Radiation Therapy; no role in management of bladder cancer
Robert E. Donohue M.D.
Denver VAMC
University of Colorado

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. propria
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 co-
morbidities, location[s] of tumor
skill of M.D.
recurrence is a new tumor!
But
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
T1 84% Heney UCNA 1992

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 TRANURETHRAL RESECTION IN EVALUATING PATIENTS WITH BLADDER TUMORS
HARRY W. HERR
From the Urology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, New York

J.U. 162: 24, 1999

REPEAT TRANURETHRAL RESECTION TO EVALUATE BLADDER TUMORS

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

<table>
<thead>
<tr>
<th>Stage at 1st</th>
<th>TURBT</th>
<th>No Stage at 2nd TURBT</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>38</td>
<td>4 (10%)</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>T1</td>
<td>28</td>
<td>12 (22%)</td>
<td>11</td>
<td>0</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>T2</td>
<td>10</td>
<td>5 (50%)</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Muscle</td>
<td>22</td>
<td>4 (17%)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>No muscle</td>
<td>51</td>
<td>18 (35%)</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>73</td>
<td>31 (42%)</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>0</td>
</tr>
</tbody>
</table>

76%* persistent tumor
first TURBT repeat TURBT
T1 35 muscle 9 [26%] 5* [14%]
T2 23 no muscle 4 [17%] 11* [49%] 12* [22%] 30 [55%]

Point-Counterpoint: Radiation & Bladder Cancer
Radiation Has No Role in the Treatment of Any Stage of Bladder Cancer

~ Robert E. Donohue, MD
**TURBT peri-operative**

Immediate OR or PACU [ RR ] drug, Mitomycin C
- 40 mg in 20 ccs saline concentration
- Alkalization 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
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
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
### 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

**Currently**
- Pelvic node dissection
- Standard – Common iliac
- Extensive – IM artery
- Radical cystectomy
- Ileal conduit
- Ileo-cecal pouch
- Ileal, colonic neo-bladder

**Pelvic Invasive TCC**

**Historically**
- Pelvic node dissection
- Radical cystectomy
- Ileal conduit diversion
- Mortality 5-12%
- Morbidity 50%
- Survival – roughly 50%

**Currently**
- Pelvic node dissection
- Standard – Common iliac
- Extensive – IM artery
- Radical cystectomy
- Ileal conduit
- 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 preservation
  Chemo + Chemosensitizing 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
Bladder Preservation

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
Bladder Preservation

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

Bladder Preservation

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; 11 other Rx
24, alive and well, NED, 45%
31, functioning bladder, no T2, 58%
28, CR to chemo, 89% NED bladder
Kaufmann 1993
Bladder Preservation

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

pT0 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
CMV + ChXRT 49% 36%
ChXRT 49% 40%
now, 100 mg/M2 q 3 weeks
Bladder Preservation

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**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!

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**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

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**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

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**Bladder Preservation**

RTOG 99-06, T2- T4a
- Paclitaxel + CDDP + hyperfractionated XRT
- reTURBT < T1
  - 4 courses
  - Gemcitabine + CDDP

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Point-Counterpoint: Radiation & Bladder Cancer

Radiation Has No Role in the Treatment of Any Stage of Bladder Cancer

~ Robert E. Donohue, MD
Bladder Preservation

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.