



# Soft Tissue Tumor

**Hsin-Nung Shih M.D.**

PROFESSOR

DIVISION OF JOINT RECONSTRUCTION

DEPARTMENT OF ORTHOPEADIC

CHANG GUNG MEMORIAL HOSPITAL

CHANG GUNG UNIVERSITY, COLLEGE OF MEDICINE

TAIWAN

# Soft Tissue Tumor

## *Definition*

- ❖ Nonepithelial extraskeletal tissue
- ❖ Exclusive reticuloendothelial system, glia
- ❖ Voluntary muscles, fat, fibrous tissue, peripheral nervous system
- ❖ Derived from mesoderm (and neuroectoderm)

# Soft Tissue Tumor

## *Incidence*

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- ❖ 0.3%
- ❖ Benign: Malignant = 100:1
- ❖ (1983 Enzinger and Weiss 10:1)
- ❖ Malignant
  - 0.8% to 1% of all cancers
  - 2.0% of all cancer deaths
- ❖ 1990 Campanacci soft tissue sarcoma
  - 20 cases/million population/yr  
(twice as often as bone tumor)

## Estimated new cases of cancer by site

Site	No. cases
Lung	93,000
Breast	88,700
Colon	69,000
Lymphoma	29,000
Central nervous system	10,000
Soft tissue	4,500
Bone	1,900

Data are from National Cancer Institute's Third National Cancer Survey, 1975

# Soft Tissue Tumor

## *Pathogenesis*

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- ❖ Unknown
- ❖ Environmental factors
- ❖ Oncogenic viruses
- ❖ Immunological factors
- ❖ Genetic factors
- ❖ Radiation

# Histological Classification of Soft Tissue Tumors

- Fibrous (tissue) tumors
- Fibro-histiocytic
- Adipose tissue
- Muscle tissue
- Blood vessels
- Lymph vessels
- Synovial tissue
- Mesothelial tissue
- Peripheral nerve
- Autonomic ganglia
- Paraganglionic structures
- Cartilage and bone-forming
- Pluripotential mesenchyme
- Disputed or uncertain histogenesis
- Unclassified

# Most Common Benign and Malignant Soft Tissue Tumors

## Benign

Ganglion

Lipoma

Myoma, leiomyoma

Fibroma

Myxoma

Hemangioma,  
hemangiomatosis

Chondroma

Neurofibroma

## Malignant

Rhabdomyosarcoma

Leiomyosarcoma

Malignant fibrous histiocytoma

Fibrosarcoma

Liposarcoma

Synovial sarcoma

Soft tissue osteosarcoma

# Location

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40%	Lower extremity
20%	Upper extremity
10%	Head and neck
30%	Trunk
10%	Retroperitoneal area
Others	Chest, abdominal wall

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★ Location influence on the local treatment option





# Grading

*Broders et al 1939*

- ❖ **Cellularity**
- ❖ **Pleomorphism or anaplasia**
- ❖ **Mitotic activity**
- ❖ **Necrosis**
- ❖ **Expansive, infiltrative, invasive growth**
- ❖ **Matrix formation**
  - **hemorrhage, calcification, collagen or mucoid**

# Grading systems: histological parameters used in different grading systems

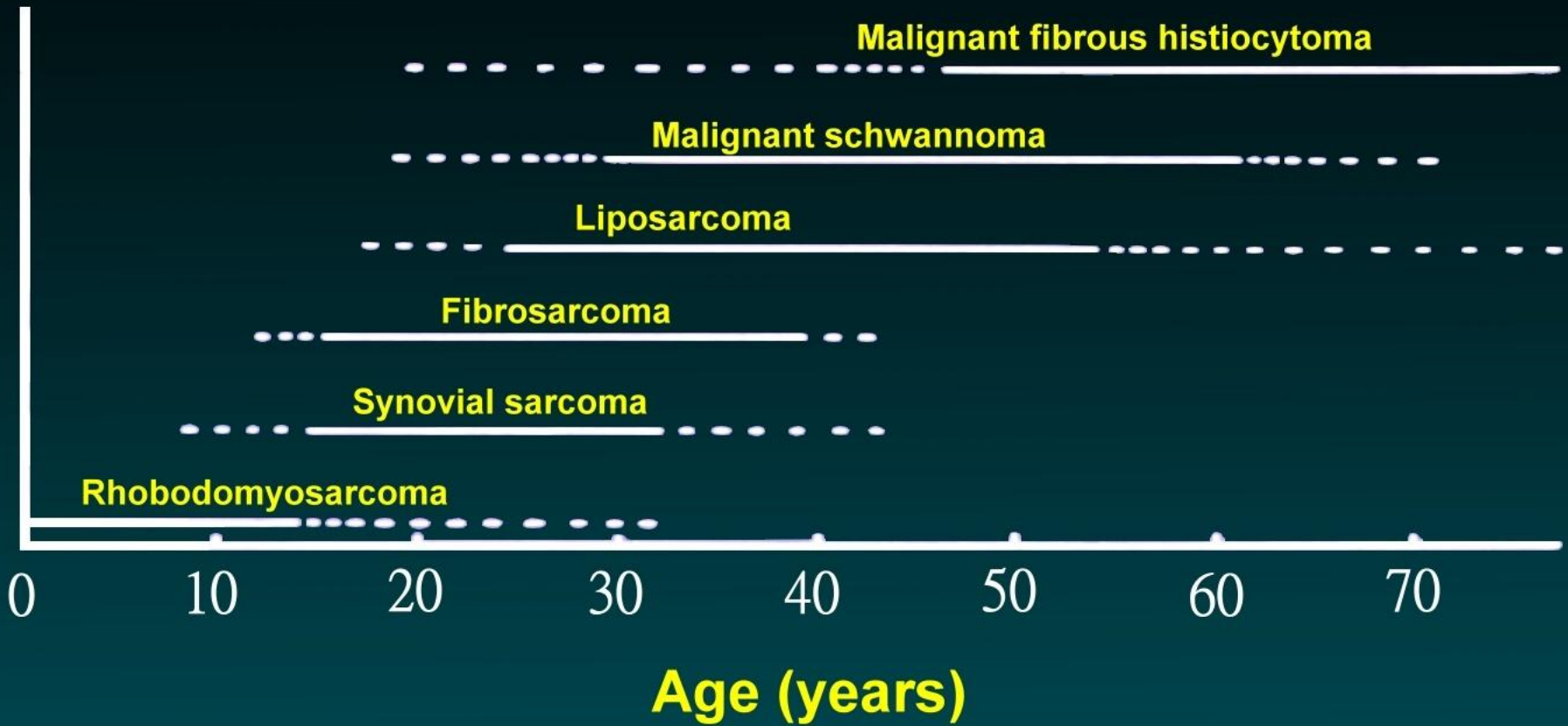
	Markhede	Myhre-Jensen	Costa	Coindre
Cellularity	+	+	+	-
Differentiation	-	-	-	+
Pleomorphism	+	+	+	-
Mitotic rate	+	+	+	+
Necrosis	-	+	+	+

# Definition of grading parameters

Parameter	Score
<b>Degree of differentiation</b>	
Close resemblance to adult tissue	1
Cell type clearly recognizable	2
Cell type uncertain . . . . .	3
<b>Necrosis</b>	
No necrosis . . . . .	1
<50% necrosis . . . . .	2
>50% necrosis . . . . .	3
<b>Mitotic figures</b>	
0-9/10 HPF. . . . .	1
10-19/10 HPF. . . . .	2
20+/10 HPF . . . . .	3
<b>Total score</b>	
Grade	
Grade I . . . . .	2,3
Grade II . . . . .	4,5
Grade III . . . . .	6,7,8

\*Modified from Coindre, J.M., et al, Cancer 58:306, 1986





## Histological type

## Histological grade

I II III

Fibrosarcoma  
Infantile fibrosarcoma  
Dermatofibrosarcoma protuberans  
Malignant fibrous histiocytoma  
Liposarcoma  
    Well-differentiated liposarcoma  
    Myxoid liposarcoma  
    Round cell liposarcoma  
    Pleomorphic liposarcoma  
Leiomyosarcoma  
Rhabdomyosarcoma  
Angiosarcoma  
Malignant hemangioendothelioma  
Synovial sarcoma  
Malignant mesothelioma  
Malignant schwannoma  
Neuroblastoma  
Ganglioneuroblastoma  
Extraskeletal chondrosarcoma  
    Myxoid chondrosarcoma  
    Mesenchymal chondrosarcoma  
Extraskeletal osteosarcoma  
Malignant granular cell tumor  
Alveolar soft part sarcoma  
Epithelioid sarcoma  
Clear cell sarcoma  
Extraskeletal Ewing's sarcoma

	I	II	III
Fibrosarcoma			
Infantile fibrosarcoma			
Dermatofibrosarcoma protuberans			
Malignant fibrous histiocytoma			
Liposarcoma			
Well-differentiated liposarcoma			
Myxoid liposarcoma			
Round cell liposarcoma			
Pleomorphic liposarcoma			
Leiomyosarcoma			
Rhabdomyosarcoma			
Angiosarcoma			
Malignant hemangioendothelioma			
Synovial sarcoma			
Malignant mesothelioma			
Malignant schwannoma			
Neuroblastoma			
Ganglioneuroblastoma			
Extraskeletal chondrosarcoma			
Myxoid chondrosarcoma			
Mesenchymal chondrosarcoma			
Extraskeletal osteosarcoma			
Malignant granular cell tumor			
Alveolar soft part sarcoma			
Epithelioid sarcoma			
Clear cell sarcoma			
Extraskeletal Ewing's sarcoma			

# Staging System

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American Joint Committee

(AJC)

Enneking System

# AJC staging of soft tissue sarcomas: definitions of TNMG

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## T: Primary tumor

T1 Tumor less than 5 cm

T2 Tumor 5 cm or greater

T3 Tumor that grossly invades bone, major vessel, or major nerve

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## N: Regional lymph nodes

N0 No histologically verified metastasis to regional lymph nodes

N1 Histologically verified regional lymph node metastasis

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## M: Distant metastasis

M0 No distant metastasis

M1 Distal metastasis

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## G: Histological grade of malignancy

G1 Low (well-differentiated)

G2 Moderate (moderately well-differentiated)

G3 High (poorly differentiated)

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Modified from Russell, W.O., et al.: Cancer 40:1562, 1977



# AJC staging of soft tissue sarcomas: definitions of stages

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## Stage I

Stage Ia (G1T1N0M0): Grade 1 tumor less than 5 cm in diameter with no regional lymph node or distant metastasis

Stage Ib (G1T2N0M0): Grade 1 tumor 5 cm or greater in diameter with no regional lymph node or distant metastasis

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## Stage II

Stage IIa (G2T1N0M0): Grade 2 tumor less than 5 cm in diameter with no regional lymph node or distant metastasis

Stage IIb (G2T2N0M0): Grade 2 tumor 5 cm or greater in diameter with no regional lymph node or distant metastasis

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## Stage III

Stage IIIa (G3T1N0M0): Grade 3 tumor less than 5 cm in diameter with no regional lymph node or distant metastasis

Stage IIIb (G3T2N0M0): Grade 3 tumor 5 cm or greater in diameter with no regional lymph node or distant metastasis

Stage IIIc (G1-3T1-2N1M0): Tumor of any grade or size with regional lymph node but no distant metastasis

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## Stage IV

Stage IVa (G1-3T3N0-1M0): Tumor of any grade and any size that grossly invades bone, a major vessel, or a major nerve with or without regional lymph node metastasis but without distant metastasis

Stage IVb (G1-3T1-3N0-1M1): Tumor with distant metastasis

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Modified from Russell, W.O., et al.: Cancer 40:1562, 1977



# Cytoplasmic staining for glycogen in soft tissue tumors

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## Usually glycogen positive

## Variable

## Usually glycogen negative

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Rhabdomyosarcoma

Liposarcoma

Fibrosarcoma

Mesothelioma

Leiomyosarcoma

Dermatofibrosarcoma protuberans

Chondrosarcoma

Angiosarcoma

Malignant fibrous histiocytoma

Clear cell sarcoma

Epithelioid sarcoma

Hemangiopericytoma

Ewing's sarcoma

Carcinoma

Synovial sarcoma

Alveolar soft part sarcoma

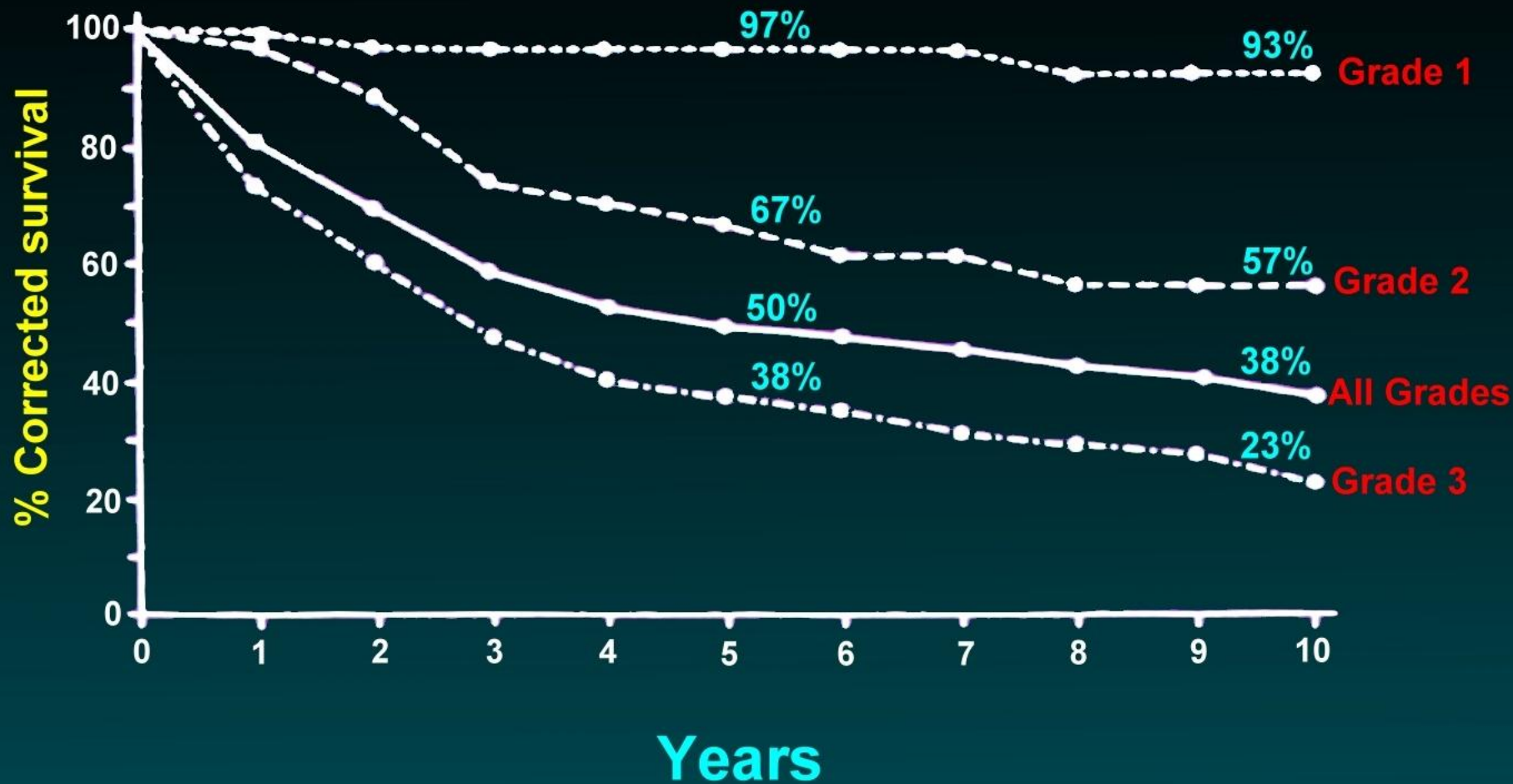
Malignant melanoma

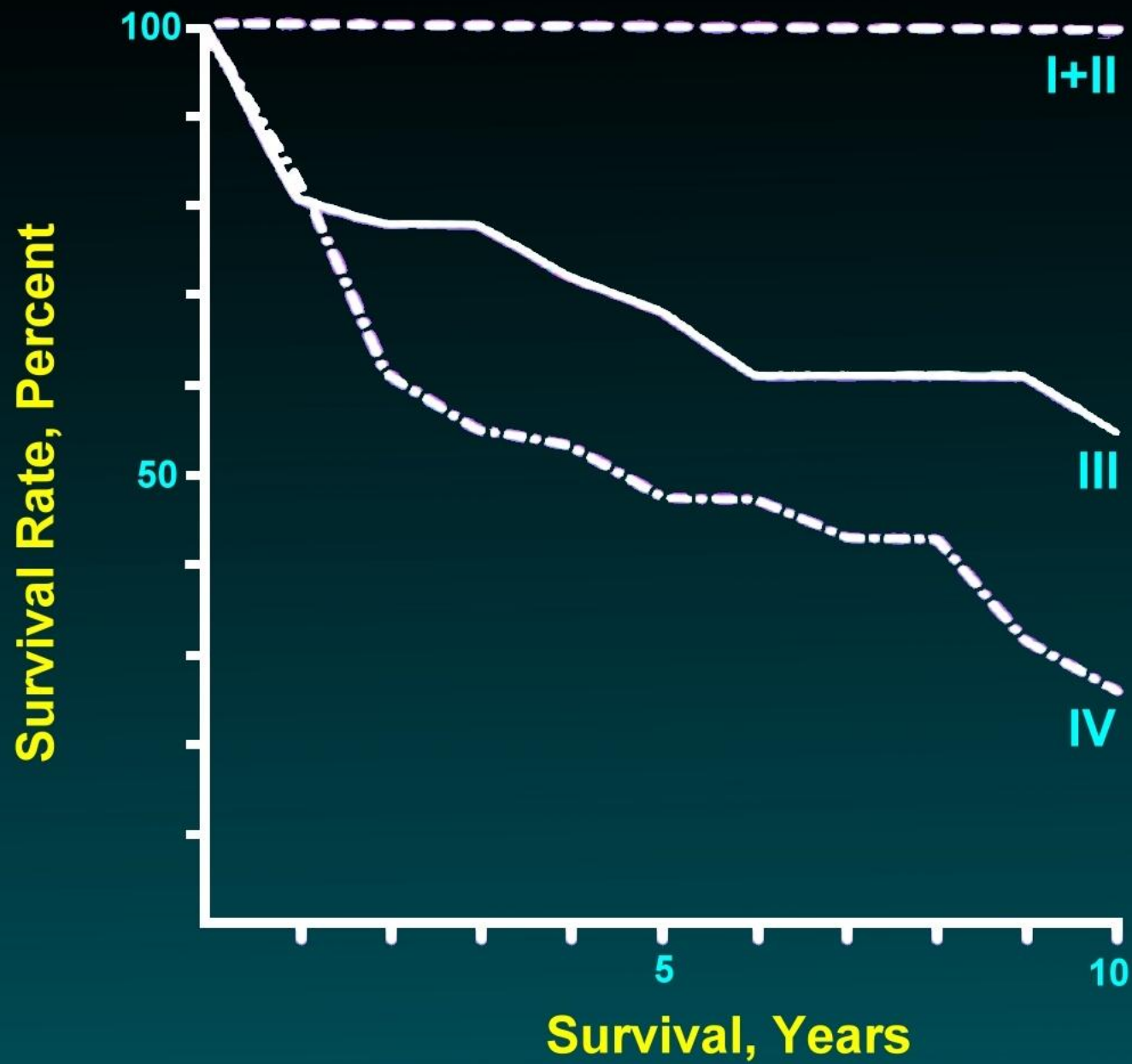
Malignant schwannoma

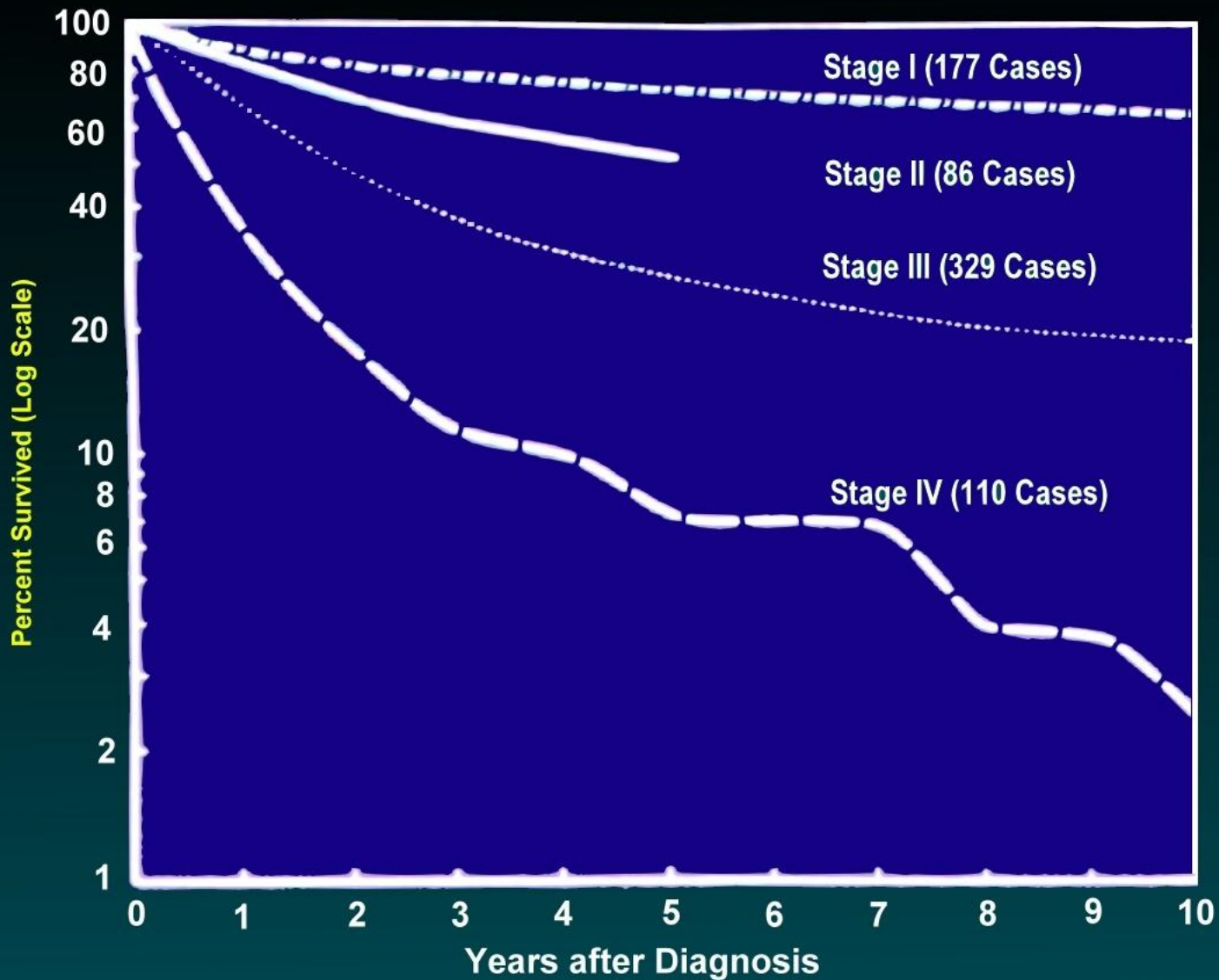
Neuroblastoma

Paraganglionoma

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American Joint Committee Staging System.  
Survival curves of 702 soft tissue sarcomas. stages I to IV.

# Soft Tissue Tumor

## *Clinical Evaluation*

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- ❖ Physical examination
  - ❖ Plain X-ray
  - ❖ CT scan
  - ❖ MRI
  - ❖ Bone scan
  - ❖ Angiogram
  - ❖ Others
-

# Soft Tissue Tumor

## *Physical Examination*

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**Extend of local spread =  
presence of metastasis**

- ❖ **Size**
  - ❖ **Fixation to structures**
  - ❖ **Relationship to biopsy site**
  - ❖ **Lymph node involvement**
  - ❖ **Functional status of involved part**
  - ❖ **Confound anatomical structures  
compromise optimal surgical or radiation  
therapy**
-

# Enneking Staging System

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- ❖ Surgical rather than histological
- ❖ Emphasis on compartmentalization in the extremities



# Margin In Anatomical Compartments

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**Exception**

**Groin, Knee, Ankle**

**Popliteal space**



91 7 1



# Soft Tissue Tumor

## *Physical Examination*

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***Not Reliable***

**In benign and malignant  
(except unchanged mass for years)**

**→ Biopsied tissue and histological  
evaluation**

# Lymph Node Metastasis

◎ **5% incidence**

- ❖ 20% epithelioid sarcoma
- ❖ 17% synovial sarcoma
- ❖ 12% rhabdomyosarcoma
- ❖ Clear cell sarcoma

- Poor prognosis
- Rare long-term survivor

*Surgery 1978 Weingrad and Rosenberg*

# Metastasis of Soft Tissue Sarcoma

- ❖ 5% to 10% in all cases
- ❖ Depend on the site of lesions
- ❖ 107/307 (35%) local recurrence or distant metastasis
- ❖ 52% in lunge (extremity 70%)
- ❖ Retroperitoneal through abdomen
- ❖ Truncal sarcoma > extremity sarcoma

## Actuarial distant control rates at 5 years among 141 pts with G2-3 extremity sarcoma with control of primary lesion after treatment by RT and surgery

Tumor Size (mm)	No. Patients	Acturial 5-year distant control
< 25	16	0.92
26-50	42	0.76
51-100	47	0.67
101-150	17	0.42
>150	19	0.26
<b>Total</b>	<b>141</b>	<b>0.64</b>

Rosenberg, Suit, Baker 1985

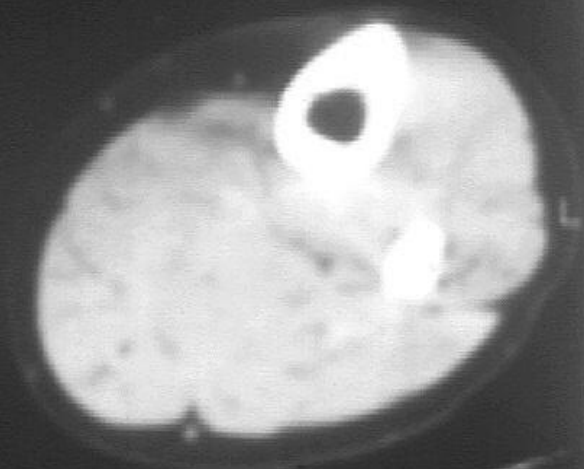
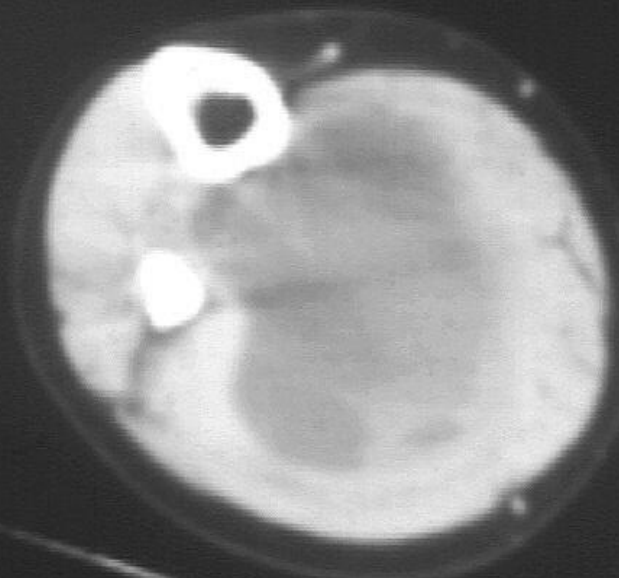
# Natural History

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- ❖ Local recurrence
- ❖ Distant metastasis







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RUN 41  
RT

CGMH LINCOLN  
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LAT  
TIBIA



W 384  
L -42



# Site of Soft Tissue Sarcoma

- ❖ Resectability of a lesion
- ❖ Potential for local control
  
- Head and neck – vital structures
- Simon and Enneking JBJS 1976
  - Local recurrence following surgery
    - Buttock – 38%      Groin – 14%
    - Thigh – 15%      B-K – 0%

# Biopsy

- ❖ Fine-needle aspiration
  - ❖ Needle biopsy
  - ❖ Excisional biopsy (<3 cm)
  - ❖ Incisional biopsy (>3 cm)
- 
- Frozen section
  - Lymph node

# Surgery

*no additional adjuvant therapy*

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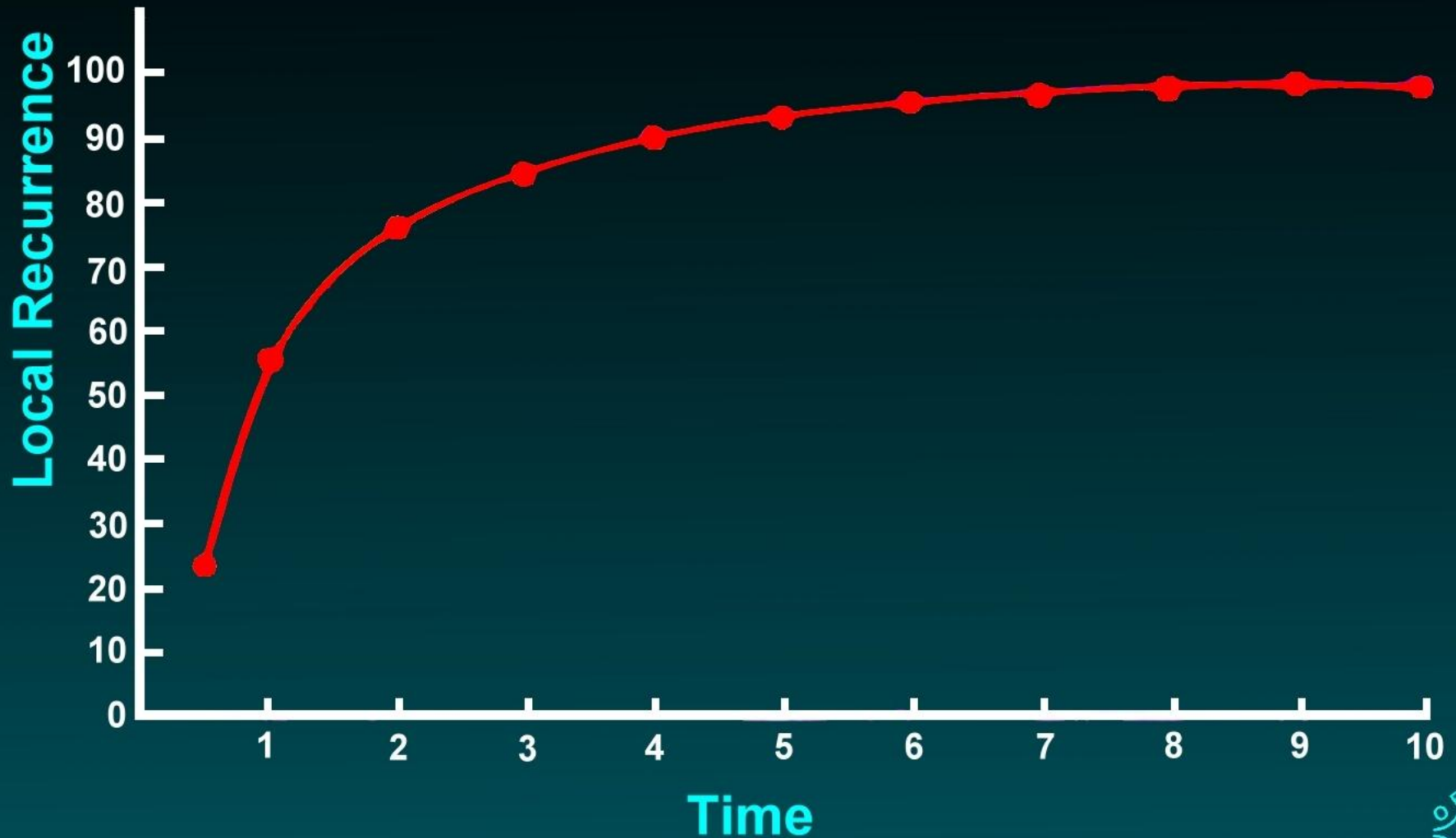
- ❖ **More** radical surgical procedures
- ❖ **Lower** local failure rate

## Local failure rates in patients with high-grade extremity sarcomas treated by surgery and postoperative radiation

Center	No. patients	Follow-up (years)	Local failure +distant metastases
MGH	72	1-18	12
NCI	128	1-7	10
M.D. Anderson	229	4-22	51
<b>Total</b>	<b>429</b>		<b>73 (17%)</b>



## % Local Recurrences (of those who will recur) VS Time Following Curative Surgery





## Preoperative radiation followed by surgery in patients with extremity soft tissue sarcomas

Treatment	n	Local Recurrence (%)	Disease-free Survival (%)	Satisfactory function (%)
RT/limb salvage	19	1(5)	11(58)	12(63)
Limb salvage	19	7(37)*	7(37)	13(68)
Amputation	16	2(13)	11(69)	2(13)

\*  $p < 0.05$  compared with RT/limb salvage group; not significantly different from amputation group.

From Enneking, W.F., and McAuliffe, J.A.: Adjunctive preoperative radiation therapy in treatment of soft tissue sarcomas: a preliminary report. *Cancer Treat. Symp.* 3:37-42, 1985

## Surgical procedures for soft tissue extremity sarcomas

Margin	How margin achieved		Plane of dissection	Microscopic appearance
	Limb-salvage	Amputation		
Intracapsular	Intracapsular piecemeal excision	Intracapsular amputation	Within lesion	Tumor at margin
Marginal	Marginal en-bloc excision	Marginal amputation	Within reactive zone-extracapsular	Reactive tissue ± microsatellites tumor
Wide	Wide en-bloc excision	Wide through bone amputation	Beyond reactive zone through normal tissue within compartment	Normal tissue ± “skip lesions”
Radical	Radical en-bloc resection	Radical exarticulation	Normal tissue extracompartmental	Normal tissue

Adapted from Enneking, W.F.:

Staging of musculoskeletal neoplasms. In Current concepts of diagnosis and treatment of bone and soft tissue tumors. Heikberg 1984 Springer-Verlag

## Local control of soft tissue sarcomas of the extremities by radical surgery

	Simon and Enneking	Shiu et al
<b>Total no. patients</b>	<b>54</b>	<b>297</b>
<b>Radical local resection</b>	<b>25(46%)</b>	<b>158(53%)</b>
<b>Amputation</b>	<b>29(54%)</b>	<b>139(47%)</b>
<b>Local control</b>		
<b>Radical local resection</b>	<b>88%</b>	<b>72%</b>
<b>Amputation</b>	<b>79%</b>	<b>93%</b>
<b>Overall</b>	<b>83%</b>	<b>82%</b>

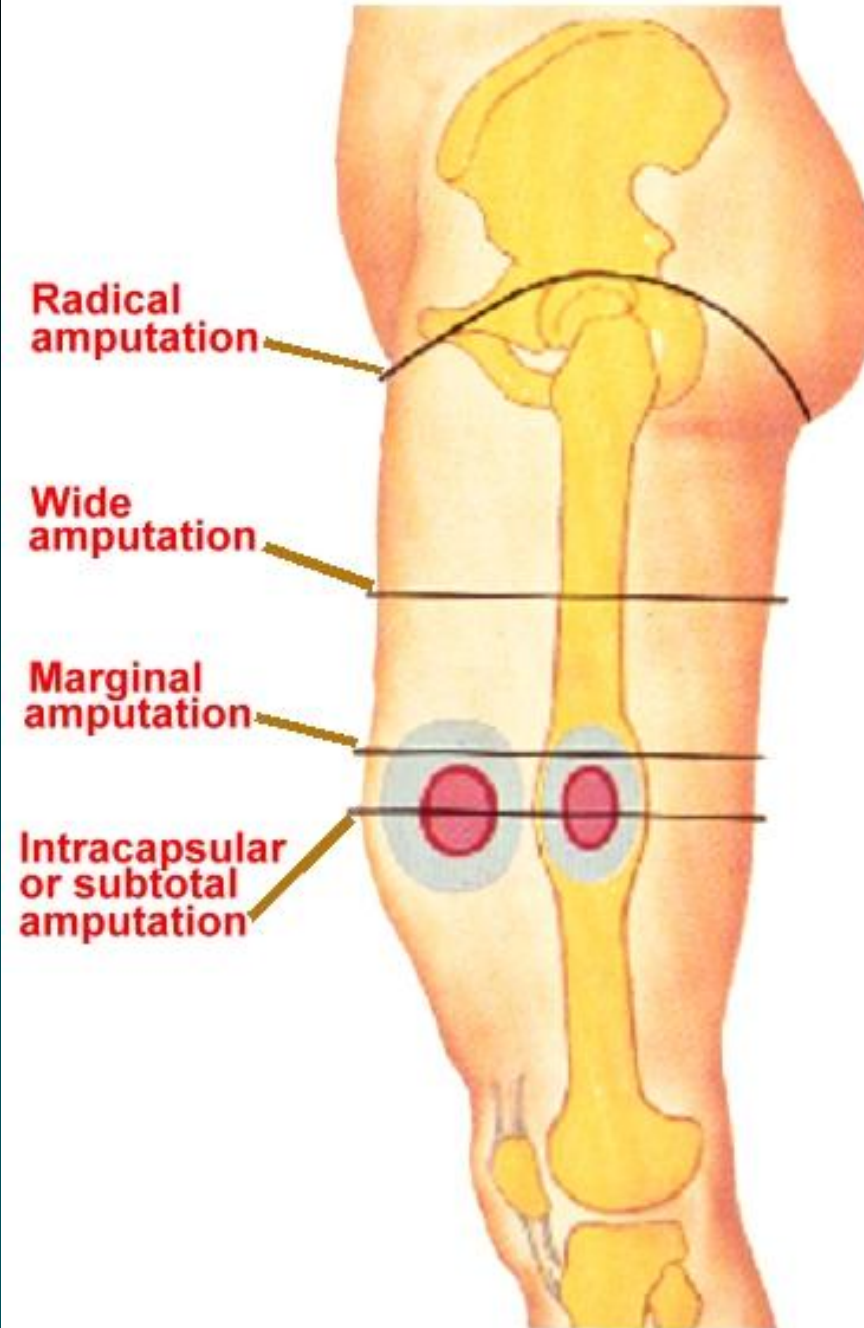
From Rosenberg SA, Suit HD, and Baker LH: Sarcomas of the soft tissue. In DeVita VT, Hellman S and Rosenberg SA (editors). Cancer: principles and practice of oncology, et. 2, Philadelphia, 1985, JB Lippincott Co.

## Adequacy of margins of radical surgery related to local failure rate

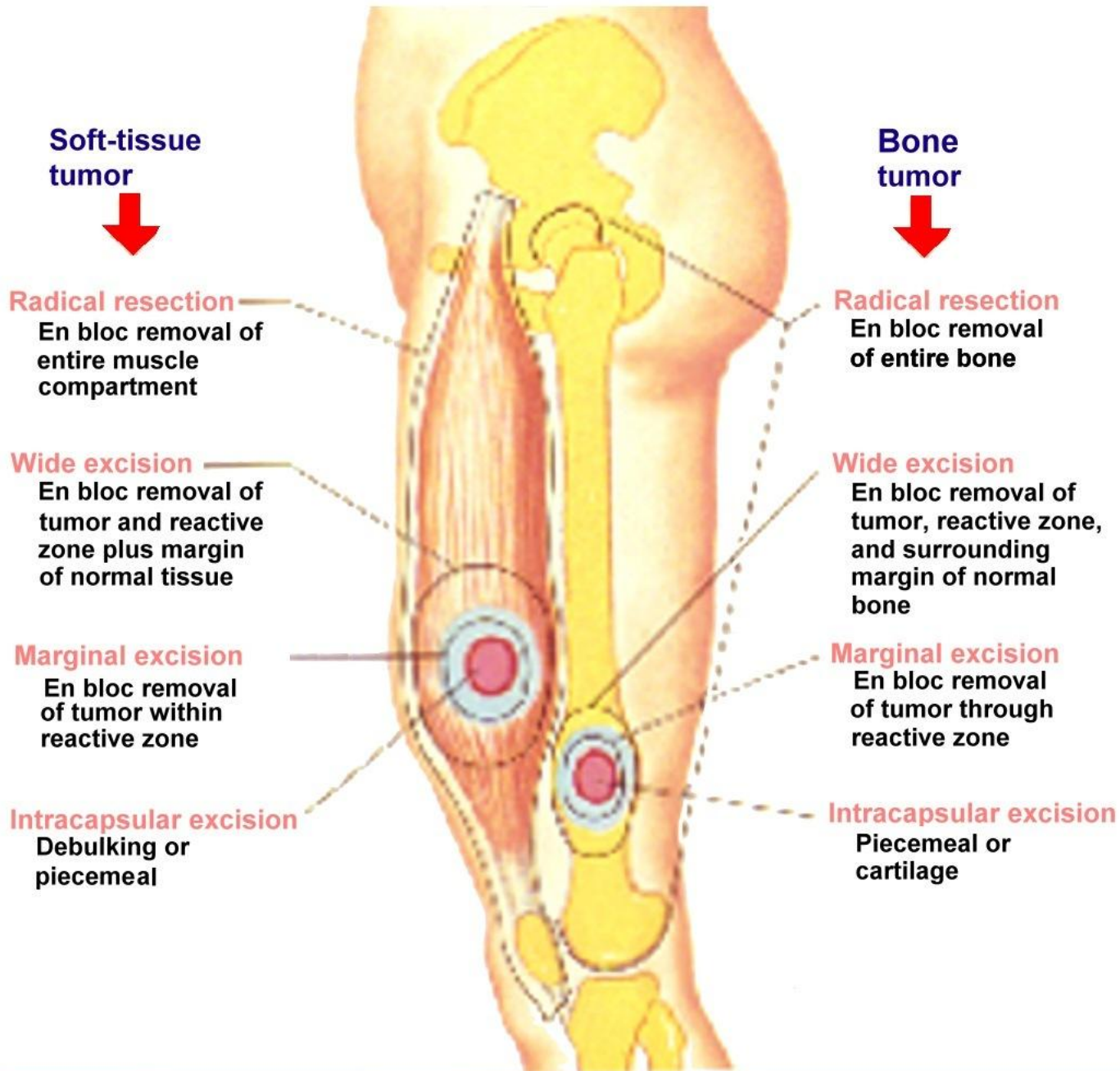
Series	Negative margins	Positive margins
	NO. local failures/total failures	
Simon and Enneking	1/46	8/8
Markhede et al	5/76	16/19
Total	6/122 (5%)	24/27 (89%)

From Rosenberg SA, Suit HD and Baker LH:  
 Sarcomas of the soft tissue. In DeVita VT, Hellman S, and Rosenberg SA (editors): Cancer: principles and practice of oncology, ed. 2, Philadelphia, 1985, JB Lippincott Co

# Amputations



## Limb-salvage procedures



# Extremity Surgical Therapy

## ❖ Intracapsular excision

- – Tumor at margin

## ❖ Marginal excision

- – Reactive tissue  $\pm$  microsatellites tumor

## ❖ Wide excision

- – Normal tissue  $\pm$  skip lesions

## ❖ Radical excision

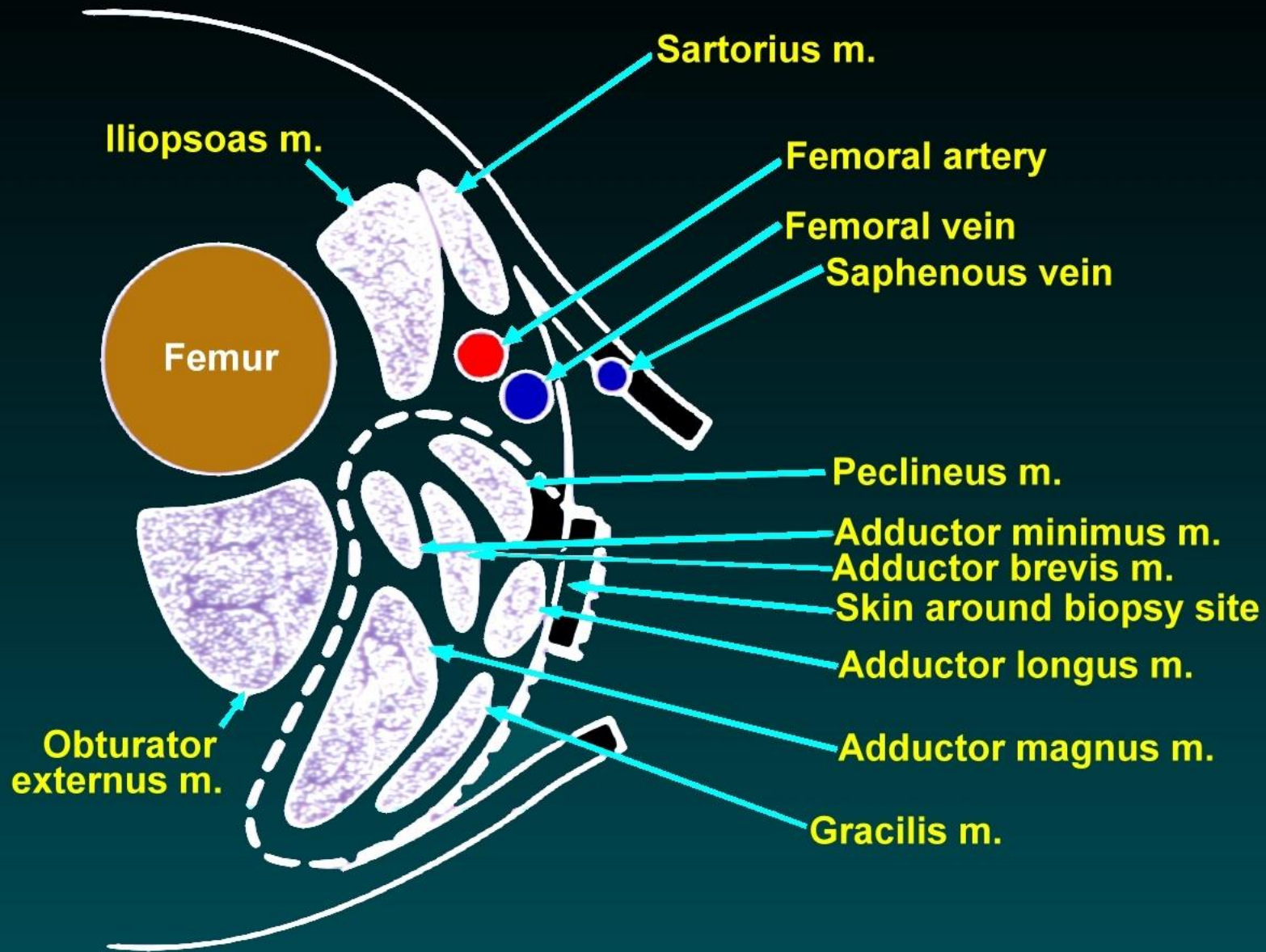
- – Normal tissue

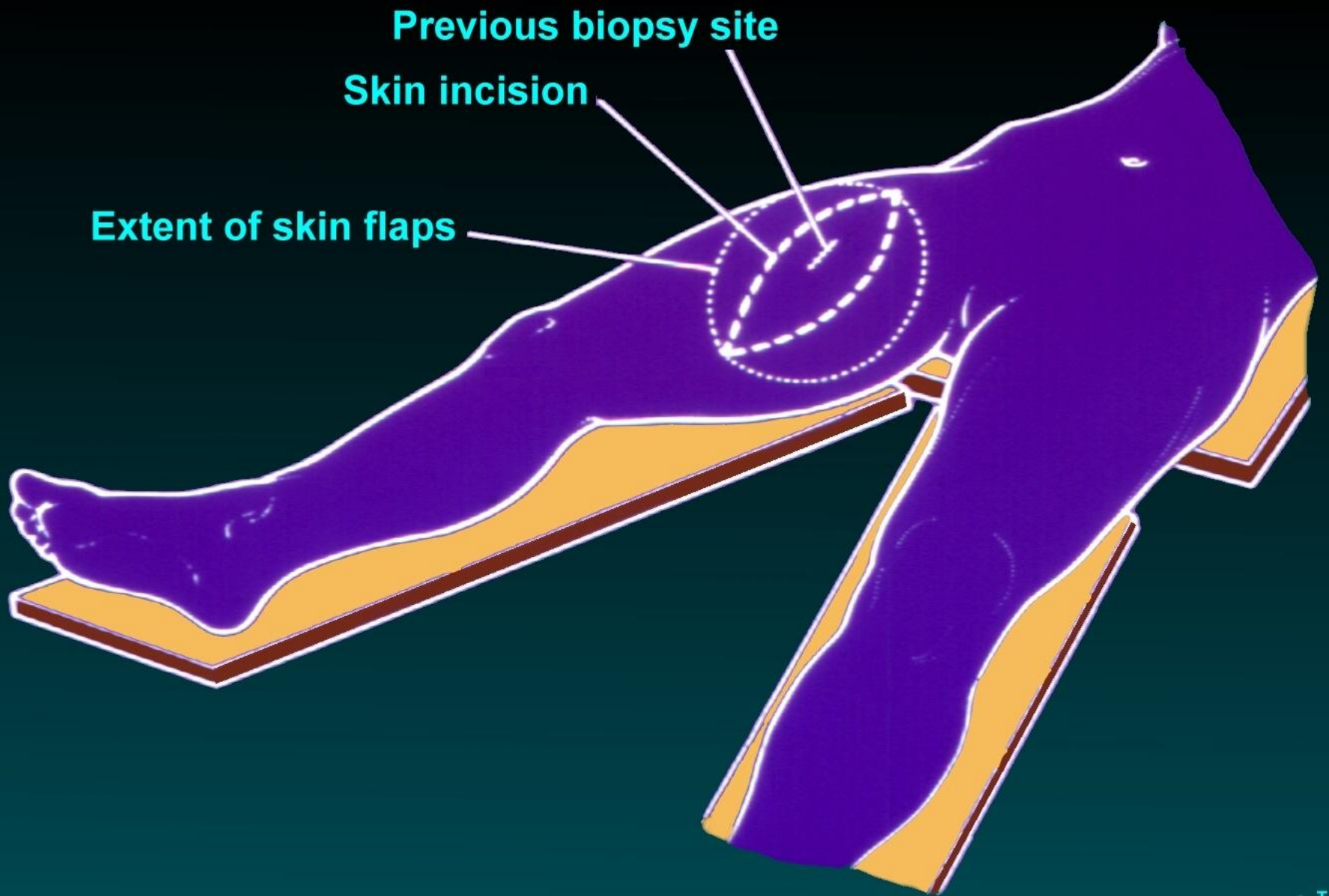
# Limb-sparing Procedures

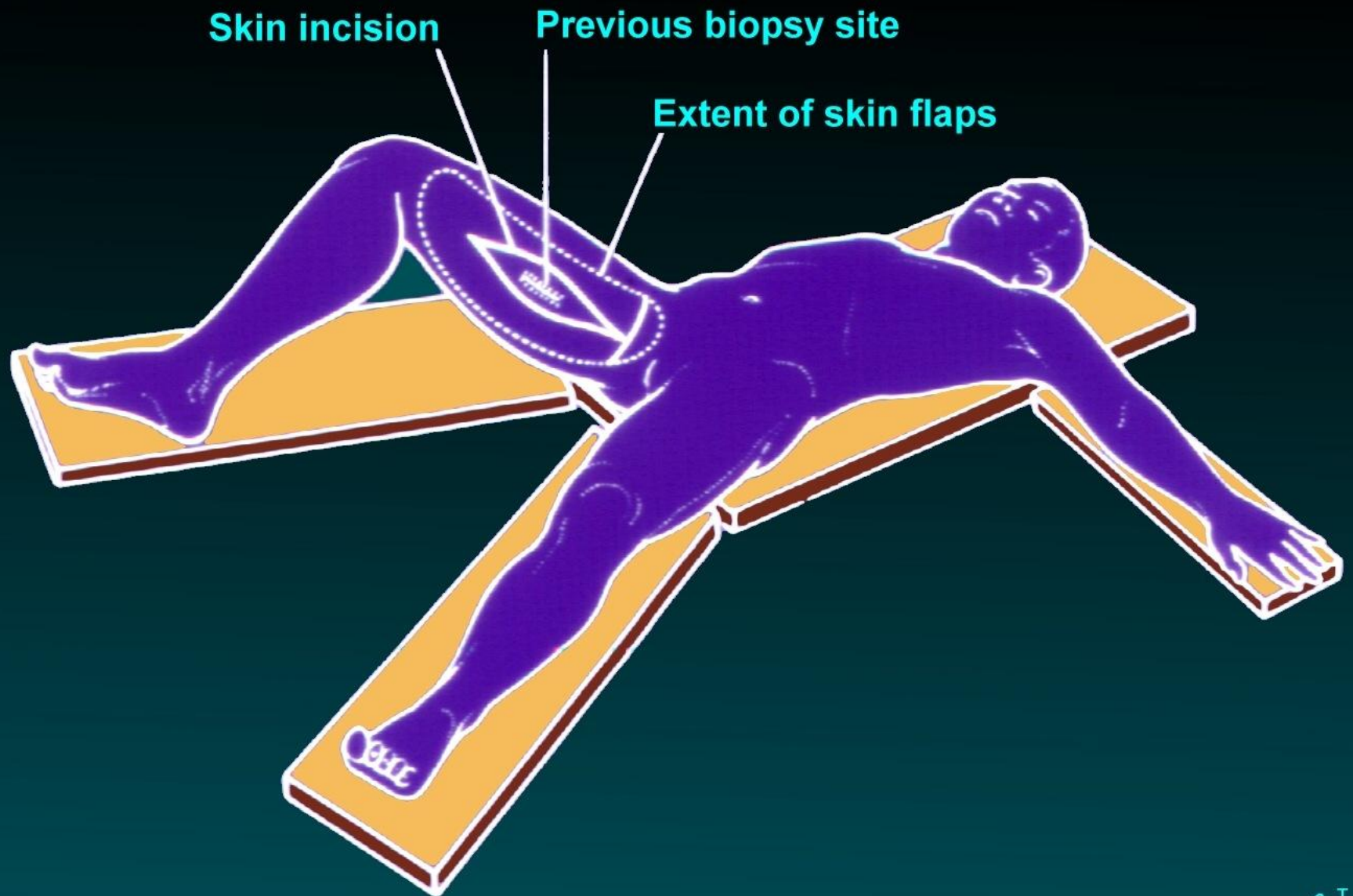
## *Wide local excision*

- ❖ Most common procedure  
+ post-op RT
- ❖ Several cm away from tumor  
(+ skin, scar, closed tumor)
- ❖ Lymph node dissection
- ❖ Mark the margin



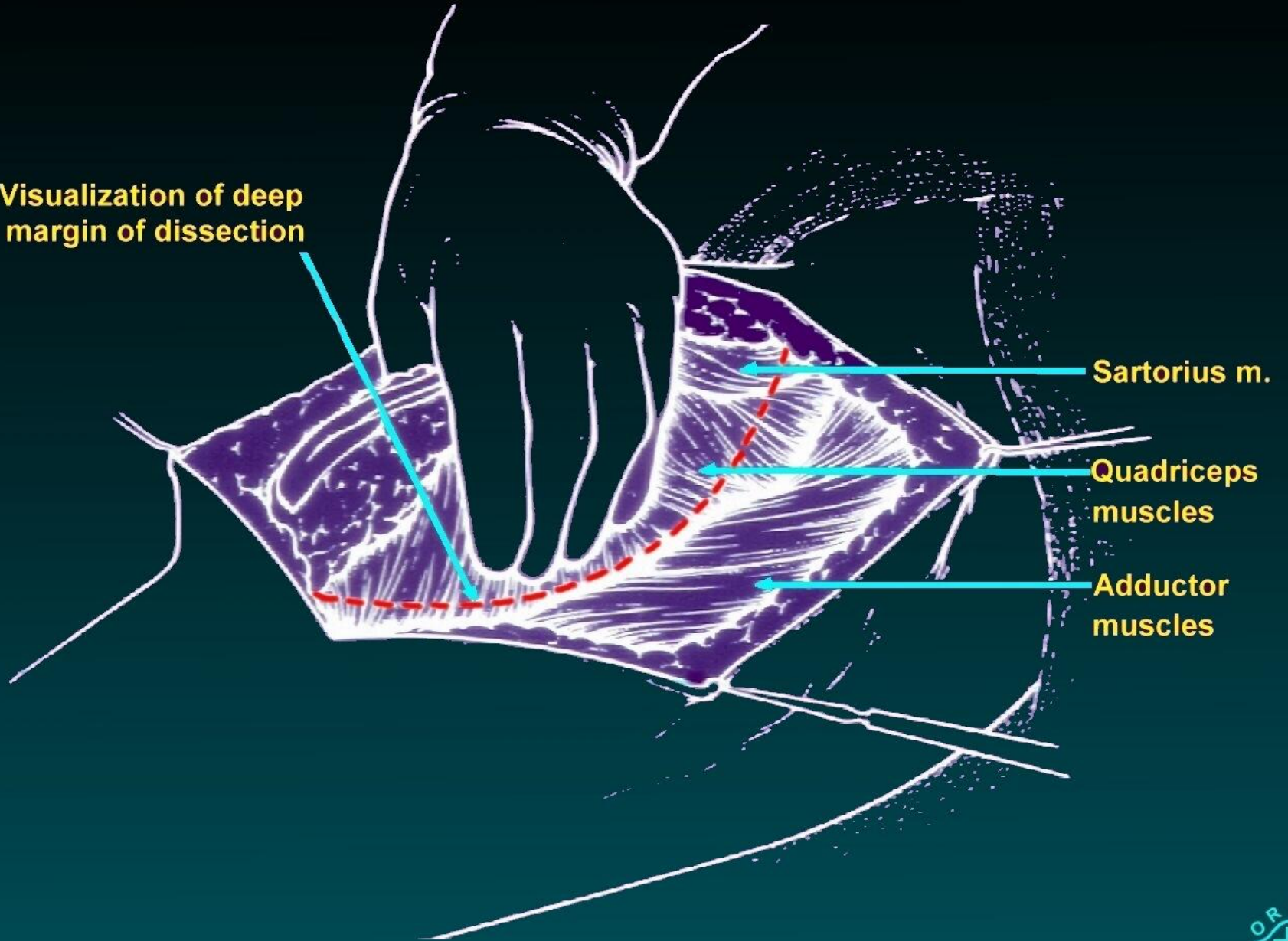








**Visualization of deep margin of dissection**

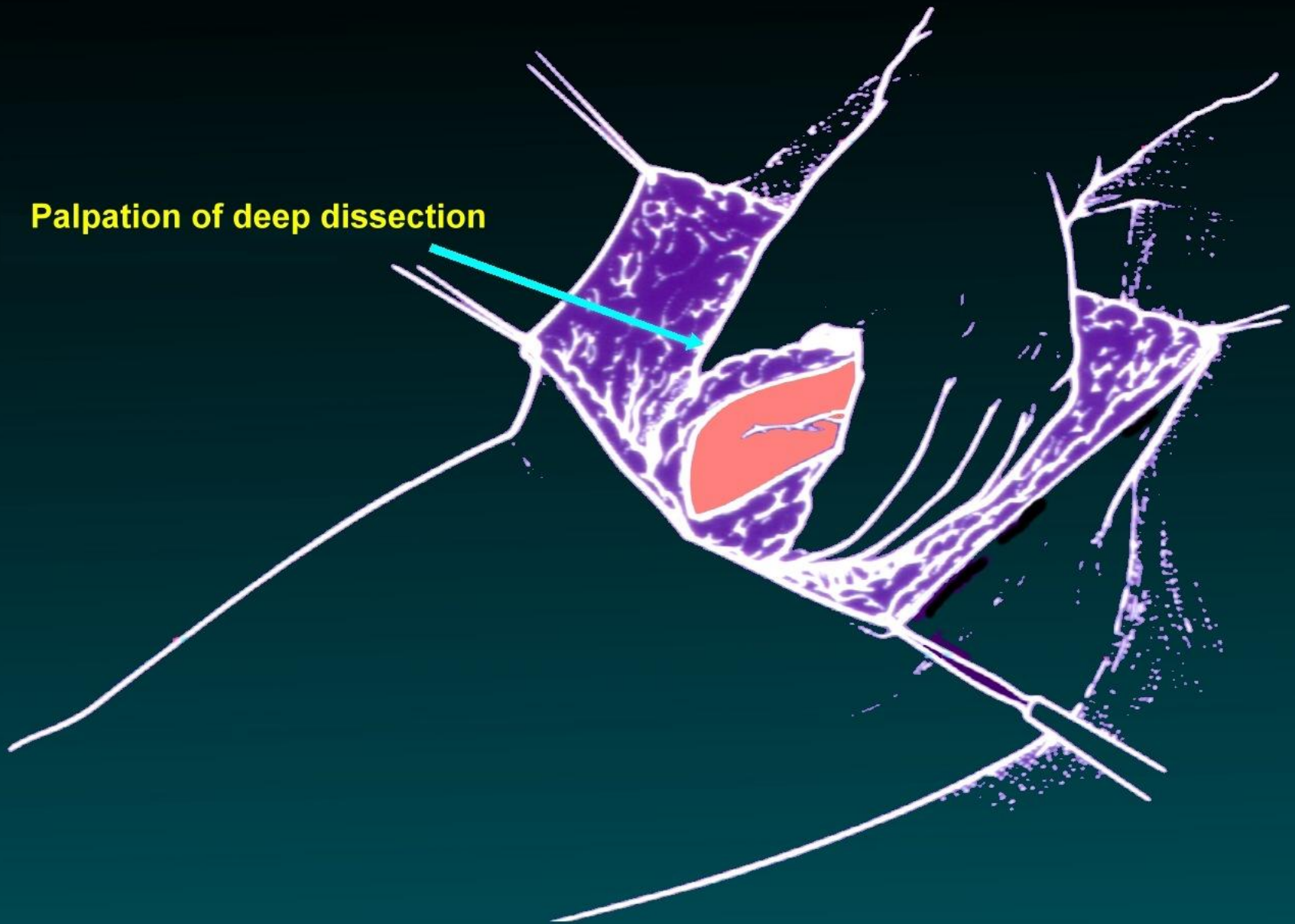


**Sartorius m.**

**Quadriceps muscles**

**Adductor muscles**

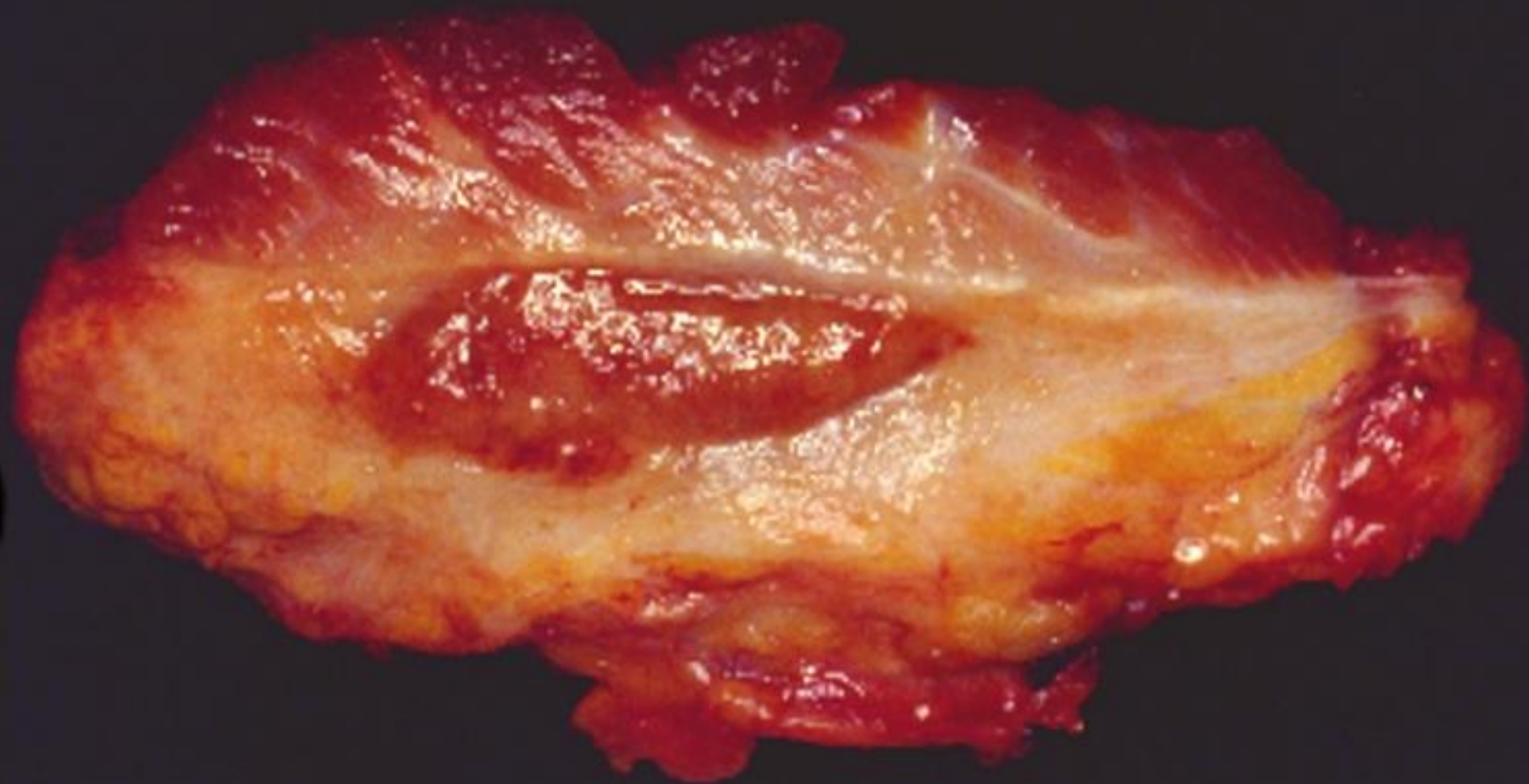
**Palpation of deep dissection**



**Suction Drain**







1 2 3 4 5 6 7 8 9 10 11

# Radiation Therapy

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- ❖ Potent treatment modality
- ❖ Not surgical candidates
- ❖ Reduce the morbidity of surgery
- ❖ Reduce the dosage of radiation in combination treatment



# Pre-operative Radiation

## *Advantage*

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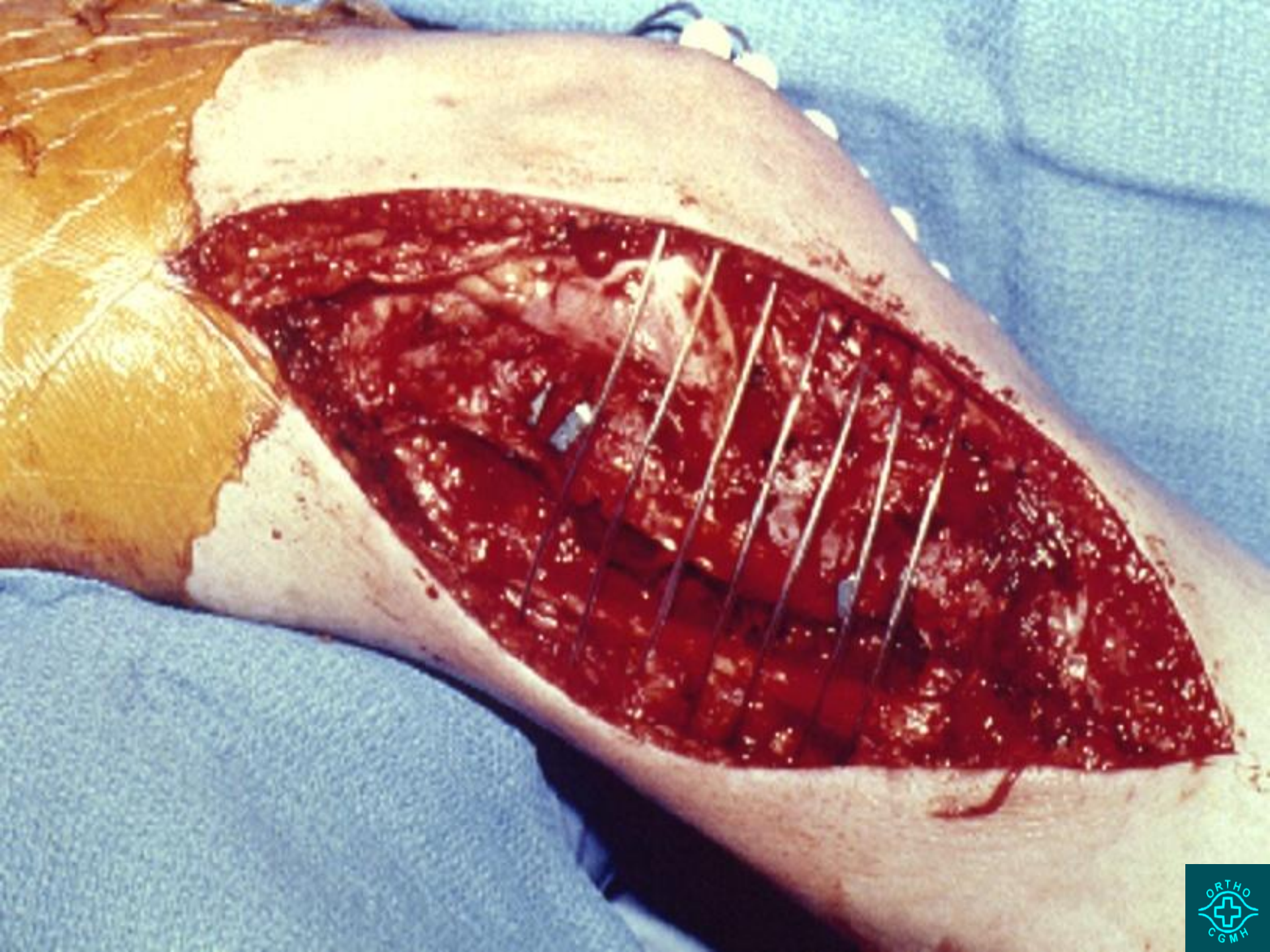
- ❖ Restricted volume
- ❖ Lesser surgical resection
- ❖ Reduce the seeding

# Intraoperative Radiotherapy

*Shiu MSKH 1984*

*Iridium – 192 implants*

- ❖ Little experience
- ❖ Localized delivery of radiation
- ❖ Delivery during post-op hospital stay





# Radiation Therapy Alone

## *Result*

### ❖ MSKH (McNeer 1968)

- 15/25 > 5 yrs free disease

### ❖ MGH 65 Gy

- 61% > 4yrs local control

### ❖ NCI (Kinsella and Glatstein)

- 22/29 local control
- 6/29 disease free

# **Surgery** *Local Failure*

- ❖ **Before 1950s – local excision**  
**60-80% (90%)**
- ❖ **Wide excision 30%-50%**
- ❖ **Radical excision 20%**

# Surgery + Post-op RT

- ❖ No delay in surgery  
(psychological advantage)
- ❖ Fewer radiation – induced complication
- ❖ Grading the specimen
- ❖ Exact tumor defined



# Adjuvant Chemotherapy

## ⊙ Controversial

### ❖ Advantage

- ❑ MSKCC 85% to 90% (+)
- ❑ NCI (1975-1981) 84% to 60% (-)
- ❑ Gherlinzoni (1986) 79% to 54% (-)

### ❖ Negative

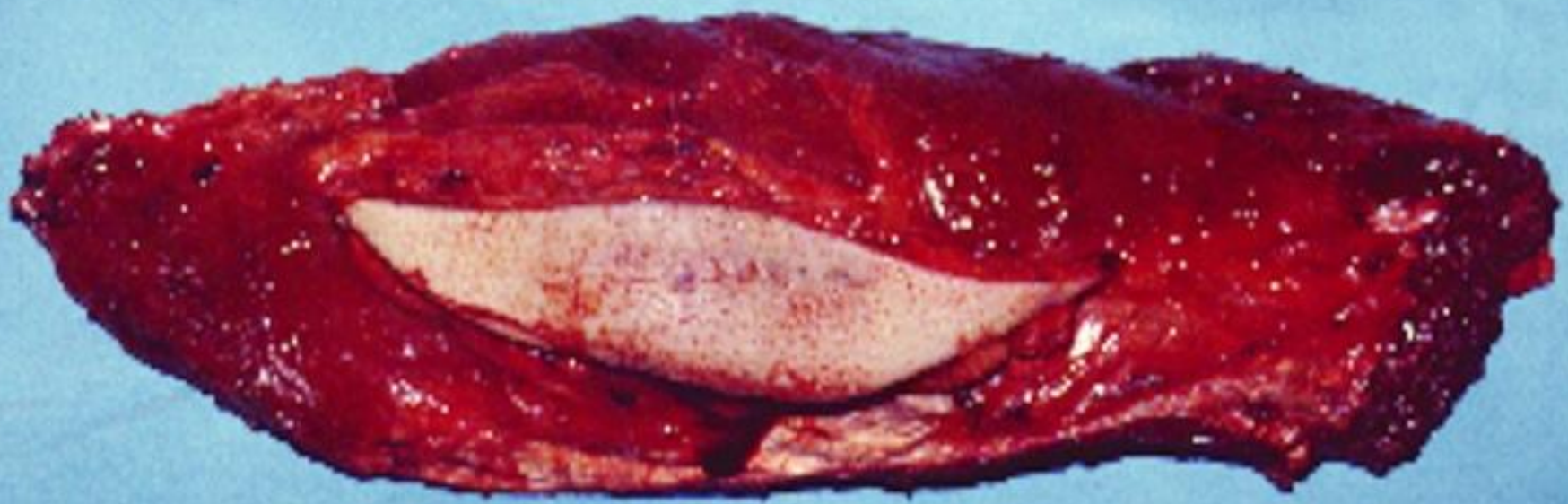
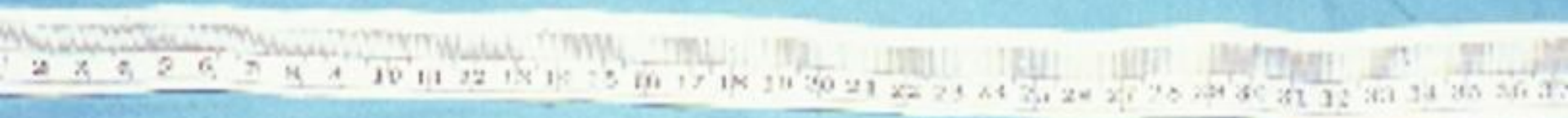
- ❑ Mayo Clinic (1984) Dr. Edmonson
- ❑ Antman and Bramwell (1985)

















## **Local Control and Radical Margin** *(No additional adjuvant therapy)*

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- ❖ **Proximal thigh and groin**
  - **Easy failure**
- ❖ **Radical amputation for leg and foot tumor – 100%**

**NCI and MSK cancer center 1975, 1985**

## Five-year actuarial local control and survival results after preoperative radiation therapy of extremity soft tissue sarcomas (Massachusetts General Hospital experience)

Stage*	No patients	5-year results local control	Disease-free survival
IA	5	1.00	1.00
IB	13	1.00	1.00
IIA	19	0.79	0.81
IIB	17	0.74	0.59
IIIA	13	1.00	0.83
IIIB	20	0.72	0.48
IIIC-IVA	3	0.75	1.00
Total	90	0.83	0.74

\*AJC staging classification

From Suit HD, Mankin HJ, Schiller AL, et al: Results of treatment of sarcoma of soft tissue by radiation and surgery at Massachusetts General Hospital, cancer Treat, Symp. 3:43-47, 1985

# Modification of Radiotherapy

© *Eilber et al UCLA 1985*

- ❖ Initial IA doxorubicin (30 mg/day x 3)
- ❖ RT 3.5 Gy fractions x 10 days
- ❖ 1-2 wks interval
- ❖ Wide or marginal excision



# Modification of Radiotherapy

© *Eilber et al UCLA 1985*

## ⊕ **Result**

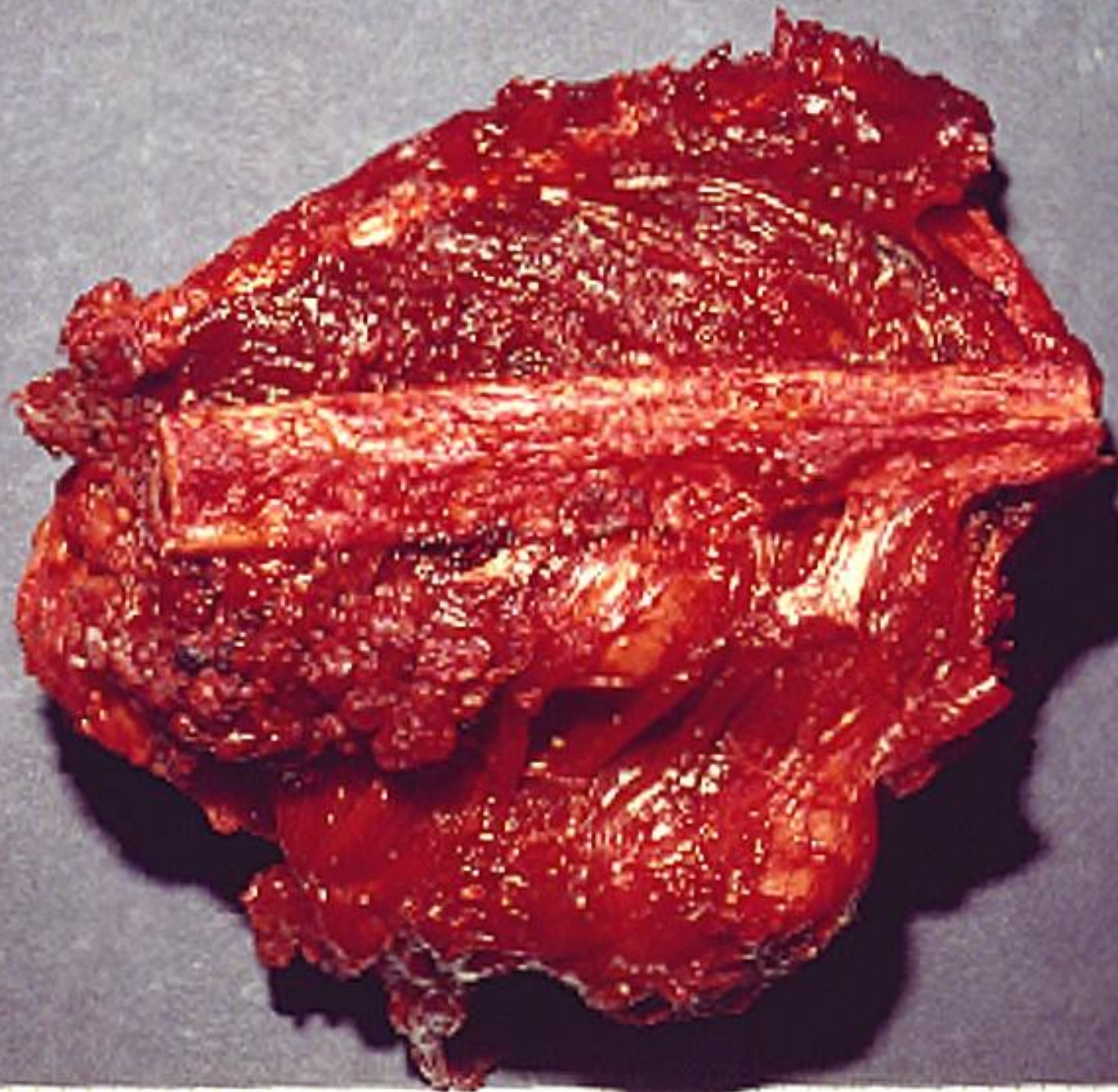
- ❖ 3/77 (4%) initial amputation
- ❖ 3/77 (4%) local recurrence
- ❖ 64% disease free > 5 yrs
- ❖ 35% complication rate in 13/77 (17%)
  - 17.5 Gy pre-op RT
  - 25% complication rate
  - 8% local recurrence



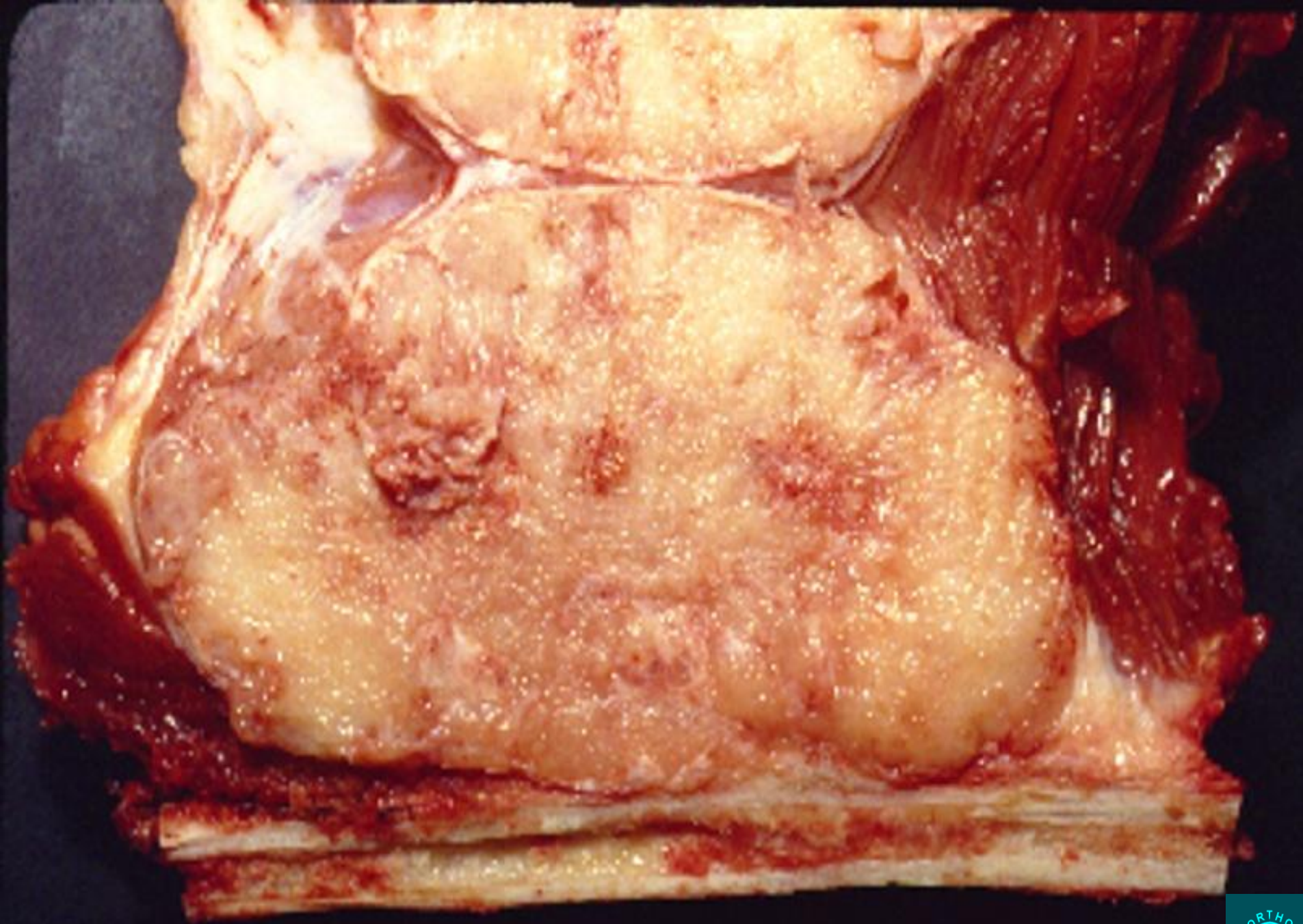




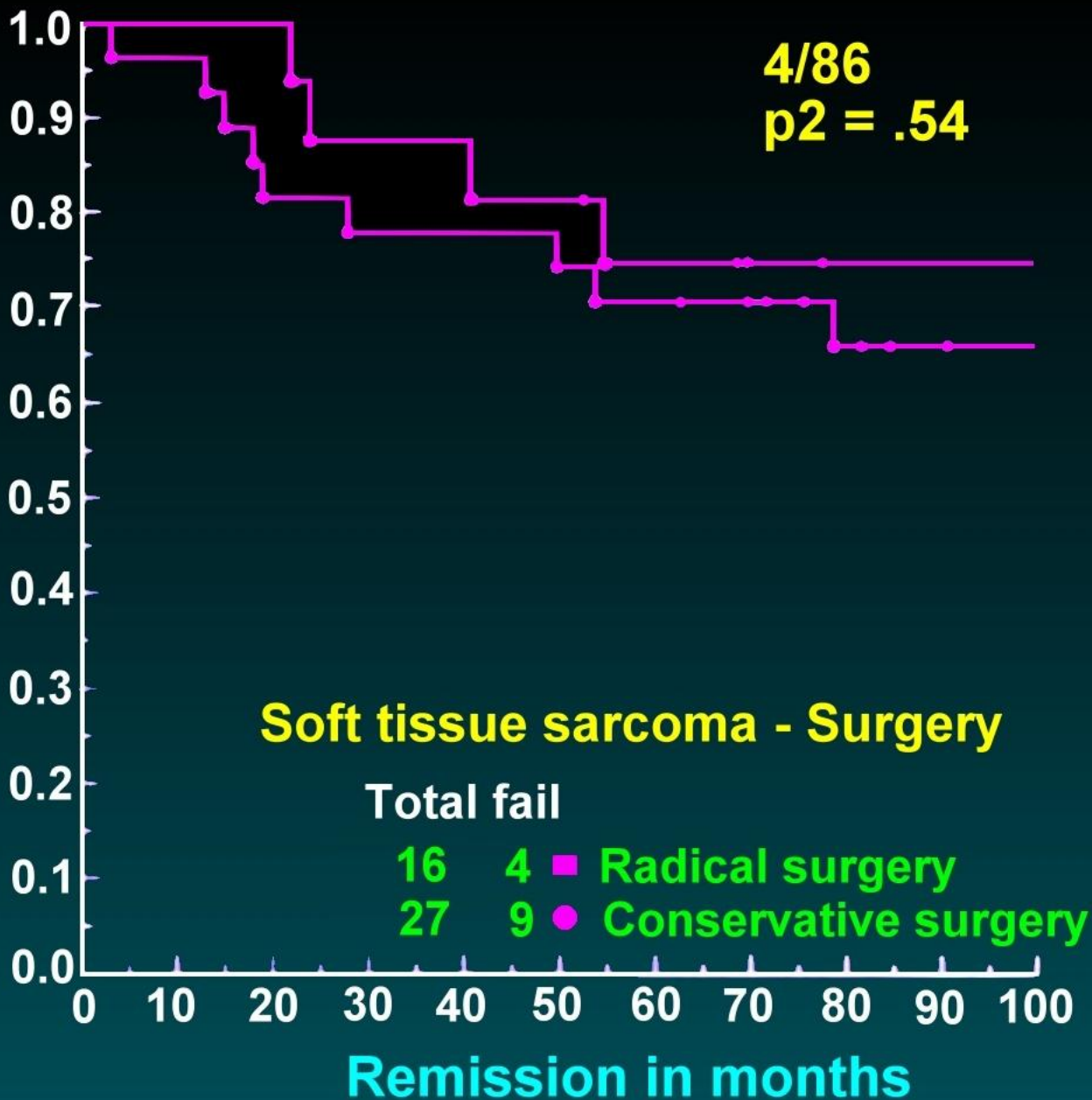






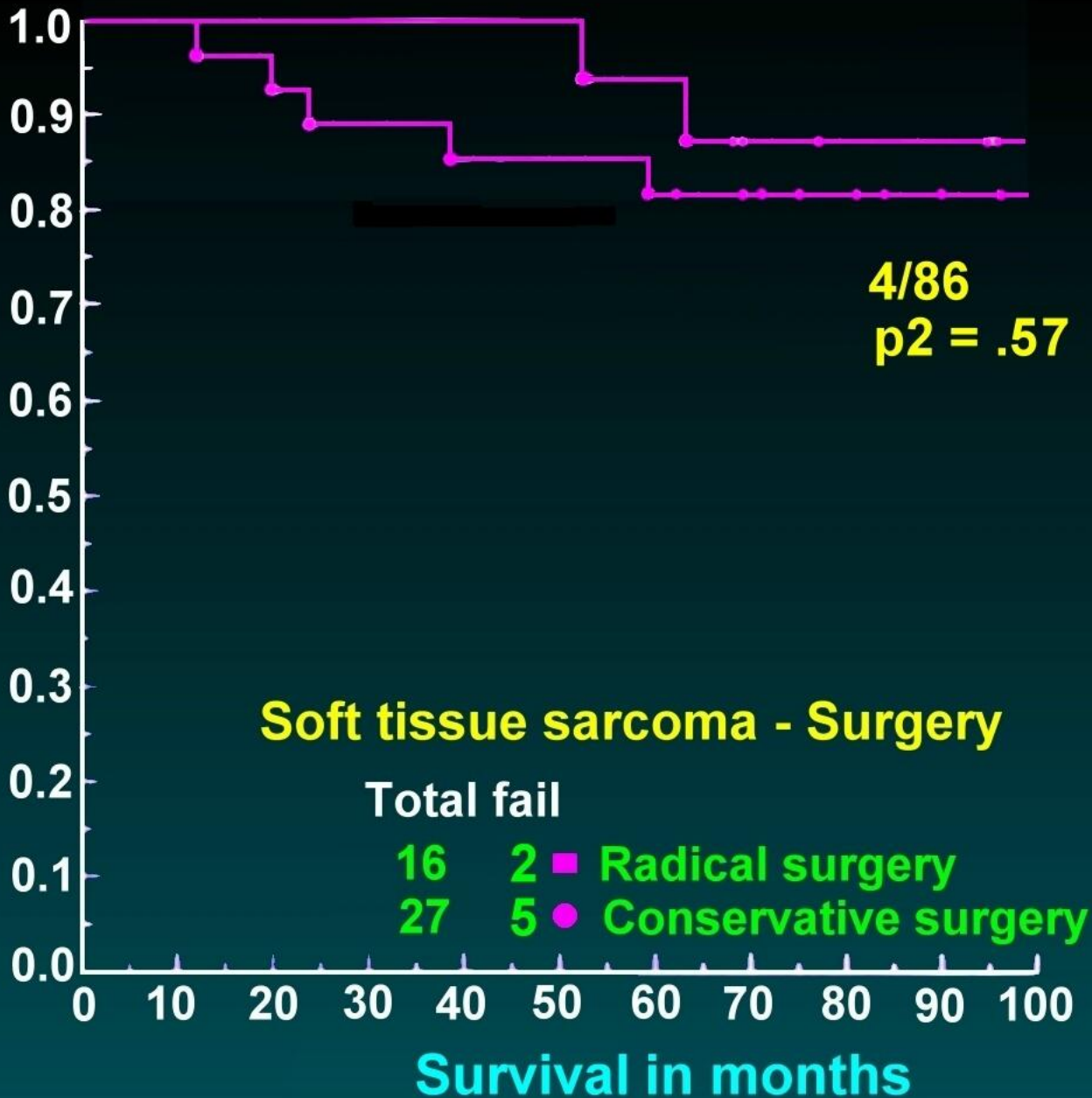


Proportion in remission



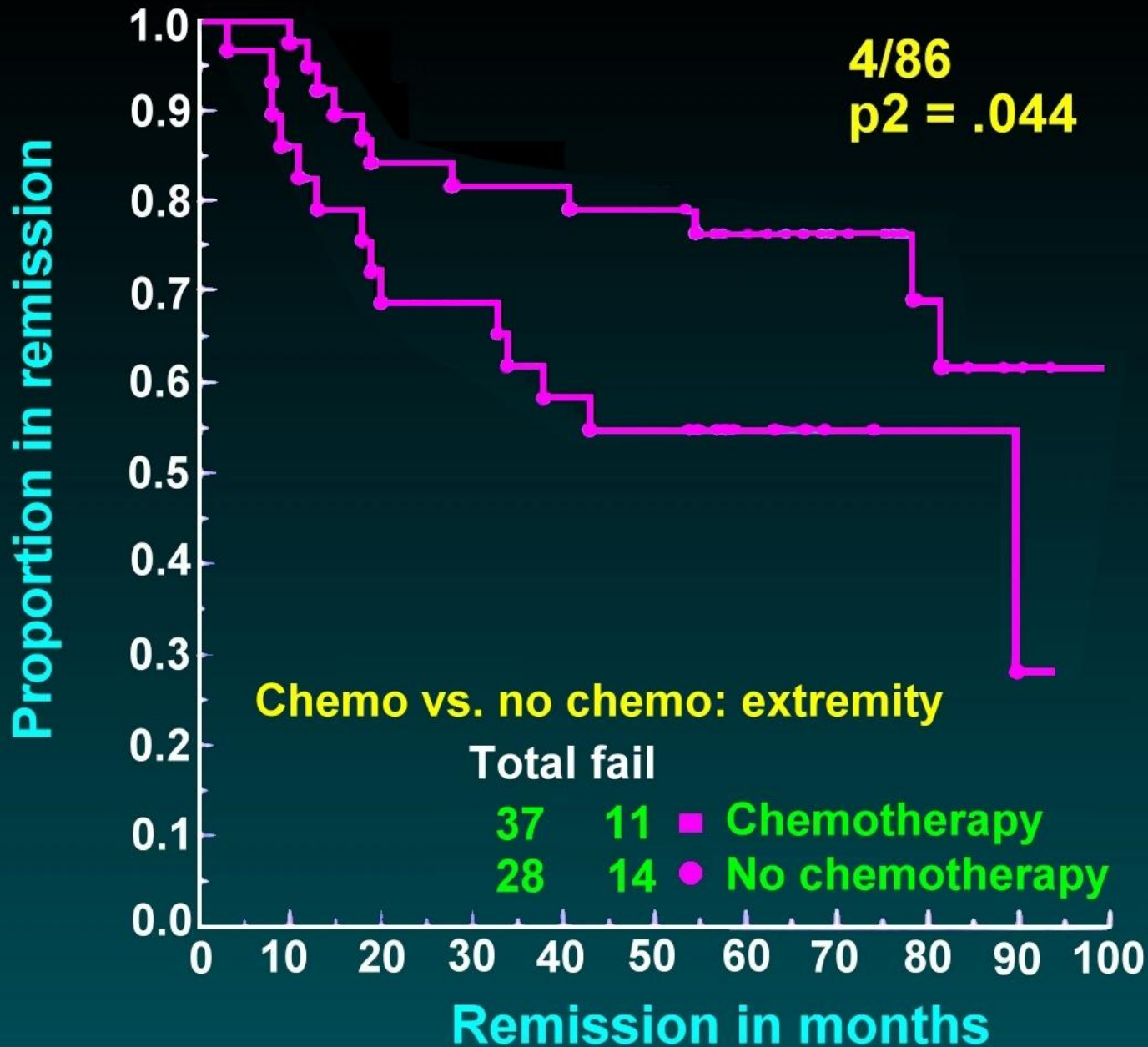


Proportion Surviving

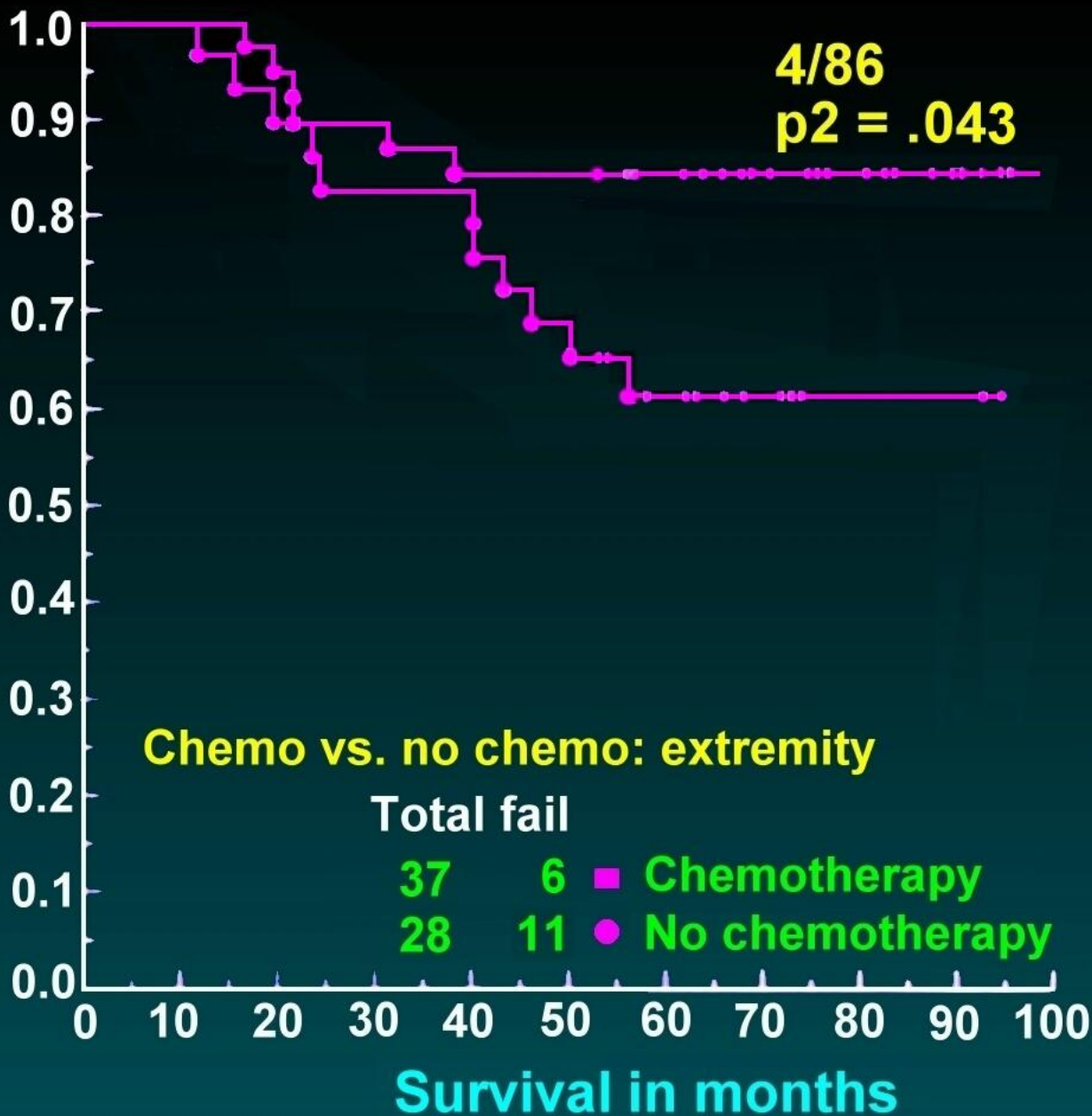


# Adjuvant Chemotherapy

- ❖ Doxorubicin 25%  
(2.5% complete + 22.5% partial)
  - ❖ Dimethyltriazenoimidazole (DTIC)  
15% (in 109 patients)
  - ❖ Combination 32%
- Current standard choice  
*Doxorubicin-based combination*



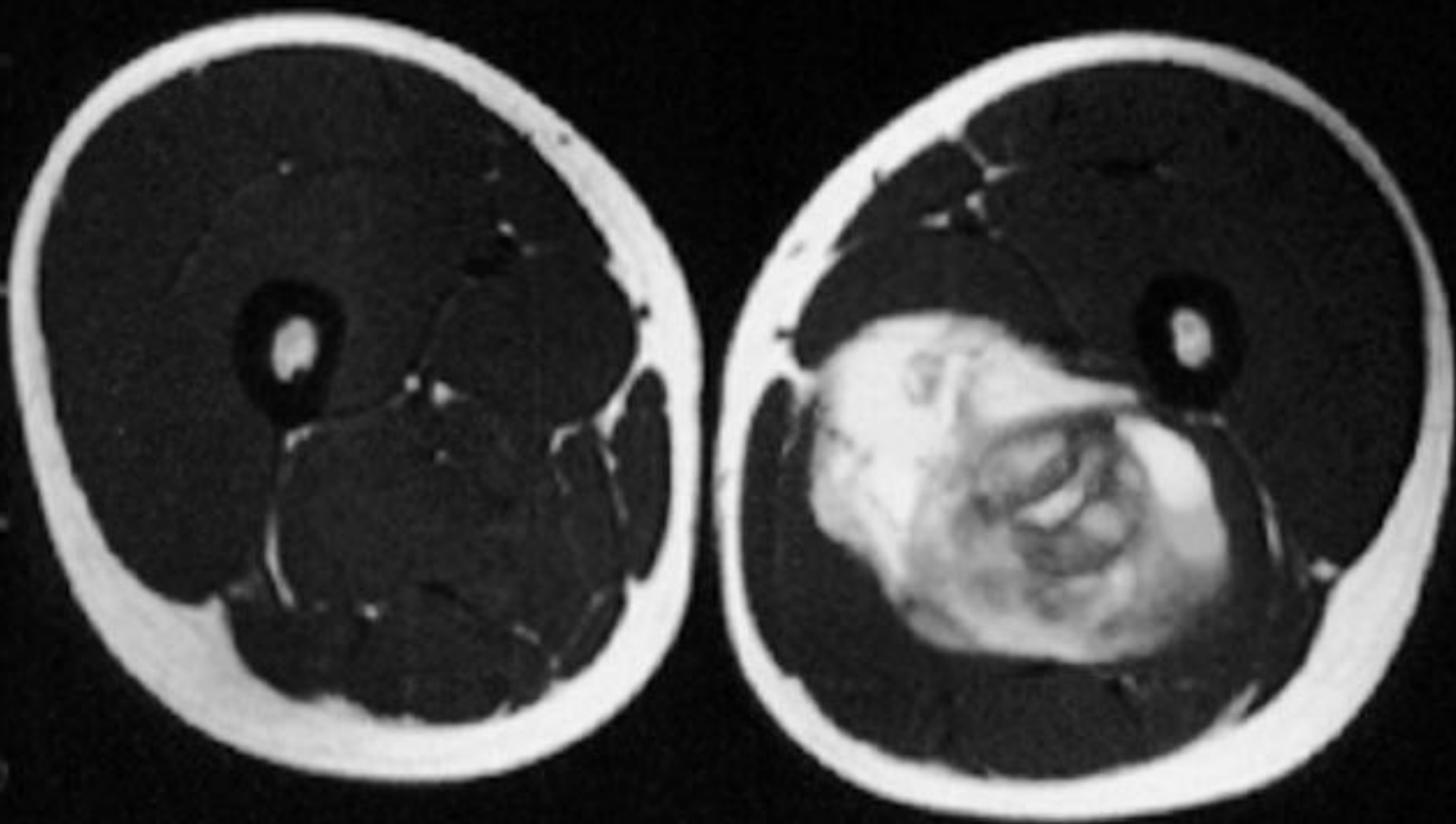
Proportion Surviving







2775



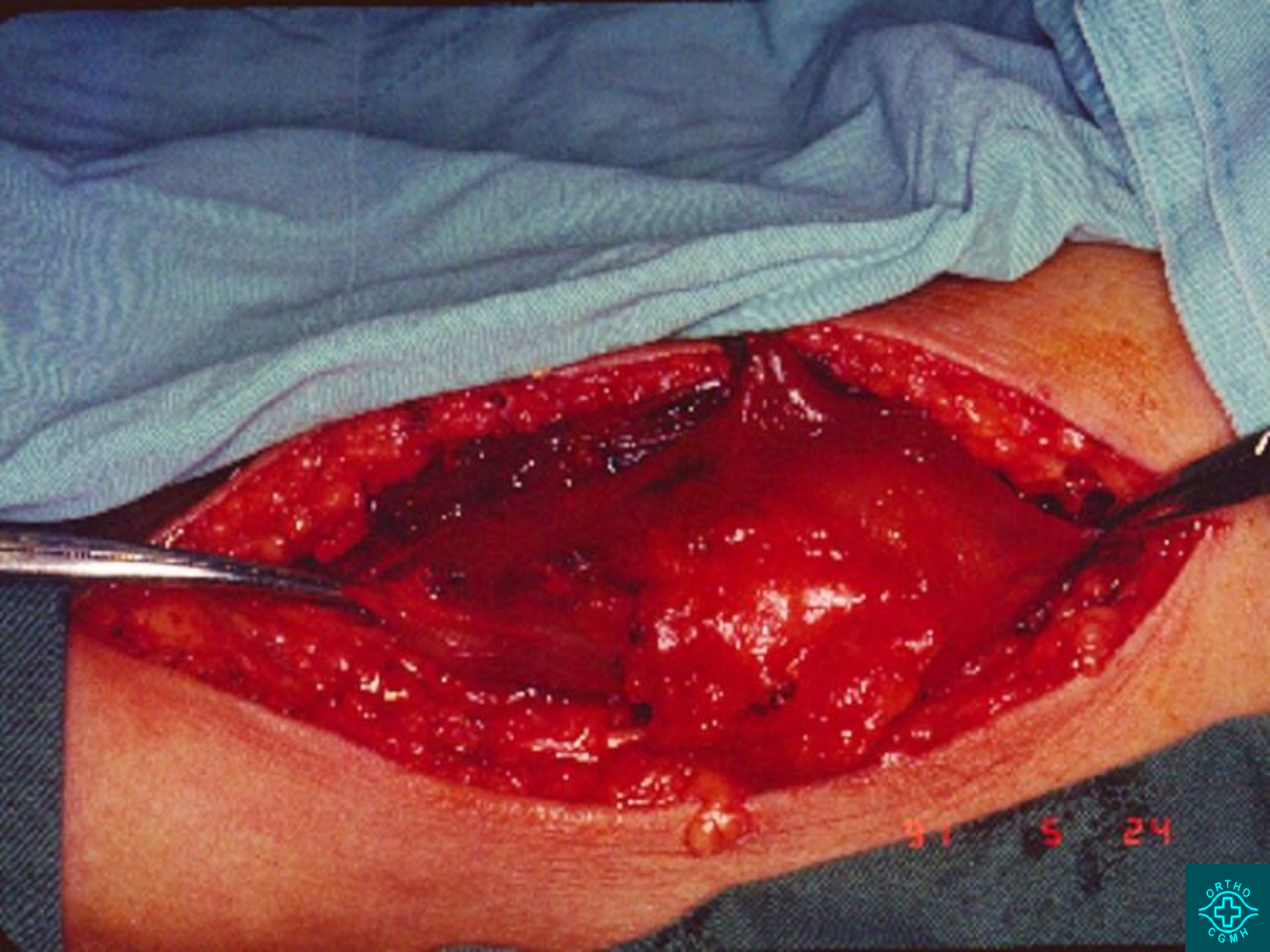
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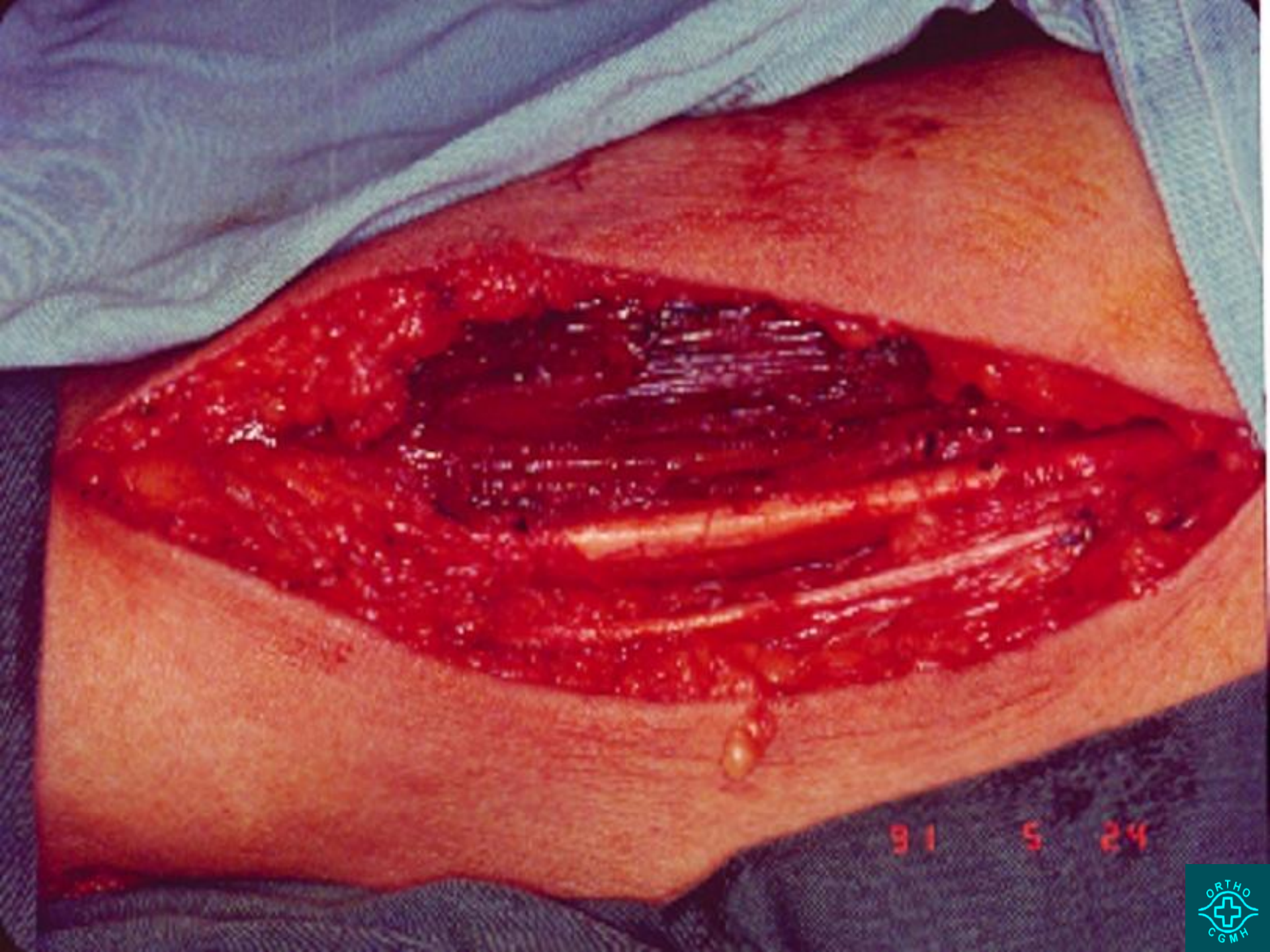
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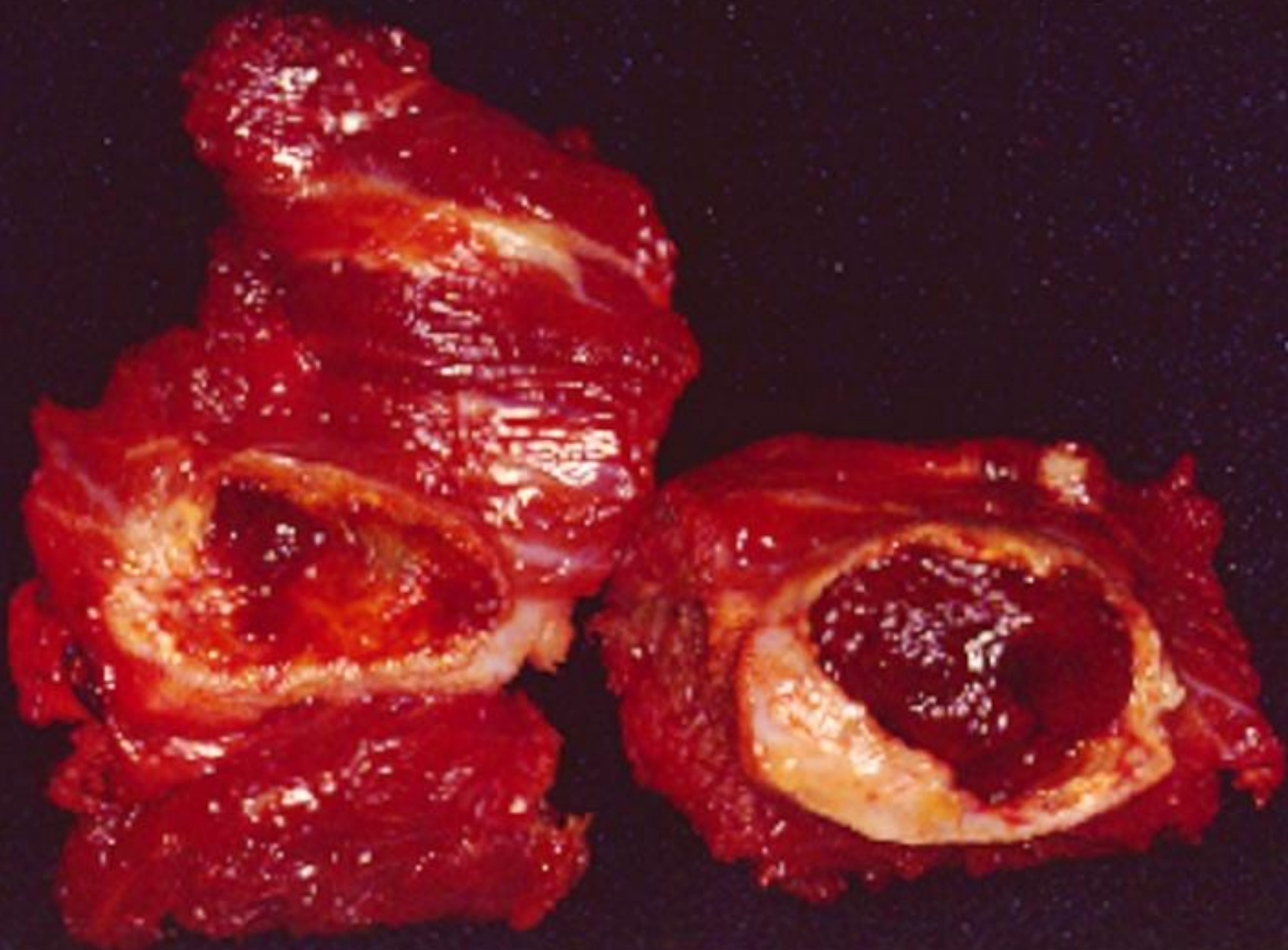
31 5 24

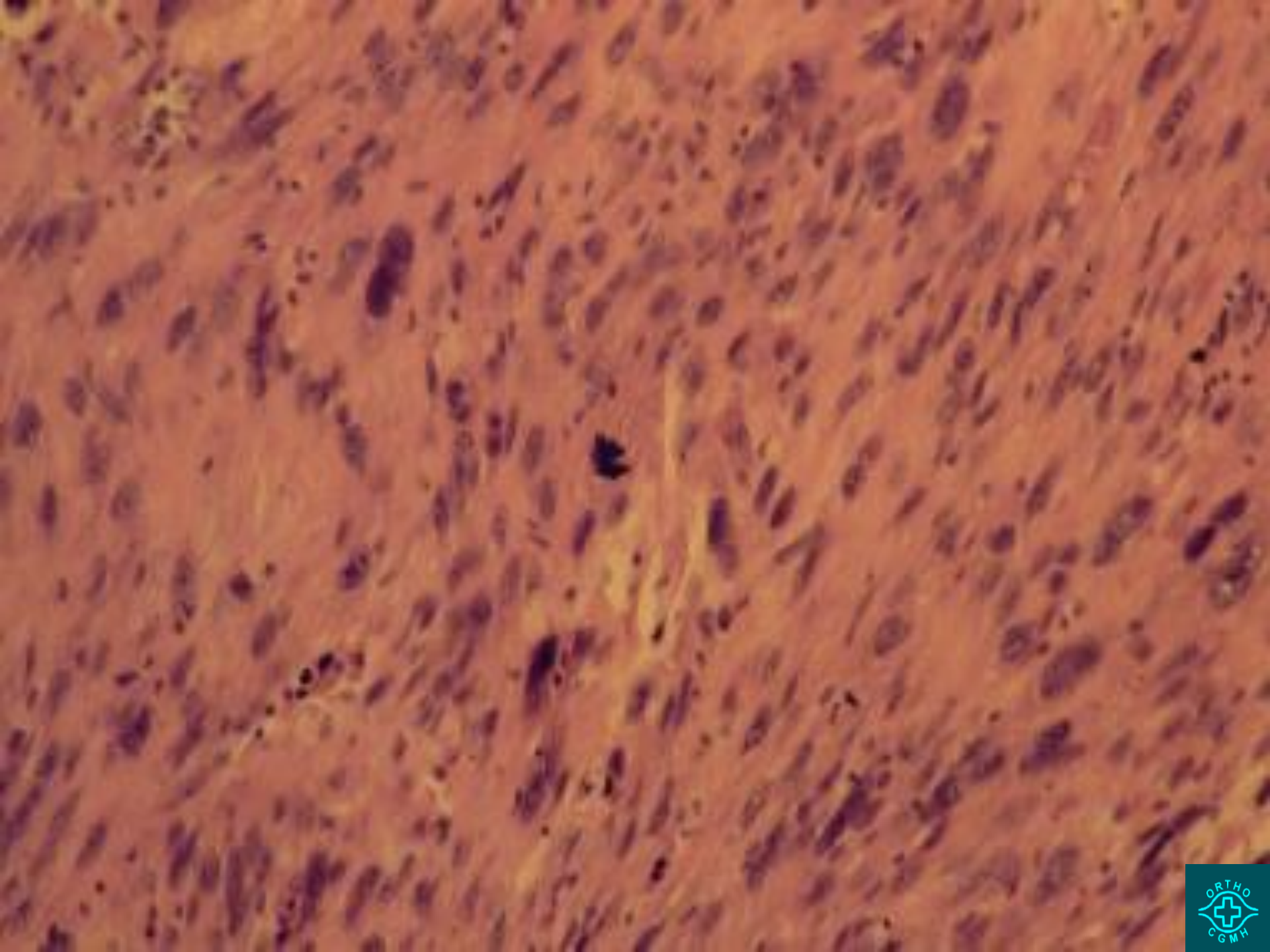




91 5 24



















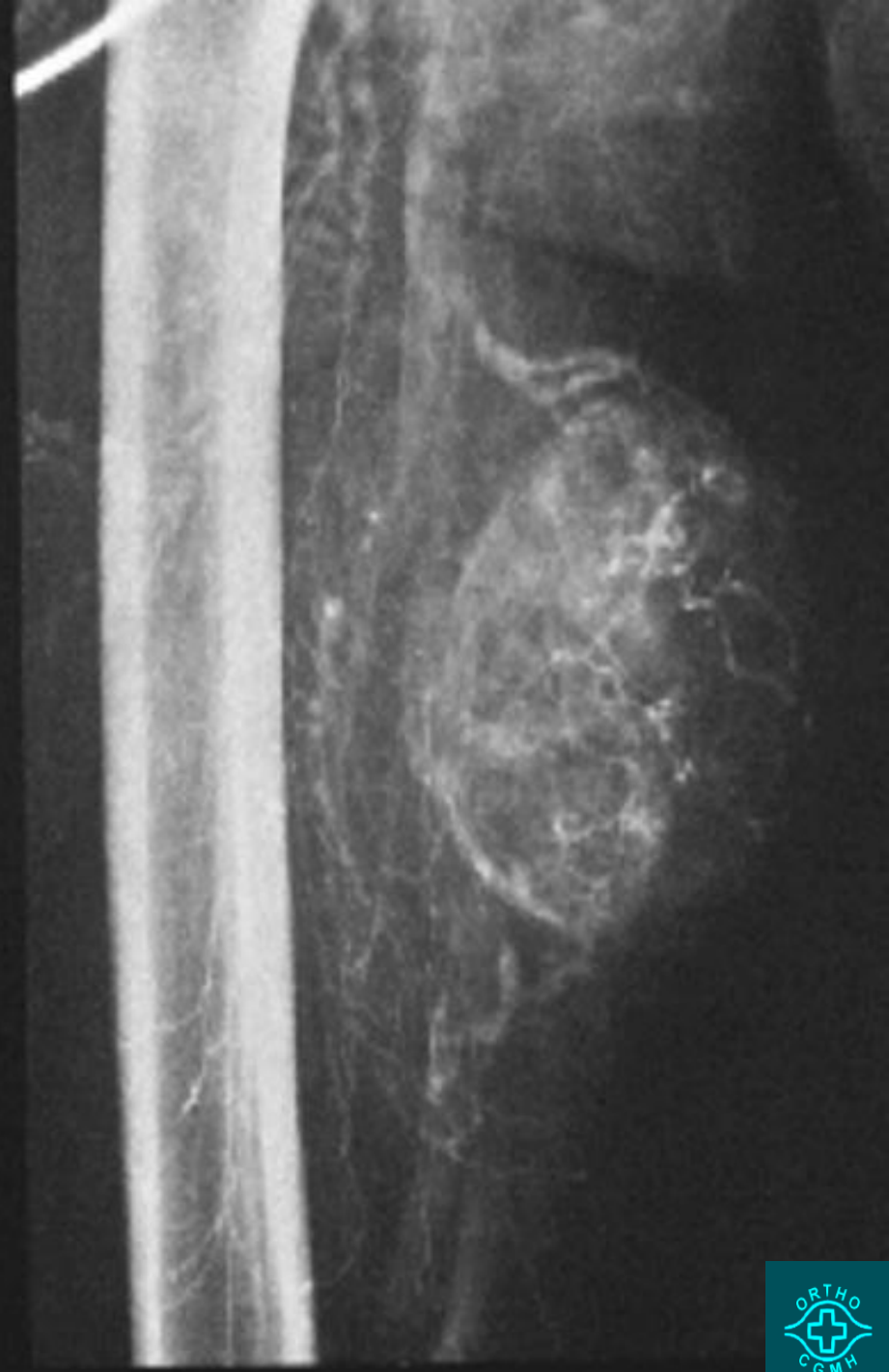
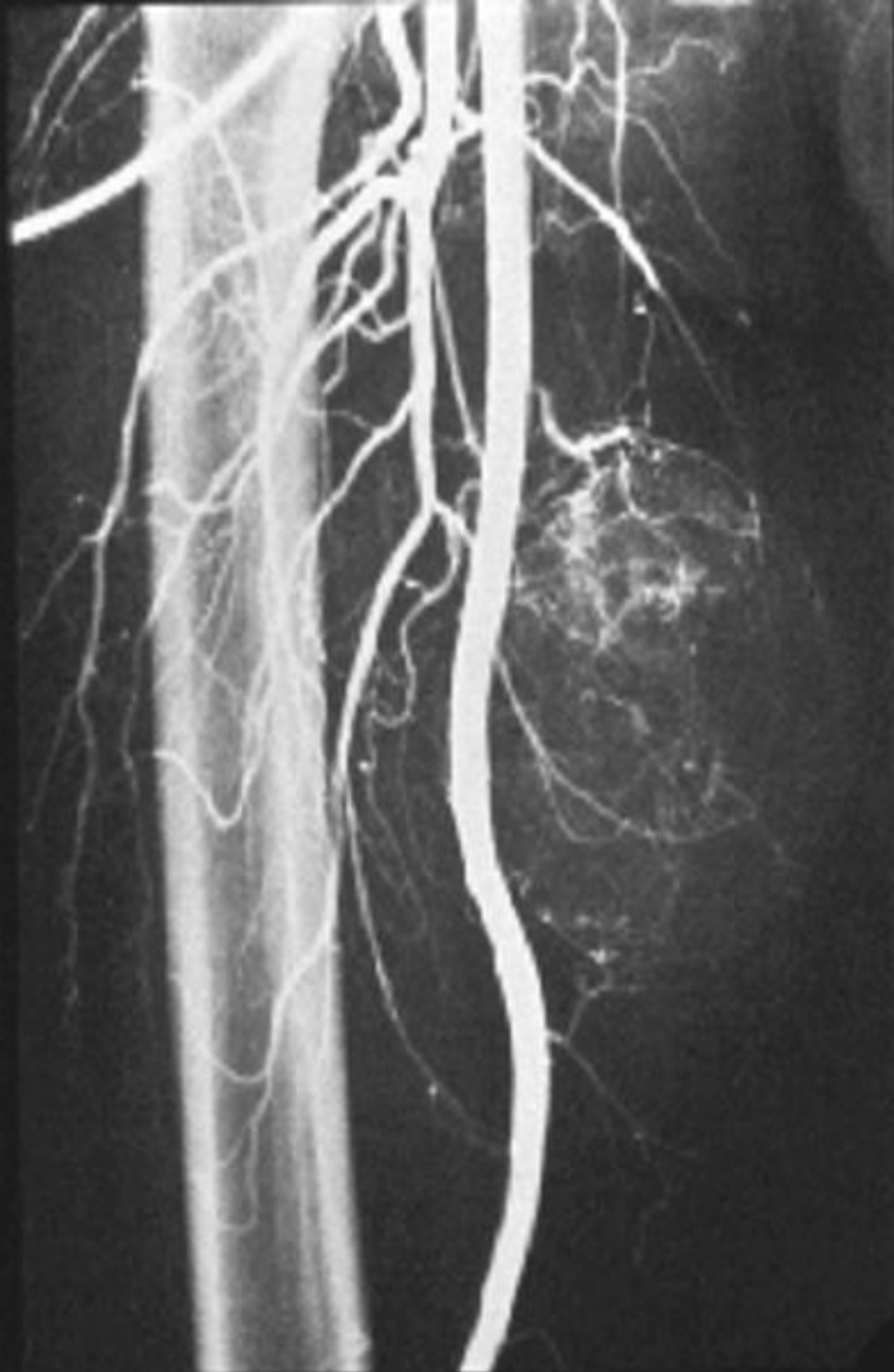
A-P



L'r Lat (L't)

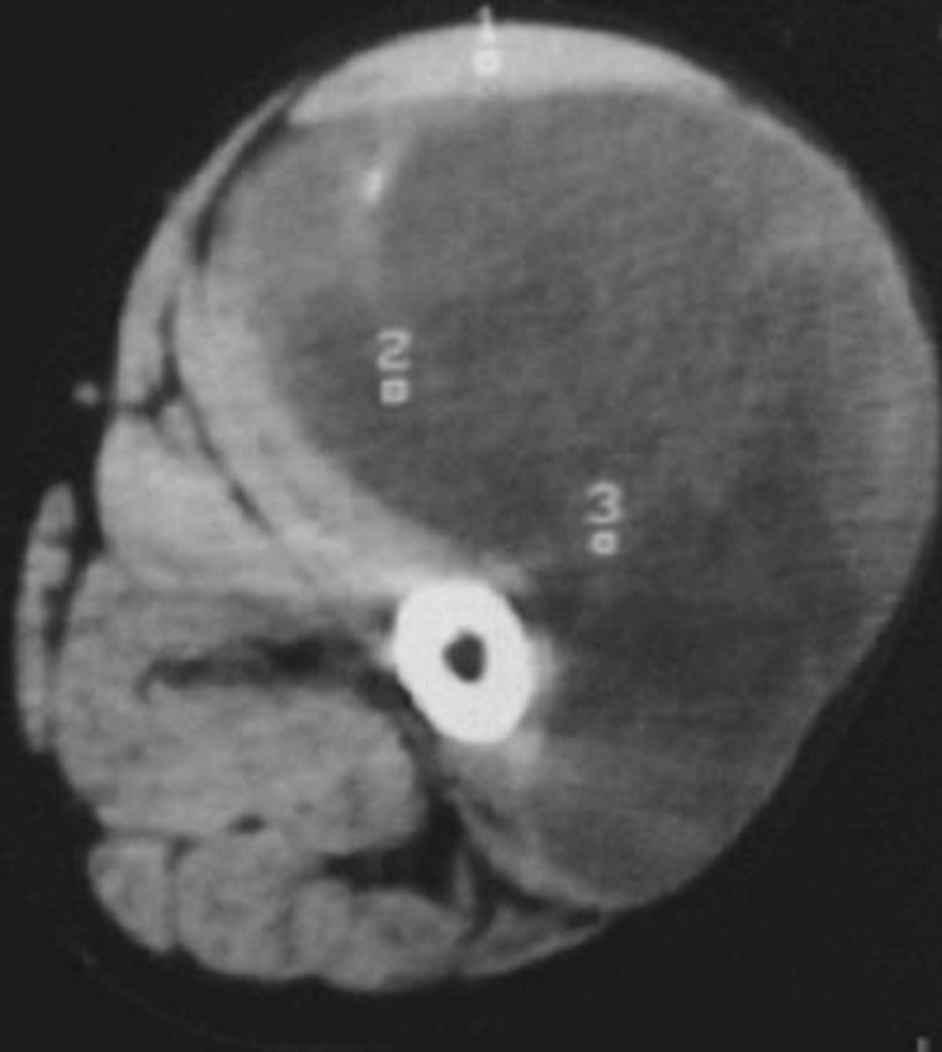
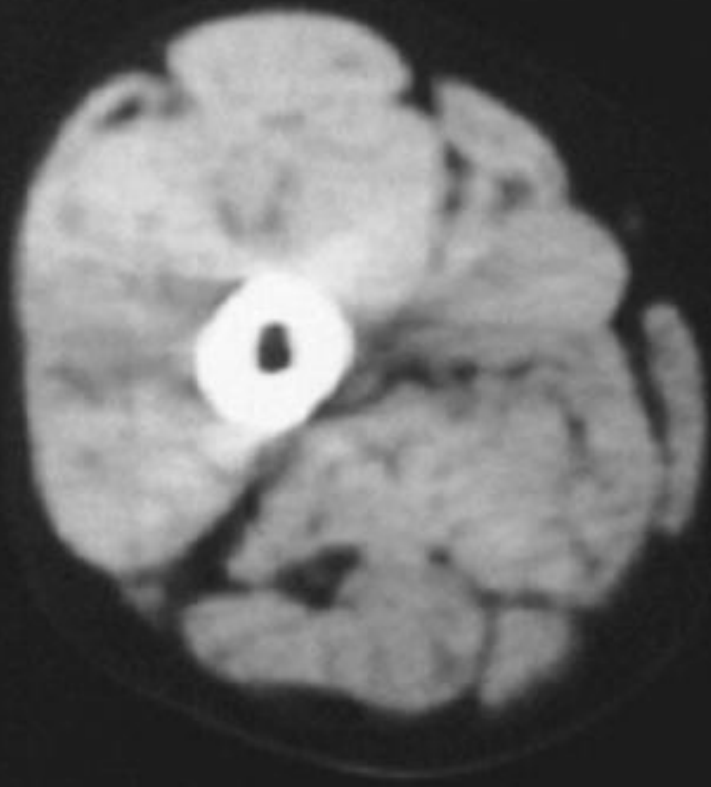
10. 4.2 5

10. 4.2 1



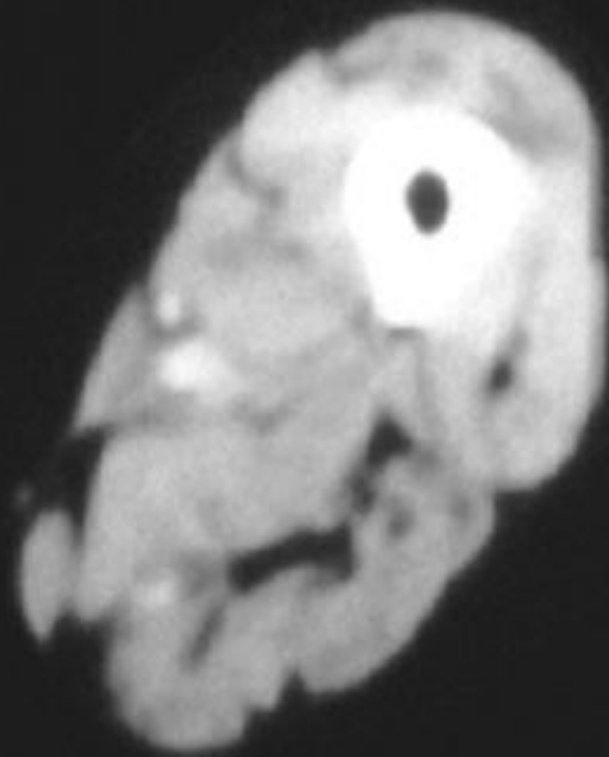
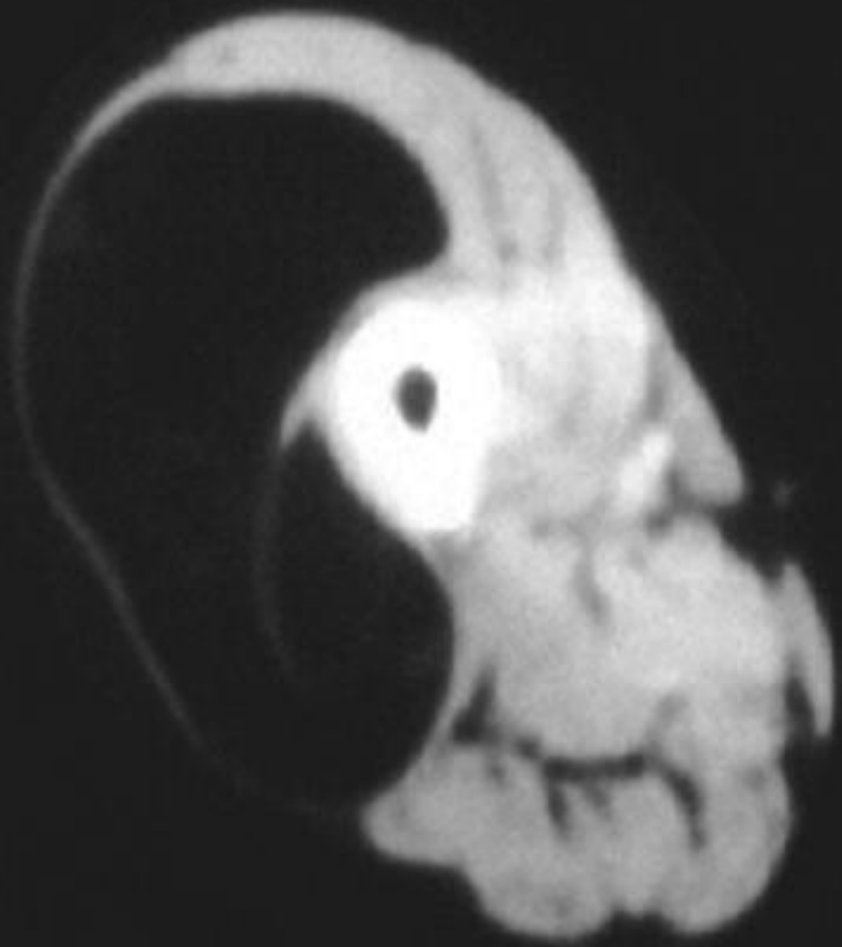
FOV 42 W  
K 00  
Y 00  
STD

11/21/11  
F 1



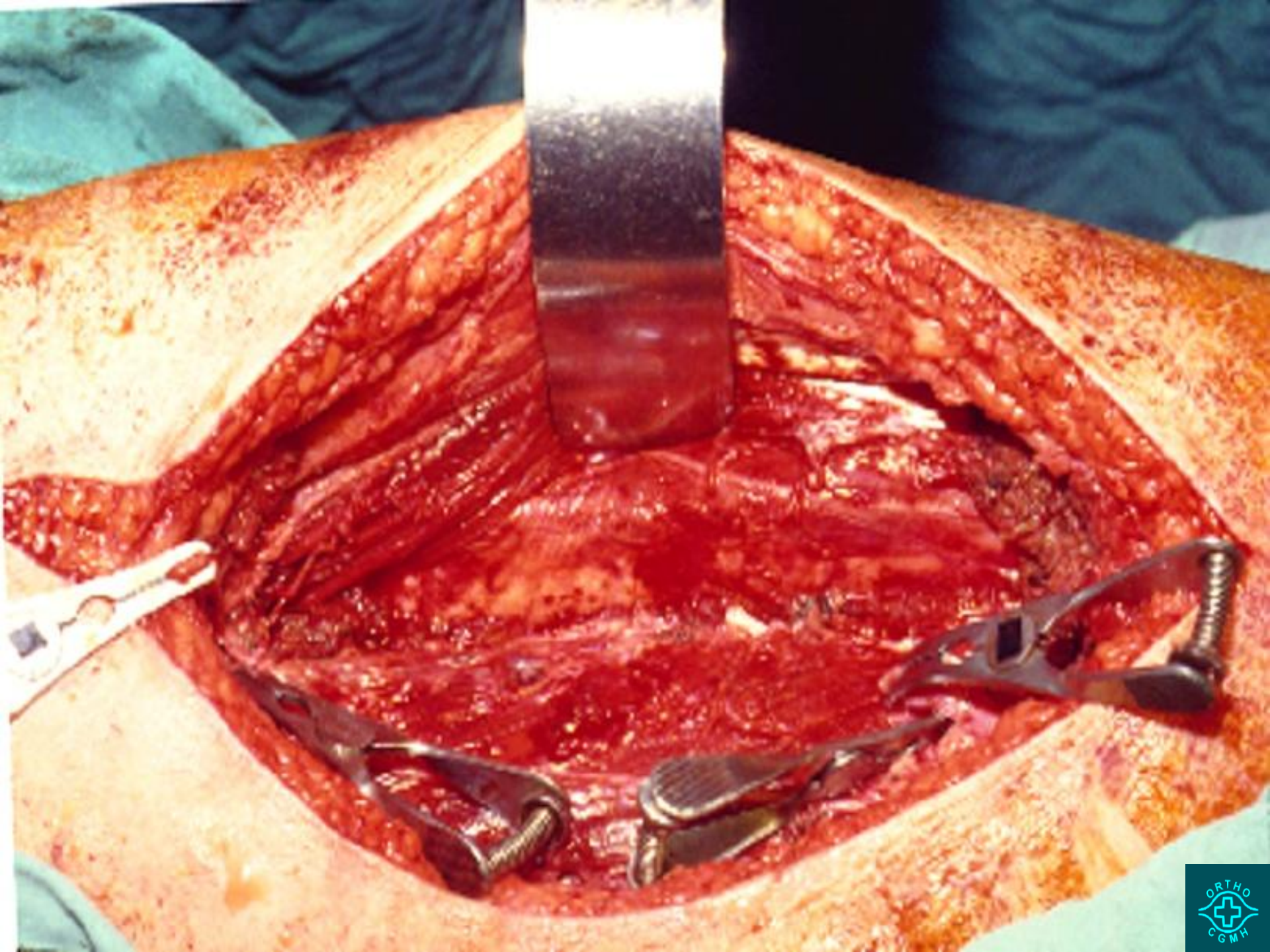
R



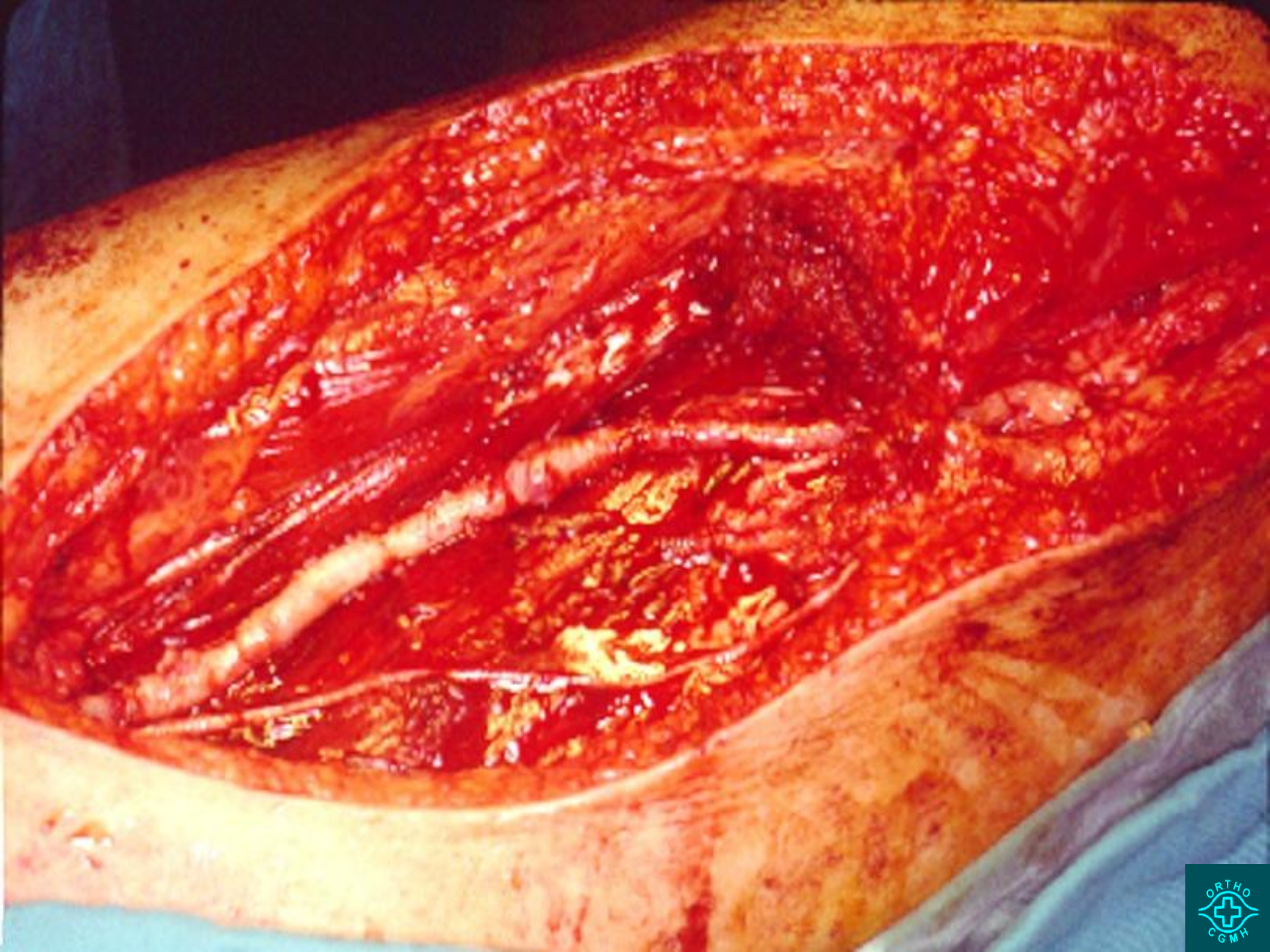


R











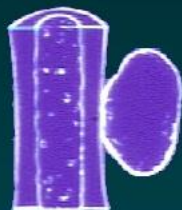
**Soft Tissue Mass**



**Sharp Margin**

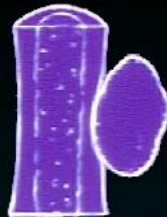


**ill-defined Margin**



**Bone Contact**

**Bone**



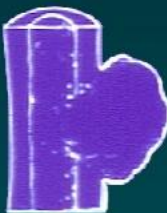
**Scalloped with Sharp Margin**



**Scalloped with Sclerotic Margin**



**ill-defined Erosion**



**Cortical Destruction with Marrow Extension**

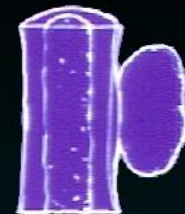
**Multiple Bones**

**Erosion Across Joint**



**Erosion Between Bones**

**Periosteal Reaction**



**Solid**



**Agressive: Early**



**Agressive: Late**

# Differential Diagnosis: Primary Soft Tissue Tumor vs. Primary Bone Tumor

**Epicenter**

**Bevel**

**Periosteal Reaction**

**Size of Lesion**

**Primary  
Soft  
Tissue  
Tumor**



**outside cortex**



**cortex beveled  
toward bone**

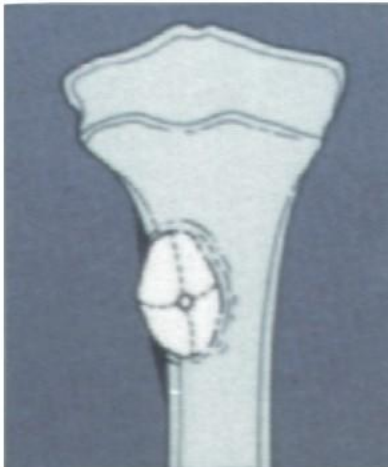


**absent**

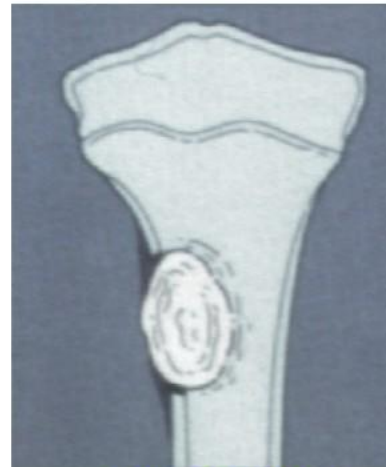


**small bone lesion  
large soft tissue mass**

**Primary  
Bone  
Tumor**



**Within bone**



**cortex beveled  
toward soft tissue**



**present**



**significant bone destruction  
small soft tissue mass**





# CHANG-GUNG MEMORIAL HOSPITAL LINKOU MEDICAL CENTER TAIWAN

**THANK YOU !!**

