Randomized Prospective Study of the Benefit of Adjuvant Radiation Therapy in the Treatment of Soft Tissue Sarcomas of the Extremity

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Purpose: **This randomized, prospective study assesses the impact of postoperative external-beam radiation therapy on local recurrence (LR), overall survival (OS), and quality of life after limb-sparing resection of extremity sarcomas.**

Patients and Methods: **Patients with extremity tumors and a limb-sparing surgical option were randomized to receive or not receive postoperative adjuvant external-beam radiotherapy. Patients with high-grade sarcomas received postoperative adjuvant chemotherapy whereas patients with low-grade sarcomas or locally aggressive nonmalignant tumors were randomized after surgery alone.**

Results: **Ninety-one patients with high-grade lesions were randomized; 47 to receive radiotherapy (XRT) and 44 to not receive XRT. With a median follow-up of 9.6 years, a highly significant decrease (P_2 = .0028) in the probability of LR was seen with radiation, but no difference in OS was shown. Of 50 patients with low-grade lesions (24 randomized to resection alone and 26 to resection and postoperative XRT), there was also a lower probability of LR (P_2 = .016) in patients receiving XRT, again, without a difference in OS. A concurrent quality-of-life study showed that extremity radiotherapy resulted in significantly worse limb strength, edema, and range of motion, but these deficits were often transient and had few measurable effects on activities of daily life or global quality of life.**

Conclusion: **This study indicates that although postoperative external-beam radiotherapy is highly effective in preventing LRs, selected patients with extremity soft tissue sarcoma who have a low risk of LR may not require adjuvant XRT after limb-sparing surgery (LSS).**

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THE TREATMENT OF patients with soft tissue sarcomas of the extremities has served as a model for the development of treatment strategies using adjuvant therapies to preserve function and achieve long-term survival. Although surgery remains the mainstay of therapy for primary lesions, both chemotherapy and radiotherapy (XRT) have been extensively used in the treatment of high-grade tumors in attempts to optimize cure rates and patient quality of life. The earliest and now widely accepted advance was the replacement of radical or amputative surgery with limited, limb-sparing surgery (LSS) followed by high-dose radiotherapy. Studies by Suit et al,[1] Lindberg et al,[2] and McNeer et al[3] showed that LSS and XRT could achieve local control rates of greater than 80%, which appeared similar to rates of local control achieved with radical surgery and superior to historic data that showed local control rates of 10% to 50% with LSS alone.[4,5] A single, prospective, randomized trial was performed that showed similar rates of disease-free (DFS) and overall survival (OS) for patients treated with amputation or the combination of LSS and XRT.[6]

The use of LSS and XRT has been widely accepted in the last two decades, and the rate of amputation for extremity sarcoma has fallen to less than 10% in the United States.[7] Despite this overall improvement in functional outcome, problems and questions still remain. High-dose XRT to the extremity is costly and can result in significant functional impairment of the limb and, in some cases, complications leading to amputation.[8] When XRT is given routinely as a postoperative adjuvant modality, many patients, perhaps a majority, who would not have recurred locally are nevertheless subjected to the potential consequences of XRT. Furthermore, the impact of local recurrence (LR) on OS is not clear. Although LR of sarcoma has often been associated with poorer survival in retrospective studies,[9,10] this may not be a causal relationship but an association that identifies patients with intrinsically more aggressive tumors.[11-14] Therefore, strategies to achieve optimal local control must consider not only actuarial LR rates, but also the costs of attaining those results.

The other major adjuvant modality used in high-grade extremity sarcomas is chemotherapy. Conflicting results have been reported with the use of doxorubicin-based postoperative adjuvant chemotherapy.[15-18] Based on early results of a randomized National Cancer Institute (NCI) study using doxorubicin, cyclophosphamide, and methotrex-

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ate that showed significantly improved local control, DFS, and OS,[18] all NCI patients with high-grade extremity sarcomas receive postoperative adjuvant chemotherapy. On further follow-up, statistical analysis showed these benefits to be of borderline significance or no longer significant.[19] Recently, a meta-analysis of more than 1,500 patients in 14 randomized trials evaluated the benefit of doxorubicin-based chemotherapy in patients with resectable primary soft tissue sarcoma and showed that chemotherapy decreased LR, distant recurrence, and improved recurrence-free survival, but its impact on OS was not statistically significant ($P = .12$) (Tierney et al, unpublished observations). Based on preliminary analysis of our adjuvant chemotherapy trial, we included adjuvant chemotherapy uniformly in designing a subsequent trial evaluating the role of adjuvant XRT in the treatment of high-grade sarcomas of the extremities. In this study, all patients with a high-grade extremity sarcoma and an LSS option were treated with surgery and postoperative chemotherapy and were randomized to receive or not receive postoperative XRT. The study end points were LR, DFS, and OS. In addition, patients with low-grade sarcomas of the extremity, whose tumors are often locally aggressive but only rarely metastatic, are often considered for postoperative XRT to reduce the incidence of morbid, locally invasive recurrences. The overall impact of this approach on net limb function and LR has not been analyzed in a prospective randomized fashion. Therefore, we conducted a simultaneous trial in which patients with low-grade extremity sarcoma first underwent limb-sparing resection and were then randomized to receive or not receive adjuvant XRT. In both studies, concurrent prospective quality-of-life and functional studies were performed to evaluate the effect of XRT on these parameters.

PATIENTS AND METHODS

A total of 141 patients with extremity soft tissue tumors were randomized. Between 1983 and 1991, 91 patients with high-grade extremity sarcomas who had undergone LSS within the previous 4 months were randomized to receive chemotherapy alone or concurrent chemotherapy and XRT. Patients with evidence of metastatic disease, a history of a second malignancy, or contraindications to receiving doxorubicin, cyclophosphamide, or XRT were excluded. Patients who presented with recent excision of their primary tumors were widely re-excised at the NCI, unless clear documentation was available to confirm the adequacy of the previous surgery. As a minimum, surgery had to result in the removal of all gross disease. In patients with a prior operation, definitive surgery was planned to entirely encompass the previous surgery, including all biopsy and drain sites. Wherever possible, a margin of 1 to 2 cm of normal tissue or an uninvolved fascial boundary was maintained around the tumor specimen. This standard was compromised only if a limited positive (or close) surgical margin would spare the patient the disabilities resulting from resection of major nerves, vessels, or weight-bearing bone. Resections included periosteum or vessel adventitium in continuity where necessary. Patients with gross residual tumor or multiple, widely positive margins following maximum LSS were offered amputation and not included in the study.

All pathology specimens were reviewed by one pathologist to confirm tumor grade. Grading was based on pleomorphism, mitoses, cellularity, and necrosis as previously described.[20]

Following primary wound healing, patients with high-grade tumors were then randomized to receive chemotherapy with or without XRT. This randomization used fixed blocks and was stratified for grade 2 tumors versus grade 3 tumors, proximal limb tumors versus distal limb tumors, and positive surgical margins versus negative margins (<1 mm $v \geq 1$ mm). Chemotherapy and XRT were given concurrently (beginning within 1 week of each other) and started no more than 4 months following definitive surgery. The chemotherapy administered consisted of doxorubicin 70 mg/m^2 intravenous (IV) bolus and cyclophosphamide 700 mg/m^2 IV infusion. Both drugs were given on day 1 of a 28-day cycle, and a total of five cycles were given. Radiation was begun concurrently with the start of chemotherapy, and consisted of 4,500 cGy to a wide field followed by an 1,800 cGy boost to the tumor bed (as defined by perimeter surgical clips). Care was taken to avoid circumferential limb irradiation and unnecessary irradiation of joints and tissues not at risk, through the use of filters, compensatory wedges, and electrons. One hundred eighty cGy fractions were given 5 days a week for a total of 6 to 7 weeks of therapy. Therapy was delayed for marked cutaneous reactions or wound complications. All patients were followed up by clinical assessment and chest radiograph every 2 to 3 months for 2 years, 3 to 4 months for 2 more years, and 6 to 12 months at 4 years and beyond. Periodic computerized tomography (CT) scans were obtained of the chest in all patients, and of the surgical site, if physical assessment was difficult. Yearly bone scans were also obtained in most patients with high-grade tumors. If patients developed metastatic disease, they were censored in follow-up for LR, as careful screening of the primary site was often no longer warranted.

Fifty patients with low-grade tumors were randomized within 4 months of definitive resection, and those randomized to receive XRT were treated with the same dose and technique as patients irradiated for high-grade tumors. A fixed block randomization with stratification for primary versus recurrent tumors, grade 1 versus aggressive benign lesions and positive versus negative surgical margins was used. Patients with low-grade tumors were examined and underwent chest radiograph (or CT scan) every 3 to 4 months for 2 years, then every 4 to 6 months for 2 years, and yearly beginning at 5 years. Limb CT or magnetic resonance imaging (MRI) scans were obtained periodically on patients who were difficult to assess on physical examination.

Quality-of-life data were collected in a prospective fashion from patients entered onto this protocol. A previous article described the instruments used and preliminary data at 6- and 12-month follow-ups.[21] In brief, patients underwent serial physical assessment and grading according to defined criteria, measuring joint range of motion, strength, edema, gait, and use of orthoses. The first three parameters were rated 0 to 3 (0, normal; 1, mildly impaired; 2, moderately impaired; and 3, severely impaired) with range of motion measured and rated by a standardized scale. Independence in activities of daily living were assessed using a modified Erdman scale.[22] In addition, a battery of psychosocial questionnaires were administered at each assessment, including the Functional Living Index—Cancer (FLIC) as an assessment of global quality of life.[23] This entire process was performed before commencing any postoperative adjuvant therapy, and at scheduled time points over the subsequent 5 years. For the current analysis, data at 3 to 6 months, 12 to 18 months, 24 to 30 months, and 36 to 42 months after surgery (designated 6 months, 12 months, 24 months, and 36 months, respectively) were initially analyzed in an unpaired fashion

comparing the two treatment arms at each time point. Because patient function varied widely because of the location and extent of the extremity involvement, functional assessments were also analyzed as a change from baseline assessment for all patients completing a baseline assessment before beginning XRT.

For statistical comparisons of metastasis-free, LR-free, and overall survival between treatment arms, the log rank method[24] was used. Median potential follow-up is defined as the median interval from the on-study date to the time of data analysis. The probabilities of event-free survival were computed using the method of Kaplan and Meier.[25] In comparing group characteristics, the Fisher's exact test, or the test of Mehta and Patel[26] was used, where appropriate. All P values are two tailed.

RESULTS

All Randomized Patients

A total of 141 patients with extremity soft tissue tumors of either high or low grade were randomized to receive (70 patients) or not receive (71 patients) postoperative external-beam XRT. These patients displayed a variety of histologic tumor types (Table 1). Overall, one patient who received XRT developed an LR, whereas there were 17 LRs when XRT was not given (Fig 1). Because of significant differences in prognosis, in all subsequent analyses, patients with high- and low-grade tumors are reported separately.

Patients With High-Grade Sarcoma

Among the 91 patients diagnosed with high-grade extremity sarcomas, 47 were randomized to receive chemotherapy alone and 44 to receive XRT with chemotherapy. Among four patients who violated protocol, three were randomized to receive no radiation and one to receive radiation. All of these violations involved refusal to receive or complete chemotherapy. All analyses presented include these four patients, but elimination of these patients did not alter any conclusion. Patient characteristics were well balanced between arms (Table 2) without significant differences in sex, race, tumor site, tumor size, or tumor grade. Patients receiving XRT had slightly more resections with close margins and slightly fewer with widely negative margins, but these differences did not reach significance. Seventy-seven percent of patients randomized to radiation and 89% of patients randomized to no radiation received more than 90% of their planned chemotherapy (P = .16; Fisher's test). Full-dose XRT was completed in all patients randomized to that treatment. Fifty-seven percent of patients required brief interruptions of their XRT for desquamation, but there were no major or acute toxicities seen from radiotherapy.

Table 1. Tumor Histology

	n
High-grade tumors	
Synovial cell sarcoma	26
Malignant fibrous histiocytoma	23
Liposarcoma	11
Spindle cell sarcoma (not specified)	10
Malignant schwannoma	9
Leiomyosarcoma	4
Epithelioid sarcoma	2
Alveolar soft part sarcoma	2
Angiosarcoma	1
Fibrosarcoma	1
Extraskeletal chondrosarcoma	1
Pleomorphic rhabdomyosarcoma	1
Low-grade tumors	
Liposarcoma, myxoid	20
Liposarcoma, well-differentiated	6
Malignant fibrous histiocytoma	6
Desmoid, extraabdominal	5
Spindle cell sarcoma (not specified)	4
Dermatofibrosarcoma protuberans	4
Chondrosarcoma	2
Leiomyosarcoma	2
Malignant schwannoma	1

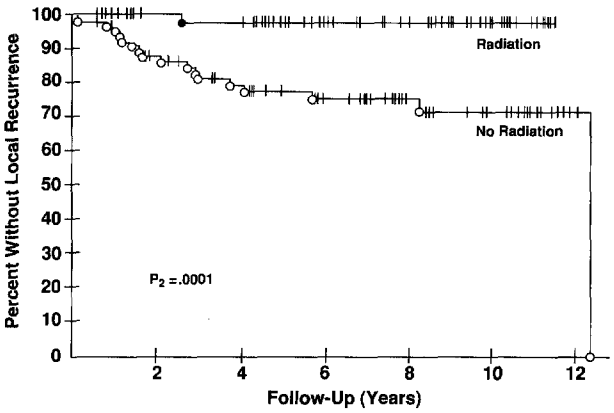

Fig 1. Local recurrence-free survival for all patients with soft tissue tumors of the extremity randomized to receive or not receive adjuvant postoperative external-beam XRT. Patients who develop metastatic disease are censored for LR.

With a median potential follow-up of 9.6 years (range 4.3 to 12.3 years), there have been no LRs (as the site of initial recurrence) in patients randomized to receive XRT and nine LRs in patients randomized to not receive XRT (P_2 = .003). The estimated actuarial local failure rate at 10 years in patients randomized to receive only chemotherapy is 22% (95% confidence interval; range, 12% to 37%) (Fig 2). Despite the difference in LR rate, there was no difference in the probability of distant metastatic disease in the two treatment groups (Fig 3; P_2 = .64). Furthermore, the estimated 10-year OS for the two arms is similar at 75% for patients receiving radiation and 74% for patients not receiving radiation (Fig 4; P_2 = .71; 95% confidence interval on the difference in OS at 10 years = −18% to +19%). With the small number of patients failing locally in this study, LR

Table 2. Patients With High-Grade Sarcoma

	No XRT		Adjuvant XRT		Patients With LR
	No.	%	No.	%	No.
Total patients randomized	47		44		9
Protocol violators	3	6	1	2	1
Sex					
Male	26	55	20	45	6
Female	21	45	24	55	3
Site					
Proximal upper extremity	7	15	6	14	2
Distal upper extremity	5	11	2	5	1
Proximal lower extremity	25	53	21	48	6
Distal lower extremity	10	21	15	34	0
Tumor					
Grade 2	26	55	24	55	4
Grade 3	21	45	20	45	5
Tumor size (cm; maximum diameter)					
0-1.9	4	9	3	7	0
2.0-4.9	15	32	16	36	3
5-9.9	17	36	18	41	4
≥10.0	11	23	6	14	2
Not available	0	0	1	2	0
Surgical resection margin					
Positive (<1 mm)	4	9	3	7	1
Negative; close (1-10 mm)	14	30	8	18	3
Negative; wide (>10 mm)	5	11	12	27	0
Negative; not specified	5	11	4	9	2
No tumor in re-resection	18	38	17	39	3
Not available	1	2	0	0	0

was significantly associated with the absence of XRT, but not with tumor size, margin status, tumor grade, or amount of chemotherapy received (Table 2). Of the nine patients with LR, four experienced synchronous distant metastases and three of these patients have died of metastatic sarcoma (Table 3). One patient with an LR and a solitary pulmonary

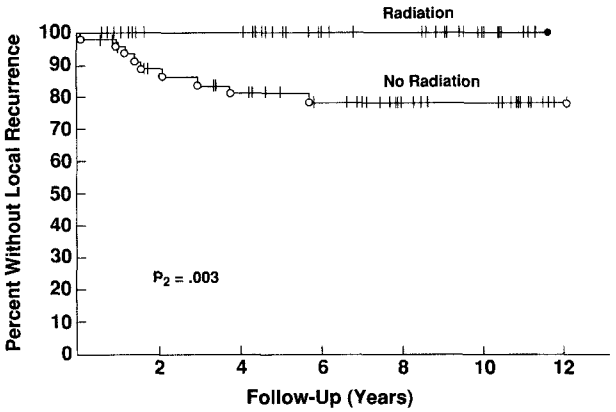

Fig 2. Local recurrence-free survival in patients with high-grade, locally resectable extremity soft tissue sarcomas randomized to treatment with surgery and adjuvant chemotherapy versus surgery, adjuvant chemotherapy, and postoperative XRT. LR occurred only in the absence of XRT.

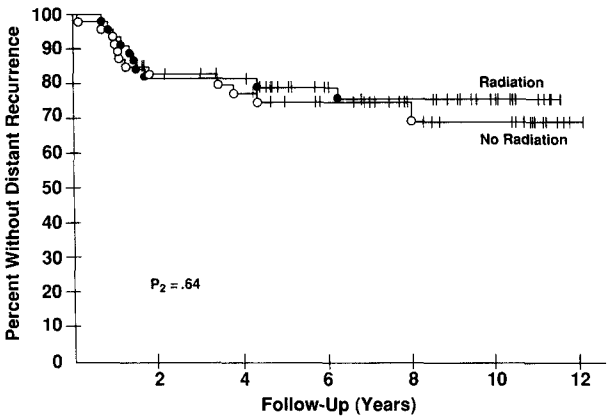

Fig 3. Metastatic DFS of patients with high-grade extremity sarcoma randomized to receive surgery and chemotherapy versus surgery, chemotherapy, and XRT.

metastasis and the other five patients with isolated LRs all underwent surgical resections and have remained free of metastases 4, 5, 6, 7, 7, and 8 years following resection of their recurrences. These six local recurrences were treated with amputation in two cases and wide local re-excision and postoperative XRT in four cases.

Patients With Low-Grade Sarcoma

Twenty-six patients with low-grade extremity sarcomas were randomized to receive adjuvant XRT and twenty-four were randomized to treatment with surgery only. Demographic characteristics in these two patient populations were evenly distributed (Table 4). There was one protocol violation in which a patient refused XRT after randomization. She is included in all analyses according to randomization. With a median follow-up of 9.9 years (range 1.4 to 12.4 years), eight patients randomized to not receive XRT have locally recurred, and one treated with XRT has locally recurred

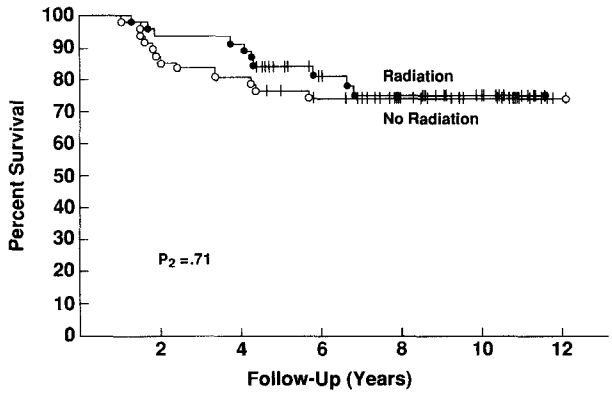

Fig 4. Overall survival of patients with high-grade extremity sarcoma randomized to treatment with surgery and adjuvant chemotherapy versus surgery, chemotherapy, and XRT.

Table 3. Patients With High-Grade Soft Tissue Sarcoma and LRs After Surgery

Treatment of LR	Distant Recurrence	Survival
Amputation	Yes (synchronous)	DOD
None	Yes (synchronous)	DOD
None	Yes (synchronous)	DOD
WLE and XRT	Yes (synchronous)	NED (7)*
WLE and XRT	No	NED (8)*
WLE and XRT	No	AWD (7)*
Amputation	No	NED (4)*
WLE and XRT	No	NED (6)*
Amputation	No	NED (5)*

Abbreviations: WLE, wide-local excision; DOD, died of disease; NED, no evidence of disease; AWD, alive with (local) disease.

*Follow-up after local recurrence (years).

($P = .016$) (Fig 5). If the nine patients with desmoid tumors or dermatofibrosarcoma protuberans (rather than true grade 1 sarcomas) are excluded from the analysis, then six of 19 patients not receiving XRT and one of 22 patients receiving XRT have locally recurred ($P = .067$). The patient recurring after XRT was initially treated with a lateral arm field and recurred at the margin of this field in the medial arm. Of the nine patients with LR, one required amputation for a massive proximal thigh recurrence and promptly developed high-grade pulmonary metastases, one declined further treatment, and one had a palliative re-resection in the face of advanced cardiac disease. The other six patients underwent

Table 4. Patients With Low-Grade Sarcoma

	No XRT		Adjuvant XRT		Patients With LR
	No.	%	No.	%	No.
Total patients randomized	24		26		9
Protocol violators	0	0	1	4	0
Sex					
Male	17	71	15	58	6
Female	7	29	11	42	3
Site					
Proximal upper extremity	5	21	7	27	2
Distal upper extremity	1	4	1	4	0
Proximal lower extremity	15	63	12	46	5
Distal lower extremity	3	13	6	23	2
Tumor grade					
Benign	5	21	4	15	2
Grade 1	19	79	22	85	7
Tumor size (cm)					
0-1.9	2	8	2	8	0
2.0-4.9	4	17	8	31	2
5.0-9.9	8	33	9	35	3
≥10.0	10	42	7	27	4
Surgical resection margin					
Positive (<1 mm)	7	29	4	15	4
Negative; close (1-10 mm)	6	25	4	15	2
Negative; wide (>10 mm)	0	0	1	4	0
Negative; not specified	2	8	7	27	2
No tumor in re-resection	9	38	10	38	1

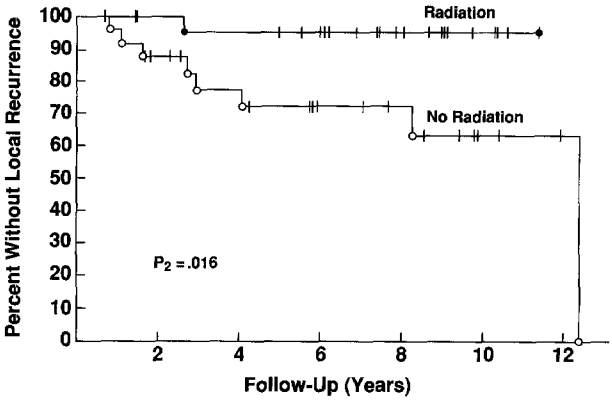

Fig 5. Local recurrence-free survival of patients with low-grade extremity tumors treated with surgery alone, or surgery and postoperative adjuvant XRT.

local re-excisions and irradiation and have not locally recurred 14, 19, 51, 59, 74, and 84 months after their re-excisions. There have been four deaths from metastatic disease among patients with low-grade tumors (two in each treatment arm), with only one of these patients having a local recurrence.

Quality-of-Life Studies

As a group, patients receiving XRT had significantly decreased joint motion in the affected limb compared with patients not given XRT when analyzed 6, 12, 24, and 36 months after surgery. Muscle strength was lower 12 months after surgery with adjuvant XRT, but this was of borderline significance. Greater edema was found in this treatment group during the first year after surgery. No significant differences in these parameters were identified between the two treatment arms on baseline assessments before XRT (Table 5). When these parameters were analyzed for change

Table 5. Quality-of-Life Assessment

		Mean Score			
Evaluation Point (months)	Treatment Arm	Muscle Strength (0-3)*	Joint Motion (0-3)*	Edema (0-3)*	FLIC Score (0-154)†
Baseline	No XRT	0.57	0.69	0.34	112
	XRT	0.53	0.90	0.36	114
6	No XRT	1.07	0.87‡	0.44‡	125
	XRT	0.98	1.41	0.91	118
12	No XRT	0.80	0.82‡	0.43	127
	XRT	1.11	1.52	0.62	129
24	No XRT	0.66	0.51‡	0.39	130
	XRT	0.94	1.59	0.56	125
36	No XRT	0.77	0.65‡	0.23	127
	XRT	0.75	1.41	0.50	131

*0 = normal function/best score.

†154 = FLIC best score.

‡Significant difference from patients who received XRT ($P < .05$).

from baseline for the two treatment groups, a persistent reduction in joint motion and transient, but significant, increases in limb weakness and edema were confirmed in patients given XRT (not shown). Despite these findings, there were no significant differences between patients in the two treatment arms as measured by a global quality-of-life scale (FLIC) or in performance of activities of daily living (quantitated by the modified Erdman scale).

DISCUSSION

The development of treatment strategies for patients with primary soft tissue sarcoma have emphasized local control with maintenance of limb function, OS, and quality of life. External-beam radiotherapy has been widely advocated as a means of improving local control after limb-sparing procedures, although its effectiveness in this role has never been definitively determined. In addition to its effectiveness, it is also important to assess the impact of adjuvant XRT on long-term function and quality of life, because many patients with sarcoma may not recur locally after surgery alone, but might have to endure complications of prophylactic XRT for many decades. Historically, limited surgery alone has resulted in excessively high rates of LR. With the current understanding of optimal surgery and the availability of other adjuvants such as chemotherapy, a re-evaluation of the efficacy and overall benefit of adjuvant XRT for soft tissue tumors of the extremities was undertaken.

In this prospective randomized trial, adjuvant postoperative external-beam radiotherapy was shown to result in a statistically significant reduction in LRs in patients with either high-grade or low-grade extremity tumors. Overall survival and nonlocal recurrences were nearly identical for patients receiving or not receiving radiation. Thus the conclusions regarding adjuvant XRT for patients with sarcoma are similar to conclusions reached for the use of adjuvant, postoperative XRT in patients with primary breast and rectal cancer, where local control was enhanced without significant differences in overall survival.[27,28] Brennan et al,[13] Pisters et al,[14,29] and Harrison et al[30] have performed the only other randomized trial addressing this issue in patients with sarcoma. They used brachytherapy instead of external-beam radiotherapy to treat adults with soft tissue sarcomas, and saw a smaller impact on local control from adjuvant XRT in patients with high-grade tumors, and no effect in patients with low-grade tumors. This difference in result in patients with low-grade tumors raises the possibility that brachytherapy may be clinically inferior to external-beam radiotherapy in this setting.

The estimated LR rate of patients in this study who did not receive adjuvant XRT was 22% at 10 years for patients with high-grade tumors. This may be attributable either to the adjuvant chemotherapy given to patients with high-grade tumors, or to the limited number of resections resulting in positive surgical margins. Patients in whom complete tumor resection could not be accomplished without ablating all meaningful limb function were offered amputation and were not included in this trial. Therefore, the conclusions of this study are pertinent only to patients who undergo a satisfactory local excision with negative or minimal microscopically positive resection margins and cannot be safely extrapolated to patients with frankly inadequate tumor resections.

With different strategies yielding similar overall survival rates, recommendations for the use of XRT may rest primarily on quality-of-life issues and individual patient risk factors for LR. Although this study had too few local failures to identify risk factors for LR (other than lack of XRT), previous studies have suggested that previous recurrence and surgical margins have the greatest impact on local recurrence.[31,32] It is of interest to note that no patient in this trial who had a widely negative resection margin locally recurred. For the four patients in this study with high-grade primary tumors who suffered LR and synchronous metastatic disease, the timing of these recurrences suggested that the primary tumor, rather than the LR, was the likely source of those metastases, although this issue cannot be definitively resolved. It remains likely that the impact of their LR was overshadowed by their distant metastatic disease, and, in fact, three of these patients have died of their metastatic tumor. All other patients (including one with resection of a solitary pulmonary metastasis) have had resection of their LR and have not developed metastatic disease. For four patients, control of their LR eventually required limb amputation, and the consequences of not administering XRT to these patients must be judged against the impact of administering apparently unnecessary radiation to approximately 75% to 80% of the patients in the other treatment arm (patients who would not have locally recurred after surgery and chemotherapy only).

In an attempt to clarify these issues, this study was performed with a concurrent prospective quality-of-life investigation. All significant differences in functional parameters between the two treatment arms favored patients not given XRT. The primary areas showing a difference were muscle strength, edema, and joint motion. Because these differences were often transient and not debilitating, overall satisfaction and activities of daily living were not consistently degraded by the administration of XRT. Therefore, this study suggests that when XRT can be administered with minimal toxicity and long-term side effects, its significant contribution to local sarcoma control following limited resection is of value.

When the expected toxicity of XRT is high and the risk of LR is predicted to be low (based on surgical margins, tumor size and location, or other parameters), surgery without adjuvant XRT may be the treatment of choice.

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