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## Original Paper

# The Role of Radiotherapy in the Local Management of Dermatofibrosarcoma Protuberans

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**Dermatofibrosarcoma protuberans (DFSP), a fibrohistiocytic tumour of intermediate malignancy, has a strong tendency to recur locally. Wide local excision is the recommended treatment modality. A retrospective analysis was performed on 38 consecutive DFSP patients presenting to The Netherlands Cancer Institute, to define the role of radiotherapy. Of the 21 patients treated surgically (all with negative resection margins) seven recurred, a local control probability of 67%. Combined modality treatment was given to 17 patients. Prior to radiotherapy, these patients experienced 33 occurrences of DFSP, but after irradiation only three recurrences were seen, a local control probability of 82%. These results are in keeping with the recent literature where increasing value is being given to both adjuvant and curative radiotherapy in the local management of DFSP. We recommend radiotherapy in DFSP patients where repeated surgery may cause mutilation or functional impairment. © 1997 Elsevier Science Ltd.**

**Key words:** dermatofibrosarcoma protuberans, radiotherapy, surgery, treatment outcome

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## INTRODUCTION

DERMATOFIBROSARCOMA PROTUBERANS (DFSP) is a rare mesenchymal neoplasm involving the skin and subcutis. DFSP is classified as a “fibrohistiocytic” tumour, is composed of fibroblast-like and histiocyte-like cells, and is of intermediate malignancy. The cell of origin is thought to be a fibroblast or myofibroblast with histiocytic properties [1–3].

DFSP is predominantly seen on the trunk, back and proximal extremities, but a few facial and genital localisations have been described [2–8]. Males are more commonly affected than females, primarily in the third and fourth decade of life. A report of a congenital case has also been published [2, 3, 9].

The tumour arises in previously healthy skin or in scars, areas of repeated trauma [10], vaccination sites [11, 12] or irradiated skin [13]. It presents as a slowly growing multinodular or plaque-like mass, fixed to the skin and often surrounded by a red-blue halo. Without any apparent cause,

the tumour may suddenly progress rapidly. Patients with enormous masses do not demonstrate cachexia as is usually seen with other advanced malignancies.

The clinical course is characterised by a strong tendency to recur locally after initial treatment, usually within 3 years. The disease-free interval between recurrences shortens progressively [2, 8, 14–16]. Pulmonary and regional lymph node metastases are rare, and are usually preceded by multiple local recurrences. The incidence is less than 5% [8, 13, 17–23].

Microscopically, a poorly circumscribed, cellular, spindle cell proliferation is seen in the dermis, which invariably shows irregular extension into the subcutaneous fat. The tumour has a storiform (rushmat-like) pattern, and up to 5 mitoses per high-power field may be seen. Myxoid or frank fibrosarcomatous areas may occasionally be present, either in the primary tumour or in the recurrences [2, 3, 24]. A melanin pigment-containing variant also exists: the Bednar tumour [2, 3].

Immunohistochemistry shows that tumour cells are positive for vimentin and CD34. The latter was thought to be a specific marker for endothelial cells, but is now known to

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have a broader reactivity. Its usefulness in DFSP is in distinguishing scar tissue from residual tumour [25–30], and in the differential diagnosis from benign fibrous histiocytoma and its cellular variant, both of which are CD34 negative.

Other differential diagnoses to be considered include atypical fibroxanthoma and malignant fibrous histiocytoma; these tumours show marked cellular pleomorphism in contrast to DFSP, which is cytologically relatively bland.

Cytogenetic analysis has been performed on a small number of cases, and a ring chromosome 17 has been described [31–33]. A balanced 46,XY,t(X;7) translocation has been found [34], as has a (2;17) translocation [35].

Wide local excision is the recommended treatment modality in DFSP. Moh's micrographic surgery is an elaborate technique, but recurrences after this type of surgery are seldom seen. Therefore, this procedure has been recommended when treating children and/or areas not suitable for extensive surgery [8, 36–46].

The role of radiotherapy is as yet undefined. However, local control can be achieved by radical radiotherapy [2, 47–54].

In an attempt to improve the understanding of the role of radiotherapy in the local management of DFSP, a retrospective analysis was performed on all consecutive DFSP patients presenting for treatment in The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital (NKI/AvL) between January 1978 and December 1994.

## PATIENTS AND METHODS

Between 1978 and 1994, 38 DFSP patients were treated in the NKI/AvL. Both patients treated primarily in our institute and those referred during the course of their disease were eligible for analysis. All pathology slides and reports were reviewed in our institute, including the cases where the primary surgery was performed elsewhere. Thus, the extent of surgery is known both for patients operated on elsewhere and patients who had surgery in the NKI/AvL.

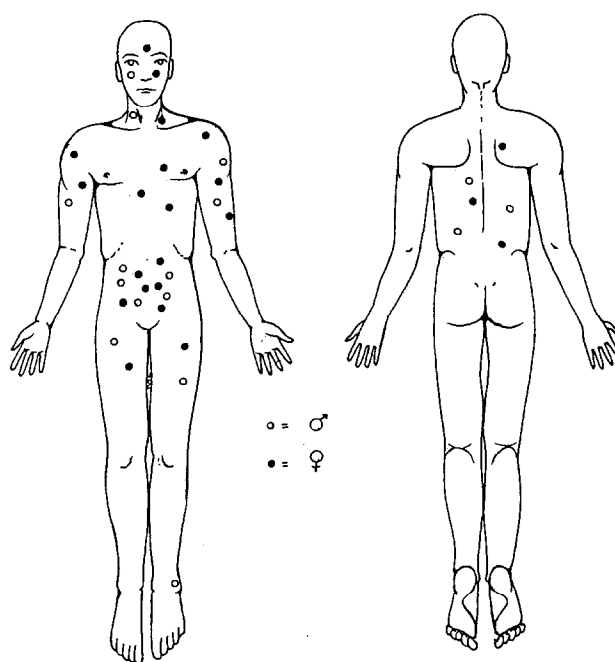
Wide negative surgical margins were defined as margins >1 cm after fixation.

A total of 22 females (median age 40 years, range 27–72 years) and 16 males (median age 38 years, range 21–81 years) were treated.

The most frequent localisations were the skin of the abdomen (11 patients, 29%) and the arms (8 patients, 21%). The back (6 patients, 16%), the face and neck (5 patients, 13%) and the legs (5 patients, 13%) were less often involved (see Figure 1).

Of 38 patients, 33 are still in follow-up. 3 have been lost to follow-up after 4, 10 and 14 years without evidence of DFSP. One patient died of intercurrent non-malignant disease 3 years after successful treatment for DFSP. The last patient died of a cytologically proven liver metastasis of rectal cancer without evidence of DFSP, which had been treated 4 years previously.

To analyse the role of radiotherapy, we divided our patient population into two groups; group I consists of 21 patients who had surgery only, group II of 17 patients who received postoperative radiotherapy at some time in the course of their disease. The indications for radiotherapy were: in 7 patients because of recurrent disease, in 7 patients because of narrow margins, in 5 patients because of positive margins and in 2 patients because of local infiltration anaesthesia as part of their surgery. A total of 4



**Figure 1. Tumour localisations. The abdominal wall was the most frequent localisation. There are no differences between males and females.**

patients had two of these indications for radiotherapy. None of our patients were irradiated for gross disease. 10 patients were irradiated as part of their initial treatment: 7 because of narrow margins, 2 because of positive margins and 1 for local infiltration anaesthesia. Two patients were irradiated at first recurrence, 4 at the second recurrence and 1 at the third recurrence. In all of them, the macroscopic tumour was removed before radiotherapy. None were irradiated for gross disease.

Of 17 irradiated patients, 1 had a total dose of 50 Gy, 13 had a total dose of 60 Gy, 1 patient had 64 Gy and 2 patients had 66 Gy. All patients were irradiated with daily fractions of 2 Gy. Electron beams were used for 11 patients, 6 patients received equally weighted mixed beam treatments (5 patients megavoltage photons and 1 patient 250 kV photons) (see Table 1).

All patients in the surgery alone group (group I) had repeated surgery, if necessary, until adequate wide negative surgical margins were obtained.

Time to local recurrence was analysed for first, second and third recurrence by the Kaplan–Meier method. Differences were tested by the log-rank test for significance.

## RESULTS

### Results of surgery only

21 of the 38 patients were surgically treated only, consisting of a “wide local excision” proven by negative surgical margins. If margins were narrow or positive (<1 cm after fixation), repeated surgery was performed until negative margins were obtained. A total of 1–4 operations (mean 2.5) per patient were performed.

Of these 21 surgically treated patients, 7 recurred. 6 of these patients recurred once, after a mean disease-free survival of 68 months (range 17–120 months). Of these 6 patients, 5 were operated on in referring hospitals, 1 in our institute. Since receiving salvage treatment in the NKI/AvL,

Table 1. Radiotherapy specifications

Radiotherapy indications	Number	Radiotherapy dose	Number	Radiotherapy technique	Number
Recurrence	7	25 × 2 Gy	1	Electrons	11
Narrow margins	7	30 × 2 Gy	13	Electrons plus 250 kV photons	1
Positive margins	5	32 × 2 Gy	1	Electrons plus megavoltage photons	5
Local infiltration anaesthesia	2	33 × 2 Gy	2		

5 of them are controlled and in follow-up for a mean of 56 months (21–111 months), 1 was lost to follow-up after 48 months without evidence of disease. One patient suffered two recurrences (both while treated elsewhere), was salvaged surgically in the NKI/AvL, and remains disease free for 42 months.

12 out of the 14 patients without recurrence were operated on in NKI/AvL, 2 in referring hospitals. All these 14 patients are in continuing disease-free follow-up with a mean of 83 months (range 24–168 months).

#### Results of surgery and adjuvant radiotherapy

The remaining 17 patients were irradiated during the course of their disease, because of the various reasons as shown in Table 1. 4 patients had two indications for radiotherapy. 10 patients were irradiated as part of their initial treatment, 2 patients after the first recurrence, 4 patients after the second and 1 after the third recurrence. Prior to radiotherapy, these 17 patients experienced 33 occurrences of DFSP. After radiotherapy, only 3 recurrences were seen; twice after 13 months, once after 40 months. The 14 patients without recurrence since radiotherapy have a mean DFS of over 9 years, varying from 4 to 17 years.

#### Analysis of recurrences

A total of 24 recurrences were seen; 15 first recurrences, 6 second recurrences and 3 third recurrences (Figure 2).

The interval between the primary treatment and the first recurrence compared to the interval between the first recurrence and the second was more or less the same. Patients with 3 recurrences had their third recurrence relatively soon after their second. Recurrences in our patient population also tended to occur long after the primary treatment. The median time to relapse was approximately 3.5 years for first and second recurrence, but approximately 1 year for third relapse. The last relapse in the patients with recurrences was not seen until after more than 10 years follow-up.

#### Treatment institute

Of the 38 patients, 14 were primarily treated elsewhere and then referred to the NKI/AvL (13 because of recurrence). 24 were treated in our institute since first DFSP presentation. Therefore, the population of patients treated in the NKI/AvL is a negatively selected group. Despite this, there is a trend towards better local control after treatment in our institute (Figure 3).

#### Analysis of prognostic factors

Since 14 patients were first treated outside the NKI/AvL, the information we have on primary tumour size is limited. Therefore, size cannot be analysed as a prognostic factor for recurrences.

We tested site as a prognostic factor. Compared to other localisations, DFSP tends to recur less frequently when

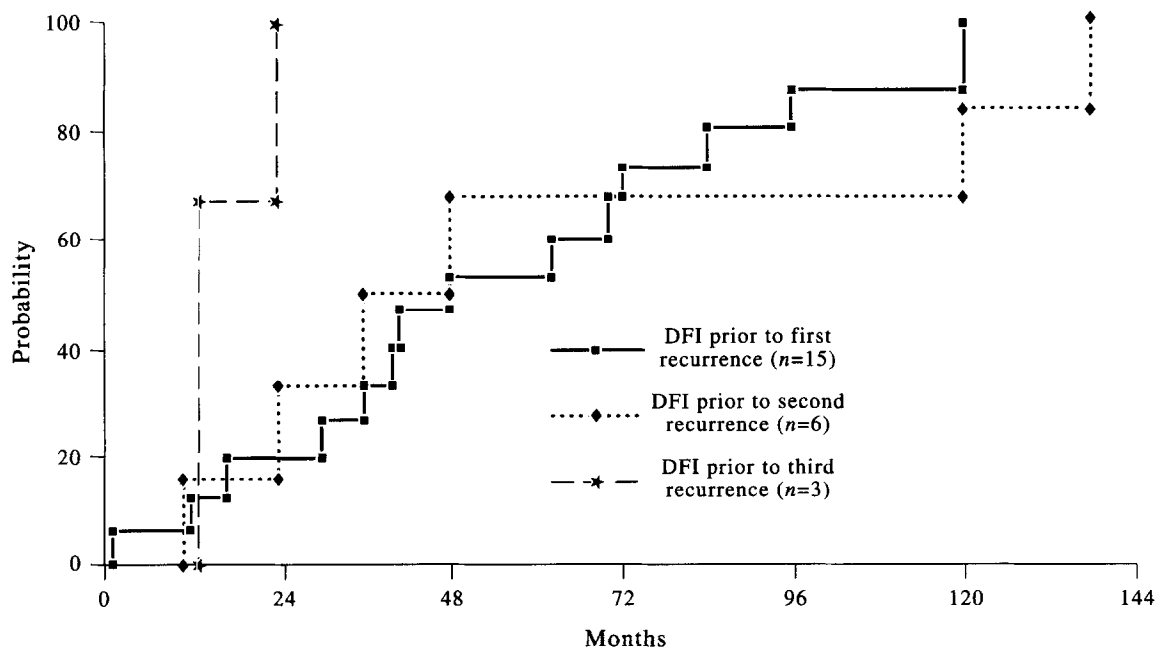
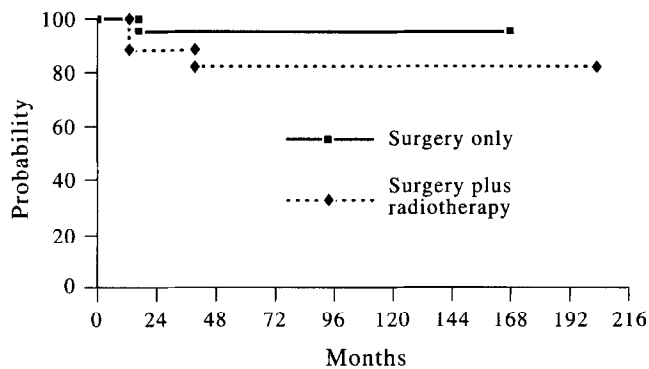


Figure 2. Cumulative incidence of recurrences in recurring patients. The disease-free interval (DFI) between recurrences is shown, per group normalised to 100%. No progressive shortening of the disease-free interval prior to recurrences, as is described in the literature, was seen. A relapse can be a late event.



**Figure 3. Local control after treatment in the NKI/AvL. There is a trend towards better local control after referral to The Netherlands Cancer Institute, though differences were not statistically significant (log-rank test).**

localised on the trunk. However, this difference was not statistically significant ( $0.1 < p < 0.2$ ).

No difference between males and females was found among the patients with recurrences.

#### *Surgery failures*

Of the 7 patients recurring after surgery only, 2 were operated on twice, 5 patients had 3 operations. This was not significantly different from the number of surgical interventions among the patients without recurrences. None of these patients received radiotherapy as part of their salvage treatment. Based upon our patient analysis, we cannot tell whether they would have been better off with earlier radiation.

#### *Radiotherapy failures*

3 patients failed after adjuvant radiotherapy. One patient recurred at the portal margin after  $33 \times 2$  Gy with 17 MeV electrons. The second patient recurred in the skin transplant flap applied to close the surgical defect. She was irradiated because of positive margins after two operations to a dose of  $30 \times 2$  Gy with 8 MV photons without bolus. (Adding bolus would have increased skin dose and might have prevented the recurrence.) The last patients recurred in field despite  $33 \times 2$  Gy with 8 MeV electrons after two surgical failures. All these patients underwent successful salvage surgery.

## DISCUSSION

We have shown in our series that radiotherapy may play a role in the local management of DFSP. The patients treated by surgery only invariably had a wide local excision but recurrence nevertheless occurred in 7 of 21 cases (1 patient twice), a local control probability of 67%. Of 17 patients with less adequate surgery (positive or narrow margins or local infiltration anaesthesia) who received adjuvant irradiation, only 3 recurred, a local control of 82%. The results are not statistically significant (log-rank test) due to the relatively small number of patients.

Most published series study the results of surgery in treating DFSP. The chance of a local recurrence is related to the tumour-free resection margins including fascia or periosteum beneath the tumour, but less to the diameter of the lesion [8, 40, 44].

Radiotherapy, particularly in older publications [48, 50], is discouraged, but these reports rarely specify the irradiation dose and techniques applied. However, in the recent literature, increasing value is being given both to postoperative and curative radiotherapy (Table 2).

According to Taylor and Helwig [55], "radiotherapy has no apparent influence upon the subsequent course of the tumour, but few data were available as to the amount of radiation administered". However, only 6 out of 115 patients were irradiated in this series. Rinck and associates [52] showed that inadequate radiotherapy, either in total dose or in applied technique, may not control DFSP. In this paper, DFSP recurred after 30 Gy in 9 fractions (50 kV X-rays), whereas another tumour was controlled after 60 Gy in 30 fractions (110 kV X-rays). Oehler and associates [51], based on an analysis of 19 patients, suggested that postoperative irradiation should be given to all patients to prevent major radical surgery. Marks and associates [49] successfully irradiated 3 patients with radiotherapy as the sole treatment modality (67–75 Gy).

Suit and associates [53, 54] treated 4 patients and controlled them all with radical radiotherapy, 3 of these were recurrences following prior surgery (67–75 Gy by means of electron beams and brachytherapy). Another 15 patients were irradiated postoperatively (50–78 Gy); 12 of them were controlled (33–124 months follow-up). In 1956, Doornink controlled 3 large DFSP of the scalp by giving 45

**Table 2. Literature concerning radiotherapy in managing DFSP**

Author, year (Ref)	Number of patients	Recurrences in surgery patients	Recurrences in surgery plus radiotherapy patients	Recurrences in radiotherapy patients
McGregor 1961 [50]	10	0/8 2–6 years FU	0/1 lost to FU	0/1 20 years FU
Taylor 1962 [55]	115	4/98 (extent of surgery unknown) 1–17 years FU	?/6	
Rinck 1982 [52]	1, 46 years FU			1/2 (1 patient with 2 tumours) NED after 60 Gy failure after 30 Gy
Oehler 1988 [51]	19	0/4 (all complete resection) 2–17 years FU	4/19 (extent of surgery unknown) 3–29 years FU	
Marks 1989 [49]	10, 1–8 years FU		0/9 (all complete resection)	0/1
Suit 1995 [53]	16, 1–10 years FU		2/12 (extent of surgery unknown)	0/4
Suit 1996 [54]	18, 1–13 years FU		3/15 (12/15 positive margins)	0/3 (~9 years FU)
This study	38, 1–22 years FU	7/21	3/17	

FU, follow-up.

Gy in 15 fractions with 140 Kv X-rays using a 3 mm Al filter [47].

The regression after curative irradiation is slow and a small fibrotic lesion may remain present; a similar phenomenon is seen after radiotherapy for desmoid tumours [56].

A prospective randomised trial in a rare tumour such as DFSP is not feasible. Treatment regimes must be based on experience. Wide local surgery, if anatomically possible, can provide adequate local control of DFSP. We recommend radiotherapy in DFSP patients where repeated surgery may cause mutilation or functional impairment. A high probability of local control may then be expected.

Patients should be followed up for life because recurrence can be a late event.

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