Soft-tissue Sarcomas

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Abstract

This article discusses the epidemiology, diagnosis, and management of primary soft-tissue sarcomas (STS). These musculoskeletal tumors are a rare and heterogeneous group of malignancies, which are best managed by multidisciplinary teams in specialist sarcoma referral centers. Historically, the standard for local control of these tumors has been amputation. Evolutions in multimodality treatment have seen a shift toward preservation of the limb. Advances in limb-sparing surgery have seen the quality of life in sarcoma patients to improve drastically; however, unplanned surgical excision of STS remains a major treatment dilemma in the control of local disease.

Keywords: *Limb-sparing surgery, musculoskeletal oncology, orthopedic tumors, sarcoma, soft-tissue sarcoma, unplanned excision of sarcoma*

MeSH terms: *Sarcoma, limb prosthesis, biopsy, tumors*

Introduction

Soft-tissue sarcomas (STS) are a rare and heterogeneous group of tumors, arising in connective tissues embryologically derived from the mesenchyme. There are a dozens of subtypes [Table 1] arising from cartilage, muscle, blood vessels, nerves, and fat.[1] Sarcomas make up <1% of all neoplasms, which often results in a delay in diagnosis.[2] Sarcomas are best managed at specialist referral centers, and suspected cases are recommended to be referred promptly, allowing for further investigation and review by a multidisciplinary team (MDT). Surgery remains the mainstay of treatment, supported by advancing multimodal therapies including chemotherapy and radiotherapy. This review discusses the diagnosis and management of sarcomas, along with the clinical challenges faced in orthopedic oncology.

Epidemiology and Classification

Sarcomas occur in 2–4 people per 100,000 population and its >50 subtypes are divided into two broad categories: STS and bone sarcomas.[2] Bone and STS are classified according to the "World Health Organization Classification of Tumours of Soft Tissue and Bone," as a part of the "International Classification of Diseases," which provides universal nomenclature for use by all international sarcoma centers.[1]

Key Points

- Sarcomas are tumors of mesenchymal origin
- Sarcomas make up <1% of all cancers
- Sarcomas occur in 2–4 people per 100,000 population
- Malignant fibrous histiocytoma is (MFH) no longer a sarcoma subgroup, the new diagnosis of exclusion is undifferentiated pleomorphic sarcoma (UPS)
- Most common STS are as follows:
  - Leiomyosarcoma
  - Liposarcoma.

STS diagnoses predominate over bone sarcoma diagnoses with a 4:1 incidence ratio, and there is a male preponderance for the incidence, with a ratio of approximately 1.4:1, male-to-female ratio.[3] The incidence reaches 230/million/year in the age group of 85 years and above, which shows a male predominance with an increase in the male:female ratio to 1.9:1.[4] Anatomically, the extremities are the most common site for STS, with the lower limb being a more common location than the upper limb, with a 28% to 12% distribution of all STS, respectively. The thigh is the most common site in the body for STS, with 44% of all extremity STS.[3]

Incidence and distribution

Bone sarcoma-to-STS incidence ratio is 1:4. There is a greater male preponderance of 1.4:1, male:female. The

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Table 1: Primary soft-tissue tumors

Tumour types	Sub-Types
Adipose	Benign
	Lipoma
	Malignant
	Well-differentiated liposarcoma
	Myxoid liposarcoma
Fibrous	Benign
	Nodular fasciitis
	Deep fibromatosis
	Malignant
	Fibrosarcoma
	Inflammatory fibrosarcoma
	Postradiation fibrosarcoma
	Cicatricial fibrosarcoma
Cartilage and bone forming	Malignant
	Extraskeletal chondrosarcoma
	Extraskeletal osteosarcoma
Skeletal muscle	Benign
	Rhabdomyoma
	Malignant
	Alveolar rhabdomyosarcoma
	Embryonal rhabdomyosarcoma
	Ectomesenchymoma
Smooth muscle	Benign
	Leiomyoma
	Malignant
	Leiomyosarcoma
	Epithelioid leiomyosarcoma
Vascular	Benign
	Hemangioma
	Intermediate malignancy
	Hemangioendothelioma
	Hemangiopericytoma
	Malignant
	Angiosarcoma
Nerve sheath	Benign
	Schwannoma
	Neurofibroma
	Malignant
	Malignant schwannoma
	Neuroepithelioma
	Malignant granular cell tumor
	Malignant peripheral nerve sheath tumor
Synovial tumors	Malignant
	Synovial sarcoma
	Malignant giant cell tumor of tendon sheath
Pleomorphic tumors	Malignant
	Myxofibrosarcoma
	Angiomatoid fibrous histiocytoma
	Giant cell-rich anaplastic carcinoma
	Leiomyosarcoma with osteoclastic giant cell reaction
	Giant-cell rich osteosarcoma
	Undifferentiated high-grade pleomorphic sarcoma
	Undifferentiated pleomorphic sarcoma with prominent inflammation

median age of diagnosis is 59 years. Bimodal distribution of STS peaking in the 5th and 8th decades.

Soft-tissue sarcomas

STS most commonly occur in the extremities, with 40% of all STS. Predominantly in the lower limbs (28%) versus upper limbs (12%). The thigh is the most common site in the body, accounting for 44% of all extremity STS.

The adverse prognostic factors for soft tissue sarcomas' are: Size, increasing age, high grade, metastasis at diagnosis, local recurrence at diagnosis (following unplanned excision), positive surgical margin, deep to muscular fascia, high levels of tumor necrosis.[5-7]

Diagnosis

Sarcomas present in a variety of ways, but regardless how a suspected sarcoma initially presents, the means of confirming the sarcoma remains the same i.e. by complete anatomic imaging and tissue diagnosis.

Clinical presentation

Given the heterogeneity of STS, it is not possible to specifically define the clinical features of a presenting sarcoma. Soft-tissue lumps showing any of the following clinical features are to be considered malignant until proven otherwise: increasing in size, >5 cm, deep seated, and/or painful. The greater the number of these clinical features being present, the greater the risk of a soft-tissue mass being a malignancy; with increasing size being the best individual indicator.[8]

Ultrasound scan

Ultrasound scan (USS) is commonly used for the investigation of superficial STS. It is readily accessible and is used to confirm the presence and evaluate the size and depth of a soft-tissue mass. USS may play a role in guidance for core-biopsy sampling of superficial masses. However, if a malignancy is suspected, then magnetic resonance imaging (MRI) and computed tomography (CT) scans are required prior to biopsy sampling, allowing for assessment and staging to be completed using images which have not yet been altered by intervention.[9] A note of caution – beware the chronic hematoma as USS can also be misinterpreted with a common USS misdiagnosis being chronic hematoma, which can lead to erroneous care.

Plain X-ray

Although X-rays are not particularly useful for the assessment of STS, they can provide valuable information. Calcification of a soft-tissue mass may indicate an extraosseous bone-forming sarcoma or synovial sarcoma. Myositis ossificans, a calcified hematoma and hemangiomas with phleboliths, while common, is associated with distinct presenting histories.[10]

Magnetic resonance imaging

MRI scans are routinely used to detect and evaluate STS [Figure 1a]. Its high level of soft-tissue contrast and anatomical detail mean that even small soft tissue can be detected with a great accuracy.[9] MRI scans of the affected region should include the whole anatomical compartment, the involved site, and its adjacent joints.

Signs on MRI which can be indicative (not diagnostic) of a malignancy are: Deep-seated large mass, heterogeneous signal, surrounding edema, associated destruction of bone.

MRI plays an essential role in the local staging of tumors such that no surgery is to be performed nor biopsy taken until an MRI is carried out. Biopsy planning with the use of cross-sectional imaging, such as MRI, ensures that other compartments are not contaminated and that the interpretation of images is not compromised by post biopsy edema or hemorrhage.[9,11]

MRI is extremely valuable in locating neurovascular structures and defining specific muscular compartments being affected, as well as showing the spread of individual muscles by the tumor. These factors play an essential role in determining the tumor's resectability and the anticipated quality of surgical margins.[9,12]

Computed tomography

CT is readily available and can be used in cases where MRI is contraindicated or where CT may better delineate areas of periosteal bone formation, micro-calcification, and cortical destruction. If faint calcification is seen on X-ray, a followup CT may be more useful than MRI given CT's higher sensitivity to calcification.[9] CT is not routinely used for local staging; however, it is essential in systemic staging where its role is to exclude pulmonary metastatic disease.[9] CT plays a significant role during tissue diagnosis of suspected STS [Figure 1b], used for guidance during core-needle biopsy sampling.

Positron emission tomography-computed tomography

Positron emission tomography-CT (PET-CT) is a nuclear medicine investigation which combines PET's ability to detect the distribution of metabolic or biochemical activity with CT's precise anatomic imaging, thereby defining the location of STS primary tumors and metastasis. Previously, identifying disease during the initial staging of sarcomas has been done by plain chest X-ray or chest CT and bone scintigraphy.[9] The staging system primarily used for STS is the American Joint Committee on Cancer [Table 2]. Evidence has shown that PET added to conventional imaging improved preoperative staging,[13] and recently, PET-CT scans have been shown to have a higher sensitivity, specificity, accuracy, negative predictive value, and positive predictive value than PET or CT alone and is therefore recommended as a part of routine diagnostic imaging in STS.[14,15]

Biopsy

Tissue biopsy of STS is an essential part of both diagnosis and management, with inadequate or inaccurate biopsies usually leading to poorer outcomes. Such poor outcomes include higher mortality rates and reduced opportunity for limb salvage. Biopsy techniques include core-needle biopsy with CT guidance [Figure 2] and open biopsy, with fine-needle biopsy not being sufficient as it does not provide information regarding the structure of the tumor,

Table 2: American Joint Committee on Cancer/ International Union against cancer tumor node metastasis staging system

Stage	Grade	Size (cm)	Metastasis
1	Low grade	≤8	None
1b	Low grade	>8	None
2	High grade	≤8	None
2b	High grade	>8	None
3	Any grade	Any	Skip metastasis
4	Any grade	Any	Distant metastasis at diagnosis

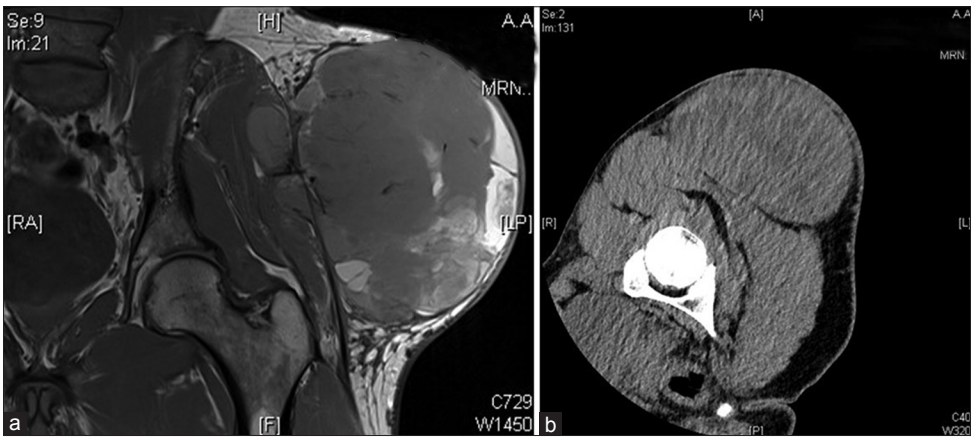

Figure 1: (a) Magnetic resonance imaging and (b) Computed tomography of a left gluteal synovial sarcoma. This patient successfully underwent wide resection and plastic reconstruction with a latissimus dorsi flap

which is essential for accurate tumor diagnosis. Biopsy specimens undergo a range of investigations, including immunohistochemistry, flow cytometry, and cytogenetics. The most routinely used grading system for bone and STS is the Fédération Nationale des Centres de Lutte Contre le Cancer grading system, which is displayed in Table 3.

Poorly planned biopsies have been shown to result in greater adverse outcomes than those which are appropriately planned, this includes the need for more amputations due to biopsy-related local contamination and subsequent spread of disease.[16] Given the associated risks, it is recommended that centers which are not able to adequately investigate the patient should refer to sarcoma specialist centers before performing a biopsy.[16-18]

Imaging Key Points

- USS: USS is used to confirm the presence and evaluate the size and depth of a soft-tissue mass. If malignancy is suspected, then an MRI is required. Beware the diagnosis of a chronic hematoma
- X-ray: Calcification of a soft-tissue mass is a potential indication of a malignancy
- MRI: Adequate scans will include the whole anatomical compartment, the involved site, and its adjacent joints. Essential for local staging of disease
- CT: Essential in systemic staging where its role is to exclude pulmonary metastatic disease. Used for guidance in core-biopsy sampling
- PET-CT: Recommended as a part of routine systemic staging
- Tissue biopsy: Gold standard for confirming sarcoma diagnosis. Recommended to be performed by a specialist referral center.

Inappropriate Excision of Sarcomas

Management of STS outside of specialist sarcoma referral centers results in significantly worse clinical outcomes. Adverse outcomes include increased morbidity from subsequent, potentially more complex surgeries and increased mortality.[19-22] Unplanned sarcoma excision refers to removal of a mass without the knowledge of its malignant nature and without the application of sarcoma-appropriate oncologic margins. Evaluation prior to a planned oncological excision involves complete anatomic MRI of the affected part, CT of the chest, and tissue biopsy.[23]

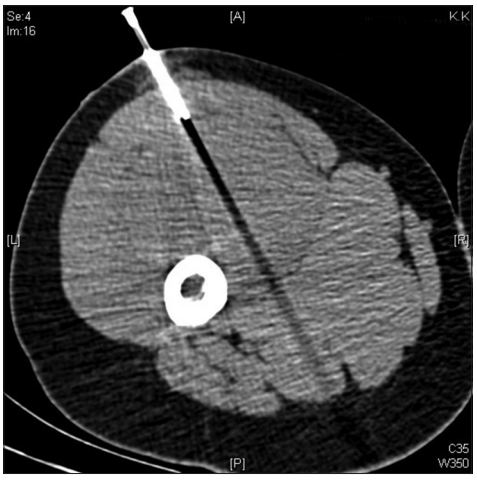

Figure 2: Computed tomography guided core-needle biopsy of a left thigh, in Ewing's sarcoma

A general practitioner (GP) will see many hundreds of benign tumors in their lifetime of clinical practice, but can be expected to only see one or two patients with STS.[24] Benign soft-tissue lumps, outnumbering malignant STS, present diagnostic difficulties, particularly to the uninitiated. Earlier diagnosis would result in improved survival and allow for less-damaging surgery being performed. Surgeons inappropriately excising STS include general surgeons, plastic surgeons, and nononcologically trained orthopedic surgeons, at times excising masses without definite knowledge what is contained inside [Figure 3a].

Knowledge that reexcision referrals are coming from these clinicians can allow for targeted education regarding safe and appropriate management. Educational interventions have been directed at these groups of surgeons, as well as GPs, however this problem has persisted. Inappropriate excisions account for a frightening 18% to 53% of total referrals at a number of specialist sarcoma centers.[22,25-27]

These inappropriately excised STS have been shown to have a 29% lower survival rate, 35% lower metastatic-free survival rate, and a 22.6% higher local recurrence rate.[23] Poor planning leading to recurrence can also result in necrotic, fungating, and infected tumors [Figure 3b]. Numerous studies have demonstrated that, as a downstream effect of inappropriate excision, 7.4%–18.5% of cases require amputation [Figure 3c] to achieve local control.[16,23,28] In addition to amputations, many patients require complex surgeries as a direct result of biopsy or excision prior to specialist referral. A recent study by Potter *et al*. showed that 32% of their sarcoma referrals had undergone nononcological excision at the time of presentation and were more likely

Table 3: Fédération Nationale des Centres de Lutte Contre le Cancer grading system

Tumor differentiation	Necrosis	Mitotic count (*n* per 10 high-power fields)
1: Well	0: Absent	1: *n* <10
2: Moderate	1: <50%	2: 10-19
3: Poor (anaplastic)	2: ≥50%	3: *n* ≥20

The sum of the scores of the three criteria determines the grade of malignancy. Grade 1=2 or 3, Grade 2=4 or 5, Grade 3=6

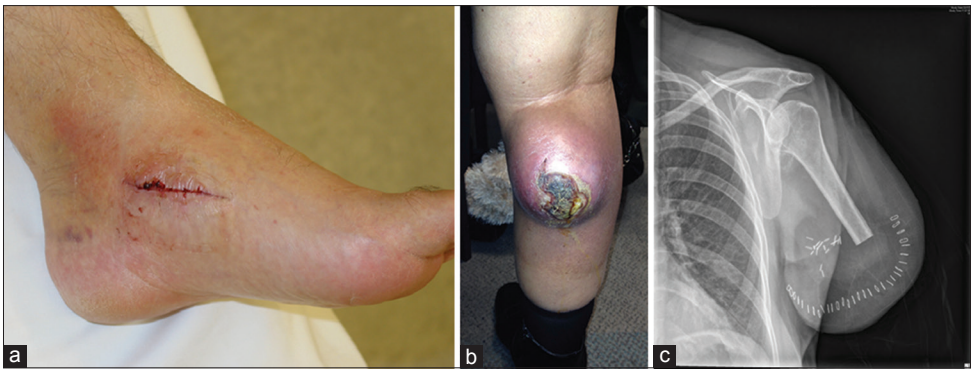

Figure 3: Inappropriate excisions. (a) Tibial neurovascular structure bruising is seen, a small lump believed to be a hematoma was excised, then found to be a synovial sarcoma. (b) Fungating right lower-leg tumor. This patient had undergone an unplanned excision of a small mass by a general surgeon, which turned out to be a sarcoma. Subsequently, the sarcoma locally recurred, rapidly grew, and began to fungate. (c) Forearm undifferentiated pleomorphic sarcoma, underwent unplanned excision prior to referral. Local recurrence resulted in the patient requiring above-elbow amputation

to require more complex surgery, including skin grafts or flap coverage. This subset of patients had a significantly higher rate of local recurrence (34% vs. 6%), despite the additional surgery.[20] This shows that, despite the best efforts of sarcoma specialists to salvage a chance at good therapy, excision prior to diagnosis and referral can potentially have an irreversible downstream effect on a patient's life.

Size Matters

The larger a STS is at referral, the worse the chance of cure.[5,29-31] A recent study analyzed 1460 STS and argued that, if a clinician discovered a soft-tissue mass bigger than 5 cm and growing, they should be very suspicious for sarcoma.[29] Analysis revealed that the average size of a referred sarcoma was 10.2 cm, and that mortality increased with increasing size at presentation, showing a patient with a STS up to 15 cm had a 3.5 times greater risk of dying than a patient with a tumor <5 cm at diagnosis ($P < 0.0001$) [Figure 4]. Given the description that "golf ball-sized mass" having been used to describe potential STS, the same authors established an educational program for referring clinicians. The intervention involved a mail package with a golf ball (4.2 cm in diameter), inscribed with "Is this Sarcoma?," along with a brochure explaining all deep-seated soft-tissue masses larger than a golf ball and red flag indicators for STS needed a diagnosis and referral to a sarcoma center.

Analysis revealed a very successful outcome, with a 37% increase in referrals.[32]

Common Features of a Malignant Lump

- Lump >5 cm
- Lump increasing in size
- Lump deep to the fascia
- Pain.

Figure 4: Golf ball sized 4.2 cm. Consider any lump bigger than this to be a sarcoma until proven otherwise

Key Points

- Soft-tissue masses which are >5 cm or are deep seated should always undergo MRI and tissue diagnosis prior to excision
- The care of patients diagnosed with STS should be supervised by a sarcoma specialist center MDT
- Excision of a STS should be performed by an orthopedic surgeon with specialist sarcoma training
- Unplanned sarcoma excision can lead to:
  - Increased mortality
  - Increased complex surgery including flaps
  - Increased local recurrence
  - Increased metastatic disease
  - Increased amputation.

Surgery

Surgery remains the primary treatment modality for STS. Decisions about the optimal surgical procedure for the primary tumor are based on the tumor location,

tumor size, involvement of adjacent anatomical structures, patient preference, and response to neoadjuvant therapies. Such decisions are often made with the consultation of an MDT. The primary aim of curative surgery is to excise the whole tumor with tumor-negative margins.

Local staging of disease is essential for surgical planning. As discussed earlier, imaging of the affected site should include plain radiographs, CT, MRI, or PET. The tumor size, capsule, consistency, site, shape, edge, and adjacent structures are vital pieces of information for planning the surgical margins and reconstructions after assessing response to neoadjuvant therapies.[33] Given that evidence of metastasis will likely affect the nature of care, all efforts to diagnose metastasis should be undertaken.[34]

STS have a predilection to grow in a centrifugal manner, which pushes the surrounding tissue aside as they grow. During this process, a pseudocapsule of compressed tissue and inflammation develops around the tumor, which often contains micro-satellites of tumor tissue.[11] Sarcomas commonly arise intracompartmentally (one anatomic compartment) and become extracompartmental once they grow to a size that exceeds the confines of the original compartment.[11] There are four primary forms of surgical margins in sarcoma surgery [Figure 5].

Intralesional

This form includes excision of a STS with microscopic disease remaining and potentially macroscopic disease. Intralesional excision may be planned, such as in palliative procedures, or unplanned, in which case the patient will require re-excision, if adequate margins can be achieved with acceptable morbidity.[8]

Marginal

Excision of tumor from within the surrounding reactive zone, no adjacent structures are excised. In cases where a tumor is directly adjacent to vital neurovascular structures, marginal margins combined with adjunct radiotherapy can be performed in place of wide resection margins [Figure 6].

Wide

The entire tumor is excised with a border of normal tissue encasing 100% of the tumor's margins. The resected specimen includes at least 2 cm of the normal tissue in the longitudinal plane and one named normal anatomic boundary in the radial plane. At times, an adjacent bone must be excised, in the rare event where removal of soft tissue alone in the radial plane is not sufficient to achieve a wide margin [Figure 5]. Local structures including blood vessels, peripheral nerves, and muscles are often excised in a bid to achieve a wide margin, often requiring reconstruction from other surgical specialties such as vascular and plastic surgery [Figure 7a and b].

Radical

This form indicates an extracompartmental excision involving all compartments that contain tumor. Commonly involves amputation of a limb; however, a radical margin is still possible with limb salvage. Despite having an extremely low recurrence rate (<5%), it is uncommonly performed due to high morbidity. Indications for a radical margin include local recurrence.[11]

Regardless of the histotype of a tumor or its grade, wide-margin excision is the surgical preference, as macroscopic residual disease imparts a poor prognosis and local control is not guaranteed to be achieved even with the addition of postoperative radiotherapy.[35]

As discussed above, the primary aim of surgery for STS is resection of the tumor with negative oncologic margins. A secondary goal is to reconstruct the site of the lesion

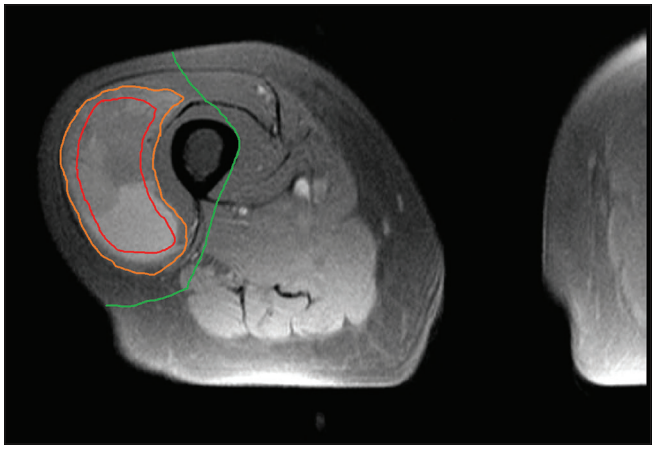

Figure 5: Axial MRI showing surgical margins of a right-sided thigh undifferentiated pleomorphic sarcoma. Red circle (innermost) represents an intralesional margin. Yellow circle (2nd from center) represents a marginal excision. Green circle (outermost line) represents a wide excision

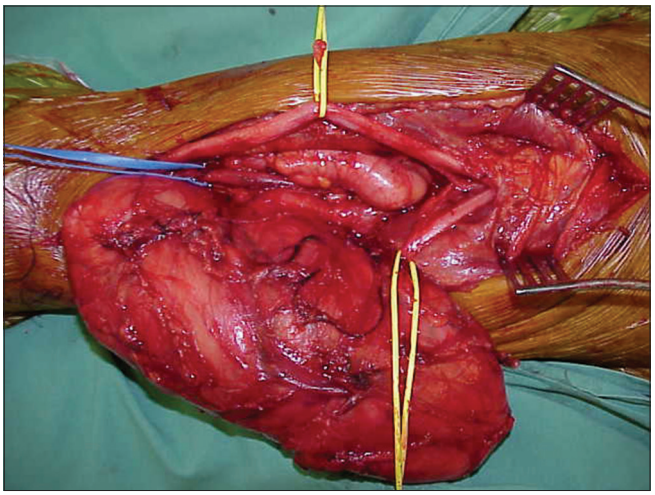

Figure 6: The intraoperative photograph showing the marginal excision of a high-grade liposarcoma

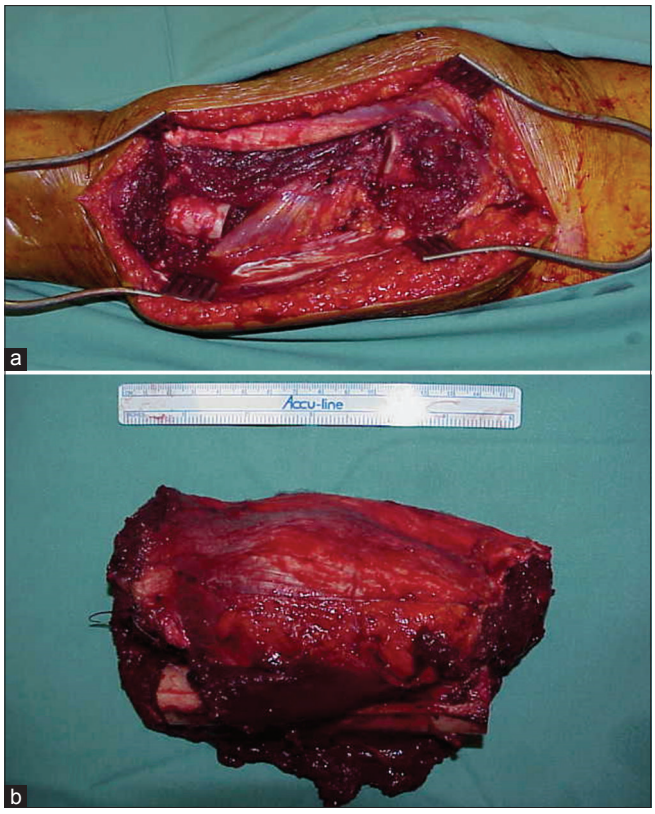

Figure 7: Peroperative clinical photographs (a) The cavity remaining following the wide-margin excision of a tumor of the thigh, where soft tissue and a section of femur, which the tumor had engulfed, were also excised. (b) The excised undifferentiated pleomorphic sarcoma from a patient's thigh. Note the surrounding soft tissue and femur to achieve the wide margin

Table 4: Chemosensitivity in soft-tissue sarcomas

Relative chemosensitivity	STS
Chemoinsensitive	Alveolar soft part sarcoma
	Extraskeletal myxoid chondrosarcoma
Relatively chemo insensitive	Malignant peripheral nerve sheath tumor
	Myxofibrosarcoma
	Dedifferentiated liposarcoma
	Clear cell sarcoma
	Endometrial stromal sarcoma
Moderately chemosensitive	Pleomorphic liposarcoma
	Epithelioid sarcoma
	Pleomorphic rhabdomyosarcoma
	Leiomyosarcoma
	Angiosarcoma
Chemosensitive	Desmoplastic small round cell tumor
	Synovial sarcoma
	Spindle cell sarcoma
	Myxoid/round cell liposarcoma
	Uterine leiomyosarcoma
Chemotherapy integral to management	Ewing's sarcoma family tumors
	Embryonal and alveolar rhabdomyosarcoma

STS=Soft-tissue sarcomas

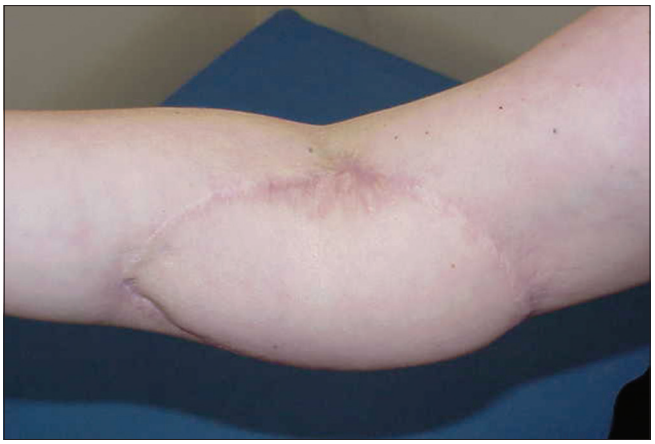

Figure 8: Clinical photograph showing a medial forearm reconstruction, with a skin and muscle flap, following the wide excision of a synovial sarcoma

such that it will enable the highest level of function for the patient. It is imperative, however, that the decision surrounding how the site will be reconstructed does not detract from the need to achieve an oncologically safe margin. Means of reconstructing a surgical site following STS resection include skin and muscle flaps [Figure 8].

Chemotherapy

Despite surgery being a universal treatment option for STS, adjuvant chemotherapy helps a limited number of subtypes and is often guided by the histology of the tumor [Table 4]. Chemotherapy is deemed an essential part of standard treatment for Ewing's sarcoma and osteosarcoma,[12] but routine use in STS remains largely unproven.[8] Standard treatment often comprises preoperative neoadjuvant systemic combination therapy, involving chemotherapy, surgical excision, and postoperative adjuvant chemotherapy.[36]

The principle behind neoadjuvant chemotherapy is to administer cytotoxic drugs soon after diagnosis, in a time frame where metastatic potential is possibly minimal and to enable assessment of the histologic response to chemotherapy in the excised tumor.[37] The response to chemotherapy is a strong prognostic factor to outcome, allowing for detection of poor responders who may need altered management to those who have a good response.[11]

Radiotherapy

Radiotherapy has a well-established role in the treatment regimen of both localized and metastatic STS. Three randomized controlled trials have confirmed that surgery combined with radiotherapy is the most effective management for most localized high-grade STS of the extremity.[38-40] The National Cancer Institute trial conducted in 1982 established limb-sparing surgery combined with radiotherapy as the new standard of management after revealing that amputation and limb-sparing surgery had equal survival rates.[38] The trials undertaken by Yang *et al*. and Pisters *et al*. in the late 1990s examined the effect of radiotherapy versus no radiotherapy

in patients with high-grade STS undergoing limb-sparing surgery, both trials showed improved local control with adjuvant radiotherapy.[39,40]

The primary purpose of radiotherapy is to inactivate the microscopic extensions of tumor which are surrounding the tumor capsule, reducing surgical potential for seeding and histologically positive margins, subsequently lowering the rate of local recurrence. Local recurrence rates as high as 30% were reported prior to the use of radiotherapy.[41] A dramatic drop in the local recurrence rate to below 15% was seen when combined radiotherapy and surgery was introduced.[42]

Various combinations of treatment are practiced, including both neoadjuvant (preoperative) radiotherapy and postoperative radiotherapy. One of the largest scale trials conducted to compare preoperative to postoperative radiotherapy, known as the National Cancer Institute of Canada SR2 trial, revealed that STS patients treated with postoperative radiotherapy had more subcutaneous fibrosis (48% vs. 31.5%), joint stiffness (23% vs. 17.8%), and extremity edema (23% vs. 15.1%), when compared to the preoperative radiotherapy.[43] However, despite the benefits of reduced late toxicity in preoperative radiotherapy, it comes with the trade-off of an 18% increased risk of acute major wound complications (35% vs. 17%), in favor of postoperative radiotherapy.[44] Given that wound healing is a serious risk for recovery, a number of measures can be taken to minimize the risk, including appropriate tissue handling, elimination of dead spaces, sufficient operative bed drainage, use of vascularized soft-tissue reconstructions where possible, and minimal tension wound closure.[11] Brachytherapy is a useful option in the treatment of STS, with advantages including targeted dose distribution, low integral dose, and short treatment times. There is no evidence, however, to support improved wound healing with brachytherapy over external beam radiotherapy for STS. Ultimately, the clinician should select the combination of modalities that are most familiar to the treating team and suitable to the patient.[45,46]

Key Points

- Preoperative chemotherapy and radiotherapy is essential in treating bone and STS, respectively
- Benefits of adjuvant therapy include: reducing tumor size, sterilizing tumor margins, inducing tumor necrosis, and treating metastatic disease
- Chemotherapy is fundamental in treating osteosarcoma and Ewing's sarcoma family tumors
- Radiotherapy reduces local recurrence in high-grade STS of the extremities
- Benefits of preoperative radiotherapy include less subcutaneous fibrosis, less joint stiffness, and less edema than postoperative radiotherapy, but is associated with greater wound breakdown.

Recent Advances

The 4th edition of the "WHO Classification of Tumours of Bone and Soft Tissue," published in 2013, provides the most advanced sarcoma nomenclature. The most significant of recent changes made by the WHO classification system is the removal of "MFH," which for decades was the most common type of STS. Extensive histopathological investigation revealed that the MFH category comprised upward of five different sarcomas and was subsequently replaced. Having formerly been considered a diagnosis of exclusion, the new category, for those sarcomas which do not fall under the diagnostic requirements of other specific types, is "UPS."[1]

Advances in adjuvant therapies have seen current radiotherapy become centered on the practice of image-guided radiotherapy. This involves the use of CT and MRI to enhance target and normal tissue localization for radiotherapy planning and delivery. A benefit of image-guided radiotherapy is that, if during the course of treatment, imaging demonstrates anatomical changes, the radiation plan can be modified to reflect these changes.[47] This intensity modulation based on changes seen in imaging during the course of therapy has been shown to reduce wound complications by 12.5% (30.5% vs. 43%), as compared to previous radiotherapy modalities used in trials three decades earlier.[48]

As advances in surgical managements have progressed, there has been a greater demand on the orthopedic oncologist to perform more limb-sparing surgery. The late 1970s saw an increase in limb-sparing techniques, albeit with a major complication rate upward of 30%,[11] with many patients subsequently undergoing amputation. Tumor size is a common predictor of amputation with only 8% of those patients with small (<5 cm) tumors requiring amputation compared to 39% of those with tumors >25 cm.[29] Limb-sparing surgery can be considered once the indications and contraindications for surgery are discussed [Table 5].[34]

Conclusion

STS are rare, heterogeneous tumors, whose morbidity and mortality rates have significantly reduced over the past half century due to advances in surgical techniques, adjuvant therapies, and diagnostic modalities. Steps continue to be taken to ensure that all patients with musculoskeletal tumors receive appropriate care, by educating the medical community about the adverse consequences of unplanned tumor resection and late referrals. The most important factor to be mindful of when managing orthopedic tumors is that the greatest outcomes for patients come from MDTs at specialist sarcoma referral centers. It is nothing short of exciting to envisage how patients will be managed at these centers in another half century.

Table 5: Limb-sparing surgery indications

Indications for limb-sparing surgery	Contraindications for limb-sparing surgery
Tumor resection can be achieved with oncologically sound margins	Surgical margins are expected to be inadequate for managing the primary tumor
Expected survival is long enough to justify complex surgery	Survival is not expected to exceed 3 months
The patient refuses an amputation and accepts the risk of local recurrence from inadequate margins	Gross contamination of the adjacent soft-tissue compartments with tumor due to poorly performed biopsy, inadvertent surgery with positive margins, or pathologic fracture
Palliating patients with limb disease that is easily and safely operated on to improve quality of life	Local or systemic sepsis is a concurrent problem

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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