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A Clinicopathological Study on Local Extension in Musculoskeletal Sarcoma

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Abstract

To clarify the biological barrier effect on the local extension of musculoskeletal sarcomas, a clinicopathological study was carried out retrospectively and prospectively in 21 patients (24 operations) with skeletal sarcomas and 11 patients (13 operations) with soft tissue sarcomas.

Clinically, no local recurrence was observed in cases that the operation was performed with a radical surgical margin, whereas one local recurrence was observed even in the only case operated with a wide surgical margin.

The results of these surgical procedures showed that radical local control may be achieved by a carefully planned procedure within the limits of a wide margin, considering the minor barrier that may exist in a compartment.

The histological findings observed from the specimens including surrounding normal tissue, suggest that the epimysium, epiphyseal cartilage, aponeurosis, muscle fiber and the synovial layer act as minor barriers.

Introduction

Surgical treatment remains the primary therapeutic apporach to musculoskeletal malignancies despite gradual changes in the system of treatment brought about by the advancements in adjuvant therapeutic modes such as chemotherapy, radiotherapy, and immunotherapy. Surgical treatment itself has achieved a marked improvement with grading of lesions by the Surgical Staging System (SSS) introduced by *Enneking*, which allows determination of the extent of radical resection based on clear identification of barriers in the body. However, local procedures for maximum functional limb saving are ardently desired as alternatives to amputation or disarticulation, which currently constitutes the primary treatment of musculoskeletal malignant tumors. The surgical margin may be reduced even when extensive resection is indicated by *Enneking*'s system by selection of a more suitable surgical plane of resection and a better definition of the minimum area of excision that guarantees local cure. Therefore, the barrier effect of each tissue at which the

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resection may be made must be urgently and more precisely defined at different stages of the disease based on clinical and histological examination of the manner of tumor extension.

Materials and Methods

We studied 37 patients with primary musculoskeletal malignancies (24 with bone and 13 with soft tissue lesions) treated at our department during an 8-year period from 1976 to 1984 (Tables 1A and 1B).

The results of 24 operations in 21 patients with malignant bone lesions and 13 operations in 11 patients with soft tissue sarcomas were clinically evaluated either prospectively more than 9 months after the operation or retrospectively if the outcome could be determined within 9 months by, for example, comfirmation of local recurrence. The lesions were assessed and the areas of excision determined according to the SSS, and the effectiveness of local control was evaluated.

Histopathological studies were made in resected specimens in which normal tissues around the lesion were preserved. The 11 patients with bone malignancies consisted of 7 with osteosarcoma, 3 with malignant fibrous histiocytoma of bone, and 1 with chordoma ; the 7 patients with soft tissue malignancies consisted of 2 with leiomyosarcoma, and 1 each with rhabdomyosarcoma, malignant fibrous histiocytoma of the soft tissue, liposarcoma, synovial sarcoma, and malignant melanoma of the soft part. Pathological specimens were prepared by sectioning the resected tissue en bloc, and treating slices of each block by hematoxylin-eosin, Masson-trichrome, or reticulin staining. Macroscopic and microscopic examinations were made for the mode of tumor extension and the biological barrier effect of each tissue.

Results

I. Operation and Outcome

1) Malignant Bone Tumors

Table 2A shows the surgical margin and the number of patients showing local recurrence for lesions of each stage in the 24 operations in 21 patients. Intracapsular excision was performed in 4 patients : one each with sacrococcygeal chordoma, chondrosarcoma originating from a thoracic vertebral body, osteosarcoma identification of which as a malignant bone tumor was clinically and pathologically difficult, and primary malignant fibrous histiocytoma of bone which was originally considered clinically and radiologically to be a cancer metastasis to the bone and treated by palliative surgery. Three patients were operated on with marginal surgical margin.

Of the patients operated on with wide surgical margins, one patient with a stage IIB osteosarcoma (Case 2) underwent what *Enneking* termed wide amputation, exhibited no local recurrence, but developed lung metastasis 8 months later. Local prodedure with a wide margin was performed in two patients with a stage IB lesion (Cases 15 and 21) and another with a stage IIA lesion (Case 13), who showed uneventful postoperative courses for 20, 11 and 21 months, respectively. In case 20, who had had a stage IIB osteosarcoma, pulmonary metastases were found at twelve months postoperatively, however no local recurrence was noted in her right shoulder

Table 1. List of the Patients

case	Name	Age sex	Histology	Site	Stage	Procedure	Recurrence (months)	Metastasis (months)	Follow up (months)	Prognosis
1	M.W.	37M	CS	l. Scapula	III	Forequarter amp.	+ (27)	+	33	Died
2	I.K.	67F	OS	l. Femur	II B	Wide amp.	−	+ (8)	34	Died
3	Y.K.	33M	MGCT	r. Humerus	II B	Radical amp.	−	+ (5)	11	Died
4	K.M.	43F	OS	r. Metatarsal	II B	Radical amp.	−	−	72	NED
5	K.I.	51M	OS	r. Tibia	III	AK amp.	−	+	12	Died
6	Y.W.	17M	OS	l. Tibia	II B	Radical amp.	−	+ (26)	61	Alive after Resect. of Pulm. Meta.
7	K.K.	44M	MFH	l. Tibia	II B	Radical amp.	−	−	60	NED
8	T.K.	66M	MGCT	l. Femur	I B	Radical amp.	−	−	49	NED
9	M.F.	16F	OS	l. Tibia	II B	Radical amp.	−	+ (5)	20	Died
10	Y.S.	21M	OS	l. Femur	II B	Marginal ex.	+ (1)	+ (4)	12	Died
11	I.Y.	37M	MFH	l. Femur	II B	Radical amp.	−	+ (14)	34	NED
			MFH	r. Humerus	III	Wide ex.	+ (18)	−	20	Local recurrence
12	K.T.	58F	Chordoma	Sacrum	I B	Intracapsular ex.	+ (8)	−	24	Local recurrence
13	T.A.	57F	MFH	l. Femur	II A	Wide ex.	−	−	21	NED
14	K.J.	64F	MFH	l. Femur	II B	Intracapsular ex.	+ (6)	/	/	/
			MFH	l. Femur	II B	Radical amp.	−	+ (8)	14	Died
15	A.Y.	64F	CS	l. Scapula	I B	Wide ex.	−	−	20	NED
16	M.D.	14M	OS	l. Tibia	II B	Radical amp.	−	−	12	NED
17	K.M.	16M	OS	l. Tibia	II B	Radical amp.	−	+ (2)	11	Died
18	U.Y.	65M	CS	Vertebra	II B	Intracapsular ex.	+	+ (2)	9	Died
19	H.T.	18M	OS	Sacrum	II B	Biopsy only	/	+ (2)	10	Died
20	K.S.	15F	ABC	r. Humerus	II B	Intracapsular ex.	+ (6)	−	/	/

			OS	r. Humerus	II B	Wide ex.	−		+	(12)	15	Alive after Resect. of Pulm. Meta.
21	H.M.	38 F	MFH	l Humerus	I B	Wide ex.	−		−		11	NED
22	H.O.	21 F	MFH	r. Femur	II B	Biopsy only	/		−		1	Died
23	K.A.	14M	OS	r. Femur	II B	Wide ex.	−		−		8	NED
24	A.K.	10 F	OS	l. Tibia	III	Ak amp.	−		+	(2)	8	Died
			OS	r. Radius		Marginal ex.	+					
25	R.I.	20 F	RHBD	l. Thigh	III	None						Died
26	S.A.	67M	RHBD	l. Thigh	II B	Radical dis.	−		−		71	NED
27	F.M.	71 F	LEIO	r. Periscapular	II B	Intracapsular	+	(3)	−			
					II B	Intracapsular	+	(3)	+	(5)	6	Died
28	S.N.	66M	EXTOS	l. Groin	II B	Marginal ex.	+	(9)	−		14	Died
29	T.N.	39M	SYN	r. Hand	II B	Wide amp.	+	(4)				
					II B	Wide ex.	−		+	(8)	33	NED
30	A.N.	38M	LIPO	l. Periscapular	II B	Marginal ex.	+	(4)	+	(2)	8	Died
31	M.S.	59M	MFH	l. Hand	III	BE amp.	−		+		2	Died
32	S.H.	60M	MFH	r. Thigh	II A	Wide ex.	−		−		27	NED
33	Y.K.	18 F	RHBD	r. Foot	III	Marginal ex.	+	(1)	+		9	Died
34	K.T.	40 F	RHBD	r. Thigh	II A	Wide ex.	−		−		19	NED
35	Y.S.	43M	LIPO	r. Wrist	I B	Wide ex.	−		−		17	NED
36	M.K.	60M	LEIO	r. Upper arm	II A	Wide ex.	−		−		18	NED
37	M.T.	40 F	MAMES	l. Elbow	III	Wide ex.	−		+		9	Died

OS=osteosarcoma, CS=chondrosarcoma, MGCT=malignant giant cell tumor, MFH=malignant fibrous histiocytoma
NED=no evidence of disease, AK=above-knee, dis.=disarticulation, amp.=amputation, ex.=excision, RHBD=rhabdomyosarcoma
LEIO=leiomyosarcoma, LIPO=liposarcoma, EXTOS=extraskeletal osteosarcoma, MAMES=malignant melanoma of soft part
SYN=synovial sarcoma, BE=below-elbow

Table 2A. Recurrence Rate According to Surgical Stage and Procedure of Skeletal Sarcoma

Stage	Procedure							
	Intracapsular		Marginal		Wide		Radical	
	Loc.	Amp.	Loc.	Amp.	Loc.	Amp.	Loc.	Amp.
I A	—	—	—	—	—	—	—	—
I B	1/1	—	—	—	0/2	—	—	0/1
II A	—	—	—	—	0/1	—	—	—
II B	3/3	—	1/1	—	0/1	0/1	—	0/9
III	—	—	1/1	1/1	0/1	—	—	0/1

Table 2B. Recurrence Rate According to Surgical Stage and Procedure of Soft Tissue Sarcoma

Stage	Procedure							
	Intracapsular		Marginal		Wide		Radical	
	Loc.	Amp.	Loc.	Amp.	Loc.	Amp.	Loc.	Amp.
I A	—	—	—	—	—	—	—	—
I B	—	—	—	—	0/1	—	—	—
II A	—	—	—	—	0/3	—	—	—
II B	2/2	—	2/2	—	0/1	1/1	—	0/1
III	—	—	1/1	—	0/1	—	—	—

Table 2C. Recurrence Rate According to Surgical Stage and Procedure of Musculoskeletal Sarcoma

Stage	Procedure							
	Intracapsular		Marginal		Wide		Radical	
	Loc.	Amp.	Loc.	Amp.	Loc.	Amp.	Loc.	Amp.
I A	—	—	—	—	—	—	—	—
I B	1/1	—	—	—	0/3	—	—	0/1
II A	—	—	—	—	0/4	—	—	—
II B	5/5	—	3/3	—	0/2	1/2	—	0/10
III	—	—	2/2	1/1	0/2	—	—	0/1

Loc,: local procedure Amp.: amputation or disarticulation

operated by a wide margin. All patients whose surgical margin was regarded as radical underwent limb amputation, and showed no local recurrence.

2) Malignant Soft Tissue Tumors

The 13 lesions of soft tissue malignancies were 4 rhabdomyosarcomas, 2 leiomyosarcomas, 2 liposarcomas, 2 soft tissue MFH, and 1 each of synovial sarcoma, soft tissue osteosarcoma, and malignant melanoma of soft part. Four of these lesions were seen in the thigh, 2 each in the periscapular region and the hand, and 1 each in the upper arm, forearm, elbow, groin, and sole of the foot.

Four of the patients were treated initially at our department, but the other 9, including 2 cases referred to us immediately after simple excision, had undergone some surgical intervention, posing difficulties in staging as well as treatment. Staging of the lesions after simple excision was made according to the extent of the compartment showing scar or granulation. Excision of

the biopsy route, which was suspected to be contaminated with tumor cells, was considered to suffice as the additional procedure for lesions shortly after initial surgical intervention, since their extracompartmental spread appeared unlikely, and such a simple excision operation was considered not to affect the initial staging of the lesions.

Table 2B shows the surgical margin and the number of recurrent cases for each stage of the 13 primary lesions in the 11 patients who were observed for more than 9 months postoperatively. Local recurrence occurred after 6 operations in 5 patients (Cases 27, 28, 29, 30, and 33) with soft tissue malignancies, being more frequent than in those with bone malignancies. It was detected, moreover, within 4 months of the operation in 4 of the patients. Unlike bone malignancies, local recurrence preceded metastasis except in 1 patient (Case 30), and it served as an index of prognosis. Amputation of the limb was performed only in 2 patients, i.e. 1 with rhabdomyosarcoma of the proximal portion of the thigh, in which bone invasion was anticipated (Case 26), and 1 with synovial sarcoma of the dorsum of the right hand (Case 29), suggesting that local procedures should be considered first for soft tissue malignancies. Local procedures with wide surgical margins were performed in 4 patients : 1 each with stage IB liposarcoma of the distal forearm, stage IIA MFH of the thigh, leiomyosarcoma of the upper arm, and rhabdomyosarcoma of the thigh. None of these patients exhibited local recurrence or metastasis for a mean postoperative period of 20 months.

3) Overall Results

Results of 37 surgical procedures for bone and soft tissue sarcomas at our department are summarized in Table 2C.

Excision was performed with a marginal margin in 3 patients with stage IIB lesions and 3 patients with stage III lesions, all of whom died from local recurrence. These results suggest that simple shelling out type excision at the margin of the capsule-like structure invariably leaves tumor cells on the plane of excision. Of the patients who underwent wide margin excision, recurrence was observed on the proximal side of the surgical scar of 1 patient with synovial sarcoma of the dorsum of the hand. Local control could be achieved, however, by additional excision with a wide margin.

Of the stage II patients treated at our department, the survival rate was compared between 8 patients who underwent wide margin excision and 10 patients who underwent radical margin excision using a log-rank plot as shown in Figure 1. Although the observation period was short in some patients, no significant difference had been observed until the time of this study. The absence of difference in the state of local control or prognosis suggests that the results of our wide margin excision are comparable to those of *Enneking*'s radical margin excision.

In stage III patients, on the other hand, consideration of life expectancy often leads to preference of local procedures for temporary local control to limb amputation. Even in the stage III condition, individual lesions can be classified into stage IA, IB, IIA, or IIB and local procedures may be applied according to this classification. Stage III patients may, therefore, be regarded as subjects suited for evaluation of the relationship between the surgical margin and local control. Table 3 summarizes the staging of the metastatic lesions in Case 11 and 37 and effecti-

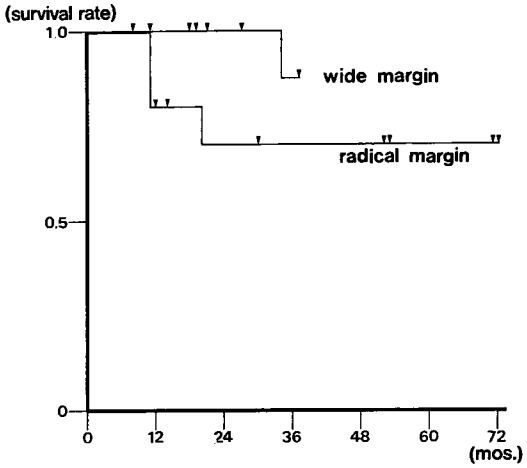


Fig. 1. Survival of 19 patients with stage II musculoskeletal sarcomas resected through the wide or radical margin.

veness of local procudures on the control of these lesions. Case 11 was evaluated as stage III due to the bone matastasis to the right upper arm, but the primary as well as the metastatic lesion was completely controled and no new metastatic lesions were found in the lung or any other organs 14 months after the surgery. In this patient, a change of diagnosis to metachronous multiple MFH of the bone is under consideration. Even in Case 37, in which a number of metastatic lesions developed in the muscles, no local recurrence was noted during her life at sites where the excision was made with a wide or more extensive margin.

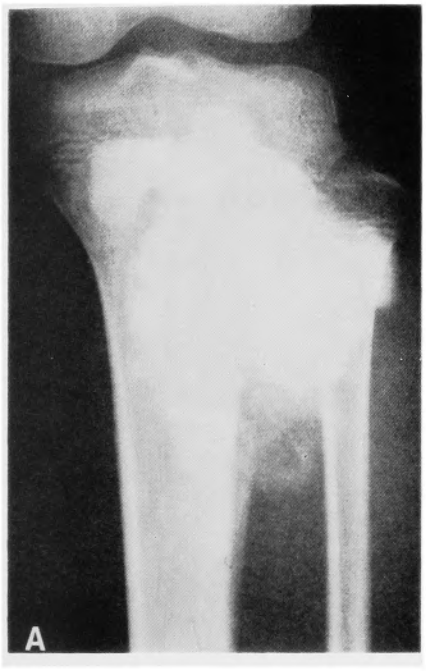
II. Histopathological Examination

Primary malignant bone tumors occur most commonly in the metaphysis, which is a site of both clinical and surgical importance. A tumor originating in the metaphysis first spreads to the spongy bone of the epiphysis and diaphysis. If the growth plate has already been closed, the tumor readily infiltrate into areas under the articular cartilage. If the epiphisial cartilage is remaining, the tumor expansion is temporarily blocked, but in a more advanced stage, continuous

Table 3. Evaluation of the Surgical Site of the Local Tumor in Patients with Stage III

	Site	Surgical Site		Local Procedure	Follow-up	Recurrence
Case 11	R. Humerus	Intraosseous with pathologic fracture	In.	Wide excision (+TSR)	14 m.	No
Case 37	L. Elbow	Antecubital fossa	Ex.	Wide excision	9 m.	No
	L. Lower leg	M. Gastrocnemius	In.	Radical excision	9 m.	No
	L. Hip	M. Gluteus maximus	In.	Wide excision	6 m.	No
	R. Thigh	M. Quadriceps	Ex.	Marginal excision	4 m.	Yes
	L. Thigh	M. Biceps femoris	In.	Radical excision	5 m.	No
	R. Back	M. Latissimus dorsi	Ex.	Marginal excision	2 m.	Yes
	R. Elbow	Multicentric	Ex.	Marginal excision	3 m.	Yes

In.=intracompartmental, Ex.=extracompartmental



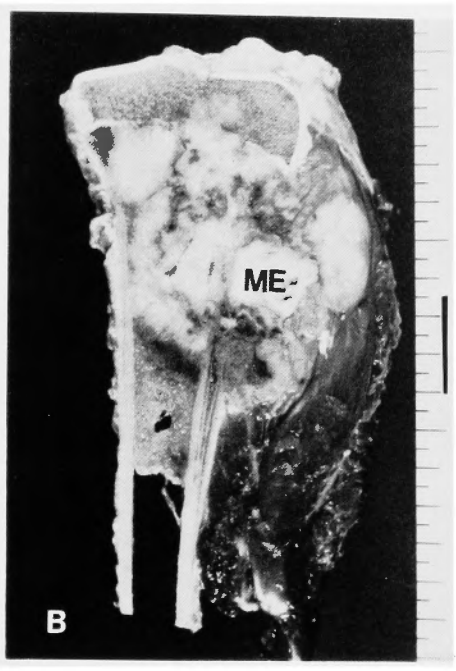


Fig. 2. A 10 year-old female with stage III osteosarcoma of the proximal tibia had above-knee amputation.

A. An X-ray after the biopsy shows the sclerotic lesion with a lump of methacrylate.

B. A cut surface of the specimen is presented. The biopsy window is marked by the plug of methacrylate(ME),. Central penetration of the open growth plate permitted extension into the epiphysis.

C. A radiograph of the slice of the specimen demonstrates predominantly osteoblastic lesion.

D. A low-power photomicrograph shows the tumor(OS) extended through the channel of the epiphyseal plate(EP).

E. A photomicrograph shows the lesion invaded into the fat marrow without any encapsulation.

F. A photomicrograph demonstrates the lesion extended out of the cortical bone (arrow).

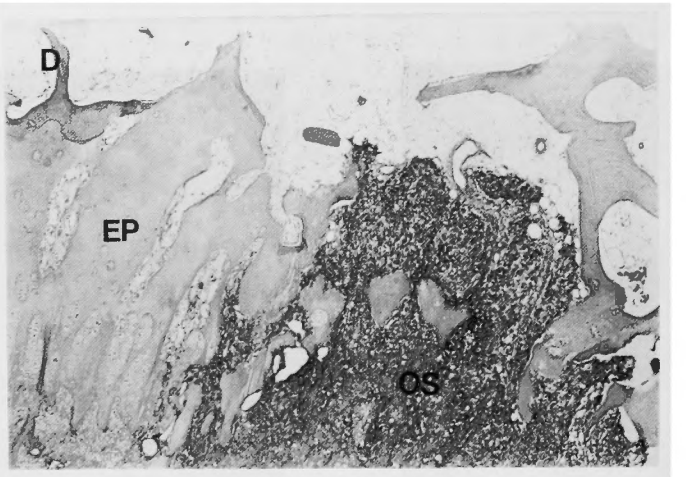


Fig. 2. D

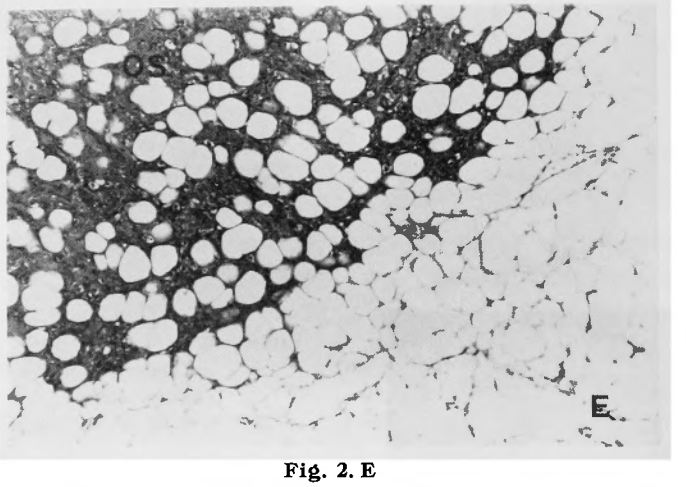


Fig. 2. E

infiltration is seen limited to the center of the epiphysis correnponding to the position of the central vascular channel (Fig. 2). Expansion of the tumor in patients with the closed growth plate is continuous directly from the metaphysis.

The tumor invades with its growth the surrounding soft tissue via less resistant structures such as ligaments attached to the epiphysis and the attachment of fibrous layer of the articular capsule to the bone, and spreads to the underlining layer of the synovial membrane. Release of tumor cells through the synovial membrane to the joint cavity is, however, rare (Fig. 3). In the terminal stage, the tumor having invaded under the surface of the synovial membrane, among the muscle fibers, and within the tendons and ligaments begins to extend to the outside of the fascia and aponeurosis. This developmental process is schematically represented in Fig. 4.

As for intramuscular sarcoma, the tumor was seen to grow among the muscle fibers and bundles along the long axis (Fig. 5). Against the tumor extension, the muscle tissue exerted a barrier effect vertically to the course of muscle fibers by forming a thick and dense layer with a capsule-like structure, which is composed of atrophied and degenerated muscle fibers, due to com-

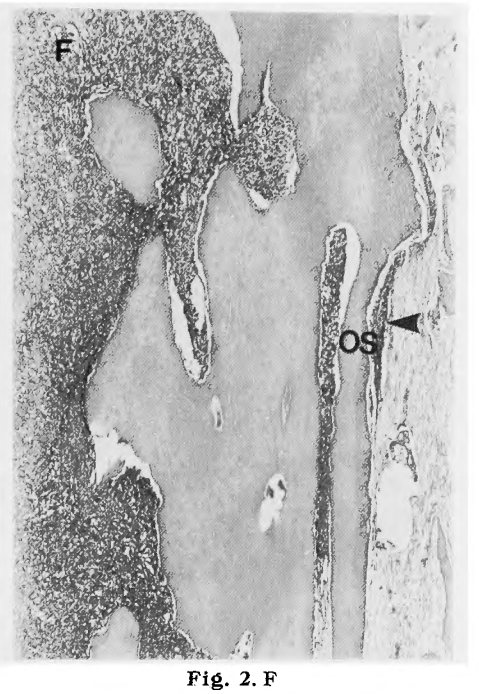


Fig. 2. F

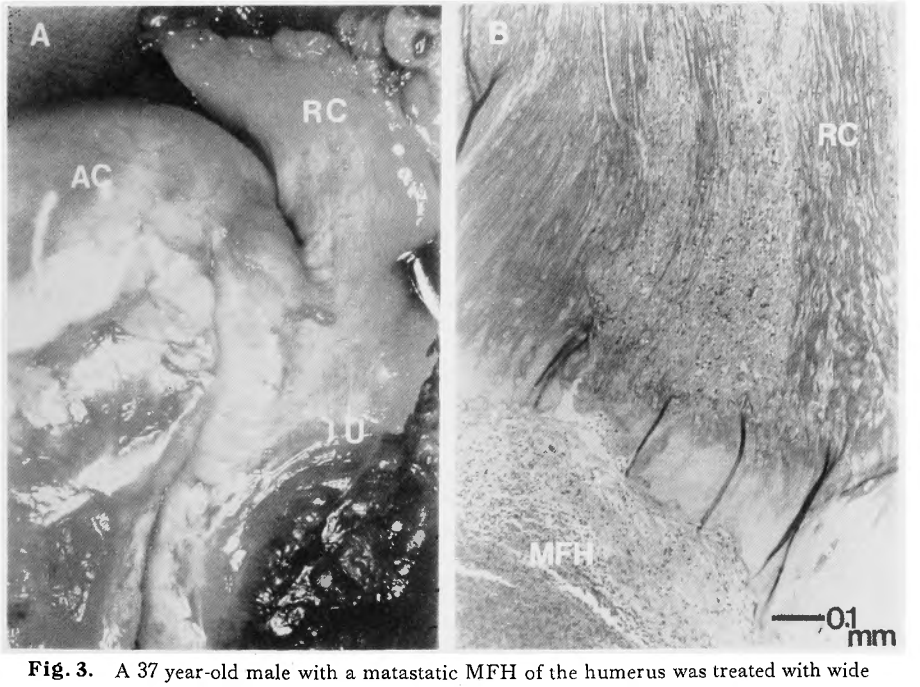


Fig. 3. A 37 year-old male with a matastatic MFH of the humerus was treated with wide excision of the proximal humerus and adjuvant chemotherapy.
A. A surgical specimen of the humeral head(AC) demonstrates the perichodral lesion(T) and the rotator cuff (RC).
B. A photomicrograph shows the lesion invaded into the tendon of the rotator cuff. [Masson-trichrome stain]

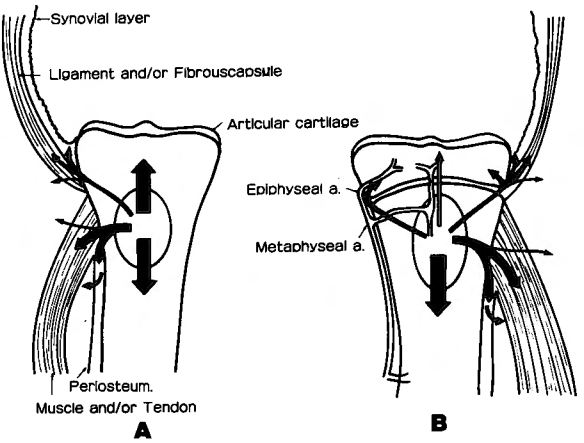


Fig. 4. Schematic drawing of tumor extension related to the minor barrier
The epiphyseal plate is closed (A) or opened (B).

pression associated with the tumor growth. Spaces between muscle fibers, however, were extended and showed edematous changes accompanied by neovascularity and diffuse infiltration of tumor cells.

The tumor infiltrated not only into the surrounding reactive layer, but even to sites where the muscle tissue appeared macroscopically normal, forming small lesions of skip metastasis among the muscle fibers and bundles containing satellites. In this instance, similarly to the fascia, the

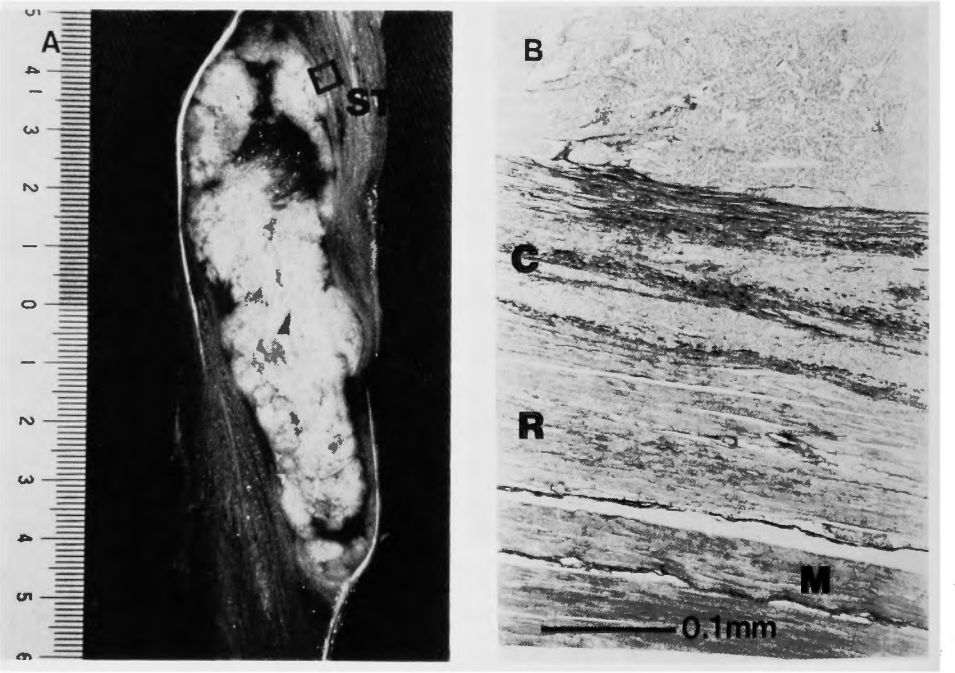


Fig. 5.

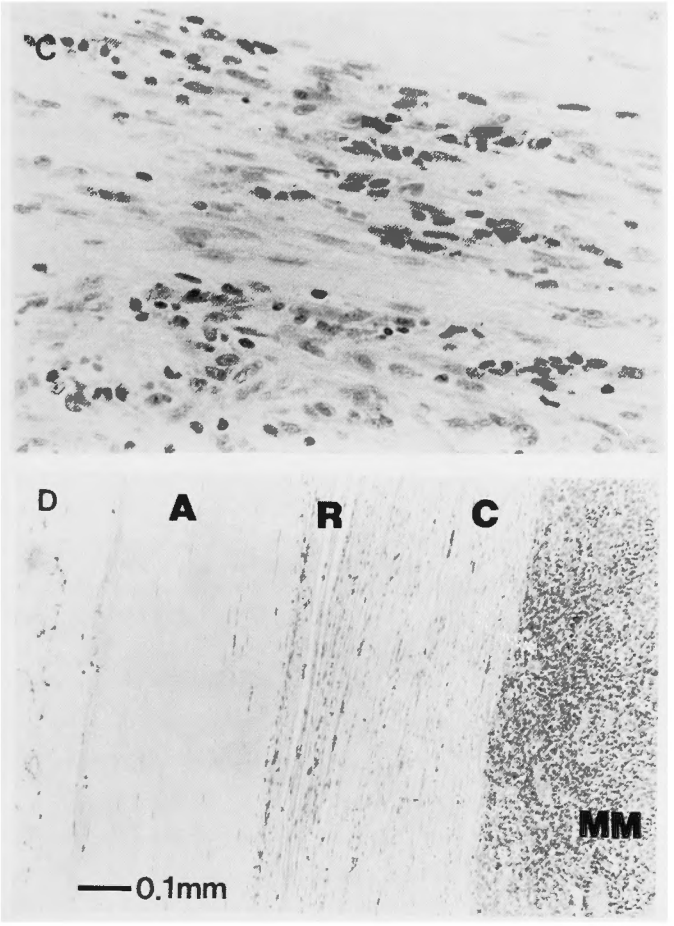


Fig. 5. A 40 year-old female with stage III malignant melanoma of soft part
A. A cut surface of the specimen of the long head of biceps femoris. Intramuscular lesion extended in the direction of muscle fibers.
B. A low-power photomicrograph shows the pseudocapsule(C), surrounding reactive zone(R), and muscle(M). [Masson-trichrome stain]
C. A high-power photomicrograph shows the pseudocapsule made of lymphocyte, plasma cell, fibrous connective tissue cell and sarcoma cell with melanin pigments. [H-E stain]
D. A low-power photomicrograph demonstrates the transition from the lesion (MM) to the pseudocapsule(C), to the reactive muscle(R), and to the non-reactive aponeurosis(A). [H-E stain]

aponeurosis functioned as a barrier against the tumor extension. In Figure 6, this developmetal pattern is schematically represented and an optimal area of excision is shown with a solid line.

Discussion

Musculoskeletal tumors vary in the degree of malignancy, but complete removal of local lesions is a common requirement for their treatment[2,3]. Failure in local control results in a low survival rate, because of a close relationship between the persistence of tumor cells at the excision

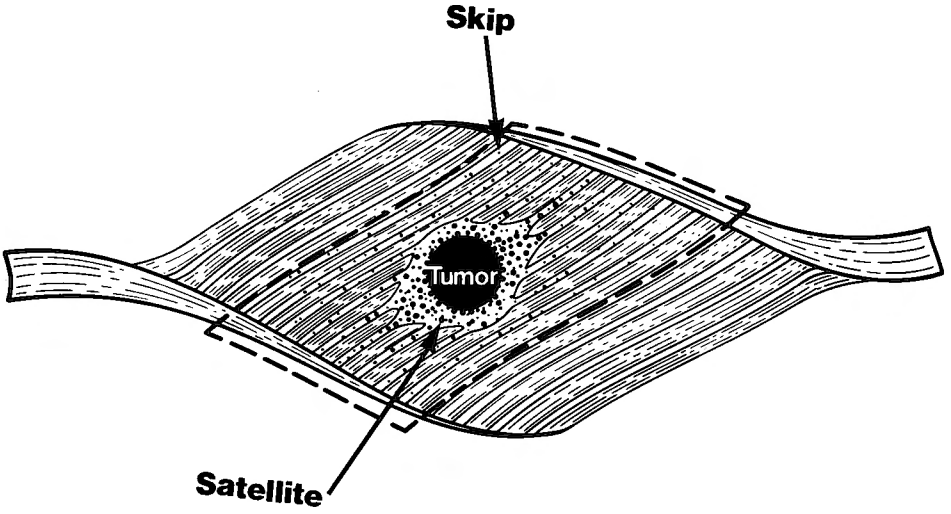


Fig. 6. Grown pattern of the intramuscular sarcoma
The relation between muscle fiber and sarcomatous lesion is shown. An area encircled by a broken line shows the wide margine excision, however a radical local control may be expected because all of the daughter lesions is fully removed.

site and the development of metastasis[4]. Although chemotherapy may be useful for the control of micro-metastatic lesions including skip metastases, it is considered to be ineffective for lesions having grown larger than a certain size, and uncertainty of its effects does not permit reduction of the surgical margin.

Above-knee amputation is widely accepted for malignancies of the proximal end of the tibia both to assure the cure and to facilitate application of a prosthesis. *Marcove*[14] and *Watts*[20] advocated resection of the distal end of the femur along with the patella for a tumor of the proximal end of the tibia having extended to the epiphysis to eliminate the possibility of skip metastasis beyond the knee joint or intraarticular extension. However, en bloc resection as a more conservative alternative to limb amputation has also been performed for bone malignancies when the patients rejected the radical procedure, in combination with adjuvant radiotherapy or chemotherapy, and improvements in the biomaterials[16,17]. The local recurrence rate of 9% (6 of the 66 patients) reported by *Marcove* after en bloc resection of osteosarcoma[14] is comparable to that after amputation. *Marcove*[14] removed the entire femur together with the surrounding normal tissues to a sufficient thickness and replaced it with a metal prosthesis. For tumors near the joint, total removal of the joint was performed with subsequent joint replacement. Eilber[5] reported a local recurrence rate of less than 3%, a value even lower than that after amputation, by combining chemotherapy and radiotherapy with a wide margin resection.

The relationship between the extent of resection for primary bone malignancies, notably osteosarcoma, and the rate of local recurrence was described in 1980 by *Enneking* et al by introducing the concepts of the barrier to the tumor extension provided by certain tissues and the compartments within the barriers[7-10]. The Surgical Staging System devised according to these concepts is accepted widely as accurate criteria for determination of the optimal plane of resection.

This achievement may be appreciated as a landmark in the progress of surgical treatment for musculoskeletal sarcomas[13].

Soft tissue malignancies also vary widely in the origin as well as the degree of malignancy, but rates of local recurrence and metastasis are known to be nearly uniform among all these tumor types[8,9,18]. The local recurrence rate is high as 62%[18], after simple excision of the lesion, suggesting the inadequacy of local control by this procedure and necessity of reevaluation of the excision area.

A consideration on the pseudocapsule, around which simple excision is made, appears to be in order. *Bowden*[1] suggested that the pseudocapsule is produced by flattening of tumor cells, and that these cells, in contact with the surrounding normal tissues, retain the ability of invasive proliferation. *Simon*[18], on the other hand, stated that the pseudocapsule is formed by growth of reactive fibrous connective tissue of the host, but the tumor cells penetrate the structure and are present diffusely among the muscle fibers and between the muscle layers. According to Kawaguchi[12], the pseudocapsule consists of collagen fibers and fibroblasts produced due to compression and resultant degeneration of normal tissues by the rapidly growing tumor. The capsule is liable to lamellar detachment, and the tumor cells infiltrate into the external reactive zone. The capsule formation is less notable along the course of muscle fibers but more notable vertically to the course. *Pack*[15] considered the pseudocapsule to be a structure formed by aggregation of fibrous components of the tumor and not encapsulating the tumor. *Enneking*[9,10] speculated that the excentric growth of the tumor causes the flattening and the parallel arrangement of the tumor cells in the periphery along with atrophy of the replaced normal tissues due to compression, resulting in a capsule-like appearance. He also observed vascularization and edema, and abundant satellite lesions especially in malignant lesions, in the surrounding reactive zone.

We consider that the capsule of the malignant tumor is composed of tumor cells, interstitial tissue, and mesenchymal cells originating from the surrounding tissues, and is formed within the periphery of the tumor including the reactive zone. It, therefore, does not constitute the border of the tumor or enlarge with the growth of the tumor, but is being remodeled toward the outside by generation and resorption in progress at various rates. When the capsule tissue remained even in a small portion of the resection surface, local recurrence was invariably observed in our patients[11].

Instead of simple excision, wide resection in which the lesion is removed with normal tissues completely surrounding it may be necessary for complete local control. However, this leads to the problems of how wide the margin should be and how can the margin be measured during surgery. Although surgery with a margin of a few centimeters was reported to have resulted in a recurrence rate of 7%, this margin is clearly inadequate for radical resection. *Eilber*[5] reported that most of local recurrent lesions were observed on the surface of resection, and regarded contamination during surgery as primarily responsible for the recurrence. They, therefore, advocated en bloc resection of the entire muscles possibly contaminated during the tumor excision including the origin and the insertion as well as the skin, subcutaneous tissues, and soft tissues with a sufficient margin[1,15]. However, as was clear by our observations, the presence of a daughter

lesion beyond the capsule rather than the operative contamination is more responsible for the local recurrence. *Enneking* divided these daughter lesions into satellites and skip lesions (local metastases), and considered that the extent of their spread is limited within the barriers resistant to tumor infiltration, and that radical resection of even highly malignant lesion can be achieved by resection of only the entire compartments invaded by the tumor. This definition of the surgical margin based on anatomy is far more practical than a margin merely assumed to be a given distance away from the border of the lesion, and is clinically useful.

As such barriers, *Enneking*[7] suggested the cortical bone and articular cartilage in bone, articular cartilage and joint capsule in joints, the major fascial septa containing a muscle group of common function and tendinous origin and insertion in soft tissues. The epiphysial cartilage was considered by many investigators including *Rosa*i et al to be a barrier from observations of primary tumors of the metaphysis, but *Enneking*[6] and *Simon*[19] excluded it as a barrier. While admitting from our clinical findings that the metaphysial cartilage is resistant to the tumor expansion for a certain period from the early developmental phase, we also encountered many cases in which the lesion continuously extended to the epiphysis through the vascular channel presumably located in the center relatively early in the developmental process. The epiphysial cartilage, therefore, is considered to be a weaker barrier than the articular cartilage.

Kawaguchi[12] observed a barrier effect against soft tissue tumors in the connective tissues of fascia, periosteum, and joint capsule as well as the vascular adventitia and epineurium. He also considered a margin of 10 cm along the axis of the muscle from the limit of the tumor to suffice and resection of the entire muscle including the origin and the insertion to be unnecessary. Thus, the concept of the barrier varies among authors and has not yet to be established. Although *Enneking* defined only the tissues with notable resistance to the tumor expansion as barriers, all tissues are considered to possess barrier effects of varying degrees.

A total excision of a compartment is considered necessary according to *Enneking's* SSS regardless of the position of the tumor in the compartment or its size, but such an approach cannot be accepted by today's standards. In order to minimize the area of resection without reducing the chance of cure, grading of all tissues as minor barriers may be useful for surgery since each tissue is considered to have a barrier effect of specific magnitude. Incorporation of these minor barriers within *Enneking*'s compartments is expected to contribute to an improvement in the success rate of conservative surgery for functional limb preservation.

Our histopathological studies indicated the following routes of tumor expansion. Primary bone malignancies occur most commonly in the metaphysis, a site adjacent to the joint which is of clinical as well as surgical importance. A tumor originating at this site first spreads toward the epiphysis and marrow cavity composed of spongy bone. The advance of the tumor is temporarily prevented if the epiphysial cartilage is present ; the tumor readily extends to areas immediately under the articular cartilage if the epiphysial plate has been closed. In the next stage, the cortical bone of the metaphysis is resorbed, and the tumor projects out of the bone at the insertion of the tendons, accompanied simultaneously by notable subperiosteal mesenchymal reaction. In a more advanced stage, the tumor develops continuously into the epiphysis, penetrating the epiphysial

cartilage, even if it is present, through the central vascular channel. By this time, the tumor having infiltrated via the attachment of ligaments and fibrous joint capsule is seen under the synovial lining. In the terminal stage, the tumor under the surface of the synovial membrane, among muscle fibers, and within tendons and ligaments extends diffusely, forming a reactive zone even outside the fascia and aponeurosis. The advance toward the marrow cavity, however, is limited. Thus, we conceive what may be called minor barriers with different barrier effects rather than barriers with a uniform strength.

Development of soft tissue malignancies is inherently related to the properties of the facia, muscles, nerves, and blood vessels. The muscle, a structure consisting of an aggregation of muscle fibers enveloped by the epimysium, in particular, constitutes with the fascia the largest compartment. The knowledge of tumor extension patterns within the muscle bears special importance in reducing surgery for functional preservation.

The tumor grows in the muscle while displacing the normal muscle fibers. This enlarges interfibrous spaces along the long axis of the muscle, and the tumor infiltrates these spaces by forming satellites. Vertically to the course of muscle fibers, the thickness of the reactive zone is smaller, but satellites formed within this thin layer are likely to migrate along the long axis of the muscle and produce skip metastases at distant sites. Muscle bundles, therefore, are considered to act as a barrier against the tumor expansion vertically to the axis of the muscle.

Conclusion

To explore the possibility of functional preservation by reducing the surgical margin for musculoskeletal malignancies, 32 patients treated at our department were classified according to *Enneking*'s Surgical Staging System, and the relationship between the surgical margin in a total of 37 operations and their results, particularly in terms of the rate of local recurrence, was studied. Although our results supported the validity of SSS, the rate of complete cure was high even after wide margin resection. Margins of surgical specimens (11 bone malignancies and 7 soft tissue malignancies) were histopathologically evaluated for pattern of tumor extension as well as for relative barrier effects of different anatomical structures. The epiphysial cartilage, aponeurosis, synovial membrane of the joints and synovial bursa, muscle fiber, and epimysium were suggested to function as minor barriers.

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和文抄録

骨・軟部悪性腫瘍の局所進展に関する臨床病理学的研究

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〔研究目的〕 骨・軟部悪性腫瘍の患肢温存療法における局所の根治性の獲得には，より遠隔位での充分な切除が必要であり，患肢温存のためには切除を最小限に止めたいという予盾があり，その解決の基準として1980年Enneking が提唱した Surgical Staging System の評価は高いものがある．これは腫瘍の拡がりに対する明確な barrier（皮質骨，筋膜，腱など）によって囲まれる compartment を規定し，腫瘍の占局部位によって外科的切除面を設定していくものである．これを厳密に適応すると，悪性度が高く，局所浸潤性の著しい腫瘍に対しては患肢温存の適応はなく，臨床上，実際経験される患肢温存成功例を説明しえない．局所根治性を保証しうる外科的切除面を設定するためには，腫瘍の局所進展に対する各組織の barrier としてのランク付けを行なうことが望まれ，この目的遂行のため，以下の研究を立案実施した．

〔材料および方法〕 愛媛大学整形外科学教室において開設以来取扱った骨・軟部悪性腫瘍のうち術後９ケ月以上経過したもの，およびそれ以内でも既に局所再発のみられた症例を用いた．骨悪性腫瘍21症例24回手術，および軟部悪性腫瘍11症例13回手術について，stage 別に局所の根治性を検討した．手術材料のうち，周囲に健常組織が充分保存されていた標本を対象に病理組織学検討を行なった．それらは骨肉腫７例，骨悪性線維性組織球腫３例，脊索腫１例，平滑筋肉腫２例，横紋筋肉腫，軟部悪性線維性組織球腫，脂肪肉腫，滑膜肉腫，軟部悪性黒色腫各１例であった．標本はスライスとした後分割し，病理標本を作製し，腫瘍の浸潤範囲と宿主の組織反応を指標として検討した．

〔結果および考察〕

1. 臨床的検討：実施された手術の切除面と局所再発の関係を検討した結果，切除面が intracapsular または marginal margin であった12手術例では全例局所再発がみられたのに対し，wide margin で施行された13手術例では１例にのみ４ケ月で再発をみたが，他は９ケ月以上再発はなかった．Radical margin で実施された12手術例では，局所再発はみられなかった．以上の結果より，被膜近傍での単純切除は禁忌である反面，wide margin でも根治性が得られる可能性が示された．

2. 病理学的検討：腫瘍辺縁部に膠原線維，線維芽細胞によりなる被膜を，さらにその外方に反応層を認めた．この被膜は浸潤を示す腫瘍の成長とともに外側に remodelling されていくと考えられた．

骨幹端に原発した腫瘍の局所浸潤様相より経時的変化を推定した結果は，腱，靱帯の骨付着部への浸潤は骨髄への浸潤のつぎに起こるが，骨端軟骨は腫瘍の骨端への浸潤に対し一旦は barrier となりうるものの，比較的早期に破られる様子が観察された．

関節隅角部は腫瘍浸潤に対し一つの抵抗減弱部であるが，関節内穿破はみられず，滑膜表層には barrier effect が認められた．筋肉内では筋線維方向にはその間を容易に浸潤し satellite を形成するが，垂直方向では反応層の幅は狭く，筋線維束は腫瘍の横軸方向への進展に対し minor barrier effect を有していた．

〔まとめ〕 骨・軟部悪性腫瘍の罹患局部に関連して，骨端軟骨，滑膜表層，筋線維束，腱膜，筋上膜は minor barrier effect を有しており，これをもって major barrier に囲まれた compartment 中に小区域を設定することが可能であると考えられた．