Overview of Soft tissue Sarcoma Pathology Aspect

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Introduction

Classification of soft tissue tumors

Biological behaviors of soft tissue tumors

- Benign, Intermediate, Malignant

Incidence: determined by age groups

Locations

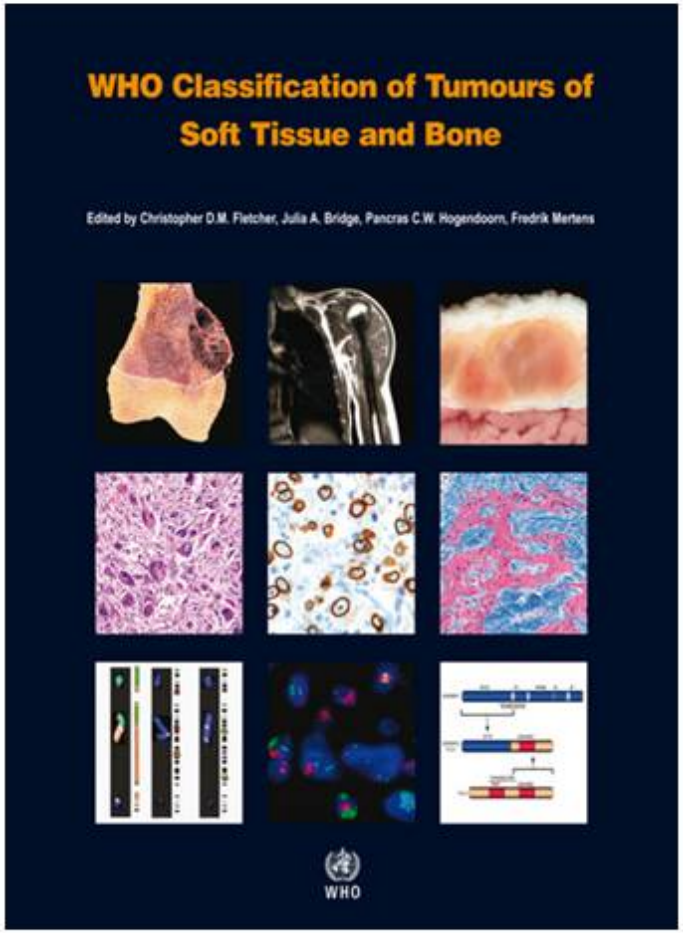
- Anatomic distributions
- Deep vs. Superficial

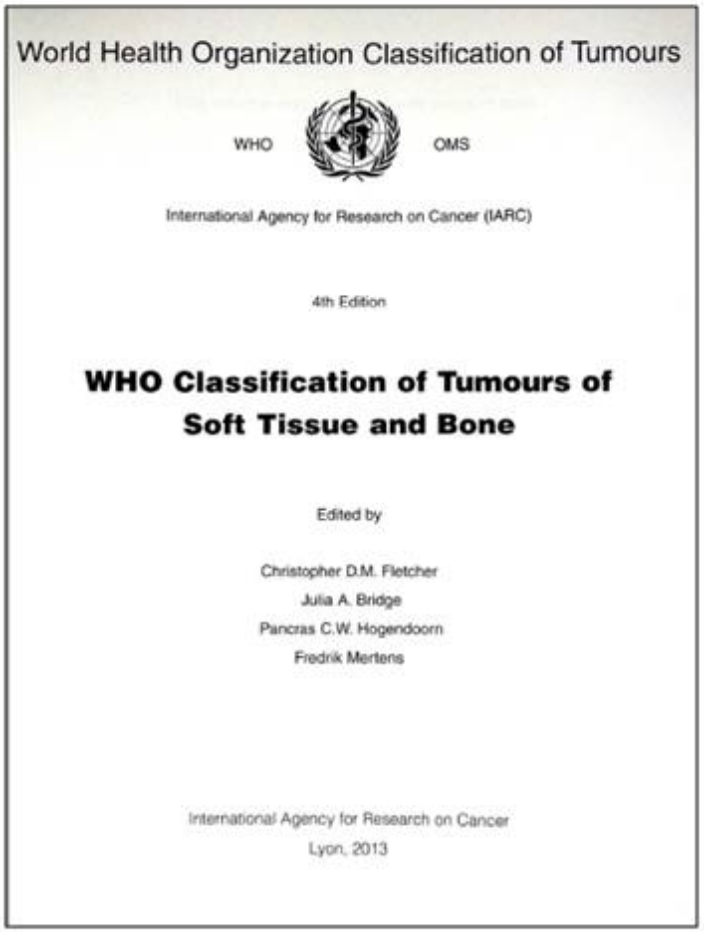
Pathological Diagnosis

- **Pattern approach**
- **IHC panels**

Molecular Genetic

WHO Classification 2013





WHO Classification 2013

WHO classification of tumours of soft tissue[a,b]

ADIPOCYTIC TUMOURS

Benign

Lipoma	8850/0
Lipomatosis	8850/0
Lipomatosis of nerve	8850/0
Lipoblastoma/lipoblastomatosis	8881/0
Angiolipoma	8861/0
Myolipoma	8890/0
Chondroid lipoma	8862/0
Extra-renal angiomyolipoma	8860/0
Extra-adrenal myelolipoma	8870/0
Spindle cell/pleomorphic lipoma	8857/0
Hibernoma	8880/0

Intermediate (locally aggressive)

Atypical lipomatous tumour/ well differentiated liposarcoma	8850/1 8850/3

Malignant

Dedifferentiated liposarcoma	8858/3
Myxoid liposarcoma	8852/3
Pleomorphic liposarcoma	8854/3
Liposarcoma, not otherwise specified	8850/3

FIBROBLASTIC / MYOFIBROBLASTIC TUMOURS

Benign

Nodular fasciitis	8828/0*
Proliferative fasciitis	8828/0*
Proliferative myositis	8828/0*
Myositis ossificans	
Fibro-osseous pseudotumour of digits	
Ischaemic fasciitis	
Elastofibroma	8820/0
Fibrous hamartoma of infancy	
Fibromatosis colli	
Juvenile hyaline fibromatosis	
Inclusion body fibromatosis	
Fibroma of tendon sheath	8813/0
Desmoplastic fibroblastoma	8810/0
Mammary-type myofibroblastoma	8825/0
Calcifying aponeurotic fibroma	8816/0*
Angiomyofibroblastoma	8826/0
Cellular angiofibroma	9160/0
Nuchal-type fibroma	8810/0
Gardner fibroma	8810/0
Calcifying fibrous tumour	8817/0*

Intermediate (locally aggressive)

Palmar/plantar fibromatosis	8813/1*
Desmoid-type fibromatosis	8821/1
Lipofibromatosis	8851/1*
Giant cell fibroblastoma	8834/1

Intermediate (rarely metastasizing)

Dermatofibrosarcoma protuberans	8832/1*
Fibrosarcomatous dermatofibrosarcoma protuberans	8832/3*
Pigmented dermatofibrosarcoma protuberans	8833/1*
Solitary fibrous tumour	8815/1*
Solitary fibrous tumour, malignant	8815/3
Inflammatory myofibroblastic tumour	8825/1
Low-grade myofibroblastic sarcoma	8825/3*
Myxoinflammatory fibroblastic sarcoma/ Atypical myxoinflammatory fibroblastic tumour	8811/1*
Infantile fibrosarcoma	8814/3

Malignant

Adult fibrosarcoma	8810/3
Myxofibrosarcoma	8811/3
Low-grade fibromyxoid sarcoma	8840/3*
Sclerosing epithelioid fibrosarcoma	8840/3*

SO-CALLED FIBROHISTIOCYTIC TUMOURS

Benign

Tenosynovial giant cell tumour	
localized type	9252/0
diffuse type	9252/1*
malignant	9252/3
Deep benign fibrous histiocytoma	8831/0

Intermediate (rarely metastasizing)

Plexiform fibrohistiocytic tumour	8835/1
Giant cell tumour of soft tissues	9251/1

SMOOTH MUSCLE TUMOURS

Benign

Deep leiomyoma	8890/0

Malignant

Leiomyosarcoma (excluding skin)	8890/3

PERICYTIC (PERIVASCULAR) TUMOURS

Glomus tumour (and variants)	8711/0
Glomangiomatosis	8711/1*
Malignant glomus tumour	8711/3
Myopericytoma	8824/0
Myofibroma	8824/0
Myofibromatosis	8824/1
Angioleiomyoma	8894/0

SKELETAL MUSCLE TUMOURS

Benign

Rhabdomyoma	8900/0
Adult type	8904/0
Fetal type	8903/0
Genital type	8905/0

Malignant

Embryonal rhabdomyosarcoma (including botryoid, anaplastic)	8910/3
Alveolar rhabdomyosarcoma (including solid, anaplastic)	8920/3
Pleomorphic rhabdomyosarcoma	8901/3
Spindle cell/sclerosing rhabdomyosarcoma	8912/3

VASCULAR TUMOURS OF SOFT TISSUE

Benign

Haemangioma	9120/0
Synovial	
Venous	9122/0
Arteriovenous haemangioma/malformation	9123/0
Intramuscular	9132/0
Epithelioid haemangioma	9125/0
Angiomatosis	
Lymphangioma	9170/0

Intermediate (locally aggressive)

Kaposiform haemangioendothelioma	9130/1

Intermediate (rarely metastasizing)

Retiform haemangioendothelioma	9136/1*
Papillary intralymphatic angioendothelioma	9135/1
Composite haemangioendothelioma	9136/1
Pseudomyogenic (epithelioid sarcoma-like) haemangioendothelioma	9136/1
Kaposi sarcoma	9140/3

Malignant

Epithelioid haemangioendothelioma	9133/3
Angiosarcoma of soft tissue	9120/3

CHONDRO-OSSEOUS TUMOURS

Soft tissue chondroma	9220/0
Extraskeletal mesenchymal chondrosarcoma	9240/3
Extraskeletal osteosarcoma	9180/3

GASTROINTESTINAL STROMAL TUMOURS

Benign gastrointestinal stromal tumour	8936/0
Gastrointestinal stromal tumour, uncertain malignant potential	8936/1
Gastrointestinal stromal tumour, malignant	8936/3

NERVE SHEATH TUMOURS

Benign

Schwannoma (including variants)	9560/0
Melanotic schwannoma	9560/1*
Neurofibroma (incl. variants)	9540/0
Plexiform neurofibroma	9550/0
Perineurioma	9571/0
Malignant perineurioma	9571/3
Granular cell tumour	9580/0
Dermal nerve sheath myxoma	9562/0
Solitary circumscribed neuroma	9570/0
Ectopic meningioma	9530/0
Nasal glial heterotopia	
Benign Triton tumour	
Hybrid nerve sheath tumours	9563/0*

Malignant

Malignant peripheral nerve sheath tumour	9540/3
Epithelioid malignant peripheral nerve sheath tumour	9542/3*
Malignant Triton tumour	9561/3
Malignant granular cell tumour	9580/3
Ectomesenchymoma	8921/3

TUMOURS OF UNCERTAIN DIFFERENTIATION

Benign

Acral fibromyxoma	8811/0
Intramuscular myxoma (including cellular variant)	8840/0
Juxta-articular myxoma	8840/0
Deep ("aggressive") angiomyxoma	8841/0*
Pleomorphic hyalinizing angiectatic tumour	8802/1*
Ectopic hamartomatous thymoma	8587/0

Intermediate (locally aggressive)

Haemosiderotic fibrolipomatous tumour	8811/1*

Intermediate (rarely metastasizing)

Atypical fibroxanthoma	8830/1
Angiomatoid fibrous histiocytoma	8836/1
Ossifying fibromyxoid tumour	8842/0
Ossifying fibromyxoid tumour, malignant	8842/3*
Mixed tumour NOS	8940/0
Mixed tumour NOS, malignant	8940/3
Myoepithelioma	8982/0
Myoepithelial carcinoma	8982/3
Phosphaturic mesenchymal tumour, benign	8990/0
Phosphaturic mesenchymal tumour, malignant	8990/3

Malignant

Synovial sarcoma NOS	9040/3
Synovial sarcoma, spindle cell	9041/3
Synovial sarcoma, biphasic	9043/3
Epithelioid sarcoma	8804/3
Alveolar soft-part sarcoma	9581/3
Clear cell sarcoma of soft tissue	9044/3
Extraskeletal myxoid chondrosarcoma	9231/3
Extraskeletal Ewing sarcoma	9364/3
Desmoplastic small round cell tumour	8806/3
Extra-renal rhabdoid tumour	8963/3
Neoplasms with perivascular epithelioid cell differentiation (PEComa)	
PEComa NOS, benign	8714/0*
PEComa NOS, malignant	8714/3*
Intimal sarcoma	9137/3*

UNDIFFERENTIATED/UNCLASSIFIED SARCOMAS

Undifferentiated spindle cell sarcoma	8801/3
Undifferentiated pleomorphic sarcoma	8802/3
Undifferentiated round cell sarcoma	8803/3
Undifferentiated epithelioid sarcoma	8804/3
Undifferentiated sarcoma NOS	8805/3

[a] The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) (916A). Behaviour is coded /0 for benign tumours, /1 for unspecified, borderline or uncertain behaviour, /2 for carcinoma in situ and grade III intraepithelial neoplasia, and /3 for malignant tumours; [b] The classification is modified from the previous WHO histological classification of tumours (870A) taking into account changes in understanding of these lesions. * These new codes were approved by the IARC/WHO Committee for ICD-O in 2012.

Soft Tissue Tumors

- Embryologically derived from ***mesoderm*** (some from neuroectoderm): fibrous, muscle (striated/smooth), adipose, vessels, nerves
- Benign : Malignant = 200+: 90 entities

- Many soft tissue tumors does not require IHC for Dx.
- No specific IHC for distinguishing benign/malignant
- For diagnosis sarcoma, need MALIGNANT features
  (mitosis, necrosis, nuclear atypia, nuclear hyperchromasia, hypercellularity)
- Need IHC panel for tumor cell type identification

Biological behavior

Benign

eg. Lipoma

- Closely resemble normal tissue
- Non-destructive growth
- Cured by complete local excision
- Rare recurrence
- No metastasis

Malignant tumor (Sarcoma) :

eg. Liposarcoma, undiff. Pleomorphic sarcoma (UPS / MFH)

- Locally destructive growth
- High recurrence rate
- Distant metastasis - common:
    - Low-grade (histologic grade I) ~ 2-10%
    - High-grade (histologic grade II-III) ~ 10-100%

Intermediate (locally aggressive):

eg. Desmoid fibromatosis

- Infiltrative, locally destructive growth pattern,
- No metastasis
- Rx. wide excision

Intermediate (rarely metastasizing):

eg. Solitary fibrous tumor (SFT/hemangiopericytoma)

- Locally aggressive, metastases risk <2 %
- Not reliably predictable on histomorphology
- Rx. wide excision + F/U

Age-related incidence

Some Sarcomas are relatively specific to particular age groups

- Childhood - RMS, neuroblastoma, Ewing
- Young Adult - Synovial sarcoma , ASPS, DSRCT
- Old age - Liposarcoma, Undiff. pleomorphic sarcoma (UPS/MFH)

Information on the Request Form

- **Duration**

  (wk/mo, nodular fasciitis, myxoFS)
- **Size**
- **Depth**

  (deep/superficial, Pleo.LPS/Pleo.lipoma)
- **Surrounding structure**

  (knee mass !?!, sciatic nerve mass !?!)
- **Past history**

  (previous Sx/RT, dd.LPS/radiation Sarx)

Location & site distribution

Deep Soft Tissue - Most

- 75% Large muscles of extremities ***esp. thigh***
- 10% Retroperitoneum

Superficial sarcoma

- eg. Dermatofibrosarcoma protuberans (DFSP), Epithelioid sarcoma, Angiosarcoma, myxofibrosarcoma

Region specific

- Hand & wrist:- Epithelioid sarcoma
- Scalp:- Angiosarcoma
- Knee/ankle:- Synovial sarcoma
- GU, orbit:- Rhabdomyosarcoma

Incidence

- **<** 1% of the overall human malignancy
- Life-threatening (2% of all cancer deaths)
- 3/4 = Undiff. high-grade pleomorphic sarcoma (UPS/MFH), Liposarcoma, Leiomyosarcoma, Synovial sarcoma, Malignant peripheral nerve sheath tumor (MPNST)

Diagnosis

Surgical biopsy

- **Core needle biopsy (CNB)**: at least 3-5 cores, 14-16 guage needle size, put in > 1 blocks
- **Open biopsy**: when CNB fail to Dx.

Cytology

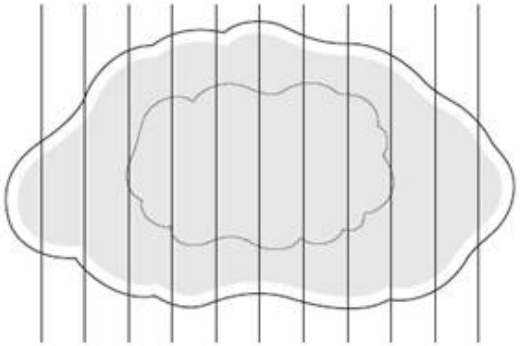
- Limited role: monitoring recurrence/metas. In known Dx. Sarx
- NOT recommend for primary Dx. for Sarx

Diagnosis

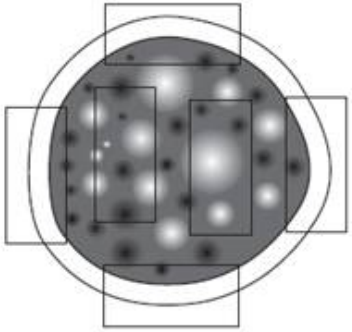
Frozen section

- To determine low-grade vs. high-grade
  (NOT… benign vs. malignant)
- Assess margin
  (EXCEPT… myxoFS, wd.LPS, desmoid tumor)
- Confirm fresh/viable tissue

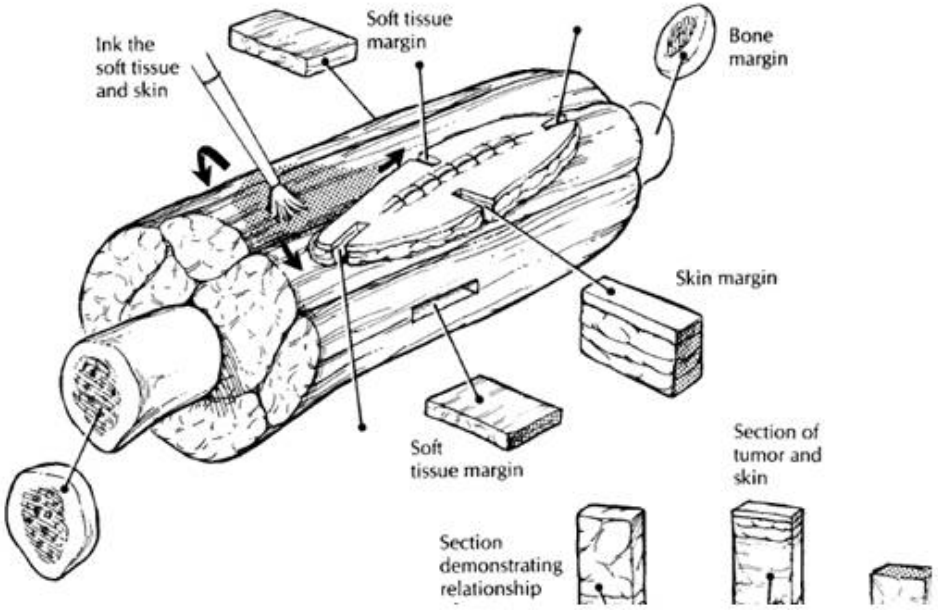
Tissue Sampling



Paint externally and cut into multiple transverse slices



Sample non-necrotic tumour and tumour in relation to the margins of excision



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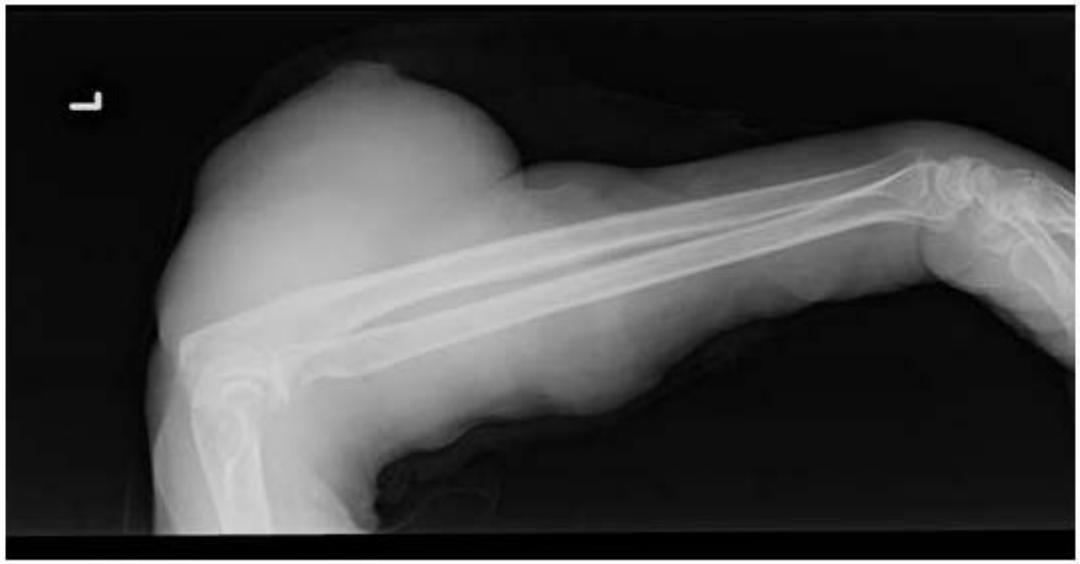
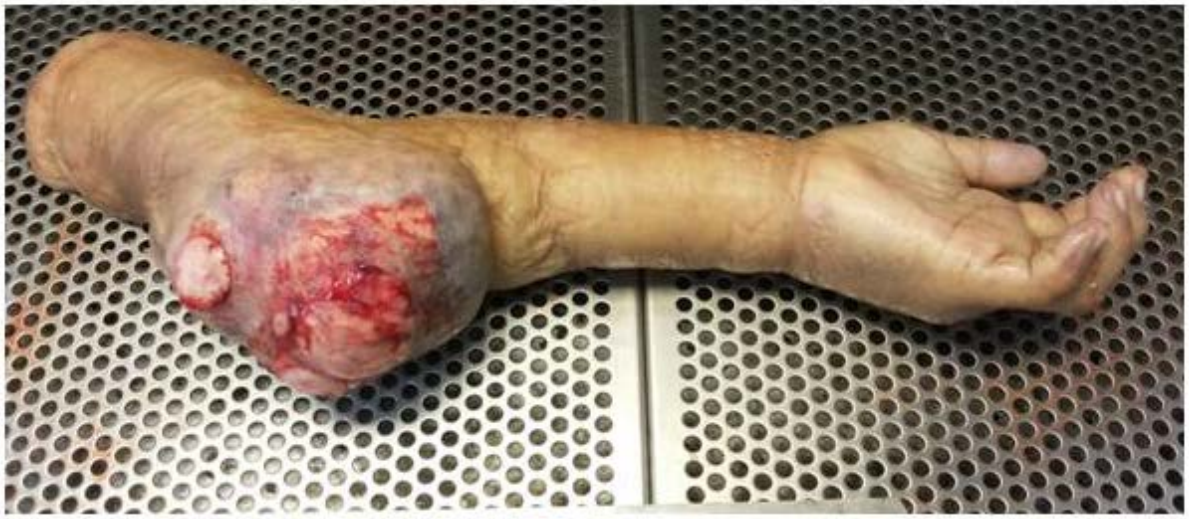
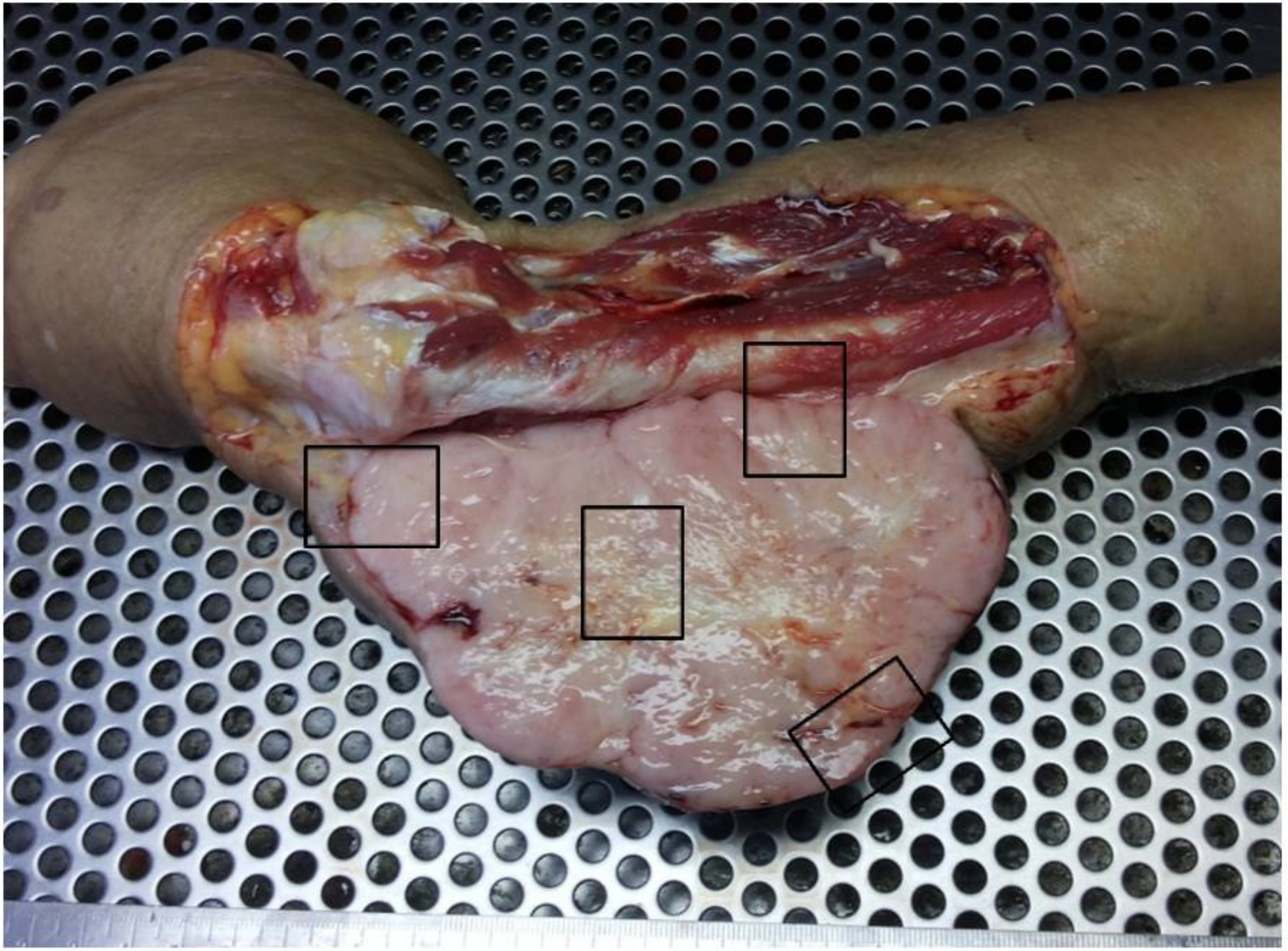
2. Rubin BP, Antonescu CR, Gannon FH. Members of the Cancer Committee, College of American Pathologists. Protocol for the examination of specimens from patients with tumors of bone. Arch Pathol Lab Med. 2010 Apr;134(4):e1-7.
3. Derek C. Allen, Iain Cameron. Histopathology Specimens. Springer-Verlag London Limited 2004.
4. William H. Westra, Surgical Pathology Dissection. 2nd Ed. Springer-Verlag New York

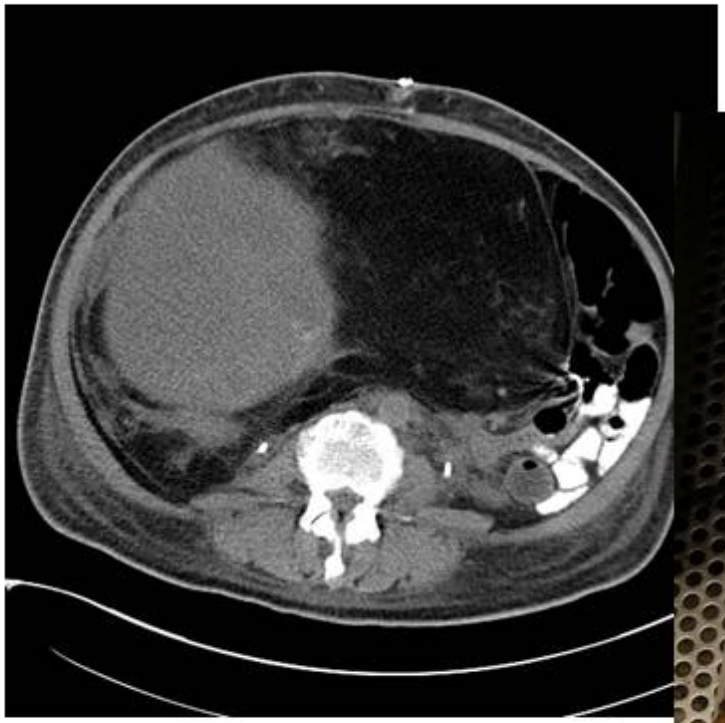
Undiff. Pleomorphic Sarcoma

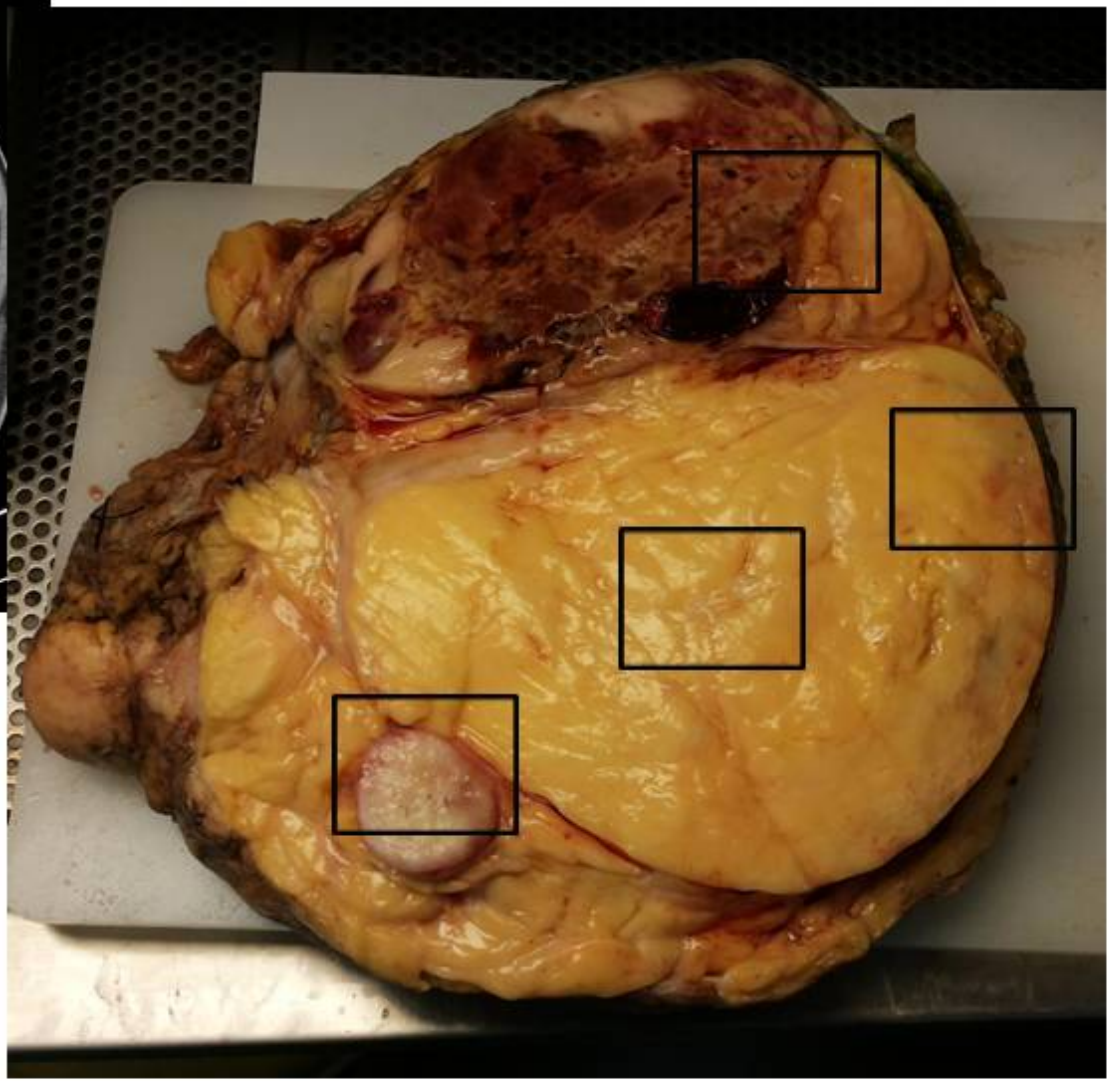




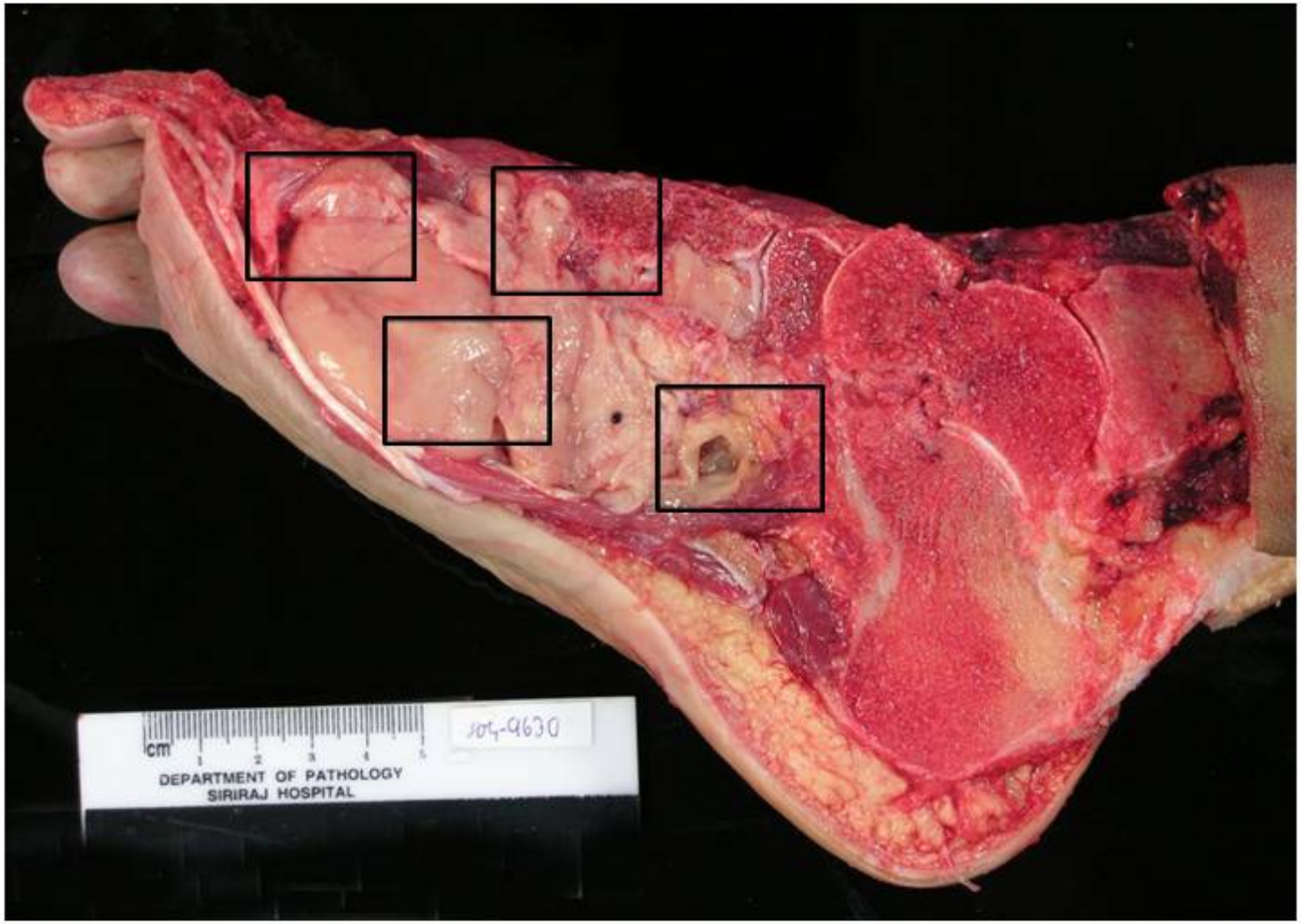


Dediff Liposarcoma





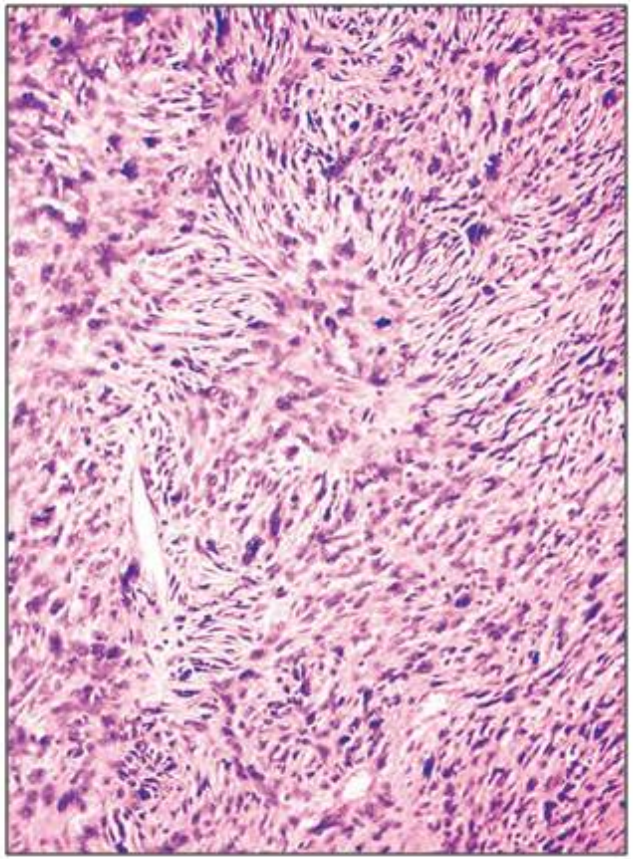
Synovial sarcoma



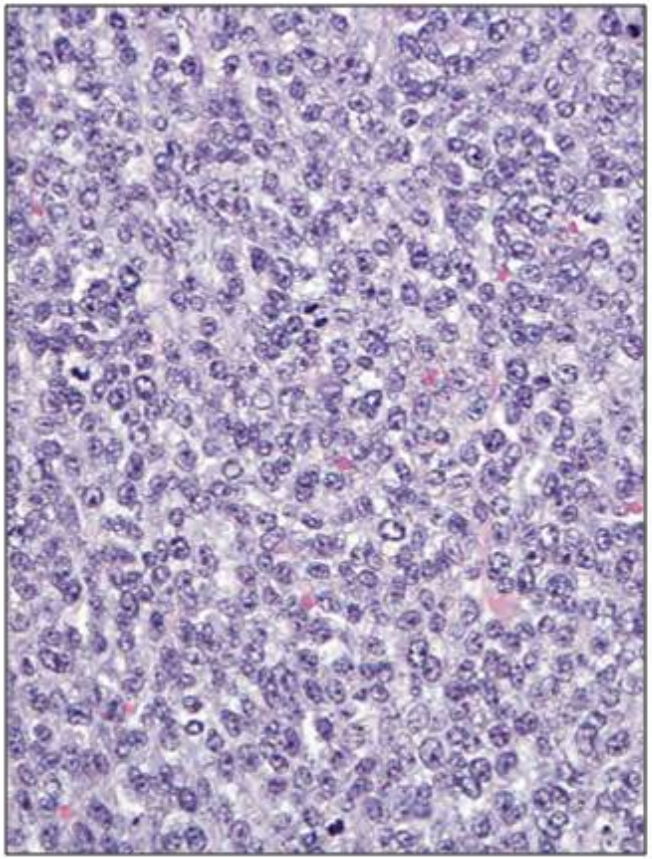
Comment

- Extensive necrosis precluded our interpretation; Rebiopsy/excision might be helpful
- The low grade sarcoma in this small biopsy might not represent the whole tumor.
- Due to discordance between radiographic/pathologic finding, recommend rebiopsy/open biopsy for definite diagnosis.

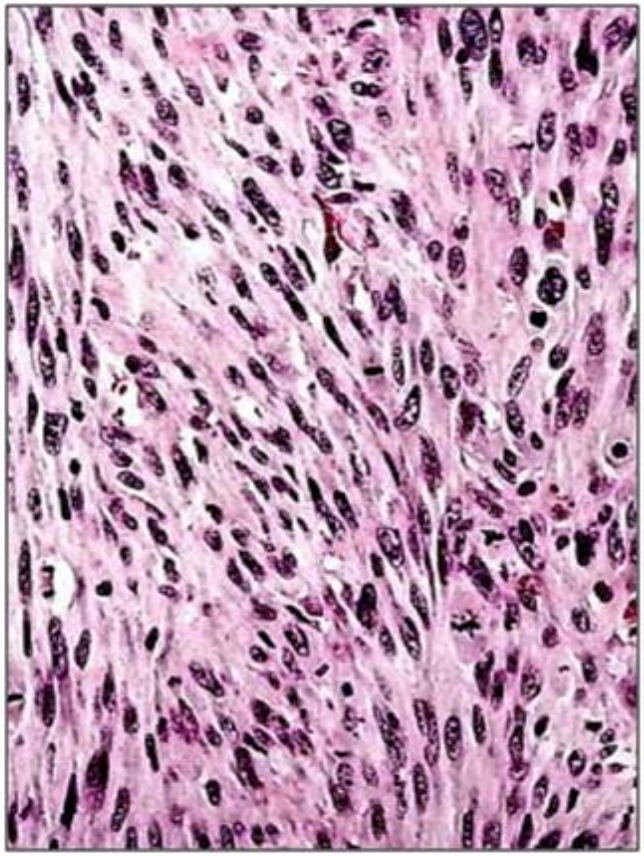
Pattern Recognition (+ DDx)



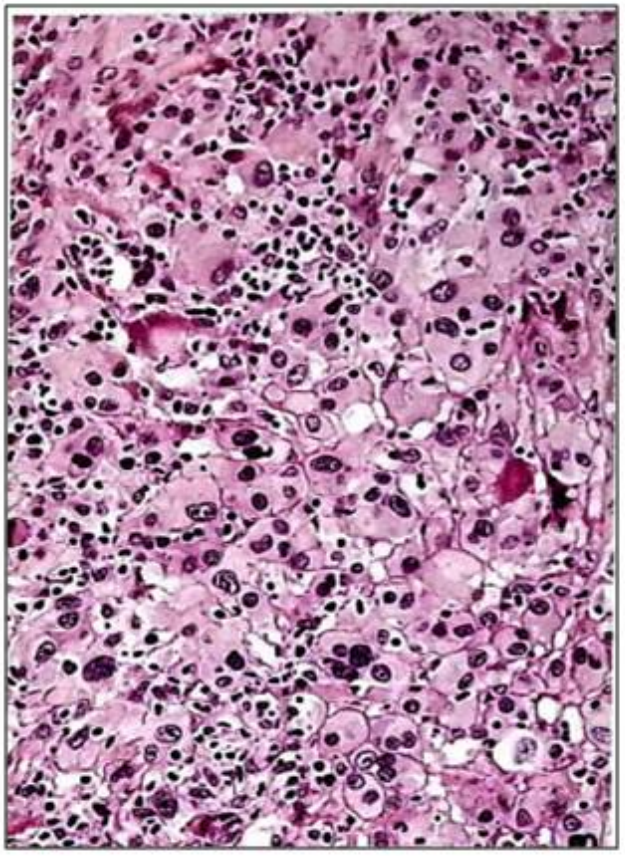
Pleomorphic cells



Round cells



Spindle cells



Epithelioid cells

Diagnosis on Histologic Pattern & IHC Results +/- Molecular studies

- Pleomorphic tumors
- Small blue round cell tumors
- Monomorphic spindle cell tumors
- Epithelioid cell tumors

Morphology of Cells in Soft Tissue Tumors

Morphology	Features	Tumor Type
Pleomorphic cell	Anaplastic cell, enlarged nuclei	UPS (MFH), Schwannoma, Pleomorphic variant of LPS, RMS, LMS,
Round cell	Size of a lymphocyte with little cytoplasm	Rhabdomyosarcoma, Ewing sarcoma/PNET, lymphoma, PDSS
Spindle cell	Rod-shaped, long axis twice as great as short axis	PDSS, MPNST, Fibrosarcoma, LMS, Schwannoma
Epithelioid cell	Polyhedral with abundant cytoplasm	(Carcinoma, Melanoma) Epithelioid sarcoma, ASPS, Epithelioid variant of LMS, AS, MPNST.

UPS (MFH): undiff.pleomorphic sarcoma (malignant fibrous histiocytoma), RMS: rhabdomyosarcoma, LMS: leiomyosarcoma, PNET: primitive neuroectodermal tumor, PDSS: poorly diff. synovial sarcoma, MPNST: malignant peripheral nerve sheath tumor, ASPS: alveolar soft part sarcoma, AS: angiosarcoma

Diagnosis on Histologic Pattern, No IHC Requirement

- Benign & malignant lipomatous lesions
- Low-grade fibrous lesions
- Benign vascular lesions
- Myxoid tumors of deep soft tissue
  - Myxofibrosarcoma
  - Myxoid LPS
  - Extraskeletal myxoid chondrosarcoma (EMC)

IHC Panel for Pleomorphic Malignant Tumors

	CK	S100	CD30	SMA	desmin
CA	+	-	-	-	-
Melanoma	-	+	-	-	-
ALCL	-	-	+	-	-
LMS	+ / -	-	-	+	+
RMS	-	-	-	-	+
MPNST	+ / -	+ / -	-	-	-
UPS (MFH)	-	-	-	+ / -	-

CA: carcinoma, ALCL: anaplastic large cell lymphoma, LMS: leiomyosarcoma, RMS: rhabdomyosarcoma, MPNST: malignant peripheral nerve sheath tumor, UPS (MFH): undiff.pleomorphic sarcoma (malignant fibrous histiocytoma)

IHC Panel for Small blue Round Cell Tumors

	CK	S100	CD45	TdT	Desm	CD99
Ewing	+ / -	+ / -	-	-	-	+
Lymphoma	-	-	+	+	-	+ / -
RMS	-	-	-	-	+	-
PDSS	+	+ / -	-	-	-	+ / -
DSRCT	+	-	-	-	+	-
CA	+	-	-	-	-	-
Melanoma	-	+	-	-	-	-
Lymphoma	-	-	+	+	-	+ / -

Ewing: Ewing sarcoma, RMS: rhabdomyosarcoma, PDSS: poorly diff. synovial sarcoma, DSRCT: desmoplastic small round cell tumor, CA: carcinoma

IHC Panel for Monomorphic Spindle Cell Tumors

	CK	S100	CD34	SMA	CD117
SS	+ / -	+ / -	-	-	-
MPNST	-	+ / -	-	-	-
FS / DFSP	-	-	+ / -	+ / -	-
LM / LMS	-	-	-	+	-
SFT	-	-	+	-	-
GIST	-	+ / -	+ / -	+ / -	+
Schwannoma	-	+	-	-	-

SS: synovial sarcoma, MPNST: malignant peripheral nerve sheath tumor, FS/DFSP: fibrosarcoma/dermatofibrosarcoma protuberans, LM/LMS: leiomyoma/leiomyosarcoma, SFT: solitary fibrous tumor (hemangiopericytoma), GIST: gastrointestinal stromal tumor

IHC Panel for Malignant Epithelioid Cell Tumors

	CK	S100	CD45	CD30	CD31	SMA
CA	+	-	-	-	-	-
Melanoma	-	+	-	-	-	-
E-MPNST	+ / -	+	-	-	-	-
ALCL	-	-	+ / -	+ / -	-	-
Epitheloid sarc	+	-	-	-	-	-
E-AS	+ / -	-	-	-	+	-
E-LMS	+ / -	-	-	-	-	+

CA: carcinoma, E-MPNST: epithelioid malignant peripheral nerve sheath tumor, ALCL: anaplastic large cell lymphoma, E-AS: epithelioid angiosarcoma, E-LMS: epithelioid leiomyosarcoma

Cont’