

Treatment of Bladder Cancer at the Rotterdam Radiotherapy Institute (R.R.T.I.)

With Special Reference to Bladder Radium Implantation and Preoperative Radiotherapy followed by Cystectomy

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Summary. Between 1950 and 1972, a total of 2031 cases of bladder cancer were treated in the R. R. T. I. The policy differed according to size and stage of the disease as well as to the general condition of the patient. Best results were achieved by radium implantation of solitary lesions less than 5 cms in diameter. Preoperative radiotherapy followed by cystectomy was the treatment of choice for cases of T₃ category. The remaining T₁ and T₂ cases were treated surgically, while T₄ cases were managed with external irradiation alone.

Key words: Bladder cancer - Radium implants - Preoperative radiotherapy - Results.

The incidence of bladder cancer in the Netherlands has been on the upward trend since the 1960's, when it was 10 males and 3 females per 100,000 population, while in 1969 it had risen to 14 males and 3 females per 100,000 population (2). The treatment of this disease has achieved a great uniformity at the R. R. T. I. since 1950. Since then all patients with bladder cancer have been seen in combined uro-radiotherapeutic clinics in which all patients are examined, staged and treated according to a strict schema to which all the urologists of the district adhere.

MATERIAL AND METHODS

Before deciding on treatment, every patient undergoes a full clinical assessment which includes:

1. Physical Examination
2. Radiological Examination: Thorax, I. V. P. Skeletal Survey, Lymphography for cystectomy patients

3. Isotopic Examination Bone scan
Lymph scan
(before X-Ray examination)
4. Blood Examination Full blood count
+ blood group
Glucose
Sedimentation rate
Blood chemistry
C. E. A. (since 1975)
5. Urine Examination Routine
Culture and sensitivity
Cytology
C. E. A. (since 1975)
6. Bimanual Examination Under Anaesthesia (B. E. U. A.) for staging

The staging is done routinely under general anaesthesia - according to the U. I. C. C. criteria - in which cystoscopy, B. E. U. A. followed by TUR for pathological confirmation are mandatory.

The treatment is prescribed according to a rigid protocol depending upon the size, extent,

Table 1. R.R.T.I. (1974) Carcinoma^a of the bladder treated between 1950 and 1972^b

Type of Treatment	
Radium Implantation	615
External Irradiation Supervoltage	1004
External Irradiation Orthovoltage before 1957	98
Vaginal Radium Application with or without external radiation	27
Intravesical Cobalt ⁶⁰ Beads curative	26
Intravesical Cobalt ⁶⁰ Beads palliative combined with external radiation	58
Preop. X + Cystectomy (5 without Preop. X)	151 ⁺
T. U. R. (2 segmental resections)	52
Total	2031 ^c

^a Excluding Carcinoma-in-Situ and Papilloma (115)

^b Cystectomy cases up to 7/74

^c Excluding 23 untreated patients (condition too poor)

and stage of the disease. This can be summarised as follows:

1. Mainly solitary T₁, 2 and 3^NX^MO
<5 cm ϕ Radium Implant.
2. All other cases were treated with External Radiotherapy 6500 rads in 6 1/2 weeks (until 1966).
3. In 1965, intracavitary Co⁶⁰ beads were used for a few in situ or diffuse T₁ cases but was soon abandoned.
4. Since 1966, all cases not suitable for a Radium implant were treated with Preoperative Radiotherapy 4000 rads in 4 weeks followed by total cystectomy.
5. Since 1972, this policy was applied only to T₃ cases, while T₁ and 2 cases were treated surgically.
6. T₄^NX^MO was mostly treated with radical External Radiotherapy.

From 1950 to 1972, a total of 2031 cases of bladder cancer were treated in the R.R.T.I. Details are shown in Table 1.

The average age of the patients grouped according to treatment and sex shows significant differences (Fig. 1). The external irradiation group consists of the oldest patients, while the radium implants group contains the middle aged patients and the youngest patients constitute the preoperative irradiation plus cystectomy group. In all groups the females were older than the males. Thus, the three groups are not comparable because of the different tumour and patient characteristics.

The 3- and 5-year actuarial uncorrected survival rates - in relation to the T-categories - of the various treatment modalities are shown in Figure 2. Radium implants yielded the best results although comparison between groups is not permissible.

Carcinoma of the Bladder treated by Radium Implants (1, 7)

Indications

1. One solitary or two small lesions in close proximity to each other.
2. Stages T₁-2- or 3 (early).
3. Not more than 5 cm in diameter.
4. The general condition of the patient must be fit for surgical and anaesthetic intervention.

Technique

1. For T₁-2 tumours a single plane implant is indicated where the needles are inserted parallel to the mucosa (Fig. 3).

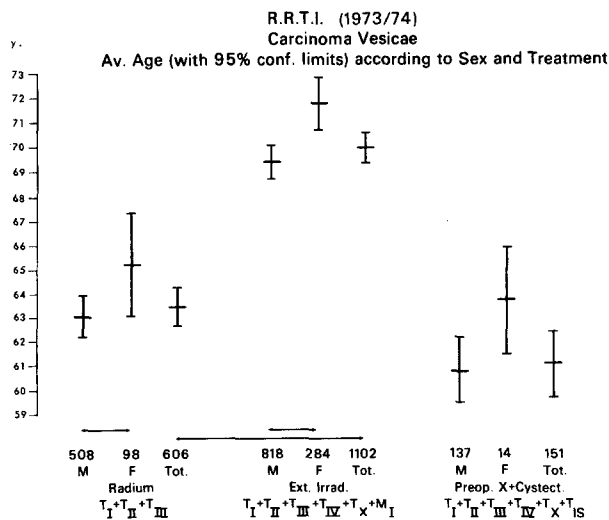


Fig. 1

R.R.T.I. (1973/74)

Carcinoma Vesicae

3- and 5 y. Act. Surv. acc. to T-Category and Treatment

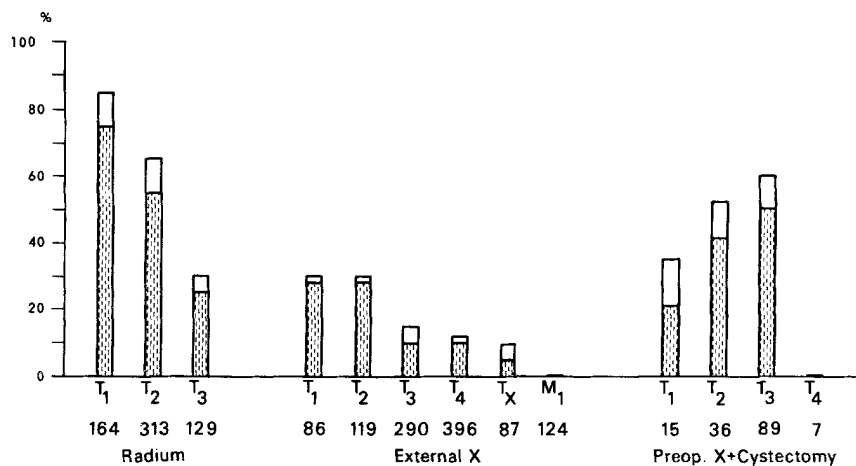


Fig. 2

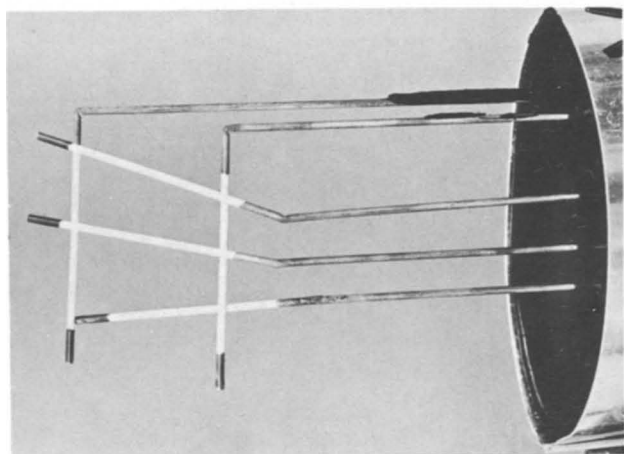


Fig. 3. Device for single plane Radium implantation

2. Similar lesion in the dome of the bladder can be treated by partial resection and closure of the bladder. Radium needles are then inserted from outside subserosally along the suture line (Fig. 4).

3. A two plane implant - when the needles are inserted in two planes, one submucosally from inside, the other subserosally from outside - is applicable for the less bulky T3 cases.

4. For bulky T3 tumours, a volume implant is applicable, though this is rarely practised as a routine.

The distribution of T-categories among the 615 patients treated by implantation is shown in Table 2.

51% of all cases belonged to category, T2 while 26% of the cases were T1 and 21% T3.

Five T4, 4 carcinoma in situ and papillomas recognised retrospectively were excluded.

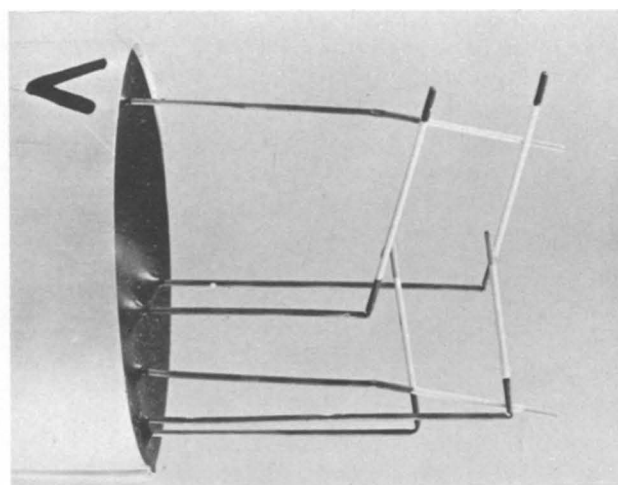


Fig. 4. Device for Radium implantation from the bladder exterior

Table 2. R.R. T. I. (1973) Carcinoma of the Bladder treated by radium implant

Distribution of T-categories		
T ₁	164	26 %
T ₂	313	51 %
T ₃	129	21 %
T ₄	5	2 %
prost.		
^a T _{IS} , Pap.	4	
Total	615	100 %

^a Diagnosed as "Cancer" initially

The average age of patients treated with radium was 63 years. There was no difference in age distribution among the T-categories (Fig. 5).

With increasing T-category, the percentage of poorly differentiated tumours increased and the percentage of differentiated tumours decreased. This finding is in accordance with Jewett's concept of grade-linked "speed", i. e. growth rate of the tumour (Fig. 6). The actuarial uncorrected survival rate decreases with increasing T-category as shown in Figure 7.

From 1956 to 1962 - post radium external irradiation of 3×350 rads to the skin was given because of scar recurrences. After 1962, this scar irradiation was replaced by pre-operative irradiation 3×350 rads to the mid-plane of the pelvis. The incidence of scar recurrence after radium implants in the various T-categories and their sub-groups is shown in Table 3. In the T1 category, no scar recurrences were observed and external irradiation was discontinued for this group in 1969.

In the T2 category, the incidence of scar recurrences decreased from 6% for the sub-group without additional external irradiation to 0% for the sub-group receiving external irradiation prior to the insertion of the radium implant.

In the T3 category sub-group without additional external irradiation, the incidence of scar recurrences was significantly higher than in the sub-group with post-radium external irradiation and there were no scar recurrences in cases of pre-radium external irradiation. Of 606 patients with bladder cancer T1, 2 & 3 treated with radium, 259 died within 5 years. The causes of death are detailed in Table 4.

Carcinoma of the Bladder Treated by Preoperative Radiotherapy followed by Cystectomy (3, 4, 5, 6, 8, 9, 10)

Since 1966, cases of bladder cancer too big for local implantation but still operable, have been given preoperative radiotherapy followed by cystectomy. A total number of 79 patients were treated between 1966 and 1971. The indications for preoperative irradiation followed by cystectomy are summarised in Table 5. Radiotherapy was given on 6 MeV Linear Accelerator via two parallel opposing fields covering the true pelvis (recently the 5th lumbar vertebra has also been included) and delivering a total tumour dose of 4000 rads in 20 daily fractions of 200 rads over 25 days. Cystectomy followed one week later (no lymphadenectomy). Figure 8

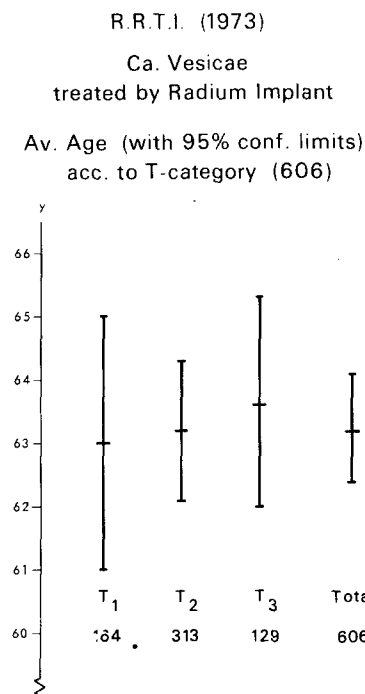


Fig. 5

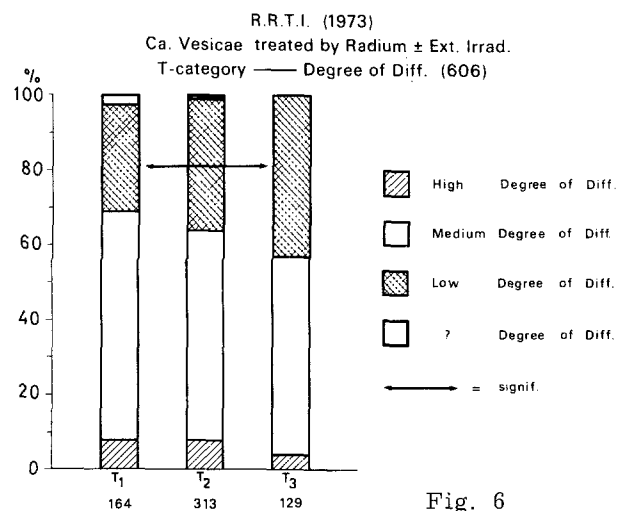


Fig. 6

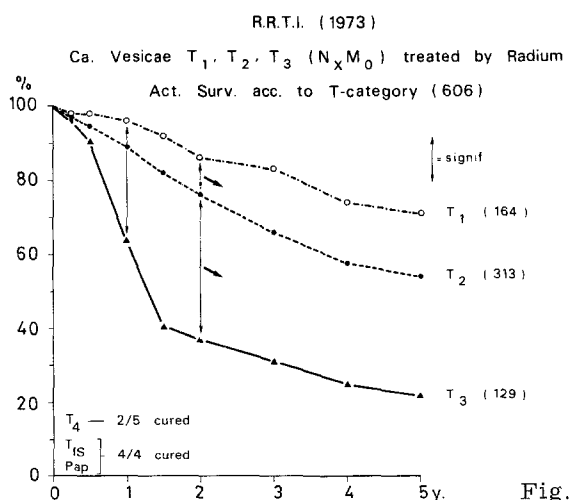


Fig. 7

R.R.T.I. (1971)
Carcinoma Vesicae
5-Years Prognosis after Preop.Irrad.+Radium*, Ext.Irrad.^o and Cystectomy

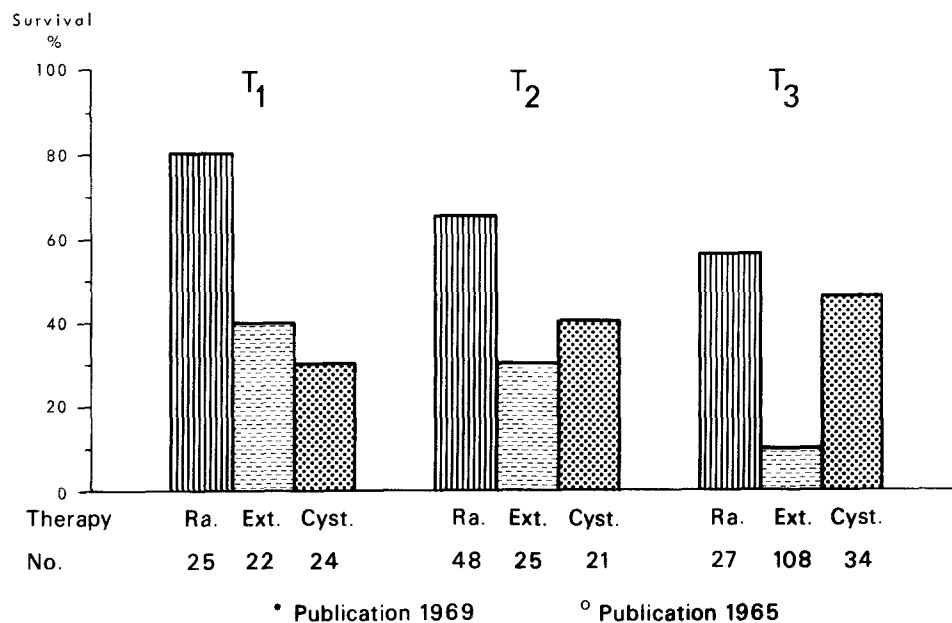


Fig. 8

Table 3. R.R.T.I. 1973
 Carcinoma of the Bladder treated by radium
 + Ext. X. Scar Implants ↔ Ext. Irradiation
 (606)

	No Ext. Irrad.		Postop. Ext. Irrad.		Preop. Ext. Irrad.	
T _I	0/40	0%	0/24	0%	0/100	0%
T _{II}	2/32	6%	1/79	1.3%	0/202	0%
T _{III}	7/31	23%	3/55	5.5%	0/43	0%

shows the 5-year follow up results of the various treatments in relation to the T-categories. There was a decrease in survival with either radium or external irradiation with increasing T-category, while there was an improvement in the prognosis with preoperative radiotherapy followed by cystectomy with the increasing T-category. Up to 1974, a total of 151 patients had been treated with preoperative radiotherapy followed by cystectomy. The average age was about 61 years. Females were older than males (Fig. 9).

The actuarial uncorrected survival shows that patients with T4 had the worst prognosis,

while patients with T3 had the best prognosis, followed by T2 and T1 (Fig. 10). T-category is a clinical staging arrived at after B. E. U. A. Once the patient had the preoperative radiotherapy a second B. E. U. A. is done to assess the change in the T-category, which is then noted and recorded, and the patient proceeds to surgery. The surgical specimen is then examined histologically and the degree of infiltration in the bladder wall is noted and referred to as P-category. It was found that in two-third of cases the P-category was less than the corresponding T-category. This T-reduction was attributed to the preoperative radiotherapy. Only in 9 out of 151 cases (6%) was there preoperative understaging.

Patients in the T2 category that showed T-reduction (Fig. 11) (i.e. "P" 0, 1S, or 1) had a significantly better prognosis than those without T-reduction (including 5 understaged patients T2 → "P" 3).

As the bladder is completely removed, a better prognosis related to T-reduction might reflect a favourable response to radiotherapy of involved lymph nodes in the pelvis). In the T3 category, survival was poorest in cases which showed no T-reduction (T3 → "P" 3). It was considerably better in cases when there was a T-reduction (T3 → "P" 0, 1 or 2) (Fig. 12). This might reflect the same lymph node effect (vide supra).

Table 4. R.R.T.I. (1973)
Carcinoma of the Bladder treated by Radium
(606) Causes of Death (within 60 months)

	Number	% of 606 Cases
Loc. Recurrence (+ Mets)	84	14
Mets (without Loc. Rec.)	80	13
2nd Bladder Cancer	5	1
Complications	12	2
Intercurrent	78	13
CVA	27	
2nd Cancer	24	
Other Causes	27	
All Causes	259	43

Table 5. R.R.T.I. Carcinoma of the Bladder

Indication for Preop. Irradiation + Cystectomy

- Category	T ₁		
	T ₂	N _X M ₀	φ >5 cm
	T ₃		
	T ₄	prostatic or 'small' pelvic fixation	

- General condition permitting radical surgery

Therefore in 1974 it was decided that on the second B.E.U.A., cases that showed no T-reduction should proceed to a second course of radiotherapy and not to surgery.

DISCUSSION

Radium implantation in carefully selected cases of bladder cancer has yielded the best results so far. That is why and whenever pos-

R.R.T.I. (1974)
Ca. Vesicae
treated by Preop. X + Cystectomy (151)
Av. Age (with 95% conf. limits) acc. to Sex.

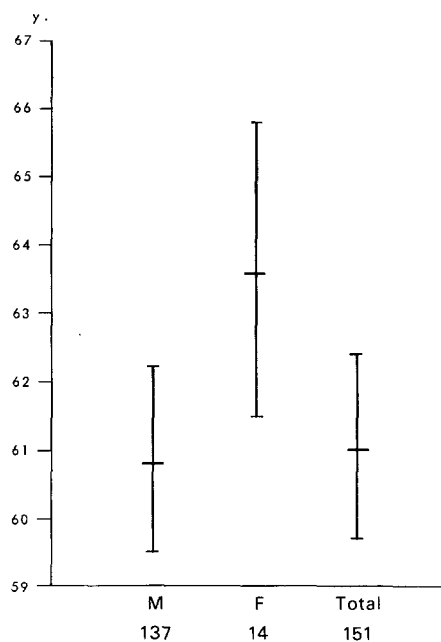


Fig. 9

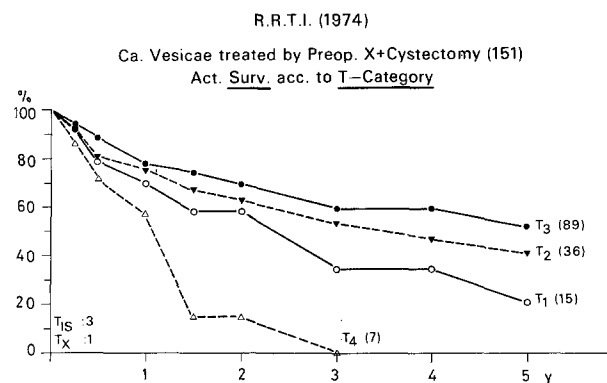


Fig. 10

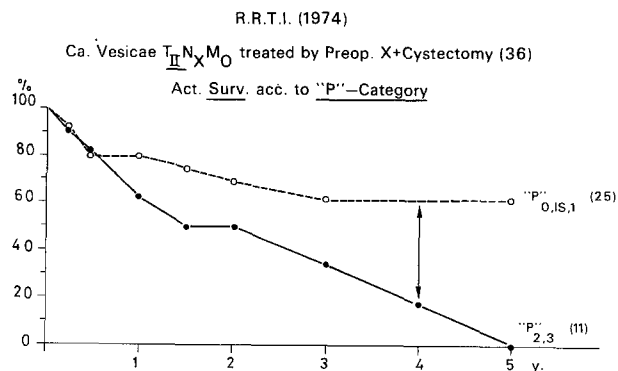


Fig. 11

R.R.T.I. (1974)

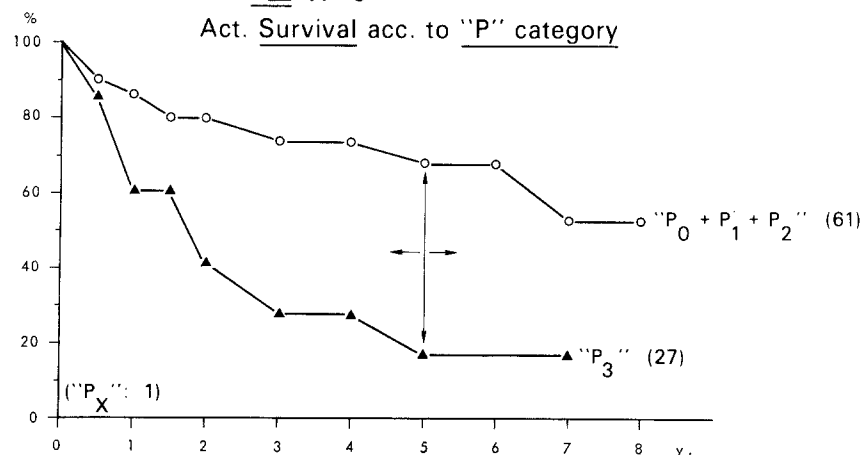
Carcinoma Vesicae $T_{III}N_XM_0$ treated by Preop. X + Cystectomy (89)

Fig. 12

sible, this method of treatment will be practised since its results are far superior to other methods, yet morbidity is negligible and side effects are practically non-existent.

On the other hand preoperative radiotherapy followed by simple cystectomy is recommended for T3 cases but only when the patients are in good general conditions and fit for major surgery.

T1 and T2 tumours are treated surgically whenever possible. In the cases where patients are not fit for surgery or refuse operation then external irradiation is the only alternative. T4 tumours are invariably treated with external irradiation (exceptionally they are treated in a similarly to T3).

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