A System of Staging Musculoskeletal Neoplasms

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A system for staging benign and malignant musculoskeletal lesions is presented. This system, first devised at the University of Florida in 1977, was based on data assembled from 1968 through 1976. It was field tested by the Musculoskeletal Tumor Society and published in *Clinical Orthopaedics and Related Research* in 1980. In the ensuing five years, the system has undergone refinement. It has recently been adapted by the American Joint Committee Task Force on Bone Tumors and proposed by them to the International Union Against Cancer (IUCC) for international usage. Based upon histologic grade (G), anatomic site (T), and presence or absence of metastases (M), it describes the progressive stages, irrespective of histogenesis, that assess the progressive degrees of risk to which the patient is subject. This system articulates well with current radiologic techniques of staging and serves as a useful guide in the selection of an appropriate definitive surgical procedure. Its usage permits comparative end result studies on the effect of surgical and nonsurgical methods of management.

The purposes of a staging system for musculoskeletal neoplasms are to (1) incorporate the significant prognostic factors into a system that describes progressive degrees of risk of local recurrence and distant metastases to which a patient is subject, (2) stratify the stages so they have specific implications for surgical management, and (3) provide guidelines for adjunctive therapies. Over a number of years, staging systems for various classes of malignant tumors have been developed under the auspices of the American Joint Committee for Cancer Staging and End Results Reporting (AJC). The systems vary among cancers related to the natural course of a particular type of cancer. In 1980, a system for the surgical staging of musculoskeletal sarcoma was proposed, studied, and adopted by the Musculoskeletal Tumor Society[4] and subsequently adopted by the AJC.

In this review, the natural evolution of benign and malignant lesions of connective tissue derivation that led to the staging system, the system for both benign and malignant lesions, its articulation with surgical treatment, and early experience with its use will be described.

NATURAL EVOLUTION

The natural course in progression from the most benign to the most malignant connective tissue tumor is the same, lesion for lesion, whether the tumor arises in bone or somatic soft tissue. A fibrosarcoma behaves as a fibrosarcoma whether it arises in soft tissues and invades bone or *vice versa.* Aggressive benign fibrous lesions in soft tissue (fibromatosis) behave the same as their counterparts arising in bone (desmoplastic fibroma). Therefore, a common staging system was devised for bone and soft tissue, as opposed to separate systems for bone and soft tissue lesions. The system, as befits the natural history, applies only to lesions of connective tissue histogenesis and not to primary lesions of round cell origin (leukemias, lymphomas, myeloma, Ewing's sarcoma) or metastatic lesions.

The significant progressive changes in the biologic behavior of musculoskeletal lesions are (1) localized, latent or static, inactive, be-

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nign; (2) localized, active, benign; (3) aggressive, invasive, but still benign; (4) indolent, invasive, malignant, low risk of regional lymphatic or distant metastases; (5) rapidly growing, destructive, malignant, high risk of local, regional, and distant metastases; and (6) regional and/or distant metastases. Each of these progressions has distinctive clinical, radiographic, and histologic features that form the basis for the staging system and will be presented in some detail. The radiographic features that express these evolutionary changes in skeletal lesions have been previously studied and classified by their probability of occurrence by Lodwick *et al.*[11]

(1) *Inactive benign lesions* are usually asymptomatic, discovered incidentally, and seldom related to pathologic fracture or mechanical dysfunction. They may slowly attain large size but eventually reach a steady state where they no longer grow. They appear quite responsive to contact inhibition and remain completely encapsulated. They remain intracompartmental and seldom deform the compartmental boundaries of cortical bone, articular cartilage, or dense fascial septae. When palpable in soft tissue, they are often small, movable, nontender, with little or no significant enlargement on subsequent clinical observation. Radiographic characteristics are lesions that are well marginated by a mature shell of cortical-like reactive bone without deformation or expansion of the encasing bone (Lodwick IA). Angiographic staging studies show little or no increase in isotope uptake and no significant reactive neoangiogenesis about the lesion or intralesional neoangiogenesis. Computed tomographic (CT) scanning shows a homogenous density, well-marginated, with no cortical broaching or cross-fascial extension.

The histologic characteristics of the lesion are (1) low cell-to-matrix ratio; (2) mature, well-differentiated matrices; (3) benign cytologic characteristics (no hyperchromasia, anaplasia, or pleomorphism), (4) encapsulation by mature fibrous tissue or cortical bone; and (5) little or no reactive mesenchymal proliferation, inflammatory infiltrate, or neoangiogenesis about the lesion.

(2) *Active benign lesions* are mildly symptomatic, discovered because of discomfort, and occasionally associated with pathologic fracture or mechanical dysfunction. They grow steadily and continue to enlarge during observation. They appear responsive to contact inhibition but not at normal levels, as they can expand by deformation of overlying cortical bone, articular cartilage, or fascial septae. They remain encapsulated and have only a thin layer of filmy areolar tissue forming the reactive zone between the lesion and surrounding normal tissue. When palpable in soft tissue, they are usually small, movable, moderately tender, and grow slowly during clinical observation. Radiographic characteristics of active lesions in bone are well-, but irregularly-marginated defects. The margin is a mature cancellous ring rather than a cortical shell, and the inner aspect is often irregular or corrugated, giving a septated appearance. Expansion, bulging, or deformation of the combination of overlying cortex/reactive bone (Lodwick IB) is frequently observed.

Staging studies show increased isotope uptake that conforms closely to the limits of the radiographic defect and reactive changes. A thin but discernible rim of reactive neoangiogenesis about the lesion is often observed but seldom any significant intralesional neoplastic neoangiogenesis. CT scanning shows a homogenous density, irregular but intact reactive bone, expansion of the overlying cortex, and intracompartmental containment by bone or fascia. The histologic characteristics of active benign lesions are (1) a relatively balanced cell-to-matrix ratio with homogenous distribution of the matrix; (2) well-differentiated matrices; (3) benign cytologic characteristics; (4) an intact capsule of mature fibrous tissue and/or cancellous bone; (5) a narrow zone of mesenchymal, inflammatory, and vascular reactive tissue between the capsule and the surrounding normal tissue; and (6) resorption of preexisting bone by osteoclasts rather than by neoplastic cells as the mechanism of expan-

sion. Intermittent areas of resorption often produce an irregular, serrated, sometimes corrugated interface between the capsule and the adjacent reactive bone.

(3) *Aggressive benign lesions* are often symptomatic, discovered because of discomfort and/or a growing mass, and, when in a stress-bearing bone, associated with a pathologic fracture. When palpable in the soft tissues, they grow rapidly, sometimes alarmingly. These lesions are frequently tender and may have an inflammatory-like appearance. They are little affected by contact inhibition and readily penetrate or permeate the natural barriers to tumor growth: cortical bone, fascial septae, and in some cases, articular cartilage or joint capsules. They penetrate the capsule with finger-like extensions protruding directly into the surrounding zone. The reactive zone is thick, edematous, and often inflammatory. These aggressive lesions invade by destroying or resorbing the restraining bone or fascia and permeate into adjacent tissues or compartments rather than expanding by concomitant endosteal resorption and subperiosteal apposition.

When aggressive benign lesions involve unrestrained areas (medullary canal, cancellous bone, advential intermuscular planes within muscle bellies, pararticular tissues), they extend rapidly, although usually preceded by a pseudocapsule of reactive tissue.

Aggressive soft tissue lesions are usually firm, fixed, tender, and have a rapid growth history. The radiographic features of aggressive benign lesions are a ragged permeative interface with adjacent bone, incomplete attempts at containment by reactive bone, cortical destruction, endosteal buttresses and periosteal Codman's triangles, and rapid soft tissue extension (Lodwick IC). Staging studies often reflect the aggressive nature and behavior of these lesions. Isotope scans show increased uptake in both the early vascular phase and the late bone phase. The extent of the increased uptake is often well beyond the apparent radiographic limits. Angiograms show a distinct reactive zone of neovasculature on the early arterial phase and an intralesional hypervascular blush on the late venous phase of the study. CT scans show nonhomogenous mottled densities with defects in attempts at reactive containment, early extracompartmental extension from bone, and indistinct margins in soft tissues. Otherwise, occult involvement of major neurovascular bundles is often shown by either angiography or CT scans in aggressive soft tissue lesions.

Histologic features of aggressive lesions are (1) high cell-to-matrix ratio; (2) clearly differentiated matrices of varying maturity; (3) predominately benign cytologic characteristics without anaplasia or pleomorphism, but with frequent hyperchromatic nuclei; mitoses are occasionally encountered, and vascular invasion within the lesion may also be found; (4) finger-like projections of tumor extend through gaps in the capsule and grow into the surrounding reactive zone; these extensions usually maintain continuity with the main mass, although occasional apparently isolated satellites are seen; and (5) a thick, succulent zone of reactive tissue is interposed between the penetrated capsule and the more peripheral normal tissue. This zone or pseudocapsule encircles but does not inhibit growth of an aggressive tumor. The reactive zone prevents tumor nodules from extending directly into normal tissue. Destruction of surrounding bone is by reactive osteoclasts rather than by tumor cells, although fingers of tumor grow rapidly into the reactive bone.

Despite the benign cytologic characteristics, the invasive behavior of these lesions is more like that of a low-grade malignancy than of an active benign process. The reliability of the benign cytologic features is occasionally challenged by the occurrence of distant, usually pulmonary, metastases. These metastases look histologically as benign as the primary tumor and have a much better prognosis than the metastases of frankly malignant lesions.

(4) *Low-grade sarcomas* have all the invasive growth mechanisms of local malignancy, but have a low risk of distant metastases and an indolent rate of evolution. With time,

and particularly with repeated cycles of unsuccessful excisions and recurrences, the risk of dedifferentiating into high-grade and distant metastases is increased.

Low-grade sarcomas often present as a slow-growing, painless mass with an indolent but steady growth rate. They are seldom symptomatic. They stimulate generous amounts of reactive bone or fibrous tissue that often impart a false impression of encapsulation. They are not inhibited by the natural barriers to tumor growth, but their extension through them is one of gradual erosion rather than rapid destruction. Their relentless progression often produces extraosseous or extracompartmental extension and neovascular bundle involvement. They seldom traverse articular cartilage or joint capsule to extend intraarticularly. They may, however, stimulate reactive synovitis and effusion when adjacent to joints in either bone or soft tissue. Similarly, they do not extend through tendon sheath, nerve sheath, or the outer adventitial layer of major arteries but tend to push these structures aside. Tendons, nerves, and vessels, however, are often involved by the reactive zone about the lesion.

When low-grade sarcomas arise in the soft tissue, they are apt to be small, superficial, fixed, nontender, and without inflammatory signs from the reactive zone. The radiographic features of low-grade skeletal sarcomas are similarly apt to be less ominous than many aggressive benign lesions (Lodwick II). They often have a generous reactive rim of cancellous bone admixed with defects of extracapsular and/or soft tissue extension. Buttressing in the medullary canal, external Codman's triangles, and especially endosteal scalloping are features of these lesions. Staging studies again accurately reflect the behavior of these lesions. Isotope scans in both bone or soft tissue show increased early and late uptake that is more extensive than the radiographic limits would suggest. The angiographic findings show little or no reactive neovasculature or intralesional neoangiogenesis and often appear deceptively benign. CT findings are of nonhomogenous density, a thick perforated ring of reactive bone, and occult soft tissue or intraosseous extension.

The histologic features of locally invasive low-grade malignancies are (1) a relatively even proportion of cells to matrix; (2) well-differentiated and usually mature matrices; (3) malignant cytologic characteristics, *e.g.*, anaplasia, pleomorphism, and hyperchromasia, with a modest number of mitoses (consistent with Broder's Grades 1 and occasionally 2 in other malignancies[2]; (4) varying amounts of necrosis, hemorrhage, and vascular invasion are found in these lesions that are seldom seen in benign lesions; and (5) numerous interruptions in the continuity of the capsule where the tumor extends directly into the reactive zone, which, in turn, forms a pseudocapsule about the lesion. In the reactive zone, nodules of isolated tumor-forming satellites are almost universally found. Skip lesions in normal tissue beyond the reactive zone are rarely if ever seen about low-grade lesions.

Due to the indolent growth rate of low-grade locally invasive sarcomas, they remain contained by the natural barriers to tumor growth within their compartments of origin for long periods. With their ability to destroy or pervade normal tissue, however, they eventually extend through their barriers to involve adjacent extracompartmental tissues. Metastasis to regional lymph nodes is unusual. Distant pulmonary metastases occur late in the course and are often solitary.

(5) *High-grade sarcomas* usually appear as destructive symptomatic masses that are often associated with pathologic fractures when they involve bone. They stimulate generous amounts of reactive tissue, but overgrow it so rapidly that they appear to have little or no pseudoencapsulation. They are uninhibited by the natural barriers to tumor growth and rapidly extend into adjacent tissues by destruction of cortical bone, fascial septae, articular cartilage, or joint capsules. They quickly extend extracompartmentally, involve adjacent neurovascular bundles, and extend proximally along ill-defined extracompartmental fascial

plane and spaces. They often cross epiphyseal growth plates, and although they respect articular cartilage will extend intra-articularly at sites of capsular or ligamentous attachment.

High-grade sarcomas of soft tissue origin are usually deep, large, fixed, tender, and stimulate a soft, edematous, succulent inflammatory-like reaction about them. The radiographic features of high-grade sarcomas arising in bone are quite predictive of their behavior (Lodwick III). The reactive response is so rapidly destroyed that the interface between the lesion and the surrounding bone is poorly marginated with a diffuse permeative border. Patchy cortical destruction, early occult soft tissue extension, obliteration of periosteal reaction with only small Codman's triangles remaining, and ill-defined intramedullary extension beyond the extent suggested by the periosteal reaction are all features of high-grade primary skeletal sarcomas.

Staging studies are usually accurate in suggesting their high-grade nature. Isotope scans show increased uptake both early and late that extends beyond the radiographic limits of the lesion. Increased isotope uptake in radiographically normal bone adjacent to high-grade soft tissue sarcomas may be the only clue of occult reaction to the soft tissue lesion. They may also be the first hint of a "skip" metastasis. Angiograms show a vigorous zone of reactive neovasculature about the lesion on the early arterial phase and often a hypervascular intralesional "blush" on the late venous phase. The extent of involvement of neurovascular bundles is often best shown on angiography: CT scans show occult intraosseous extension, skip lesions in the medullary canal, occult soft tissue extension, and extracompartmental extension through cortical bone and across fascial septae.

The histologic features of high-grade sarcomas are (1) high cell-to-matrix rate; (2) poor differentiations of immature matrices; (3) all the cytologic characteristics of high-grade malignancy, *e.g.*, abundant mitoses, vascular invasion, necrosis, hemorrhage, and direct destruction of normal tissue by tumor cells

TABLE 1. Stages of Musculoskeletal Lesions

Benign
1. Latent
2. Active
3. Aggressive
Malignant
I. Low grade without metastases
A. Intracompartmental
B. Extracompartmental
II. High grade without metastases
A. Intracompartmental
B. Extracompartmental
III. Low/high grade with metastases
A. Intracompartmental
B. Extracompartmental

(findings of Broder's Grade 2, 3, or 4 lesion[2]; (4) little or no encapsulation and isolated satellites in the pseudocapsule of reactive tissue about the lesion; and (5) skip metastases, *e.g.*, isolated nodules of tumor in the normal tissue well beyond the reactive zone, in a significant proportion (*ca.* 25%) in both bone and soft tissue sarcomas.[3] In bone, they are either in the medullary canal or occasionally transarticular in an adjacent metaphysis. In soft tissue, they may occur more proximally in either the ill-defined extracompartmental spaces and planes or within skeletal muscle.

High-grade sarcomas quickly cross barriers to tumor extension and a relatively small proportion (*ca.* 10%) are still intracompartmental at the time of presentation. The majority extend extracompartmentally; an occasional lesion, usually of soft tissue origin, will develop with regional lymphatic metastasis; and a significant proportion (*ca.* 10%) will present with distant (usually pulmonary) metastases.

These behavioral changes (latent, active, aggressive, invasive, destructive, and metastatic) that form the basis of the staging system together with their clinical, radiographic, and staging studies are summarized in Tables 1 (summary), 2 (benign) and 3 (malignant).

THE STAGING SYSTEM

The system is based on the interrelationship of three factors: (1) grade (G), (2) site (T), and

TABLE 2. Stages of Benign Musculoskeletal Lesions

	1	*2*	*3*
Grade	G_0	G_0	G_0
Site	T_0	T_0	T_{1-2}
Metastases	M_0	M_0	M_{0-1}
Clinical course	Latent, static, self-healing	Active progressing, expands bone or fascia	Aggressive, invasive, breaches bone or fascia
Radiographic grade	I_A	I_B	I_C
Isotope scan	Background uptake	Increased uptake in lesion	Increased uptake beyond lesion
Angiogram	No neovascular reaction	Modest neovascular reaction	Moderate neovascular reaction
CT	Crisp, intact margin—well defined capsule homogeneous	Intact margin "expansile"—thin capsule homogeneous	Indistinct broached margin—extracapsular and/or extracompartmental extension non-homogeneous

(3) metastases (M). Each of these in turn is stratified by components that influence both prognosis and response to treatment.

GRADE

The grade is an assessment of the biologic aggressiveness of the lesion. It is not a purely histologic assessment (as in Broder *et al.*'s[2] 1, 2, 3, 4 grading of malignancies), nor a purely radiographic assessment (as in Lodwick's IA, IB, IC, II, and III radiographic classification of probabilities),[11] nor a purely clinical reflection of growth rate, doubling time, size, temperature, tissue pressure, or biochemical markers. It is a blending of all of these into patterns. The three stratifications of grade are G_0, G_1, and G_2. Their identifying characteristics are:

G_0 (Benign): *Histologic*—benign cytology, clearly differentiated, low to moderate cell-to-matrix ratio. *Radiographic*—Lodwick IA, IB, or IC ranging from clearly marginated to those with capsular broaching and soft tissue extensions. *Clinical*—Distinct capsule, no satellites, no skips, rare metastases, variable growth rate, predominantly in adolescents and young adults.

G_1 (Low-grade malignant): *Histologic*—Broder's Grades 1 and some 2. Few mitoses, moderate differentiation, distinct matrix. *Radiographic*—Lodwick II with indolent invasive features. *Clinical*—Indolent growth, extracapsular satellites in the reactive zone, no skips and only occasional distant metastases.

G_2 (High-grade malignant): *Histologic*—Broder's Grades 2, 3, and 4. Frequent mitoses, poorly differentiated, sparse and immature matrix. High-grade cytologic features: anaplasia, pleomorphic, and hyperchromatic. *Radiographic*—Lodwick III: destructive, invasive. *Clinical*—Rapid growth, symptomatic, both satellites and skips, occasional regional and frequent distant metastases.

The behavior of G_0 benign lesions may be latent, active, or aggressive. Their histologic features are often poor indicators of their behavior, and within this spectrum G_0 lesions are often better predicted by their radiographic, staging, and clinical features (Table II). The histologic characteristics of G_1 low-grade sarcomas make their distinction from G_2 high-grade lesions on histologic grounds predictably accurate, and their radiographic staging and clinical features are supportive and confirmatory of the histologic distinction.

TABLE 3. Stages of Malignant Musculoskeletal Lesions

	I_A	I_B	II_A	II_B	III_A	III_B
Grade	G_1	G_1	G_2	G_2	G_{1-2}	G_{1-2}
Site	T_1	T_2	T_1	T_2	T_1	T_2
Metastasis	M_0	M_0	M_0	M_0	M_1	M_1
Clinical course	Symptomatic indolent growth	Symptomatic mass indolent growth	Symptomatic rapid growth	Symptomatic rapid growth fixed mass pathological fracture	Systemic symptoms palpable nodes pulmonary symptoms	
Isotope scan	Increased uptake	Increased uptake	Increased uptake beyond radiographic limits	Increased uptake beyond radiographic limits	Pulmonary lesions no increased uptake	
Radiographic grade	II	II	III	III	III	
Angiogram	Modest neovascular reaction, involvement neurovascular bundle	Modest neovascular reaction, involvement of neurovascular bundle	Marked neovascular reaction—no involvement of neurovascular bundle	Marked neovascular reaction—involvement neurovascular bundle	Hypervascular lymph nodes	
CT	Irregular or broached capsule but intracompartmental	Extracompartmental extension or location	Broached (pseudo) capsule—intracompartmental	Broached (pseudo) capsule—extracompartmental	Pulmonary lesions or enlarged nodes	

TABLE 4. Surgical Grade (G)

Low (G_1)	*High (G_2)*
Parosteal osteosarcoma	Classic osteosarcoma
Endosteal osteosarcoma	radiation sarcoma
	Paget's sarcoma
Secondary chondrosarcoma	Primary chondrosarcoma
Fibrosarcoma, Kaposi's sarcoma atypical malignant fibrosis histiocytoma	Fibrosarcoma malig. fib. histiocytoma undiff. primary sarcoma
Giant cell sarcoma, bone	Giant cell sarcoma, bone
Hemangioendothelioma hemangiopericytoma	Angiosarcoma hemangiopericytoma
Myxoid liposarcoma	Pleomorphic Liposarcoma
	Neurofibrosarcoma (Schwannoma)
	Rhabdomyosarcoma
	Synovioma
Clear cell sarcoma, tendon sheath epitheliod sarcoma	
Chordoma	
Adamantinoma	
Alveolar cell sarcoma	Alveolar cell sarcoma
Other and undifferentiated	Other and undifferentiated

However, it may be difficult to distinguish G_0 from G_1 lesions on purely histologic features, and, in many instances, the radiographic and particularly the staging studies may be of more value than the histologic findings (Table 3).

A promising new method of assessing grade is the determination of the nuclear DNA concentration (ploidy) by flow cytometry. Individual cell nuclei are stained with a specific fluorescent DNA dye and the concentration is assessed rapidly by fluorometric assay of the cells as they pass through a focused laser beam. Normal cells are euploid and so are most G_0 lesions. G_1 lesions have increased amounts of cells in normal replicative activity (tetraploidy). G_2 lesions have both abnormal numbers of cells in tetraploidy but also may show an abnormal cell line (aneuploid) quite distinctive for high-grade neoplasms. These correlations between ploidy and prognosis have been shown to be valid for other classes of neoplasia—particularly myelomas and lymphomas—and preliminary results suggest that this technique may be quite helpful in connective tissue lesions.[10]

In summary, surgical grading into G_0, G_1, or G_2 requires histologic, radiographic, and clinical correlation to achieve accuracy and reliability. Although certain histogenic types of sarcomas may have a preponderance of their lesions G_1 or G_2 (Table 4), each lesion must be assessed on its own characteristics before a grade is assigned. For example, most parosteal osteosarcomas are G_1, but a few dedifferentiate into G_2 lesions and accordingly have a much more ominous prognosis. Conversely, although most classic osteosarcomas are G_2, occasionally one will be G_1 with a much more favorable prognosis.

SITE

The anatomic setting of the lesion has a direct relationship to the prognosis and the choice of surgical procedure. The three strata of anatomic settings are T_0, T_1, and T_2. These are determined primarily by clinical and radiographic techniques. Staging studies (isotope scanning, angiography, CT, and NMR imaging, ultrasonography, myelography, *etc.*) can make valuable contributions in preoperatively assessing the anatomic setting.

T_0: the lesion remains confined within the capsule and does not extend beyond the borders of its compartment of origin. While the boundaries of the capsule and/or the compartment of origin may be distorted or deformed, they both remain intact.

T_1: the lesion has extracapsular extensions, either by continuity or isolated satellites, into the reactive zone, but both the lesion and the reactive zone about it are contained within an anatomic compartment bounded by the natural barriers to tumor extension: cortical bone, articular cartilage, joint capsule, or the dense fibrous tissue of fascial septa, ligaments, or tendon (sheath). To be classified as T_1, both the lesion and its (pseudo)capsule must be within the compartment. If the reactive zone

extends outside the compartment while the tumor remains within, the lesion is classified as extracompartmental. The anatomic compartments of both bone and soft tissue are shown in Table 5.

Three particular points about compartmentalization require elaboration. The skin and subcutaneous tissue are classified as a compartment, even though there are no longitudinal boundaries. In the transverse dimension, however, the deep fascia forms an effective barrier between the subcutaneous and deeper tissues. The parosseous compartment is a potential compartment between cortical bone and overlying muscles. Lesions on the surface of bone that have not invaded either the underlying cortical bone or the overlying muscle but have pushed them apart are defined as intracompartmental. Lesions within muscular compartments that contain more than one muscle (*e.g.*, the volar compartment of the forearm) are considered intracompartmental despite involving more than one muscle.

T_2: lesions extending beyond compartmental barriers into the loosely bounded fascial planes and spaces that have no longitudinal boundaries are extracompartmental or T_2. Extracompartmental involvement may be either by virtue of extension of a previously intracompartmental lesion, by arising *de novo* in the extracompartmental tissues, or by inadvertent transmission by trauma or surgical excision. The various sites that are extracompartmental are shown in Table 5. Almost without exception, lesions (or their reactive zones) that abut or involve major neurovascular bundles are extracompartmental by virtue of the extracompartmental location of these structures.

TABLE 5. Surgical Sites (T)

Intracompartmental (T_1)		*Extracompartmental (T_2)*
Intraosseous	→	Soft tissue extension
Intraarticular	→	Soft tissue extension
Superficial to deep fascia	→	Deep fascial extension
Parosseous	→	Intraosseous or extrafascial
Intrafascial compartments		Extrafascial planes or spaces
Ray of hand or foot		Mid- and hindfoot
Posterior calf		Popliteal space
Anterolateral leg		Groin–femoral triangle
Anterior thigh		Intrapelvic
Middle thigh		Midhand
Posterior thigh		Antecubital fossae
Buttocks		Axilla
Volar forearm		Periclavicular
Dorsal forearm		Paraspinal
Anterior arm		Head and neck
Posterior arm		
Periscapular		

METASTASIS

In most staging systems for carcinomas, metastases are stratified by virtue of being regional (N for nodes) or distant (M) since the prognosis and treatment is significantly different for these two sites of metastasis.

For sarcomas, metastatic involvement of either regional lymph nodes or distant organs has the same ominous prognosis, and both are designated by M. There are only two strata of metastasis: M_0 and M_1. M_0 indicates no evidence of regional or distant metastases, while M_1 signifies either regional or distant metastases.

These three factors, G, T, and M, are combined to form the criteria for the progressive stages of benign and malignant lesions (Table 1). Benign lesions that are designated by Arabic numerals 1, 2, or 3 are synonymous with latent, active, or aggressive. The characteristics of Stage 1 latent, Stage 2 active, and Stage 3 aggressive lesions are shown in Table 2, and were described in detail as the latent, active, and aggressive progressions in the preceding section on evolution. As indicated, Stages 1, 2, and 3 correspond closely to the Lodwick classification of radiographic features as IA, IB, and IC.

Malignant lesions that are designated by the Roman numerals I, II, or III are synonymous with low-grade, high-grade, and metastatic. These three stages of sarcomas are further

TABLE 6. Surgical Margins

Type	*Plane of Dissection*	*Microscopic Appearance*
Intracapsular	Within lesion	Tumor at margin
Marginal	Within reactive zone—extracapsular	Reactive tissue ± microsatellites tumor
Wide	Beyond reactive zone through normal tissue	Normal tissue ± "skips"
Radical	Normal tissue extracompartmental	Normal tissue

stratified into A or B depending on whether the lesion is anatomically intracompartmental (A) or extracompartmental (B). The characteristics of these malignant lesions are shown in Table 3, and were described in detail as low-grade invasive and high-grade destructive lesions in the evolution of connective tissue lesions. Their radiographic characteristics correspond closely to Stages II and III in the Lodwick classification. Only after each lesion has been studied clinically, radiographically, and biopsied for histogenic typing and cytologic grading can it be staged according to its characteristics. Although particular lesions tend to cluster in particular stages (*i.e.*, >90% of classic osteosarcomas present as Stage IIB) others tend to be more evenly distributed (*i.e.*, giant cell tumors of bone approximately 10% Stage 1, 75% Stage 2, and 15% Stage 3).

Clearly, a particular lesion may undergo transition from one stage to another. Benign lesions that are Stage 2 active or even Stage 3 aggressive during adolescence frequently undergo involution into Stage 1 latent lesions after growth has ceased. On the other hand, certain benign lesions of any stage may undergo transformation into Stage I, II, or even III sarcomas. Obviously, high-grade Stage II and occasionally low-grade Stage I lesions become Stage III lesions after presentation by virtue of either regional or distant metastases. Certain factors have been implicated directly or by inference in the upstaging of benign or malignant lesions. Radiation has been held responsible for transition of giant cell tumor, chondroblastoma, and other benign lesions to sarcomas. Repeated inadequate surgical interventions have been implicated in the evolution of low-grade fibrous lesions into high-grade fibrosarcomas and in the dedifferentiation of Stage I parosteal osteosarcoma into Stage II or III high-grade osteosarcoma.

ARTICULATION WITH SURGICAL TREATMENT

Articulating the staging system with the surgical treatment of connective tissue tumors requires precise definitions of the procedures as well as the stages. The traditional terms of incisional biopsy, excisional biopsy, resection, and amputation are difficult to define in either biologic, anatomic, or physical terms. After a number of physical and surgical criteria were postulated, a method of definition was devised, based on the margin the procedure obtained in relation to the lesion and the barriers to its extension.

The four oncologic surgical margins, the plane of dissection that achieves them, and the microscopic appearance of the tissue at the margin of the wound are shown in Table 6. The four margins are described in surgical terms (intracapsular, marginal, wide, and radical), and they reflect the progressive barriers to tumor extension in their natural evolution, *e.g.*, the (pseudo)capsule, reactive zone, intracompartmental normal tissue, and compartmental boundaries. Although marginal, wide, and radical margins may all be tumor-free, the residual reactive tissue at a marginal margin often contains extensions or satellites, and the residual normal intracompartmental tissue beyond a wide margin occasionally contains skip lesions. For high-grade sarcomas only a radical margin with an intact barrier of normal tissue between the margin and the reactive zone consistently and reliably can be called tumor-free.

Determinations of margins may be estimated by inspection of the cut surface of either bone or soft tissue. Tetracycline-labeling may be quite helpful in visually identifying the type of osseous margin as it distinguishes reactive from normal bone. Often specimens will have to be taken for histologic study from questionable areas to verify whether non-neoplastic tissue at a margin is reactive or normal. The microscopic appearance of wide and radical margins are histologically identical (*i.e.*, normal) and the distinction as to the type of margin obtained is made by identifying whether or not the margin is beyond a compartmental barrier. This is usually done by gross inspection or radiographic examination of the specimen. As shown in Table 7, each of the four margins can be achieved by a local or limb-salvaging procedure or an amputation, making eight possible oncologic procedures.

The four types of limb-salvaging procedures are (1) intracapsular excision, *i.e.*, debulking, cyto-reductive excision, *etc.*, done piecemeal within the (pseudo)capsule; (2) marginal (local) excision, *i.e.*, *en bloc* excisional biopsy, shell-out, *etc.*, done *en bloc* extracapsularly within the reactive zone; (3) wide (local) excision, *i.e.*, *en bloc* excision done through normal tissue beyond the reactive zone, but within the compartment of origin leaving *in situ* some portion of that compartment; or (4) radical (local) resection, *i.e.*, *en bloc* excision of the lesion and the entire compartment of origin leaving no remnant of the compartment of origin.

The terms excision and resection are coupled with wide and radical to emphasize the biologic differences between the two procedures. Wide excision and radical resection are correct; by definition wide resection or radical excision become incompatible terms. This is important conceptually, if not semantically, because in Europe, the term "radical," in terms of margin, is synonymous with tumor-free and can in the above terms be either marginal, wide, or radical. Therefore, in the European literature, excision and resection are used interchangeably, with "radical" taken to mean any local procedure with a tumor-free margin.

TABLE 7. Musculoskeletal Oncologic Surgical Procedures

Margin	*How Margin Achieved*	
	Limb salvage	Amputation
Intracapsular	Intracapsular piecemeal excision	Intracapsular amputation
Marginal	Marginal *en bloc* excision	Marginal amputation
Wide	Wide *en bloc* excision	Wide through-bone amputation
Radical	Radical *en bloc* resection	Radical exarticulation

The other four types of oncologic procedures are amputations that achieve various margins, and whose levels pass (5) within the (pseudo)capsule (intracapsular amputation); (6) through the reactive zone (marginal amputation); (7) through normal tissue proximal to the reactive zone, but with the compartment of involvement, usually a through-bone (wide amputation); and (8) proximal to the involved compartment, usually a disarticulation (radical amputation, because it removes the entire compartment at risk).

In terms of these definitions, articulation of the stages with the surgical margins and procedures can be done with anatomic and biologic meaning rather than in less significant physical dimensions. The articulation for benign lesions is shown in Table 8, and the articulation for malignant lesions is summarized in Table 9.

BENIGN LESIONS

Stage 1 latent lesions have a negligible recurrence rate following intracapsular excision (*i.e.*, curettage, piecemeal removal), because their natural history is to heal spontaneously. Examples would be a ganglion, nonossifying

TABLE 8. Articulation of Benign Stages with Surgical Margins

Stage	*Grade*	*Site*	*Metastasis*	*Margin for Control*
1	G_0	T_0	M_0	Intracapsular
2	G_0	T_0	M_0	Marginal or ? intracapsular plus effective adjuvant
3	G_0	T_{1-2}	M_{0-1}	Wide or ? marginal plus effective adjuvant

fibroma, solitary eosinophilic granuloma, simple cyst, giant cell tumor of tendon sheath, *etc.*, whose behavior was latent. *En bloc* marginal or even wide excision, if feasible, without additional morbidity or disability, while desirable for insurance, is unnecessary to achieve a low-risk margin for Stage 1 lesions.

Stage 2 active lesions have a significant recurrence rate after intracapsular procedures and negligible recurrence rates after marginal *en bloc* excision. Since active lesions are by definition intracapsular (T_0), dissection through the extracapsular reactive zone carries little risk of leaving residual neoplastic tissue with a marginal margin. When obtaining a marginal margin by an *en bloc* excision carries a significant risk of morbidity or disability, then either these risks or the risks of recurrence after an intracapsular procedure must be assumed or consideration be given to extending the margin of an intracapsular procedure to the equivalent of a marginal (or better) margin by the use of nonsurgical adjuvants. Because both chemotherapy and radiation therapy are effective by virtue of their effect on mitotically active cells, their effectiveness on benign G_0 lesions is limited, and the side effects make their use inappropriate. Physical adjuvants such as phenol, hypertonic saline, merthiolate, methyl methacrylate, and repeated freezing and thawing (cryosurgery) have all had trials and advocates. Only cementation with thermal (and perhaps chemotoxic necrosis) and cryosurgery producing cell rupture have been documented to produce significant extensions of surgical margins.[6,7] Both have been shown to produce millimeters of necrosis, and, when used appropriately and judiciously, can reliably extend an intracapsular margin to become the equivalent of a marginal margin with significant reduction in recurrence rates for active Stage 2 benign lesions.

Stage 3 aggressive benign lesions with their extracapsular extensions (T_1 or even T_2) have high recurrence rates after either intracapsular or marginal procedures. Wide surgical margins beyond the extensions in the reactive zone are the least that provide a low-risk procedure for these aggressive lesions. Marginal procedures

TABLE 9. Articulation of Malignant Stages with Surgical Margins

Stage	*Grade*	*Site*	*Metastasis*	*Margin for Control*
I_A	G_1	T_1	M_0	Wide—usually excision
I_B	G_1	T_2	M_0	Wide—consider amputation *vs.* joint or neurovascular deficit
II_A	G_2	T_1	M_0	Radical—usually resection or wide excision plus effective adjuvant
II_B	G_2	T_2	M_0	Radical—consider exarticulation or wide excision or amputation plus effective adjuvant
III_A	G_{1-2}	T_1	M_1	Thoracotomy—radical resection or palliative
III_B	G_{1-2}	T_2	M_1	Thoractomy—radical exarticulation or palliative

coupled with effective adjuvants may be clinically prudent when location makes wide surgical procedures impractical. Thermotherapy has been ineffective, albeit largely untried; but radiation therapy, when coupled with marginal excision, has considerably reduced the risk of recurrence. Surgically inaccessible lesions such as aggressive fibromatosis, aggressive recurrent aneurysmal bone cysts, and aggressive giant cell tumors are in this category. The effectiveness of physical adjuvant for Stage 3 lesions has not been as extensively investigated as for Stage 2 lesions, but may be rational in lieu of disabling wide procedures. Despite their appeal, to date no combination of adjuvant/marginal surgery has been as effective as wide surgery. When prior recurrences after inadequate excisions have occurred, the pattern of local dissemination is often so diffuse that only amputation offers a practical method of achieving a low-risk wide margin.

MALIGNANT LESIONS

Stage IA: Low-grade G_1 locally invasive tumors with predilection for occult extracapsular satellites in the enveloping reactive zone have high recurrence rates after either intracapsular or marginal procedures. Wide procedures are low-risk, and because of their intracompartmental location, Stage IA lesions are usually excellent candidates for excision rather than amputation. Marginal excision plus an effective adjuvant is less risky than marginal excision alone, but identification of an effective adjuvant is difficult. Adjuvant radiation therapy has been effective in reducing the incidence of recurrence after marginal excision in soft tissue lesions, but of limited value in skeletal lesions. Chemotherapy has been ineffective in G_1 sarcomas. Physical adjuvants are largely untested, but as their effectiveness is difficult to predict and usually measured in millimeters, they would not seem rational for G_1 sarcomas that have a low incidence of recurrence after wide procedures.

Stage IB: Extracompartmental G_1 lesions require the same margins as their intracompartmental counterparts. The extracompartmental location often makes a wide margin unattainable by anything short of amputation or wide excision with sacrifice of significant neurovascular or articular structures. Marginal surgery coupled with an adjuvant is no more effective in IB than in IA lesions. When the extracompartmental status has occurred as a result of recurrences after prior inadequate excision, achieving a wide margin in the face of widely disseminated occult disease by limb-salvaging excision becomes less and less practical, and amputation more and more a serious consideration.

Stage IIA: High-grade, high-risk destructive lesions are seldom intracompartmental and have a significant incidence of skips. Low-risk control is offered by either radical resection (frequently practical in the unusual circumstance of intracompartmental confinement), radical amputation, or by the combination of a wide margin and an effective adjuvant(s). Soft tissue sarcomas are more often still intracompartmental and radiation therapy is an effective adjuvant for local control of the majority of the various histogenic types (exception: chemotherapy is more effective in rhabdomyosarcoma) of soft tissue sarcomas. Chemotherapy may be effective in assisting local control in some skeletal lesions, *i.e.*, osteosarcoma and perhaps malignant fibrous histiocytoma, while in others, *i.e.*, chondrosarcoma and fibrosarcoma, it has little benefit. It is quite clear, however, that all combinations of wide surgery with adjuvant therapy carry a significantly greater risk of local recurrence than a radical procedure (approximately 25% *versus* <5%), whether achieved by limb salvage or amputation.

Stage IIB: Radical margins are the most effective way of assuring local control and in IIB lesions are often attainable only by disarticulation. Wide margins, coupled with adjuvant therapy, have significant risks of recurrence in their own right and often achieve only marginal margins because of the proclivity of these lesions to have occult proximal microextensions along the major neurovascular bundles.

The risk of local recurrence in Stage IIB sarcomas treated by wide excision without adjuvant therapy is 40%–60%, and with adjuvant therapy in responsive lesions is 20%. When the wide margin is achieved by through-bone amputation, the risk of recurrence with effective adjuvant is less than with wide excision, approximately 10% rather than 20%.

Stage III: Control of the disease requires both the appropriate surgical management of the primary plus control of the pulmonary or other distant metastases. When the appropriate wide or radical procedure entails significant morbidity or disability, a lesser palliative procedure may be rational unless control of the metastasis can be reasonably anticipated. Both preliminary aggressive chemotherapy (with decision as to subsequent thoracotomy) and definitive surgical treatment of the primary tumor, based on the response of the metastases to the chemotherapy or, alternatively, aggressive thoracotomy and definitive radical surgery followed by postoperative adjuvant chemotherapy in the clinically tumor-free state, are recommended by some authors, although long-term results are not yet known. Either procedure appears preferable to palliation alone as each has significant salvage rates at five years.

DISCUSSION

In its preliminary trials by the Musculoskeletal Tumor Society, this staging system was shown to be practical, reproducible, and of significant prognostic value for sarcomas of both bone and soft tissue origin.[4] Subsequent reports have shown its value in surgical planning and treatment evaluation.[1,5,8,9,12]

Some misconceptions of the original presentation of the definitions of surgical margins and procedures in 1980 need clarification. The common misconceptions concern methods for description of the margins (and procedures) about superficial lesions, extracompartmental lesions, and lesions that are inadvertently entered but subsequently reexcised. A superficial lesion in the skin and/or subcutaneous tissue that has not penetrated the deep fascia is intracompartmental. *En bloc* removal with a plane of dissection to the deep fascia and through normal tissue well around the lesion obtains an extracompartmental radical margin in depth (on the other side of the deep fascia, a natural barrier), but only a wide margin circumferentially (there are no natural barriers within skin and subcutaneous tissue, and so an extracompartmental radical margin in the defined sense is not possible). This ambiguity has been resolved by arbitrarily calling a margin less than 5 cm about the reactive zone wide, and a margin more than 5 cm radical. This dimension was chosen in conformity with the melanoma experience. Thus, a superficial IA lesion excised *en bloc* to the deep fascia with a surrounding margin of 2 cm has been widely excised, while the same lesion with a 6-cm margin about it has been radically resected. Whether or not these physical dimensions are appropriate for the articulation of margin and stage remains to be seen.

Extracompartmental "B" lesions, whether by extension or origin, by definition cannot be radically resected because the extracompartmental spaces and planes have no longitudinal barriers. For such lesions, a local procedure that removes *en bloc* a lesion with a margin of normal tissue is a wide excision for an *en bloc* removal. Procedure of an extracompartmental lesion that is beyond natural barriers in the transverse plane but by definition cannot be radical in the longitudinal sense is arbitrarily defined as a radical resection when the longitudinal margin is at the same level as the origin or insertion of the adjacent muscles. For example, a lesion in the subsartorial canal abutting the femoral neurovascular bundle that was removed *en bloc,* including the bundle with a plane of dissection beyond the fascial boundaries of the canal (*i.e.,* radical transversely), but with a proximal and distal margin less than the musculotendinous junctions of the sartorius, would have been widely excised. The same procedure with the proximal and distal margins at or beyond the musculotendinous junctions of sartorius would be

a radical resection. If the lesion were removed *en bloc* by dissection within the canal sacrificing the bundle, the procedure would be a marginal excision. If the lesion were dissected away from the bundle preserving the bundle, the procedure would be designated as either an intracapsular or marginal excision, depending on whether the dissection was within the (pseudo)capsule or extracapsular reactive zone.

If a lesion involves two compartments, *i.e.*, a lesion arising in bone extending into the adjacent soft tissues, then, to achieve a radical margin, both compartments would have to be removed *en bloc in toto*. For example, to achieve a radical resection of a lesion of the distal femoral metaphysis extending into the posterior thigh would require removal of the entire femur, hamstrings, and sciatic nerve *en bloc*. From the above, it is evident that in certain instances the only practical way of achieving a radical margin is by amputation. This may be particularly true in certain anatomic sites (*i.e.*, popliteal fossae, femoral triangle, axillae, antecubital fossae, flexor canal of the forearm) where a radical margin can be obtained by resection, but the virtually functionless salvaged limb hinders rather than aids rehabilitation.

When lesions are entered, the wound is being contaminated and all the tissues exposed are at risk for recurrence. If these at risk tissues are not removed, the margin is intracapsular. If the tissues are removed, the margin becomes what the subsequent removal achieves in relation to the lesion as if the exposure had not happened. The procedure is said to be a contaminated procedure. For example, if a lesion in the quadriceps were inadvertently entered exposing the rectus femoris muscle and the lesion subsequently widely excised with a cuff of normal tissue, the procedure would be designated a contaminated wide excision, because some of the exposed more proximal rectus femoris would remain in the wound.

If, under the same circumstance, the entire quadriceps compartment were removed *en bloc* by extracompartmental dissection, then the procedure would be a (uncontaminated) radical resection. This means that after incisional biopsy, the entire tract at risk must be appropriately excised *en bloc* with the lesion and tissues to achieve wide or radical margins. It also means that if the (pseudo) capsule is inadvertently entered during attempted excisional biopsy, a great deal more tissue will have to be removed to achieve an uncontaminated wide or radical margin than if such contamination had not occurred. In certain instances, contamination may take place in such a way that the only way of achieving an uncontaminated wide or radical margin is by amputation (previously unnecessary to achieve an uncontaminated wide or radical margin) and in other circumstances (*e.g.*, the pelvis) inadvertent contamination may make obtaining an uncontaminated margin of any kind impossible.

It is evident that continuous refinement and classification of these terms, definitions, and concepts are needed for them to be of optimal value. A serious consideration of stratification of Stage III is also in order. It is becoming clearer that the prognosis of a patient who develops a solitary pulmonary metastasis from a G_0 or G_1 primary tumor some years following local control is significantly different than multiple metastases from a G_2 lesion at the time of presentation or shortly after apparent local control of the primary lesion.[12] It may well be that meaningful stratifications will offer guidelines for the management of these lesions.

The final objective of this staging system—development of guidelines for adjunctive therapy—has yet to be realized. The effectiveness of adjuvant therapy continues to be judged by survival rates of various histogenic types of sarcomas, largely ignoring the influence of the stage, surgical margin, or adequacy of the surgical procedure on survival rates. This lamentable state is exemplified by the fact that one decade after the enthusiastic widespread adoption of prophylactic chemotherapy, serious doubt continues whether the increase in survival rates during this period is the result of adjuvant chemotherapy or improvement in staging techniques with resultant

improvements in surgical control of the primary tumor. In the light of this, it would seem obvious that data concerning staging, surgical margins, and surgical procedures must be gathered to establish significant variables in the assessment of the current explosive proliferation of protocols for adjunctive management of musculoskeletal lesions.

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