Eur J Cancer, Vol. 29A, No. 5, pp. 664–668, 1993.
Printed in Great Britain

0964–1947/93 $6.00 + 0.00

Papers

Increased Incidence of Sarcoma in Patients Treated for Testicular Seminoma

Grete Krag Jacobsen, Anders Mellemgaard, Svend Aage Engelholm and Henrik Møller

In a nationwide cancer registry analysis of second primary malignancies in 6187 men with testicular cancer in the period 1943–1987, 13 sarcomas were found, yielding a 4-fold increase of the relative risk (RR). The majority of sarcomas occurred in men with seminoma, and the increased incidence was seen irrespectively of time since the diagnosis of testicular cancer. The interval between the testicular cancer and the sarcoma varied from 5–34 years. After investigation of the hospital records and re-examination of the histological specimens, 3 patients were excluded. In spite of this, the RR was still considerably increased (at least 3-fold). Seven of the 10 sarcomas were found to be located within the field of the radiation treatment administered and three at the periphery. The absolute number of these secondary sarcomas is low, but the risk of developing such neoplasms and other malignancies should, even so, be kept in mind in the follow-up of testicular cancer patients.
Eur J Cancer, Vol. 29A, No. 5, pp. 664–668, 1993.

INTRODUCTION

THE STUDY of multiple primary malignant neoplasms occurring in the same person may yield an insight into the aetiology of the neoplasms and into the possible carcinogenic effect of the treatment [1]. For subjects with germ cell tumours, which comprise pluripotent cell types, the possibility furthermore exists that a second primary tumour is actually a metastatic lesion from the germ cell tumour [2, 3].

Efficacious radiotherapy for seminoma and more recently, cisplatin-based chemotherapy for non-seminoma and disseminated seminoma has resulted in a large number of long-term survivors after testicular germ cell cancer [4, 5]. In a nationwide cancer registry analysis of second primary malignancy occurring after a diagnosis of testicular cancer in Denmark in the period 1943–1987, an increased incidence of malignant neoplasms of various types and locations was found [6]. The highest relative risk (RR) was found for sarcomas and these neoplasms are described in the present paper. Results regarding other secondary malignancies are given elsewhere [6].

PATIENTS AND METHODS

The Danish Cancer Registry has since 1943 registered all cases of malignant neoplasms occurring within the whole country. When two supposedly independent malignant neoplasms occur in the same person, two separate records exist in the register. Details about the register information have previously been given [6]. The relative risk of different neoplasms were calculated in the person-time experience from date of diagnosis with testicular cancer to death, emigration or 31 December 1987 whichever occurred first. The incidence of second primary malignant neoplasms in testicular cancer patients was compared with the corresponding incidence rate in the Danish population as a whole using indirect age standardisation for age and calendar time. Results were expressed by the relative risk (RR) with the associated 95% confidence interval calculated on the basis of the exact binomial probabilities.

In the period 1943–1987, a total of 6187 men with testicular cancer were registered: 3256 (53%) seminomas, 2560 (41%) non-seminomas and 361 (6%) other and unspecified types. In the course of 59 000 person-years of follow-up, 459 second primary malignant neoplasms were observed, 337 in patients with seminoma, 98 in patients with non-seminoma and 24 in patients with other and unspecified types. The mean duration of follow-up for seminomas was 11.6 years, for non-seminomas 7.4 years and for other and unspecified types 5.9 years.

A total of 13 males were identified who had a history of testicular cancer and sarcoma, occurring in that order. Another 6 males were identified who developed both types of neoplasms but with the sarcoma occurring before the testicular cancer. For all these men, hospital records, including treatment records, were procured and investigated. Histopathological descriptions, slides and/or tissue blocks were obtained, if available, from the departments of pathology. New slides for special staining and immunohistochemistry were cut if indicated.

Postorchidectomy treatment has changed during the period studied. Since 1930, postoperative radiation was given as a routine treatment of germ cell tumours, seminomas as well as non-seminomas. Between 1930 and 1960, treatment was given by 250–300 kV on posterior fields. Thus, doses of 20–25 Gy were given to the paraaortic lymph nodes during 3–4 weeks. In the early 1960s, supervoltage radiotherapy was introduced when ^{60}Co equipment became available, and the fields of treatment was also changed to include the ipsilateral pelvic lymph nodes.

Correspondence to G.K. Jacobsen, Department of Pathology, Gentofte Hospital, DK-2900 Hellerup, Denmark; A. Mellemgaard and H. Møller are at the Danish Cancer Registry, Institute of Cancer Epidemiology, Danish Cancer Society, Copenhagen; and S.A. Engelholm is at the Department of Oncology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark.
Revised 8 Sep. 1992; accepted 21 Oct. 1992.

Furthermore, the dose was increased to 30–35 Gy during 3–4 weeks. From the early 1970s most patients in Denmark were treated on anterior fields by 22–32 MV radiation (Betatron's) or anterior/posterior by linear acceleration with 6 MV. In the same period lymphangiography was introduced for staging procedure, and in the stage II patients the radiation dose was increased to 40–45 Gy. After 1985, radiotherapy was only administered to patients with stage II seminomas and to patients with seminoma relapse in retroperitoneal lymph nodes.

From 1973 chemotherapy comprising bleomycin and vinca-alkaloids was given to stage II patients in eastern Denmark in addition to radiation, and from 1978 all stage II patients with non-seminomas nationwide received cisplatin-based combination chemotherapy.

RESULTS

A total of 13 secondary sarcomas occurred in the cancer registry in the cohort of testicular cancer cases in the investigated period from 1943–1987 (Table 1). The expected number was 3.27 assuming the national incidence rate to apply, yielding a relative risk of 4.0 (95% CI: 2.1–6.8). The majority of sarcomas occurred in men with seminoma and as seen in Table 1 the incidence was increased regardless of period of follow-up. A test for trend over time divided into three periods of follow-up was not significant. The interval between the testicular tumour and the sarcoma varied from 5 to 34 years (Table 2). In addition, 6 sarcomas which occurred before the diagnosis of testicular cancer were identified in the register (Table 3). 3 cases occurred prior to seminomas and 3 cases prior to non-seminomas. The interval between the sarcoma and the testicular tumour varied from 1 to 24 years.

After reinvestigation of the histological material available, 3 cases of sarcoma secondary to testicular cancer were not confirmed. The first case was a fault of registration. The second case which was registered as sarcoma of the thyroid gland was found to represent a poorly differentiated (anaplastic) carcinoma. The third case had primarily been diagnosed as angiosarcoma of the liver but turned out to represent peliosis. The results of the microscopical re-examination of the primary testicular cancers and the secondary sarcomas are given in Table 2.

Among the remaining 10 cases the primary diagnosis of pure seminoma was changed to non-seminoma in 1 case (no. 9) because small components of embryonal carcinoma and immature teratoma were found at re-examination of the tumour slides. Consequently, the group included eight pure seminomas and two non-seminomatous tumours although with a predominant component of seminoma. During the investigation 1 more case of sarcoma (dermatofibrosarcoma protuberans) secondary to testicular cancer was found, but as the sarcoma occurred in 1988, this case was not included in the calculation of RR.

Table 1. Number of observed (n) and expected (e) cases, relative risks (RR) and 95% confidence intervals of sarcoma after diagnosis with testicular cancer, according to the cancer registry records

	n	*e*	RR	(95% CI)
Total	31	3.27	4.0	(2.1–6.8)
Histology				
Seminoma	11	2.36	4.7	(2.3–8.3)
Non-seminoma	1	0.75	1.3	(0.0–7.4)
Other and unspecified	1	0.16	6.4	(0.2–34.8)
Latency (years)				
0–9	5	1.49	3.4	(1.1–7.8)
10–19	4	0.95	4.2	(1.1–10.8)
20+	4	0.83	4.8	(1.3–12.3)

The sarcoma diagnosis of the 11 cases was confirmed at re-examination and further subclassification was performed in 2 cases (nos 1 and 4).

All but two treatment reports were obtainable and confirmed that postoperative radiotherapy had been administered. Although information on radiotherapy was not reconfirmed in the remaining cases, it is likely that patients with seminomas diagnosed during the 1950s were given routine treatment. Thus 8 cases of sarcomas occurring after testicular cancer were located within an area possibly affected by the given radiotherapy while 3 cases occurred at the periphery of the radiation field, namely in the axilla (2 cases) and at the proximal thigh in the regio trigonum scarpae.

In the group of 6 cases of sarcomas and subsequent testicular cancer one was revised from undifferentiated sarcoma to malignant lymphoma of B-cell type after immunohistochemical investigation. 2 cases were revised from fibrosarcoma of subcutanous tissue to malignant fibrous histiocytoma and 1 case was found to be an eosinophillic granuloma which is not considered a malignant neoplasm. Results of the microscopical re-examination are shown in Table 3.

The sarcomas appearing prior to testicular cancer occurred on the limbs.

DISCUSSION

Among survivors of testicular cancer registered in the countrywide Danish Cancer Registry in the period 1943–1987, an increased incidence of malignant neoplasms was found [6]. The incidence of sarcomas was four times higher than expected. Since the data in the register has been collected and registered over many years, we took the opportunity to re-examine the cases to confirm the diagnoses and to obtain more detailed information about tumour location and postoperative treatment. After histological re-examination 2 cases were excluded because the final diagnosis was revised to carcinoma and peliosis, respectively. A third case was found to be a fault of registration. These corrections resulted only in a slight decrease in the calculated RR, but since the diagnosis on which the expected numbers are based have not been likewise revised the originally calculated RR is valid. Although in relative terms, the risk of sarcomas was increased about 4-fold in the cohort, the absolute incidence of sarcomas remained fairly low. Ten years or longer after testicular cancer diagnosis, eight sarcomas occurred in the 2241 patients who survived 10 years, giving an absolute risk of 0.4%.

The primary testicular tumours were also revised and the diagnoses were reconfirmed. In one tumour, small non-seminomatous tumour components were found. These components were examined with particular interest in the presence of sarcomatous elements which were, however, not found. Therefore, the second primary sarcomas in these cases are unlikely to represent metastatic lesions from the germ cell tumours. In addition, none of the sarcomas had the appearance and location of metastatic deposits from testicular germ cell cancer.

Until cisplatin-based chemotherapy was introduced in the late 1970s, the only treatment for germ cell tumours was surgery followed by radiotherapy [4, 7]. Patients with non-seminomat-

Table 2. Results of re-examination of tissue slides and investigation of hospital records on 11 men with sarcomas secondary to testicular cancer diagnosed 1943–1987 in Denmark

	Testicular cancer				Secondary sarcoma				Interval Years between 1st and 2nd malignancy
Case no.	Year of diagnosis	Years of age	Tumour type	Postop. therapy	Year of diagnosis	Age (years)	Tumour type	Location	
1	43	22	S	RT	77	57	Mesenchymal chondrosarcoma	III costa dx.	34
2	54	53	S	RT	75	74	Leiomyosarcoma	Small intestine	21
3	55	34	S	RT	65	44	Fibrosarcoma	Axilla	10
4	56	46	S	n.a.	73	63	Liposarcoma	Axilla	17
5	57	32	S	n.a.	79	54	Malignant fibrous histiocytoma	Regio lumbalis	22
6	58	47	S	RT	83	71	Fibrosarcoma	Regio trigonum scarpae dxt.	24
7	66	35	S+EC	RT	76	45	Malignant fibrous histiocytoma	Regio lumbalis	10
8	67	41	S	RT	86	60	Malignant mesothelioma	Pleura	19
9	71	42	S+EC+IMT	RT	80	51	Leiomyosarcoma	Regio lumbalis	9
10	74	36	S	RT	79	41	Leiomyosarcoma	Abdomen, behind the caecum	5
11*	77	32	EC+YST+IMT	RT	88	43	Dermatofibrosarcoma protuberance	Regio supra-scap. sin.	11

* Not included in calculations for RR.
S = seminoma, EC = embryonal carcinoma, IMT = immature teratoma, YST = yolk sac tumour, RT = radiotherapy, n.a. = treatment record not available.

Table 3. Results of re-examination of tissue slides and investigation of hospital records on 6 men with sarcomas diagnosed 1943–1987 in Denmark and followed by testicular cancer

	Primary sarcoma			Secondary testicular cancer				Interval Years between 1st and 2nd tumour
Case no.	Year of diagnosis	Age (Years)	Tumour type	Location	Year of diagnosis	Age (Years)	Type	
1	49	13	Malignant fibrous histiocytoma	Forearm	73	37	EC+IMT	24
2	54	56	Myofibrosarcoma	Femur	75	77	S	21
3	55	17	Malignant fibrous histiocytoma	Crus	60	22	S	5
4	68	34	Osteogenic sarcoma	Femur	69	34	S+EC	1
5	75	54	Malignant lymphoma	Reg. colli lat.	79	58	EC+S	4
6	77	41	Eosinophilic granuloma	Mandible, scapula and os cranii	83	47	S	6

EC = embryonal carcinoma, IMT = immature teratoma, S = seminoma.

ous tumours often died within 1 or 2 years from the diagnosis, while many patients with seminomas, which are radiosensitive, were cured and survived for many years. This effect of the treatment is evident in the present material. All but two treatment reports were obtainable and confirmed that postoperative radiotherapy had been administered and the location of the sarcomas was found to be within the field of radiation, except in 3 patients who had their sarcomas located at the periphery of the radiation field, namely at the axilla and the proximal thigh.

The histological type of the sarcomas varied. Leiomyosarcomas were most frequent (3 cases) followed by malignant fibrous histiocytomas (2 cases) and fibrosarcomas (2 cases). Leiomyosarcoma following radiotherapy for testicular cancer has to our knowledge only been reported once [8]. Fibromatosis and fibrosarcomas are more likely to follow radiation therapy [9].

In a review of 53 post-irradiation soft tissue sarcomas from the Armed Forces Institute of Pathology malignant fibrous histiocytoma was the most frequent histological type followed by osteosarcoma and fibrosarcoma [10], while osteosarcoma was found to be the largest group of post-irradiation sarcomas reviewed by Robinson *et al.* [11]. The differences in the sarcoma types may partly be explained by difference in location of primary tumours and field of irradiation. Thus, osteosarcoma has been found to be particularly frequent following irradiation for breast cancer with the majority arising in the scapula followed by humerus, clavicle, ribs and sternum [11], probably due to greater bone than soft tissue absorption of irradiation. Likewise bone sarcomas were also most frequent in a Danish series of post-irradiation sarcomas of the shoulder girdle [12]. In patients with testicular cancer the field of irradiation is different and does not contain the same variety of bones as in the above mentioned series of patients.

The present material includes one case of malignant mesothelioma and we are aware that a case of malignant mesothelioma of the peritoneal cavity following radiotherapy for seminoma of the testis has also been published [13]. It should be noted that we did not find angiosarcomas, which may also follow irradiation [14, 15], as the only case occurring in this series was revised to peliosis of the liver.

Previous studies of second primary malignancies in patients treated for testicular tumours have found increased incidence of various malignancies including germ cell tumours, tumours in the urinary and gastrointestinal tracts, leukaemia, skin cancer and lung cancer [16–21] but only one other study mentions increased incidence of malignancies of connective tissue but without further specification [1]. The international collaborative study among cancer registries of second malignancies following testicular cancer including part of the present material, reports increased incidence of malignancy of bone and connective tissue [19]. The number of patients in these studies except the latter are however limited and the observation periods are shorter than in the present.

The increased incidence of sarcoma was seen irrespective of time since the diagnosis of testicular cancer, which in this study also means irrespective of the type of radiation therapy, since the therapy changed during the observation period from orthovoltage to supervoltage and latest to irradiation by linear acceleration. Robinson *et al.* [11] found that differences occurred in latency between those patients treated with orthovoltage and supervoltage with the shortest interval in the supervoltage group. Although our figures are small for such an evaluation, the tendency is at least in accordance to this as the latency interval decreased from approximately 21 years before 1960 to approximately 11 years after supervoltage therapy was introduced. To investigate whether sarcoma especially affects testicular cancer patients, we also retrieved from the registry files cases of sarcomas occurring prior to testicular cancer. Only 4 proper cases were found, 2 in patients with seminomas and 2 in patients with non-seminomas. The histological subtypes of the sarcomas did not differ essentially from the subtypes of the secondary sarcomas, but it was noteworthy that the primary sarcomas were located on the limbs contrary to the secondary sarcomas located centrally in or on the body, further indicating the association with the given radiotherapy.

Our findings show an increased RR for sarcomas after testicular cancer, probably caused by the radiation treatment of the testicular cancer. The absolute number of these secondary sarcomas is low, although in relative terms the incidence is increased by 3–4-fold. The risk of developing these neoplasms and the other malignancies encountered in testicular cancer patients [6] should be considered when treatment regimes are planned. At the present time the policy of treatment of stage I seminoma is under discussion. In other countries, postoperative radiotherapy administered to irradiate possible occult metastases is widely performed and recommended although this treatment is unnecessary in almost 80% of these patients [22, 23]. Although uncommon, the risk of developing second primary malignancy in testicular cancer patients should be kept in mind in the follow-up of these patients. The present study elucidates only the sequelae after the treatment of seminoma, while the next decades will reveal long term sequelae of the successful treatment that was introduced in the late 1970s in both seminoma and non-seminoma patients [7, 22].

1. Boice DJ, Storm HH, Curtis RE, *et al.* Introduction to the study of multiple primary cancers. In: Multiple Primary Cancers In Connecticut and Denmark. *Natl Cancer Inst Monogr* 1985, **68**, 3–9.
2. Ahmed T, Bosl GJ, Hajdu SI. Teratoma with malignant transformation in germ cell tumors in men. *Cancer* 1985, **56**, 860–863.
3. Ulbright TM, Loehrer PJ, Roth LM, Einhorn LH, Williams SD, Clark SA. The development of non-germ cell malignancies within germ cell tumors. *Cancer* 1984, **54**, 1824–1833.
4. Schultz H, Arends J, Brincker H, *et al.* DATECA-projektet. Det danske testiscancerprojekt. (English summary). *Ugeskr Laeger* 1978, **42**, 2563–2566.
5. Daugaard G, Hansen HH, Rørth M. Treatment of malignant germ cell tumours. *Ann Oncol* 1990, **1**, 195–202.
6. Møller H, Mellemgaard A, Jacobsen GK, Pedersen D, Storm HH. Incidence of second primary cancer following testicular cancer. *Eur J Cancer* 1993, **29A**, 672–676.
7. Schultz HP, von der Maase H, Rørth M, Pedersen M, Nielsen ES, Walbom-Jørgensen S, the DATECA study group. Testicular seminoma in Denmark 1976–80. *Acta Radiol Oncol* 1984, **23**, 263.
8. Lynch DF, Herr HW. Radiation-induced sarcoma following radiotherapy for testicular tumor. *J Urol* 1981, **126**, 845.
9. Pettit VD, Chamness JT, Ackerman LV. Fibromatosis and fibrosarcoma following irradiation therapy. *Cancer* 1954, **7**, 149–158.
10. Laskin WB, Silverman TA, Enzinger FM. Post-radiation soft tissue sarcomas: An analysis of 53 cases. *Cancer* 1988, **62**, 2330–2340.
11. Robinson E, Neugut AI, Wylie P. Clinical aspects of postirradiation sarcomas. *J Natl Cancer Inst* 1988, **80**, 233–240.
12. Steinke NMS, Østgaard SE, Jensen OM, Nordentoft AM, Sneppen O: Irradiation-induced sarcomata of the shoulder girdle. *Ugeskr Læger* 1991, **153**, 1655–1657.
13. Stock RJ, Fu YS, Carter JR. Malignant peritoneal mesothelioma following radiotherapy for seminoma of the testis. *Cancer* 1979, **44**, 914–919.
14. Maddox JC, Evans HL. Angiosarcoma of skin and soft tissue: a study of 44 cases. *Cancer* 1981, **48**, 1907–1921.
15. Chen KTK, Hoffman KD, Hendricks EJ. Angiosarcoma following therapeutic irradiation. *Cancer* 1979, **44**, 2044–2048.

16. Kleinerman RA, Liebermann JV, Li FP. Second cancer following cancer of the male genital system in Connecticut, 1935–82. In: Multiple Primary Cancers in Connecticut and Denmark. *Natl Cancer Inst Monogr* 1985, **68**, 139–147.
17. Hay JH, Duncan W, Kerr GR. Subsequent malignancies in patients irradiated for testicular tumours. *Br J Radiology* 1984, **57**, 397–602.
18. Fosså SD, Langmark F, Aass N, Andersen A, Lothe R, Børresen AL. Second non-germ cell malignancies after radiotherapy of testicular cancer with or without chemotherapy. *Br J Cancer* 1990, **61**, 639–643.
19. Kaldor JM, Day NE, Band P, *et al.* Second malignancies following testicular cancer, ovarian cancer and Hodgkin's disease: an international colaborative study among cancer registries. *Int J Cancer* 1987, **39**, 571–585.
20. Hellbardt A, Rene-Olivier M, Obradovic M, Mermillod B, Paunier J-P. The risk of second cancer (sc) in patients treated for testicular seminoma. *Int J Rad Oncol Biol Phys* 1990, **18**, 1327–1331.
21. Kim JH, Chu FC, Woodard HQ, Melamed MR, Huvos A, Cantin J. Radiation-induced soft-tissue and bone sarcoma. *Radiology* 1978, **129**, 501–508.
22. Glanzmann C, Schultz G, Lütolf UM. Lond-term morbidity of adjuvant infradiaphragmatic irradiation in patients with testicular cancer and implications for the treatment of stage I seminoma. *Radiother Oncol* 1991, **22**, 12–8.
23. Duchesne GM, Horwich A, Dearnaley DP, Nicholls J, *et al.* Orchidectomy alone for stage 1 seminoma of the testis. *Cancer* 1990, **65**, 1115–1118.
24. von der Maase H, Engelholm SA, Rørth M, *et al.* The DATECA study group. Non-seminomatous testicular germ cell tumours in Denmark 1976–80. *Acta Radiol Oncol* 1984, **23**, 255.

Acknowledgements—We are grateful to all the departments of oncology, radiotherapy and pathology because they made it possible to investigate hospital records and review histological specimens. We thank Gitte Grandt Pedersen for typing the manuscript.

Eur J Cancer, Vol. 29A, No. 5, pp. 668–671, 1993.
Printed in Great Britain

0964–1947/93 $6.00 + 0.00

Induction Chemotherapy and Intensification with Autologous Bone Marrow Reinfusion in Patients with Locally Advanced and Disseminated Breast Cancer

Nanno H. Mulder, Paula O.M. Mulder, Dirk Th. Sleijfer, Pax H.B. Willemse, Els van der Ploeg, Wil V. Dolsma and Elisabeth G.E. de Vries

In 56 patients with disseminated or locally advanced breast cancer it was attempted to reach a state of no evidence of disease by a remission induction regime containing prednisone, 5-fluorouracil, methotrexate, doxorubicin and vincristine. If successful, patients received an intensification regimen consisting of cyclophosphamide (7 g/m²) and etoposide (1.5 g/m²) with autologous bone marrow reinfusion. The complete remission rate of the induction regimen was 52% and the partial remission rate 42%. 32 patients received the intensification regimen. Two toxic deaths occurred. The median time to disease progression in the group with disseminated disease was 15 months. After a median observation of 4 years, 11 out of 19 patients with locally advanced breast cancer were free of disease. It is concluded that this approach may lead to prolonged disease-free survival in patients with locally advanced breast cancer, but does not influence the survival in disseminated disease.
Eur J Cancer, Vol. 29A, No. 5, pp. 668–671, 1993.

INTRODUCTION

PATIENTS WITH disseminated breast cancer are not curable by present day chemo-, hormonal or immunotherapy or combinations of treatment modalities. Even in cases of a complete remission, characteristically reached in approximately 20% of patients by chemotherapy, remission duration is limited and all patients relapse [1]. Partial remissions are even shorter and median survival is less than 2 years [2]. Patients with locally advanced disease, inflammatory breast cancer, thoracic wall infiltration or gross axillary involvement have a prognosis comparable to those with systemic disease [3–5].

Breast cancer is, however, sensitive to chemotherapy, and a case can be made for better results of more intensive regimens [6]. Therefore, the use of ablative doses of chemotherapy with bone marrow rescue seems to be a valid option to study. The results of such treatment in patients who have measurable tumours indicate high remission rates but usually short remission duration and survival [7–16].

These results parallel those with acute leukaemia, where cure is uncommonly achieved by ablative treatment in relapse, but the same therapy in remission can cure [17]. Clearly, the optimal

Correspondence to N.H. Mulder.
N.H. Mulder, D. Th. Sleijfer, P.H.B. Willemse and E.G.E. de Vries are at the Department of Medical Oncology; P.O.M. Mulder is at the Department of Intensive Care Medicine; E. van der Ploeg is at the Department of Surgical Oncology; and W.V. Dolsma is at the Department of Radiotherapy, University Hospital Groningen, Oostersingel 59, 9713 EZ Groningen, The Netherlands.
Received 5 Oct. 1992; accepted 25 Nov. 1992.