TABLE 119e-1 AMERICAN JOINT COMMITTEE ON CANCER STAGING SYSTEM FOR SARCOMAS

Histologic Grade (G)	Tumor Size (T)	Node Status (N)	Metastases (M)
Well differentiated (G1)	≤5 cm (T1)	Not involved (N0)	Absent (M0)
Moderately differentiated (G2)	>5 cm (T2)	Involved (N1)	Present (M1)
Poorly differentiated (G3)	Superficial fascial involvement (Ta)		
Undifferentiated (G4)	Deep fascial involvement (Tb)		
Disease Stage	**5-Year Survival, %**		
Stage I	98.8		
A: G1,2; T1a,b; N0; M0			
B: G1,2; T2a; N0; M0			
Stage II	81.8		
A: G1,2; T2b; N0; M0			
B: G3,4; T1; N0; M0			
C: G3,4; T2a; N0; M0			
Stage III: G3,4; T2b; N0; M0	51.7		
Stage IV	<20		
A: any G; any T; N1; M0			
B: any G; any T; any N; M1			

subsequent excision without compromising a definitive resection. Lymph node metastases occur in 5%, except in synovial and epithelioid sarcomas, clear-cell sarcoma (melanoma of the soft parts), angiosarcoma, and rhabdomyosarcoma, where nodal spread may be seen in 17%. The pulmonary parenchyma is the most common site of metastases. Exceptions are GISTs, which metastasize to the liver; myxoid liposarcomas, which seek fatty tissue; and clear-cell sarcomas, which may metastasize to bones. Central nervous system metastases are rare, except in alveolar soft part sarcoma.

Radiographic Evaluation Imaging of the primary tumor is best with plain radiographs and magnetic resonance imaging (MRI) for tumors of the extremities or head and neck and by computed tomography (CT) for tumors of the chest, abdomen, or retroperitoneal cavity. A radiograph and CT scan of the chest are important for the detection of lung metastases. Other imaging studies may be indicated, depending on the symptoms, signs, or histology.

STAGING AND PROGNOSIS

The histologic grade, relationship to fascial planes, and size of the primary tumor are the most important prognostic factors. The current American Joint Committee on Cancer (AJCC) staging system is shown in Table 119e-1. Prognosis is related to the stage. Cure is common in the absence of metastatic disease, but a small number of patients with metastases can also be cured. Most patients with stage IV disease die within 12 months, but some patients may live with slowly progressive disease for many years.

TREATMENT SOFT TISSUE SARCOMAS

AJCC stage I patients are adequately treated with surgery alone. Stage II patients are considered for adjuvant radiation therapy. Stage III patients may benefit from adjuvant chemotherapy. Stage IV patients are managed primarily with chemotherapy, with or without other modalities.

SURGERY

Soft tissue sarcomas tend to grow along fascial planes, with the surrounding soft tissues compressed to form a pseudocapsule that gives the sarcoma the appearance of a well-encapsulated lesion. This is invariably deceptive because "shelling out," or marginal excision, of such lesions results in a 50–90% probability of local recurrence. Wide excision with a negative margin, incorporating the biopsy site, is the standard surgical procedure for local disease. The adjuvant use of radiation therapy and/or chemotherapy improves the local control rate and permits the use of limb-sparing surgery with a local control rate (85–90%) comparable to that achieved by radical excisions and amputations. Limb-sparing approaches are indicated except when negative margins are not obtainable, when the risks of radiation are prohibitive, or when neurovascular structures are involved so that resection will result in serious functional consequences to the limb.

RADIATION THERAPY

External-beam radiation therapy is an adjuvant to limb-sparing surgery for improved local control. Preoperative radiation therapy allows the use of smaller fields and smaller doses but results in a higher rate of wound complications. Postoperative radiation therapy must be given to larger fields, because the entire surgical bed must be encompassed, and in higher doses to compensate for hypoxia in the operated field. This results in a higher rate of late complications. Brachytherapy or interstitial therapy, in which the radiation source is inserted into the tumor bed, is comparable in efficacy (except in low-grade lesions), less time-consuming, and less expensive.

ADJUVANT CHEMOTHERAPY

Chemotherapy is the mainstay of treatment for Ewing's primitive neuroectodermal tumors (PNET) and rhabdomyosarcomas. Meta-analysis of 14 randomized trials revealed a significant improvement in local control and disease-free survival in favor of doxorubicin-based chemotherapy. Overall survival improvement was 4% for all sites and 7% for the extremity site. An updated meta-analysis including four additional trials with doxorubicin and ifosfamide combination has reported a statistically significant 6% survival advantage in favor of chemotherapy. A chemotherapy regimen including an anthracycline and ifosfamide with growth factor support improved overall survival by 19% for high-risk (high-grade, ≥5 cm primary, or locally recurrent) extremity soft tissue sarcomas.

ADVANCED DISEASE

Metastatic soft tissue sarcomas are largely incurable, but up to 20% of patients who achieve a complete response become long-term survivors. The therapeutic intent, therefore, is to produce a complete remission with chemotherapy (<10%) and/or surgery (30–40%). Surgical resection of metastases, whenever possible, is an integral part of the management. Some patients benefit from repeated surgical excision of metastases. The two most active chemotherapeutic agents are doxorubicin and ifosfamide. These drugs show a steep dose-response relationship in sarcomas. Gemcitabine with or without docetaxel has become an established second-line regimen and is particularly active in patients with undifferentiated pleomorphic sarcoma (UPS) and leiomyosarcomas. Dacarbazine also has some modest activity. Taxanes have selective activity in angiosarcomas, and vincristine, etoposide, and irinotecan are effective in rhabdomyosarcomas and Ewing's sarcomas. Pazopanib, an inhibitor of the vascular endothelial growth factor, platelet-derived growth factor (PDGF), and c-kit is now approved for patients with advanced soft tissue sarcomas excluding liposarcomas after failure of chemotherapy. Imatinib targets the KIT and PDGF tyrosine kinase activity and is standard therapy for advanced/metastatic GISTs and dermatofibrosarcoma protuberans. Imatinib is now also indicated as adjuvant therapy for completely resected primary GISTs. Three years of adjuvant imatinib appears to be superior to 1 year of therapy for high-risk GISTs, although the optimal treatment duration remains unknown.