

SMALL-VOLUME HIGH-DOSE RADIATION THERAPY IN CARCINOMA OF THE URINARY BLADDER

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External irradiation can be used for treatment of carcinoma of the bladder as a single method or in combination with surgery. In most centres for radiation therapy a large volume, including the whole bladder and the regional lymph nodes, is irradiated both when combined treatment and irradiation alone is planned (GOFFINET et coll. 1975, BIRKHEAD et coll. 1976, WASSIF & VAN DER WERF-MESSING 1978, BACKHOUSE 1979, CUMMINGS et coll. 1979, GOSPODAROWICZ et coll. 1981, SHEHATA et coll. 1983). Some other authors have, in view of the moderate sensitivity to radiation of bladder carcinoma, recommended irradiation of the tumour with a narrow margin of normal tissues, according to the so-called small-volume high-dose principle (PATERSON 1963, POINTON & EVANS 1969, EDSMYR 1975). This technique has been used at this Institute, and an attempt to estimate its clinical value is now presented.

Material and Methods

From January 1970 to December 1975, 176 patients (157 men, 19 women; mean age 59, range 31 to 75 years) with microscopically confirmed bladder carcinoma were irradiated with curative intention. Patients with non-invasive papillomas were not included.

The clinical staging was performed according to the modified Jewett-Strong system (JEWETT & STRONG 1946): Stage A, tumour not invading beyond the lamina propria; Stage B, invasion of the muscle; Stage C, perivesical invasion, with a palpa-

ble but movable extravesical mass (includes prostatic invasion); Stage D, tumour fixed to the pelvic side wall.

All patients were referred for radiation therapy by the urologists cooperating with the Institute. In 87 patients (49.4%) transurethral resection was performed some time before irradiation. The patients with stages A and B were not suitable for more radical surgery because of medical reasons, multiplicity or large size of the tumour which contraindicated segmental resection, or because the patients refused the proposed surgical treatment. Patients with extravesical extension were routinely referred for radiation therapy.

Treatment. All patients were treated with ^{60}Co teletherapy. The identification of the target volume was based on bimanual examination, cystoscopy, and cystography. In some patients control radiography was performed with the therapeutic cobalt beam.

In 146 patients a three-field technique was used as described by PATERSON. The Figure shows the field arrangement and dose distribution. In 30 obese patients a four-field technique was used. The field sizes varied from 7.5 cm $\times$ 7.5 cm to 10 cm $\times$ 12 cm. The standard tumour dose was 60 Gy in 20 fractions over 4 weeks.

Reaction and complications. In most of the patients a bladder reaction (dysuria and urinary frequency) and rectal reaction (diarrhoea) of mild or moderate degree occurred toward the end of the

Accepted for publication 23 June 1983.

irradiation course. In 161 patients (91.5%) the reaction did not cause any interruption and the planned therapeutic dose was delivered. In 8 patients an interruption of treatment for several days was necessary, and in another 5 patients the radiation therapy was not completed because of severe bladder or rectal reaction. In one case the treatment was not completed due to viral hepatitis, and one patient died of diabetic coma during radiation therapy.

A severe late complication occurred in only one patient, who developed gross contracture of the urinary bladder requiring permanent ureterostomy one year after irradiation. He survived for five years without evidence of recurrence.

Results

Forty-seven patients, i.e. 26.7 per cent of those irradiated, survived for five years after irradiation and 42 of them (23.9%) without evidence of disease. The 5-year survival rates without evidence of malignancy according to clinical stage, histology, duration of symptoms, previous transurethral resection, technique of irradiation, and tolerance of therapy are shown in Table 1.

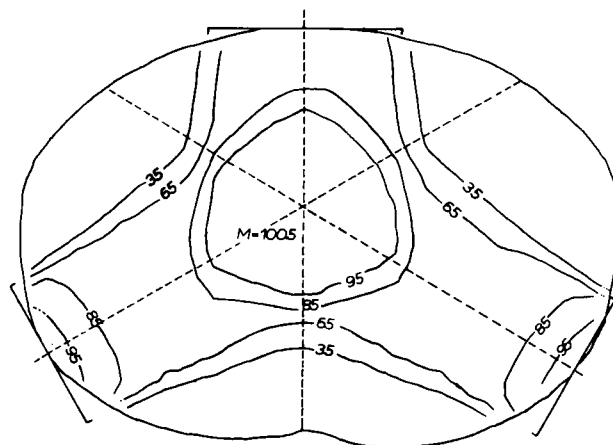
Patients with transitional cell carcinoma had a significantly better chance of survival than those with other histologic types of bladder carcinoma, and patients with symptoms of less than 3 months duration had a better chance of survival than those with a longer anamnesis (χ^2 test). No statistically significant relationship was found between survival and clinical stage, previous transurethral resection, tolerance of therapy, and technique of irradiation.

The treatment failures are shown in Table 2. The 134 patients analysed comprised 91 patients who died of carcinoma, 5 who survived for more than 5 years with carcinoma, 5 who died of some other disease without evidence of malignancy, 32 in whom the cause of death remained unknown; one patient was lost to follow-up, and was assumed in the analysis to be dead.

The most common cause of therapeutic failure was pelvic recurrence. A subsequent cystectomy was not attempted in any case.

Discussion

The results of megavoltage therapy of carcinoma of the bladder observed in this series are in agreement with those reported by other authors (EDS-



Small-volume high-dose telecobalt irradiation of bladder carcinoma. Isodose distribution using three-field technique.

MYR, EDSMYR et coll. 1978, REDDY et coll. 1978, BACKHOUSE, KAGAN et coll. 1981, SHEHATA et coll.). GOFFINET et coll. and GOSPODAROWICZ et coll. reported some survival benefit in patients with stage B, who had received irradiation of a large volume including the pelvic nodes. However, irradiation of an extended volume does not seem to influence the results essentially. In order to investigate this, irradiation of extended fields was begun in 1979, delivering to the primary tumour region 70 Gy and to the regional lymph nodes 50 Gy using conventional fractionation.

Not surprisingly, the survival rates obtained at this Institute were similar to those presented by POINTON & EVANS, who described the results of a clinical trial with comparison of small-volume high-dose orthovoltage and megavoltage irradiation of bladder carcinoma. Megavoltage irradiation gave, according to these authors, a 19.4 per cent 5-year survival rate in stage 2 and, paradoxically, 27.2 per cent in stage 3, in comparison with a 26.9 per cent symptom-free 5-year survival rate in stage B and 20.3 per cent in stage C in the present series. POINTON & EVANS used a staging system almost identical with that used in this department. They found, as was also found in the present series, that this staging system poorly discriminates between groups of patients with different chances of survival. This observation has also been made by those who have used the original or modified Jewett-Strong or TNM classifications (KAGAN et coll.). The present authors propose that for the evaluation of radiation therapy a new clinical staging system should be worked out,

Table 1

Five-year survival without evidence of disease in 176 patients with bladder carcinoma

Clinical features	No. of cases	5-year survival without evidence of malignancy	
		No.	Per cent
Stage of disease			
A	2	2	100.0
B	89	24	26.9
C	64	13	20.3
D	21	3	14.3
Histopathology			
Transitional cell carcinoma	131	36	27.4
Anaplastic carcinoma	12	1	8.3
Squamous cell carcinoma	3	0	0
Carcinoma, histologically not specified	30	5	16.7
Duration of symptoms			
Less than 3 months	13	7	53.8
3-6 months	41	9	21.9
7-12 months	54	10	18.5
Over 12 months	68	16	23.5
Previous operative procedures			
Transurethral resection	87	25	28.7
None	89	17	19.1
Tolerance of therapy			
Irradiation completed as planned	161	40	24.8
Irradiation completed at intervals	8	1	12.5
Irradiation not completed	7	1	14.3
Technique of irradiation			
Three-field technique	146	36	24.7
Four-field technique	30	6	20.0
Total	176	42	23.9

Table 2

Causes of treatment failure in 134 patients

Cause of failure	No. of cases	Per cent
Pelvic recurrence	78	58.2
Pelvic recurrence and distant metastases	7	5.2
Distant metastases only	11	8.2
Other causes	5	3.7
Cause of death unknown	32	23.9
Patient lost to follow-up	1	0.8
Total	134	100.0

taking into consideration not only the degree of invasion but also the size of the tumour. In radiation biology, the importance of tumour size for the prediction of radiation response is evident. A clinical analysis by BATATA et coll. (1981) showed less favourable 5-year survival rates for patients with tumours larger than 4 cm (26%) than for those with smaller lesions (48%).

The results of external beam radiation therapy in invasive bladder carcinoma are unsatisfactory. Pelvic recurrence is the main reason for failure. Therefore, preoperative irradiation followed by total cystectomy has been proposed (MILLER 1977, WASSIF & VAN DER WERF-MESSING, CUMMINGS et coll., WHITMORE & BATATA 1979). Recent clinical trials have shown, however, that only male patients under 65 years of age who are fit enough for radical surgery can benefit from this intensive form of combined therapy (BLOOM et coll. 1982). Patients for whom combined therapy is not feasible should have the benefit of optimal radiation therapy and, if possible, a subsequent cystectomy in case of recurrence. Better results of radiation therapy might be obtained by improvement of the therapeutic ratio. Plans at this Institute include neutron therapy for moderately advanced cases, and short-course irradiation for late cases (SKOŁYSZEWSKI et coll. 1982, SKOŁYSZEWSKI & REINFUSS 1982).

SUMMARY

The results of high-dose small-volume ⁶⁰Co teletherapy in a series of 176 patients with carcinoma of the urinary bladder are reported. Five-year survival rates without evidence of disease were 26.9 per cent in stage B, 20.3 per cent in stage C, and 14.3 per cent in stage D. The most common cause of treatment failure was pelvic recurrence, which was observed alone in 58.2 per cent and together with distant metastases in 5.2 per cent of the patients.

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