From the Orthopedic Oncology Group, University Hospital, Lund, Sweden

Prognosis in soft tissue sarcoma

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Cover:
Magnetic resonance tomogram (T2 weighted image) showing a Grade IV malignant fibrous histiocytoma in the right rectus femoris muscle of an 86-year-old woman. The tumor is separated from the bone and the large vessels by a layer of apparently uninvolved muscle and fascia. (See also Figure 10).

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Contents

Summary

Consensus is still lacking as regards which surgical procedures carry a low risk of local recurrence in soft tissue sarcoma.

A series of 81 patients with Grades I-IV soft tissue sarcomas of the locomotor system, with a minimum follow-up time of 6 years, was studied with respect to local recurrence. All the patients were operated on with wide surgical margins without adjunctive therapy. A subclassification of these margins was performed. A wide F margin, obtained by myectomy of one or several muscles, but not of the total compartment, was found to be a safe procedure, giving a local recurrence rate of less than 0.1. This applied when surgery was performed without a preceding open biopsy. For subcutaneous tumors a wide S margin, including the deep fascia, also resulted in a small local recurrence rate, even if performed after incisional biopsy or marginal surgery.

More than one half of all patients with soft tissue sarcoma in the locomotor system have tumors suitable for surgical treatment with a wide F or a wide S margin for a low local recurrence risk.

A wide margin where the surgical dissection had transgressed the muscle where the tumor was located or areolar tissue in cases of extramuscular tumor (wide AM margin) was found to result in a higher local recurrence rate, around 0.25.

There is no generally accepted staging system for soft tissue sarcomas. Those systems in most common use were not constructed after statistical multivariate analysis, whereby the strongest prognostic factors may be identified.

The staging system of the American Joint Committee (AJC), the system of Hajdu, and the Surgical Staging System (SSS) were evaluated with respect to their ability to discriminate patients with different chances for survival in a series of 122 patients operated on with wide or radical surgical margins. None of the three systems could identify patient-groups with a significantly different prognosis better than that, that could simply be done by the histologic malignancy grading of the tumors.

A multivariate analysis of variables thought to be of prognostic significance for local recurrence and survival was performed in a series of 144 patients with Grades III and IV soft tissue sarcomas. Marginal surgery, extracompartmental tumor location, and tumor necrosis increased the risk of local recurrence. Local recurrence, male sex, malignancy grade IV, tumor necrosis, and increasing tumor size increased the risk of tumor-related death. In a new multivariate analysis that only included patients operated on with a wide or radical margin, it was found that male sex, malignancy grade IV, tumor necrosis, and tumor size >10 cm could be used as prognostic

predictors. Survival decreased when there was an increasing number of these risk factors present. For patients with 0 or 1 risk factor, the 6-year survival rate was 1.0 as compared with 0.33 in patients with 3 or 4 risk factors. The risk factor model could also be applied after surgery with a marginal margin. For patients with 3 or 4 risk factors, the type of surgical treatment seemed to be of less importance for the prognosis. Many of these patients presumably had micrometastases at the time of presentation.

The risk-factor model was evaluated by multivariate analysis in a new series of 88 patients with Grades III and IV soft tissue sarcomas. In this series the prognostic significance of malignancy grade, tumor necrosis, and tumor size >10 cm was verified. Male sex was not a risk factor in this analysis. Instead, intratumoral vascular invasion, seldom discussed in the prognosis of soft tissue sarcoma, significantly increased the risk of tumor-related death. In this series a model with four risk factors, including vascular invasion, could also be constructed. Patients with 0 or 1 risk factor had a 3-year survival rate exceeding 0.9 . Patients with 3 or 4 risk factors had a survival rate of 0.2 .

The findings in the multivariate analyses suggest that all the patients with a Grade III sarcoma-except when the tumor is larger than 10 cm *and* shows necrosis or vascular invasion-and all the patients with a Grade IV sarcoma, but no other risk factor, could be adequately managed simply with treatment of the primary tumor. These cases, estimated to comprise around one half of all patients with Grades III and IV tumors, should not be included in trials with chemotherapy.

Prognosis in Grades III and IV sarcomas is probably determined more by additional risk factors in the host and tumor than by the type of surgical treatment; local recurrence after surgery with a wide or radical margin is in many cases probably only a predictor of a grave prognosis and not the reason for metastases.

Introduction

The treatment of patients with a soft tissue sarcoma was mainly surgical until about 15 years ago. Since then, surgery, combined with radiotherapy and chemotherapy, has become increasingly common (Eilber et al. 1985, Lindberg 1985, Suit et al. 1985 a, b). Local, i.e., limb-sparing surgery, supplemented with *radiotherapy*, has diminished the high amputation rate – previously considered necessary for local control – without increasing the risk of local recurrence (Leibel et al. 1982, Eilber et al. 1985, Enneking & McCarthy 1985). *Chemotherapy* has been claimed to eradicate micrometastatic disease, which is responsible for overt metastases and death in patients without signs of dissemination of the disease at the time of diagnosis of the primary tumor. The effect of adjuvant chemotherapy in soft tissue sarcoma is, however, still being debated (Antman et al. 1985, Bramwell et al. 1985, Rosenberg et al. 1985, Alvegård 1986, Potter et al. 1986). Before the era of combined therapy, some patients, even with highly malignant tumors, escaped local recurrence and metastatic disease after only local surgery. However, the definition of the surgical procedures and of the host and tumor variables that characterized these patients has met with difficulties. Thus, the anatomic definition of surgical procedures with a low risk of local recurrence is still controversial; and except for histologic malignancy grade, there is no consensus as to which other tumor and host factors can be used to identify the patient in whom the risk of metastatic disease is low. Consequently, there is no generally accepted staging system for soft tissue sarcomas such as exists for most types of cancer. Because there are complications from radiotherapy and chemotherapy (Eilber et al. 1985, Lindberg 1985), the identification of patients who can be cured by only local surgery is important. Several studies by the Orthopedic Oncology Group in Lund have addressed the definition of surgical margins and prognostic factors in patients with soft tissue sarcomas and were summarized by Rydholm (1983).

This presentation summarizes the findings of the further analyses by the Group (constituted by orthopedic surgeons, pathologists, medical oncologists, cytologists, radiologists), which have aimed at defining those combinations of surgical, tumor, and host variables that indicate a good chance of cure for the soft tissue sarcoma patient by exclusively local surgery (Rydholm, Rööser, Persson 1986; Rydholm, Rööser 1987; Rööser, Attewell, Rydholm 1987; Rööser, Attewell, Berg, Rydholm 1987a, b; Rööser, Berg, Ranstam, Rydholm, Willén unpublished data).

The local recurrence rate after surgical procedures with different margins was analyzed to define which procedures were adequate to achieve a low risk of local recurrence.

Risk factors for tumor-related death were analyzed to define low- and high-risk patients. Data from these analyses were used to construct models for prognostication.

Definitions, patients, statistics

Definitions

Soft tissue sarcomas were malignant mesenchymal tumors of the locomotor system, i.e., trunk and extremities. Tumors in the head, viscera, retroperitoneum, and those strictly located in the cutis were excluded, as were Kaposi's sarcoma, dermatofibrosarcoma protuberans, and Stewart-Treeves tumors.

Histologic type was determined in accordance with the WHO International Reference Centre for Histological Definition and Classification of Soft Tissue Tumors (Enzinger et al. 1969).

Histologic malignancy grading was determined on a four-grade scale based on mitotic frequency, cellularity, cellular atypia, and cellular pleomorphism. Grade I was the least and Grade IV the most malignant tumor (Kindblom et al. 1975, Angervall 1981, Markhede et al. 1982, Merck et al. 1983, Rydholm et al. 1984).

Necrosis was determined microscopically in slides from different parts of the tumor. When the longest crossection of one necrotic area in a slide occupied at least the diameter of one low power field = 4.3 mm. (Carl Zeiss 10x ocular, 2.5x plane lens), the tumor was classified as necrotic. Tumors with less, or no, necrosis were defined as nonnecrotic. The length of the largest necrotic area found microscopically was also analyzed as a continuous variable. Only areas of coagulation necrosis, with or without leukocytic infiltration, were taken into account (Figure 1). Cystic areas were included only when at least one slide from the cyst wall showed coagulation necrosis. Areas with mucinous degeneration or avascular myxoid cysts were not considered to be necrotic, and neither were areas of hyaline scar tissue or fibroblastic proliferation, which possibly represent organizing necrosis.

Vascular invasion was defined as microscopic evidence of tumor extension into the lumen and/or through the wall of a blood or lymphatic vessel of any dimension (Figure 2). Sarcomas that could be demonstrated as having originated from the wall of a vessel, i.e., some leiomyosarcomas and hemangiotheliosarcomas, were also considered to show vascular invasion.

All histologic evaluation were performed by N. O. Berg and H. Willén, Department of Pathology, University Hospital, Lund, pathologists in the Orthopedic Oncology Group.

Compartmentalization of a tumor was determined according to Enneking et al. (1980, 1981). Thus, a subcutaneous tumor without involvement of the deep fascia was intracompartmental. A deep tumor confined to one compartment was intracompartmental whether or not it was intramuscular or extramuscular. All the other tumors were extracompartmental.

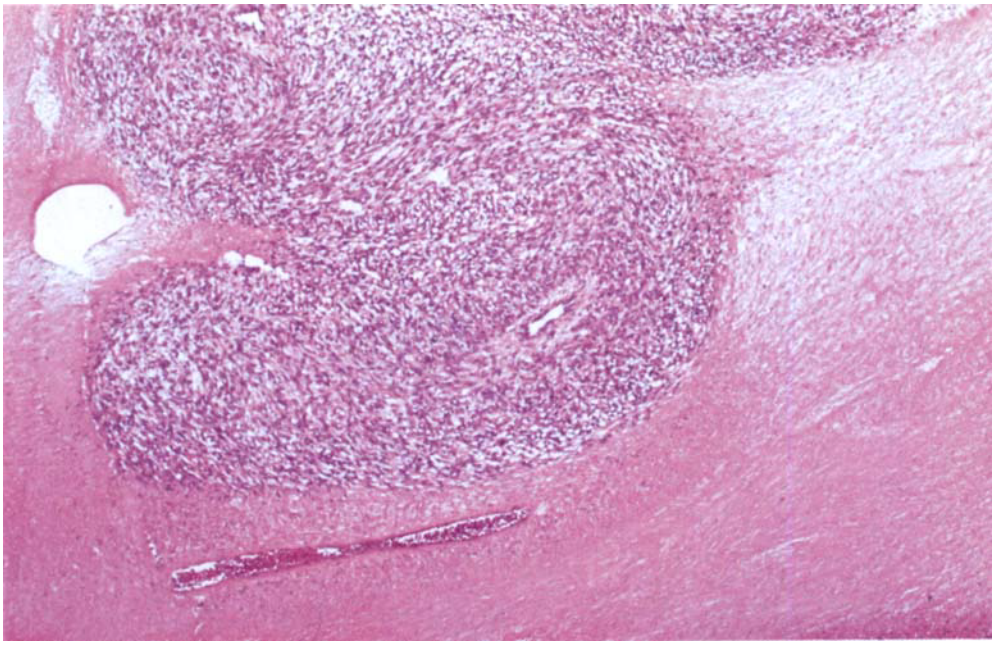

Figure 1a. Coagulation necrosis (bottom) in a Grade III leiomyosarcoma in the thigh of a 64-year-old woman. The patient died of metastases 28 months after diagnosis of the primary tumor. Photo by N.O. Berg, M.D., Department of Pathology, University Hospital in Lund (Figures 1 and 2).

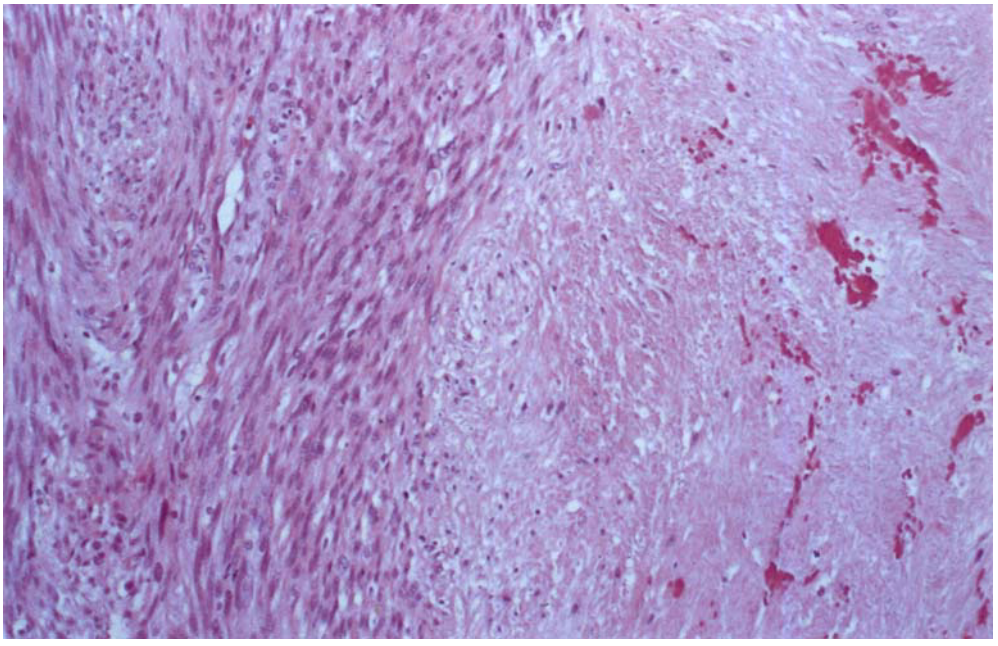

Figure 1b. Coagulation necrosis (right) in a Grade III leiomyosarcoma in the lower leg of a 67-year-old woman. The patient was alive with no sign of disease 60 months after diagnosis of the primary tumor.

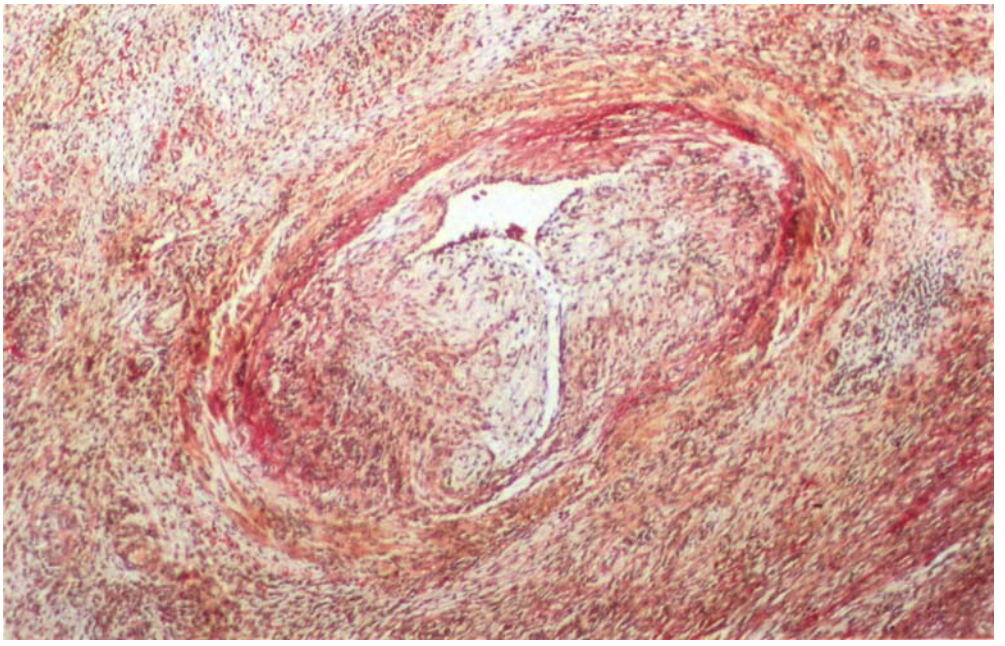

Figure 2a. Vascular invasion by tumor in a Grade III malignant fibrous histiocytoma in the lower leg of a 64-year-old woman. A soft tissue metastasis of the ipsilateral thigh diagnosed at 36 months was widely excised. There were no signs of disease 48 months after diagnosis of the primary tumor.

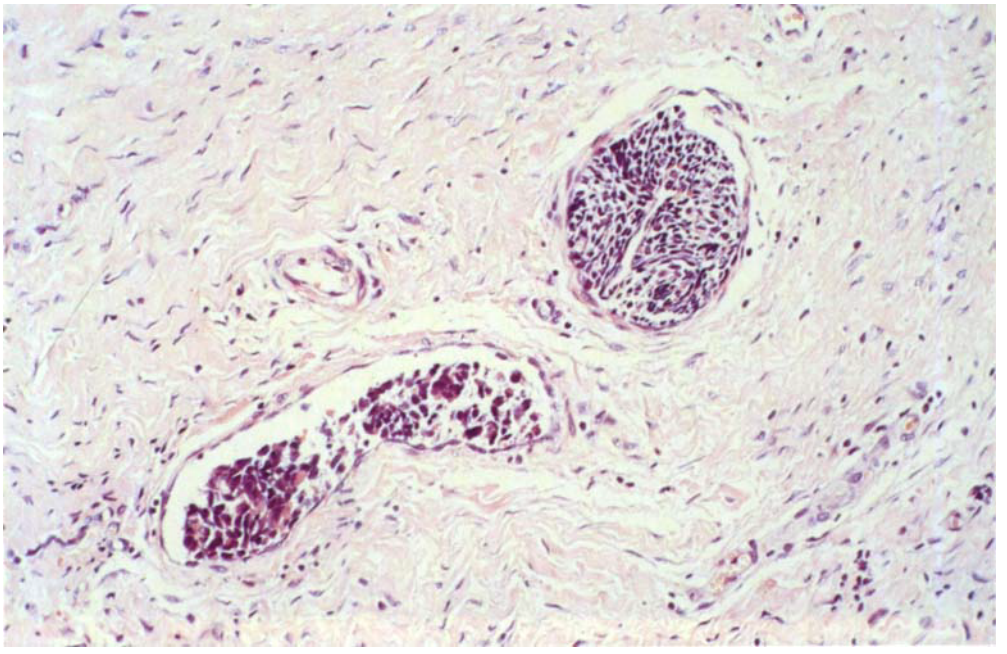

Figure 2b. Vascular invasion by tumor in a Grade IV synovial sarcoma at the knee of a 57-year-old man. The patient died of metastases 11 month after diagnosis of the primary tumor.

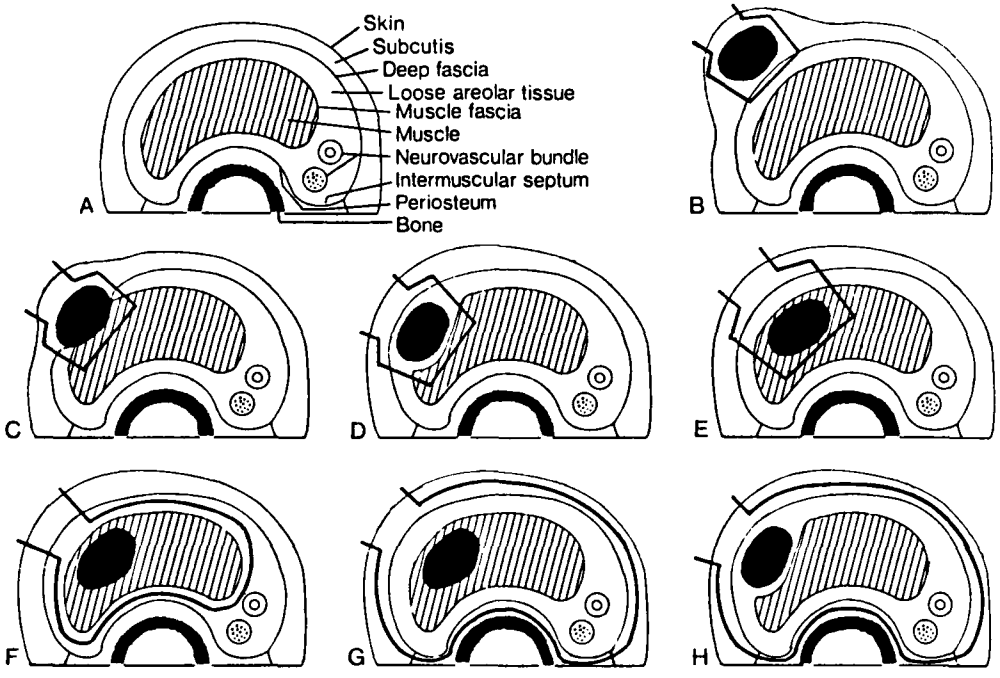

Figure 3. Schematic illustration of tumor depth, compartmentalization, and surgical margins in soft tissue sarcoma.* Surgical margins are those defined by the Surgical Staging System (SSS, Enneking et al. 1980, 1981) and those used in this report (Rydholm & Rööser 1987). W=Wide, R=Radical.

A. Cross-section. Anatomy

Tumor depth	Compartmentalization	Margin	
		SSS	This report
B. Superficial	Intra	W	W–S
		R**	R**
C. Superficial and deep	Extra	W	W–AM
D. Deep, extramuscular	Intra	W	W–AM
E. Deep, intramuscular	Intra	W	W–AM
F. Deep, intramuscular	Intra	W	W–F
G. Deep, intramuscular	Intra	R	R
H. Deep, extramuscular	Intra	R	R

* Deep extracompartmental tumors, for instance, in the groin or popliteal fossa, are not illustrated.

** The difference between a wide and a radical margin is the amount $\leqslant$5 cm, of the surrounding subcutaneous tissue.

Surgical margins (Figure 3). A marginal margin (shelling out, enucleation, excisional biopsy) was defined according to Enneking et al. (1980, 1981). An excision undertaken with the intention of achieving a more superior margin was classified as marginal if the tumor was exposed, even if in only a small part of the specimen. A wide margin implied en bloc excision of the tumor with a surrounding cuff of macroscopically uninvolved tissue (Enneking et al. 1980, 1981). No microscopic tumor growth should be seen at the excision margin. Three wide-margin subtypes were defined (Rydholm & Rööser 1987). A wide S margin (*s*ubcutaneous) resulted when a subcutaneous tumor that did not involve the deep fascia was excised with a cuff of healthy subcutaneous tissue and with the deep fascia beneath the tumor included in the specimen. A wide F margin (*f*ascia) was achieved when a deep tumor was excised with the specimen bounded by uninvolved and unopened fascia in all directions (primary myectomy) without the removal of the total compartment; the margin was constituted by muscle fascia and/or deep fascia or major septae. A wide AM margin (*a*reolar, *m*uscle) was obtained when a deep tumor was widely excised and where some or all boundaries of the specimen were not fascia, but muscle tissue or loose areolar tissue. A radical margin was defined according to Enneking et al. (1980, 1981). Amputation was not regarded as a surgical margin per se, but was classified according to the type of margin achieved.

Patients

Series I comprised all the 237 patients with a soft tissue sarcoma of the locomotor system diagnosed from 1964 through 1978 in the southern region of Sweden (1.3 million inhabitants). The series was population-based and unselected, because patients treated outside the Orthopedic Oncology Group in Lund were also included. None of the patients had overt metastases at the time of diagnosis of the primary tumor, and all of them were treated by at least a marginal excision. Fifty-nine patients had Grade I or Grade II tumors, and 178 patients had Grade III or Grade IV tumors. Data for these patients have been reported earlier (Rydholm 1983). Since that report, follow-up has continued, and the minimum follow-up time in the series was now 6 years or until death, whereas the maximum follow-up time was 21 years. No patient was lost to follow-up.

Series II included 88 patients with Grades III and IV soft tissue sarcomas of the locomotor system diagnosed from 1979 through 1983 in the southern region of Sweden; these patients were operated on with at least marginal surgery and did not have overt metastases at the time of diagnosis of the primary tumor. The series comprised all patients in the region who fulfilled these criteria. The minimum follow-up time was 3 years or until death and the maximum, 7 years. No patient was lost to follow-up.

From these two series, patients were categorized into five groups: A-E (Figure 4).

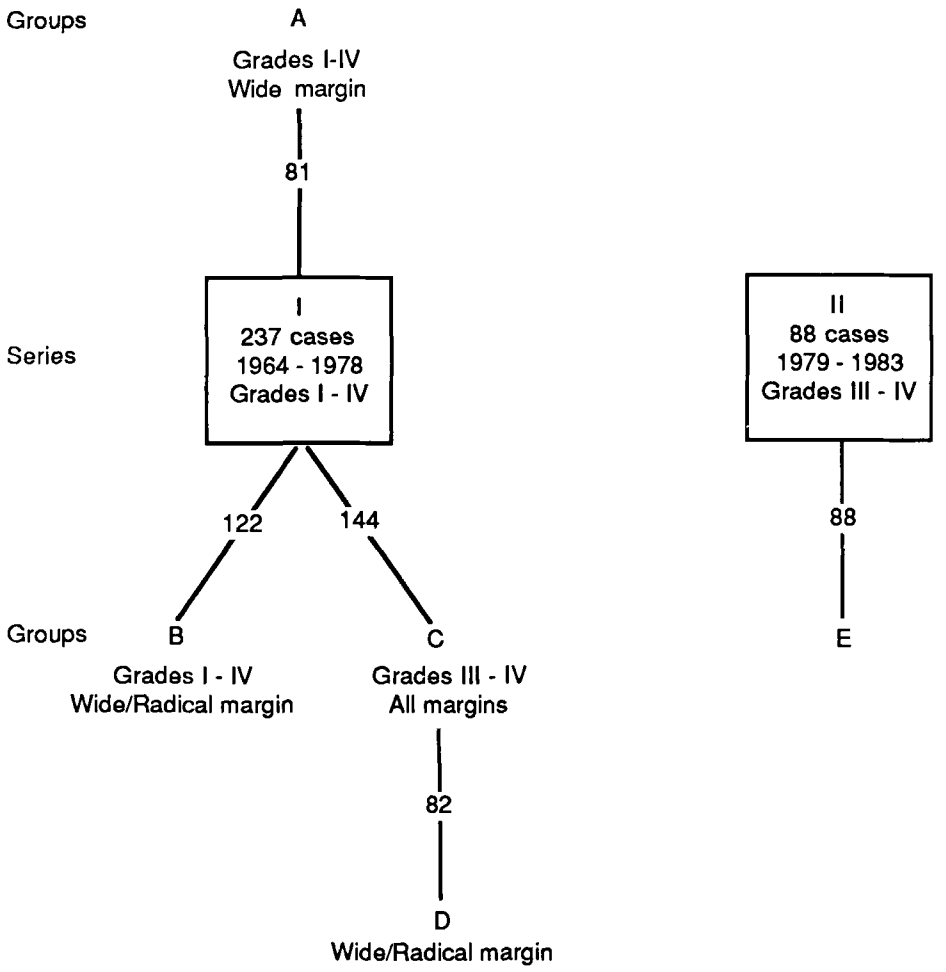

Figure 4. Accrual of patients with soft tissue sarcomas from two series to five different groups. In group A the local recurrence rate after surgery with different types of wide margins was analyzed. In groups B–E prognostic variables for tumor-related death were analyzed.

Statistics

In the multivariate analyses the Cox proportional hazards model was used (Kalbfleisch & Prentice 1980). This model analyses the joint influence of prognostic variables on the *theoretically expected* end event-in this presentation, *local recurrence* or *tumor-related* death. Allowance is made for censoring of the patients. The prognostic influence of a variable is calculated as its regression coefficient (ß)-the higher the value of which, the more important it is. The risk of local recurrence or tumor-related death associated with a certain value of a variable, the Relative Risk (RR), is expressed as $e\beta^x$ where

x is the difference between the actual value of the variable and another value (= 1 in case of a dichotomous variable). When analyzing local recurrence as a prognostic factor for tumor-related death, the hazard (death) rate was not assumed to be equal before and after a local recurrence, and the variable was thus analyzed as dependent of time.

The significance of the prognostic variables included in the model was assessed by the Wald statistic.

Observed cumulative rates of local recurrence and survival, as opposed to the *expected values*, were calculated by the life-table technique and expressed as Kaplan-Meier curves. The curves were compared by the generalized Wilcoxon test.

Crude overall rates for local recurrence and survival were compared by two-sided chi-square tests with Yates continuity correction. When comparing continuous variables the two-sided Student's *t*-test for difference of means was used.

In all statistical analyses performed, results were considered significant if the obtained *P* values were <0.05. However, when evaluating independence between prognostic variables obtained by multivariate analysis, several (n) tests were carried out simultaneously. With a significance level of 5 percent, there was a random chance for significance in one out of 20 tests. Therefore, the *P* value required to achieve a significance level of 5 percent in an individual test was set at 0.05/n according to the correction formula of Fisher.

The statistical analyses were performed by R. Attewell, Department of Occupational Medicine, University Hospital, Lund and J. Ranstam, Department of Community Health Sciences at Malmö General Hospital, University of Lund.

Local recurrence after different surgical margins

Marginal excision of a sarcoma is unsuitable as definitive treatment due to the high risk of local recurrence with which it is associated. The Surgical Staging System (Enneking et al. 1980) defines two separate margins superior to the marginal margin with decreasing risk of local recurrence: viz., the wide and the radical margin. However, depending on which type of tissue constitutes the wide margin, a refined classification with three different subtypes can be made: wide S, F, and AM (see definitions). After surgery with these three types of wide margin, the local recurrence rate was evaluated in group A. Also, the local recurrence rate after a wide F margin was analyzed in Grades III and IV tumors specifically; a wide excision of high-grade malignant tumors has been associated with a high risk of local recurrence (Enneking et al. 1980, 1981).

Patients and methods (group A)

In 81 patients, all collected from series I, the local recurrence rate after surgical treatment alone with different types of wide margins was analyzed (Rydholm & Rööser 1987). Of 237 patients in series I, 115 were operated on with a marginal margin, 23 with a radical margin, and 18 other patients received adjunctive radiotherapy or chemotherapy. All of these patients were excluded, thus leaving 81 patients for analysis. There were 55 men and 26 women; their mean age was 54 (6–87) years; and the mean size of the superficial tumors was 4.5 (1–11) cm, compared with 6.5 (1–13) cm for the deep ones. Malignant fibrous histiocytoma was the most common histogenetic type (23 cases), and the thigh was the most common location (29 cases). Nine tumors were Grade I or II, and 72 tumors were Grade III or IV. All the tumors were classified with respect to compartmentalization (Table 1). The surgical margin achieved was wide S in 34 cases, wide F in 14 cases, and wide AM in 33 cases. Included in these figures are six amputations, which thus were not classified separately, but according to the margin achieved by this procedure.

By adding 4 patients from series II and excluding 2 from series I (with Grades I and II tumors), a specific analysis was made of the local recurrence rate in 16 consecutive patients with deep, intracompartmental Grades III and IV tumors (Rydholm et al. 1986). This subset thus comprised 12 of the 14 patients in group A who were operated on with a wide F margin. In this subset, there were 7 men. Malignant fibrous

Table 1. Local recurrence rate related to compartmentalization, histologic malignancy grade (I–IV), and three subtypes of the wide surgical margin in 81 patients with soft tissue sarcomas

Surgical margin	Intra				Extra				Total
	I	II	III	IV	I	II	III	IV	
Wide AM	–	1/1	1/5	1/3	0/2	3/6	0/8	3/8	9/33
Wide S	0/4	0/9	2/13	0/8	–	–	–	–	2/34
Wide F	0/1	0/1	1/3	0/9	–	–	–	–	1/14
Total	0/5	1/11	4/21	1/20	0/2	3/6	0/8	3/8	12/81

histiocytoma was the most common histogenetic tumor type (6 cases) and the thigh, the most common location (11 cases). All 16 patients were operated on from 1970 through 1980 by primary myectomy (wide F margin). Surgery thus consisted of removal of one or several muscles, but not the total compartment. Preoperative fine-needle aspiration cytology was performed in 13 cases. No adjunctive radiotherapy or chemotherapy was given. For these 16 patients the minimum follow-up time was 5 years or until death, and the maximum follow-up time was 14 years.

Observations

Twelve of the 81 patients developed local recurrence. Eight of these occurred within 2 years after surgery and 11 within 5 years. The local recurrence rate was 9/33 (0.27) after a wide AM margin, 2/34 (0.06) after a wide S margin, and 1/14 (0.06) after a wide F margin (Table 1, Figure 5). The local recurrence rate was thus lower after an S or F margin than after an AM margin ($P < 0.05$). Neither the histologic grade of the tumor (Grades I and II versus Grades III and IV) nor the number of operations performed to reach the definitive margin influenced the local recurrence rate (Tables 1 and 2). There were no more local recurrences in intracompartmental tumors than in extracompartmental ones after a wide AM margin (Table 1).

Table 2. Local recurrence rate related to number of surgical procedures performed to achieve the final margin in 81 patients with soft tissue sarcomas

	Number of procedures	
	1	>1
Wide AM	2/9	7/24
Wide S	0/7	2/27
Wide F	1/14	–
Total	3/30	9/51

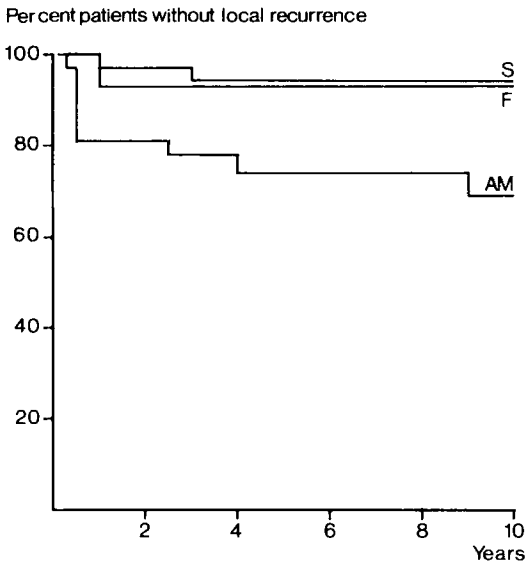

Figure 5. Cumulative rate of freedom from local recurrence in 81 patients with Grades I–IV soft tissue sarcomas operated on with different types of wide margins. (n_S 34, n_F 14, n_{AM} 33).

Among the 16 patients with Grades III and IV tumors operated on with primary myectomy, there was one local recurrence, diagnosed 10 months postoperatively.

Comments

The local recurrence rate was higher after a wide excision with a margin constituted of muscle or areolar tissue (AM margin) than with a margin made up of subcutaneous fat and deep fascia (S margin for subcutaneous tumors) or muscle fascia (F margin for deep tumors). The subclassification of wide margin that we have constructed is thus meaningful. The local recurrence rate after surgery with a wide S or a wide F margin, irrespective of malignancy grade, was as low as that following a "radical resection" as reported by Enneking et al. (1980, 1981). These findings indicate that surgical treatment with an S margin is sufficient for most subcutaneous tumors. This margin can always be achieved by local surgery. Local surgery with a wide F margin also suffices as local treatment for intramuscular tumors even when high-grade. The wide F margin is obtained by primary myectomy, i.e., surgery without prior open biopsy or marginal excision. A myectomy after an open biopsy could not be designated as a wide F margin; the fascial containment was broken before definitive surgery, and thus the margin is, at best, a wide AM margin.

That primary definitive surgery with a wide F margin is a low-recurrence risk procedure for sarcoma is further supported by Berlin et al. (1987), who reported a combined Lund-Gothenburg series of 113 patients with virgin deep-seated sarcomas of the extremities. The only treatment given was surgery performed without prior open

biopsy. The local recurrence rate was 2/43 (0.05) after a wide F margin (in that report called wide extramuscular margin) compared with 6/34 (0.18) after a wide AM margin (called wide intramuscular margin). The local recurrence rate was no higher in Grades III and IV tumors than in those of Grades I and II.

An accurate preoperative diagnosis as regards benign versus malignant tumor can, in most cases, be made from the combined information obtained by clinical, cytologic, and radiologic (CT, MRI) examinations (Åkerman et al. 1985, Pettersson et al. 1987, Rydholm et al. 1987). Thus, primary surgery signifies only a small risk of removing a benign tumor with an unnecessary large margin because of a falsely malignant preoperative diagnosis. This risk is acceptable; the functional loss after myectomy of even several muscles is most often small (Markhede & Nistor 1979, Markhede & Stener 1981), as is also the case after wide excision of a superficial tumor.

In several modern treatment protocols, local surgery is routinely combined with radiotherapy to decrease the risk of local recurrence. However, radiotherapy, which is not without side-effects, is not indicated after surgery with a wide S or a wide F margin. Thus, more than half of the patients in group A required only local surgery by these margins to achieve local control. Conversely, the local recurrence rate after an AM margin was 0.27; but a local recurrence risk of 70 per cent has been reported after wide excision of high-grade, extracompartmental tumors (Enneking 1983). Radiotherapy may, therefore, be considered after surgery with an AM margin. So-called conservative surgery-probably including both marginal and some wide AM margins-combined with radiotherapy, has recently been reported to give local recurrence rates around 15 per cent or less (Eilber et al. 1985, Enneking & McCarthy 1985, Suit et al. 1985, Suit et al. 1985). Thus, limb-sparing, combined treatment should be an alternative to amputation or disarticulation in patients where local surgery alone is associated with a high recurrence rate. Local surgery and radiotherapy should also be considered for tumors where myectomy is unsuitable (previous surgery) or where a radical excision, although nonablative, implies sacrifice of major nerves, such as in the posterior thigh, the calf, or the anterior forearm.

Survival related to patient, tumor, and treatment variables

Soft tissue sarcomas demonstrate a remarkable biological heterogeneity: There are many different histogenetic types and large variations in local aggressiveness and metastatic potential.

Prognostication of soft tissue sarcoma patients is thus important. Patients with a low risk of metastatic disease should not be subjected to chemotherapy, considering its potentially dangerous side-effects. Further, comparison between different series of patients treated according to different protocols is only possible by using a generally accepted staging system. Systems in current use are those of the American Joint Committee (AJC) (Russell et al. 1977), the system of Hajdu (Hajdu 1979), and the Surgical Staging System (SSS) (Enneking et al. 1980).

The prognostic power of these three systems was evaluated and found poor (group B). Therefore, variables with potential prognostic value with respect to survival in Grades III and IV tumors were analyzed (groups C, D, E). A prognostication model derived from multivariate analysis was constructed (group D) and tested in another series of patients (group E).

Evaluation of the systems of AJC, Hajdu, and SSS

Patients and methods (group B)

Almost all the 122 patients in series I who were operated on with a wide or radical margin could be staged according to AJC (n117), Hajdu (n121) and SSS (n120) and the cumulative survival rate at 6 years was analyzed (Rööser et al. 1987). No patient had overt metastases at the time of diagnosis of the primary tumor.

AJC uses for staging histologic malignancy grade (low, intermediate, high), tumor size ($\gtrless$5 cm), and tumor extension (invasion of bone, major vessel, or nerve). Hajdu's system is based on the number of negative prognostic signs, which are high histologic malignancy grade (two-grade scale), deep tumor location, and tumor size >5 cm.

The SSS was designed for both bone and soft tissue lesions and also provides guidelines for the type of surgical treatment. A tumor is classified with respect to surgical grade. For soft tissue sarcomas this grading is mainly based on Broders' et al. (1939) histologic grading (Broders I-II = low, Broders III-IV = high). The second variable is tumor compartmentalization (intracompartmental or extracompartmental) according to location.

When translating our four-grade malignancy scale into the AJC system, Grades I and II tumors were classified as low malignant tumors (Grade 1), Grade III tumors as intermediate malignant tumors (Grade 2), and Grade IV tumors as highly malignant tumors (Grade 3). For the SSS and Hajdu systems, Grades I and II tumors were classified as low malignant tumors (Grade I) and Grades III and IV, as highly malignant tumors (Grade II). An analysis was also made for the SSS by classifying Grades I, II, and III tumors as low malignant tumors and Grade IV as highly malignant tumors.

Observations

In the AJC system only Stage IIIb patients had a markedly lower survival rate than the other stages (0.60 versus 0.91 in Stage IIIa, $P=0.08$). No difference between any other two consecutive stages was significant (Table 3).

Table 3. Cumulative 6-year survival rate in different stages in the AJC system in 117 patients with soft tissue sarcomas operated on with a wide or radical margin. G=malignancy grade, T=tumor-size extension

Stage	n	Fraction survivors
Ia, (G1,T1, N0, M0)	14	1.0
Ib (G1,T2, N0, M0)	13	0.92
IIa (G2,T2, N0, M0)	20	0.84
IIb (G2,T2, N0, M0)	25	0.91
IIIa (G3,T1, N0, M0)	11	0.91
IIIb (G3,T2, N0, M0)	34	0.60

In the Hajdu system, Stage III patients had a survival rate of 0.65, which was less than for Stage II patients (0.94), ($P<0.01$). No other difference in pairs of consecutive stages was significant (Table 4). In the analysis of the SSS with Grades I and II classified as low malignant tumors, no two consecutive stages showed a significantly different survival rate (Table 5). With malignancy Grades I, II, and III classified as low malignant tumors, the only significant difference in pairs of consecutive stages was between I B (0.96) and II A (0.69) ($P<01$) (Table 5), although the survival in stage II B was lower, 0.48.

Table 4. Cumulative 6-year survival rate in different stages in Hajdu's system in 121 patients with soft tissue sarcomas operated on with a wide or radical margin

Stage	n	Fraction survivors
0	7	1.0
I	27	0.89
II	34	0.94
III	53	0.65

Table 5. Cumulative 6-year survival rate in different stages in the Surgical Staging System in 120 patients with soft tissue sarcomas operated on with a wide or radical margin

Stage	n[a]	Fraction survivors	n[b]	Fraction survivors
I A	16	0.94	44	0.90
I B	11	1.0	28	0.96
II A	62	0.78	34	0.69
II B	31	0.74	14	0.48

[a] Histologic Grades I and II=low, (G_1), III and IV=high (G_2),
[b] Histologic Grades I to III=low (G_1), IV=high (G_2).

Comments

The lowest survival rate was 0.48 (Stage II B in the SSS). The high survival rates are probably due to the fact that the base series was population-based and thus unselected, comprising many patients with small tumors; 0.4 had tumors <5 cm. Furthermore, only patients with tumors in the trunk and extremities, those without overt metastases at presentation, and those subjected to a reasonable treatment, i.e., surgery with a wide or a radical margin, were included.

All three staging systems could separate patients with different prognoses only as well as could histologic malignancy grade alone. It has been repeatedly demonstrated that histologic malignancy grade is a strong prognostic factor in soft tissue sarcoma. Because not all the patients having tumors of the highest malignancy grade died from their disease, more variables are apparently necessary for prognostication. However, the other variables used in these three systems did not increase their prognostic power significantly.

By the methods that can now be applied to histologic grading, malignancy grading on two levels (Hajdu, SSS) is too crude; grading in four groups can separate different prognostic groups (Kindblom et al. 1975, Angervall 1981, Merck et al. 1983, Angervall et al. 1986). There is a strong association between two of Hajdu's variables, size and depth (Rydholm 1983). Thus, the use of both variables probably does not increase the discriminating capacity substantially.

The concept of tumor compartmentalization (SSS) was introduced by Enneking et al. (1980). It is important in the classification of surgical margin, but its prognostic power as regards survival remains to be proven. Stage A (intracompartmental) sarcoma includes subcutaneous tumors that, as a group, are much smaller than deep sarcomas, which comprise the majority of Stage B tumors. Thus, a possible prognostic influence of compartmentalization could be explained by different tumor sizes. In fact, in a multivariate analysis of several factors, including tumor size and compartmentalization, the latter variable was shown not to have significance with regard to survival. (Rööser et al. 1987).

Neither Russell et al. (AJC) (1977) nor Hajdu (1979) specified the type of treatment of the primary tumor in the series that formed the basis for their respective staging system. Any possible influence of local control on prognosis was, therefore, not considered. To be really useful, a staging system must be able to predict prognosis in relation to a defined treatment. In addition, sarcomas of the trunk and the extremities should probably be staged separately from those of the head and viscera (Enneking et al. 1980, Heise et al. 1986). The findings in this analysis show that only strong factors contributing independently to prognostication should be included in staging systems. Owing to complex covariations, independent factors can be identified only by multivariate analysis. Such analyses were performed in groups C, D, and E.

Prognostic factors in grades III and IV soft tissue sarcomas

Prognostic factors were analyzed in three patient groups: C, D, and E.

Patients and methods (group C)

From the 237 patients in series I, the 59 cases with Grades I and II sarcomas were excluded. In the remaining 178 patients, compartmentalization data was missing in 8, data on tumor size in 1, and the slides were not available for evaluation of necrosis in 25. Thus, complete clinical and histologic data permitting a multivariate analysis of potential prognostic variables were available in 144 patients (Rööser et al. 1987). There were 87 men and 57 women; the mean age was 56 (16–88) years; and the mean tumor size was 7 (1–30) cm. Malignant fibrous histiocytoma was the most common histogenetic tumor type, 38 cases (Table 6). Tumor necrosis was defined as a necrotic area >4.3 mm in any slide preparation from the tumor.

Twenty-two patients were also treated by radiotherapy and 18 by chemotherapy using nonstandardized protocols.

Because a previous multivariate analysis including these 144 patients could not detect any prognostic difference between patients operated on with a wide or a radical margin (Rydholm 1983), they were grouped together (16 radical and 66 wide excisions). Fourteen variables were analyzed for influence on the expected local recurrence rate

and 15 variables (including local recurrence) for effect on the expected survival (Table 6). Age and size were analyzed as continuous variables.

Table 6. Variables multivariately analyzed for prognostic influence on local recurrence and tumor-related death in 144 patients with Grades III and IV soft tissue sarcomas

Variable	n	Patients with local recurrence	Patients died of tumor
Age			
<50 years	51	14	17
>50 years	93	34	38
Sex			
Male	87	27	40
Female	57	21	15
Symptoms			
No pain	105	32	29
Pain	39	16	26
Histologic type			
Malignant fibrous histiocytoma	38	13	15
Leiomyosarcoma	22	7	10
Liposarcoma	19	5	6
Neurogenic sarcoma	17	8	10
Synovial sarcoma	16	6	6
Other types	32	9	8
Malignancy Grade			
III	63	19	15
IV	81	29	40
Tumor necrosis			
No	69	17	14
Yes	75	31	41
Tumor depth			
Superficial	47	11	10
Deep	97	37	45
Size			
<6 cm	77	22	19
>6 cm	67	26	36
Compartmentalization			
Intracompartmental	90	20	26
Extracompartmental	54	28	29
Fine-needle aspiration			
Performed	93	31	38
Not performed	51	17	17

(Continued on next page)

Table 6 (continued)

Variable	n	Patients with local recurrence	Patients died of tumor
Number of operations for primary tumor			
1	72	28	30
>1	72	20	25
Surgical margin			
Marginal	62	37	33
Wide or radical	82	11	22
Radiotherapy			
No	122	38	43
Yes	22	10	12
Chemotherapy			
No	126	43	45
Yes	18	5	10
Local recurrence			
No	96	-	19
Yes	48	-	36

A second multivariate analysis of survival was carried out in an enlarged series of 177 patients. In this analysis, those 25 cases whose slides were missing and those 8 patients with no information about tumor compartmentalization were included. Thus, the effect of tumor necrosis and compartmentalization were not evaluated here, and a total of 13 variables were included in the multivariate model.

Observations

Risk factors for local recurrence

Forty-eight of the 144 (0.33) patients had local recurrence. Marginal surgery (Relative Risk, RR 6), tumor necrosis (RR 2), and extracompartmental tumor location (RR 2) increased the risk of local recurrence (Table 7).

Table 7. Risk factors for local recurrence in 144 patients with Grades III and IV soft tissue sarcomas

	Relative risk	*P* value
Marginal surgery	5.9	0.0001
Tumor necrosis	2.1	0.01
Extracompartmental location	1.9	0.003

Risk factors for tumor-related death

Fifty-five out of 144 patients (0.38) died of the tumor. Local recurrence (RR 9), histologic Grade IV (RR 3), male sex (RR 3), tumor necrosis (RR 2), and increasing size increased the risk of tumor-related death (Table 8, Figure 6).

The risk of tumor-related death increased exponentially with a RR of 1.1 for each centimeter of increment in tumor size regardless of absolute size. The increase in risk associated with an increment in size from 5 to 10 cm was 1.7, from 10 to 15 cm 1.7, and from 5 to 15 cm 3.0.

The order and strength of the risk factors were the same in all the patients when compared with only those patients who had a local recurrence.

Table 8. Risk factors for tumor-related death in 144 patients with Grades III and IV soft tissue sarcomas

	Relative risk	*P* value
Local recurrence	9	0.0001
Grade IV	3.4	0.0002
Male sex	3.4	0.0002
Tumor necrosis	2.4	0.007
Increasing size	1.1 for 1 cm increment	0.0002

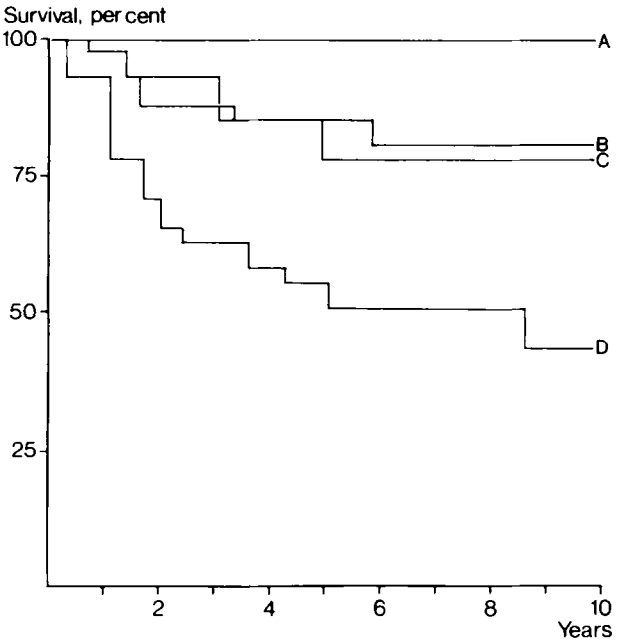

Figure 6. Cumulative survival rate, related to malignancy grade and tumor necrosis in 82 patients with soft tissue sarcomas operated on with a wide or radical margin (P=0.002).

A. Grade III, no necrosis, n23
B. Grade IV, no necrosis, n19
C. Grade III, necrosis, n17
D. Grade IV, necrosis, n23

Marginal surgery also increased the risk of tumor-related death (RR 2). When the higher risk of local recurrence after marginal surgery was taken into account, however, by the use of a separate interaction variable in the multivariate model, the relative risk of tumor-related death associated with marginal surgery per se was 0.98 (P=0.1).

In the multivariate analysis of survival in 177 patients, the same variables were significant, with the same order of prognostic importance as in the smaller series, except for tumor necrosis and compartmentalization, which were not analyzed.

Independence of risk factors

When assessing the independence of the significant prognostic variables, 21 tests were simultaneously performed. By using the formula of Fisher, the P value required for a significance level of 0.05 in an individual test was set at 0.05/21=0.0024. By this method, the only significant covariations found were between size and necrosis, between compartmentalization and surgical margin, and between local recurrence and surgical margin (Table 9). Without the correction formula, covariation was also found between malignancy grade and necrosis, and between local recurrence and necrosis. The mean size of extensively necrotic tumors was 8 cm as compared with 5 cm in nonnecrotic ones.

Table 9. Tests for independence in pairs of significant prognostic variables. A P value <0.0024 indicates a significant covariation with Fisher's correction. A P value <0.05 indicates a significant covaration without Fisher's correction

	Sex	Size	Necrosis	Compart-mentaliza tion	Local recurrence	Margin[a]
Malignancy grade	0.4	0.06	0.03	0.4	0.6	0.2
Sex		0.3	1.0	0.5	0.6	0.09
Size			0.001	0.7	0.2	0.2
Necrosis				0.5	0.05	0.5
Compartmen-talization					0.005	0.002
Local recurrence						0.0001

[a] Wide or radical versus marginal.

Considering tumor necrosis and pain from the tumor, 29/39 (0.7) painful and 46/105 (0.4) painless tumors were necrotic ($P<.01$). There was no significant relation between the histogenetic type of sarcoma and the relative frequency of necrotic tumors.

Patients and methods (group D)

Five of the factors significantly influencing local recurrence and survival in group C, namely, extracompartmental tumor location, male sex, histologic malignancy grade IV, tumor necrosis, and increasing tumor size were entered into a new multivariate analysis of survival (Rööser et al. 1987). Local recurrence as a prognostic variable for survival was omitted for predicting the prognosis from the patients' immediate postoperative status. Also, a reasonable treatment was required; from the 144 patients, those 62 operated on with a marginal excision were excluded. The analysis was thus performed in only those 82 patients operated on with a wide or radical surgical margin. There were 55 men, with a mean age of 55 (18–80) years and a mean tumor size of 7 (1–18) cm. There were 42 patients with a Grade IV sarcoma; 14 patients had tumors >10 cm, and 40 tumors were classified as necrotic tumors.

Observations

Risk factors for tumor-related death

Twenty-two of 82 patients (0.25) died of their tumor disease. Male sex (RR 8), histologic Grade IV (RR 7), and tumor necrosis (RR 5) increased the risk of tumor-related death after a wide or radical excision (Table 10). When the continuous variable tumor size was dichotomized, 10 cm best separated patients with a different prognosis (RR 6). The number of patients who died of their tumor disease for each value relative to the four prognostic variables is shown in Table 11. Tumor compartmentalization did not in itself increase the risk of tumor-related death.

Table 10. Risk factors for tumor-related death in 82 patients with Grades III and IV soft tissue sarcomas operated on with a wide or radical margin

	Coefficient(ß)	Relative risk	*P* value
Male sex	2.1	7.8	0.0002
Malignancy Grade IV	1.9	6.7	0.001
Tumor size >10 cm	1.7	5.5	0.002
Tumor necrosis	1.5	4.5	0.0004

Table 11. Distribution of 82 patients with Grades III and IV soft tissue sarcomas operated on with wide or radical margin relative to four prognostic varables

Variable	n	Tumor-related deaths
Sex		
Male	55	19
Female	27	3
Malignancy Grade		
IV	42	17
III	40	5
Tumor size		
>10 cm	14	7
<10 cm	68	15
Tumor necrosis		
Yes	40	17
No	42	5
Total	82	22

Patients and methods (group E)

The Cox proportional hazards model was used to evaluate the validity of the risk factors of tumor-related death, previously identified in group D (male sex, histologic Grade IV, tumor size >10 cm, tumor necrosis) in another unselected and population-based series of 88 patients with Grades III and IV soft tissue sarcomas of the locomotor system (series II), (Rööser et al. unpublished data).

Complete clinical data and histologic slides were available in all the cases. Diagnosis of local recurrence was confirmed by histologic examination in all but 1 case.

Tumor necrosis was analyzed both according to the previous criterion (>4.3 mm) and as a continuous variable, utilizing the length of the largest microscopically necrotic area found when examining slides from different parts of the tumor.

Also analyzed was a new variable: microscopic vascular invasion by tumor, which was recently shown to be a risk factor in soft tissue sarcoma (Trojani et al. 1984). Vascular invasion was observed in 23 of the 88 tumors. In addition, local recurrence as a potential risk factor for tumor-related death was included in the multivariate model. There were 44 men and 44 women, and the mean age was 61 (22–88) years. The mean tumor size was 7 (1–30) cm, and 23 tumors were larger than 10 cm. Fifty-eight tumors were deep, and the thigh was the most common location (36 cases). Forty-six patients had Grade IV tumors. Malignant fibrous histiocytoma was the most common histogenetic type (27 cases).

Four patients were operated on with a radical margin and 60, with a wide margin. In 13 cases the wide margin was achieved by excision of one of several muscles, but not the total compartment without prior open biopsy (primary myectomy). Twenty-four patients were operated on with a marginal excision, the majority being either intentionally marginal and planned in cooperation with the radiotherapist or intended to be wide, but the tumor was exposed in some small area. Twelve of the marginally operated on cases received postoperative radiotherapy by fractionated doses to a total of 51 Gy. Radiotherapy was also given to 1 patient in whom the margin first was considered to be marginal. Reexamination showed that the specimen was bounded, however, by a layer of uninvolved fascia. Thus, the margin was reclassified as wide.

As a part of the Scandinavian Sarcoma Group (SSG) study, 8 randomized patients were given systemic postoperative chemotherapy (Adriamycin 60 mg/m^2 body-surface area, on nine occasions). Seven patients diagnosed before the start of the SSG study also received this treatment, the indications being large tumor size and/or the highest malignancy grade. All of these 15 patients were included in the analysis because no effect of chemotherapy was found in the SSG study (Alvegård 1986).

Observations

Local recurrence

The local recurrence rate was 5/64 (0.08) after a wide or radical excision, 1/12 (0.08) after a marginal excision and radiotherapy, and 7/12 (0.6) after marginal excision only (P=0.0001 for the difference between the two former groups and the latter group).

Metastasis

Thirty of 88 patients (0.34) developed metastases. In 25 cases, these were pulmonary only, whereas in 4 cases, bone, soft tissue, regional lymph nodes, or viscera were involved, and in 1 patient there was dissemination to both the lungs and other sites. In 20 of the cases (0.67) the metastases were diagnosed within 1 year after primary surgery and in 22 (0.73) within 2 years.

Tumor-related death

Twenty-five of 88 patients (0.28) died of their tumor disease. The figure was 6/13 (0.5) in those with local recurrence and 19/75 (0.25) in those without local recurrence (NS). The death rate was 7/15 (0.5) in patients treated with adjunctive chemotherapy and 18/73 (0.25) in the others.

Risk factors for tumor-related death

Malignancy grade IV, tumor size >10 cm, and microscopic vascular invasion were risk factors for tumor-related death in the multivariate analysis (Table 12). Necrosis, defined as >4.3 mm in any slide preparation from a tumor, was not a significant risk factor (P=0.23). When the length of the largest necrotic area found was dichotomized, however, the presence of such an area >11 mm was found to be a risk factor (Table 12). Male sex and local recurrence were not prognostic for tumor-related death (P=0.73 and P=0.79). The distribution of patients and tumor-related deaths relative to the four significant prognostic variables are shown in Table 13.

Table 12. Risk factors for tumor-related death in 88 patients with Grades III and IV soft tissue sarcomas

	Relative risk	*P* value
Malignancy grade IV	4.0	0.02
Tumor size >10 cm	3.2	0.01
Tumor necrosis	3.0	0.02
Vascular invasion by tumor	2.6	0.02

Table 13. Distribution of 88 patients with Grades III and IV soft tissue sarcomas relative to four prognostic variables

Variable	n	Tumor-related deaths
Malignancy grade		
IV	46	21
III	42	4
Tumor size		
>10 cm	23	12
<10 cm	65	13
Tumor necrosis		
>11 mm	25	13
<11 mm	63	12
Vascular invasion by tumor		
Yes	23	12
No	65	13
Total	88	25

Comments: groups C, D, E

The risk factors for tumor-related death found in groups C, D, and E are summarized in Table 14. In group C, the high risk of local recurrence after marginal surgery and the strong association between local recurrence and tumor-related death (Markhede et al. 1982, Merck et al. 1983) was confirmed. Tumor necrosis also increased the local recurrence risk, as did extracompartmental tumor location.

Table 14. Risk factors for tumor-related death found in 3 different analyses of patients with Grades III and IV soft tissue sarcomas

Risk factor	Group C	Group D	Group E
Local recurrence	+	...	–
Malignancy grade IV	+	+	+
Male sex	+	+	–
Tumor necrosis			
>4.3 mm	+	+	–
>11 mm	...	...	+
Tumor size			
Continuously increasing	+	...	...
>10 cm	...	+	+

Confirming earlier findings, histologic Grade IV versus Grade III (Kindblom et al. 1975, Markhede et al. 1982, Merck et al. 1983) and large tumor size (Sears et al. 1980, Eilber et al. 1985) increased the risk of tumor-related death. Male sex also made the prognosis worse, which is not commonly reported, though shown by Hajdu et al. (1977), Wright et al. (1982), Chase & Enzinger (1985), and Alvegård (1986).

Tumor necrosis was a strong predictor of fatal outcome. This has also been shown by Ekfors & Rantakokko (1978), DeStefani et al. (1982), Costa et al. (1984), Trojani et al. (1984), Chase & Enzinger (1985), Donhuijsen et al. (1986), although the criteria for the classification of necrosis have differed. Necrosis increased the risk of both local recurrence and tumor-related death, which may indicate that local and distant aggressiveness are correlated in sarcoma. The prognostic strengths of the host and tumor-related risk factor were approximately the same before and after local recurrence, and also when there was no recurrence. This suggests that local recurrence and metastatic spread in many cases may be more two different expressions of malignant potential than causally related.

Marginal surgery doubled the risk of tumor-related death. This effect seemed to be mediated via the increased risk of local recurrence after a marginal excision. It may be, however, that there has been a bias, giving a higher risk for marginal surgery in tumors prone to disseminate. Mandard et al. (1981) found that the prognosis of soft

tissue sarcomas in the extremities was better after "adequate excision" than when macroscopic or microscopic tumor was left in the patient. However, microscopically infiltrating sarcoma, especially large ones, were adequately excised in a lower frequency than small, well-delineated tumors. These findings were interpreted as indicating a correlation between loco-regional and general malignancy.

Enneking (1983) has reported a close association between malignancy and infiltrative growth. However, it is not clear whether he includes infiltrative growth as a factor when determining grade. In the malignancy-grading system used in this presentation, infiltrative growth was not included; there seems to be no clear-cut covariation between histologic malignancy grade and infiltrative growth (Berg, Willén unpublished observations). Therefore, infiltrative tumor growth may be another prognostic factor for soft tissue sarcoma, as shown for many carcinomas.

In group D, only those patients from group C who were operated on with a wide or radical margin were included in the analysis. All the factors that increased the risk of death from tumor after surgery with all the margins were significant risk factors also after surgery with a wide or radical margin only. When tumor size was dichotomized, 10 cm best separated patients with different prognoses. In the staging systems of AJC and that of Hajdu, a tumor larger than 5 cm is considered to make the prognosis worse. This smaller figure may be due to the fact that sarcomas in the head and viscera were also included in the series from which these staging systems were derived. The criterion we found, 10 cm, was derived from multivariate analysis, whereby allowance was made for other factors covarying with size, such as malignancy grade and tumor necrosis.

In group E, a prognostic significance for tumor-related death was confirmed for three of the four risk factors previously identified in group D; histologic Grade IV, tumor size >10 cm, and tumor necrosis. Thus, further evidence is added to the previously found prognostic importance of necrosis.

Male sex was not a prognostic factor in group E, which was in contrast to what was found in groups C and D. The reasons for this are unclear.

Microscopic intratumoral vascular invasion, rarely discussed in the prognosis in soft tissue sarcoma (Mandard et al. 1981, Trojani et al. 1984, Chase & Enzinger 1985), was found to be a risk factor for tumor-related death, similar to what has been shown for several types of carcinoma (Willén 1984). If vascular invasion is used for prognostication, it is important to recognize that histologic evaluation requires an awareness of the artefacts that can simulate vascular invasion and that can result from traumatic handling or improper fixation of the tissue (Willén 1984).

Whereas local recurrence was a risk factor for tumor-related death in group C, it was not in group E. Here, local recurrence could not be proven to influence survival, which was also reported by Shiu et al. (1975), Leibel et al. (1982), Bramwell et al. (1985), Brennan et al. (1985). The difference in the findings made in groups C and E may be due both to an increased relative prognostic strength of risk factors unrelated to treatment in the latter series (vascular invasion was introduced and the extent of necrosis analyzed as a continuous variable) and to the generally good local control in the latter series during the minimum follow-up time of 3 years; only 12 of 88 patients were treated with marginal surgery without radiotherapy and altogether only 13 had a local recurrence.

Markhede et al. (1982) reported that in half of their cases with metastases, these appeared within 1 year after surgery. In their study, however, Grades I and II sarcomas were included. In Grades III and IV tumors, overt spread occurs earlier in the course of the disease (Rydholm 1983). Thus, in group E the proportion of patients whose tumor metastasized within 1 year was higher-namely, two thirds-relative to all the patients whose tumor metastasized.

Pulmonary metastases, at least less than 2.5 cm in diameter, probably grow with a constant doubling time, resulting in an exponential growth (Collins et al. 1956, Meyer 1972, Pearlman 1979). It can be calculated that a nodulus measuring 1 cm in diameter may in this way have doubled its volume 30 times from a single cell (Collins et al. 1956).

Doubling times for metastases from fibrosarcoma may range between 11 and 274 days (Pearlman 1979), and an average value of 42 days was reported for metastases from sarcomas of miscellaneous histogenesis (Spratt & Spratt 1964). Thus, it is reasonable to assume that any pulmonary metastasis that measures 1 cm or more within 1 year after diagnosis of the primary tumor – whether the spread took place by a single cell or a multicellular embolus – was implanted before surgery. This may apply to the majority of metastasizing Grades III and IV tumors.

Multivariate-derived prognostication models

Prognostication models were constructed in two patient groups: D and E.

Group D

There were 16 possible combinations of the four risk factors (male sex, Grade IV, tumor size >10 cm, tumor necrosis). The algebraic sum of the regression coefficients (ß), calculated for those risk factors present, was inversely related to the *expected* 6-year survival as calculated by the Cox model. This relation could also be expressed as a diminishing survival probability with an increasing number of risk factors present (1.0 for 0 factor, 0.98–0.96 for 1 factor, 0.89–0.78 for 2 factors, 0.45–0.25 for 3 factors, 0.02 for 4 factors).

Observed survival related to number of risk factors

The cumulative survival rate was calculated for three groups of patients. All the patients with 0 or 1 risk factor survived. The 6-year survival rate was 0.75 for patients with 2 risk factors and 0.33 for patients with 3 or 4 risk factors (Figure 7). The three Kaplan-Meier curves were pairwise different from each other. (P=0.009 for 0 or 1 factor versus 2 factors, P=0.003 for 2 factors versus 3 or 4 factors).

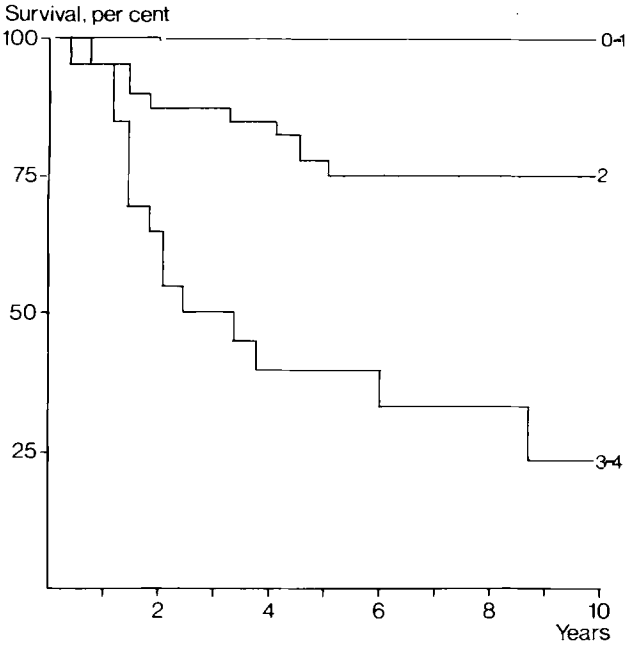

Figure 7. Cumulative survival rate with different number of risk factors in 82 patients with Grades III and IV soft tissue sarcomas after surgery with a wide or radical margin. (n_{0-1} 28, n_2 34, n_{3-4} 20).

Local recurrence related to number of risk factors

Five of 20 patients with 3 or 4 risk factors had local recurrence as compared with 6 of 62 patients with 2 risk factors or less (difference not significant).

Group E

The *expected* 3-year survival rates for the totally 16 possible combinations of the four risk factors (Grade IV, size >10 cm, necrosis, vascular invasion) were 0.96 for 0 factor, 0.92–0.86 for 1 factor, 0.76–0.60 for 2 factors, 0.40–0.22 for 3 factors, and 0.02 for 4 factors.

Observed survival related to number of risk factors

Cumulative survival rates for patients with 0 or 1, 2 and 3, or 4 risk factors were calculated in those 76 patients treated by wide or radical excision or marginal excision and radiotherapy (Figure 8). Thus, those 12 treated with marginal surgery without radiotherapy were excluded. The 3-year survival rate was over 0.9 for the 38 cases with 0 or 1 risk factor.

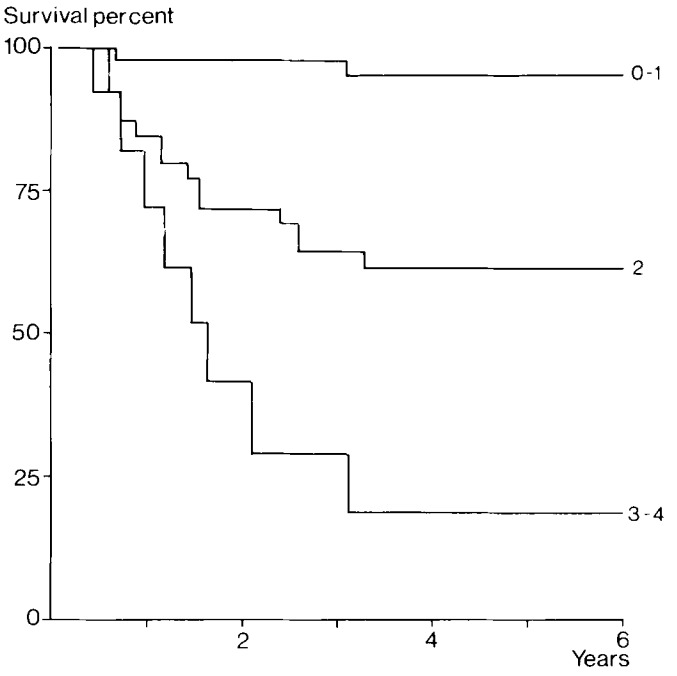

Figure 8. Cumulative survival rate related to number of risk factors in 76 patients with Grades III and IV soft tissue sarcomas operated on with a wide or radical margin, or with a marginal margin and radiotherapy.
(n_{0-1} 38, n_2 26, n_{3-4} 12).

For the 26 patients with 2 risk factors, the 3-year survival rate was 0.65. No patient in this group was treated with marginal surgery only. Twelve of the 76 patients had 3 or 4 risk factors and a 3 year survival rate of 0.2.

The Kaplan-Meier curves for patients with a consecutively higher number of risk factors were pairwise different from each other ($P=0.001$ and $P=0.001$ for 0 or 1 factor versus 2 factors, $P=0.04$ and $P=0.01$ for 2 factors versus 3 or 4 factors).

In those 12 patients treated with marginal surgery without radiotherapy, 1 of 9 patients with 0 or 1 risk factor and all 3 patients with 3 or 4 risk factors died of their tumor disease. No patient with 2 risk factors was treated with marginal surgery without radiotherapy.

Local recurrence related to number of risk factors

In the whole series of 88 patients, there were somewhat more local recurrences with 3 or 4 risk factors (4/15) compared with 2 or fewer risk factors (9/73) (difference not significant). Also, the death rate in patients with local recurrence was higher when 3 or 4 risk factors were present (4/4) as compared with 2/9 for patients with 2 or fewer factors.

Comments

In group D, by using a model with four risk factors that were identified by multivariate analysis, a group of patients (28/82) with an excellent prognosis after wide or radical excision of a Grade III or Grade IV sarcoma could be defined. These 28 patients, who had 0 or 1 risk factor, had the same survival rate as those 28 patients with Grades I and II tumors in base series I who were operated on with the same margin (0.96) (Rööser et al. 1987). These two groups comprised one half of all the patients with Grades I-IV sarcomas operated on with a wide or radical margin. The findings indicate that besides patients with Grades I and II sarcomas, those with 2 or fewer risk factors should not be randomized to trials with adjunctive chemotherapy. Such trials have been performed, but with conflicting results and conclusions (Yap et al. 1983, Antman et al. 1985, Bramwell et al. 1985, Rosenberg et al. 1985, Potter et al. 1986, Alvegård 1986). One reason for the discrepant results of adjuvant therapy may be that a different fraction of patients with a uniformly good prognosis, in spite of their having histologically high-grade tumors, were included. This would tend to mask possible effects of chemotherapy. Candidates for trials with chemotherapy should only be patients with 3 or 4 risk factors, where the 6-year survival rate was below 0.35.

When the risk factor model was applied to the 62 patients of the 144 in group C who were operated on with a marginal margin, there was also a decreasing survival rate with an increasing number of risk factors (Rööser et al. 1987). Patients with 2 or fewer risk factors who were operated on with a wide or radical margin had a survival rate that even at 10 years was around 0.30 higher than that after marginal surgery. They also had fewer local recurrences (6/62 compared with 24/42). For patients with 3 or 4 risk factors, the 10-year survival rate was only 0.1 higher after surgery with a wide or radical margin than after marginal surgery despite fewer local recurrences (5/20 compared to 13/20). Even after surgery with a wide or radical margin, the more aggressive nature of the tumors in patients with 3 or 4 risk factors manifested itself by somewhat more local recurrences than in cases with 2 or fewer factors. It is not likely that dissemination in patients with many risk factors occurred secondary to local recurrence because prognosis was grave even in cases with local control. Probably the majority of these patients had occult tumor spread when the primary tumor was diagnosed. Pulmonary metastases have been reported to be invisible on chest radiographs during the longest period of their existence; metastatic seed has been extrapolated to have occurred years before diagnosis of the primary tumor (Collins et al. 1956, Schwartz 1961, Pearlman 1979, Rööser et al. 1987). In patients with 2 or fewer risk factor, the better survival seen after surgery with a wide or radical margin may be interpreted as an effect of local control. However, there may be other characteristics in the tumor, not here analyzed, which are associated with an increased risk of both marginal surgery and a worse prognosis. Infiltrative growth may be such a factor (Mandard et al. 1981).

Even in group E, a prognostication model based on the number of risk factors present could significantly separate three groups of patients with a different prognosis, as in group D. The patients with 0 or 1 risk factor had a 3-year survival rate of 0.9 and comprised a subset of more than one half of the series. They should have a good chance of being cured after treatment of only the primary tumor. Adjunctive chemotherapy

does not seem to be indicated in these patients. For patients with 3 or 4 risk factors, the prognosis was dismal irrespective of the type of surgical treatment.

Also in group E, there was a tendency for more local recurrences in patients with 3 or 4 risk factors as compared with cases with 2 or fewer factors. Local recurrence was no risk factor per se for tumor-related death in this series, however, which further indicates that prognostic factors in the host and/or tumor may determine prognosis more than different types of surgical treatment.

When the 82 patients in group D who were operated on with a wide or radical margin were combined with those 76 cases in group E who were treated with a wide or radical margin or with marginal surgery and radiotherapy, the crude tumor-related death rate could be related to two common risk factors (Grade IV, size >10 cm) and one criterion (necrosis) with slight differences in definition. Patients with Grade III sarcomas, except when larger than 10 cm and necrotic, and those with a Grade IV tumor as the sole risk factor, comprising altogether two thirds of the combined series, had a death rate of 0.14 compared with 0.53 in the remaining one third (Figure 9).

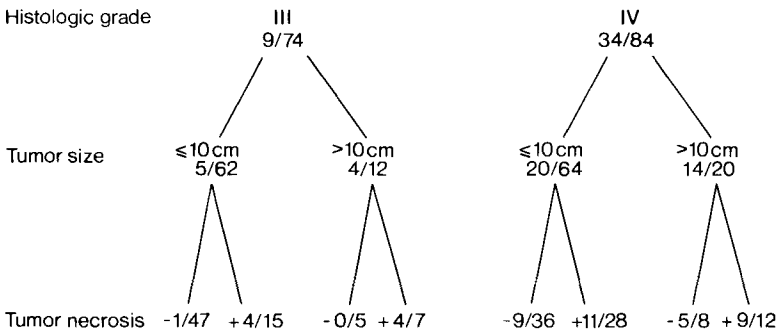

Figure 9. Tumor-related death rate related to malignancy grade, tumor size, and tumor necrosis in 158 patients with soft tissue sarcomas operated on with a wide or radical margin (146) or marginal margin and radiotherapy (12). Combined data from groups D and E.

The findings in groups C, D, and E demonstrate the usefulness of the proportional hazards model when analyzing prognostic factors for such heterogeneous tumor types as soft tissue sarcomas. By the Cox-model, prognostic variables with quantitated strength are obtained which allows selection of the most important prognostic factors and permits comparisons between independent series.

Discussion

Local recurrence related to surgical margins

The most commonly used system for definition of surgical margins in sarcoma is the Surgical Staging System (SSS) constructed by the Musculoskeletal Tumor Society (Enneking et al.). This system was also used in this report. The local recurrence rate after surgery with a wide margin as defined in the SSS was 0.15 (12/81). However, by defining three types of wide margin, according to the type of tissue that constituted the margin, a meaningful subclassification could be made; two of the subtypes were found associated with a local recurrence rate around 0.05. Thus, surgery with a wide S or a wide F margin is effective in accomplishing local cure-without adjuvant therapy-even in high-grade malignant tumors. These margins can be achieved by local surgery with small loss of function.

Enneking (1983) stated that a local recurrence rate of 30–70 per cent is to be expected after procedures leading to a wide margin in high-grade tumors. He did not, however, analyze the local recurrence rate after myectomy in virgin tumors because open biopsy before definitive surgery was considered necessary. It may be true that a radical margin is required for deep tumors if open biopsy or marginal surgery has preceded definitive treatment. Enneking did not specifically analyze the recurrence rate in subcutaneous tumors either. The findings in this report indicate that a wide margin is sufficient even when an incisional biopsy or a marginal excision has preceded definitive surgery in subcutaneous sarcoma.

A wide F margin implies surgery without open biopsy; the patient must be referred to the treatment center before any surgery. Deep tumors or those larger than 5 cm are much more likely to be to be sarcomas (Rydholm 1983). By using these criteria as guidelines for referral of patients with virgin soft tissue lesions from peripheral hospitals, the Orthopedic Oncology Group in Lund received more than four fifths of *all* the patients with deep extremity sarcomas diagnosed in the region from 1982 through 1985 as "untouched" tumors. The cost was 10 patients with benign tumors suspected of malignancy referred for every sarcoma patient (Rööser et al. 1987, Rydholm et al. 1987).

The concept of primary surgery, i.e., removing a tumor after only clinical and radiologic diagnosis, was developed by Stener (Stener & Stener 1958, Stener 1978). Combined clinical, cytologic, and radiologic diagnosis has been shown to discriminate sarcoma accurately from benign tumor in more than 90 per cent of the cases (Åkerman

et al. 1985, Rydholm et al. 1987). The functional loss after myectomy of even several muscles in, for instance, the thigh is small (Markhede & Stener 1981), and the consequences of an exceptional misdiagnosis appear to be acceptable. However, when amputation is considered, open biopsy is generally indicated.

The topographic identification of tumors suitable for local surgery has been enhanced by the use of computed tomography and magnetic resonance imaging. By these methods the relationship of a tumor to muscles, fascias, major vessels and bone, can often be visualized (Pettersson et al. 1987) (Figure 10).

Patients with subcutaneous tumors, who all can be treated by local surgery with a wide S margin, comprise at least one third of the patients with soft tissue sarcoma in the locomotor system (Rydholm et al. 1984). The relative frequency of tumors suitable for myectomy with a wide F margin is about one third of the deep-seated sarcomas in the extremities (Berlin et al. 1987, Rydholm et al. unpublished data). *Thus, more than one half of the patients with soft tissue sarcoma in the locomotor system primarily have tumors that can be operated by local surgery without adjuvant therapy with small loss of function and with a low risk of local recurrence. Tumors suitable for this treatment can be defined by only clinical, cytologic and radiologic examinations. Therefore, routine treatment with surgery combined with radiotherapy is not indicated.*

Patients operated on with a wide AM margin had a local recurrence rate of 0.27. This group included both patients with extracompartmental tumors and those with

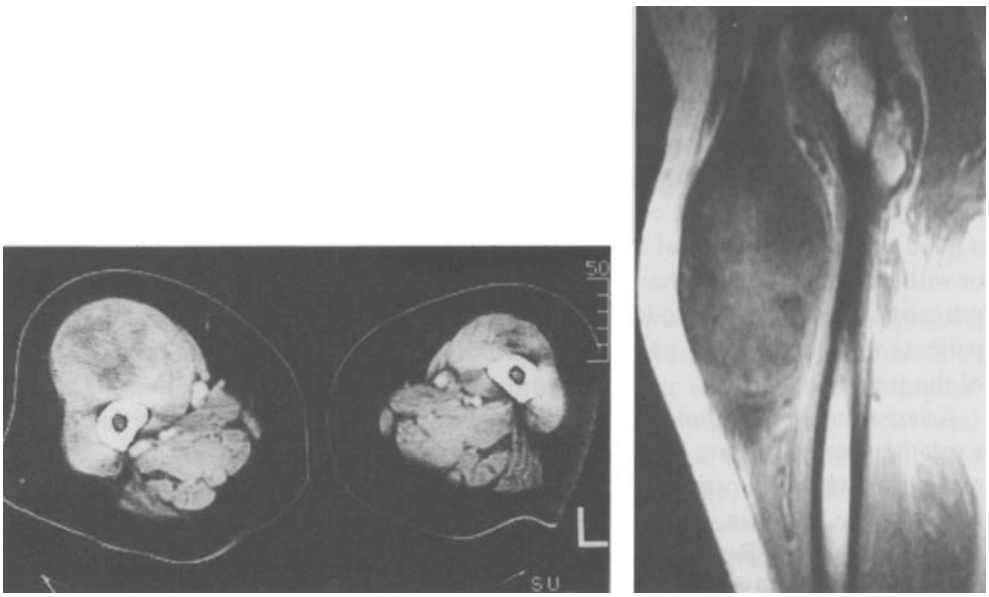

Figure 10. A Grade IV malignant fibrous histiocytoma located in the right rectus femoris muscle of an 86-year-old woman. Computed tomogram (left), magnetic resonance tomogram (right). The patient was referred with a virgin tumor and surgery, with excision only of the rectus muscle (primary myectomy), was performed after fine-needle aspiration cytology showed sarcoma. No adjunctive therapy was given. There was no evidence of disease and no functional deficit 1 year after surgery (see also cover).

intracompartmental tumors where the surgical dissection had transgressed the muscle where the tumor was located or, in the case of extramuscular tumors, loose areolar tissue. The risk of local recurrence after a procedure with a wide AM margin roughly corresponds to that following a "radical resection" of an extracompartmental tumor (Enneking 1983). This may indicate that the difference between the wide AM margin and the radical margin for extracompartmental tumors may be small. Therefore, local surgery combined with radiotherapy, rather than ablative surgery, should be considered in patients where it is not possible to obtain fascial containment of the tumor or where such a procedure implies sacrifice of major nerves. "Conservative surgery" and radiotherapy has resulted in local recurrence rates of 10–20 per cent, in several series, with a functional limb in 70–80 per cent of the cases (Suit et al. 1975, Morton et al. 1976, Lindberg 1985, Enneking & McCarthy 1985).

One fourth of the patients operated on with a wide AM margin and two thirds of those operated on with a marginal margin had local recurrence. It remains to be analyzed whether tumors with marked infiltrative growth, such as is commonly described for malignant fibrous histiocytoma (Kyriakos & Kempson 1976, Weiss & Enzinger 1978, Enzinger & Weiss 1983), recurred more often. Less infiltrative sarcoma may not require radiotherapy after wide AM surgery; and for the most encapsulated tumors, even a marginal excision may suffice as definitive treatment.

Survival related to patient, tumor, and treatment variables

Differences in outcome among patients with malignant disease may be more a function of strong host- and tumor-related prognostic factors than due to differences in therapy (Sather 1986). Consequently, identification of prognostic factors is important because modern treatment must be carefully tailored to the patient's prognosis. Patients with a good prognosis after local surgery alone should not be overtreated by amputation or with radiotherapy and chemotherapy. The same holds true for patients with a poor prognosis irrespective of today's treatment modalities. In addition, the inclusion of patients with a uniformly good prognosis in clinical trials may mask possible effects of the treatments tested.

A large number of clinical and biological observations at the time of diagnosis of a soft tissue sarcoma have been found to be important predictors of the outcome. Overt metastases when the primary tumor is diagnosed, histologic malignancy grade, tumor necrosis, size, location, depth, sex, and age have all been found to influence prognosis (Hajdu et al. 1977, Russell et al. 1977, Hajdu 1979, Enneking et al. 1980, Sears et al. 1980, Abbas et al. 1981, Markhede et al. 1982, Wright et al. 1982, Merck et al. 1983, Costa et al. 1984, Angervall et al. 1986). As more prognostic factors are identified, staging of patients for prognostication obviously becomes increasingly complex. This augments the value of statistical multivariate methods where the relative strength and independence of prognostic factors can be estimated. None of the three staging systems in current use-the AJC system, Hajdu's system, or the SSS-was based on multivariate analysis. None of them could define more than two patient groups with significantly

different prognoses when tested on a population of patients who had received reasonable surgical treatment. In all three systems, only histologic malignancy grade appeared to be a significant independent prognostic variable. The AJC system uses a three-grade malignancy scale, whereas the other two use a two-grade malignancy scale. By using only two histologic grades, prognostic information is lost (Angervall et al. 1986). The SSS does not use tumor size as a prognostic variable, and AJC and Hajdu use 5 cm as the cut-off point for different prognosis with regard to tumor size. According to our findings, this criterion should probably be adjusted upwards – at least for tumors of the locomotor system. Suit et al. (1985) proposed a modification of the AJC size criterion, introducing <5, 5–15, and >15 cm as separate prognostic intervals. Tumor compartmentalization according to the SSS is related to the risk of local recurrence (Enneking et al. 1980, 1981, Rööser et al. 1987). However, it was not found to be a prognostic factor per se for survival.

The multivariate-analyzed series in this presentation were population-based and thus unselected; all the cases treated outside the Orthopedic Oncology Group in Lund were also included. In addition, no patient was lost to follow-up. There are two reasons why this probably increases the validity of the results when compared with series where only patients referred to cancer centers are included. The two reasons, then, are no *referral bias,* i.e., patients with small and/or superficial tumors treated at peripheral hospitals are also included, and no *follow-up bias,* i.e., patients with local recurrence and/or metastatic disease are probably overrepresented when follow-up is incomplete.

We analyzed only patients with Grades III and IV sarcomas because the good prognosis for patients with Grades I and II tumors has been repeatedly demonstrated (Markhede et al. 1982, Merck et al 1983, Rydholm 1983). For the latter patients, no factor other than histologic grade is thus required for prognostication.

Prognostic factors

In groups C and D, histologic Grade IV, large size, tumor necrosis, and male sex were the most important host and tumor-associated predictors for tumor-related death in patients without overt metastases when the primary tumor was diagnosed. Marginal surgery, extracompartmental location, and tumor necrosis increased the risk of local recurrence. In the new group E of 88 patients sex did not significantly influence prognosis. This deviation from previous findings confirms the importance of study replication in independent series when prognostic factors are evaluated, as emphasized by Hannequin et al. (1986). In group E a new factor, microscopic vascular invasion, increased the risk for tumor-related death.

Vascular invasion and tumor necrosis are not commonly discussed as independent prognostic factors in soft tissue sarcoma. Some evidence has accumulated, however, as regards the prognostic importance of necrosis (Ekfors & Rantakokko 1978, DeStefani et al. 1982, Costa et al. 1984, Trojani et al. 1984, Chase & Enzinger 1985, Donhuijsen et al. 1986). The mechanism of necrosis is not understood. Widespread central necrosis has, however, been associated with a high intratumoral pressure

(Young et al. 1959, Wiig et al. 1981, Rööser et al. 1987) that may, in turn, be caused by rapid tumor growth and correlated with biological aggressiveness.

Vascular invasion by tumor is even more sparsely analyzed as a prognostic factor in soft tissue sarcoma than is necrosis. It has, however, been used as a factor in the prognostication of carcinoma (Willén 1984). Trojani et al. (1984) found that microscopically verified local tumor emboli were correlated with a high rate of metastases in sarcoma. Mandard et al. (1981) and Chase & Enzinger (1985) also showed that vascular invasion in a tumor could be related to distant spread.

The finding of necrosis and vascular invasion as prognostic factors shows that by histologic variables it is possible to define subsets with different prognoses even in patient groups having tumors of the same high malignancy grade.

Prognostication models

There is a consensus that simple shelling out of a sarcoma without adjunctive radiotherapy is, in general, insufficient treatment. Therefore, those patients who were operated on with a reasonable procedure, i.e., wide or radical excision, were analyzed separately. In group D, by simple counting of the risk factors male sex, Grade IV, tumor size >10 cm and tumor necrosis, a large group of patients with a prognosis as good as in Grades I and II sarcomas could be identified. Patients with 0 or 1 risk factor had a good prognosis after treatment of the primary tumor alone and would not have benefited from chemotherapy.

Similarly, in group E, using a new risk factor, microscopic vascular invasion, a model with four risk factors could identify a group of patients with 0 or 1 risk factor that comprised more than one half of the series and that could be predicted to have a good prognosis after treatment of just the primary tumor. *Thus, at least one half of the patients with Grades III and IV sarcomas, commonly called high-grade malignant, can be identified and predicted to have a good prognosis after treatment of the primary tumor. These patients should not be included in trials with chemotherapy.*

In both series where four-factor models were used, patients with 3 or 4 risk factors had a chance for long-term survival of less than 0.25 in spite of surgery with a wide or radical margin. In many of these cases micrometastases were probably established at the time of presentation. Thus, they were, by either of the two models, definitely candidates for trials with adjunctive chemotherapy.

Type of surgical treatment and local control related to survival

In group C, local recurrence was a strong risk factor for tumor-related death, confirming previous reports by Markhede et al. (1982), Merck et al. (1983), Bertoni et al. (1985). The higher survival after surgery with a wide or radical margin compared with that after a marginal excision in patients with few of the risk factors defined in group D was paralleled by fewer local recurrences. However, there probably is a correlation between local aggressivity and metastatic potential in sarcoma as also evidenced by the finding in study group C; viz., that tumor necrosis increased the risk

of both local recurrence and death from tumor. An apparent influence of surgery and/or local recurrence on survival may, therefore, result from a certain bias. That is, there may be a higher risk that among large and/or aggressive tumors a margin that was intended to be wide, particularly of the S or AM type, becomes marginal after histopathologic examination (Mandard et al. 1981, Abbatucci et al. 1986). Analogously, the local recurrence rate after a specified surgical margin may be higher in patients with tumors prone to metastasize (Enneking 1983). In groups D and E, there were more local recurrences in patients with 3 or 4 risk factors, who comprised one fourth of group D and one fifth of group E. Prognosis, however, was not significantly related to local control in the multivariate analysis performed in group E. Thus, local recurrence heralded a fatal course in those patients where prognosis was poor even after local control, i.e., those with 3 or 4 risk factors. Conversely, local recurrence was not a strong harbinger of tumor-related death in those four fifths of the patients who had 2 or fewer risk factors. In group C the host- and tumor-related risk factors had approximately the same prognostic strength for tumor-related death before and after local recurrence and in patients without local recurrence. These findings further indicate that local regrowth, when associated with a grave course might not have been the causative agent of metastases.

In series of patients with sarcomas of the extremities comprising both patients operated on with limb-sparing surgery and those treated by amputation, there has probably been a selection of cases with extensive tumors for the latter treatment (Brennan et al. 1985). Because only the margin in the longitudinal plane has to be considered in amputation, good local control is more easily achieved by this treatment. Thus, in reports by Shiu et al. (1975), Leibel et al. (1982), Brennan et al. 1985, Berlin et al. (1987), there were much fewer local recurrences after amputation than after local surgery. Survival was no better or worse, however, after ablative surgery. Chase & Enzinger (1985) who analyzed sarcomas in several locations and Potter et al. (1985), reporting high-grade tumors, found that local recurrence influenced prognosis very little. In most patients with high-grade tumors who develop metastases, these are diagnosed within 1 year after primary surgery whether local control has been achieved or not. Occult dissemination before the time of presentation is likely to have occurred in these cases and may be the main pattern of distant spread in Grades III and IV sarcomas.

Among patients with Grades III and IV sarcomas those with few additional host and/or tumor related-risk factors have a less risk of having established micrometastases at the time of presentation. It is presumably mainly among these cases that local control influences survival. However, for most patients, prognosis seems to be determined already at the time of diagnosis of the primary tumor. "Current emphasis on local control may be much less important in survival than is thought" (Brennan et al. 1985).

The future

Prognostication in soft tissue sarcoma could probably be additionally improved if prognostic factors were separately analyzed in each of the different histogenetic types of tumors; prognostic factors probably operate with different strengths in different histologic entities. Because of the rareness of soft tissue sarcoma, only three histologic types, namely, liposarcoma, synovial sarcoma, and myxofibrosarcoma have been analyzed by multivariate methods (Kindblom et al. 1975, Wright et al. 1982, Merck et al. 1983). However, apart from the study by Wright et al., where tumor size was found to be the single most important predictor of the prognosis, the relative strengths of the risk factors found were not quantitated. Prognostic factors other than clinical and/or histologic ones will be identified in soft tissue sarcoma: Keen et al. (1985) found that aneuploidy was related to local and/or distant aggressive behavior in leiomyosarcoma. Kreicbergs et al. (1987) and Åkerman et al. (1987) found a higher proportion of aneuploid tumors in Grade IV than in Grade III sarcomas. Thus, DNA-ploidy level may be correlated with prognosis in soft tissue sarcoma.

Cytogenetic studies of the karyotypes in soft tissue tumors have just begun. To date, specific chromosomal rearrangements have been identified in only a small number of cases, which include lipoma, myxoid liposarcoma, malignant fibrous histiocytoma, and synovial sarcoma (Heim et al. 1986, 1986, Turc-Carel et al. 1986 a, b, Mandahl et al. 1987).

Whether there is a relationship between specific chromosomal aberrations and prognosis, as has been shown for several hematologic neoplasias, it remains to be seen.

Conclusions

I. Subcutaneous and intramuscular sarcomas, constituting one half of all the soft tissue tumors in the locomotor system, can be treated by local surgery with a low risk of local recurrence and minor loss of function. Adjunctive radiotherapy is not indicated for these patients.

II. One fourth of the patients with soft tissue sarcomas have tumors of histologic malignancy Grades I or II. The vast majority of these patients survive after treatment of only the primary tumor. For patients with Grades III and IV sarcomas, commonly called high-grade sarcoma, several other prognostic factors for tumor-related death can be identified. By using these factors, one half of the patients could be predicted to have a good prognosis.

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Coded data, Series I and II

Key to data

A. Age at diagnosis — years

B. Sex — 1=Male, 2=Female

C. Histologic type
1=Malignant fibrous histiocytoma
2=Liposarcoma
3=Leiomyosarcoma
4=Neurogenic sarcoma
5=Synovial sarcoma
6=Angiosarcoma
7=Fibrosarcoma
8=Myxofibrosarcoma
9=Other types
10=Sarcoma NOS

D. Malignancy grade — 1–4

E. Tumor necrosis series I — 0=<4.3 mm, 1=>4.3 mm

E. Tumor necrosis series II — length in mm

F. Vascular invasion by tumor — 0=No, 1=Yes

G. Location
1=Shoulder girdle
2=Upper arm
3=Elbow
4=Forearm
5=Wrist, hand
6=Buttock
7=Hip girdle, groin
8=Thigh
9=Knee
10=Lower leg
11=Ankle, foot
12=Neck
13=Trunk

H. Depth — 1=Subcutaneous, 2=Subfascial

I. Size — largest diameter in cm

J. Symptoms — 0=No pain, 1=Pain

K. Preoperative fine needle aspiration cytology — 0=Not performed, 1=Performed

L. Definitive surgical margin for primary tumor — 3=Marginal, 4=Wide or radical

M. Adjunctive chemotherapy — 0=No, 1=Yes

N. Adjunctive radiotherapy — 0=No, 1=Yes

O. Local recurrence — 0=No, 1=Yes

P. Time for first local recurrence — months

Q. Time for second local recurrence — months

R. Number of local recurrences

S. Follow-up time — months

T. Time for death — months

U. Cause for death — 1=Tumor-related, 2=Other disease

Series I

Case	A	B	C	D	E	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U
1	63	1	2	3	0	8	2	12	0	1	4	0	0	0			0	116		
2	54	2	2	3	1	8	2	17	0	1	3	0	1	0			0	103		
3	5	1	5	3		4	2	4	0	0	4	0	0	0			0	147		
4	84	2	3	2	0	11	2	8	0	1	3	0	0	0			0		50	2
5	87	1	3	4		8	1	4	0	0	3	0	0	0			0		76	2
6	17	1	10	3	1	8	2	8	0	0	4	0	0	0			0	182		
7	16	1	9	4	1	1	2	5	0	0	3	0	1	1	8	1			8	1
8	65	2	5	3	0	1	2	3	0	1	3	0	0	0			0	112		
9	59	1	1	3	1	10	2	3	1	0	4	0	0	0			0		10	1
10	59	1	2	4	0	1	1	9	1	0	3	0	0	0			0		26	1
11	66	2	1	4		8	2	15	1	1	3	0	0	1	4		1		4	1
12	68	1	8	3	0	8	1	5	0	1	4	0	0	0			0	75		
13	61	2	2	4	1	1	2	12	1	1	3	0	1	1	3	1			7	1
14	61	1	8	2	0	10	1	3	0	0	3	0	0	1	18		1	156		
15	68	2	8	3	0	8	1	6	0	0	4	0	0	0			0	74		
16	60	1	4	2	1	6	2	13	0	1	3	0	0	1	12	24	3		164	1
17	64	2	6	2	0	1	2	2	0	0	3	0	0	0			0	106		
18	63	2	2	3		4	2	2	0	1	3	0	0	1	17		1	123		
19	54	1	1	3	1	12	2	11	0	0	3	0	0	1	4		1		9	1
20	64	2	8	4	1	10	1	6	0	1	4	0	0	0			0		102	2
21	63	1	7	2	0	13	1	1	1	0	4	0	0	0			0	109		
22	55	1	1	4	1	8	1	9	0	1	4	0	0	0			0	83		
23	58	1	7	4	0	12	2	2	0	0	4	0	0	0			0	156		
24	50	2	1	4	1	8	2	14	1	0	3	1	1	0			0		28	1
25	56	2	4	4	1	8	2	10	1	0	3	0	0	1	10		1		25	1
26	55	1	4	2	0	6	2	7	0	0	3	0	0	1	20	36	3		87	1
27	57	2	7	3	0	2	1	2	0	0	4	0	0	0			0	153		
28	63	2	1	4	0	8	2	8	0	1	3	1	0	1	11		1	84		
29	58	1	3	4	1	6	2	10	0	0	4	0	0	0			0	152		
30	55	2	3	3	1	8	1	3	0	0	3	0	0	0			0	170		
31	58	1	4	4	0	13	1	2	0	0	4	0	0	0			0	139		
32	52	1	2	3	1	9	1	7	1	0	3	0	0	1	32		1		62	1
33	54	2	3	3	0	7	1	3	0	1	4	0	0	0			0		30	1
34	55	1	11	4	1	8	2	16	1	1	3	1	0	1	4		1		9	1
35	58	1	6	3	0	12	2	5	0	1	4	0	0	0			0	125		
36	58	1	7	2	0	12	2	1	0	0	4	0	0	0			0	118		
37	49	1	4	3	1	11	2	6	1	0	4	0	0	0			0	220		
38	56	1	3	4	0	8	1	3	0	0	4	0	0	0			0		79	2
39	55	2	2	2	0	8	2	26	0	0	3	0	0	1	114		1	145		
40	58	1	8	3	0	1	2	2	0	1	4	0	0	1	12		1	101		
41	60	2	6	3	0	3	1	2	0	0	4	0	0	0			0	72		
42	59	1	3	4	0	3	2	6	0	1	4	0	0	0			0	88		
43	59	2	2	3	0	8	2	7	0	1	4	1	0	0			0	83		
44	57	1	4	4	1	8	2	9	1	0	4	0	0	0			0		31	1
45	47	2	1	1	0	8	1	1	0	0	3	0	0	0			0	227		
46	70	1	1	1	0	12	1	2	0	0	4	0	0	0			0	168		
47	52	2	2	2	0	8	2	8	0	1	4	0	0	0			0	158		
48	59	2	1	4	0	8	2	4	0	1	4	1	0	0			0	72		
49	58	1	2	4	0	8	2	2	0	0	4	0	0	0			0	84		
50	45	1	3	4	1	8	2	9	1	0	3	1	1	0			0	240		
51	69	1	3	4	0	4	2	17	0	1	4	1	0	0			0		52	1
52	52	1	1	3	0	10	2	5	0	0	4	0	0	0			0	156		
53	45	2	2	2		7	1	4	0	0	3	0	0	0			0	231		
54	51	1	3	4	0	6	1	5	0	0	4	0	0	0			0	153		
55	57	2	5	3	0	1	2	7	0	1	3	1	0	1	19	21	2		63	1
56	57	1	1	2	0	10	1	4	0	0	4	0	0	0			0	91		
57	57	1	4	1	0	1	1	2	0	0	4	0	0	0			0	80		
58	45	1	10	4	1	1	2	10	1	1	4	0	0	1	2		1		3	1
59	50	2	7	3	0	9	1	5	0	1	4	0	0	0			0	156		
60	55	1	2	1	0	8	2	23	0	1	4	0	0	0			0	90		

Case	A	B	C	D	E	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U
61	53	1	4	3	0	5	1	1	1	0	4	0	0	0			0	119		
62	42	2	3	3	0	2	1	1	0	0	3	0	0	1	9		1	238		
63	52	1	4	2	1	6	1	16	0	1	3	0	0	0			0	113		
64	50	1	1	4	1	8	2	7	0	0	3	0	0	0			0		49	1
65	44	2	2	3	0	8	1	7	0	0	4	0	0	0			0	238		
66	46	1	4	3	0	7	1	6	0	0	3	0	0	1	6		1		90	1
67	43	2	4	3	0	5	2	2	0	0	3	0	0	1	23		1	204		
68	44	2	4	4		1	2	9	1	0	3	0	0	1	3	12	2		17	1
69	44	1	1	4	1	8	2	9	1	1	4	1	0	0			0		27	1
70	39	1	9	4	1	13	2	10	0	0	3	0	0	0			0		8	1
71	51	1	3	3	0	8	1	2	0	0	4	0	0	0			0	91		
72	44	1	5	4	0	10	2	8	1	1	4	0	0	0			0	167		
73	51	2	1	4		9	1	5	0	0	4	1	0	0			0	71		
74	51	1	10	4	0	8	1	2	0	0	4	0	1	1	6		1		6	1
75	50	1	2	3	1	13	1	6	0	0	4	0	0	0			0	75		
76	44	2	2	2	0	8	1	6	0	1	4	0	0	0			0	145		
77	48	2	1	3	1	8	2	12	0	1	4	0	0	1	8		1	104		
78	38	1	4	3	1	8	2	11	1	1	4	0	0	0			0		53	1
79	49	1	1	3	0	13	2	4	0	0	4	0	0	0			0	76		
80	45	2	11	3		10	2	3	0	1	4	0	0	0			0	124		
81	49	2	6	2	0	12	2	6	0	1	3	0	1	0			0	69		
82	36	1	5	4	1	13	2	10	0	0	3	0	0	1	3	12	2		15	1
83	44	2	5	3	0	11	2	2	0	0	3	0	0	1	130		1	140		
84	40	1	8	2		13	1	5	0	0	3	0	0	0			0	166		
85	40	1	2	3	1	10	2	11	0	0	4	0	0	0			0		81	1
86	42	2	2	1	0	13	2	7	0	0	3	0	0	0			0	121		
87	33	1	6	4		2	2	2	0	0	3	0	1	0			0	211		
88	42	1	2	2	0	8	2	5	0	1	4	0	0	0			0	100		
89	41	1	7	3	0	13	1	1	0	0	4	0	0	0			0	101		
90	39	2	11	2	0	9	2	3	1	0	4	0	0	0			0	126		
91	38	1	7	3	1	1	1	6	0	0	4	0	0	1	36		1	134		
92	33	2	9	4	1	8	1	5	0	0	3	0	0	0			0	191		
93	34	1	11	4	0	1	2	10	0	0	3	0	0	0			0	182		
94	40	1	2	3	0	8	2	12	0	1	4	0	0	0			0	99		
95	35	2	9	3	1	10	2	11	0	0	4	0	0	0			0	149		
96	33	2	1	3	1	2	2	8	0	0	4	0	0	0			0	176		
97	30	1	4	4		8	2	8	0	0	4	0	0	0			0		132	1
98	36	1	5	4	1	8	2	5	0	0	4	0	0	1	15		1		34	1
99	28	1	5	4	0	9	2	7	0	0	4	1	0	0			0		73	1
100	38	1	1	4	0	6	1	3	0	0	4	0	0	0			0	84		
101	31	2	1	3	0	4	1	1	0	0	3	0	0	0			0	154		
102	32	2	5	4	1	7	2	5	0	0	3	1	1	1	8		1		9	1
103	29	1	2	2	0	6	2	15	1	0	3	0	0	1	4		1		24	1
104	30	1	5	4	1	8	2	13	1	0	4	0	1	1	4		1		16	1
105	25	2	5	4	1	10	2	3	1	0	4	0	0	0			0		40	2
106	37	1	11	4	0	8	1	2	0	0	3	0	0	0			0	72		
107	22	1	3	2		8	2	15	1	0	3	0	0	0			0	238		
108	35	2	4	3	1	8	2	6	0	0	3	0	0	1	7		1	84		
109	36	1	7	1	0	5	2	2	0	0	3	0	0	0			0	72		
110	32	2	8	1	0	2	2	14	0	1	3	0	0	0			0	123		
111	30	2	2	3	1	10	2	12	1	0	4	0	0	0			0	141		
112	22	1	1	1	0	13	1	2	0	0	4	0	0	0			0	118		
113	30	1	11	3	0	5	2	6	0	0	4	0	0	0			0	137		
114	24	2	1	3		8	1	4	0	0	3	0	0	1	5		1	212		
115	22	2	1	2		13	2	3	0	0	4	0	0	0			0	234		
116	30	2	2	2	0	7	2	13	1	0	4	0	0	1	111		1	121		
117	32	1	4	4	0	1	2	4	1	1	3	0	1	0			0	86		
118	31	1	5	4	1	4	2	6	1	1	4	1	0	0			0	94		
119	32	1	10	3		8	2	2	0	0	4	0	0	0			0	73		
120	32	1	8	2	0	8	2	4	0	1	3	0	0	0			0	76		

Case	A	B	C	D	E	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U
121	25	1	7	2	0	13	2	10	0	1	4	0	0	1	12	42	5	142		
122	28	2	6	2	0	2	1	4	0	0	4	0	0	0			0	105		
123	29	1	1	4	0	8	2	5	1	0	4	1	0	0			0		27	1
124	18	1	5	3	1	4	1	4	0	0	4	0	0	0			0	214		
125	25	1	5	4		3	2	8	1	0	4	0	0	0			0		39	1
126	21	1	4	4	0	8	2	10	1	0	4	0	0	0			0		61	1
127	27	1	9	4	1	13	2	8	1	1	3	1	0	0			0	96		
128	19	2	2	2		13	2	3	0	0	3	0	0	1	12	16	1	191		
129	21	1	5	3	0	11	1	2	1	0	4	0	0	0			0	158		
130	26	1	6	2	0	7	2	5	0	0	3	0	0	0			0	82		
131	19	1	4	3	1	8	2	4	1	0	3	0	0	0			0	139		
132	20	1	5	4	0	8	2	7	0	0	4	1	0	0			0	106		
133	21	1	9	3	0	5	1	2	0	0	4	1	0	0			0	72		
134	15	2	7	2	0	10	1	2	0	0	4	0	0	0			0	97		
135	5	1	5	3		4	2	4	0	0	4	0	0	0			0	118		
136	10	1	11	3		5	2	2	0	0	3	0	0	0			0	84		
137	2	2	9	4		13	2	3	0	0	3	1	0	0			0	156		
138	85	1	5	4		8	1	8	0	0	3	0	1	1	10	12	2		12	2
139	88	1	7	2		4	2	5	0	0	3	0	0	0			0		3	2
140	84	2	4	3		8	1	6	0	0	3	0	0	0			0		27	1
141	85	1	3	4	1	1	2	10	0	0	3	0	0	1	1	5	3		12	1
142	81	2	1	4		6	2	7	0	0	3	0	0	1	24		1		24	1
143	87	2	6	4	1	10	1	3	0	1	3	0	0	0			0		83	2
144	81	1	6	2	0	13	1	12	0	0	3	0	0	0			0		43	2
145	80	1	1	4	1	2	2	4	0	0	4	0	0	1	48	54	2		126	1
146	80	2	1	4	1	2	2	12	0	1	3	0	1	0			0	14	18	2
147	81	1	2	4	0	13	2	7	0	0	3	0	0	0			0		10	2
148	79	2	8	2		9	1	3	0	0	3	0	0	1	6	99	2		132	2
149	80	2	2	3	0	2	2	8	0	1	3	0	0	1	45	51	3	98		
150	78	2	1	4	1	3	1	11	0	0	4	0	0	0			0		64	2
151	87	1	3	4	0	8	1	4	0	0	3	0	0	0			0		76	2
152	78	2	1	3	1	2	2	14	0	1	3	0	1	1	18		1		19	1
153	83	1	11	4	1	13	2	7	1	0	3	0	1	1	4		1		7	1
154	86	1	3	3	1	13	1	5	0	0	3	0	0	0			0		16	1
155	78	1	6	4	1	1	2		0	0	3	0	0	1	4	8	2		19	1
156	87	1	1	2	0	2	1	5	0	1	4	0	0	0			0		50	2
157	78	2	1	4		9	2	12	0	0	3	0	0	0	1	2	1		83	2
158	80	1	11	4	0	2	2	7	0	0	3	1	0	1	7		1		21	1
159	78	1	3	3	1	8	1	4	0	0	4	0	0	1	7	12	2		21	1
160	79	1	1	4	1	10	2	8	1	0	3	0	0	1	7		1		12	1
161	83	1	1	4	0	4	1	4	0	0	3	0	0	1	6		1		7	2
162	87	1	1	4	1	10	1	6	0	0	3	0	0	1	6		1		13	1
163	75	1	1	4	1	8	1	6	0	0	3	0	0	1	5	10	2		20	1
164	81	2	7	3	1	1	2	4	1	1	3	0	0	1	4	18	2		24	1
165	80	1	1	4	1	8	1	3	0	0	3	0	0	1	3	15	2		19	1
166	80	2	1	3		8	2	6	0	0	3	0	0	0			0		18	2
167	81	2	7	2	0	13	1	5	0	0	3	0	0	0			0		70	2
168	80	2	3	3	1	4	1	6	0	1	4	0	0	0			0	114		
169	81	2	1	4	1	11	2	6	0	1	3	0	0	1	4		1		6	2
170	79	1	6	2	1	1	2	13	0	0	3	0	0	0			0		21	2
171	82	1	3	3	0	8	2	1	0	0	4	0	0	0			0		6	2
172	82	2	1	4	0	8	2	10	0	1	4	0	0	0			0	76		
173	71	2	1	4	1	8	2	20	0	0	3	0	0	1	3	12	2		14	1
174	70	1	4	1	1	12	2	7	0	0	3	0	0	1	71		1		72	1
175	78	2	1	3	0	10	1	4	0	0	3	0	1	0			0		111	2
176	78	1	2	4	1	13	2	23	0	1	3	0	0	0			0		4	2
177	71	1	6	2	0	10	1	5	0	1	4	0	0	0			0	173		
178	79	1	1	1	0	13	1	6	0	1	4	0	0	0			0	79		
179	68	2	5	4	1	8	2	14	0	0	3	0	0	0			0		9	1
180	72	1	3	4	1	4	1	11	0	1	4	0	0	0			0		16	1

Case	A	B	C	D	E	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U
181	72	1	1	4		8	1	10	0	0	3	0	0	0			0		10	1
182	78	2	1	2		13	1	13	0	0	4	0	0	0			0		27	1
183	70	2	1	4	0	8	2	7	1	0	3	0	1	1	24		1		27	1
184	78	2	1	3	0	8	2	10	0	1	3	0	0	1	12	36	3		68	1
185	78	1	2	4	0	4	1	3	0	0	3	0	0	0			0		7	2
186	64	2	3	4	0	6	1	7	0	0	3	0	0	1	2		1		213	2
187	74	2	1	3		11	2	5	0	0	4	0	0	0			0		114	2
188	74	2	3	4	1	8	2	8	1	1	4	0	0	1	12	27	4		50	1
189	66	1	9	4		2	2	10	1	0	4	0	0	0			0		27	1
190	63	1	2	3		2	2	30	0	0	3	0	0	1	1	19	1		29	1
191	69	2	9	4		10	2	7	0	1	4	0	0	0			0		6	1
192	75	1	3	3	1	4	1	6	0	0	4	0	0	0			0		21	2
193	72	2	7	2	0	8	1	2	0	0	3	0	0	1	8		1	129		
194	66	1	3	3	1	8	2	18	1	1	4	0	1	1	12	16	2		30	1
195	71	2	2	3	0	8	2	30	0	1	3	0	0	1	24		1		27	1
196	72	2	2	4	1	8	2	10	0	1	4	0	0	0			0	120		
197	64	2	2	3		8	2	11	0	0	3	0	0	1	14		1	220		
198	73	1	1	2	1	8	2	5	0	0	4	0	0	1	17	36	2		62	2
199	68	1	6	2	0	8	2	10	0	1	3	0	0	1	26		1		30	1
200	64	2	1	3	0	13	1	6	0	0	3	0	0	0			0	215		
201	71	1	11	4		6	1	8	0	0	4	0	0	0			0		118	2
202	73	2	1	4	1	8	2	14	1	1	4	0	0	0			0		35	2
203	66	1	5	3	0	13	2	6	0	1	4	0	0	0			0	181		
204	69	1	8	2		4	1	3	0	0	3	0	0	0			0	142		
205	64	2	8	2	1	10	2	14	0	0	3	0	0	0			0		163	2
206	65	2	1	4	0	13	1	4	0	0	4	0	0	0			0	181		
207	68	2	1	4	1	8	2	15	0	0	4	0	0	0			0		21	1
208	64	2	2	2		8	1	3	0	0	4	0	0	0			0	189		
209	68	2	1	4	1	4	2	3	0	0	4	0	0	1			0		128	2
210	69	2	6	3	0	13	2	5	0	0	3	0	0	0			0	138		
211	69	2	1	3	0	6	1	2	0	1	4	0	0	0			0		100	2
212	66	1	8	3	1	6	2	10	0	1	4	0	1	0			0	154		
213	70	1	2	2	0	8	2	7	0	1	4	0	0	1	30		1	111		
214	71	2	1	4	1	8	2	8	0	1	4	0	0	0			0	94		
215	67	2	7	1	1	7	1	2	1	0	3	0	0	1	24		1	128		
216	66	2	10	1	0	1	2	8	0	0	4	0	0	0			0		36	2
217	67	1	3	3	1	8	2	3	1	1	3	0	0	1	16		1		64	1
218	71	1	8	2	0	8	1	3	0	0	4	0	0	0			0		74	2
219	66	2	3	4	1	9	2	5	0	0	4	0	0	1	0		0		65	1
220	63	2	1	4	1	10	1	9	0	1	3	0	0	1	2	5	3		10	1
221	61	1	1	1	0	11	2	2	0	0	4	0	0	0			0	196		
222	73	2	1	4	0	8	2	7	0	1	4	0	0	0			0	72		
223	61	1	2	4	1	13	2	12	0	0	3	0	0	0	11		1		17	1
224	57	1	4	3	0	3	2	3	0	0	3	0	0	1	4		1		18	1
225	62	1	3	4	1	8	2	5	1	0	4	1	1	0			0		19	1
226	59	1	2	1	0	1	1	7	0	0	3	0	0	1	30		1	211		
227	66	2	5	4	0	2	2	5	0	1	4	0	0	0			0	124		
228	64	1	10	4	0	8	2	8	1	0	4	0	0	0			0		12	2
229	62	1	1	4	1	8	2	5	0	0	4	0	0	0			0		170	2
230	66	1	3	3		5	1	1	0	0	3	0	0	0			0		3	2
231	70	1	8	3	0	8	1	2	0	0	4	0	0	0			0		39	2
232	70	1	4	4	1	10	2	10	1	1	4	0	0	0			0		19	1
233	62	1	4	4	1	1	2	4	1	1	3	0	1	1	30		1		48	1
234	57	1	4	4	0	8	2	5	1	0	3	0	0	1	6		1		15	1
235	66	2	10	1	1	6	2	4	1	1	4	0	0	0			0	107		
236	55	2	6	3	1	2	1	7	0	0	3	0	0	1	99		1		130	1
237	64	1	8	3		8	1	7	0	0	3	0	0	0			0	123		

Series II

Case	A	B	C	D	E	F	G	H	I	L	M	N	O	P	S	T	U
1	80	2	8	3	4.2	0	9	1	5	4	0	0	0		43	2	
2	82	1	3	3	0	0	2	1	2	4	0	0	1	24	44		
3	70	1	1	3	12	1	8	2	10	4	0	0	0			68	2
4	80	1	10	4	11	1	8	2	8	4	0	0	0			19	1
5	82	1	1	4	0	1	8	1	3	4	0	0	1	36	43		
6	81	1	3	3	12	1	8	2	2	3	0	1	0		43		
7	78	2	1	3	11	0	8	1	12	4	0	0	0		66		
8	77	2	3	4	15	1	10	1	4	3	0	0	1	5		5	1
9	78	2	2	4	11	1	8	2	22	3	0	1	0			15	1
10	78	1	10	4	12	1	8	2	12	3	0	0	1	6		24	1
11	79	1	1	3	0	0	1	2	12	3	0	0	0			41	2
12	77	2	4	4	2	0	1	2	6	3	1	0	0		42		
13	73	1	2	4	20	0	8	2	30	4	0	0	0			6	1
14	77	2	3	3	7	0	8	1	6	4	0	0	0			15	2
15	75	2	2	3	1	0	8	2	12	4	0	0	0		36		
16	74	1	11	4	0.5	0	8	2	14	4	0	0	0			8	1
17	71	2	2	4	30	0	8	2	11	4	0	0	0			12	1
18	71	1	7	3	1.5	0	1	2	3	3	0	1	0		69		
19	74	1	1	4	14	0	4	1	5	4	0	0	0		44		
20	70	1	1	4	0	0	1	2	7	4	0	0	0		78		
21	74	2	2	4	12	1	13	2	10	4	0	0	0		47		
22	71	1	2	4	5	0	8	2	18	3	0	1	0		57		
23	70	1	3	3	3.5	0	8	1	2	4	0	0	0		65		
24	72	1	1	3	0	0	4	2	5	4	0	0	0		36		
25	68	1	5	4	5.5	0	4	2	8	4	0	0	0			9	1
26	69	2	10	4	20	0	2	2	11	4	1	0	1	6		25	1
27	68	1	1	4	7	0	10	1	4	3	0	1	1	8		29	1
28	69	2	3	3	0	0	10	1	3	4	0	0	0		51		
29	66	1	1	4	2	1	8	2	15	4	0	0	0			75	1
30	67	2	3	3	11	0	10	1	4	4	0	0	0		60		
31	65	2	1	3	0.5	0	10	2	4	4	0	0	0		69		
32	64	2	10	3	11	0	8	2	17	3	0	0	1	45	80		
33	67	2	11	4	7	1	1	2	7	4	0	0	0		42		
34	64	2	4	3	0.5	0	12	2	3	3	0	0	0		79		
35	66	1	1	4	20	0	10	2	20	4	1	0	0			20	1
36	64	2	3	3	20	1	8	2	7	3	0	1	0			28	1
37	63	1	1	4	9	0	13	2	12	4	0	0	1	18	66		
38	64	2	1	3	8	1	10	2	6	3	0	1	0		43		
39	65	2	1	3	0	0	8	2	3	4	1	0	1	21	41		
40	60	2	10	3	1	0	1	2	4	4	0	0	0		79		
41	62	1	5	3	0	0	11	1	2	4	0	0	0		41		
42	60	2	1	3	0	0	10	1	6	4	1	0	0			37	1
43	60	2	3	4	12	0	6	2	12	3	0	1	0			10	2
44	58	2	5	4	6	2	5	2	7	4	0	0	0			8	1
45	59	1	1	4	16	0	8	2	14	4	0	0	0			10	1
46	67	2	1	4	11	0	3	1	3	4	1	0	0		64		
47	60	1	1	4	4.4	0	8	2	6	4	0	0	0		38		
48	56	1	6	4	0	1	7	2	6	3	0	1	0		60		
49	56	1	2	4	12	0	8	2	8	4	0	0	0			17	1
50	55	1	3	4	9	0	8	2	11	4	0	0	0			14	1

Case	A	B	C	D	E	F	G	H	I	L	M	N	O	P	S	T	U
51	57	1	5	4	0	1	9	2	5	4	0	0	0			11	1
52	54	2	5	3	12	1	8	2	11	4	0	0	0			18	1
53	58	2	5	3	0	0	11	2	3	4	0	0	0		40		
54	51	1	1	4	30	0	8	2	9	4	1	0	0		72		
55	50	2	1	4	0	0	7	1	3	4	0	0	0		70		
56	48	2	2	3	4.2	0	9	2	7	4	0	0	0		76		
57	49	1	3	3	0	0	10	1	2	3	0	0	0		55		
58	47	2	1	4	11	1	2	2	5	4	0	0	0		79		
59	44	1	3	3	7	0	10	1	2	4	0	0	0		71		
60	45	1	3	3	0	0	10	1	2	3	0	0	0		42		
61	45	2	3	3	5	1	1	2	3	4	0	0	0		53		
62	45	2	2	3	0	0	8	2	8	4	0	0	0		44		
63	40	1	4	4	12	0	10	2	4	4	0	0	0		87		
64	41	2	3	4	3	1	3	2	17	3	1	1	0			35	1
65	40	1	3	3	0	0	1	2	6	4	1	0	0		65		
66	43	2	3	3	5.5	0	7	1	6	4	1	0	0		45		
67	42	1	5	3	0	0	7	1	1	4	0	0	0		43		
68	38	1	1	4	14	0	10	1	5	4	0	0	0		62		
69	39	1	9	4	0	0	10	2	5	4	0	0	0		48		
70	38	1	2	4	7	0	8	2	12	4	1	1	0		42		
71	35	1	9	4	0	1	4	2	6	4	1	0	0			9	1
72	33	2	6	4	2.5	0	2	1	3	4	0	0	0		79		
73	34	2	2	4	15	0	7	2	8	4	1	0	0		64		
74	35	2	6	3	15	1	10	1	6	4	1	0	0			41	1
75	29	1	6	3	0	0	8	1	6	4	0	0	0		48		
76	26	2	5	3	0	0	9	2	2	4	0	0	0		49		
77	26	1	5	3	0	0	4	2	2	4	1	0	0		40		
78	24	2	4	4	20	0	8	2	10	3	0	1	0		55		
79	22	1	9	4	12	0	5	2	3	3	1	1	1	8		30	1
80	86	1	2	3	5.5	0	8	2	15	3	0	0	0			30	2
81	86	2	1	3	1	0	8	2	8	4	0	0	0			45	2
82	88	1	7	4	12	0	13	1	16	3	0	0	1	4		11	1
83	85	2	1	3	1	0	10	1	3	3	0	0	1	10	73		
84	85	1	1	4	13	1	8	2	9	4	0	0	0			6	2
85	83	2	3	4	4.4	0	10	2	3	4	0	0	0			24	2
86	86	2	8	3	13	0	10	1	6	3	0	0	1	11	36		
87	86	2	8	3	11	1	8	1	12	4	0	0	0		38		
88	82	1	1	4	11	0	2	1	7	4	0	0	0			64	2