

# Radiation Therapy in Advanced Bladder Cancer

가톨릭대학교 의과대학 치료방사선과학교실

## 최 일 봉

### Definitive Radiotherapy (RT)

#### 1. Eligibility

- 1) "Unfit" for cystectomy due to comorbid conditions or disease extent
- 2) Refuse cystectomy

#### 2. RT TECHNIQUE

- 1) Have the bladder empty to assist setup reproducibility and adequate coverage of the tumor at each treatment
- 2) Foley catheter is inserted and 25 to 30 ml of radiopaque contrast material in addition to 10 to 15 ml of air for bladder visualization
- 3) Rectal tube with barium contrast to visualize the rectum

#### 3. RT FIELDS

- 1) Initial fields: To encompass entire bladder and 1st echelon draining LNs
  - Superior border: L5-S1 interspace
  - Inferior border: Bottom of the obturator foramen
  - Lateral border: 2 cm beyond the bony pelvic side walls
  - Anterior border: 2-3 cm margin anterior to the air bubble

- Posterior border: 2-3 cm margin posterior to the bladder to incorporate presacral LNs

- 2) Cone-down fields: 3 Dimensional Plan to cover the tumor within the bladder

#### 4. RT DOSE

- 1) Initial fields: daily 180 cGy, 5 times a week, up to 4500 cGy
- 2) Cone-down fields: daily 180 cGy, up to 1980 cGy
- 3) Total dose (TD) is brought to 6480 cGy.

#### 5. Cystoscopic Evaluation

- 1) During RT  
Frequent cystoscopic evaluations to further assess the response as a means of selecting the most optimal treatment approach.

2) 4 to 8 weeks following completion of RT±CT and any patient with persistent and invasive tumor was referred for salvage cystectomy before local regrowth could occur.

#### 6. RESULTS

- 1) Inferior survival to those obtained with cystectomy, due to  
(1) Partly difficult rendering the bladder tumor free by ERT alone

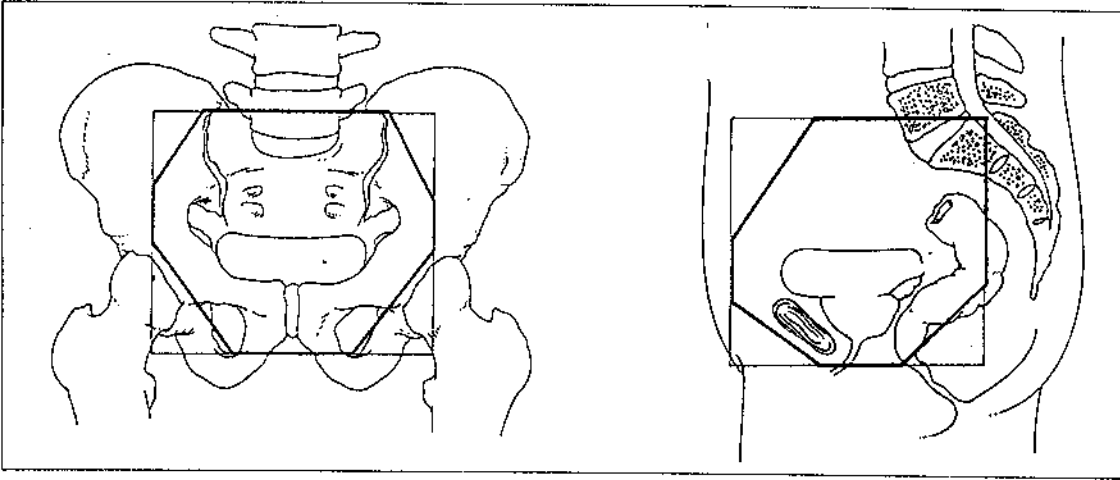


Fig. 1.

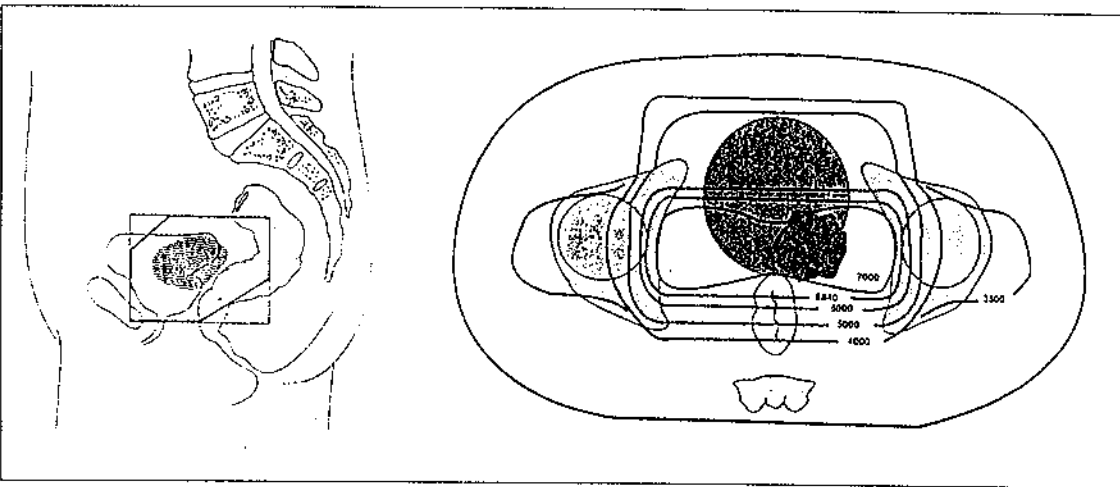


Fig. 2.

- (2) And the continued risk for developing new tumors in the organ left in situ.
- 2) CR: 40-52% (based on cystoscopy and biopsy)
- 3) PR or PD without metastasis: Salvage cystectomy
- 4) 5Y bladder free of disease: 35-45%
- 5) 5YS: 23% to 40%

#### 7. PROGNOSTIC FACTORS for Local Control, Freedom from metastasis, and Survival

1) Clinical CR Most Important (MDACC 1994)

5YS	Overall	CR	Non-CR
	20%	50-70%	10-20%

**Table 1. Results Following external Beam Irradiation Alone**

Series	No. of patients	Clinical stage	5-Year survival	5-Year local bladder control
London hospital (#22)	182	T2-T3	40%	41%
U.K. Co-op group (#48)	157	T3	23%	45%
Princess margaret hosp. (#13)	121	T2-T4a	40%	35%
Sydney, prince of wales (#31)	342	T1-T4b	-	45%
Belgium/Netherlands group (#5)	147	T2-T3	31%	35%

**Table 2. Treatment of Invasive Bladder Cancer with Definitive External Beam Irradiation**

Author (year)	Np. patients	Clinical stage 5-year survival		
		T2	T3	T4
Rider <sup>92</sup> (1972)	554	50	18	20
Miller & Johnson <sup>93</sup> (1973)	109		20	
Goffinet <sup>96</sup> (1975)	384	42	35	8
Morrison <sup>94</sup> (1975)	40		40	
Greiner <sup>95</sup> (1977)	225		28	10
Blandy <sup>96</sup> (1980)	404	27	38	9
Gospodarowicz <sup>†13</sup> (1980)	355	50	28-38*	14-40*
Goodman <sup>97</sup> (1981)	560		38	7
Bloom <sup>98</sup> (1982)	85		31	
Gospodarowicz <sup>†</sup> (1985)	121	59	29-52*	
Shipley <sup>16</sup> (1985)	55		39	6
Yu <sup>99</sup> (1985)	257	42	24	
Duncan & Quilty <sup>100, 101</sup> (1986)	963	40	26	12
Davidson <sup>†</sup> (1990)	709	49	28	2
Greven <sup>103</sup> (1990)	116	59	10	0

\* T3b-a, T4b-a.

† Cause specific corrected survival.

For patients who achieve Initial CR: Favorable outcomes (Pollack A; 1994)

2) Shipley W et al (1987)

- (1) Depth of invasion by Staging
- (2) Tumors greater than 5 cm
- (3) Residual disease after TURB
- (4) Radiographic evidence of Ureteral Obstruction with Hydronephrosis

3) Fox Chase Cancer Center (1992)

- (1) Preclinical T stage
- (2) Hb level
- (3) Grade I/II III  
5YS 43% 27%

4) Gospodarowicz M et al (1989)

Papillary or mixed tumor morphology vs solid

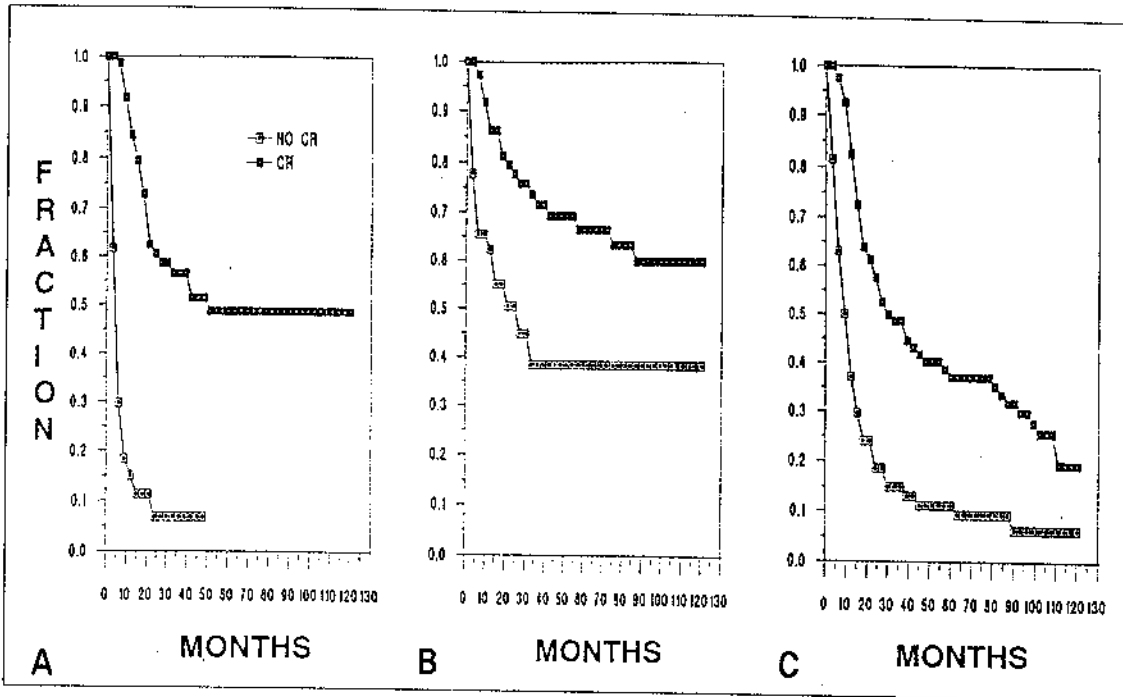


Fig. 3. Actuarial pelvic control (A), freedom from metastases (B), and overall survival (C) broken down by whether clinical complete response was seen at the first follow-up cystoscopy.

tumors

## 8. TOXICITIES

- 1) Irritative symptoms from the bowel and the bladder, inflammation of the skin & fatigue
- 2) A persistent proctitis, with bleeding and secretion of mucus, is rare but does occur, and bowel obstruction be severe enough to require surgical extirpation.
- 3) markedly reduced bladder capacity resulting from fibrosis may make a cystectomy or urinary diversion necessary.
- 4) Chronic grade III/IV GU Complication: 11% (Shipley W et al; 1987). Sexual function can also be impaired.
- 5) Occurrence of secondary tumors is a potential late complication.

## RT Combined with Radical Cystectomy

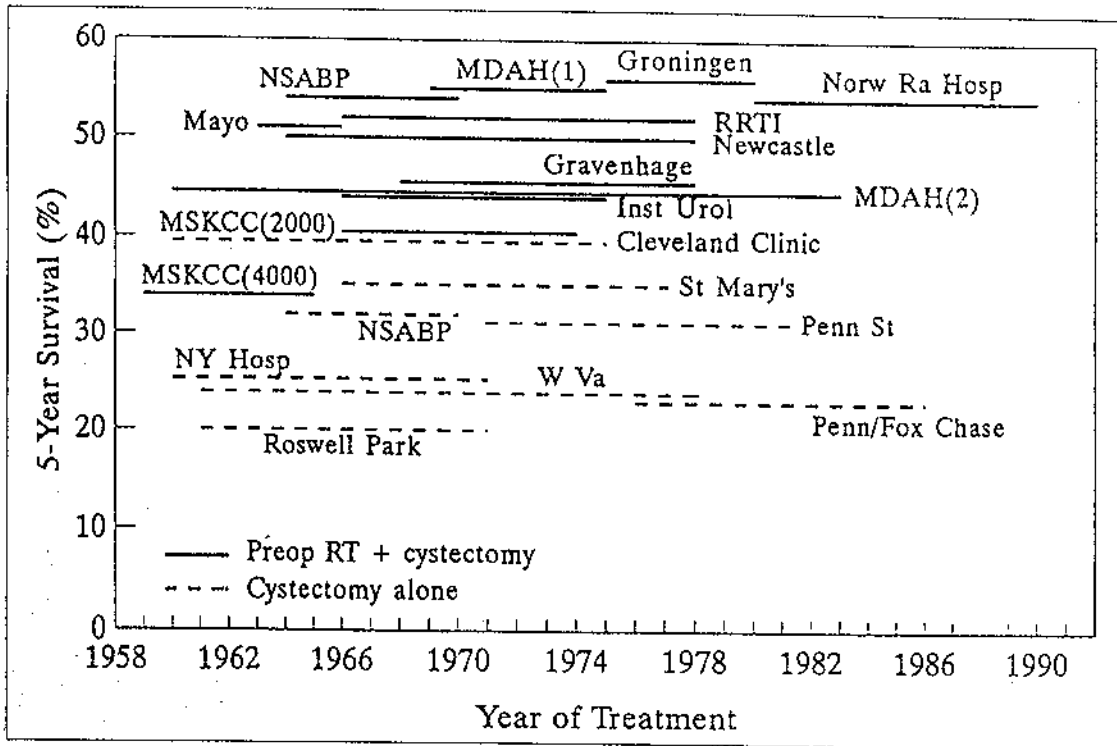
### 1. Preoperative RT/CRT

- 1) Role of Preoperative RT: Controversial
- 2) Preoperative RT: 50 Gy/5 wks followed by radical cystectomy 4-6 weeks later
- 3) If neoadjuvant chemotherapy (CMV, MV-AC) is administered, the CT is given first, followed by RT and then cystectomy. No data justify abandonment of preoperative RT in favor of neoadjuvant CT
- 4) High-Dose (45-50 Gy) preoperative RT시 5Y survival은 50% 이상이다.

**Table 3.** Incidence of Major Complications after Radiation Therapy in Patients with Bladder Cancer

Author (year)	No.	Dose (Gy)	Fraction size (Gy)	Complications (%)				
				Total	Bladder	Rectosigmoid	Small Bowel	Mortality
Miller & Johnson <sup>9,10</sup> (1973)	533	70	2.0	14	8	4	2	5
Fossa <sup>11</sup> (1984)	159	50-56	2.0	5	1	3	3	
Duncan & Quilty <sup>12</sup> (1986)	963	55-57	2.2-2.8	14	12	4	1	1
Gospodarowicz <sup>13</sup> (1991)	355	50	2.3-2.5	11	7	7		
Johnson <sup>14</sup> (1991)	262	50-77	1.5-2.5	22*	5	20		3
Mameghan <sup>15</sup> (1992)	303	45-65	1.8-2.5	5	1	4		2

\* Includes 23 of 58 (40%) Grade 1 or 2 complications.



**Fig. 4.** The 5-year survival rates after total or radical cystectomy alone for eight series of patients with clinical stage B2 to C (T3) bladder cancer are depicted according to the year patients were treated (*dashed lines*). All patients were treated between 1960 and 1986. Five-year survival rates for patients treated during this period ranged from 20% to 40% (median, 32%). The 5-year survival rates for preoperative irradiation plus total or radical cystectomy for 12 series of patients with clinical stage B2 to C (T3) bladder cancer are given according to the year patients were treated (*solid lines*). All patients were treated between 1959 and 1990. Five-year survival rates ranged from 34% to 55% (median, 50%). (Parsons JT, Million RR: Role of planned preoperative irradiation in the management of clinical stage B2-C [T3] bladder cancer in the 1980s. *Semin Surg Oncol* 5:255, 1989).

**Table 4. Survival Results for Clinical Stage T3 Bladder Carcinoma after 45-to 50-Gy Preoperative Irradiation Plus Cystectomy**

Investigator	Dates patients entered study	Clinical stage	No. of patients	Treatment	5-Yr survival rate (%)
Slack et al <sup>226</sup>	1964-1970	T2-T4	70*	45 Gy/4-4.5 wk; cystectomy 4-8 wk later	54
DeWeerd & Colby <sup>48</sup>	1963-1966	T2-T4	45	48 Gy; cystectomy; lymph node dissection	51
Chan & Johnson <sup>35</sup>	1969-1975	T3	89	50 Gy/5 wk; cystectomy 6 wk later	55
Tjabbes <sup>249</sup>	1968-1978	T3	48	45 Gy; immediate cystectomy	45
Hall & Heath <sup>83</sup>	1964-1978	T3	102	40-45 Gy/4-4.5 wk; cystectomy 1-6 wk later	50 <sup>†</sup>
Pollack et al <sup>175</sup>	1960-1983	T3	225	50 Gy/5 wk; cystectomy 4-6 wk later	45

\* Received radiation therapy, cystectomy, and "no drug" or "placebo"; patients treated with 5-fluoro-uracil were excluded.

<sup>†</sup> Overall 5-yr survival figure was not given but was calculated from available data. Survival in the 74% of patients whose tumors were downstaged was 60%, and it was 30% in the 26% of patients whose tumors were not downstaged, giving a 5-year overall survival rate of 50.4%.

(Modified from Parsons JT, Million RR: Planned preoperative irradiation in the management of clinical stage B2-C [T3] bladder carcinoma. *Int J Radiat Oncol Biol Phys* 14:797-810, 1988).

#### 5) MDACC (Pollack A et al; 1997)

- Preoperative RT may be of benefit to late-stage patients (T3b/T4)
- Downstaging: 70% of those who completed the planned treatment.

#### 2. Post-Op RT

- 1) Post-Op RT is reserved for patients with with proven disease recurrence or for patients with known significant residual disease.
- 2) However, no data support the use of postoperative RT for patients with transitional cell tumors due to significant toxicities. The incidence of small bowel obstruction can be as high as 30% if more than 45 Gy are administered (Reisinger 1992).

#### 3) Zaghoul (1992)

In Egyptian patients with squamous cell carcinoma, the pelvic recurrence rate was reduced from 50% to 10% by postoperative RT.

#### 4) CONCLUSION

- (1) It's safer to treat with preoperative RT than postoperative RT.
- (2) If the clinical setting requires postoperative RT, this should be combined with CT to keep the total RT dose modest.
- (3) RT fields should be constrained as much as possible to minimize the proportion of small intestine and the ileal conduit stoma that receives the total dose of RT.

**Table 5. Actuarial 5-year Results by Treatment for Those with and without Downstaging Using Several Endpoints**

	Percent		
	PREOP	CYST	p*
<b>p&lt;T staged</b>			
Distant metastasis freedom			
All	70	82	0.08
T2/T3a	67	100	0.0002
T3b	77	58	0.14
Disease freedom			
All	67	79	0.12
T2/T3a	66	100	0.0001
T3b	71	52	0.07
Overall survival			
All	59	65	0.12
T2/T3a	57	79	0.004
T3b	63	58	0.61
<b>p≥T staged</b>			
Distant metastasis freedom			
All	41	65	0.0002
T2/T3a	44	69	0.0007
T3b	33	50	0.27
Disease freedom			
All	33	59	<0.0001
T2/T3a	38	65	0.0001
T3b	22	44	0.15
Overall survival			
All	26	49	0.0001
T2/T3a	29	56	0.0003
T3b	20	37	0.24

\* Log-rank

p<T staged=downstaged; P≥T staged= not downstaged.

PREOP=preoperative radiotherapy plus cystectomy.  
CYST=cystectomy alone.

### 3. Comparisons of Preoperative RT and immediate Cystectomy to ERT followed by Salvage Cystectomy

#### 1) Results

DAVECA 8201 (Sell A; 1991)

	5YS	Pelvicrecur	Meta
Pre-Op RT	29%	<u>6.8%</u>	34%
ERT	23%	36%	32%
p value	0.08	46%	

MDAH (Miller LS; 1997)

Pre-Op RT	<u>46%</u>
ERT	22%
p value	<0.1

### Bladder Preservation Therapy

#### 1. ERT Alone

##### 1) Conventional Fractionation (CFX)

\* Favorable Prognostic Factors

- ① Clinical Stage: T2/T3
- ② Tumor Size: Less than 5 cm Maximum Diameter
- ③ Absence of Ureteral Obstruction

##### 2) Hyperfractionation (HFX)

To improve local control

(1) Swedish Trial (1985) (n=168), T2-T4

1 Gy t.i.d., TD: 84 Gy/8wks with an mid-course  
2-week rest

Control: 2 Gy once a day, TD: 64 Gy/8wks

**Table 6. Randomized Trials of Irradiation that did or did not defer Radical Cystectomy for Salvage of Recurrence**

Treatment	No. of patients	Clinical stage	5-year survival	% Distant metastases
M.D, Anderson hospital (#34)				
50 Gy+cystectomy	35	T3	46%	-
60 Gy+salvage cystectomy	32	T3	22%	-
U.K. Co-op group (#2)				
40 Gy+radical cystectomy	98	T3	39%	-
60 Gy+salvage cystectomy	91	T3	28%	-
National danish trial (#47)				
40 Gy+radical cystectomy	88	T3	29%	34%
60 Gy+salvage cystectomy	95	T3	23%	32%
National bladder cancer group*				
50 Gy+radical cystectomy	37	T2-T4a	27%	38%
60-68 Gy+salvage cystectomy	35	T2-T4a	40%	31%

\* S.D. Cutler, personal communication 1983.

**Table 7. Muscle-invading Bladder Cancer: Success Rates of Bladder Preservation with Monotherapy**

Treatment	No. of evaluated series	Total no. of patients	% With bladder, free of invasive recurrence
Transurethral resection alone* (18, 19)	2	331	20% <sup>†</sup>
Radiation therapy alone <sup>†</sup> (5, 13, 22, 31, 48)	5	949	41%
Chemotherapy alone (cisplatin+methotrexate) <sup>†</sup> (14, 15)	1	27	19%

\* Used selectively as monotherapy, most patients had cystectomy

<sup>†</sup> No transurethral resection of tumor.

<sup>†</sup> Intravesical drug therapy often used for noninvasive recurrent tumors.

**Table 8. Muscle-invading Bladder Cancer: Complete Response Rates after Monotherapies and Combined Modality Therapies**

Treatment	No. of evaluated series	Total no. of patients	% Complete responses
Radiation therapy alone (13, 22, 40, 51)	4	721	45%
Chemotherapy alone (9, 16, 26, 28, 30, 41)	6	301	27%
TURBT plus Chemotherapy (17, 37, 39, 45)	4	225	51%
TURBT plus Chemo-radiotherapy (3, 6, 11, 55)	4	218	71%

Modified with permission from Kioso et al. (27)

TURBT, transurethral resection of tumor.



**Table 9. Five-year Bladder Relapse Rates and Survival Rates after Treatment of T3 Bladder Carcinoma with Removable Interstitial Sources**

Study	Treatment	Clinical stage	No. of patients	Bladder relapse rate* (%)	Survival rate (%)
Williams et al <sup>275</sup>	<sup>182</sup> Ta	T3	24	29	21
Van der Werf-Messing et al <sup>259</sup>	EB (10.5 Gy) plus radium	T3	63	33	39
Van der Werf-Messing et al <sup>258</sup>	EB (10.5 Gy) plus radium plus EB (30 Gy)	T3	41	-	57
Mazeron et al <sup>145</sup>	EB (8.5 Gy) plus partial cystectomy plus <sup>192</sup> Ir	T3	5	0	25
Boiteux et al <sup>20</sup>	EB (10.5 Gy) plus partial cystectomy plus <sup>192</sup> Ir	T3a	26	15	47
Van der Werf-Messing & van Putten <sup>260</sup>	EB (40 Gy) plus radium within 1 wk	T3	42	14	54

EB, external-beam radiation therapy

\* relapse in the original site or elsewhere in the bladder.

**Results.**

①

5YS	HFX (84 Gy)	CFX (64 Gy)
All	34%	22% (p=.01)
T2	37%	33% (NS)
T3	37%	16% (p<.05)
T4	22%	15% (NS)

More benefit in T3

② Without significant increase in toxicities

(2) RTOG 8308 (1988)

Phase I/II; 1.2 Gy b.i.d., TD: 60, 64.8, 69.6 Gy

Results

① Phase I treatment: well tolerated

② G3/4 T: 11% at the highest dose level

③ Acceptable late morbidity

(3) Royal marsden hospital (1992)(n=85)

1.8-2 Gy b.i.d., TD 57.6-64 Gy/32fx/26 days

Results: CR:80% [3-6 mos after, by cystoscopy]

**2. Interstitial Brachytherapy**

1) Eligibility

Monnen (1994): Only 10% of pts with invasive bladder cancer met these criteria

(1) Solitary nonrecurrent tumors of clinical stages T2/T3a

(2) Less than 5 cm in diameter

(3) Fit for surgery with adequate bladder capacity

2) Usually preceded by ERT to shrink the tumor and improve the geometry of the the implant

3) Indications for preoperative or interstitial irradiation in conjunction with partial cystectomy

(1) The tumors arise in the fixed portion of the bladder

(2) Require ureteral reimplantation

4) Local control: 75-80%  
5YS: 50-76%

5) Recurrence  
In original lesion: 28%  
Elsewhere in the bladder: 5%

6) Rotterdam Group (1989)  
T2 (n=328), T3(n=63)

Preoperative RT (3 fractions of 3.5 Gy) followed by radium implantation

Results	5YLR	5YS
T2	16%	56%
T3	28%	37%

7) French Group (1992)

pT1(n=98), pT2(n=66), pT3a (n=26), pT3b (n=9), pT4 (n=1)

Pre-Op ERT (TD 11 Gy, mean 5.4 Gy/fr) + partial cystectomy with LAD + iridium implant

Results

(1) Recur: n=36, at original site (n=9), at different site (n=19)

(2) 5YS: 67%

pT1: 77%

pT2: 63%

pT3: 47%

(3) Serious Complication

Hematuria (n=8)

Chronic Cystitis (n=17)

Fistulas (n=11)

### 3. Combined Modality Treatments (CMT)

1) Objectives

- (1) Eradication of local tumor
- (2) Maintenance of normal organ function
- (3) Improvement in quality of life (QOL)
- (4) Prevention of distant metastases

2) Salvage cystectomy

Reserved for isolated bladder recurrence after chemoradiotherapy (CRT)

3) Eligibility

(1) Muscle-invasive (T2-4) or

(2) High-risk T1

① G III/IV

② Associated Tis/Ta

③ Tumor diameter > 5 cm

④ Residual and nonresectable tumor after TURB

⑤ Multifocality

⑥ Multiple recurrences

(3) No metastasis

(4) No prior pelvic RT

(5) Transitional histology

4) Selective Bladder-sparing approaches: Favorable Group

(1) T2/T3a (2) Unifocal (3) Not associated with Tis or the prostatic urethra (4) Capacity of the UB

(5) Rb-positive and p-53-negative (MSKCC)

5) RT Field: small pelvic fields

### 4. Results for CMT

- Higher rate of pCR after TUR + CRT than after TUR + CT

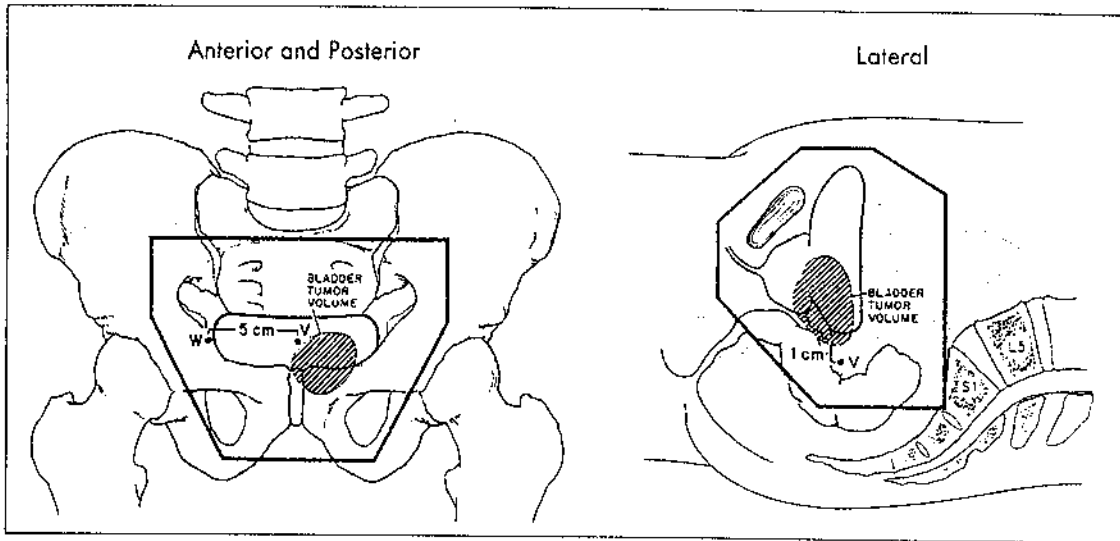


Fig. 5. Small pelvic irradiation fields used in combination with systemic chemotherapy in the treatment of invasive bladder cancer (Courtesy Dr. W.U. Shipley).

- Comparable survival to radical cystectomy with a high rate of bladder preservation (BP)

1)

	pCR	BP	Survival
TUR+C/RT	60-80%	50-70%	45-52% (5y)
↗ CR			57% (4y)
↘ Non-CR			11% (4y)
TUR+CT	20-30%	20%	

#### RTOG 8512 (1993)

##### 2) Eligibility

- (1) T2-T4, N0-N2, M0 who have residual tumor following initial TUR [considered for cystectomy]
- (2) All histologies
- (3) KPS > 70

##### 3) Objectives

- (1) To determine the CR, toxicity of CMT, degree of downstaging
- (2) To refine criteria for identifying the population with high permanent tumor control

##### 4) Regimen

Concurrent C (100 mg/m<sup>2</sup>)/RT(40 + 24 Gy, 2 Gy/ fr)(n=47)

##### 5) Schema

##### 6) Results

- (1) CR: 66%
- (2) All local failures occurred during the first 12 months  
3Y freedom from invasive recurrence: 73%
- (3) 3YS: 64%, BP: 40%

RTOG 8802 (1996)

tumor following initial TUR

(2) All histologies

(3) KPS>70

1) Eligibility

(1) T2-T4, N0-N3, M0 who have residual

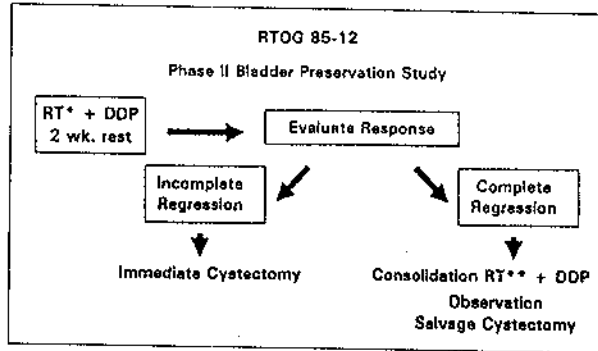


Fig. 6. Treatment schema. \*RT=2 Gy/day×4 wks. for 40 Gy; DDP=Cisplatin 100 mg/M2 IV day 1, 22 of RT. \*\*RT=2 Gy/day to 24 Gy Total; DDP=Cisplatin 100 mg/M2 IV day 1 of RT.

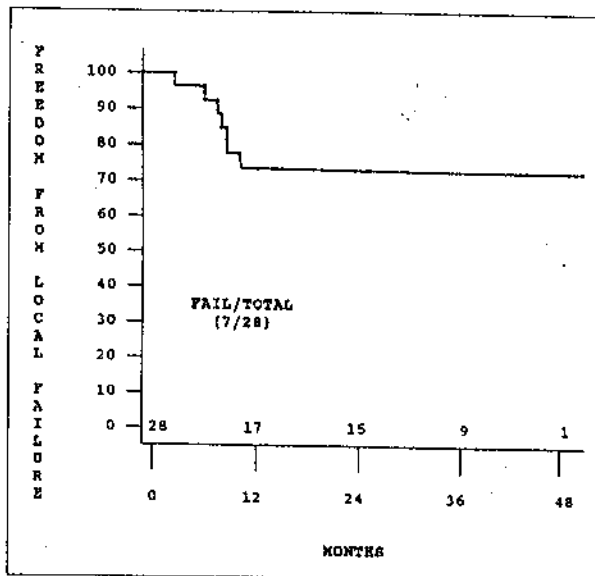


Fig. 7. Freedom from local (invasive only) failure of 28 evaluable patients who achieved complete response to cisplatin/radio therapy. Patients who recurred in the bladder with noninvasive tumors are not considered failures

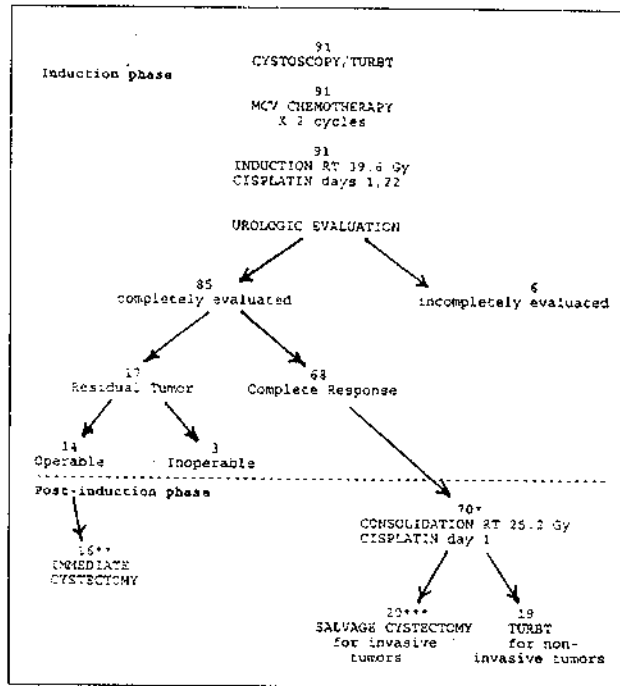


Fig. 8. Treatment schema. Numbers of patients treated at each phase are shown. Rt, radiotherapy; TURBT, transurethral resection of bladder tumor. \* Includes 66 patients with complete response, 2 with incomplete evaluations, and 2 inoperable patients with residual tumor \*\* includes 14 operable patients with residual tumor, 1 incompletely evaluated patient, and 1 with complete response; \*\*\* includes 19 patients completely evaluated with complete response and 1 incompletely evaluated.

## 2) Objectives

- (1) To assess the safety, the CR, DFI, pattern of failure, and survival
- (2) To refine criteria for identifying the population with high permanent tumor control
- (3) To examine the value of cell DNA analysis by flow cytometry in predicting patients whose tumor will achieve rapid response
- (4) To study QOL

Table 10. Sites of First Treatment Failure

Site	No.	%
Induction failure	17	19
Bladder-only relapse	37	41
Invasive cancer	18	
Noninvasive tumor	19	
Regional nodes	2	2
Distant metastases	6	7
Death without cancer	5	5
NED	24	26
Total	91	100

Abbreviation; Ned, no evidence of disease.

**Table 11. Acute Toxicity (%) of Chemoradiotherapy in Sequential RTOG Studies**

Toxicity	Present study, MCV/Cisplatin/RT (n=91)		Earlier Study, <sup>10</sup> Cisplatin/RT (n=47)	
	Severe	Any	Severe	Any
Bladder	3	40	0	38
Rectal	0	34	0	47
Bowel	1	35	2	28
Nausea	3	75	8	73
Mucosal	3	29	0	0
Anemia	0	37	0	35
WBC	12	71	6	63
Platelet	2	8	4	8
Renal	2	32	2	42
Neurologic	0	5	2	2

NOTE. See Cox et al<sup>15</sup> for standard RTOG toxicity grading criteria. Patients with RTOG grade 3 or 4 toxicity are listed as severe.

**Table 12. Studies of Chemoradiotherapy and Selective Bladder Preservation**

First author	No. of patients	Drugs	Complete response (%)	Bladder preserved (%)	Actuarial survival rate (%)
Cervek <sup>20</sup>	45	MCV	62	68	73 (2-year)
Housse <sup>21</sup>	54	F*C*	74	NA	59 (3-year)
Kaufman <sup>14</sup>	53	MCV/C*	67 <sup>†</sup>	58	66 (3-year)
Rebischung <sup>22</sup>	29	F*C*	69	69	56 (2-year)
Rifkin <sup>23</sup>	91	MCV±A	57	52	63 (2-year)
Russell <sup>24</sup>	34	F*	?	70	64 (4-year)
Tester, updated <sup>10</sup>	42	C*	66	52	52 (5-year)
Present study	91	MCV/C*	75	60	62 (4-year)

Abbreviations; M, methotrexate; C, cisplatin; V, vinblastine; A, doxorubicin; F, fluorouracil

\* Chemotherapy drug given concurrently with radiotherapy

<sup>†</sup> Twenty-eight of 42 patients who completed treatment achieved a complete response.

4YS: 62%

3) Regimen

4YBP: 44%

TUR + MCV (x2) + C/RT (39.6 + 25.2 Gy, 1.8

4Y DM: 22%

Gy/fr)(n=91)

At recurrence ⇒ Salvage cystectomy ⇒ 30-40% survival

4) Schema

5) Results

Toxicity: Greater incidence of mucositis, diarrhea, leukopenia than RTOG 8512

Induction Failure (non-CR): 19%

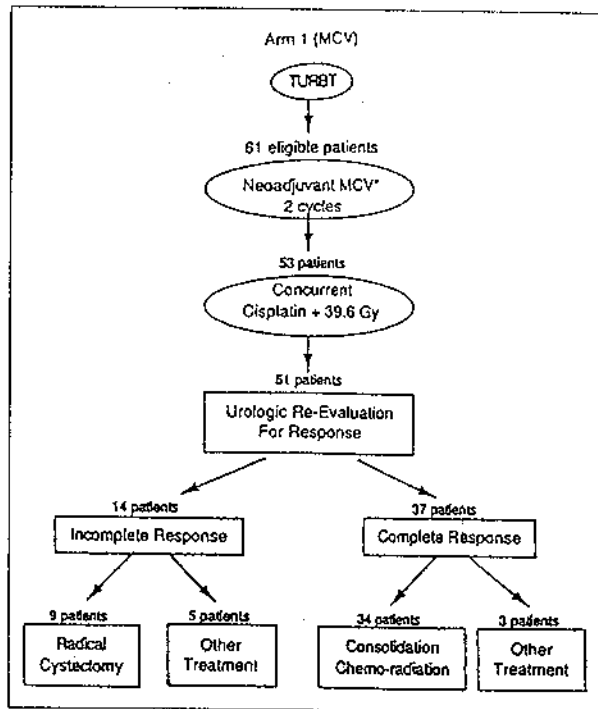


Fig. 9. Arm 1 of RTOG 89-03 for the treatment of invasive bladder cancer with combined TURBT, chemotherapy, and radiation therapy for attempted bladder preservation.

Table 13. Treatment-Related Toxicity

	Grade 3 or greater	
	Arm 1 (MCV)	Arm 2 (no MCV)
During neoadjuvant MCV, %		
Leukopenia	21	-
Thrombocytopenia	5	-
Neutropenic fever	23	-
Infection	8	-
Nausea/vomiting	23	-
Late morbidity, %		
Hematologic	13	6
Renal	8	2
Neurologic	2	2
Cardiac	0	2
Bladder	13	8
Intestinal	8	5

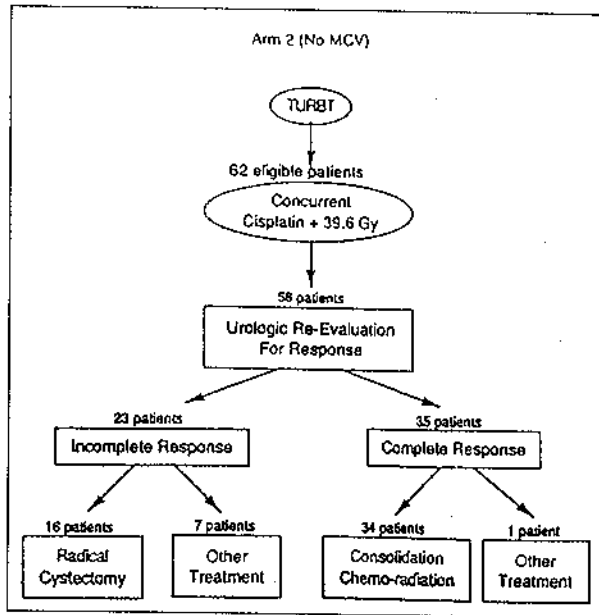


Fig. 10. Arm 2 of RTOG 89-03 for the treatment of invasive bladder cancer with combined TURBT and concurrent chemotherapy and radiotherapy for attempted bladder preservation.

Table 14. Results by Treatment Assignment, Status After TURBT, and Presence or Absence of Hydronephrosis

Patient group	No.	Alive, %	cCR Rate, %	Total pelvic failure, %	Distant failure, %*	Alive with intact bladder, %*
All eligible	123	50	59	12	35	38
Treatment assignment						
MCV	61	49	61	9.8	33	36
No MCV	62	50	55	14.5	39	40
Status after TURBT						
Visibly complete	88	55	65	13	34	43
Visibly incomplete	32	53	44	12	38	26 <sup>†</sup>
Hydronephrosis						
Absent	99	54	64	11	35	39
Present	24	33 <sup>†</sup>	38 <sup>†</sup>	25	42	33

Abbreviation: cCR, clinical complete response, ie, tumor site rebiopsy negative and cytology negative

\* Actuarial rate at 5 years

<sup>†</sup> p=.06.

<sup>†</sup> p=.02.



Severe leukopenia: 12%

No TRD (treatment related death)

6) Discussion

Doxorubicin: not used because 3-drug regimen can downstage significantly primary tumor.

**RTOG 8903 (1998)**

T2-4

Arm 1: MCV(x2) + 39.6 Gy/cisplatin(C)(x2) (n=61)

2: 39.6 Gy/C(x 2) (n=62)

↙ If CR-Additional 25.2 Gy [Total 64.8 Gy]/C

↘ If non-CR-Cystectomy

1) SCHEMA

2) Results

Completion 5YS 5YDM 5YFB (Functioning Bladder)

Arm 1	67%	48%	33%	36%
2	81%	49%	39%	40%

⇒ Addition of MCV: No further benefit

3) In the future

(1) Molecular tumor subtype: predict success with bladder-conserving treatment

(2) New CT Regimen: Taxol, Gemcitabine AHFX (Accelerated hyperfractionation)

RT: to improve LC

(3) New CT Combinations: to reduce DM

**적 입 령**

- 1. 1978년 가톨릭대학교 의과대학 졸업
- 2. 1983년 방사선과 전문의 취득
- 3. 1990년 - 91년 미국 미네소타대학 교환교수
- 4. 1992년 - 현재 가톨릭대학교 의과대학 치료방사선과 과장
- 5. 1999년 - 현재 가톨릭대학교 의과대학 치료방사선과 교수