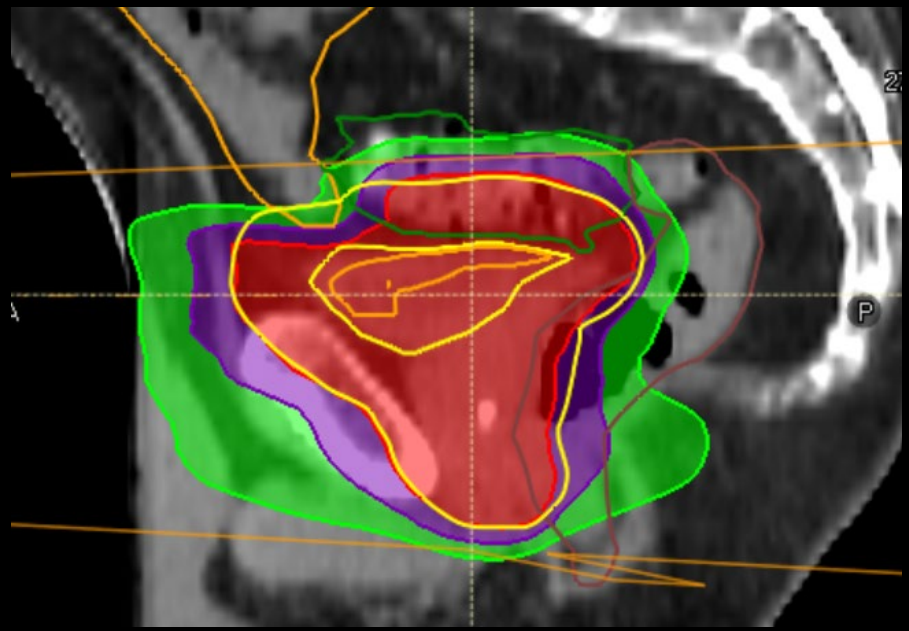
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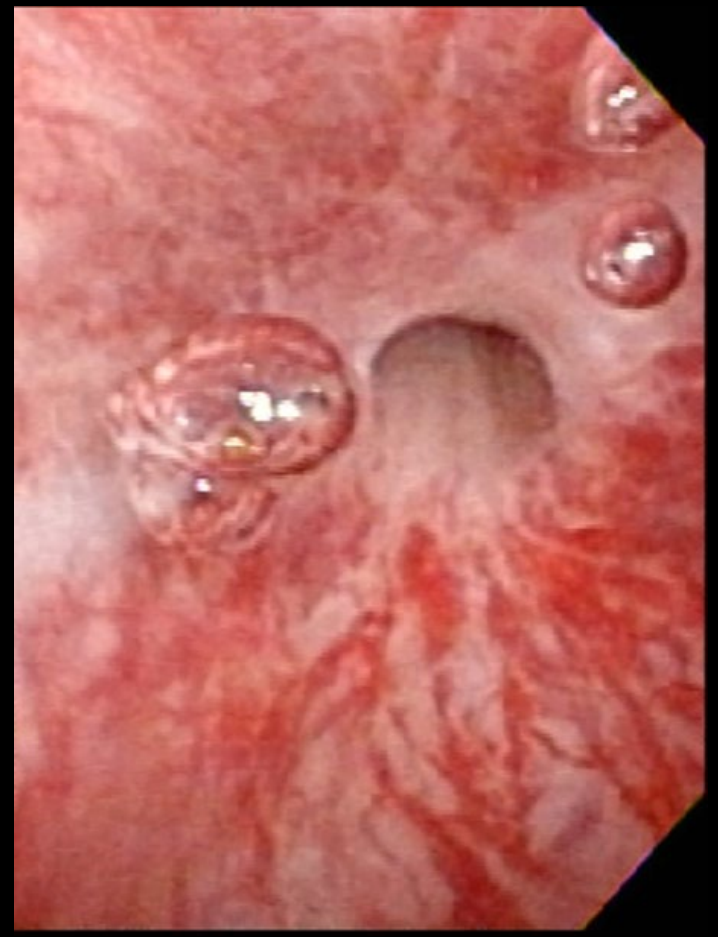
CASE 1

- Required intermittent catheter use for 1-2 months due to urinary obstruction requiring nursing home level care following chemoRT
- Living situation returned to pre-treatment baseline 2 months after treatment
- 2 years out with negative restaging cystoscopy and reimaging to date.
- Voids normally and has no late bladder or bowel toxicity.



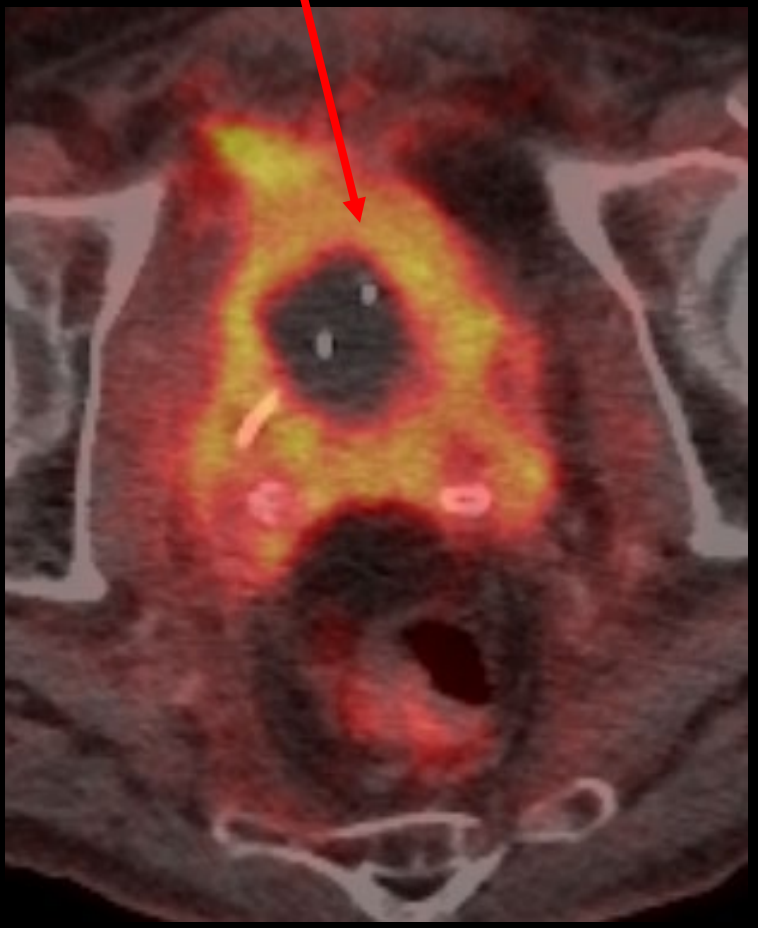
4 month post chemoRT cysto with cystitis changes, no residual disease or new lesions

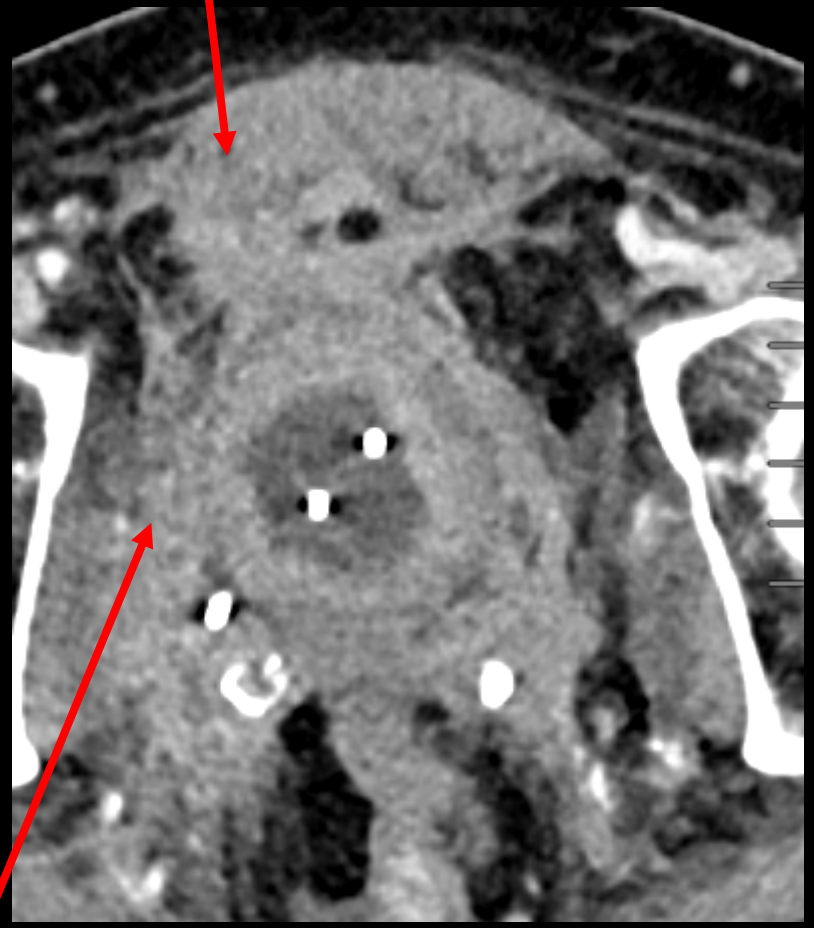
CASE 2

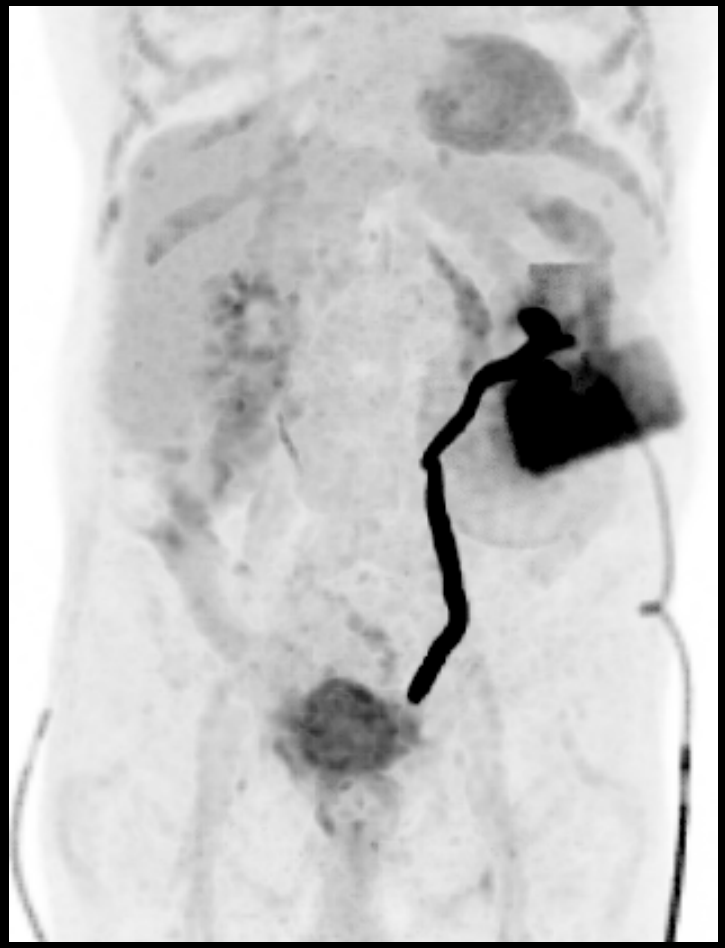
- 69 year old with HTN, HLD, COPD, GERD, and spinal stenosis developed 30 lb weight loss and pelvis/right groin pain.
- CT showed markedly abnormal bladder wall thickening R>L with non-mass like thickening extending to and invading the R obturator and rectus abdominal musculature
- Cysto, partial TURBT, R ureteral stent placement performed. Pathology confirmed urothelial carcinoma with muscularis propria invasion (at least T2)
- Post-op course complicated by acute renal failure, re-imaging showed hydronephrosis bilaterally and percutaneous nephrostomy tubes were placed.
- PET/CT showed no pathologic adenopathy or distant disease
- Clinically staged IVA, T4b N0 M0
- Non-operable due to extent of local disease. Good systemic therapy candidate (once renal function recovered)

Diffuse wall thickening, PCNT in place so no drainage of PET tracer to bladder

Abdominal rectus muscle invasion



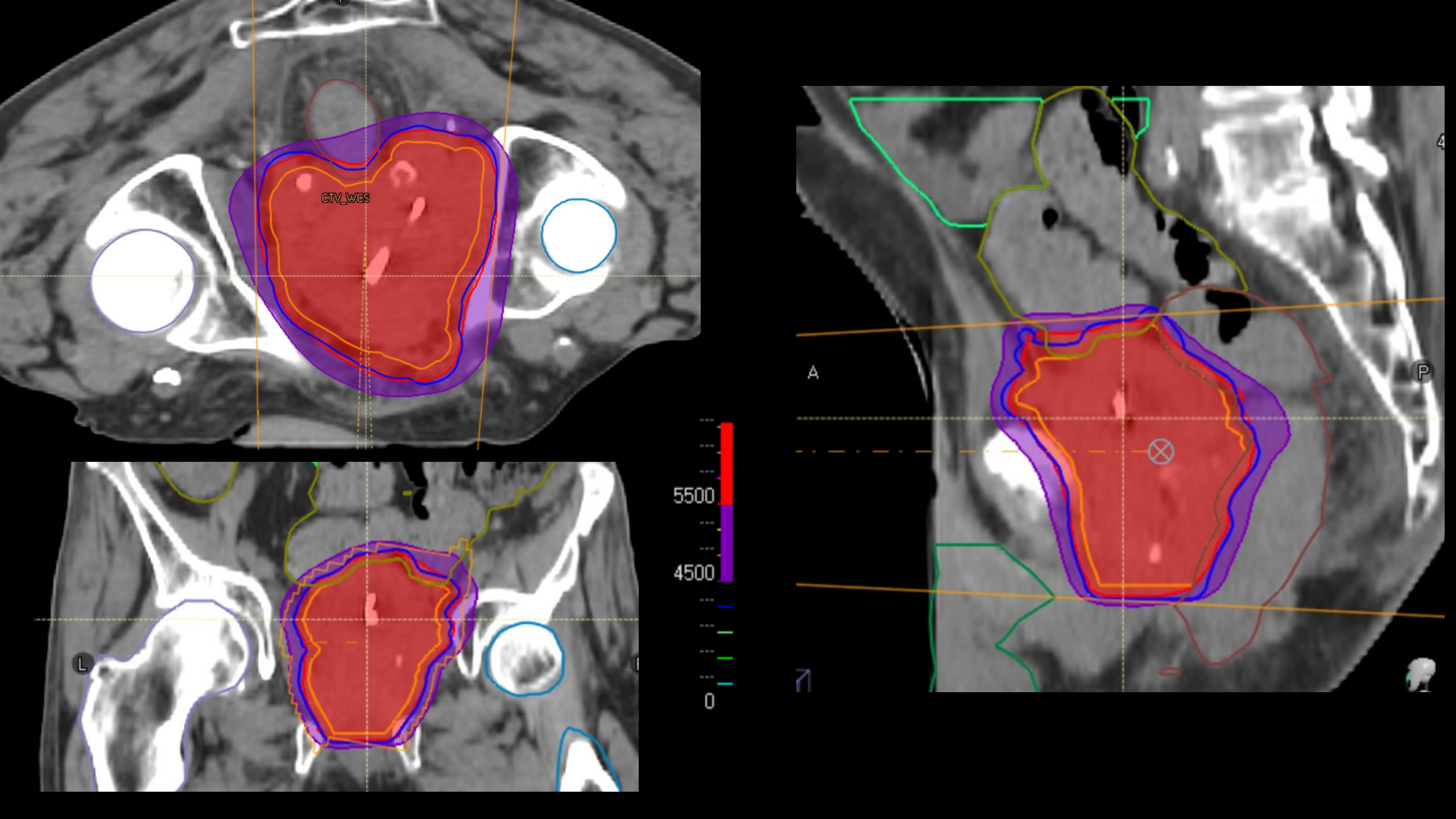




Obturator muscle invasion

CASE 2

- TUMOR BOARD FAVORED APPROACH WAS PALLIATIVE SYSTEMIC THERAPY +/- PALLIATIVE RADIATION FOR OBSTRUCTIVE SYMPTOMATOLOGY AND PAIN
- PATIENT ADAMANTLY DESIRED AGGRESSIVE CARE, WAS RE-PRESENTED
- DEFINITIVE CHEMORADIATION OFFERED AFTER EXTENSIVE COUNSELING REGARDING RISKS OF TREATMENT GIVEN HIS EXTENT OF DISEASE AND GUARDED ONCOLOGIC OUTCOMES WITH T4B DISEASE
- ULTIMATELY, HE UNDERWENT CURATIVE INTENT CHEMORADIATION ENCOMPASSING THE WHOLE BLADDER + EXTRAVESICULAR EXTENDING DISEASE
  - 55 GY IN 20 FRACTIONS
  - CONCURRENT 5-FU/MMC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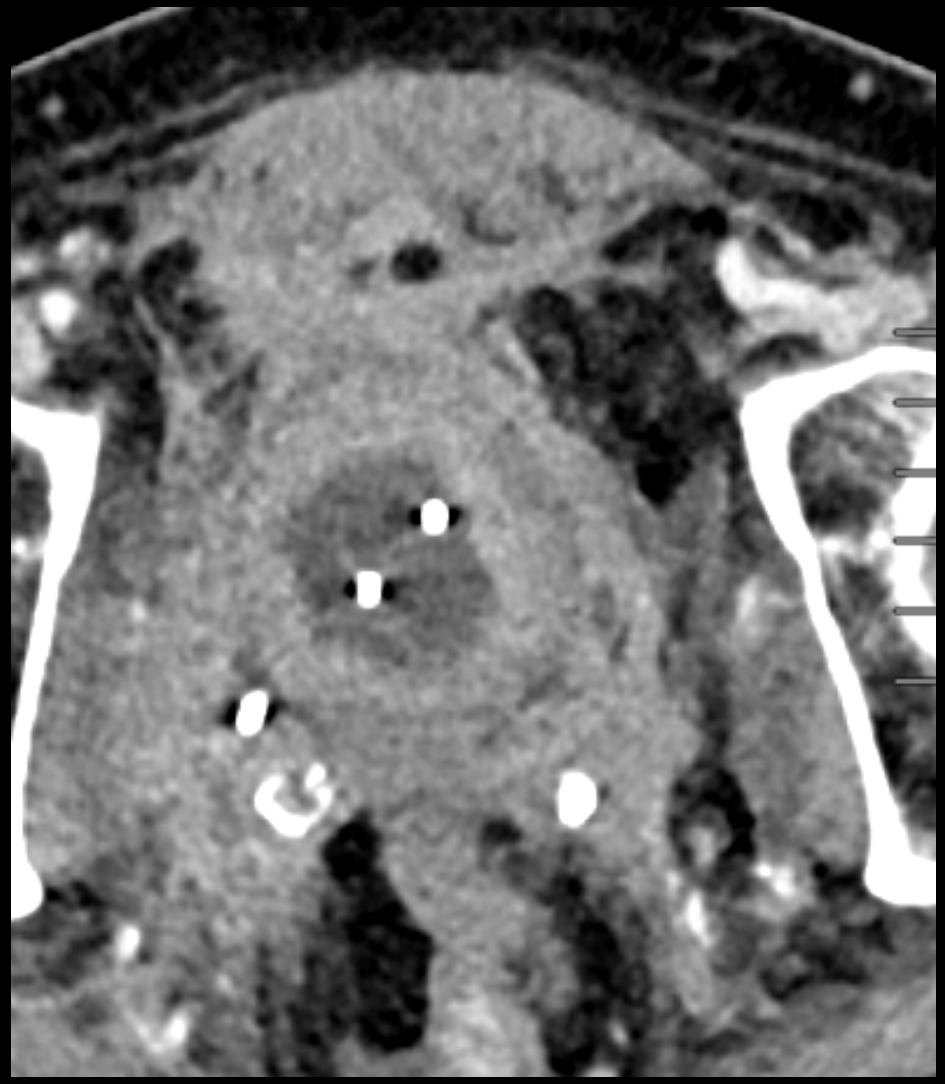
CASE 2

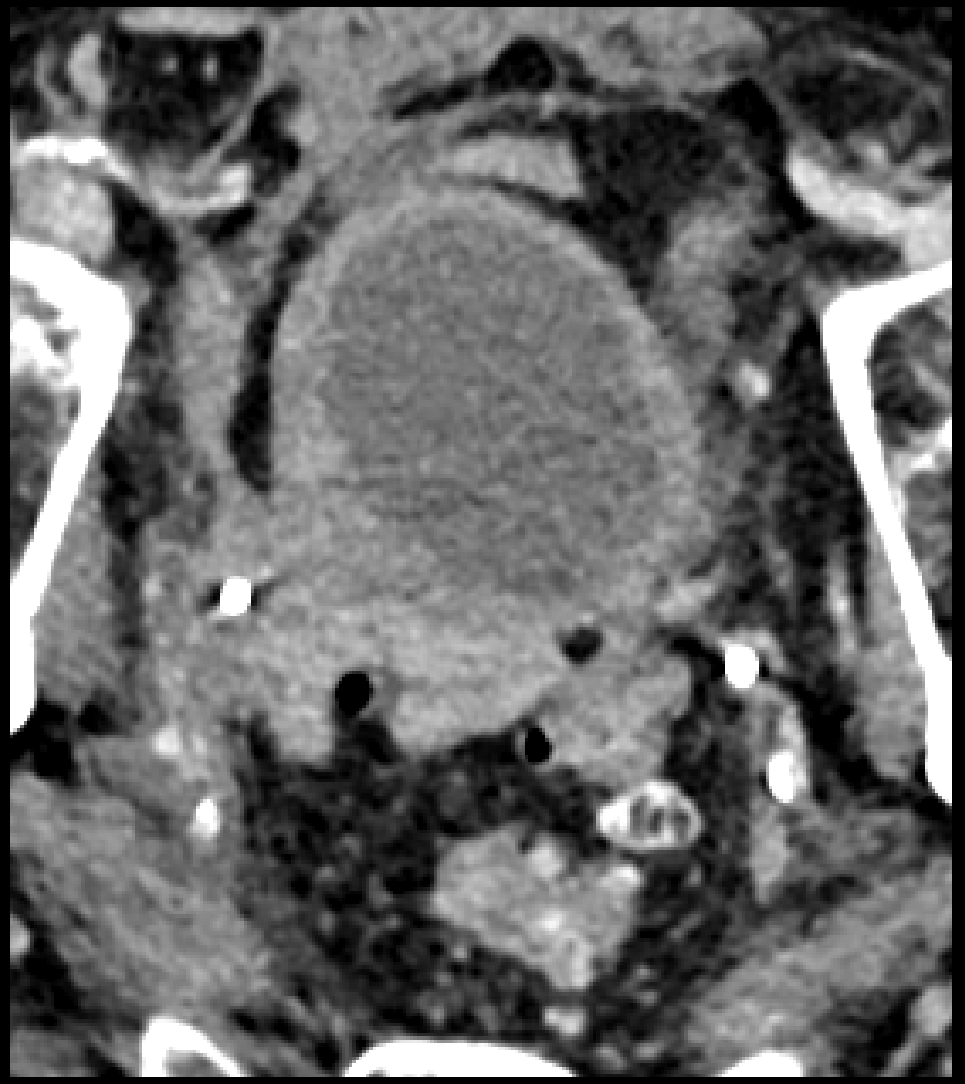
- Analgesia regimen was able to be discontinued mid-treatment
- Radiation enteritis required loperamide. Radiation proctitis was managed with hydrocortisone/pramoxine foam and sucralfate enemas.
- 2 months out from treatment acute pelvic toxicities resolved. He gained 20 lbs and returned to modified duties at work.

- 1 year out from treatment percutaneous nephrostomy tubes were able to be transitioned to indwelling ureteral stents. Extremely difficult exchange due to chronic blader wall/ureteral pelvic junction obstruction and fibrosis.
- Was able to return to full time work after PCNT transitioned to stents.
- No late bowel toxicity

Pre-treatment T4b disease presentation

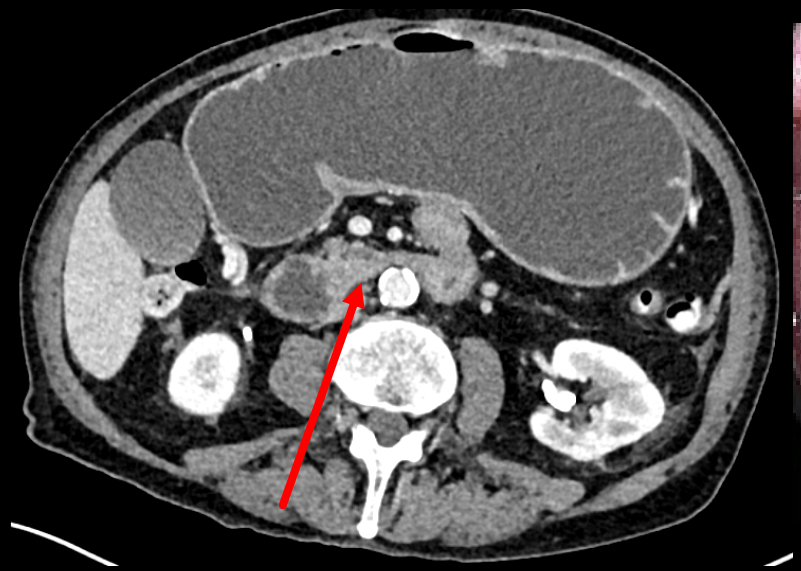


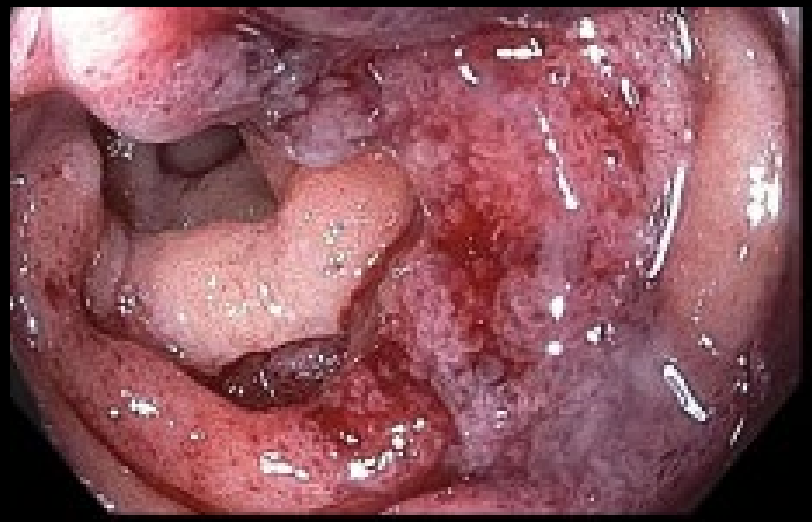
Post-treatment surveillance CT with thickening at Right UPJx from fibrosis. Improved obturator and rectus muscle wall stranding/tissue planes

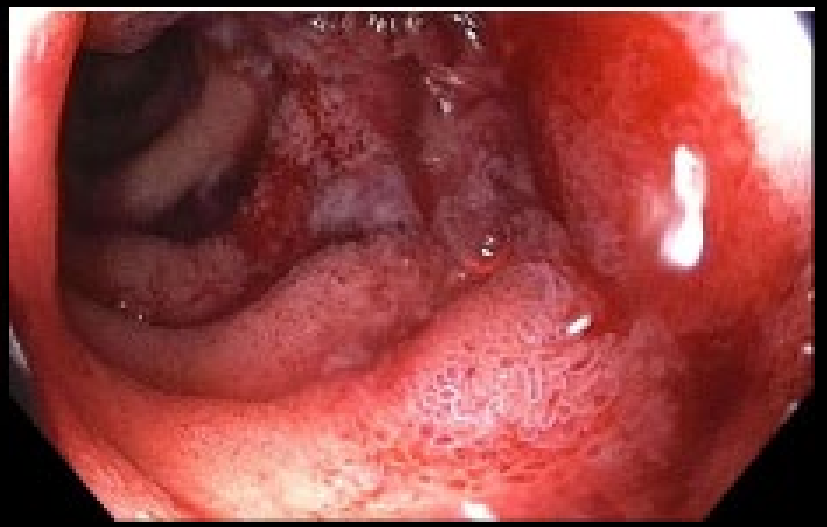


CASE 2

- 1.5 YEARS OUR FROM TREATMENT HE DEVELOPED NAUSEA, VOMITING, AND EARLY SATIETY.
- CT SHOWED BOWEL OBSTRUCTION PATTERN WITH GASTRIC DISTENSION AND A DISTAL DUODENUM TRANSITION POINT.
- EGD WITH BIOPSY OF 3RD PORTION OF DUODENUM OBSTRUCTING ULCER SHOWED METASTATIC UROTHELIAL CARCINOMA.
- RESTAGING CYSTOSCOPY AND PELVIS IMAGING TO DATE NEGATIVE FOR LOCAL OR REGIONAL PROGRESSION







BLADDER PRESERVATION CHEMORT SUMMARY

- Ideal candidates rarely exist
- Dose/Fractionation schedule and treatment targets are provider dependent
  - 4 vs 6-7 week course[1,8-10,16,18]
  - Role of mid-treatment cysto should be reviewed at tumor board[8,9,14,15,18]
  - Elective Lymph node coverage is controversial[14-17,19,20]
  - Elective inclusion of prostate is controversial[8-10,14,15,19]
  - Opinions are mixed on common iliac nodal (N3) management (Curative vs Palliative)[1,2]
- Concurrent chemo improves outcomes when added to radiation
  - CR rates, LRC, DFS, and DMFS[8-10]
  - No randomized data to support one concurrent systemic agent over another[1]
- Radiation *alone* can be curative and/or offer meaningful pelvic control[10]
- Incorporation of immunotherapy with chemoRT is undefined[18]

Outline

- Introduction
- Workup, Staging
- Definitive Management Options
- Bladder Preservation Principles
- Cases and Controversies
- **Future Directions**

Trimodality Therapy for Muscle-Invasive Bladder Cancer: Recent Advances and Unanswered Questions

Current Oncology Reports (2020) 22: 14
https://doi.org/10.1007/s11912-020-0880-5

Di Maria Jiang[1] · Peter Chung[2] · Girish S. Kulkarni[3] · Srikala S. Sridhar[4]

Concurrent with radiotherapy		
NCT03747419 (DFCI 18-464)	Phase II	Avelumab every 2 weeks for 6 doses
NCT03702179 (IMMUNOPRESERVE)	Phase II	Durvalumab 75 mg plus tremelimumab 75 mg every 4 weeks for 3 doses
NCT02662062 (PCR-MIB)	Phase II	Pembrolizumab 200 mg every 3 weeks plus cisplatin, pembrolizumab continued until 12 weeks
NCT02621151 (15-00220)	Phase II	Pembrolizumab 200 mg every 3 weeks for 3 doses plus gemcitabine
NCT03993249 (HGCG 0000020479)	Phase II	Nivolumab and standard of care chemoradiotherapy
Adjuvant post chemoradiotherapy		
NCT03768570 (CCTG BL13)	Phase II	Durvalumab 1500 mg every 4 weeks for a maximum of 12 months
NCT03697850 (BladderSpar)	Phase II	Atezolizumab 1200 mg ever 3 weeks for a maximum of 12 months
NCT03171025 (NEXT)	Phase II	Nivolumab iv 480 mg every 4 weeks for a maximum of 12 months.
Both concurrent and adjuvant		
NCT02560636 (PLUMMB)	Phase I	Pembrolizumab 100-200 mg every 3 weeks starting 2 weeks prior to radiotherapy, continued for a maximum of 12 months
NCT03844256 (CRIMI)	Phase I/II	Nivolumab 480 mg every 4 weeks, or Nivolumab 3 mg/kg and ipilimumab 1 mg/kg every 3 weeks, or Nivolumab 1 mg/kg and ipilimumab 3 mg/kg every 3 weeks, combined with mitomycin and capecitabine Optional nivolumab every 4 weeks continued for a maximum of 52 weeks
NCT04073160 (TRIO Bladder)	Phase I	Durvalumab 1500 mg plus tremelimumab 75 mg every 4 weeks followed by concurrent durvalumab 1500 mg every 4 weeks, based on molecular subtypes Durvalumab may be continued for a maximum of 1 year
NCT03775265 (SWOG S1806)	Phase III	Atezolizumab and physician's choice concurrent chemotherapy (cisplatin, gemcitabine, or 5-fluorouracil and mitomycin). Atezolizumab every 3 weeks starting with concurrent chemotherapy, continued for a maximum of 6 months
NCT03620435 (ML-39576)	Phase II	Atezolizumab 1200 mg iv every 3 weeks, continued for a maximum of 1 year

Efficacy and Safety of Bladder Preservation Therapy in Combination with Atezolizumab and Radiation Therapy (BPT-ART) for Invasive Bladder Cancer: Interim Analysis from a Multicenter, Open-label, Prospective Phase 2 Trial

Received Sep 2, 2022; Accepted for publication May 8, 2023

Int J Radiation Oncol Biol Phys, Vol. 117, No. 3, pp. 644–651, 2023

pCR Rates:

RT Alone: 44-61%[10]

ChemoRT: 66-69%[8-10,16]

Immuno RT: 70-85%[21]

ChemoImmuno RT: ?

Induction?

Maintenance?

BLADDER SPARING THERAPIES FOR UROTHELIAL CANCER: A RADIATION ONCOLOGIST'S PERSPECTIVE

MINNESOTA SOCIETY OF CLINICAL ONCOLOGY
2024 SPRING CONFERENCE, 04/24/2024

QUESTIONS?

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904-327-6313

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EXTRA SLIDES

BLADDER SPARING THERAPIES FOR UROTHELIAL CANCER: A RADIATION ONCOLOGIST'S PERSPECTIVE

MINNESOTA SOCIETY OF CLINICAL ONCOLOGY
2024 SPRING CONFERENCE, 04/24/2024

PET/CT in Bladder Cancer: An Update

Kirsten Bouchelouche, MD, DMSc

Semin Nucl Med 52:475-485

Seminars in NUCLEAR MEDICINE

- Primary site staging data limited by radiotracer accumulation in the bladder
  - post-void hydration or diuretic protocols are under investigation
  - CT and MRI data has equivalent or superior sensitivity/specificity
- Lymph node staging of PET CT: sen. is 23-100% and spec. 33-100%
  - Up to 25% of T2 disease can have +LN
  - Up to 50% of T3 disease can have +LN
- Distant Mets staging of PET CT: sen. is 50-100% and spec. 86-100%
  - changes management over CT/MRI alone 68% of time
- PET CT is Superior to conventional imaging in identifying recurrences
- Emerging prognosis data for Neoadjuvant systemic therapy response assessment

The increasing indications of FDG-PET/CT in the staging and management of Invasive Bladder Cancer

Nicolas Pavlos Omorphos, B.Sc., M.B.B.S., M.R.C.S.[a,*], Aruni Ghose, M.B.B.S.[b,c,f], John D.B. Hayes, B.Sc. (Hons) M.B.Ch.B., M.R.C.S. (Ed)[d,e], Abhinav Kandala[d], Prokar Dasgupta, M.Sc.(Urol), M.D., D.L.S., F.R.C.S., F.R.C.S.(Urol), F.E.B.U.[c,h,i], Anand Sharma, M.B.B.S, M.D., M.R.C.P., M.R.C.P Medical Oncology, D.Phil.[e,f,g], Nikhil Vasdev, D.Sc., M.Ch.(Urology), F.R.C.S.(Urology)[d,e,i]

Urologic Oncology: Seminars and Original Investigations 40 (2022) 434–441

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UROLOGIC ONCOLOGY

The evolving indications of FDG-PET/CT in muscle-invasive bladder cancer based on the current recommendations of the European Association of Urology, European Society for Medical Oncology and American College of Radiology Appropriateness Criteria [14,26,43]

Diagnosis	Allows better assessment of a patient's response to NAC
	Used in detection of both Lymph node metastases and distant
	F-FDG is used for whole-body imaging, and utilises the increased use of glucose by malignant cells – which clinicians can use to identify local/distant metastases before they are signalled by conventional imagining modalities
	Improved diagnostic accuracy of PET/CT, and F-FDG PET/CT by combinations of axial based LN size and SUV_{max} criteria allowed high sensitivity as well as specificity in pre-operative detection of bladder cancers, lymph node metastases, pelvic lesions, and distant metastases
	Imaging here allows early visualisation of metabolism alternations
	It has an 83% sensitivity with a 94% specificity for the detection of chemo-sensitive tumours
Follow up	F-FDG-PET/CT proven to reliably monitor response to chemotherapy in various cancers
	High efficacy in bladder cancer, with a 92% sensitivity of F-FDG-PET/CT in detecting residual invasive bladder cancer, and a 95.2% accuracy in detecting post-treatment recurrence outside the urinary tract, especially for bone lesions
	FDG-PET/CT has a sensitivity and specificity of 78.5% and 95.6% respectively in identifying complete pathologic response
Treatment	F-FDG-PET/CT shown to influence patient management and is a prognostic indicator of PFS and OS
	F-FDG-PET/CT should be included in oligometastatic disease staging to minimise the risk of overtreatment, when radical treatment options are being considered
	Currently recommended by the American College of Radiology for patients with MBIC (from skull-base to mid-thighs)

Long-Term Outcomes in Patients With Muscle-Invasive Bladder Cancer After Selective Bladder-Preserving Combined-Modality Therapy: A Pooled Analysis of Radiation Therapy Oncology Group Protocols 8802, 8903, 9506, 9706, 9906, and 0233

Raymond H. Mak, Daniel Hunt, William U. Shipley, Jason A. Efstathiou, William J. Tester, Michael P. Hagan, Donald S. Kaufman, Niall M. Heney, and Anthony L. Zietman

"RTOG Experience"

VOLUME 32 · NUMBER 34 · DECEMBER 1 2014

JOURNAL OF CLINICAL ONCOLOGY

- 468 PTS, 6 RTOG BLADDER PRESERVATION STUDIES
  - T2 - 61%, T3 - 35%, T4A - 4%
  - MINI-PELVIS INITIAL COURSE → BLADDER BOOST (STANDARD)
  - MOSTLY SPLIT COURSE W/ CYSTO RE-EVAL
  - VARIOUS CONCURRENT CHEMO, SOME NEOADJ/ADJ CHEMO
- 69% HAD COMPLETE RESPONSE
- 5 YEAR OS 57%, 10 YEAR OS 36%
- 5 YEAR DSS 71%, 10 YEAR DSS 65%
- 10 YEAR: NON-INVASIVE LF RATE 36%, MIBC LF RATE 14%, DM RATE 35%

Long-Term Outcomes in Patients With Muscle-Invasive Bladder Cancer After Selective Bladder-Preserving Combined-Modality Therapy: A Pooled Analysis of Radiation Therapy Oncology Group Protocols 8802, 8903, 9506, 9706, 9906, and 0233

VOLUME 32 · NUMBER 34 · DECEMBER 1 2014

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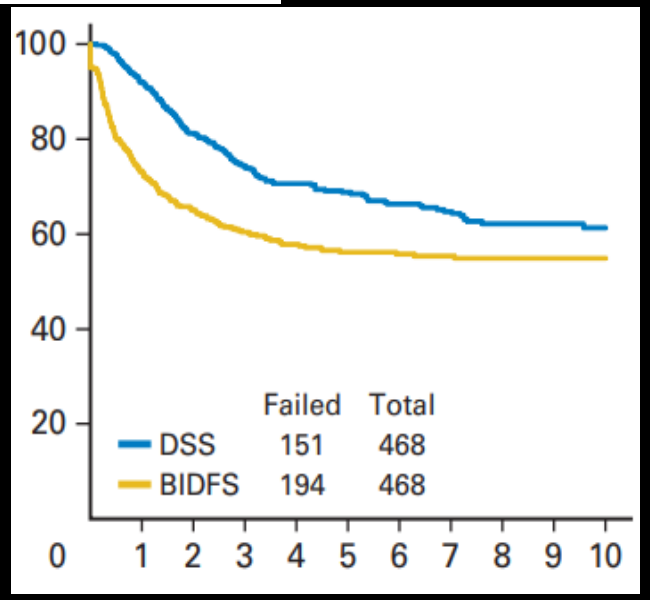
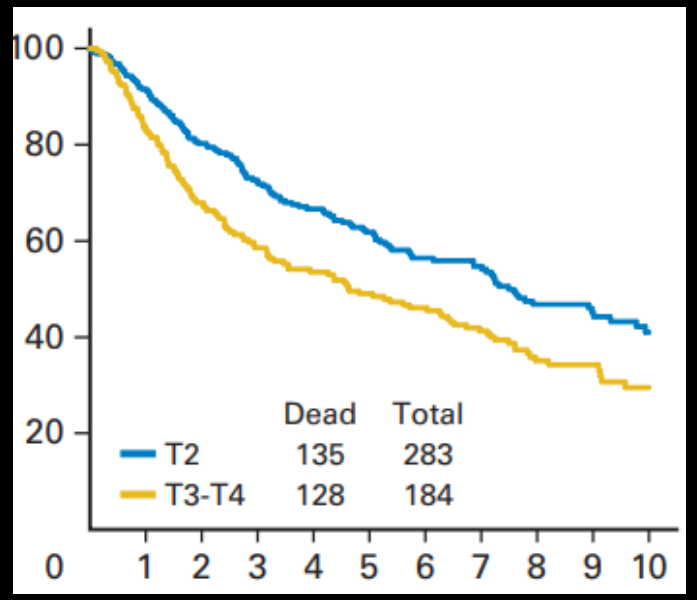
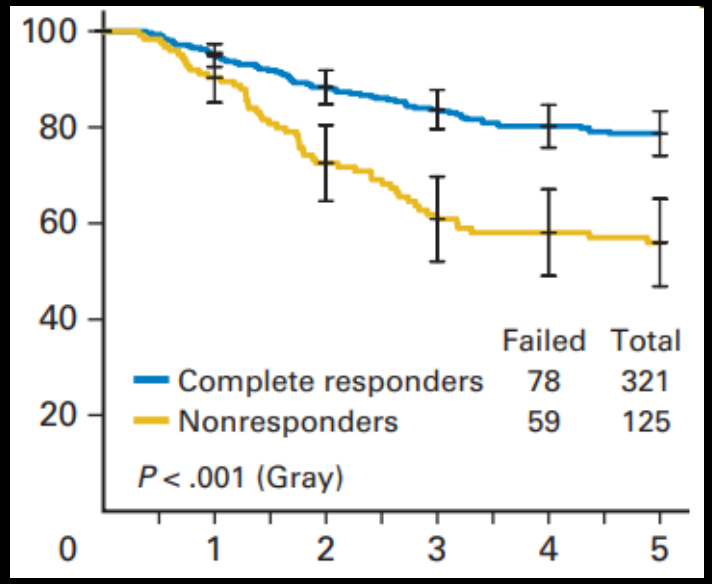
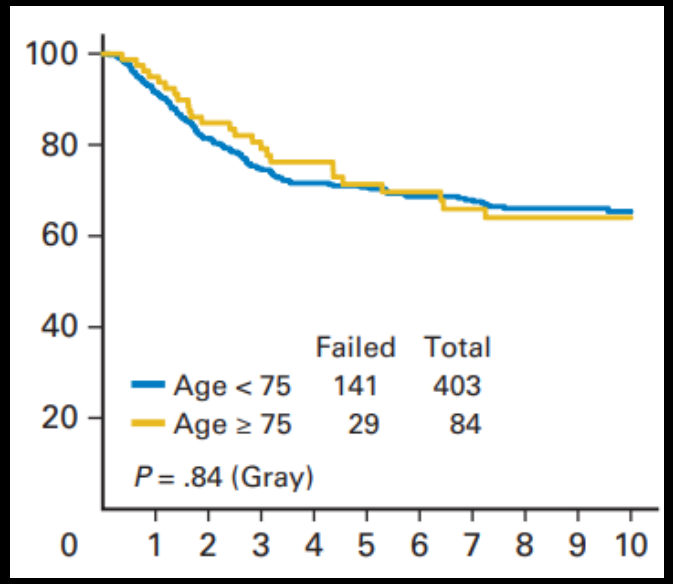
Survival (%)

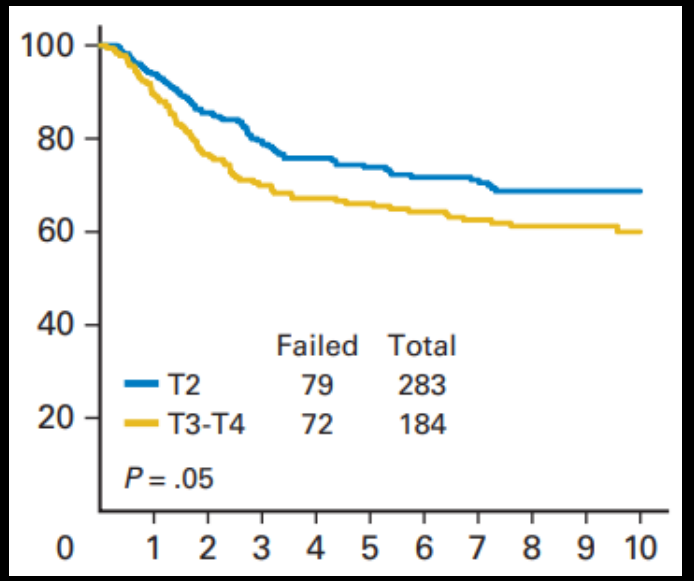




Disease-Specific Survival(%)







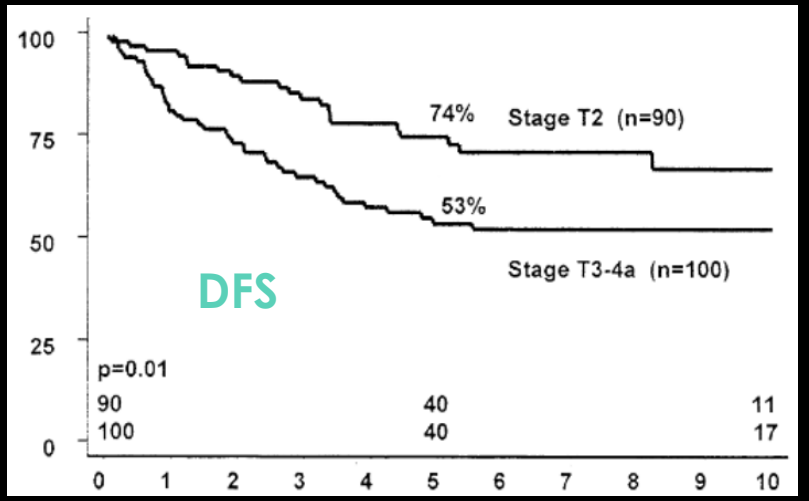
SELECTIVE BLADDER PRESERVATION BY COMBINED MODALITY PROTOCOL TREATMENT: LONG-TERM OUTCOMES OF 190 PATIENTS WITH INVASIVE BLADDER CANCER

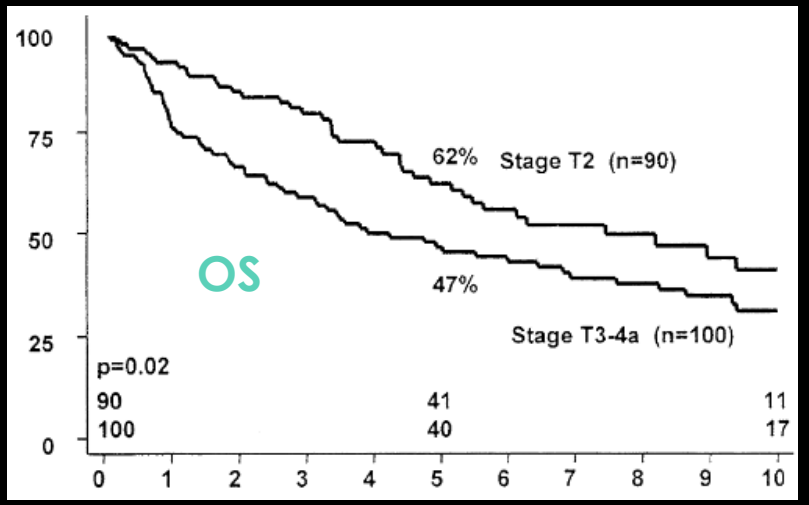
W. U. SHIPLEY, D. S. KAUFMAN, E. ZEHR, N. M. HENEY, S. C. LANE, H. K. THAKRAL, A. F. ALTHAUSEN, AND A. L. ZIETMAN

ADULT UROLOGY

"MGH Data"

- 190 PTS @ MGH, T2-T4A, BLADDER PRESERVATION
- 40 GY PELVIS → CYSTO CR? → 64.8 GY BLADDER
  - VARIOUS CISPLATIN CONCURRENT CHEMO. NEOADJ, ADJ CHEMO ALLOWED
  - APPROXIMATELY 2/3 OF PTS WERE ABLE TO PROCEED WITH BOOST
- OS: 5YR - 54%, 10YR - 36%
- DFS: 5YR - 63%, 10YR - 59%
- DSS IN PTS W/ INTACT BLADDER: 5 & 10YR - 45%





Efficacy and Safety of Bladder Preservation Therapy in Combination with Atezolizumab and Radiation Therapy (BPT-ART) for Invasive Bladder Cancer: Interim Analysis from a Multicenter, Open-label, Prospective Phase 2 Trial

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Int J Radiation Oncol Biol Phys, Vol. 117, No. 3, pp. 644–651, 2023

- Phase 2 Single Arm trial investigating Immunotherapy and Radiation
- Primary Outcome: PFS. Secondary Outcome: pCR rate
- Atezolizumab Q3 weeks x 8 cycles + pelvic RT (lower dose than standard)
  - mini-pelvis RT 41.4 Gy/23 fxn and 16.2 Gy/9 fxn whole bladder boost
  - 57.6 Gy total dose (whereas conventional fractionation s.o.c dose is 64.8 Gy)
- T2-3 (38 pts), some very high risk T1 (7 pts)
  - Excluded T4, tumor >5 cm, hydronephrosis, autoimmune disease, prior pelvis RT
- pCR rate 84.4% (38 of 45)
- 4 of 7 without PCR had non-MIBC residual only