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# Carcinoma of the Bladder – Radiotherapy

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Summary. Differentiated transitional cell carcinoma responded better to radiotherapy than anaplastic or squamous cell carcinoma. Five year survival was higher in low stage than in high stage carcinoma, and higher in papillary than in solid carcinoma. Tumour control, but also complication rate, increased with higher radiation dose. With the introduction of a two volume irradiation technique, a large tumour dose can be given with a minimum of complications.

Key word: Urinary bladder cancer - Radiotherapy.

The results of treatment of 352 patients treated by radiotherapy only for carcinoma of the bladder are presented. The radiosensitivity of these tumours is discussed and the reasons for failure to control the disease and methods currently being tried to improve the results are considered.

## SURVIVAL RATES

The figures are taken from a previous publication (4). Table 1 shows the survival rates for a series of cases treated more than 5 years ago on an 8Mv Linear Accelerator. The results are analysed according to staging (5), histological type, and the type of tumour as seen cystoscopically. The best results were obtained in Stage T1-T2 cases; papillary tumours gave better results than solid or ulcerated tumours and the differentiated transitional cell tumours had a better survival rate than the anaplastic or squamous cell tumours: These results, which are better than previously obtained by radiotherapy, still leave considerable scope for improvement.

## THE RADIO-SENSITIVITY OF BLADDER TUMOURS

The relationship between radiation dose and tumour ablation has been examined based on the cystoscopic examination of patients up to 2 years after treatment at four different dose levels. Table 2 shows the response rate in the three histological types. Examining the largest group - the transitional cell tumours - (Table 3), it appears that the tumour control rate is highly dose dependent. Over the dose range from 4250-6250 rads the control rate increases from 38 % to 80 %. This is also shown graphically (Fig. 1).

With higher doses there is a risk of damage to normal tissues. This is difficult to express numerically as there are degrees of damage both acute and late. Table 4 considers only patients with serious late damage i. e. damage that develops months or years after treatment and is a risk to life or requires surgical treatment. This includes intestinal complications such as stricture, fistula formation and obstruction and bladder complications, such as a contracted bladder or telangiectasia with bleeding. When both control rates and complication rates are represented on one graph (Fig. 2), the difference between the curves can be regarded as the relative sensitivity of the tumour compared to the normal tissue or the therapeutic ratio.

There are several approaches which try to improve the therapeutic ratio.

### (a) The Radiation Volume

The effect of radiation on the tumour is concerned mainly with cell killing and is a function

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Table 1

ALL CASES – FIVE YEAR SURVIVAL RATES*

| | | $T_1$ $T_2$ | $T_3$ | $T_4$ | *All stages* |
|---|---|---|---|---|---|
| Transitional cell | Papillary | (74) 43·0% | (76) 30·8% | (26) 4·5% | (176) 32·0% |
| | Solid | (16) 30·0% | (42) 26·0% | (20) 6·0% | (78) 21·7% |
| | Ulcerated | — | (10) 10·0% | (6) 16·5% | (16) 12·4% |
| | All types | (90) 40·7% | (128) 27·6% | (52) 6·5% | (270) 28·0% |
| Anaplastic | Papillary<br>Solid<br>Ulcerated | All stages<br>(46) 22% | | | |
| Squamous | Papillary<br>Solid<br>Ulcerated | All stages<br>(36) 20% | | | |

* Calculated by the actuarial method.

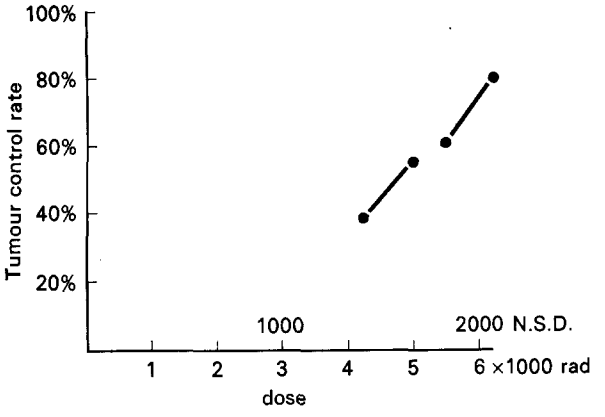


Fig. 1. Relationship between irradiation dose and tumour ablation

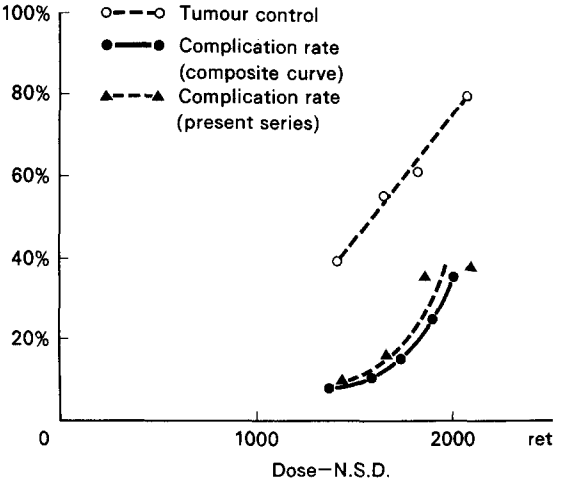


Fig. 2. Influence of irradiation dose on tumour control and complication rate

of the dose given but when we consider damage to normal tissues both the dose and the volume of tissue irradiated have to be taken into account. From the work of Cohen, and others (1), the normal tissue damage relationship is proportional to a value lying between the cube root and fifth root of the volume. If these findings are translated into practical therapy and assuming the cube root relationship, a reduction in the volume treated of 10% would permit an increase in the dose of 4% and if the volume were reduced by as much as 25% a 10% higher dose could be given. This would make an appreciable difference to the local disease control rate.

Damage to normal tissues can be minimised by reducing the dose or the volume treated. To lower the dose increases the risk of recurrence and it is generally thought preferable to reduce the total volume. This concept has led to the use of shrinking field techniques by which the size of the field is reduced as the therapy proceeds.

Our present practice is to give 5250 rads in 28 days to a wide volume which includes the primary tumour, the extra-vesical tissues and external iliac node areas and then to treat the bladder tumour volume only giving an additional 1000 to 1250 rads in 1 week (See Fig. 3). This technique has led to a very much reduced incidence of complications and in the past 5 years there have been only 3 cases showing serious complications. As this is about 1% of patients treated it may be possible to increase the tumour dose with advantage.

If tumour localisation and extent were more accurately determined the fields could be reduced still more. Precise localisation of bladder tumours is difficult but ultrasonic scanning to define extra-vesical spread and computerised axial tomography may be helpful.

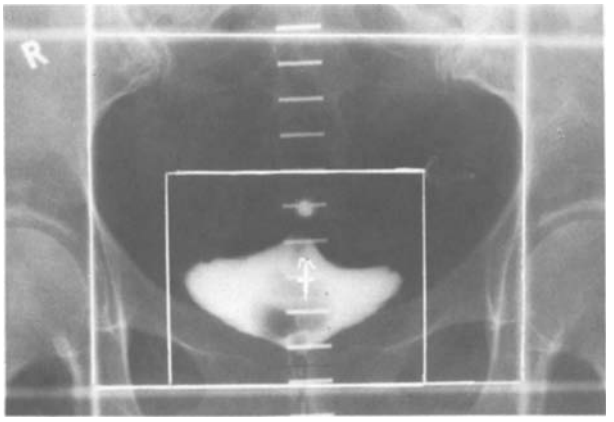

Fig. 3. Field arrangements in 2-volume technique

Table

TUMOUR RESPONSE TWO YEARS AFTER TREATMENT, $T_3$ TUMOURS

| | *No local disease* (%) |
|---|---|
| Transitional cell | 46 |
| Anaplastic | 54 |
| Squamous | 43 |

Table

TRANSITIONAL CELL TUMOURS, DOSE AND COMPLETE TUMOUR RESPONSE AT TWO YEARS

| | *All cases* | *Dose (rad)* | |
|---|---|---|---|
| | | 6250 | 5500 |
| $T_1$ $T_2$ | (90) 71% | (44) 80% | (46) 61% |
| $T_3$ | (85) 46% | 5000 (40) 55% | 4250 (45) 38% |

Table

ALL CASES – MAJOR COMPLICATION RATES

| | *Rate all cases* (%) | *High dose* (6250 rad) (%) | *Low dose* (5500 rad) (%) |
|---|---|---|---|
| $T_1$ $T_2$ | 36 | 37 | 35 |
| $T_3$ $T_4$ | 13 | (5000 rad) 16 | (4250 rad) 9·6 |

(b) Alternative Radiation Methods

Other methods which are being tried to improve the therapeutic ratio include super-fractionation, treatment under raised oxygen pressure and the use of high LET radiation, especially neutrons. The results of super-fractionation by Dr. Edsmyr's technique are most encouraging (2) but trials being carried out in the U.K. using hyperbaric oxygen in bladder cancer have not shown any advantage over the controls. Personal experience with neutron therapy is very limited because the energy of our neutron beam (7Mv) is not sufficiently penetrating and can give a satisfactory dose only to very thin patients.

Failure may also be due to spread of the disease to lymph nodes beyond the local site or to distant organs. It is known from lymphography studies that there is a high incidence of node involvement in the advanced stages. In T2 and T3 cases MacDonald (3), found incidences of 23% and 36% respectively. This raises the question as to whether the nodal areas should be included in the field in certain cases.

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