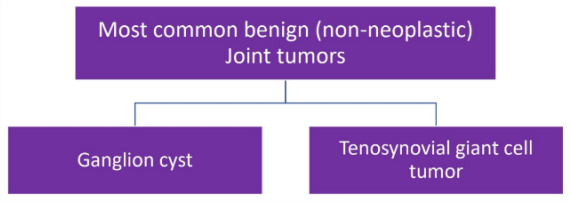
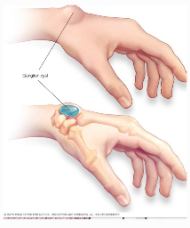
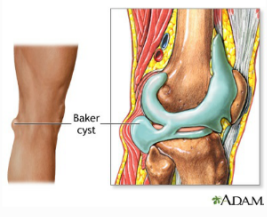
Joint tumors and tumor like conditions:

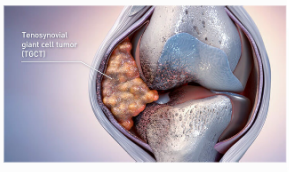


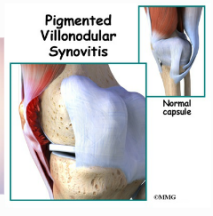
1. Ganglion cyst: (ganglion) is a misnomer, there is no actual ganglion.
- It is a **cystic bulge** around the joint, mainly in **wrist** dorsum.
- Mostly asymptomatic, but sometimes it gets bigger causing a pressure on a nerve.
- Two theories about its pathogenesis:
a. **Degeneration** of joint space leading to pseudocyst formation (fluid containing bulge).
b. **Herniation** of synovial membranes.
- Not a true cyst (because it does not have a lining), it is herniation or degenerative cyst.
- **baker's cyst** is a true synovial cyst, occurs around the **knee** joint (in its posterior side, in the popliteal fossa), & filled with fluid or a herniation process. Sometimes it causes severe pain, pressure on venous structures of the lower limb leading to **deep vein thrombosis**.



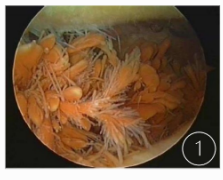


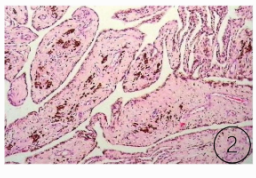
2. Tenosynovial giant cell tumor: (called to differentiate it from giant cell tumor of bone)
- A benign synovial tumor.
Translocation T(1;2), (p13q;37) which affects **type IV collagen α-3** (so it's a genetic abnormality).
- Has two types:



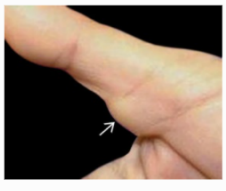


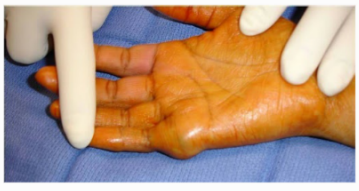
a. Diffuse (pigmented villonodular synovitis (PVNS)): more dangerous, called so because under the microscope **brown pigment** is seen (an evidence of previous bleeding) due to **hemosiderin macrophages.**
PVNS are finger-like projections into the joint (proliferation of the synovium with hemosiderin macrophages and few giant cells in the stroma). Usually affects any large joint (most commonly the knee).



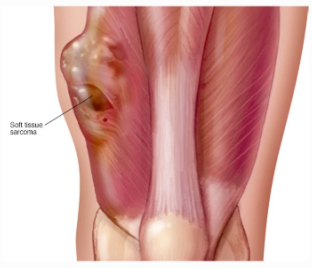


b. Localized giant cell tumor of tendon sheath (localized small hands tendons): commonly occurs in the distal aspect of joints of the **hand**. Sometimes causes pain due to pressure on a nerve. Only treated when symptomatic.



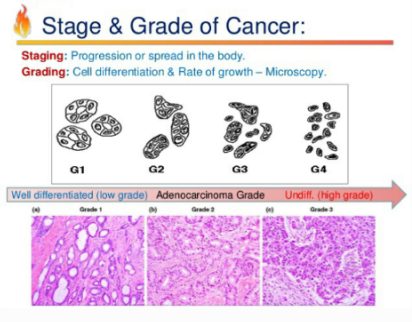


Soft tissue tumors:



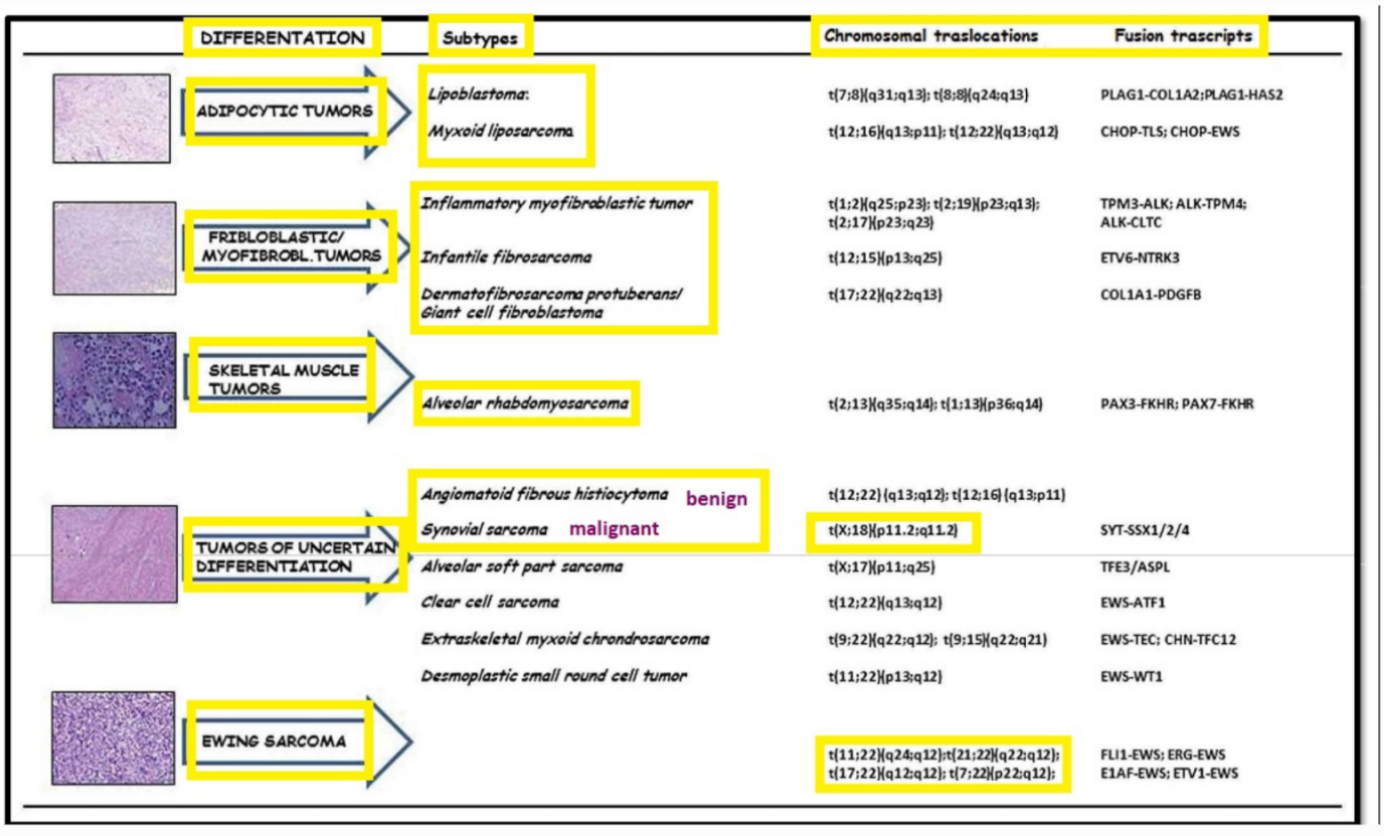
• Benign is much more common than malignant.
• Incidence is 1% with 2% cancer mortality.
• **Sarcomas** (the malignant tumors of soft tissue):
- Aggressive.
- Have **no precursor or preneoplastic lesions** (unlike dysplasia of the cervix, skin, or colon.
- Theory saye that they arise from **pluripotent mesenchymal stem cell which acquires somatic mutation.**
• There is a wide range of transferring from benign to highly malignant.
- the most common site for metastasis the **lung** (Hematogenous metastasizing).
- The most common site for sarcomas is the **extremities**, especially the **thigh**
- Sarcomas are usually **sporadic** but few can arise from **genetic mutations** such as tumor suppressor gene mutations.
- Patients with **neurofibromatosis type 1 (NF1)** are at higher risk of neurofibrosarcomas.
- Patients with **Gardner syndrome, Li-Fraumeni syndrome, Osler-Webber-Rendu Syndrome** are at higher risk of soft tissue tumors, especially sarcomas.
- Few sarcomas can occur after exposure to **radiation, burns, and toxins.**
- 15-20% of these tumors (especially sarcomas) have a **simple karyotype (a single signature mutation),** like **Ewing and synovial sarcoma**.
• 80-85% of sarcomas or aggressive malignant soft tissue tumors have a **complex karyotype** (genomic instability and a lot of mutations). Investigating these tumors for genetic abnormality is not useful because there will be multiple and many of these mutations specifically in **leiomyosarcoma (LMS) and pleomorphic sarcoma**.

Ewing sarcoma and synovial sarcoma ➡️ simple karyotype.
leiomyosarcoma (LMS) and pleomorphic sarcoma ➡️ complex karyotype.



• **Diagnosis**: grading and staging are important.
- Grade: how much the tumor looks like the primary cell of origin (well, moderate, poor diff.)
- Stage: The extent to which a cancer has developed by growing and spreading.
Pleomorphic sarcoma with multiple lung metastasis is an example of stage 4.
In low grade and localized tumors, surgical excision is curative.

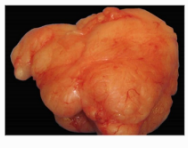
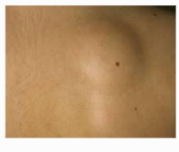
https://www.youtube.com/watch?v=qpkPKk3HxUQ



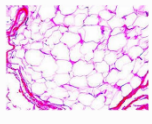
DIFFERENTATION	Subtypes	Chromosomal traslocations	Fusion trascripts
ADIPOCYTIC TUMORS	*Lipoblastoma:*	t(7;8)(q31;q13); t(8;8)(q24;q13)	PLAG1-COL1A2;PLAG1-HAS2
	Myxoid liposarcoma	t(12;16)(q13;p11); t(12;22)(q13;q12)	CHOP-TLS; CHOP-EWS
FRIBLOBLASTIC/ MYOFIBROBL.TUMORS	*Inflammatory myofibroblastic tumor*	t(1;2)(q25;p23); t(2;19)(p23;q13); t(2;17)(p23;q23)	TPM3-ALK; ALK-TPM4; ALK-CLTC
	Infantile fibrosarcoma	t(12;15)(p13;q25)	ETV6-NTRK3
	Dermatofibrosarcoma protuberans/ Giant cell fibroblastoma	t(17;22)(q22;q13)	COL1A1-PDGFB
SKELETAL MUSCLE TUMORS	*Alveolar rhabdomyosarcoma*	t(2;13)(q35;q14); t(1;13)(p36;q14)	PAX3-FKHR; PAX7-FKHR
TUMORS OF UNCERTAIN DIFFERENTIATION	*Angiomatoid fibrous histiocytoma* benign	t(12;22)(q13;q12); t(12;16)(q13;p11)	
	Synovial sarcoma malignant	t(X;18)(p11.2;q11.2)	SYT-SSX1/2/4
	Alveolar soft part sarcoma	t(X;17)(p11;q25)	TFE3/ASPL
	Clear cell sarcoma	t(12;22)(q13;q12)	EWS-ATF1
	Extraskeletal myxoid chrondrosarcoma	t(9;22)(q22;q12); t(9;15)(q22;q21)	EWS-TEC; CHN-TFC12
	Desmoplastic small round cell tumor	t(11;22)(p13;q12)	EWS-WT1
EWING SARCOMA		t(11;22)(q24;q12);t(21;22)(q22;q12); t(17;22)(q12;q12); t(7;22)(p22;q12);	FLI1-EWS; ERG-EWS E1AF-EWS; ETV1-EWS

Adipose tissue tumors: Lipomas & Liposarcomas

1. Lipoma:


- THE MOST COMMON SOFT TISSUE TUMOR.
- **Pathogenicity**: a clone that forms a benign tumor.
- **Site:** The most common location is subcutaneous tissue. (subcutis)
- Smaller than liposarcomas.
- **Gross appearance:** Soft, shiny, yellow, Well-encapsulated and well-circumscribed.



- **Histological appearance**: Mature fat cells (adipocytes).

Treatment: excision if they are big, start causing pressure, and their cosmetic appearance is not very good.

2. liposarcoma:

- MOST COMMON SARCOMAS IN ADULTS (>50 years).
- **Pathogenicity**: a clone that forms a malignant tumor.
- **Site**: The most common location is the extremities and retroperitoneum.
- Larger than lipomas.
- **Histological appearance:**

1. **Well-differentiated (atypical lipomatous tumor):** Difficult to diagnose because it looks like lipoma under the microscope. better prognosis.
2. **Myxoid**: classic, easy to diagnose under the microscope. good prognosis. t(12,16).
3. **Pleomorphic**: the most aggressive type, easy to diagnose, ugly looking. Bad prognosis.

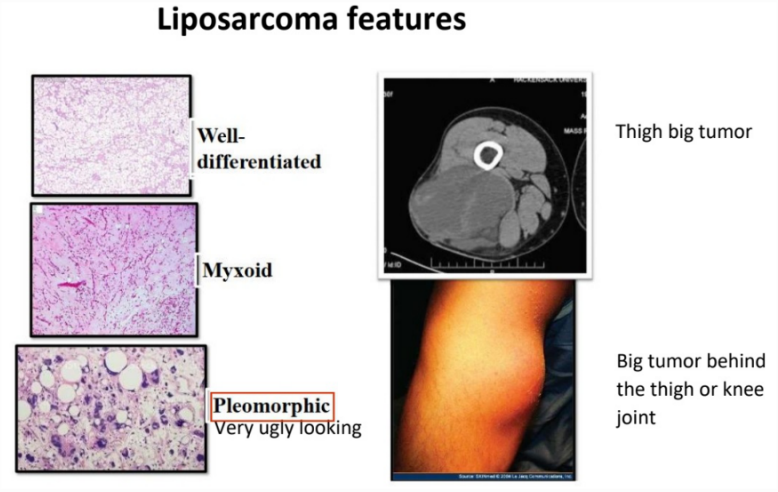
- **How to differentiate between a low grade liposarcoma (well-differentiated) and benign lipoma?** (both are histologically similar)

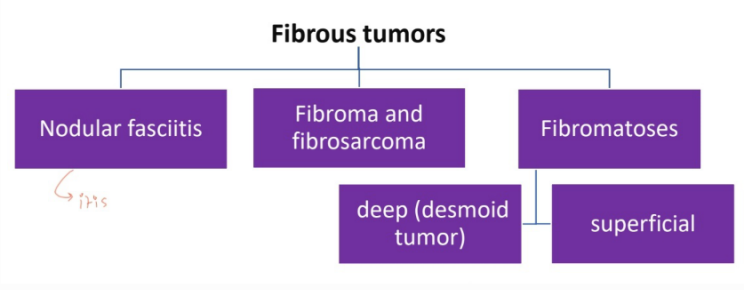
If the tumor is

- in the **Extremities or retroperitoneum** & is more than 10-15 cm in size

➡️ further analysis by **immunohistochemistry** or **FISH** analysis (more sensitive and specific) to **MDM2** gene mutations in chromosome number **12** is needed to confirm the diagnosis , IF IT TESTS POSITIVE for the MDM2 gene translocation

➡️ Liposarcoma.





Fibrous tumors:

- Nodular fasciitis:

- a clonal, t(17;22) producing MYH9-USP6 fusion gene.
- **clinical scenario:** previous history trauma, and recent rapid increase in the size of the tissue mass at the site of tumor.
- can occur anywhere.
- maybe self-limiting.
- The most important thing about nodular fasciitis is not to Mistakenly diagnose it as malignant because this exposes the patient to unnecessary harmful treatment.
- **Histological appearance: culture-like histology,** spindle cells which are bland and sometimes have frequent mitosis. Inflammatory cells such as plasma cells, neutrophils, and lymphocytes are sometimes seen.