## Point-Counterpoint: Radiation & Bladder Cancer

Radiation Has No Role in the Treatment of Any Stage of Bladder Cancer ~ Robert E. Donohue, MD

Radiation Plays a Major Role in Certain Stages of Bladder Cancer ~ David C. Beyer, MD

## Radiation Therapy; no role in management of bladder cancer

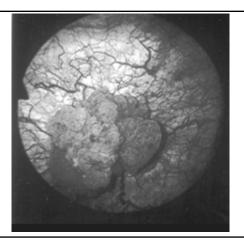
Robert E. Donohue M.D.

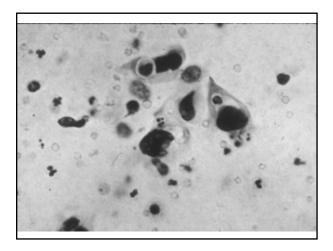
Denver VAMC

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# **TURBT** classic

hematuria
cystoscopy / cytology ?
upper tract study
cystoscopy / cytology ?
TUR resection, bladder mass





## Bladder Tumors 2009

incidence 70,980 male 52,810 female 18,170 mortality 14,330 male 10,180 female 4,150

# Transitional Cell Carcinoma

85% superficial carcinoma-in-situ
Ta epithelium
T1 LP invasion

15% invasive

85% recur 15% no recurrence

70% same stage, grade

30% increase in either or both

## **TURBT** classic

bimanual examination,
resection of tumor[s] to the
bladder wall, minimum cautery
cold cup of base, +/- M. prorpria
resection of deeper tissue [muscle?]
bladder mapping, carcinoma-in-situ

## TURBT modern

office cystoscopy, cytology, CT Scan before TURBT, [ugly] TURBT – biopsy only, slides TURBT – single, complete, slides TURBT -- staged, multiple, slides TURBT\* – second look, slides \*[all tumor gone or recent referral]

# Transitional Cell Carcinoma

persistence –inadequate TURBT size, multi-focality, patient comorbidities, location[s] of tumor skill of M.D.

recurrence is a new tumor!

T1 is superficially invasive c-i-s, untreated, invasive in 5 years

## Transitional Cell Carcinoma

recurrence and progression

Grade multi-focality 5X
1 50% [3 yrs] size 35X
2 58%
3 72% c-i-s worsens all
Stage the others
Ta 48% 30% progress

Heney UCNA 1992

T1 84%

## TURBT modern

1999 Herr – second look
2000 Solsona – post-op ChRx
2004 Silvester – post-op ChRx
2000 Lamm – maintenance BCG
1999 Hurle – upper tract studies
2002 O'Donnell – BCG +/- alpha IFN
2004 Herr – office fulguration
2007 Herr – low grade, papillary TCC

# TURBT modern

1999 Herr – second look, 2 – 6 wks, all referrals 2004 Herr – office fulguration, Lidocaine, urethra 2007 Herr – low grade, papillary TCC advantages,

THE VALUE OF A SECOND TRANSURETHRAL RESECTION IN EVALUATING PATIENTS WITH BLADDER TUMORS

HARRY W. HERR

From the Unitagy Service, Department of Surgery, Memorial Slown Kettering Cancer Center, New York, New York

J.U. 162: 24, 1999

REPEAT TRANSURETHRAL RESECTION TO EVALUATE BLADDER TUMORS

TMER 1. Comparison of bladder tumor stage after first and second transurethral resections

Stage at First	No. Pts.	No. Stage at Second Transurethral Resection (%)			
ransurethral Resection		To	Ta/Tie	71	T2
To	20	6 (30)	8 (40)	4 (20)	2 (10)
Ta T1:	18	5 (28)	7 (29)	5 (28)	1 (5)
T1:	58	13 (22)	15 (36)	14 (24)	16 (28)
Muscle	35	9 (26)	11 (31)	10 (29)	5 (14)
No muscle	23	4(17)	4 (17)	4 (17)	13 (49)
TS	54	12 (22)	7 (13)	3 (6)	30 (\$5)
Totals	150	36 (34)		134	76)

#### Herr

second look TURBT
76%\* persistent tumor
first TURBT repeat TURBT

T1 T0 T2

35 muscle 9 [26%] 5\* [14%]

23 no muscle 4 [17%] 11\* [49%]

T2 12\* [22%] 30 [55%]

## TURBT peri-operative

immediate OR or PACU [ RR ] drug,
Mitomycin C
40 mg in 20 ccs saline
concentration
alkalinization of urine
dehydrated patient
30' – 60' bladder time

TURBT
peri-operative

Mitomycin C
more effective with single tumors
single 35.8% recurrence
multiple 65.2% recurrence
5% American Urologists use this Rx
Sylvester
JU 171; 2186, 2004

#### **TURBT**

induction and maintenance rules
NPO after midnight,
negative urinalysis,
atraumatic catheterization,
gravity flow, minimum volume,
retain agent for two hours,
rotate patient, [keep him awake]

## **Induction BCG**

one or two courses
BCG q week x 6 weeks
cystoscopy / cytology 6 weeks later
negative; proceed to maintenance
positive; q week x 3 weeks [ 20% ]
cystoscopy / cytology 9 weeks later
negative; maintenance
positive; cystectomy or other RX

PERSPECTIVES IN UROLOGY: POINT- COUNTERPOINT	<ul> <li>November 5–7, 2009</li> </ul>	<ul> <li>The Scottsdale Plaza</li> </ul>	<ul> <li>Scottsdale, Arizona</li> </ul>

#### **Maintenance BCG**

maintenance BCG
weekly for 3 weeks, every 6 months
for 3 years
weekly for 3 weeks, every 12 months
for 2 years
weekly for 3 weeks, every 24 months
for 2 years

#### Maintenance BCG

induction and maintenance therapy,
if initially successful
7 year plan
cytology q 3 months
cystoscopy q 3 months
tumor marker[s] q 3 months

#### Maintenance BCG

induction and maintenance therapy,
c-i-s 84% CR 68%
papillary 87% 2y 57%
c-i-s +
papillary 77 mth 36 mth
Lamm JU
16% all courses; 25% toxicity

#### **TURBT**

induction and maintenance
urgency / frequency
Pyridium
Ditropan
other anti-cholinergics
Librium / Valium
Quinolone

8.7

#### **TURBT**

#### fever post BCG

always get a urine culture,
c-i-c infection vs BCG infection
treat with NSAIDs, must respond within
24 – 48 hours or start anti-TB Rx
culture negative for M. bovis, treat bug
culture positive for M. boivs, treat TB
wait 6 months; restart BCG at 1/100 Rx

#### **TURBT**

induction, maintenance questions

What strain of BCG is best ?

Connaught or Tice or Pasteur ?

What dose of BCG do we give ? full dose, 1/3 dose , 1/10 dose, 1/100 dose

What frequency ? q 1, 3, 5, 7, 14 days ?

#### **TURBT**

What dwell time ? 1 hour, 2 hours

What duration ? 6 OR 3 weeks=course

What timing between courses, off Rx 6 weeks induction, 9 weeks maintenance

What duration 7 years? longer, shorter,

## **Urine Markers**

NMP 22
Urovysion
BTA stat
Telomerase
Surviven
Microsatellite analysis
others

others	
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#### **Muscle Invasive TCC**

historically

neo-adjuvant radiation

Whitmore 4,000 r - 4 weeks

2,000 r - 1 week

6,000 r - 6 weeks

**Skinner** 1,500 r – 3 days

Wallace 4,000 r -

cystoscopy – no Tumor, 6,000 r

tumor - cystectomy

## **Muscle Invasive TCC**

historically

pelvic node dissection, radical cystectomy, ileal conduit diversion, mortality 5- 12% morbidity 50% survival – roughly 50%

### **Muscle Invasive TCC**

historically

pelvic node dissection, standard – obturator, hypogastric, external and common iliac nodes extensive – Inferior Mesenteric A radical cystectomy, ileal condiut, ileo-cecal pouch ileal, colonic neo-bladder

## **Muscle Invasive TCC**

currently

pelvic node dissection, standard – common iliac extensive – IM artery radical cystectomy, ileal condiut, ileo-cecal pouch ileal, colonic neo-bladder

#### **Muscle Invasive TCC**

currently
high grade, T1 disease
with negative M. propria
T2 disease,
aggressive wide re-TURBT
cystectomy
chemotherapy
bladder preservation

## **Bladder Preservation**

T1, high grade, T2
options
aggressive wide re–TURBT
cystectomy
chemotherapy
bladder presservation
Chemotherapy +
radiosensitizing agent =EBRT

### **Bladder Preservation**

T1, high grade, T2 options

aggressive wide re–TURBT cystectomy chemotherapy bladder preservation Chemo + Chemosensitizing EBRT

## **Bladder Preservation**

T1, high grade, T2 cystectomy – negative LN 50-60% pT0,T1,T2; 75-85% 5 year 20-30% T3a-b, perivesical fat, T4, 45-55% 5 year

- positive LN 20-30% any pT, pN1-3 25-35% 5 year

aggressive wide re–TURBT
20% local control
selected patients, better
T2a

external beam radiotherapy-6,000 Gy 50% likelihood of bladder control 20 – 40 % survival

## **Bladder Preservation**

external beam radiotherapy
50% likelihood of bladder control
20 – 40 % survival
subsequent randomized trials
improved local control
BUT
not survival

#### **Bladder Preservation**

T1, high grade, T2
Chemotherapy + ChXRT
parameters
solitary, early stage lesion,
no hydronephrosis,
no palpable mass,
no multifocal disease or c-i-s
no disease outside the bladder
non- constricted bladder volume

## **Bladder Preservation**

T1, high grade, T2
Chemotherapy + XRT
parameters
transitional cell carcinoma,
aggressive TURBT,
adequate renal function,
favorable – T2,
neo-adjuvant Ch Rx, pTo @ TURBT

T1, high grade, T2
Chemotherapy + ChXRT
discordance between
clinical and pathologic staging
staging
visual appearance, cytology, TURBT
at cystectomy, 33% tumor Scher
BUT
ChRx 38%, post MVAC, pTo Grossman

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111 patients, T2,T3
60 patients, [ 54%], pTo @ TURBT
43 bladder sparing
28 TURBT
15 partial
32, 74% alive; 25,58% bladder intact
17 radical cystectomy
65% 10 year survival Herr

#### **Bladder Preservation**

104 patients T2 to T4a
3 courses of Paclitaxel,
Carbo-platin and Gemcitabine,
Restaging TURBT in 74 patients
34 / 74 were pTo
10/34 immediate cystectomy
6/10 persistent tumor 60%
re-TURBT is flawed significantly white

## **Bladder Preservation**

53 patients, T2,T3,T4
TURBT
CMV – 2 courses
external beam 40Gy + CDDP
8 cystectomy; 34 CRT; 11other Rx
24, alive and well, NED, 45%
31, functioning bladder, no T2, 58%
28, CR to chemo, 89% NED bladder

Kaufmann 1993

190 patients, T2,T3,T4
TURBT
CMV - 2 courses
external beam 40Gy + CDDP
DSS DSS [b]

41 cystectomy 63% 59% 149 study 46% 45%

Shipley 2002

#### **Bladder Preservation**

3 single institution 2 RTOG pilot studies

pTo preservation 49% 5 years 38 – 43% intact bladder

pT+ cystectomy 63% 5 years

Shipley 1999

#### **Bladder Preservation**

complete response
3 single institutions
2 RTOG pilot studies

TURBT, ChRx and CRT 65 --70% survival 50 - 60% intact bladder survival 35 - 40% Shipley 1999

## **Bladder Preservation**

CRT without Ch Rx RTOG 89-03 2 cycles of cis-platinum T2,T3,T4

survival bladder 49% 36%

CMV + ChXRT 49% 36% ChXRT 49% 40% now, 100 mg/M2 q 3 weeks

8.12

opponents
metachronous bladder tumors
multifocal tumors are present
risk 50 – 60% new tumor
50% muscle invasive
25-30% non-muscle
TURBT plus BCG
urinary diversion is more difficult!

#### **Bladder Preservation**

XRT technique supine and bladder empty 40 – 45 Gy bladder + true pelvis biopsy and cytology, negative cone-downed to cystoscopically identified tumor site positive or cystectomy

#### **Bladder Preservation**

RTOG 99-06
Paclitaxel + CDDP + standard XRT
vs
hyperfractionated XRT
4 courses
Gemcitabine + CDDP Kaufman
CR 87% 2 years; 69% intact bladder
or Gemcitabine + XRT only Kent Sanger

## **Bladder Preservation**

RTOG 99-06, T2- T4a

Paclitaxel + CDDP +

hyperfractionated XRT

reTURBT < T1

4 courses

Gemcitabine + CDDP

RTOG 99-06
greater GI 3-4 toxicity from 15%
70% Rx completion [RTOG 90%]
RTOG 97-06
no Paclitaxel 4% zeitman 2003
RTOG 02-33
5 FU in place of Paclitaxel Rodel

## **Radiation Therapy**

conclusions
no large role in bladder cancer
single therapy, No
neo-adjuvant, No
bladder preservation studies
response to neo-adjuvant ChRT
decides +/- XRT
If no tumor, Why give the XRT?
If tumor present, cystectomy!

## **Radiation Therapy**

conclusions
occasional studies show an early
benefit; multi-institutional, bladder
functional reports, Uro-dynamics,
careful toxicity studies, Grades 3, 4
and 5 and quality of life issues must
be described in detail and
considered by the M.D. and patient.