



PRINCESS MARGARET CANCER CENTRE CLINICAL PRACTICE GUIDELINES

SARCOMA

SOFT TISSUE SARCOMA

Site Group: Sarcoma – Soft Tissue Sarcoma

Author: Dr. Peter Ferguson

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1. Introduction

Soft tissue sarcomas are rare tumours arising from mesenchymal tissues, representing approximately 1% of all adult malignancies. They are an extremely heterogeneous group of tumours, composed of over 50 subtypes with distinct pathologic features and clinical behaviours. The commonest subtypes are liposarcoma, leiomyosarcoma, synovial sarcoma, malignant peripheral nerve sheath tumour and undifferentiated pleomorphic sarcomas. The majority of soft tissue sarcomas arise in the extremities and trunk (80%), with 15% arising in the retroperitoneum. Soft tissue sarcomas preferentially metastasize to the lungs (90%), and regional lymph nodes (5%).

2. Prevention

Not applicable to soft tissue sarcoma.

3. Screening and Early Detection

Not applicable to soft tissue sarcoma.

4. Diagnosis

All patients with soft tissue sarcoma should be assessed in a multidisciplinary clinic with expertise in sarcoma. Local imaging of the primary tumour must include MRI for extremity and trunk locations and MRI with CT for retroperitoneal tumours. Chest CT must be done on all patients. Other staging studies are indicated for specific subtypes – Abdominal/pelvic CT for myxoid/round cell liposarcoma; CT imaging of regional lymph nodes for epithelioid sarcoma, clear cell sarcoma, angiosarcoma and rhabdomyosarcoma and synovial sarcoma.

Important staging information to be gained from imaging of the primary site includes the maximal tumour diameter (< or > 5 cm) and the relationship to the superficial fascia (deep or superficial). Other information pertinent to local treatment planning includes involvement of major vascular structures, major motor nerves, bone and pelvic/abdominal organs.

Tissue diagnosis must be obtained by core needle or open incisional biopsy. If open biopsy is undertaken, the incision must be longitudinal in the extremities and in line with the eventual definitive resection incision, with minimal contamination of the surrounding tissues. The crucial information from biopsy includes tumour grade (low, medium and high grade) and sarcoma subtype.

Staging is carried out according to the AJCC staging system, which considers the factors of tumour size and location, grade, lymph node involvement and distant metastases:

TABLE 1: AJCC version 7 staging for soft tissue sarcomas**Primary Tumor (T)**

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor 5 cm or less in greatest dimension
T1a	Superficial tumor
T1b	Deep tumor
T2	Tumor more than 5 cm in greatest dimension
T2a	Superficial tumor
T2b	Deep tumor

Note: Superficial tumor is located exclusively above the superficial fascia without invasion of the fascia; deep tumor is located either exclusively beneath the superficial fascia, superficial to the fascia with invasion of or through the fascia, or both superficial yet beneath the fascia.

Regional Lymph Nodes (N)

NX	Regional lymph nodes cannot be assessed
NO	No regional lymph node metastasis
N1	Regional lymph node metastasis

Note: Presence of positive nodes (N1) in M0 tumors is considered Stage III.

Distant Metastasis (M)

M0	No distant metastasis
M1	Distant metastasis

ANATOMIC STAGE/PROGNOSTIC GROUPS

Stage IA	T1a	NO	M0	G1, GX
	T1b	NO	M0	G1, GX
Stage IB	T2a	NO	M0	G1, GX
	T2b	NO	M0	G1, GX
Stage IIA	T1a	NO	M0	G2, G3
	T1b	NO	M0	G2, G3
Stage IIB	T2a	NO	M0	G2
	T2b	NO	M0	G2
Stage III	T2a	NO	M0	G3
	T2b	NO	M0	G3
	Any T	N1	M0	Any G
Stage IV	Any T	Any N	M1	Any G

From Edge SB, Byrd DR, Compton CC, et al (eds): AJCC Cancer Staging Manual, 7th ed. New York, Springer, 2010.

5. Pathology

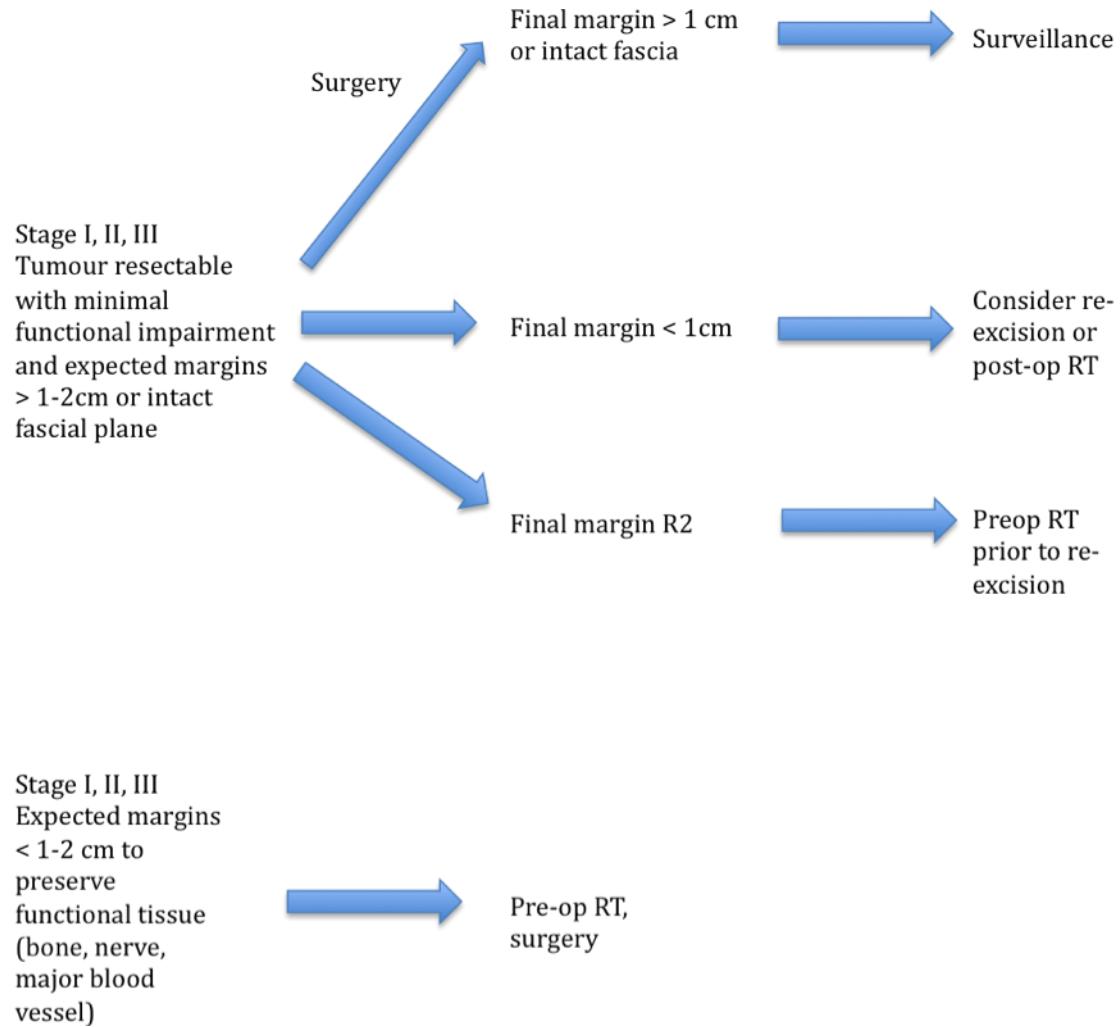
All sarcoma biopsies and resection specimens should undergo pathologic assessment by an experienced sarcoma pathologist. Biopsies should establish a malignant diagnosis, sarcoma subtype and grade. Ancillary tests such as immunohistochemistry, EM, cytogenetics and molecular genetic testing may be used in addition to morphologic assessment to establish a diagnosis, so assessment should be carried out in a site with access to the ancillary techniques.

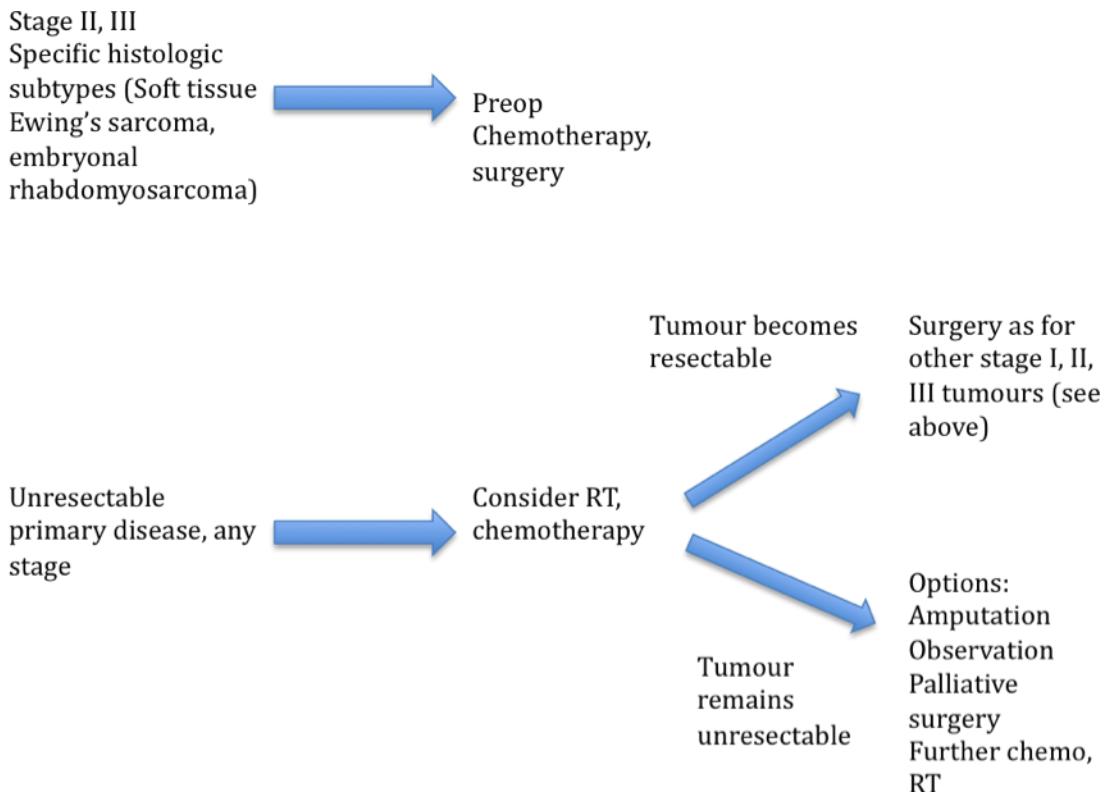
The pathology synoptic report should contain the following information: tumour location, primary diagnosis (WHO classification), depth (superficial or deep), size, histologic grade (using FNCLCC or NCIC classifications), necrosis, status of margins, status of lymph nodes, results of ancillary tests, additional features if present (mitoses, vascular invasion, character of tumour margin) and TNM stage.

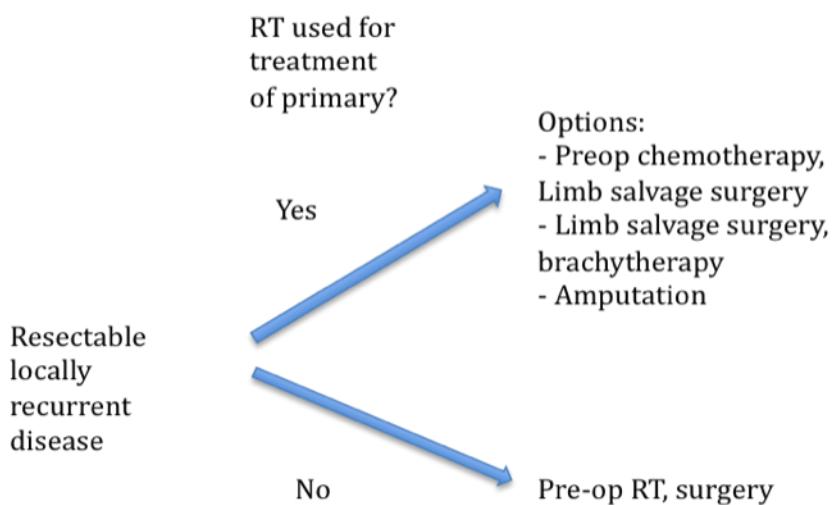
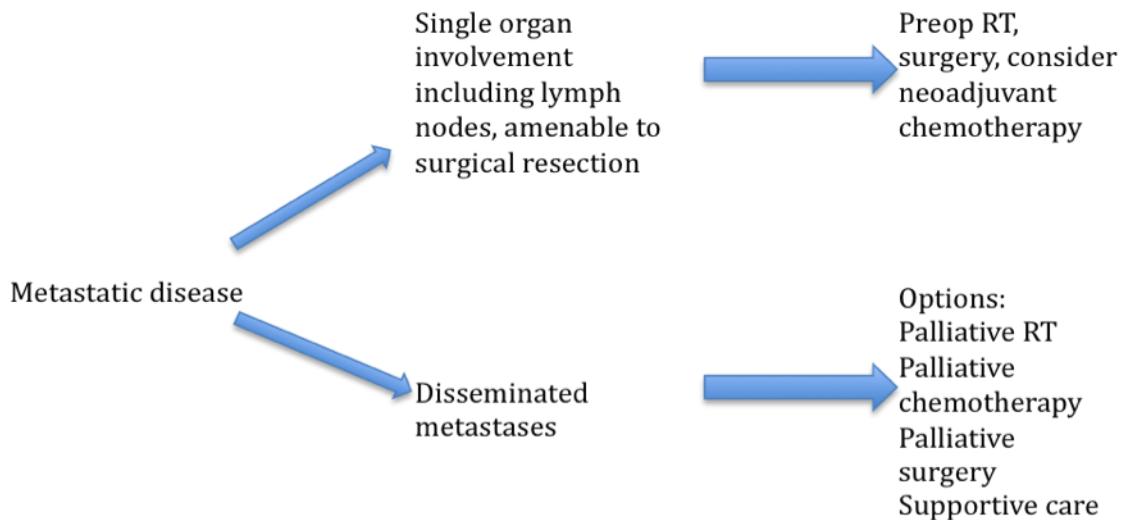
Although morphologic examination is the gold standard for most sarcoma diagnoses, molecular genetic testing has emerged as an important ancillary technique as many sarcomas feature typical and characteristic genetic abnormalities. Sarcomas whose diagnosis are confirmed using genetic testing using FISH or PCR include: Ewing's sarcoma, desmoplastic small round cell tumour, alveolar rhabdomyosarcoma, myxoid/round cell liposarcoma, atypical lipomatous tumour, dedifferentiated liposarcoma, alveolar soft part sarcoma, clear cell sarcoma, dermatofibrosarcoma protuberans, extraskeletal myxoid chondrosarcoma, fibromyxoid sarcoma and synovial sarcoma.

6. Management

6.1 Management Algorithms







For
unresectable
locally
recurrent
disease, follow
unresectable
primary
tumour
algorithm

6.2 Surgery

Biopsy of extremity, truncal, head and neck and retroperitoneal sarcomas should be done in consultation with an experienced sarcoma surgeon (for open incisional biopsy) or musculoskeletal radiologist (for core needle biopsy). Fine needle aspirate has little role in the diagnosis of sarcoma. The incision or needle track should be in line with the eventual definitive surgical incision and should be excised at the time of tumour resection.

The goal of sarcoma surgery should be resection with negative margins. If, on preoperative imaging, margins of 1-2 cm or intact fascia can be obtained without sacrificing critical structures such as bone, major motor nerves or major blood vessels, or vital organs, then surgery alone may be all that is necessary. This is usually only possible in T1a tumours.

For tumours that are close to the above structures, surgery is used with adjuvant radiotherapy and occasionally chemotherapy. When these adjuvants are used, very close negative margins are acceptable. These may be blood vessel adventitia, nerve epineurium and bone periosteum. Entire muscle compartments need not be resected unless the sarcoma is extensive.

If surgical margins are positive against critical structures such as nerves, blood vessels or bone, re-resection generally is not necessary provided adjuvant radiotherapy is used. The local recurrence rate in this situation is low. If surgical margins are grossly positive or positive unexpectedly in other anatomical areas, re-excision should be considered to minimize the risk of local recurrence.

Limb preservation should be the goal of surgery for extremity sarcomas. In cases where multiple motor nerves, blood vessels or bone require resection for negative margins, or if anticipated functional outcome with limb salvage surgery is expected to be very poor, amputation should be considered.

6.3 Chemotherapy

Chemotherapy is absolutely indicated for certain subtypes of soft tissue sarcoma, most notably soft tissue Ewing's sarcoma and embryonal rhabdomyosarcoma. Other subtypes that are often responsive include synovial sarcoma, leiomyosarcoma and some subtypes of liposarcoma (myxoid, pleomorphic, dedifferentiated). These should be given in a neoadjuvant fashion. Agents with activity in Ewing's sarcoma and rhabdomyosarcoma include vincristine, doxorubicin, cyclophosphamide, ifosfamide and etoposide. In other sarcomas, the main active agents are doxorubicin and ifosfamide.

The benefit of chemotherapy in sarcoma is unclear. Randomized trials of doxorubicin based chemotherapy shows a very small overall survival advantage. Some trials have shown decreased distant and local recurrence, albeit marginally. Chemotherapy may be utilized in some centers to try to improve resectability of stage II and III tumours.

For unresectable tumours chemotherapy may be utilized as the initial treatment to try to downstage the tumour. In some situations the tumour may become resectable and limb salvage may be undertaken.

In patients with metastatic disease, single agent chemotherapy may be utilized as the initial treatment and if there is appreciable response, resection of the primary tumour and metastases

may be undertaken providing serious functional consequences will not ensue. In these situations single agents such as doxorubicin or ifosfamide may be used.

6.4 Radiation Therapy

Radiation therapy is used in addition to surgery in the vast majority of patients with soft tissue sarcoma. The addition of radiation to surgery has allowed for limb salvage surgery in most patients, due to a much narrower surgical margin without concomitant increase in local recurrence.

Radiotherapy can be administered preoperatively or postoperatively. There is no difference in local control between the two. The main advantage to preoperative radiation is that a smaller dose (50 Gy vs. 66 Gy) and volume are utilized, both of which lead to lower rates of long term extremity fibrosis and edema, and better functional outcome scores. The main disadvantage to preoperative radiation is a near doubling of the wound complication rate (17% in postop vs. 35% in preop). Wound complications however are also modifiable. Other problems with postoperative radiation include a higher risk of radiation associated fractures and secondary sarcomas. For these reasons, many centers now utilize preoperative radiation in soft tissue sarcomas.

In T1a and T2a patients (superficial tumours), radiation may not be necessary if the expected surgical margins will be greater than 1-2 cm or intact fascia. If the margins are closer than expected on final pathologic review then postoperative radiation may be undertaken. Otherwise, if the expected surgical margins are to be less than 1 cm, in order to save critical functional structures, radiation should be considered even in low-grade tumours.

In unresectable tumours, radiation may be utilized to attempt to downstage the tumour and limb salvage surgery may then be undertaken if the tumour becomes resectable.

In patients with metastatic disease, radiation may be utilized as a palliative means to control pain and other symptoms.

In patients with locally recurrent sarcoma, the decision to utilize radiation is dependent on whether it was administered to treat the primary tumour. If not, then radiation should be given. If radiation was previously utilized, the previous radiation plan should be consulted and if further treatment often in the form of intensity modulated radiotherapy (IMRT) can be administered without exceeding the critical dose to major anatomic structures, then it may be utilized. Otherwise, chemotherapy may be utilized as an adjuvant, or surgery alone, either limb salvage or amputation, may be undertaken.

6.5 Other Therapy

This section not applicable to soft tissue sarcoma.

6.6 Oncology Nursing

Specialized nursing care is essential in the management of patients with soft tissue sarcoma. Because of the rarity of the condition, nurses knowledgeable about and experienced in caring for patients with soft tissue sarcoma contribute significantly to their outcome. Specialized surgical nursing care is important in dealing with postoperative complications and rehabilitation issues.

Similarly, chemotherapy and radiotherapy nursing care by individuals knowledgeable about sarcoma are important in managing toxicity issues and some symptom control.

7. Supportive Care

7.1 Patient Education

Because of the rarity of soft tissue sarcoma, patients often benefit from a significant educational component to their treatment. Patient based support groups are often utilized for new patients to gain insight into their disease. Educational materials prior to chemotherapy, radiation and surgery are ideal to help patients prepare for complications and toxicity.

7.2 Psychosocial Care

Social work and psychiatry are invaluable in providing support for psychosocial issues. Because many patients often travel great distances for sarcoma treatment when it is provided in quaternary care centres, social work is often important in managing social and family issues. Psychiatry may be beneficial in helping often young patients and families with coping strategies.

7.3 Symptom Management

Although most patients with soft tissue sarcoma present with painless masses, some patients may have significant symptoms if major nerves or bone are involved or if tumours are extremely large. In these situations, involvement of pain management specialists may be beneficial. The often large surgical resections for sarcoma may be associated with significant postoperative pain and the same individuals may be involved in this situation.

7.4 Clinical Nutrition

This section not applicable to soft tissue sarcoma.

7.5 Palliative Care

Patients with advanced soft tissue sarcoma often remain ambulatory and mobile. The usual course of events with patients with metastatic sarcoma is respiratory failure from multiple pulmonary metastases. Early involvement of palliative care physicians with patients with metastatic sarcoma often provides a high quality end of life experience.

7.6 Other

Patients who have undergone limb salvage surgery for sarcoma should be referred for physiotherapy/ rehabilitation. This should continue until the patient reaches their maximal functional recovery, which may take several months.

8. Follow-up Care

For the first 2 years after initial treatment, patients undergo physical examination of the primary disease site and chest x-ray. Follow-up appointments then take place every 6 months until 5 years after initial treatment and then annually until 10 years after initial treatment.

For patients who develop locally recurrent or metastatic disease, follow-up takes place at the same intervals as presentation with primary disease.

For patients who have developed metastatic disease, consideration should be given to performing intermittent chest CT scans in follow-up.

For patients who have had primary tumours in anatomic areas that are difficult to examine (retroperitoneum, pelvis) consideration should be given to performing intermittent MRI of the area.