

Clinical restaging after neoadjuvant chemotherapy for muscle invasive bladder cancer

Jared Schober, MD

Urologic Oncologist | Assistant Professor

Department of Surgery, Division of Urological Surgery

University of Nebraska
Medical Center



Nebraska
Medicine



I have no disclosures



Objectives:

- Define the clinical implication of ypT0
- Review the current state of clinical restaging after neoadjuvant chemotherapy for muscle invasive bladder cancer
- Discuss future direction to improve restaging accuracy



ypT0: Complete clinical response after neoadjuvant systemic therapy (ie. no tumor seen on final pathology)
cT0: Complete clinical response detected prior to cystectomy

Table 2. Cystectomy, chemotherapy and pT0 in treatment and control arms

	Nordic I ⁷	Nordic II ⁶	SWOG ⁵	MRC ⁸	Totals
No. NC/control intent to treat	151/160	155/154	153/154	491/485*	950/953
No. RC/total No. (%):	264/311 (85)	271/309 (88)	250/307 (81)	494/561 (88)	1,267/1,488 (85)
NC	130/151 (86)	132/155 (85)	126/153 (82)	245/284 (86)	633/743 (85)
Control	134/160 (84)	139/154 (90)	124/154 (81)	249/277 (90)	643/745 (86)
No. NC pts treated (% intent to treat)†	108 (72)	103 (66)	131 (87)†	392 (80)	734 (77)
No. pT0/total No. (%):					
NC	33/130 (25)	37/140 (26)	48/126 (38)	67/206 (33)	185/602 (31)
Control	17/134 (13)	16/139 (12)	18/124 (15)	26/211 (12)	77/605 (13)
Notes	—	Includes laparotomy in 8 pts but not RC	—	Pathology data missing on 68 pts overall	—

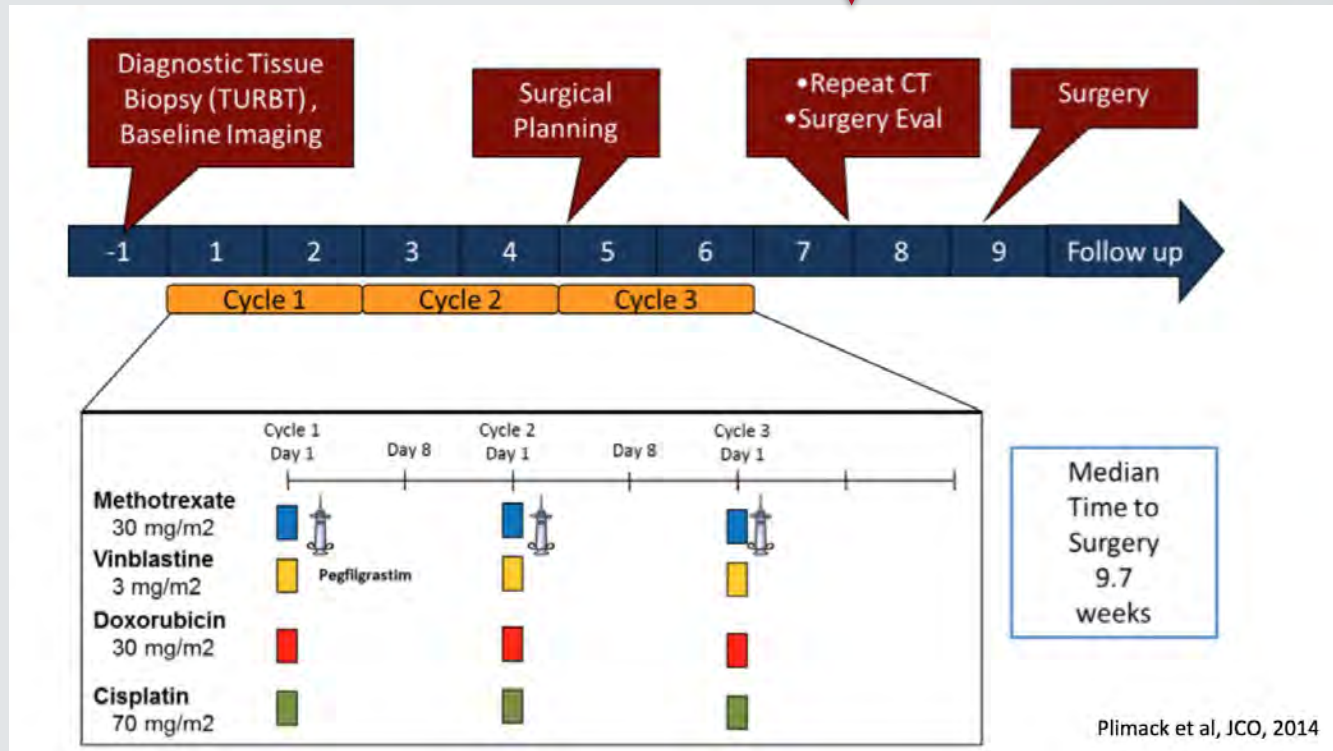
- ~30% with NAC
- ~12% with TUR alone
- Associated with >80% 10-year cancer-specific survival rates

Can we leave the bladder behind?

Lavery et al., JUrol, 2014, 191, 898
Palapattu et al., J Urol, 2006. **175**, 1645
Volkmer et al., Cancer, 2005. **104**, 2384
Tollefson et al. World J Urol, 2012, 795



Clinical Restaging



If patients could be identified as cT0 -> bladder preservation protocols



Varied Clinical Reports Suggest Worrisome Cystoscopic Miss Rate

The Utility of an Extensive Postchemotherapy Staging Evaluation in Patients Receiving Neoadjuvant Chemotherapy for Bladder Cancer

Adam C. Reese, Mark W. Ball, Nilay Gandhi, Michael A. Gorin, George J. Netto, Trinity J. Bivalacqua, and Mark P. Schoenberg

33% of seeT0, T1 or greater

J HOPKINS RETROSPECTIVE

Urology, 2014, 84, 358

Absence of Tumor on Repeat Transurethral Resection of Bladder Tumor Does Not Predict Final Pathologic T0 Stage in Bladder Cancer Treated with Radical Cystectomy

Janet Baack Kukreja^{a,c}, Sima Porten^b, Vishukamal Golla^c, Philip Levy Ho^a, Graciela Noguera-Gonzalez^{a,d}, Neema Navai^a, Ashish M. Kamat^a, Colin P.N. Dinney^a, Jay B. Shah^a

^aDepartment of Urology, University of Texas MD Anderson Cancer Center, Houston, TX, USA; ^bDepartment of Urology, University of California San Francisco, San Francisco, CA, USA; ^cDepartment of Urology, University of California Los Angeles, Los Angeles, CA, USA; ^dDepartment of Biostatistics, University of Texas MD Anderson Cancer Center, Houston, TX, USA

64% of seeT0, residual disease!

MDACC RETROSPECTIVE

EU Focus, 2018, 720

A Sequential Treatment Approach to Myoinvasive Urothelial Cancer: A Phase II Southwest Oncology Group Trial (S0219)

Ralph W. deVere White^{*,†}, Primo N. Lara, Jr.^{*,‡}, Bryan Goldman, Cathy M. Tangen, David C. Smith, David P. Wood, Jr.^{,§}, Maha H. A. Hussain^{||} and E. David Crawford

60% of seeT0, residual disease!

SWOG PROSPECTIVE

J Urol, 2009, 181, 2476



Clinical Conundrum

- Accurate preoperative prediction of pT0 could spare cystectomy in ~30% of patients.
- Requires endoscopic eval immediately prior to cystectomy
- Rigorous documentation of visual findings and pathologic sampling
- The accuracy of negative predictive value for a normal endoscopic examination was not definitively established...



Cystoscopic Evaluation Predicting pT0 Urothelial Carcinoma of the Bladder

This study is currently recruiting participants. (see [Contacts and Locations](#))

Verified March 2017 by Fox Chase Cancer Center

Sponsor:
Fox Chase Cancer Center

Collaborator:
Temple University

Information provided by (Responsible Party):
Fox Chase Cancer Center



Daniel Parker MD
@DParkerGU Follows you
Urologic Oncology Fellow, University of Oklahoma Health Sciences Center
Oklahoma City, Oklahoma

ClinicalTrials.gov Identifier:
NCT02968732

Planned: 99 pts



Matthew Zibelman
@MattZibelman Follows you



Aeen Asghar MD
@Aeen_A Follows you
Resident | Urology | @TempleUrology

Full Text View

Tabular View

No Study Results Posted

Disclaimer

How to Read a Study Record

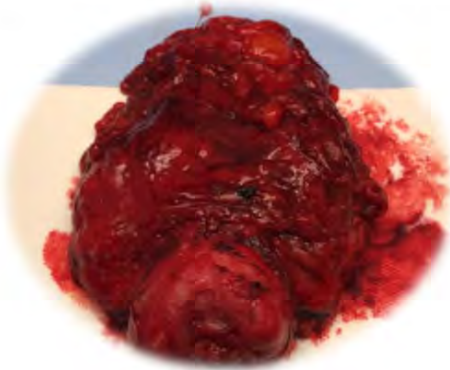
Purpose

A prospective, investigational study to assess the accuracy of standardized cystoscopic evaluation with tissue sampling performed immediately prior to definitive radical cystectomy to predict pathologic tumor stage and identify patients who may benefit from bladder preservation therapy.

AT CYSTOSCOPY:

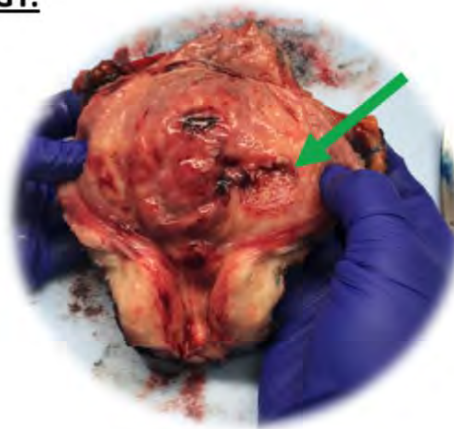
1. URINE CYTOLOGY
2. TUR MAIN TUMOR/SCAR
3. TUR 2ND TUMOR/SCAR (IF PRESENT)
4. TWO ADDITIONAL RANDOM BIOPSIES

SPECIMEN HAND-CARRIED TO PATHOLOGY:



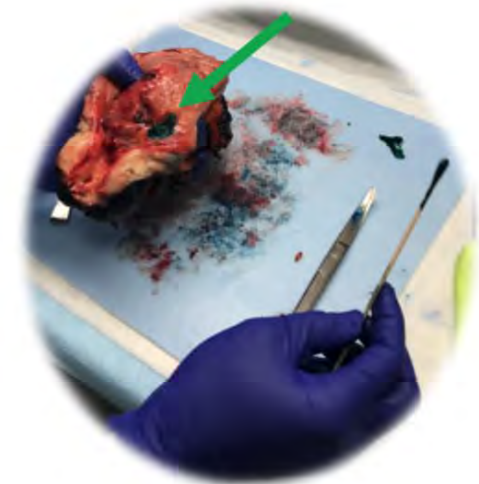
STEP A

BRING SPECIMENT TO PATH



STEP B

PATHOLOGY PA WILL BIVALVE SPECIMEN
AND UROLOGY WILL IDENTIFY TUR SITE(S)



STEP C

PATHOLOGY PA WILL INK MAIN TUR SITE
GREEN. IF 2ND TUR SITE WAS NECESSARY
(PT HAD 2ND TUMOR), 2ND SITE SHOULD BE
INKED **ORANGE**



Cystoscopy and Systematic Bladder Tissue Sampling in Predicting pT0 Bladder Cancer: A Prospective Trial



Matthew Zibelman,* Aeen M. Asghar^{1b}, Daniel C. Parker, John O'Neill, Shuanzeng Wei, Richard E. Greenberg, Marc C. Smaldone, David Y.T. Chen, Rosalia Viterbo, Robert G. Uzzo, Evan Bloom, Rutika Kokate, Daniel M. Geynisman, Pooja Ghatalia, Mengying Deng, Eric A. Ross, Elizabeth Plimack, Philip H. Abbosh and Alexander Kutikov†

From the Department of Medical Oncology (MZ, RK, DMG, PG, EPI), Fox Chase Cancer Center, Philadelphia, Pennsylvania, Division of Urological Oncology (AMA, JO, REG, MCS, DYTC, RV, RGU, EB, PHA, AK), Fox Chase Cancer Center, Philadelphia, Pennsylvania, Department of Urology (DCP), University of Oklahoma, Oklahoma City, Oklahoma, Department of Pathology (SW), Fox Chase Cancer Center, Philadelphia, Pennsylvania, Department of Biostatistics and Bioinformatics (MD, EAR), Fox Chase Cancer Center, Philadelphia, Pennsylvania

- Futility reached at 61 pts (based on the primary endpoint of NPV <70%)
 - 42 (69%) MIBC - all but 4 s/p NAC
 - 19 (31%) NMIBC
- On SEE, 31 (50.8%) patients demonstrated no visual nor biopsy-based evidence of disease (seeT0)
 - 16/31 (51.6%) residual disease (>pT0) upon RC
 - **8/31 (25.8%) residual \geq pT2 disease upon RC**
- 1 in 4 patients with seeT0 harbored MIBC

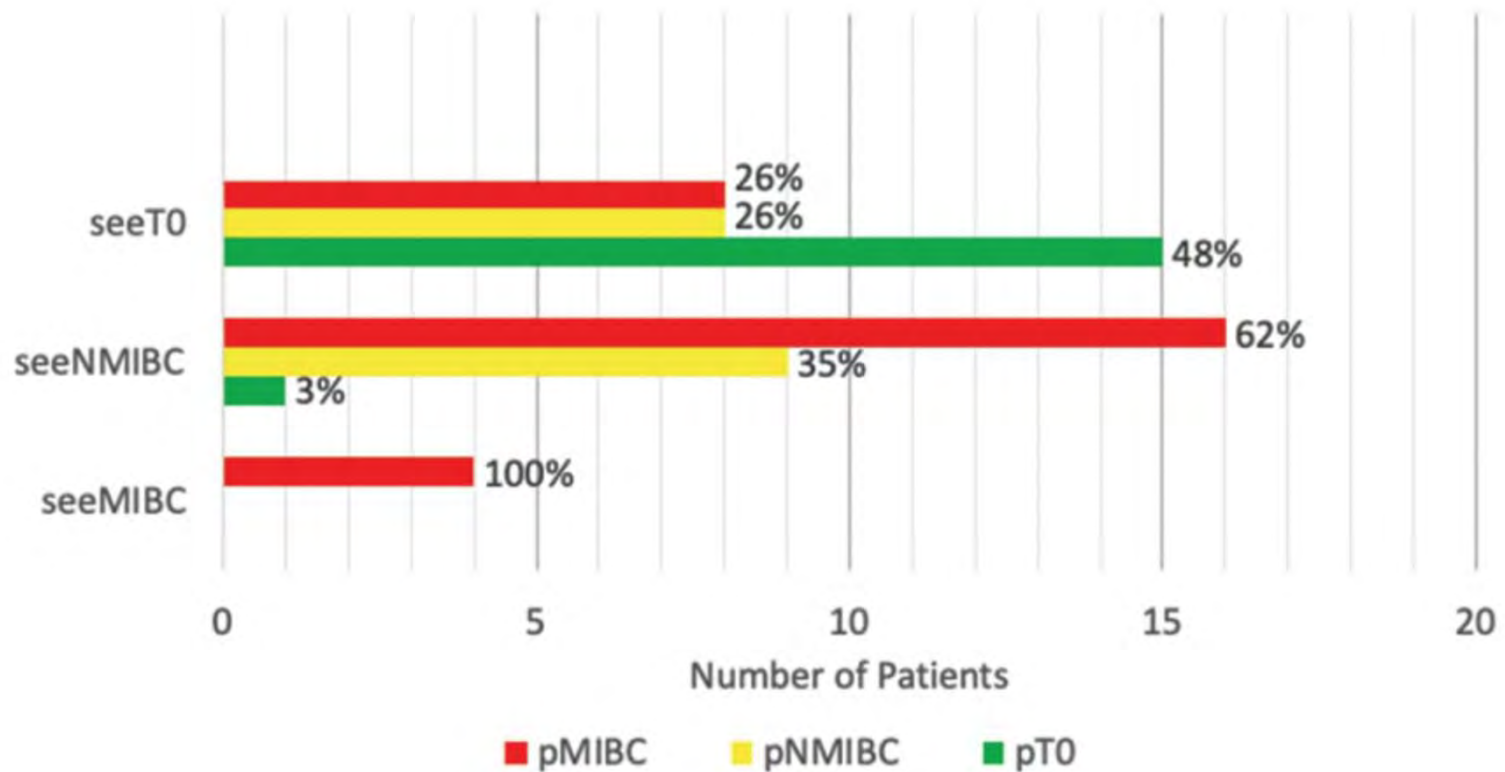
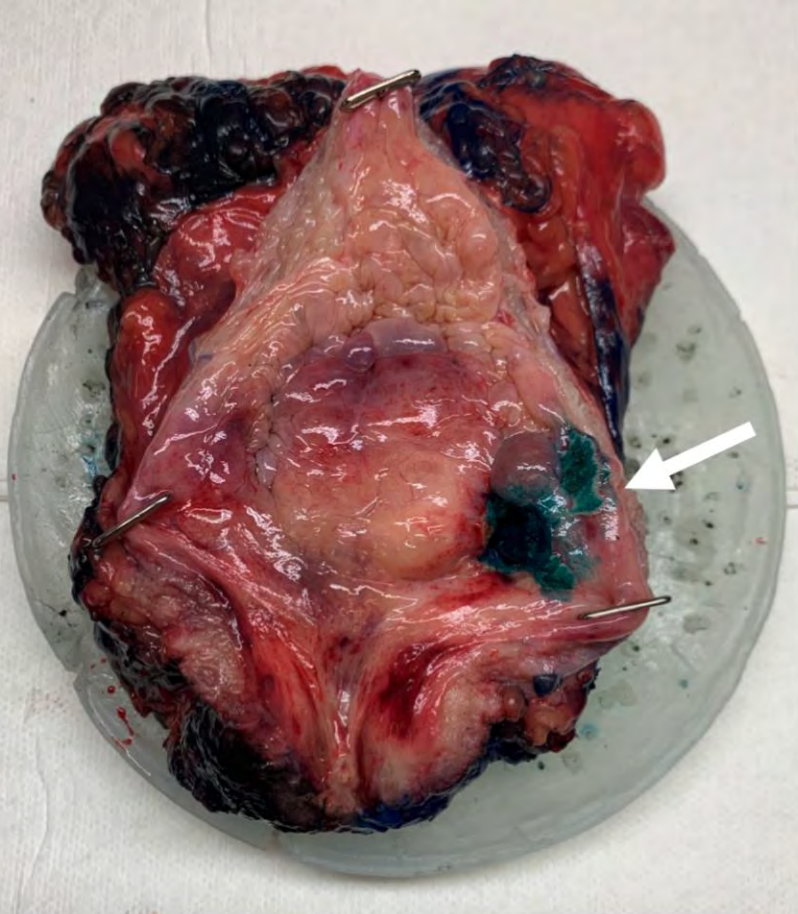

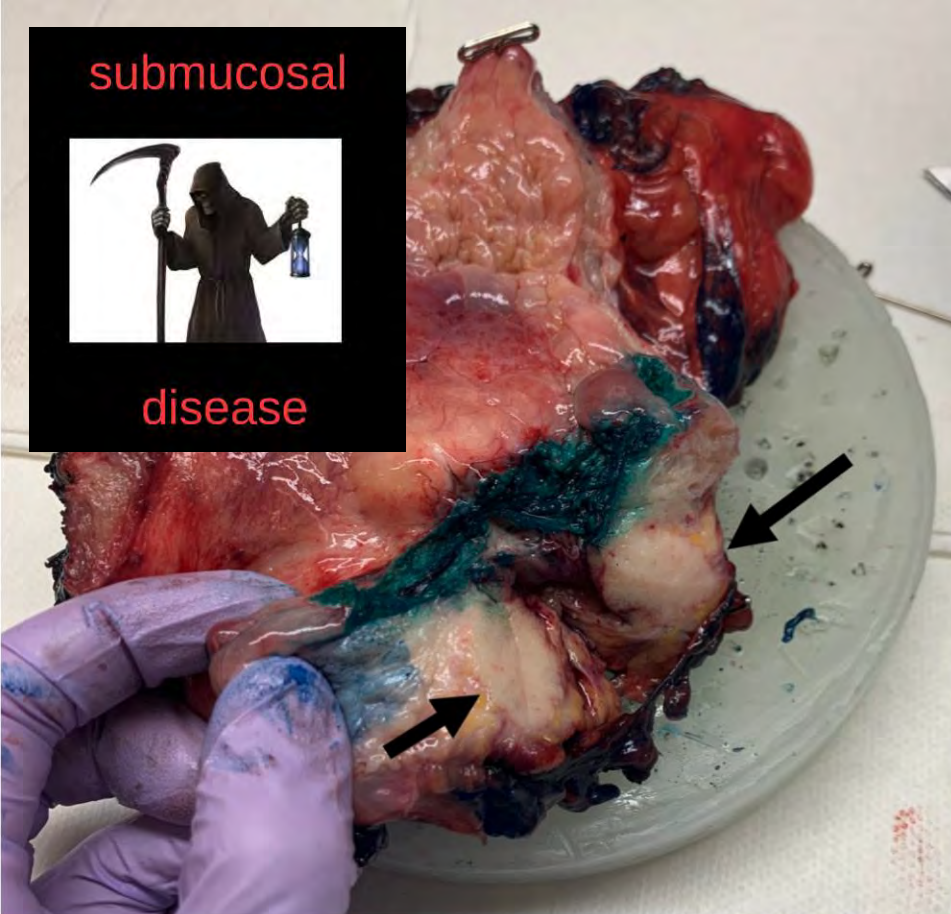


Figure 2. Agreement between SEE (seeT) and final pathology (pT) for combined cohort (61)



submucosal

disease

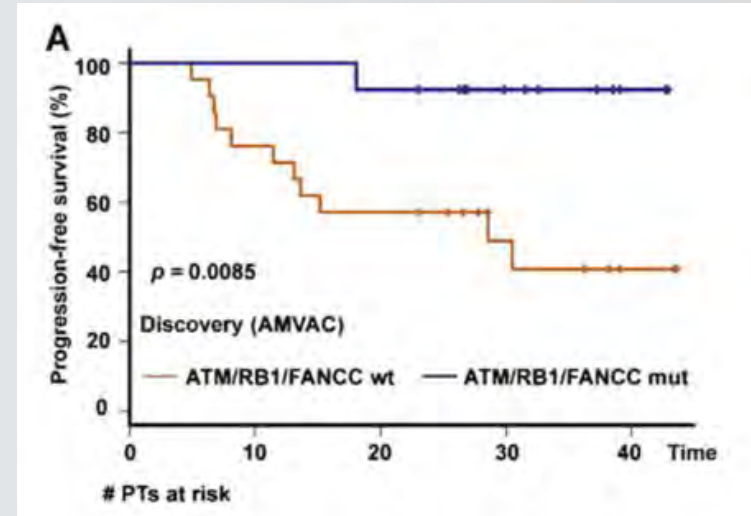




What's the next step in the progression of clinical restaging in bladder cancer?

Adjuvant Testing

- Genomic alterations predicting response and clinical benefit after neoadj therapy →
- Urine Assays for circulating free DNA (cfDNA)
- mpMRI bladder (VIRADS)
- Others



Plimack et al Eur Urol 2015



Circulating tumor DNA (ctDNA)

- Tumor specific DNA fragments in circulation
- Multiple approaches with high sensitivity
- Detection precedes radiographic progression
- Dynamic changes in ctDNA carry prognostic significance
- Resolution after NAC indicates tumor response
- Prelim data suggests could be marker for ypT0

Birkenkamp-Demtröder K et al Eur Urol 2018
Bratman et al Nat. Cancer 2020
Christensen et al JCO 2019



INSITE Trial

*INcreasing pre-**S**urgical **I**dentification of muscle
Tumor **E**valuations prior to planned cystectomy*

Single arm, diagnostic clinical trial of clinical reclassification of bladder cancer prior to cystectomy using transurethral resection, serum ctDNA, urine biopsy (cfDNA), and microbiome analysis

Goal: Increase accuracy for detecting cT0 by developing a diagnostic panel combining TURBT with adjuvant testing

Thank you!



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