1

2

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UNC CANCER NETWORK

CANCER TREATMENT IN NORTH CAROLINA **RESEARCH TO PRACTICE**

June 24, 2020

**Radiation Oncology in North Carolina:
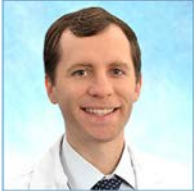Bladder Cancer Updates for 2020**

Trevor Royce, MD, MPH

5

OUR PRESENTER

Trevor Royce, MD, MPH

Dr. Trevor Royce is a clinically active radiation oncologist specializing in genitourinary malignancies (e.g. prostate and bladder cancer).

He is an engineer by training with a BS in biomedical engineering and an MS in physiology and biophysics. His formal research training included a Doris Duke Clinical Research Fellowship at the University of North Carolina and an MPH from the Harvard School of Public Health – both focused on health services research.

He also served as a Health Policy Fellow for the American Society of Clinical Oncology. He has a particular research interest in the value and financial aspects of care, and efficiency of care delivery, as well as comparative and cost effectiveness analyses.

The overarching goal of his research and national committee involvement is to impact clinical practice and health policy. He has published on cancer care utilization and patterns of practice, focusing on identifying areas of healthcare inefficiency.

6

Respond at **PollEv.com/unccn**
Text **UNCCN** to **22333** once to join, then **A, B, C, or D**

UNC CANCER NETWORK

Which one of the following is NOT typically considered a potential symptom for bladder cancer?

Blood in the urine **A**

Painful urination **B**

Pelvic pain **C**

Memory loss **D**

Answers to this poll are anonymous

7

8

To show this poll

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9

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Radiation Oncology in North Carolina: Bladder Cancer Updates for 2020

The multidisciplinary management of bladder cancer: a radiation oncologist's perspective

Trevor J. Royce MD MS MPH
Assistant Professor
Department of Radiation Oncology
UNC School of Medicine
trevor_royce@med.unc.edu

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Disclosures

- I have no disclosures.

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Objectives

- Describe the role radiation can play in the multidisciplinary management of bladder cancer
- Compare the roles of radiation and surgery in the treatment of muscle invasive bladder cancer
- Recognize the toxicities and quality of life implications of radiation therapy for bladder cancer

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Poll

- Which one of the following is NOT typically considered a potential symptom for bladder cancer?
  - » Blood in the urine
  - » Painful urination
  - » Pelvic pain
  - » Memory loss

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Poll

- Which one of the following is NOT typically considered a potential symptom for bladder cancer?
  - » Blood in the urine
  - » Painful urination
  - » Pelvic pain
  - » Memory loss

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Poll

- Which of the following cancers will be responsible for the most deaths in 2020?
  - » Melanoma
  - » Uterine/endometrial cancer
  - » Kidney/renal cancer
  - » Bladder cancer

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Poll

- Which of the following cancers will be responsible for the most deaths in 2020?
  - » Melanoma – 6,850
  - » Uterine/endometrial cancer – 12,590
  - » Kidney/renal cancer – 14,830
  - » Bladder cancer – 17,980

National Cancer Institute (seer.cancer.gov)

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Bladder Cancer Background
Anatomy

Kidney
Ureter
Bladder
Prostate gland
Urethra

WebMD

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Bladder Cancer Background
Epidemiology
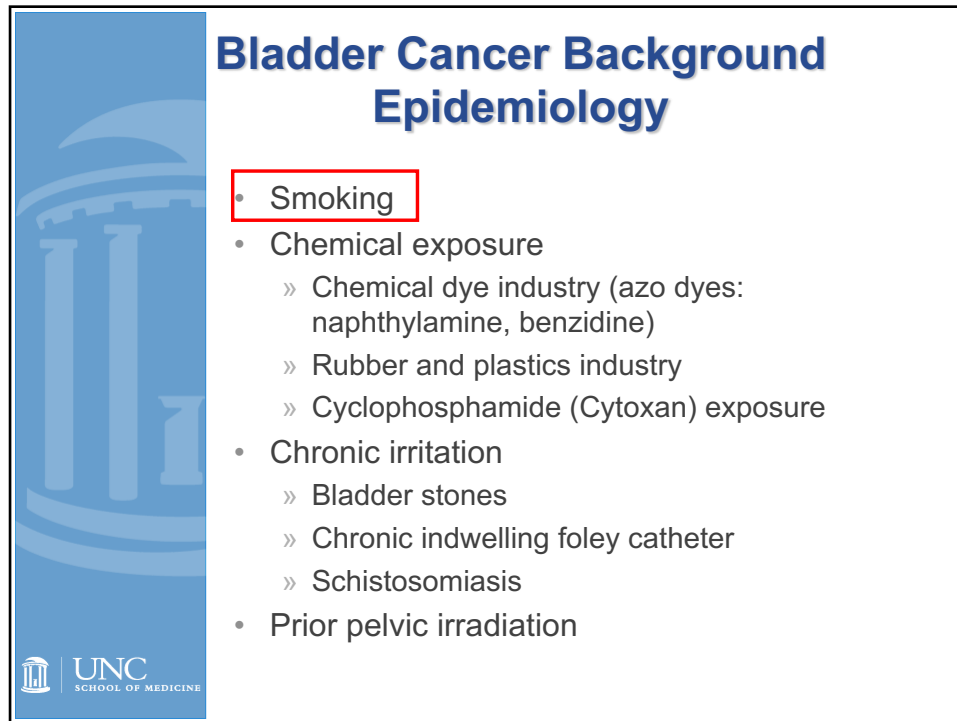
	Common Types of Cancer	Estimated New Cases 2020	Estimated Deaths 2020
1.	Breast Cancer (Female)	276,480	42,170
2.	Lung and Bronchus Cancer	228,820	135,720
3.	Prostate Cancer	191,930	33,330
4.	Colorectal Cancer	147,950	53,200
5.	Melanoma of the Skin	100,350	6,850
6.	Bladder Cancer	81,400	17,980
7.	Non-Hodgkin Lymphoma	77,240	19,940
8.	Kidney and Renal Pelvis Cancer	73,750	14,830
9.	Uterine Cancer	65,620	12,590
10.	Leukemia	60,530	23,100

Bladder cancer represents 4.5% of all new cancer cases in the U.S.

4.5%

National Cancer Institute (seer.cancer.gov)

18
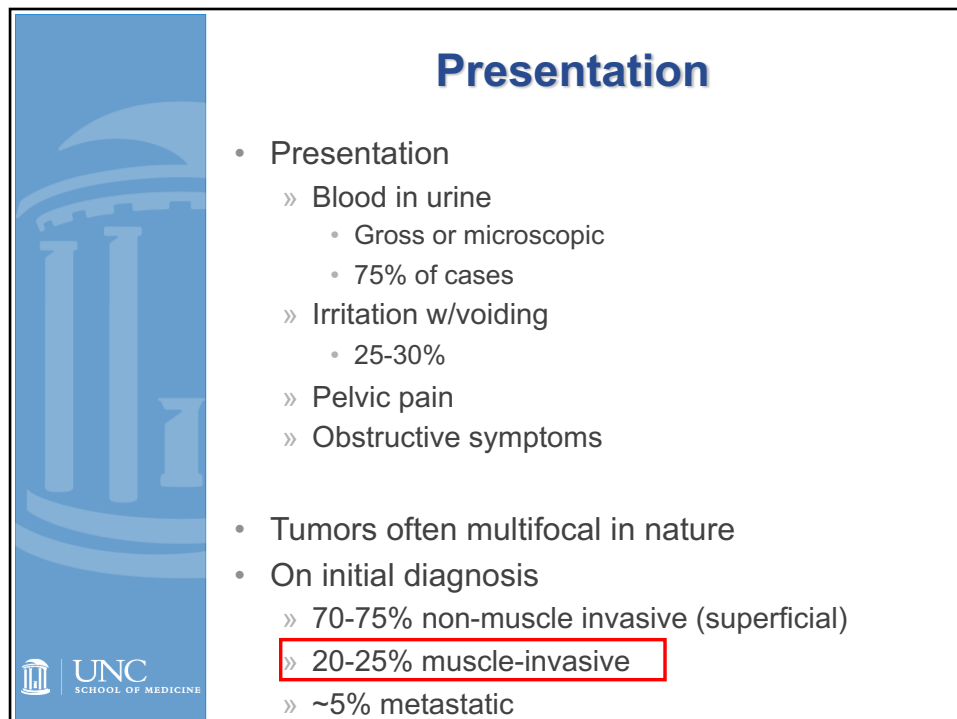
Bladder Cancer Background Epidemiology

- Smoking
- Chemical exposure
  - » Chemical dye industry (azo dyes: naphthylamine, benzidine)
  - » Rubber and plastics industry
  - » Cyclophosphamide (Cytoxan) exposure
- Chronic irritation
  - » Bladder stones
  - » Chronic indwelling foley catheter
  - » Schistosomiasis
- Prior pelvic irradiation

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Presentation

- Presentation
  - » Blood in urine
    - Gross or microscopic
    - 75% of cases
  - » Irritation w/voiding
    - 25-30%
  - » Pelvic pain
  - » Obstructive symptoms

- Tumors often multifocal in nature
- On initial diagnosis
  - » 70-75% non-muscle invasive (superficial)
  - » 20-25% muscle-invasive
  - » ~5% metastatic

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Background: Staging

Stage 0-I: Non-muscle invasive

T1: Lamina propria

Ta: Non-invasive
Tis: CIS, 'flat tumor'

T = pT

Stage II-III: Muscle invasive

T2: Muscle
   T2a: Superficial
   T2b: Deep
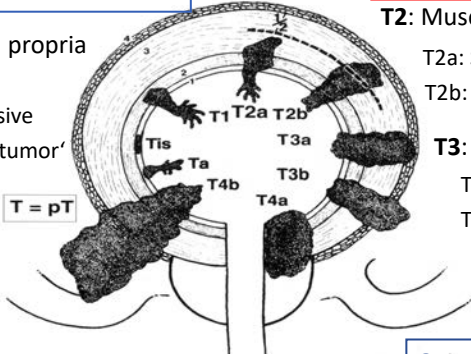
T3: Perivesical fat
   T3a: Microscopic
   T3b: Macroscopic

T4: Beyond perivesical fat
   T4a: Prostate, uterus, and/or vagina
   T4b: Pelvic/abdominal wall

Stage IV
N1: Single node in true pelvis
N2: Multiple nodes in the true pelvis
N3: Common iliac nodes
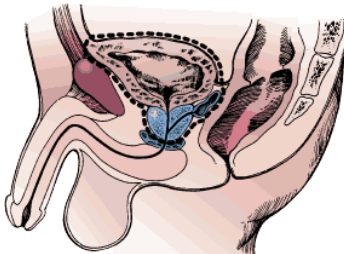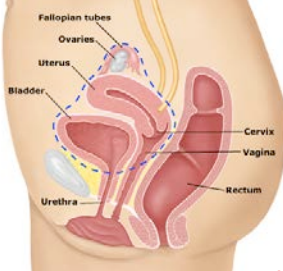
M1: Distant mets

AJCC

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Treatment: Radical Cystectomy

- Removal of bladder and pelvic lymph nodes, plus:

- Men:
  » Prostate
  » Seminal vesicles
  » Proximal vas deferens
  » Proximal urethra

- Females:
  » Uterus
  » Fallopian tubes
  » Ovaries
  » Anterior vaginal wall
  » Fascia
  » Proximal urethra

- 5% increase in 10-yr OS with neoadjuvant chemotherapy

Fallopian tubes
Ovaries
Uterus
Bladder
Cervix
Vagina
Urethra
Rectum

JAE/HROP

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Urinary diversion post-cystectomy

- Incontinent Diversion
  - » Ileal conduit urostomy
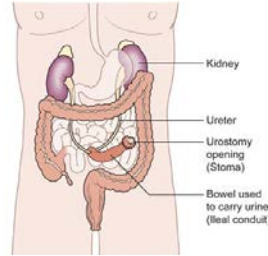
- Continent Diversion
  - Gut-derived stomal reservoir requiring intermittent catheterization

  - Gut-derived orthotopic neobladder attached to distal urethra

JAE/HROP

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https://www.coloplast.us/
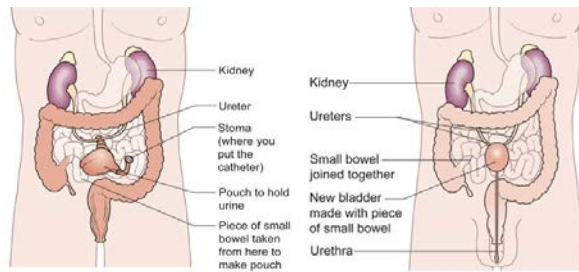
24

Are there other treatment options for bladder cancer?

Is there a way for me to keep my bladder?

Yes.

Trimodality therapy.

25

Poll

- Which are treatment options for muscle invasive bladder cancer (MIBC)?
  - » Radical cystectomy (RC) (surgical bladder removal)
  - » Trimodality therapy (TMT) (chemo/radiation – bladder preservation)
  - » All of the above

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Poll

- Which are treatment options for muscle invasive bladder cancer?
  » Radical cystectomy (surgical bladder removal)
  » Trimodality therapy (chemo/radiation – bladder preservation)
  » All of the above

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"In God we trust. All others must have data."

Bernard Fisher, MD, FACS – Surgeon and Cancer Pioneer

farrugia.com

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Organ preservation

- Organ preservation is a hallmark of modern cancer care, ideally established through randomized controlled trials

- Breast cancer: mastectomy -> breast conservation therapy
- Larynx cancer: laryngectomy -> larynx preservation
- Sarcomas: amputation -> limb-sparing

- General principles
  - » Multidisciplinary and interdependency
  - » Maximal cytoreduction: Surgery
  - » Microscopic/regional/distant disease: Systemic therapy, radiation
  - » **Goals: maintain function/preserve quality of life without compromising disease control**

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Goal: to maintain function/preserve quality of life without compromising disease control

- Is there a role for organ preservation in bladder cancer?
- What is the role of radiation?
- What is the impact on disease control?
- What is the impact on quality of life?

https://www.coloplast.us/

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Background: Radiation Strategy

- Radiation works by damaging DNA in a manner that prevents effective cellular division
- **Fractionation** – delivering radiation over many doses
  - Allows normal tissue to repair DNA damage (free radical-induced double strand breaks)
  - Tumor cells struggle with DNA damage repair due to failure of cell cycle checkpoints
  - Thus, presenting a therapeutic window that favors lethal tumor cell damage over normal cellular impairment
  - Systemic therapy ("radiosensitizer") can enhance this process

- "Conventional fractionation"
  - » Small doses of radiation daily over many weeks
  - » 1.8 – 2 Gy per daily treatment ("fraction") over 4 - 8 weeks to doses of 45 - 80 Gy

- "Moderate Hypofractionation"
  - » Larger doses over fewer weeks
  - » 2 – 4 Gy per fraction over 3-4 weeks to 35 – 50 Gy

- "Ultra hypofractionation" (stereotactic body radiation therapy, radiosurgery)
  - » Even larger doses over days
  - » >5 Gy over 1-2 weeks

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MIBC bladder-preserving TMT paradigm

Maximal transurethral resection of bladder tumor (TURBT) **U**

↓

Chemoradiation (55-65 Gy) **C + XRT**

↓

Cystoscopy for treatment response **U**

↓ ↓

Partial response → Salvage cystectomy **U**

Complete response → Surveillance cystoscopies **U**

Recurrence

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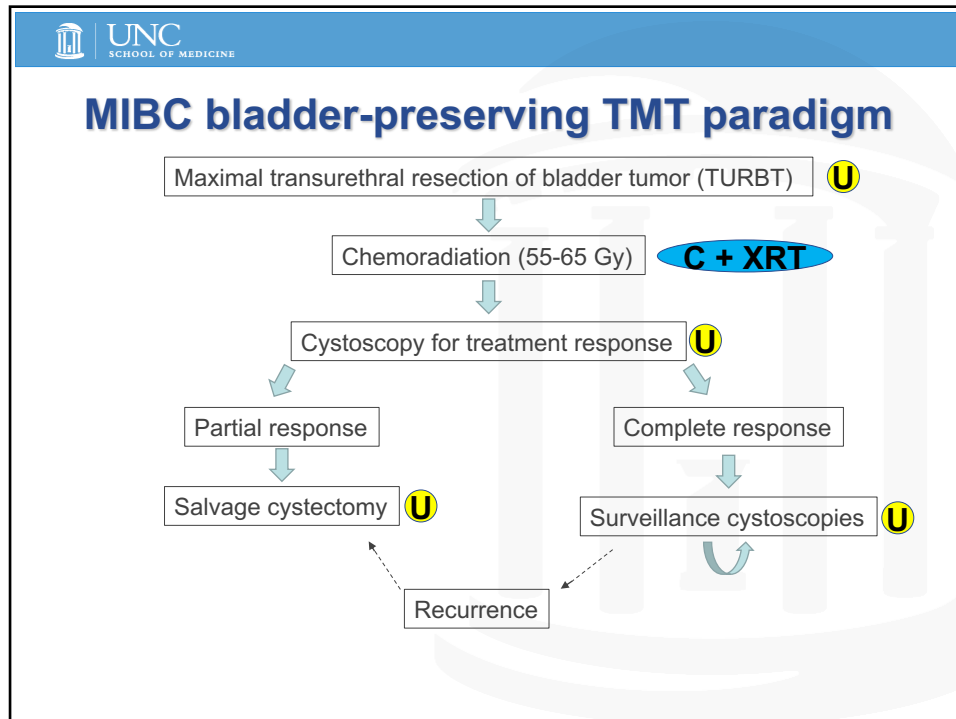
"TMT starts and end with the urologist" - William Shipley

- This includes three primary urologic interventions:
- 1) a maximal TURBT, which is associated with improvement in disease-specific survival and overall survival
- 2) if subsequent chemoradiation is unsuccessful in producing a complete response in the short term, or they relapse in the long-term, the urologist can salvage with immediate or delayed cystectomy, respectively
- 3) lifelong cystoscopic surveillance, which permits early detection and initiation of salvage therapy as needed

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What are the outcomes of TMT?

35

Background: history of TMT for MIBC

- TMT for MIBC has been systematically investigated for over three decades via consecutive institutional and cooperative group protocols and domestic and international trials.
- Long-term results of TMT are comparatively excellent in appropriately selected patients

1986-93	1994-98	1999-2018
Neoadjuvant chemo	Accelerated radiation	Enhanced Radiation sensitization
Response evaluation	Adjuvant chemotherapy	Adjuvant chemotherapy
		bidRT+C/5FU or C/Tax qdRT+Gem or 5FU/MMC
MCVx2	bidRT+C/5FU	G + C x 4
RT + C	MCV x 3	

JAE/KM/HROP

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Background: RTOG trial outcomes

- Most recent published update of completed RTOG MIBC trials: 8802, 8903, 9506, 9706, 9906, 0233.

Mak et al. J Clin Oncol 2014; 32: 3801

37

TMT relies on MDC Success: Surgery

- TURBT and Salvage Cystectomy are key to the success of TMT
  » The risk of salvage cystectomy at 5 yr was 29%.

Giacalone et al. Eur Urol 2017; 71: 952

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TMT relies on MDC Success: Systemic therapy

- BC2001. James et al. NEJM 2012.
- Randomized trial (RCT): 2x2 design. 458 patients
  - » RT +/- concurrent chemo (5FU+MMC)
  - » Whole bladder vs reduced high dose volume
- Concurrent chemo improves DFS in MIBC TMT

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Background: Improved outcomes in modern era

- Improved patient selection and improved techniques (urologic, radiation oncology, and medical oncology) have led to improvements in tumor response and survival outcomes

Years Treated	Total No. Patients	No. with CR	% CR
1986-1989	116	71	64.5%
1990-1993	64	42	67.7%
1994-1997	47	35	74.5%
1998-2001	85	64	75.3%
2002-2005	71	64	90.1%
2006-2009	49	44	89.8%
2010-2013	43	37	86.1%

T2: 47%
Hydronephrosis: 18%
Complete TURBT: 60%

T2: 93%
Hydronephrosis: 3%
Complete TURBT: 83%

Giacalone et al. Eur Urol 2017; 71: 952

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Background: "Appropriately-selected patients"

- Optimal TMT outcomes:
  - » Patient factors
    - Age, comorbidities
    - Underlying bladder function
  - » Tumor factors
    - T stage (T2 vs T3/4)
    - Presence/extent of CIS (carcinoma in situ)
    - Hydronephrosis
    - Extent of TURBT

Covariates	Comparison	Overall survival			Disease-specific survival			Bladder-intact disease-specific survival		
		HR	*p* value	95% CI	HR	*p* value	95% CI	HR	*p* value	95% CI
Age at diagnosis	Continuous	1.03	<0.001	1.01–1.04	–	–	–	–	–	–
Clinical T stage	T2 vs T3/T4a	0.57	<0.001	0.44–0.75	0.51	<0.001	0.36–0.73	–	–	–
Response to chemoradiation	Complete vs incomplete	0.61	0.001	0.46–0.81	0.49	<0.001	0.34–0.71	0.16	<0.001	0.12–0.21
Hydronephrosis	Presence vs absence	1.51	0.02	1.06–2.15	–	–	–	1.89	<0.001	1.33–2.63
Tumor-associated CIS	Presence vs absence	1.56	0.002	1.17–2.08	1.50	0.03	1.03–2.17	–	–	–
TURBT	Complete vs incomplete	–	–	–	–	–	–	0.72	0.02	0.55–0.96

CI = confidence interval; CIS = carcinoma in situ; HR = hazard ratio; TURBT = transurethral resection of bladder tumor.

Giacalone et al. Eur Urol 2017; 71: 952

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Poll

- Which of the following are relative contraindications for trimodality therapy (chemoradiation) for bladder cancer?
  - » Younger age
  - » Fewer comorbidities
  - » Poor bladder function
  - » Larger tumors (T3 tumors, >5cm; multifocal tumors)
  - » Presence of *carcinoma in situ* (CIS)
  - » Hydronephrosis
  - » Incomplete transurethral resection of bladder tumor (TURBT)
  - » All of the above

42

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43

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    - without compromising disease control

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How do RC and TMT compare?

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SPARE trial (UK)

- Closed early due to poor accrual
- 45 patients enrolled in 30 months (25 RC; 20 TMT)
- Significant non-compliance (6/25 RC patients received TMT)
- 73% long-term bladder preservation rate in TMT
- No difference in OS
- Improvement in Quality of Life (QoL) at 12 months in TMT patients. Underpowered

Huddart et al. BJU Int 2017; 120:639

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What to do when the RCT fails us?

- We must turn to alternative, lower levels of evidence (often retrospective)
- Claims-based studies
  - » Leverage large numbers to detect even modest differences
  - » Exposure misclassification
    - E.g. incorrectly identifying the technique/dose of radiotherapy; or cycles/type/timing of chemotherapy
  - » Outcome misclassification
    - E.g. incorrectly assuming that billing codes accurately capture clinical toxicities
- Patient-level studies
  - » Granular data that can be missing from claims based studies
    - E.g. baseline comorbidities and details of treatment
    - E.g. toxicity measured directly by physicians or patients
  - » Fewer subjects
  - » Lack external validity or generalizability
    - E.g. TMT at MGH
- Meta-analysis
  - » Increase sample size
  - » But only as good as the studies used ("garbage in equals garbage out"). Heterogeneity.
- Unable to adequately control for known much less unknown confounders
  - » Were those who pursued TMT appropriate RC candidates? Or RC cisplatin candidates?
- These methods have been attempted to compare RC and TMT…

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Representative recent studies comparing the efficacy (in overall survival) of trimodality therapy versus radical cystectomy.

Study	Study type	Data source	Years	Sample size		OS HR[a] (95%CI)
				TMT	RC	
Seisen 2017[1]	Claims-based	NCDB	2004-2011	1,257	11,586	1.37 (1.16-1.59)
Cahn 2017[2]	Claims-based	NCDB	2004-2013	1,489	22,680	1.58 (1.47-1.69)
Williams 2018[3]	Claims-based	SEER-Medicare	2002-2011	752	2,448	1.49 (1.31-1.69)
Kulkarni 2017[4]	Patient-level, retrospective	Institutional	2008-2013	56	56	0.85 (0.43-1.66)
Kim 2017[5]	Patient-level, retrospective	Institutional	2007-2014	29	50	0.89 (0.39-2.03)
Vashistha 2017[6]	Meta-analysis	Heterogeneous studies	1976-2015[b]	4,050	8,330	0.96 (0.72-1.29)

Abbreviations: OS, overall survival; HR, hazard ratio; TMT, trimodality therapy; RC, radical cystectomy; NCDB, National Cancer Data Base; SEER, Surveillance, Epidemiology, and End Results Program
[a]Comparing TMT (reference) to RC
[b]Study publication years

1. Seisen T, Sun M, Lipsitz SR, et al. Comparative Effectiveness of Trimodal Therapy Versus Radical Cystectomy for Localized Muscle-invasive Urothelial Carcinoma of the Bladder. *Eur Urol.* 2017;72(4). doi:10.1016/j.eururo.2017.03.038
2. Cahn DB, Handorf EA, Ghiraldi EM, et al. Contemporary use trends and survival outcomes in patients undergoing radical cystectomy or bladder-preservation therapy for muscle-invasive bladder cancer. *Cancer.* 2017;123(22):4337-4345. doi:10.1002/cncr.30900
3. Williams SB, Shan Y, Jazzar U, et al. Comparing Survival Outcomes and Costs Associated With Radical Cystectomy and Trimodal Therapy for Older Adults With Muscle-Invasive Bladder Cancer. *JAMA Surg.* 2018;77555:1-9. doi:10.1001/jamasurg.2018.1680
4. Kulkarni GS, Hermanns T, Wei Y, et al. Propensity Score Analysis of Radical Cystectomy Versus Bladder-Sparing Trimodal Therapy in the Setting of a Multidisciplinary Bladder Cancer Clinic. *J Clin Oncol.* 2017;35(20):JCO2016692327. doi:10.1200/JCO.2016.69.2327
5. Kim YJ, Byun SJ, Ahn H, et al. Comparison of outcomes between trimodal therapy and radical cystectomy in muscle-invasive bladder cancer: a propensity score matching analysis. *Oncotarget.* 2017;8(40):68996-69004. doi:10.18632/oncotarget.16576
6. Vashistha V, Wang H, Mazzone A, et al. Radical Cystectomy Compared to Combined Modality Treatment for Muscle-Invasive Bladder Cancer: A Systematic Review and Meta-Analysis of over 12,000 patients. *Int J Radiat Oncol.* 2016;97(5):1002-1020. doi:10.1016/j.ijrobp.2016.11.056
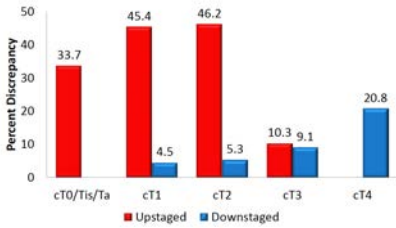
Royce 2019

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Summary: What to do when the RCT fails us?

- Many retrospective studies have tried to compare RC and TMT
- Limitations
  - » TMT patients of older and/or lower performance status
  - » Challenges with clinical staging (clinical staging w imaging a TURBT may underestimate true stage)
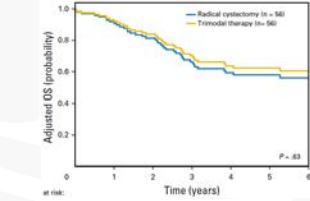 - » Actual treatment regimen often unclear

NCDB study of MIBC patients treated with upfront cystectomy

Propensity-matched study of MIBC patients receiving RC or TMT in multi-disciplinary setting at single Canadian institution:

Gray et al. IJROBP 2014; 88: 1049

Kulkarni et al. J Clin Oncol 2017; 35:2299

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    - maintain function/preserve quality of life
    - without compromising disease control

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TMT QoL

- An area ripe for investigation
- Data limited

- MGH Quality of Life Study
- 221 patients treated on TMT protocols 1986-2000 w median follow up of 6.3 years. Receive urodynamics studies and QoL questionnaires.

- 78% have compliant bladder w normal capacity and flow parameters
- 85% have no urgency or occasional urgency
- 50% of men with normal erectile function

JAE/HROP; Zietman et al J Urol 2003

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TMT QoL – UNC-MGH Study

Clinical Investigation

Quality of Life in Long-term Survivors of Muscle-Invasive Bladder Cancer

Kimberley S. Mak, MD, MPH,*,† Angela B. Smith, MD, MS,‡
Alec Eidelman, BS,§ Rebecca Clayman, BS,§ Andrzej Niemierko, PhD,§
Jed-Sian Cheng, MD,§ Jonathan Matthews, MPH,‡
Michael R. Drumm, AB,§ Matthew E. Nielsen, MD, MS,‡
Adam S. Feldman, MD, MPH,§ Richard J. Lee, MD, PhD,§
Anthony L. Zietman, MD,§ Ronald C. Chen, MD, MPH,‡
William U. Shipley, MD, FACR, FASTRO,§ Matthew I. Milowsky, MD,‡
and Jason A. Efstathiou, MD, DPhil§

*Harvard Radiation Oncology Program, Boston, Massachusetts; †Boston Medical Center, Boston
University School of Medicine, Boston, Massachusetts; ‡University of North Carolina at Chapel Hill,
Chapel Hill, North Carolina; and §Massachusetts General Hospital, Harvard Medical School, Boston,
Massachusetts

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TMT QoL – UNC MGH Study

- 206 TMT and RC patients (all fit for RC) surveyed using 6 validated QoL instruments
- TMT associated with
  - » Modestly higher general QoL (by 7-10 points)
  - » Similar urinary scores
  - » Modestly higher bowel function (by 3-7 points)
  - » Markedly better sexual QoL (by 9-32 points)
  - » Better informed decision-making (by 14 points)
  - » Less concerns about appearance (by 14 points)
  - » Less interference from cancer or cancer treatment (less life interference from cancer or cancer treatment (by 9 points)
- Hypothesis generating. Potential for real QoL benefit with TMT

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TMT QoL

Comparative Effectiveness of Bladder-preserving Tri-modality Therapy Versus Radical Cystectomy for Muscle-invasive Bladder Cancer

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Abstract

We modeled the lifetime outcomes after tri-modality therapy versus radical cystectomy in patients with muscle-invasive bladder cancer and compared the 2 strategies' effectiveness using the endpoint of quality-adjusted life years. We found that the use of tri-modality therapy resulted in greater quality of life than radical cystectomy.

Introduction: There are limited randomized data comparing radical cystectomy (RC) with bladder-sparing tri-modality therapy (TMT) in the treatment of muscle-invasive bladder cancer (MIBC). Both strategies are thought to have similar survival outcomes with different morbidity profiles. We compare the effectiveness of TMT and RC using decision-analytic modeling and the endpoint of quality-adjusted life years (QALYs). **Patients and Methods:** Using a Markov model, we simulated the lifetime outcomes after TMT versus RC ± neoadjuvant chemotherapy for 67-year-old patients with clinical stage T2-T4aN0M0 MIBC. Model probabilities and utilities were extracted from the literature. The incremental effectiveness was reported in QALYs and sensitivity analyses were performed. **Results:** For all patients with MIBC, although the model showed identical survival, TMT was the most effective strategy with an incremental gain of 0.59 QALYs over RC (7.83 vs. 7.24 QALYs, respectively). When limiting the model to favorable, contemporary cohorts in both the TMT and RC strategies, TMT remained more effective with an incremental gain of 1.61 QALYs (9.37 vs. 7.76 QALYs, respectively). One-way sensitivity analyses demonstrated the model was sensitive to the quality of life parameters (ie, the utilities) for RC and TMT. When testing the 95% confidence interval of the RC utility parameter the model demonstrated an incremental gain with TMT from −0.54 to 4.23 QALYs. Probabilistic sensitivity analysis demonstrated that TMT was more effective than RC for 63% of model iterations. **Conclusions:** This modeling study found that treatment of MIBC with organ-sparing TMT in appropriately-selected patients may result in a gain of QALYs relative to RC.

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Table 2	Markov Cohort Base Case Analysis			
Strategy	**EV (LYs)**	**Incremental Value[a]**	**EV (QALYs)**	**Incremental Value[a]**
TMT, all patients	8.89	—	7.83	—
RC, all patients	8.89	0.00	7.24	0.59
RC, favorable cohort	9.34	−0.45	7.76	0.07
TMT, favorable cohort	10.52	—	9.37	—
RC, all patients	8.89	1.63	7.24	2.13
RC, favorable cohort	9.34	1.18	7.76	1.61

Abbreviations: EV = Expected value; LY = life years; QALY = quality-adjusted life years; RC = radical cystectomy; TMT = tri-modality therapy.
[a]Incremental value of TMT strategy relative to RC strategy.

- Hypothesis generating.
- Potential for real QoL benefit with TMT.

Royce Clinical Genitourinary Cancer 2018

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"The best bladder you will ever have is the one you are born with"

-Anthony Zietman

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- Which are NCCN Category 1 recommendations for the treatment of muscle invasive bladder cancer?
  - » Radical cystectomy (surgical removal)
  - » Trimodality therapy (chemoradiation)
  - » All the above

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Poll

- Which are NCCN Category 1 recommendations for the the treatment of muscle invasive bladder cancer?
  - » Radical cystectomy (surgical removal)
  - » Trimodality therapy (chemoradiation)
  - » All the above

  - » Thus, it is essential these patients are informed of all their treatment options by being evaluated in a multidisciplinary clinic, with a team of urology, medical oncology, and radiation oncology.

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Future directions

- Adjuvant radiation following RC?
  - » Local recurrences following RC are common in a subset of MIBC patients (LRR ~10-40%)
    - pT3/T4
    - Positive margins
    - pN1-2 disease
  - » Only randomized data is from Egypt (Zaghloul et al. IJROBP 2002)
    - Accrued 1981-1984
    - RC +/- adjuvant RT
    - Improved DFS with RT (5 yr DFS ~45% vs 25%)
    - Caveats: 80% squamous, one RT arm had TID radiation
  - » NRG GU001 closed due to poor accrual

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Future directions

- Currently, no routine role for RT in management of recurrent NMIBC
- RT or chemoRT for non-cystectomy candidates?

ChemoRT for NMIBC:

RTOG 0926			
A Phase II Protocol For Patients With Stage T1 Bladder Cancer To Evaluate Selective Bladder Preserving Treatment By Radiation Therapy Concurrent With Radiosensitizing Chemotherapy Following A Thorough Transurethral Surgical Re-Staging			
Institutional TURBT for re-staging →	Full-dose Radiation* and Concurrent Chemotherapy** →	Cystoscopic Surveillance 8-10 weeks after treatment; if negative, q 3 months for the 1st year, q 4 months for year 2, q 6 months for years 3, 4, and 5*** and then annually	
Stage T1 (high grade)	*Total dose of 61.2 Gy in 34 daily fractions **Cisplatin 3 days/week during Weeks 1, 3, and 5 OR Mitomycin day 1 and 5-fluorouracil Weeks 1 and 4	***For T1 and Tcis tumor recurrence after RTOG 0926 treatment, recommend early salvage cystectomy. For Ta tumor recurrence, recommend either appropriate conservative treatment or cystectomy.	(Fully accrued; awaiting report)

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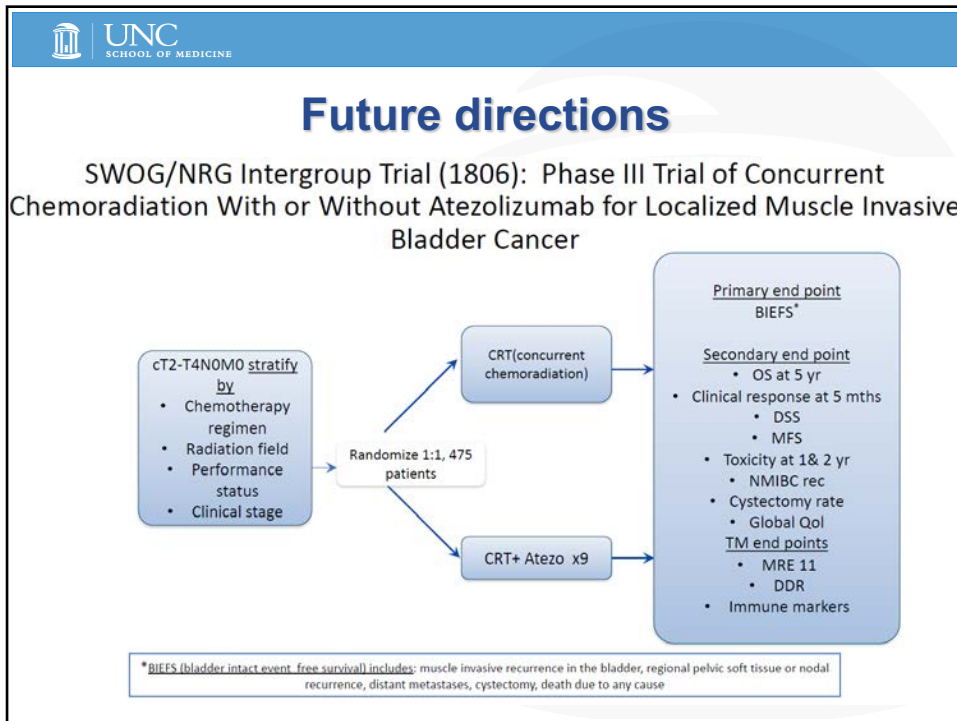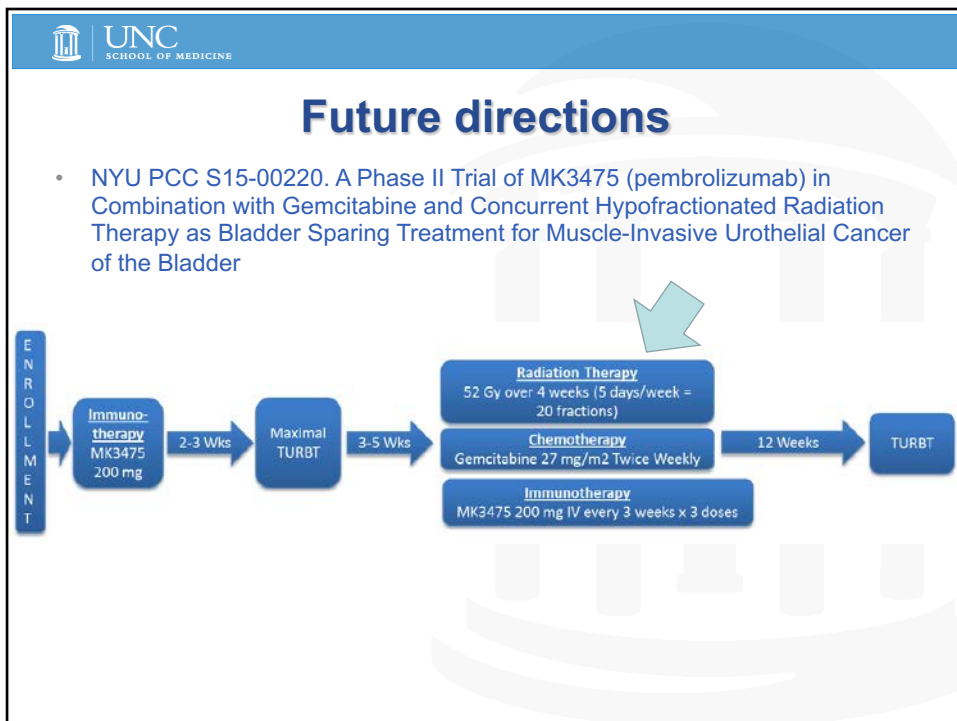
Emerging paradigms

- Multiple large genomic studies over past ~5 years have transformed understanding of MIBC biology
- Targeted agents beyond immunotherapy
  - » FDA approved erdafitinib (FGFR3 inhibitor) in April 2019…first targeted agent approved in bladder cancer
  - » MIBC has many frequently mutated cancer genes -> opportunity for other targeted agents?
- Using genomic biomarkers to guide therapy
  - » 3 on-going Phase II trials investigating chemo only (ie, no surgery or RT) for MIBC patients with tumor DNA damage repair (DDR) gene alterations who achieve complete clinical response to neoadjuvant cisplatin based chemo

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  » Navigators
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