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ADENOID CYSTIC CARCINOMA (CYLINDROMA) IN THE HEAD AND NECK

A clinical review of 82 cases

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A retrospective analysis was performed at the University Clinics in Münster of the clinical data of patients treated for adenoid cystic carcinoma (cylindroma) in the head and neck. Adenoid cystic carcinoma was first described by ROBIN (1853), who called the tumour 'tumeur hétéroadénique'. BILLROTH (1856) named it Zylindrom. In 1953 FOOTE & FRAZELL introduced the term adenoid cystic carcinoma, which now has replaced the older names.

Adenoid cystic carcinoma develops in the major and minor salivary glands, intraoral mucous glands, mucous membranes of the nose and accessory nasal sinuses, upper respiratory passages, lacrimal glands (RÖBEL 1971), ceruminal and sweat glands, and in the breast (ALBERTINI 1974).

A case of adenoid cystic carcinoma of the Gasserian ganglion region has also been reported (WILLSON & ROSEN 1974). The tumor is found most frequently in the minor salivary glands of the palate (ENEROTH et coll. 1968). Some data from the literature on the incidence in the major and minor salivary glands and in mucous glands appears in Table 1.

Though adenoid cystic carcinoma is not a common disease, it requires special attention because the prognosis depends largely on adequate initial treatment (NAU-

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Table 1

Incidence of adenoid cystic carcinoma

Author	Year	No. of cases	Incidence (per cent)
Tumours of the major salivary glands			
Koblin & Koberg	1972	215	3.2
Foote & Frazell	1953	877	4
Rafla-Demetrious	1970	268	5.2
Tumours of the mucous and minor salivary glands			
Fine et coll.	1960	79	16
Koblin & Koberg	1972	125	33.6
Rafla-Demetrious	1970	139	28.8
Thackray & Lucas	1960	80	37.5

MANN 1958, SCHETTLER & KOBLIN 1973). This tumour is characterized by slow growth (KNAK & BRANDT 1967, RAMSDEN et coll. 1973, STEINHOFF et coll. 1973, STIEBITZ 1968), frequent recurrence, and systemic spread even after long-term survival without disease (SCHETTLER & KOBLIN). General well-being may continue for a long time while the tumour progresses (FLETCHER 1973, RÖBEL). These features, as well as the low incidence of this tumour account for the rather conservative therapeutic management in the past.

In recent literature (GABKA & BEYER 1972, SCHETTLER 1972, STIEBITZ 1972, WANNENMACHER 1972) it has been emphasized that at present the treatment of choice is radical surgery. Pulmonary metastases should not exclude a patient from surgery, since these may grow slowly and without symptoms (FUCHIHATA et coll. 1973, WANNENMACHER & SCHÜTZ 1971). Long-term follow-up is essential and should not be limited to a certain period (MORAN et coll. 1961, SCHETTLER & KOBLIN).

Nowadays the value of modern radiation therapy has been established. In 1958 NAUMANN still reported no encouraging experiences with irradiation of adenoid cystic carcinomas, and KNAK & BRANDT were of the same opinion in 1967. RÖBEL considered only limited indications for radiation therapy because of the questionable sensitivity to radiation.

SCHERER et coll. (1972) have pointed out that these negative results were obtained before the introduction of ^{60}Co and megavolt therapy. They have stated that adenoid cystic carcinoma is definitely sensitive to radiation.

Modern textbooks give technical directions for the therapeutic management. FLETCHER (1973) is of the opinion that all histologic types of tumour are possible to control equally well by radiation therapy, and MOSS et coll. (1973) consider adenoid cystic carcinomas even more sensitive to radiation than other malignant

lesions of the salivary glands. Maximum tolerated doses for extended target volumes are proposed by these authors and by ARNDT (1973), who favours post-operative irradiation. Extended target volume is emphasized because of the characteristic tendency to invade nerve sheaths and to spread far beyond the clinically apparent margins of the lesion.

Good palliation, but no cure, was reported by STEINHOFF et coll. (1973) in 6 of 30 cases treated by irradiation. Better results were obtained by FUCHIHATA et coll. from combined surgical and radiologic treatment in a series of 18 cases. Four patients primarily irradiated with 9 000 to 10 000 R were reported to be free of disease after 5 years.

In their review of 134 cases of adenoid cystic carcinoma, CONLEY & DINGMAN (1974) do not give the number of patients irradiated. Their indications for radiation therapy were: (1) non-resectable recurrences, (2) to control tumour growth when the margins after surgery are not free of tumour, (3) to gain temporary local control in patients in too bad a condition for operation. The same indications have been employed in the present series as well. CONLEY & DINGMAN found that irradiation proved to be an effective and indispensable adjunct in the management of the majority of these patients. Based on 68 irradiated cases in a series of 94, STEWART et coll. (1968) conclude 'radiotherapy has made a very positive contribution to the management of these tumours'. They outline the problems encountered in evaluating the merits of radiation therapy as follows: 'Surgical accessibility and local radiation tolerance vary enormously from site to site, making it difficult to group cases for purposes of comparison. The general policy over the years has been that where tumour is accessible surgery should play the primary role, radiotherapy being reserved for inoperable or recurrent cases. This makes the comparison of like with like impossible. The radiotherapeutic approach in respect to target volume, technique and dose has varied very considerably over the period in question, thus precluding grouping by treatment technique'. The symptom-free control of the primary growth including no progress was used as the criterion of success of treatment. They point out that, following high doses, tumour residues may remain static and symptom-free for many years and that this is especially important for the elderly or for patients known to have metastases.

Material and Method of treatment

The material consisted of 82 patients treated between 1958 and 1976 for adenoid cystic carcinoma in the head and neck. Complete clinical follow-up data were available for 76 of the patients. Forty-three patients were irradiated; and 36 were treated by operation only; in 3 cases no specific treatment was given.

In spite of all shortcomings, retrospective analysis seems justified in view of the fact that adenoid cystic carcinoma is a rare tumour, and a long-term follow-up is necessary to assess the treatment results.

Table 2

Tumour location

Tumour site	No. of patients
Major salivary glands	25
Parotid	16
Submandibular	7
Sublingual	2
Minor salivary and intraoral mucous glands	42
Palate and maxillary antrum	27
Tongue	7
Lip	2
Buccal mucosa	2
Epipharynx	2
Floor of mouth	1
Lower jaw	1
Other sites	15
Trachea and bronchi	6
Larynx	2
Nose	2
Orbit	2
Auditory canal	2
Neck	1

Tumour site. Of the tumours 31 per cent were located in the major salivary glands, 51 per cent in intraoral mucous or minor salivary glands, and 18 per cent of the patients had adenoid cystic carcinoma in other regions of the head and neck (Table 2). The most common sites were the hard and soft palate.

Age and sex distribution. At the time of diagnosis the age of the patients ranged from 15 to 81 years (mean 55.4 years), 68 per cent of the patients being in the fifth and sixth decade (Fig. 1).

Six patients with adenoid cystic carcinoma of the trachea and bronchus were first treated at an average age of 48.5 years, which means that they were significantly ($p<0.1$) younger than the other patients.

The mean ages of patients with tumours of the major or minor salivary glands were 57 and 56.3 years, respectively.

KOBLIN & KOBERG (1972) reported that on an average adenoid cystic carcinomas occur 7.3 years later in intraoral salivary glands than in the major salivary glands. This statement was not confirmed in the present series.

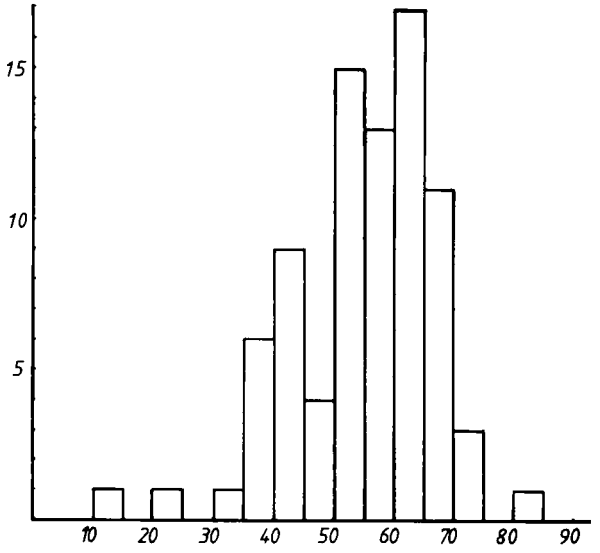

Fig. 1. Age distribution at time of diagnosis.

Of the patients 52 (63 per cent) were females; 30 (37 per cent) were males; 7 of the 9 patients under 40 years of age at the time of presentation were women. In the literature were found 656 cases. Of these 54 per cent were females and 46 per cent males, female preponderance thus being statistically significant ($p<0.05$).

Tumour size. In most cases, the clinically assessed diameter of the tumour at the time of presentation was given; in 13 cases, the data were incomplete. Detailed retrospective tumour classification according to stages as proposed for carcinomas by the UICC was not undertaken, since it did not appear to be useful in view of the various tumour sites, the number of patients, and the different modes of treatment. The diameter of the tumour was smaller than 2 cm in 11 patients, more than 5 cm in 30 cases. In 28 cases the diameter varied between those two figures. The average tumour size for 22 patients who were free of disease for 5 or more years after the initial treatment was 3.0 cm in diameter. In 16 patients with recurrence within 5 years after the initial treatment, the mean tumour size was 5.8 cm.

Duration prior to treatment. The interval between first symptoms and initial treatment ranged from a few days to 10 years; mean duration was 1.7 years (Fig. 2). The impression is that patients with adenoid cystic carcinoma do not have a long history. The present data are close to those reported by ENEROTH (1968): 37 cases, with a mean duration of 1.9 years. GABKA & BEYER, MORAN et coll. and SCHETTLER report a mean duration of 2.6, 3.5 and 4.5 years for 32, 53 and 53 patients, respectively.

Methods of treatment. The methods of treatment and the number of patients are given in Table 3. Radical surgery, if possible, has frequently been advocated in

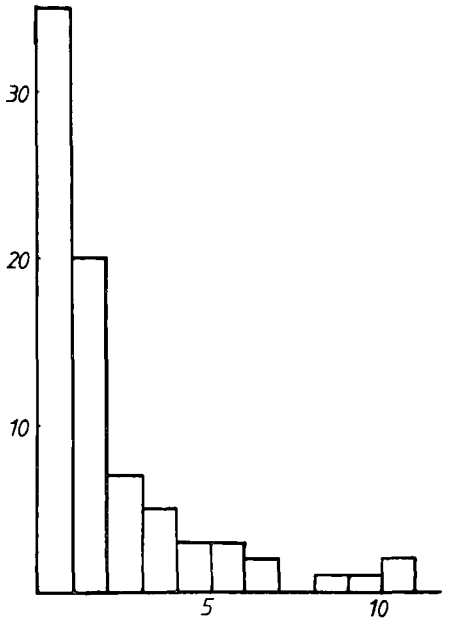

Fig. 2. Interval between first symptom and primary treatment.

recent literature (FUCHIHATA, SCHETTLER & KOBLIN, STIEBITZ 1972, WANNENMACHER). Accordingly, a change in the mode of treatment has occurred in the present series. From 1957 to 1968 radical surgery was performed in 14 patients; 22 patients received less extensive operations. From 1969 to 1976, 20 radical and 17 non-radical operations were performed.

Radiation therapy was applied at all stages of the tumour disease. In 6 inoperable patients, irradiation was the initial treatment. The tumour doses applied ranged from 55 to 85 Gy.

Postoperative irradiation was given to 5 patients after radical surgery and to 18 patients after non-radical operation. The average dose applied was 51 Gy. Three patients received total doses of more than 60 Gy and 3 less than 50 Gy (2 of these before 1961).

Local recurrence was irradiated in 25 patients; 15 of these received postoperative irradiation after repeated surgery. In 10 cases radiation therapy alone was administered. Metastases of the lungs were irradiated in one patient.

In most cases (34 patients) ^{60}Co irradiation was given; 3 received electron beam and 6 megavolt irradiation. In one case of recurrent disease 30 Gy were given intraoperatively with a ^{90}Sr source, since tolerable skin doses had been reached by prior treatment.

Results

Two years after the initial treatment 79 per cent (56/71) were living free of disease, and 13 per cent (9/71) were living with disease. Six per cent (4 patients) had died of their tumours and 2 patients had died of intercurrent disease.

Table 3

Methods of treatment

	No. of patients	Irradiation	No irradiation
No surgery	9	6	3
Non-radical surgery	39	27	12
Radical surgery	34	10	24
Total	82	43	39

Table 4

Remission

Method of treatment for recurrent disease	No. of cases	Years			
		>1	>2	>3	>5
Operation and irradiation	16	11	6	5	3
Operation only	10	8	4	1	—
Irradiation only	10	5	2	1	1
No therapy	5	2	—	—	—

Five years after treatment, 52 per cent (26/50) were living free of disease, 22 per cent (11/50) were living with disease and 26 per cent (13/50) had died of their tumours.

Ten years after treatment, 17 per cent (3/28) were living free of disease, 39 per cent (11/28) were living with disease, and 46 per cent (13/28) had died of their tumours. One patient had died of intercurrent disease. None of the 3 patients living 15 years after treatment was free of disease, 6 had died of their tumours, and one of intercurrent disease.

Determinate survival rates were calculated for the patients 2, 5, 10 and 15 years after treatment; 4 patients who had died of intercurrent disease were excluded from the calculations. In Fig. 3 the survival rates are given separately for 3 different groups of sites and for patients treated by radical or non-radical surgery. In each case, the percentage of patients living free of disease after the initial treatment is shown separately.

Seven patients who were inoperable because of extensive tumour or for other reasons were observed for 2 or more years. Of these, 5 patients had persistent or recurrent disease, one was free of disease 4 years after irradiation. Four of the patients were followed for 5 years after treatment; all died of their tumours within that period.

Table 4 gives the number of patients free of symptoms 1, 2, 3 and 5 years after different treatments for recurrence. Though the number of cases is small in each group, it is apparent that combined surgical and radiologic efforts give the best re-

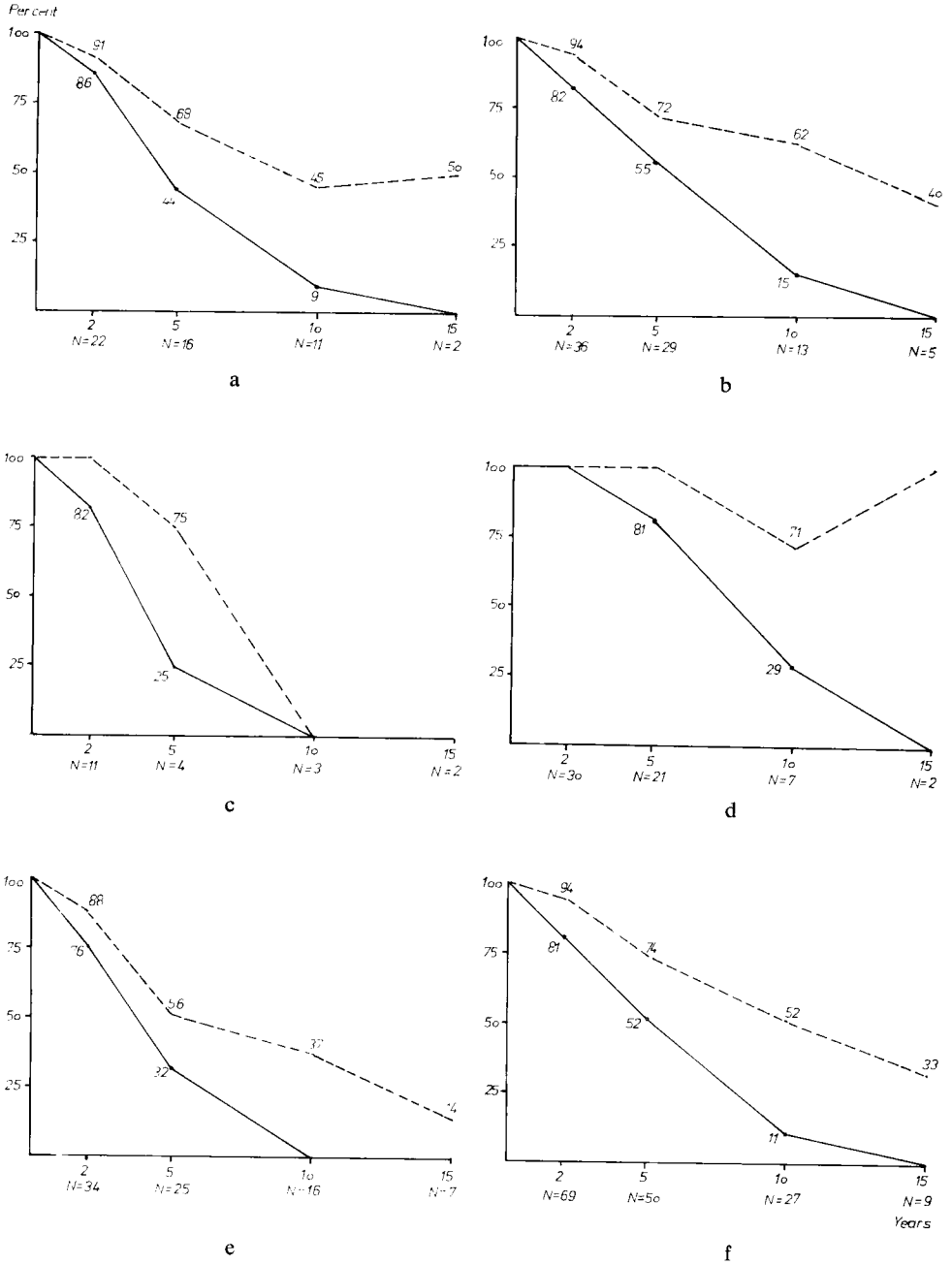

Fig. 3. Determinate survival rates (upper curves) and rates of patients with no evidence of disease after first specific treatment. N is the total number of patients in each group at a specific time. The group consisted of patients with: a) tumours in the major salivary glands, b) tumours in the minor salivary glands, c) tumours in other sites, d) tumours treated by radical surgery, e) tumours treated by non-radical surgery, f) and all cases of adenoid cystic carcinomas.

Table 5

Local recurrence

Local recurrence within year	No. of patients
1	8
2	1
3	3
4	4
5	2
6	4
7	3
8	2
9	1
10	2
Total	30

sults: 5 years after surgery and subsequent irradiation, 3 of 16 patients were still free of symptoms.

Adenoid cystic carcinoma of the trachea is associated with special treatment difficulties. The present series included 6 cases. The patients were middle-aged, and the diagnosis had been delayed by unspecific treatment for periods from 1 to 6 years. Radical surgery was usually impossible because of the tumour location. Also the radiation therapy encountered difficulties. Two patients died after 2 and 5 months, respectively, from treatment complications, 2 other patients died 4 and 5.5 years after presentation, and 2 patients are living with disease. Thus the prognosis is worse than in other tumour locations.

Local recurrence. When the period in which the patient is free of symptoms is very short, it becomes impossible to distinguish between recurrent and persistent disease. By evaluating all clinical records available, an effort was made to be as accurate as possible. Six patients were considered to have persistent disease, 4 of these being inoperable.

In 30 patients, local recurrence occurred. Eight patients were free of symptoms for less than one year; 3 of these had not been operated upon. In 10 patients, the disease-free intervals ranged from 1 to 5 years after the initial treatment. No recurrence occurred after more than 10 years (Table 5). Fourteen of the 30 patients had distant metastases as well.

Eight radically operated patients stayed free of disease for 5.3 years on an average; 21 treated by less extensive surgery developed recurrence after a mean period of 3.7 years; 7 inoperable were free of symptoms for 4 months on an average. These figures cannot be compared directly because the situation at the time of

presentation differed markedly; they are just meant to illustrate the natural history of adenoid cystic carcinoma in general.

While 20 of the 36 patients are still living, 16 with persistent and recurrent disease died within 2.5 years on an average after developing local recurrence.

Despite the discouraging general course of the disease, longlasting individual histories occurred. One patient with adenoid cystic carcinoma of the tongue died 9 years after a local recurrence; 2 patients are alive 11 years after treatment for their first recurrence. One of these patients is now free of symptoms 3 years after his fifth operation for recurrent tumour of the parotis gland; the other is living with extensive recurrence after 7 operations and 5 series of irradiation for a tumour originating in the palate.

Metastases. In 24 patients generalisation of the tumour occurred; of these, 14 also developed local recurrence.

For 12 of 82 patients, no chest films were available. Of the remaining 70 patients, 15 (21 %) had pulmonary metastases, 2 already at the time of presentation. In 13 patients, metastases were detected on an average of 3 years after initial treatment. One year later, 11 of these 13 patients were still living; after 2 years, 7 patients were alive; and after 3 years, 10 of 13 had died. One patient underwent surgery 3 years after pulmonary metastases had been detected and died 10 years later of a heart attack. Such extremely long survivals of generalized disease are frequently described in the literature. Pulmonary metastases of adenoid cystic carcinoma are not as prognostically hopeless as in other carcinomas, but, on the other hand, long-term survivals of more than 3 years are not common.

Metastases to other organs were found in 13 patients (16 %) after 4.5 years on an average. In one patient with adenoid cystic carcinoma of the buccal mucosa, osteolytic destruction in the frontal region of the skull was recognized 13 years after initial treatment. In 6 patients haematogenic spread to the lungs as well as to other organs occurred.

Discussion

It is evident that curative treatment was the aim of the irradiation in some cases; in others, palliation only was attempted. In each case, the group of patients was small. Tumour site and extension varied as widely as the histologic grade of malignancy or the number of prior treatments. A comparison of survival rates is not appropriate under these conditions. In order to evaluate the benefits of irradiation beyond giving favourable case reports, the term remission has been applied to cases with recurrent disease.

Adenoid cystic carcinoma is at present considered to be a malignant tumour. It grows relatively slowly and causes local recurrence and generalized disease even after long symptom-free periods. In the present series the duration before treatment was not as long as is frequently reported in the literature. The prognosis, as with

most tumours, depends largely on the size and location of the lesion and on adequate primary treatment. For an analysis of the treatment results, at least 10 years of observation are necessary because of the natural history of the tumour. Poor long-term survival rates have been reported previously, which may be attributed to the fact that radical surgery was not generally accepted. Anyhow this holds true in the present series, in which the primary treatment was given about 15 years ago. Nor was extended field high dose radiation common at that time. The present series indicates that these methods of primary treatment must be employed to improve the prognosis of this tumour. When an extended tumour, unfavourable location, or recurrent disease limit the possibilities of curative treatment at the time of presentation, palliative surgery and adequate irradiation should be employed, since long-term remissions are possible to achieve. These methods of treatment are especially valuable for the elderly patient. No treatment at all is evidently the worst policy. In spite of remarks in the literature emphasizing absence of sensitivity to radiation, long-term palliation is possible. A long-term clinical follow-up should be carried out carefully in order to make possible early treatment in case the disease should recur. A patient with metastases should not be excluded from treatment since the metastases may grow slowly and without symptoms.

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SUMMARY

A review of 82 cases of adenoid cystic carcinoma in the head and neck is given. Radical surgery was carried out in 33 patients and yielded the best long-term results. Radiation therapy was given to 43 patients for inoperable tumour, local recurrence or, postoperatively, for sub-clinical disease. It proved especially valuable in obtaining remissions from local recurrence.

ZUSAMMENFASSUNG

Die Arbeit gibt einen Überblick über 82 behandelte Zylindrome im Kopf-Hals-Bereich. Eine Radikaloperation wurde bei 33 Patienten durchgeführt, wobei die besten Ergebnisse erzielt werden konnten. Bei 43 Patienten wurde postoperativ bestrahlt bzw. eine primäre Strahlentherapie durchgeführt. Aus dieser Gruppe ergeben die Kombination von Operation und Bestrahlung die relativ besten Resultate, wobei besonders die rezidivfreien Intervalle verlängert werden.

RÉSUMÉ

Les auteurs présentent une revue de 82 cas de carcinome kystique adénoïde dans la tête et le cou. Une chirurgie radicale a été effectuée chez 33 malades et a donné les meilleurs résultats à long terme. Le traitement par irradiation a été administré à 43 malades pour une tumeur inopérable, une récidive locale ou, après l'opération, pour une évolution infra-clinique. Ce traitement par l'irradiation s'est montré particulièrement utile pour obtenir des rémissions sur des récidives locales.

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