

Bladder Cancer *Role of Radiation in Bladder Sparing*

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Primary Radiation for Bladder Cancer

- No modern surgery / XRT randomized trial
- Generally offered to poor surgical risk patients

Some Seminal Studies

- National Bladder Cancer Cooperative Group
- 70 patients with medical contraindications to surgery
- Cisplatin + 64.8 Gy XRT
 - 70% complete response
 - 57% 4 year survival
 - ✓ 57% for responders
 - ✓ 11% non responders

Shipley et al., JAMA 258:931, 1987

Chemotherapy Alone is Inadequate

- TUR + Chemotherapy
 - ~ 20-30 response rates
- TUR + Chemotherapy + XRT
 - ~74% response rates

Srougi & Simon, J Urol, 1994; 151:593
Given et al, Urology, 1995; 46:499

Radiation Alone May Be Inadequate

- 459 patients
- T1-T4
- Generally poor surgical risk
- 60-70 Gy with no chemo
- 5 year survival:

Overall	36%
Cause Specific	56%
Failure Free	33%

Tonoli et al; Clin Oncol, 2006 18(1):52-59

RTOG 85-12

- Candidates for Cystectomy
- 40Gy + Platinum
 - Evaluate response
 - ✓ Consolidation 24Gy + platinum
 - ✓ Cystectomy
- 66% CR
- 40% Freedom from Local Recurrence
- 40% Bladder preservation
- 73% Freedom from Invasive Recurrence

Tester, Porter, Asbell. JUROBP 1993, 25:783-790

Phase II Combined Modality

- 53 Cystectomy candidates
- TURBT / Chemo / XRT
- Evaluate at 40 Gy
 - 36 boost 24.8 Gy
 - 15 early salvage surgery
- 48% 5 year survival
- 58% bladder preservation
- 81% functioning bladder in patients with CR

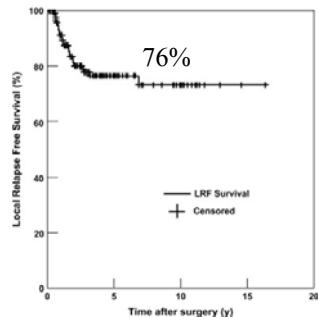
Kaufman et al., NEJM 329:1377: 1993

XRT + Brachytherapy for Bladder Cancer <5cm

- 122 patients
 - 94 men
 - 81 pT2
 - 103 Grade 3
- 10.5-40 Gy XRT with Cystotomy 10 days later
- 20-70 Gy Brachytherapy

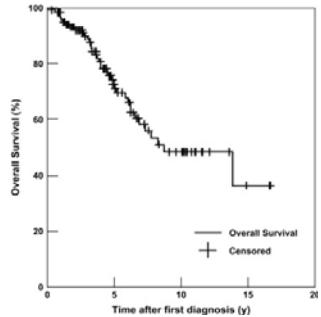
Blank et al; JUROBP 2007, 69(2):454-458

Local Relapse Free Survival



Blank et al; IJROBP 2007, 69(2):454-458

Overall Survival



Blank et al; IJROBP 2007, 69(2):454-458

Principles for RT

- XRT rarely for superficial tumors or diffuse CIS
- Precede XRT by maximal TUR of tumor
- Concurrent chemotherapy with XRT
- Simulate and treat with empty bladder
- Multiple fields
- High energy
- 40-55Gy Bladder; boost 64-66Gy total

Montie et al, JNCCN 3(1):4-34, Jan 2005

T1 Bladder Cancer

- Treated with TURBT + BCG
- Decrease recurrence by 30%
 - Still face 20-40% recurrence
- Pilot study XRT for high risk T1 bladder cancer
 - Progression 15-20%
 - Bladder preservation >80%

Weiss, C. et al. J Clin Oncol 24:2318-2324, 2006

High Risk T1 Bladder Cancer

- Grade 3
- Tumor >5 cm
- Multifocal
- Multiple recurrences
- Treat with maximum TURBT
 - RT alone (28 patients)
 - Platinum based chemo + 55.8 Gy RT (113 patients)
 - 48 months median F/U

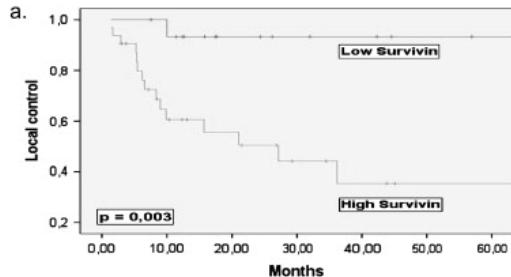
Weiss, C. et al. J Clin Oncol 24:2318-2324, 2006

Survivin in Bladder Cancer

- Protein regulates cell division and inhibition of apoptosis
- Overexpressed in human tumors
- Possible marker for early detection of bladder cancer

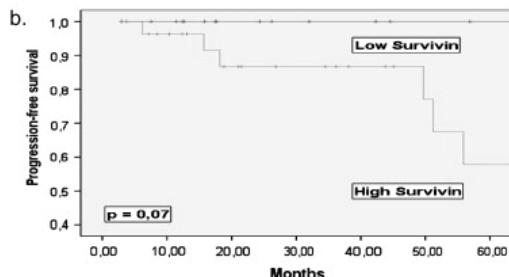
Weiss, C. et al. IJROBP V74(5): 1455-1460, 2009

Survivin Over-Expression Predicts XRT Bladder Tumor Control



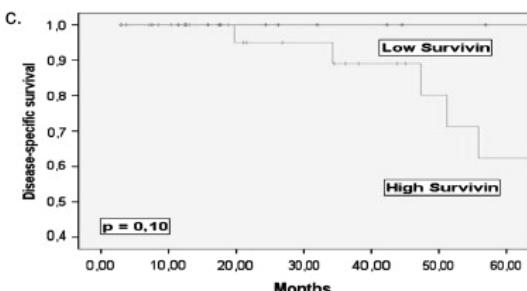
Weiss, C. et al. IJROBP V74(5): 1455-1460, 2009

Progression-free Survival



Weiss, C. et al. IJROBP V74(5): 1455-1460, 2009

Disease-Specific Survival Rates



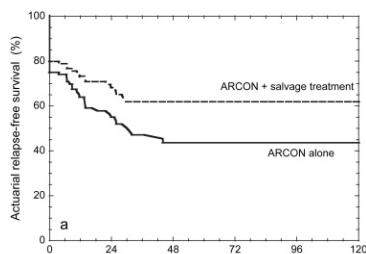
Weiss, C. et al. IJROBP V74(5): 1455-1460, 2009

“Although radical cystectomy is still considered by many to be the gold standard treatment, there is strong evidence to support the use of radical radiotherapy as an alternative.”

- Accelerated Radiotherapy, Carbogen and Nicotinamide
 - (ARCON)
- 105 patients T1G3 or \geq T2
- 55 Gy / 20 Fx's / 4 weeks

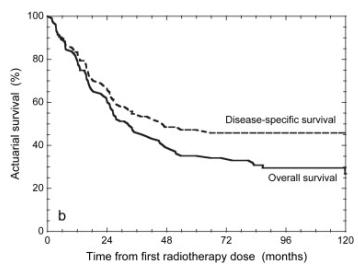
Hoskin, P. et al. IJROBP. V73(5): 1425-1431, 2009.

Bladder Cancer Relapse-free Survival after ARCON or ARCON + Salvage



Hoskin, P. et al. IJROBP. V73(5): 1425-1431, 2009.

Bladder Cancer Overall Survival & Disease-specific Survival



Hoskin, P. et al. IJROBP. V73(5): 1425-1431, 2009.

HypoFractionated ChemoRadiation

- Retrospective 26 patients, median age 80
- 37.5-40.0 Gy in 15 fractions + Platinum
- TCC or squamous cell (1)
- 39% \geq cT3
- Median survival 13.3 mos.
- Acute toxicity
 - GI 52%
 - GU 36%
 - Hematologic 36%

Ash, Welch, Winquist, Bauman; JUROBP 2007 69(3):S340

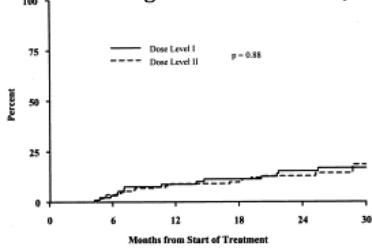
Toxicity XRT+ Brachytherapy

- Acute: Ileus, PE, Wound Dehiscence
- Late: 90% Bladder preservation
 - 5% “urinary function deterioration”
 - 3% “crippled bladder”
 - 17 second cancers
 - ✓ Only 1 in pelvis

Blank et al; JUROBP 2007, 69(2):454-458

Toxicity RTOG 94-06 (68.4-79.2 Gy)

RTOG 9406: Time to Late Grade 2 or Higher GU/GI Toxicity



Michalski et al; JUROBP 46(2):391-402, 2000

Primary XRT for Bladder Cancer

- Option for non-surgical candidates
- Option for surgical candidates desiring bladder preservation
- ~50% long term disease free survival
- >70% CR
- In RTOG studies 2/3 completed therapy with intact functioning bladder

Shipley et al. Urology 2002;60:62-67

Ongoing Studies
RTOG 0233

- Candidates for surgery
- Phase II
- TURBT
- XRT 64.3Gy
 - 44.8Gy to nodes
 - 1.6Gy bid
- + Cisplatin
- 5FU or paclitaxel
- + Adjuvant emcitabine/paclitaxel/cisplatinum

<http://rtog.org/members/active.html> Accessed Oct 2006

Ongoing Studies
RTOG 0524

- Phase I/II
- Non cystectomy candidates with muscle invasive disease
- XRT 64.8Gy
 - 1.8Gy/day
 - Reduction at 39.6Gy
 - Weekly Paclitaxel
- +/- Trastuzumab
 - Stratified by her2/neu overexpression
 - Evaluate role of EGFR

<http://rtog.org/members/active.html> Accessed Oct 2006

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