

# ACTA RADIOLOGICA

OFFICIAL ORGAN OF THE RADIOLOGICAL SOCIETIES OF  
DENMARK, FINLAND, NORWAY AND SWEDEN

Vol. 11  
Fasc. 5

THERAPY PHYSICS BIOLOGY

1972  
October

## INTRACAVITARY RADIUM TREATMENT OF MALIGNANT TUMOURS OF THE URINARY BLADDER

by

M. PEDERSEN and S. E. HERTING

The literature has from the beginning of this century contained publications dealing with the intraluminal treatment of malignant diseases of the urinary bladder with radioactive isotopes, a form of therapy that has been considerably increased by their production in atom piles. The isotopes used have been in the form of interstitially implantated radioactive media, tantalum wires (WALLACE et coll. 1952, BLOOM 1960), radon seeds (POOLE-WILSON 1950), gold grains (HODT et coll. 1952) and radium needle implantations (VAN DER WERF-MESSING 1965, 1969), as well as by the intravesical instillation of radioactive solutions, with or without a container, of Na- and Ba-isotopes (WALTON & SINCLAIR 1952) and Au- and Co-isotopes (ELLIS & OLIVER 1955, MÜLLER 1949, MEILEN 1962). Radium and cobalt sources in a balloon have also been placed centrally in the bladder (FRIEDMAN & LEWIS 1949, 1958, SELL & JØRGSHOLM 1962, SELL 1967).

The treatment results of most of these different treatment techniques have been difficult to evaluate and compare, partly because of the absence of common rules of tumour classification and partly because of the selection of patients,

From the Radium Centre and the Institute of Pathology, Odense Sygehus, Denmark.  
Submitted for publication 27 september 1971.

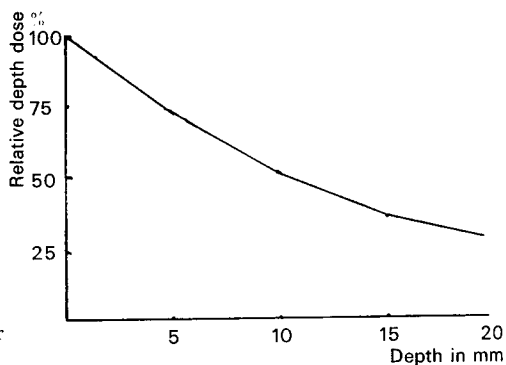


Fig. 1. Percentage depth dose in the bladder wall from a central radium source.

which presumably has often been a radical one although this is difficult to estimate from the figures. During the last years these methods of treatment, especially after the introduction of high voltage therapy in the treatment of carcinoma of the bladder have been on the decline.

The principles, the practical performance, the advantages and disadvantages, complications and fields of indication have been presented in detail by WALLACE 1959. SELL & JØRGSHOLM in a preliminary publication, described the principles in the treatment of growths of the bladder with intracavitary radium by a modified Walter-Reed technique. The results of this treatment in 50 cases of benign and malignant tumours (SELL) failed to reach those obtained by FRIEDMAN & LEWIS (1948, 1958) who in a similar number of cases in all stages from A to D<sub>2</sub> (MARSHAL'S classification 1956), obtained a 5-year crude survival rate of 56 per cent; this appeared to be a high goal to reach in this condition.

The present investigation was undertaken to deal with the results and complications in the treatment of 165 cases of malignancy and to throw further light on the usefulness of the method. Forty of these cases were part of the material published by SELL. The tumours have been reclassified, following the recommendations of the UICC, by the TNM system. They have also been graded according to the principles laid down by BERGQUIST et coll. (1965) with a grading of malignancy from 0 to IV.

*Method.* This was described in detail by FRIEDMAN & LEWIS (1958) and SELL & JØRGSHOLM. The principle consists in irradiating the bladder from the inside by means of a radium source placed centrally in the balloon of a Foley catheter 24 — 26. The balloon is distended to a volume of 40 ml and produces a relatively stable means of placing the radium source in the center of the bladder at a distance of about 4 cm from the wall; this is of course provided the lumen

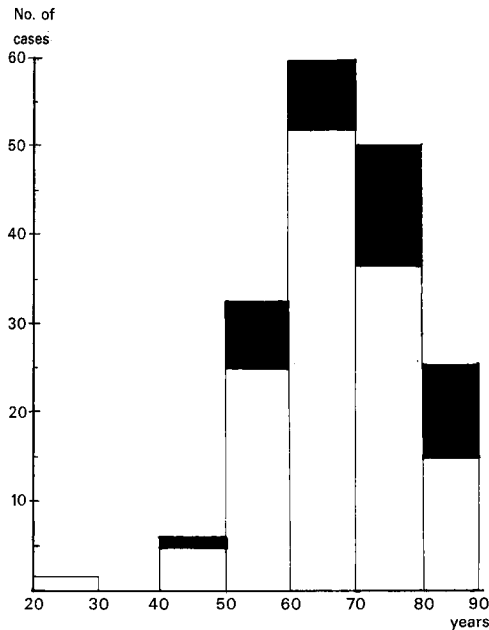


Fig. 2. Age distribution at the time of treatment. Men: white column. Women: black column.

of the bladder is not filled with any mass that displaces the balloon with the radium source. The essential part of the original Walter-Reed technique consisted in siting the catheter through a cystotomy. Large tumour processes could thus be removed and symmetric and central location of the radium source with homogeneous irradiation of the mucosa secured; furthermore, by reducing the masses, underdosage of the deepest layers of the tumour could be avoided. Only in a few of the present cases was the catheter introduced through a cystotomy; it was usually passed up the urethra and its final position controlled by cystography after the instillation of a few ml of contrast medium.

The dose to the balloon surface and the mucosa for 120 hours is approximately 3 500 rad for a 20 mg source. The treatment was usually administered in two sessions of 120 hours each with an interval of 14 days to give a total dose to the mucosa of 7 000 rad/25 days. Because of the rapidly decreasing depth dose (Fig. 1) the total dose to tumour cells lying 10 to 12 mm under the mucosa will be only 3 500 rad and at a depth of 20 mm about 1 700 to 1 800 rad/25 days.

The intention of the treatment was merely palliative in some of the cases. These were treated at one session with a total dose of 3 500 rad/5 days. The source was occasionally placed eccentrically in the balloon, e.g. in growths at base of the bladder with possible invasion of the prostate.

**Table 1***Distribution of growths and histologic type*

	Transitional-cellular	Planocellular	Other histology
Men	120	9 (6.5 %)	2
Women	25	9 (26 %)	0
Ratio: Men/Women	4.8/1	1/1	

*Material.* Most of the cases were admitted from surgical departments in the district for radiation therapy but some 5 per cent were resident outside this area and were admitted specifically for treatment in a period when highvoltage therapy for carcinoma of the bladder had not become general. The cases were selected primarily from those in which (1) surgical treatment was unsuitable, especially those with large tumours in which the alternative would be cystectomy or extensive electrocoagulation, (2) in biologically inoperable cases in which the risk of operation was considered too great, and (3) in cases in which the treatment was clearly palliative, especially in those with large bleeding tumours. Only in a few cases was the treatment part of a prescheduled treatment plan. The treatment was given to only 12 cases with no residual malignancy, the remainder not having undergone radical operation or no operation at all. An obvious selection of cases in the direction of a bad-risk material thus occurred with a large proportion of widespread and multiple tumours and a heavy load of patients in poor general condition.

A total of 181 cases were treated in the period 1958 to 1965. Eight have been omitted from the investigation because of the absence of histologic confirmation and a wrong diagnosis; 8 cases had no malignancy of the bladder and were omitted as well. Malignancy was present in 165 cases 131 of which were men and 34 women, a ratio of 3.8/1. Sixty-nine patients were over 70 (42 per cent) and 120 patients were over 60 (72 per cent); the average age for men was 67.8 and for women 63.5 years (Fig. 2).

The distribution of growths by histologic type (Table 1) indicates a surprisingly high incidence of the planocellular variety. These were mostly of low differentiation and carried a bad prognosis, because of which they have in the following tables and figures been separated from those of the pure transitional cell type.

Only one case of adenocarcinoma and one of leiomyosarcoma were registered.

All the histologic slides have been revised by one of the authors (S.E.H.) for grading of malignancy by the principle laid down by BERGQUIST et coll. (1965). The distribution of planocellular carcinomas and transitional cell

**Table 2***Distribution of tumours of different histology and grading in tumour categories T i. s. to T 4*

TNM category	Transitional cell tumours			Tumours of other histology		
	II	III	IV	Plano.	Adenoc.	Sarcoma
T in situ	21	5	0	0	0	0
T 1	10	36	5	3	0	0
T 2	3	19	2	4	0	0
T 3	2	13	13	7	1	0
T 4	1	7	8	4	0	1
Total	37	80	28	18	1	1

carcinomas grade II to IV in the clinical tumour categories T i. s. to T 4 appears from Table 2, while Table 3 presents the percentage of grades II to IV in each tumour category. As expected, tumours of grade II dominate categories T i. s. and T 1, while this grade of differentiation seldom appears in tumours of deeper infiltration. In one instance, however, a grade II tumour was in category T 4, in 2 cases in category T 3 and in 3 cases in category T 2.

Tumour classification was carried out according to the principles laid down by the UICC by means of the TNM system based on cystoscopy, biopsy and bimanual palpation under general anaesthesia. Evaluation of the N-factor has not been possible and lymphography not performed. Only in the palliative treatment group have distant metastases been demonstrated, and then only in 10 cases.

All the cases were confirmed histologically by biopsy. P-staging from histologic slides obtained at operation was possible in 82 cases. Ninety-four cases were operated upon but in 12 of these no material for histologic examination was available. Where the clinical evaluation of tumour category has been uncertain the case has been placed in the lowest of the two possible categories, risking rather an understatement than overstatement of tumour category and thereby a displacement of treatment results in a favourable direction.

The treatment must be characterised as palliative in 8 cases classified as category T 3 and in all cases of category T 4. Ten of these had distant metastases at the beginning of treatment, and in nearly all palliative cases the doses were reduced to half the usual. These 29 cases appear in some tables as a palliative treatment group.

The cases may in principle be divided into two large groups. One group, consisting of 71 cases, were not subjected to any surgical treatment before radium

**Table 3***Percentage of tumours of grades II to IV in tumour categories T i. s. to T 4 in 145 transitional cell carcinomas*

TNM category	Transitional cell tumours (%)			Total number
	II	III	IV	
T in situ	81	19	0	26
T 1	20	70	10	51
T 2	12	80	8	24
T 3	8	46	46	28
T 4	6	44	50	16

**Table 4***Distribution by primary conditions and recurrences*

Primary cases 125 } Curative Treatment } 165	} 136	No surgery	50 pat.
		Surgery + Radium: { radical op.      12 pat. conservative op. 74 pat.	
Palliative Treatment } 40	} 29		No surgery
		Surgery + Radium: { radical op.      0 pat. conservative op. 8 pat.	

therapy apart from biopsy; the other group of 94 cases had some surgical treatment before the radium therapy, the treatment being radical in only 12 patients. Eleven cases had resection of the bladder, 3 of these resections being radical; in 9 cases the treatment was performed transurethrally as electrocoagulations and electroresections, in no instance radical. Operation in the remaining 74 cases was performed transvesically with cystotomy as electrocoagulations, resections and extirpations, in only 9 cases radical.

Radium treatment following operation was administered two to three weeks later except in a few cases when the first treatment was received in immediate connection with the operation.

The distribution of 165 cases by primary conditions and recurrences, curative and palliative treatment and surgery and no surgery grouping appears in Table 4.

### Results

All the cases have been followed for at least 5 years. A total of 144 of the initial 165 cases have been controlled without loss for 7 years. The data were obtained on a fixed date, 31 December 1970, and at annual controls where

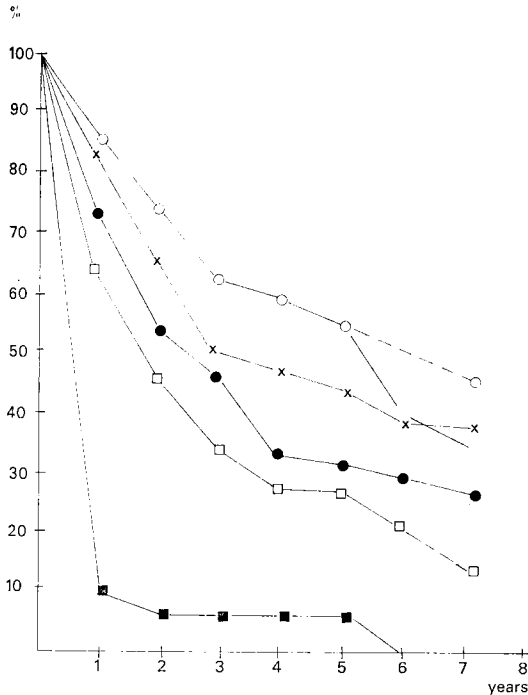


Fig. 3. Crude survival rates in 165 cases of carcinoma of the bladder of all histologic types and grades. Last part of curve for T i. s. has been computed because a rapid fall in observations between 5 and 7 years deforms the curve. (Correction: stippled line.) ○ T i. s., × T 1, ● T 2, □ T 3, ■ T 4.

cystoscopy and exploration were performed under general anaesthesia. Only for the patients of tumour category T i. s. has it been necessary to compute the 7-year survival rate, as a large drop in observations between the fifth and seventh year distorts the survival curve (Fig. 3). The survival rates enumerated in tables and figures are crude survival rates (CSR). Five of the 53 patients surviving five years without recurrence had been subjected to surgical treatment in the period between the radium treatment and 5-year observation, the CSR in reality being 5-year recurrence-free.

Twenty-one patients died without recurrence before the end of the 5-year observation. Cystoscopy at the most three months before death had failed to demonstrate any sign of residue or recurrence. The tables and figures have not been corrected for this rather large proportion of deaths without recurrence, a correction that might seem reasonable in a population of such high average age.

The CSR for cases in tumour categories T i. s. to T 4 appear in Fig. 3. For categories T i. s. and T 1 the initial steep decline in the survival curve ends at the third year and for categories T 2 and T 3 at the fourth year. Ninety

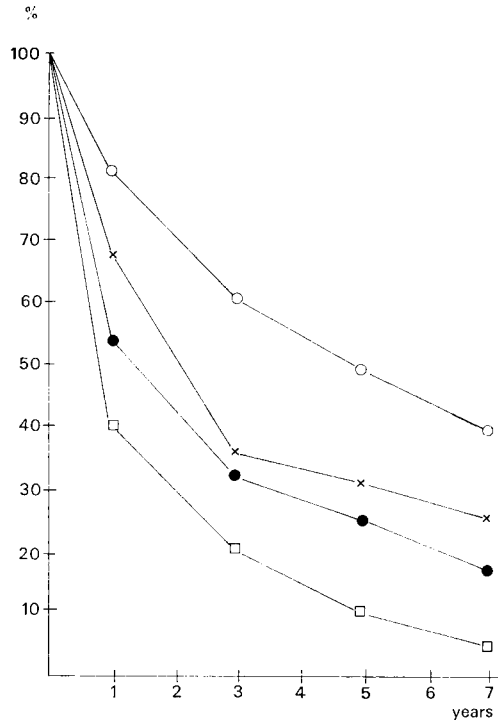


Fig. 4. Crude survival rates in 163 cases of transitional cell and planocellular carcinomas of the bladder according to histology and grade. One adenocarcinoma and a leiomyosarcoma are excluded. ○ grade II, × grade III, ● grade IV, □ planocellular.

per cent of the 29 patients in category T 4 were dead at the end of the first year; only one patient in this category survived 5 years.

By way of comparison Fig. 4 gives the CSR for cases with tumours of different grades of differentiation, transitional cell carcinomas, and planocellular carcinomas. An adenocarcinoma and a leiomyosarcoma of category T 3 and T 2 are not included, both the patients being dead at the end of the first year. The considerably better prognosis in grade II tumours is evident. Fifty-six per cent of these tumours belonged to tumour category T i. s. When all the cases are placed under one heading there appears to be little significant difference in the CSR for those with growths of grade III and IV, in spite of the fact that 75 per cent of grade IV tumours were in categories T 3 and T 4, the corresponding figure for grade III growths being only 25 per cent. When palliative cases are excluded, i.e. all cases of T 4 and 8 of those in T 3, the situation is reversed, the grade IV tumours now having a slightly better 5-year CSR than those of grade III (Fig. 5).

The difference in the CSR between grade III and the low-differentiated grade IV tumours is not significant; the slightly better prognosis for the latter in those

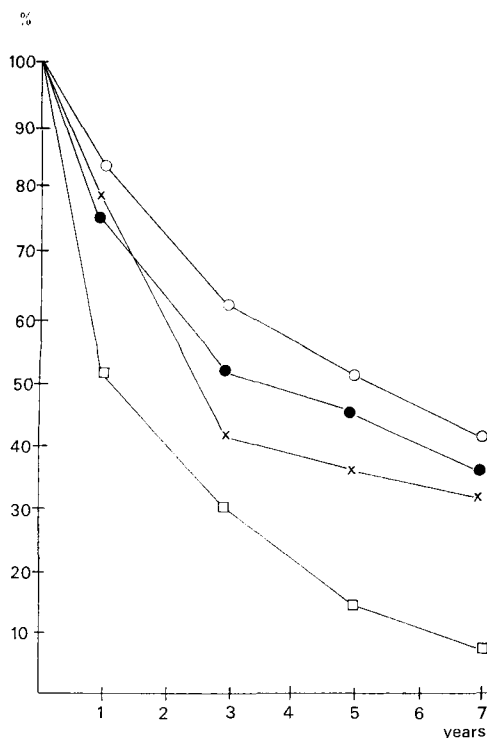


Fig. 5. The same as fig. 4 but palliative transitional cell and planocellular carcinomas have been excluded. ○ grade II, × grade III, ● grade IV, □ planocellular.

cases that were subjected to curative treatment and in which adequate tumour doses could be obtained, might indicate a higher radiation sensitivity.

The poor prognosis in planocellular carcinomas is noteworthy. Only 2 of 18 patients survived for five years, one dying without recurrence after six years, the other from distant metastases but without vesical recurrences seven years after the radium treatment.

The distribution of cases into primary cases and recurrences was 125/40. The representation of palliative cases in these two groups was 25 per cent in each, the rate of planocellular carcinomas being the same and the distribution of cases in tumour categories and grades identical. Nevertheless there was considerable difference in the CSR in the groups. The 5-year CSR for 104 primary cases treated with a curative intention was 42 per cent, while the corresponding figure in recurrences was 28 per cent; this last group consisted however only of 32 cases and the difference in CSR is not statistically significant.

The treatment results in cases of transitional cell and planocellular carcinomas treated with radium alone and with a combination of surgery and radium are

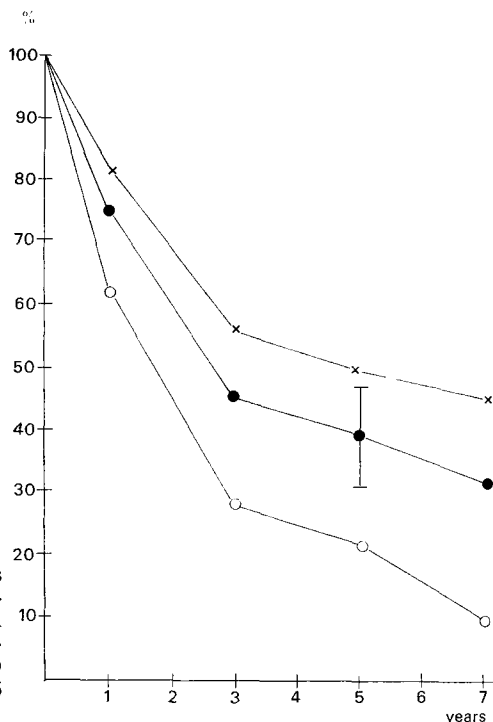


Fig. 6. Crude survival rates in 136 cases of transitional cell and planocellular carcinomas of the bladder treated with radium alone and with surgery and radium. Palliative cases have been excluded;  $2 \times SD$  has been marked.  $\times$  surgery + radium (86 cases),  $\circ$  radium alone (50 cases).

presented (Fig. 6). Palliative cases have been excluded. A total of 136 cases was treated, 50 with radium alone and 86 with radium and surgery, the first group including 8 planocellular neoplasms, the last 7 tumours of this histology. The distribution of tumour categories was, however, to the prejudice of the non-operated group, this carrying a heavy load of T 3 tumours of 15/50, i.e. 30 per cent while only 12/86 of the operated group belonged to this category, i.e. 14 per cent. Bearing this difference in selection in mind the 5-year CSR in the operated group is significantly better. Radically and unradically operated cases were not distinguished since their prognosis did not differ (Fig. 6).

The total 5-year CSR in cases with transitional cell tumours treated with radium alone was 16 per cent. When the intention of the treatment was cure the figure rose to 24 per cent. A 5-year CSR of 51 per cent was reached when the radium treatment was preceded by surgery. The results with this combined treatment are nearly identical in tumour categories T i. s., T 1 and T 2, and not much worse in T 3 (Table 5). The number of solitary tumours in the operated group was substantially higher and, as earlier mentioned, this group included fewer cases of T 3.

**Table 5**

*Five-year crude survival rates in 145 transitional cell carcinomas of the bladder, curative and palliative cases, according to treatment group. The fractions under the headings T i. s. to T 4 indicate the 5-year survivors/the number of cases treated*

	Number	Curative treatment				5-year CSR, curative	Palliative treatment		5-year CSR, total
		T i. s.	T 1	T 2	T 3		T 3	T 4	
		26	51	24	20		8	21	
No surgery	61	5/10	4/16	0/5	1/11	10/42 (24 %)	0/7	0/12	10/61 (16 %)
Surgery with residue	73	7/14	15/27	9/18	4/9	35/68 (51 %)	0/1	1/4	36/73 (49 %)
Surgery without residue	11	1/2	4/8	0/1	0	5/11 (45 %)	0	0	5/11 (45 %)

The grave outlook for patients in the palliative group is illustrated by the fact that 50 per cent of these were dead 3 months after treatment and 90 per cent after one year.

As in other published results of treatment of carcinoma of the bladder this material has indicated a better prognosis for papillomatous than for solid tumours of the transitional cell type, and the 5-year CSR for solitary tumours clearly separates them from multiple tumours (Table 6). A significant difference within 95 per cent confidence limits between solitary and multiple papillomatous tumours (61 and 33 per cent 5-year CSR, respectively) and between papillomatous and solid tumours (43 and 18 per cent 5-year CSR, respectively) was recorded in the whole material. Out of 145 transitional cell tumours, 42 were of the solid type and of these 42 only 3 growths were of grade II differentiation.

Ninety-one patients had recurrence locally in the bladder or distant metastases within the first 5 years after radium treatment. With the exception of 5 patients these were all dead before 5 years had elapsed after treatment, 50 per cent having died after 2 years and 75 per cent after 3 years. Surprisingly the time of recurrence and death seem independent of category in T i. s. to T 3 tumours, while 90 per cent of patients with T 4 tumours were dead after about a year.

Nine cases with recurrence had cystectomy between 1 and 3 years after treatment by radium. This was followed in one case by fatal complications, but by none in the others. None of these patients lived more than 2 years after operation.

The immediate mortality following treatment by radium is hard to evaluate. Only 2 patients died during the treatment, these from pneumonia and heart

**Table 6**

*Five-year crude survival rates according to type and multiplicity of transitional cell tumours. Fractions indicate number of 5-year survivors/total number of group. Planocellular tumours and tumours of other histology are not included*

	Solitary	Multiple	5-year CSR
Papillary	22/36 (61 %)	21/64 (33 %)	43/100 (43 %)
Solid	7/29 (24 %)	1/16 (6 %)	8/45 (18 %)
5-year CSR	29/65 (44 %)	22/80 (27 %)	

failure; 11 patients died within a month of treatment and within two months a total of 22 patients was dead, half of these belonging to the palliative treatment group.

*Complications.* The evaluation of complications in intracavitary radium treatment has been made difficult by the fact that in 94 cases a mixture of post-operative and postactinic sequelae arose. Infection of the bladder has often been present before the treatment, a fact that presumably plays a certain role, especially in the development of immediate reactions, and possibly in late sequelae as well; these latter may of course mask a recurrence.

Immediate complications have consisted of more or less marked symptoms of cystitis with dysuria and spasm. These have usually been relieved by suitable analgesics, often of the morphine type and psychosedatives such as largactil. Some infection of the urinary tract has usually occurred and has been treated with antibiotics. Only rarely have the immediate complications been so marked as to warrant discontinuation of the treatment. This material has not produced evidence of any connection between the severity of immediate complications and the length of interval between surgery, especially electrocoagulation, and the treatment by radium. Neither have any differences in immediate reactions been noticed between cases treated with radium alone and those undergoing surgery followed by radium. On the other hand the immediate as well as late complications have been most marked where radium has been used in the treatment of recurrences, especially in cases earlier subjected to multiple electrocoagulations.

Late sequelae were registered in 39 cases although they appeared in 12 of these in close relation to recurrences one to three years after the radium. The

**Table 7***Late sequelae in 165 patients treated with intracavitary radium for malignancy*

Complications	No. of cases	Treatment
Severe cystitis	8	Prednisone (8)
Severe cystitis and constricted bladder	14	Cystectomy (8) Ileum and bladder (1) Prednisone (5)
Severe cystitis and necrosis	8	Cystectomy (1) Resection (1) Prednisone (6)
Calculus	5	Lithotripsy (3) Prednisone (2)
Urethral stricture	6	Bougie treatment (5) No treatment (1)
Total number	41 cases /39 patients (25 %)	
Without recurrence	29 cases/27 patients (16 %)	

dominating complication was severe radiation cystitis with severe inflammatory changes, bleeding in the mucosa and layers of fibrinous incrustations, in more marked cases with necrosis, usually at the site of the primary tumour, even ending in fibrosis of the bladder wall and with a decrease in vesical volumes of 50 to 100 ml.

Severe radiation cystitis occurred in 30 cases (Table 7). This in 14 cases produced a constricted bladder and in 8 cases necrosis. Prednisone or trypanol solutions and antibiotics always formed the primary treatment. Cystectomy had to be done in 8 cases with a constricted bladder but was never fatal; it was planned in a further case but was not performed because of a large inoperable recurrence. Treatment with prednisone rendered 5 cases relatively symptom free. Necrosis was an indication for cystectomy in one case; in another resection of the bladder was done and 6 cases presented no indications for operative treatment. Of 9 patients in whom cystectomy was performed because of complications 6 survived for five years without recurrence, 2 died without recurrence and 1 patient died 2 1/2 years after cystectomy from distant metastases from a grade II tumour category T i. s.

The total number of complications amounted to 41 in 39 cases out of 165 treated (or 25 per cent) (Table 7). Twelve cases had symptoms of cystitis in close relationship to recurrence and it seems reasonable to subtract these so as to leave a rate of complications of 27/165 (16 per cent). Approximately half

these cases were subjected to surgical treatment. Operative treatment of complications in no instance led to a fatal outcome.

No renal complications have been recorded in this material.

### Discussion

The results presented seem substantially inferior to those obtained by FRIEDMAN & LEWIS (1958). The 5-year CSR for all cases of transitional cell carcinoma is 51/145 (35 per cent). This figure does not include the planocellular carcinomas whose prognosis is extremely poor with a 5-year CSR of 2/18 (11 per cent), a survival rate that corresponds with that obtained with other treatment procedures, including cystectomy.

In considering a group that may reasonably be compared to the one of FRIEDMAN & LEWIS, the cases treated by combined surgery and intracavitary radium, may be selected. Of 84 patients with transitional cell carcinoma treated with a combination of surgery and radiation therapy, 41 or nearly 50 per cent, lived for 5 years without recurrence. These were nearly evenly distributed in the tumour categories T i. s. to T 2 (Table 5). It seems fair to assume that the improvement in possibilities for a central, symmetric placing of the radium catheter and the reduction in tumour masses obtained by operation has played an essential role in securing more homogeneous irradiation of the bladder wall and higher doses to peripheral parts of the tumour.

Treatment with intracavitary radium without preceding surgery has had little success. Of 61 cases with transitional cell carcinomas so treated only 10 lived for 5 years, i.e. 16 per cent. The selection of cases for this treatment was heavy, nearly 50 per cent of the growths being of category T 3 and T 4 in contrast to a corresponding figure of 16 per cent for the operated group. But even if these advanced tumours of category T 3 and T 4 be ignored it is obvious that only in category T i. s. have the results obtained by radium treatment alone been equal to those secured by combined treatment, with a 5-year CSR of 50 per cent. The results have been considerably inferior in the categories T 1, T 2 and T 3. The distribution of tumours of grades II, III and IV has been equal, but in the non-operated group an overweight of multiple tumours was evident. It seems reasonable to assume that the results would have been better in this group if the original Walter-Reed technique with application of the radium catheter through a cystotomy had been used, or, at any rate, certain tumour ablation surgery had been performed before the introduction of the catheter.

The importance of grade of cell differentiation in assessing treatment results and procedures is hard to evaluate from this material. The prognosis in grade II tumours is significantly better than in grade III and IV tumours. This is in good agreement with the fact that grade II tumours in only 44 per cent of cases

were invasive, while the corresponding figures in grades III and IV were 94 and 100 per cent, respectively. This investigation has demonstrated no significant difference in the treatment results between grade III and grade IV tumours, but the relatively small figures prevent any realistic evaluation. It must be stressed however, that in spite of the fact that 75 per cent of grade IV tumours were in categories T 3 and T 4, while only 25 per cent of grade III tumours were in these categories, the 5-year CSR for these grades did not differ significantly.

The classification of tumours by the TNM system seems to work well. A close relationship between the 5-year CSR and T-category was evident. Grading of the tumours by their differentiation is of the greatest help in distinguishing between grade II tumours and those of grades III + IV, and of lesser significance in distinguishing grade III and grade IV tumours, at any rate when the treatment consists of a combination of surgery and radiation therapy. The authors suggest that the most accurate representation of a vesical tumour would be obtained by a combination of TNM staging, a cytologic grading by the BERGQUIST method and a classification of the growths into papillomatous and solid, differentiated and undifferentiated tumours according to the IOU system.

### Conclusion

Intracavitary treatment by radium may be eliminated as a reasonable choice among a multitude of irradiation procedures when the tumor is of category T 3 or T 4. These growths are usually of such magnitude and extend extravescially that the rapid fall in the percentage depth dose will produce a low tumour dose in peripheral tumour areas with a considerable risk of underdosage. Furthermore these advanced tumours are often associated with metastases to regional glands on the pelvic wall, glands that will be markedly underdosed. Only in palliative cases can intracavitary treatment be considered.

Leaving out of account the complications and considering the treatment results alone, intracavitary radium treatment seems very suitable for the treatment of tumours of category T i. s. with or without preceding surgery. The results in category T 1 are best when the treatment is combined with surgery, transvesical and transurethral, and the same seems to obtain in tumours with superficial muscular invasion, category T 2, and even in cases of deep muscular invasion, category T 3, but without large extravescial masses. The 5-year CSR for these three tumour stages in the present material has been 55, 45 and 40 per cent, respectively, when the treatment has been a combination of radical or conservative surgery and radium.

The treatment results are, as in all forms of treatment of vesical malignancy, best when the tumour is solitary and especially when it is papillomatous. The

limitation of the irradiation methods based on implantation techniques, tantalum wire implantation and radium needle implantation, is the magnitude of the masses, most authors considering a diameter of 4 to 5 cm as the maximum safety margin. Many of the so-called solitary tumours of the present series have had a diameter exceeding this, suggesting that intracavitary radium treatment may be a reasonable alternative to implantation. High voltage, external treatment would here most often be the method of choice, easily obtainable as it is in most centres nowadays. Complications must however be considered. These are rather heavy in intracavitary treatment, but the question arises as to whether these are not acceptable if a higher cure rate be obtainable. External high voltage therapy of vesical tumours is not without sequelae although these seem fewer (EDSMYR et coll. 1967) and of another type, especially when arising from the intestinal tract. The good results obtained in carcinoma of the uterine cervix with combined radium and external high voltage therapy suggest that a similar combination might be a possibility worthwhile investigating in carcinoma of the bladder, as an alternative to primary cystectomy. The consequence of such a treatment would doubtless be a number of secondary cystectomies because of complications, although this might not be an unreasonable price to pay if the result were higher cure rates for this very malignant condition.

The results presented were obtained in cases which because of the selection, must be characterized as bad risks and are likely the minimum obtainable with this treatment procedure. No doubt better results would be obtained in a fair clinical trial and it seems reasonable to believe that the frequency of complications could be substantially diminished if the radium therapy were combined with careful, conservative surgery and antibiotic treatment before, during and after radium therapy.

#### SUMMARY

The results and complications in the treatment of 165 cases of malignant disease of the bladder by radium alone and combined with surgery have been investigated. The importance of the tumour grading and the selection of the patient are considered. The advantages of the use of intracavitary radium as opposed to high voltage therapy is discussed. The five-year survival rate rose to about 50 per cent with radium treatment preceded by surgery.

#### ZUSAMMENFASSUNG

Die Ergebnisse und Komplikationen der Behandlung von 165 Fällen einer malignen Erkrankung der Blase durch Radium alleine oder in Kombination mit Chirurgie wurden untersucht. Die Bedeutung der Grad-Einteilung der Tumoren und der Selektion der Patienten wird hervorgehoben. Die Vorteile der Verwendung der intrakavitären Radiumbehandlung gegenüber der Hochvolttherapie wird besprochen. Die 5-Jahres-Überlebensrate stieg mit der Radiumbehandlung nach vorhergehender chirurgischer Behandlung auf etwa 50 Prozent.

## RÉSUMÉ

Les auteurs ont étudié les résultats et les complications dans le traitement de 165 cas d'affection maligne de la vessie par le radium seul et associé à la chirurgie. Ils examinent l'importance de la détermination du grade de la tumeur et de la sélection des malades. Ils étudient les avantages de l'emploi du radium intracavitaire comparé au traitement par les haut-voltage. Le taux de survie à 5 ans s'est élevé à environ 50 % des cas traités par le radium après traitement chirurgical.

## REFERENCES

- BERGQUIST A., LJUNGQUIST A. and MOBERGER G.: Classification of bladder tumours based on the cellular pattern. *Acta chir. scand.* 130 (1965), 371.
- BLOOM H. J. J.: Treatment of carcinoma of the bladder. *Brit. J. Radiol.* 33 (1960), 392.
- EDSMYR F., JACOBSSON F., DAHL O. and WALSTAM R.: Cobalt-60 teletherapy of carcinoma of the bladder. *Acta radiol. Ther. Phys. Biol.* 6 (1967), 81.
- ELLIS F. and OLIVER R.: Treatment of papilloma of bladder with radioactive colloidal gold Au-198. *Brit. med. J.* 1 (1955), 136.
- FRIEDMAN M. and LEWIS L. G.: A new technique for the radium treatment of carcinoma of the bladder. *Radiology* 53 (1949), 342.
- — Irradiation of carcinoma of the bladder by a central intracavitary radium and cobalt 60 source (the Walter Reed technique). *Amer. J. Roentgenol.* 79 (1958), 6.
- HODT H. J., SINCLAIR W. K. and SMITHERS D. N.: A gun for interstitial implantation of radioactive gold grains. *Brit. J. Radiol.* 25 (1952), 419.
- MARSHAL V. F.: Bladder tumours. A symposium. Lippincott, Philadelphia 1956.
- MEILEN P. P.: Die intravesicale Radiokobalt-Behandlung beim Harnblasenkarzinom. *Dtsch. med. Wschr.* 87 (1962), 1496.
- MÜLLER J. H.: Über die multiplen Anwendungsmöglichkeiten eines langlebigen künstlichen radioaktiven Isotops (60-Co) in flüssiger Form für die Strahlentherapie maligner Tumoren. *Schweiz. med. Wschr.* 79 (1949), 547.
- POOLE-WILSON D. S.: The treatment of carcinoma of the bladder. *Brit. J. Urol.* 22 (1950), 414.
- SELL A.: Intracavitary radium therapy of bladder tumours. *Dan. med. Bull.* 14 (1967), 21.
- and JØRGSHOLM B.: Intracavitary radium therapy of bladder tumours. *Dan. med. Bull.* 9 (1962), 189.
- UICC: Classification of malignant tumours. Union International Contre le Cancer, Geneva 1968.
- WALLACE D. M.: Tumours of the bladder. Vol. 2, p. 257. Livingstone, London 1959.
- WALLACE R. J., STAPLETON J. E. and TURNER R. C.: Radioactive tantalum wire implantation as a method of treatment for early carcinoma of the bladder. *Brit. J. Radiol.* 25 (1952), 421.
- WALTON R. J. and SINCLAIR W. V.: Radioactive solutions (Na-24 and Ba-82) in the treatment of carcinoma of the bladder. *Brit. med. Bull.* 8 (1952), 158.
- VAN DER WERF-MESSING B.: Treatment of carcinoma of the bladder with radium. *Clin. Radiol.* 16 (1965), 16.
- Carcinoma of the bladder treated by suprapubic radium implants. *Europ. J. Cancer* 5 (1969), 277.