Pathological Diagnosis of

Soft Tissue and Bone Tumors

incl. Molecular Diagnostics

PD Dr. med. Beata Bode
Institute of Surgical Pathology
University Hospital, Zurich

Review Course
„Musculoskeletal Oncology“

6th of October 2011
14.15 -14.40

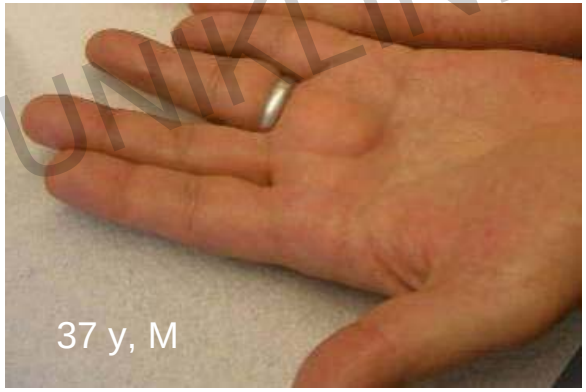
WHY PATHOLOGY?

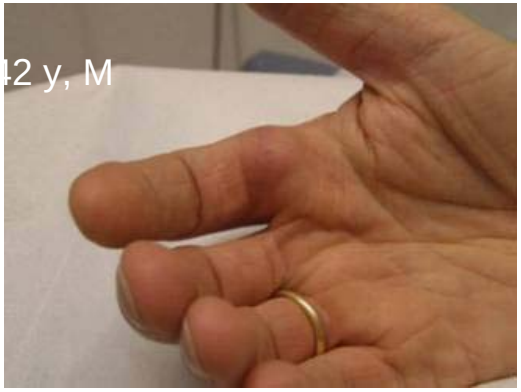
Patient with s/o muculo-skeletal neoplasia

What exactly is the problem?

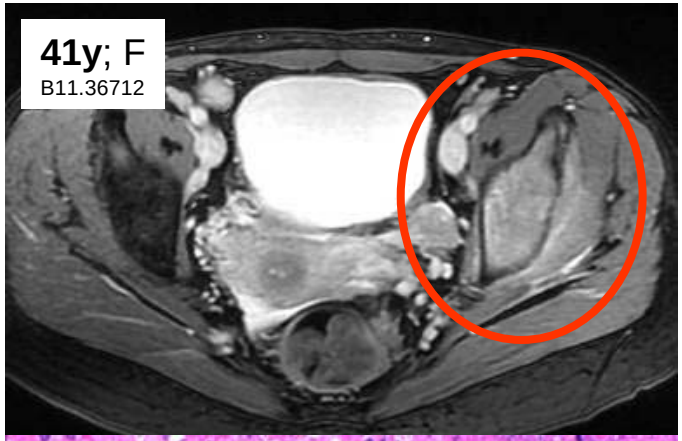
Multidisciplinary **team of physicians**

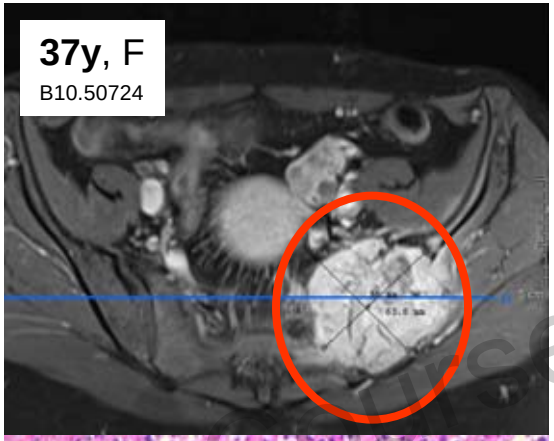
Tenosynovial giant cell tumor

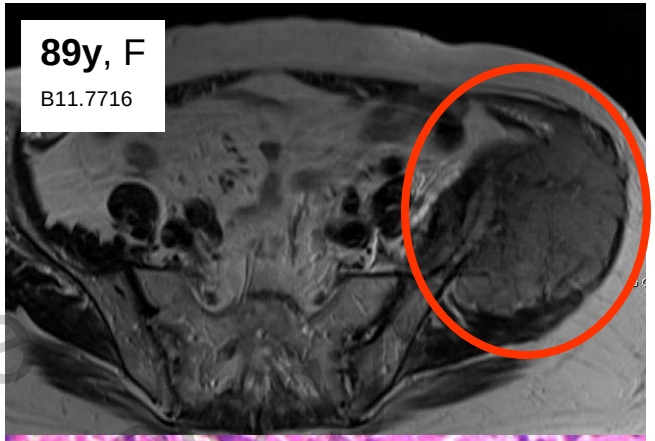


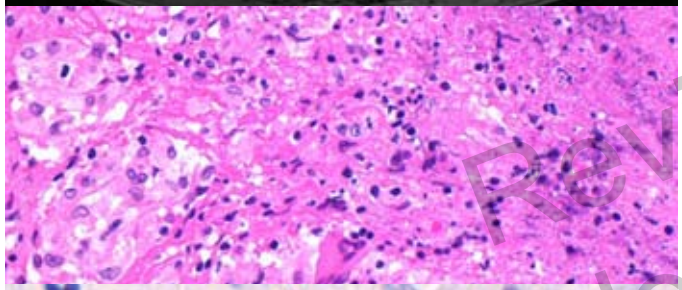


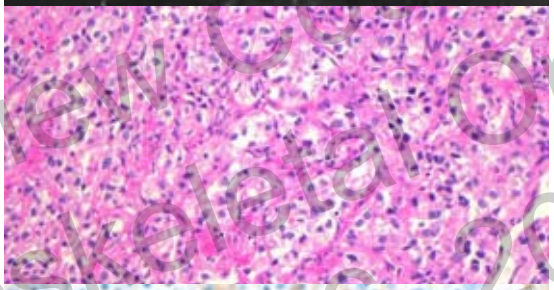
Epitheloid sarcoma

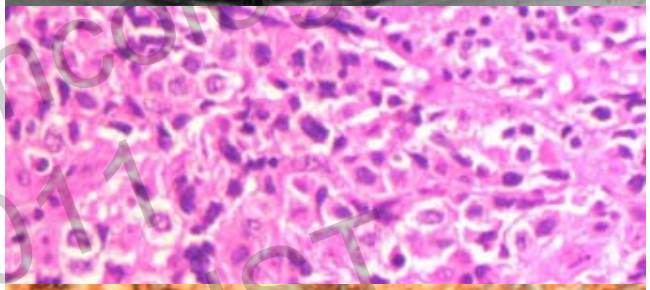


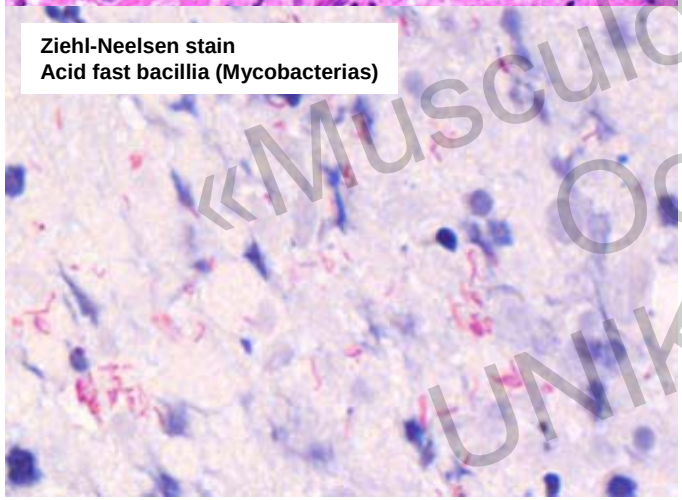


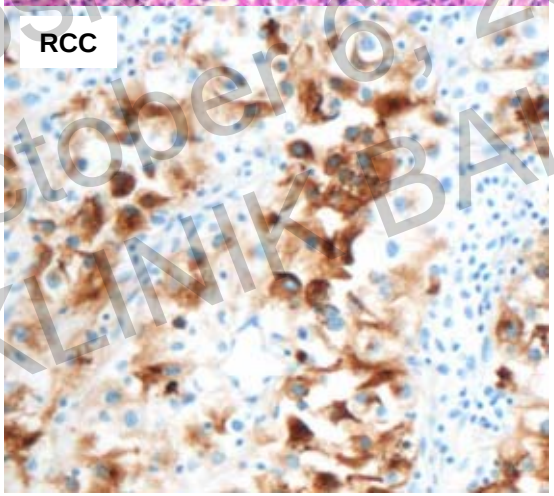


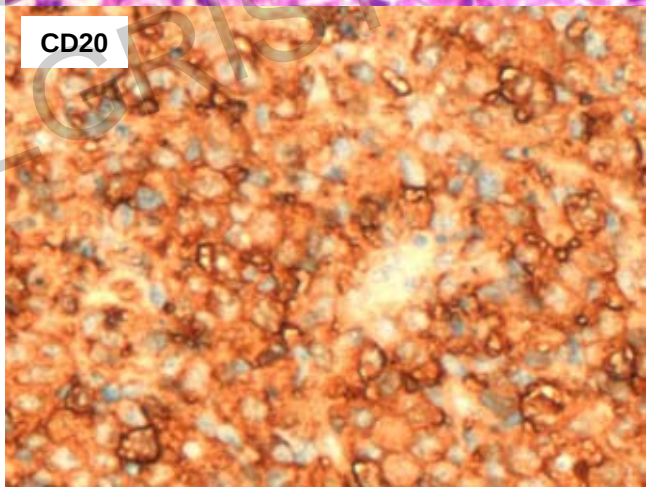












Osteomyelitis

Metastasis

Aggressive lymphoma

Primary Diagnostics

- Type of tumor
  - Benign
    - Non-neoplastic
    - Neoplastic
  - Malignant
    - Metastasis
      - Origin
    - Primary tumor
      - Malignancy grade
- Entity

Malignancy grade
Estimation of the expected clinical course according to histological and cytologial criteria
- Probability of metastases
- Survival

EXCLUSIVELY (!) ON UNTREATED PRIMARY TUMOR

- Therapy (Hormon receptors; CD20, Her2; EGFR, KRAS, CD117, etc…….)
- Prognosis (Translocations type?)

- Influence of therapy
  - chemotherapy (osteosarcoma, Ewing sarcoma)
  - radiotherapy (soft tissue sarcomas)

- Resection margins
  - Extremity sparing surgery

- Local recurrences
- Metastases

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Soft Tissue Sarcoma Trials: One Size No Longer Fits All

Pazopanib, a Multikinase Angiogenesis Inhibitor, in Patients With Relapsed or Refractory Advanced Soft Tissue Sarcoma: A Phase II Study From the European Organisation for Research and Treatment of Cancer–Soft Tissue and Bone Sarcoma Group (EORTC Study 62043)

Stefan Sleijfer, Isabelle Ray-Coquard, Zsuzsa Papai, Axel Le Cesne, Michelle Scurr, Patrick Schöffski, Françoise Collin, Lini Pandite, Sandrine Marreaud, Annick De brauwer, Martine van Glabbeke, Jaap Verweij, and Jean-Yves Blay

- Leiomyosarcomas
- Synovial sarcomas

Multicenter Phase II Trial of Sunitinib in the Treatment of Nongastrointestinal Stromal Tumor Sarcomas

Suzanne George, Priscilla Merriam, Robert G. Maki, Annick D. Van den Abbeele, Jeffrey T. Yap, Timothy Akhurst, David C. Harmon, Gauri Bhuchar, Margaret M. O'Mara, David R. D'Adamo, Jeffrey Morgan, Gary K. Schwartz, Andrew J. Wagner, James E. Butrynski, George D. Demetri, and Mary L. Keohan

- DSCRT
- SFT

Phase II Study of Sorafenib in Patients With Metastatic or Recurrent Sarcomas

Robert G. Maki, David R. D'Adamo, Mary L. Keohan, Michael Saulle, Scott M. Schuetze, Samir D. Undevia, Michael B. Livingston, Matthew M. Cooney, Martee L. Hensley, Monica M. Mita, Chris H. Takimoto, Andrew S. Kraft, Anthony D. Elias, Bruce Brockstein, Nathalie E. Blachère, Mark A. Edgar, Lawrence H. Schwartz, Li-Xuan Qin, Cristina R. Antonescu, and Gary K. Schwartz

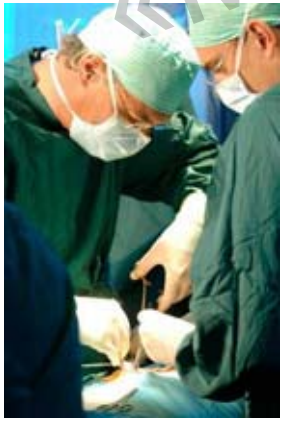
- Angiosarcomas

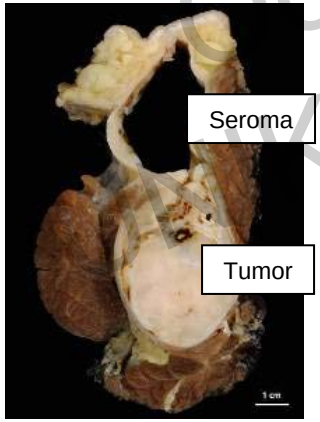
Open (surgical) biopsy

Excisional biopsy
(max 3-5 cm mass)

Incisional biopsy
(>5 cm)

Histology

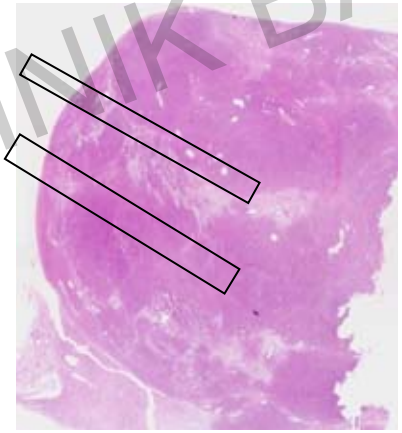




Needle biopsy

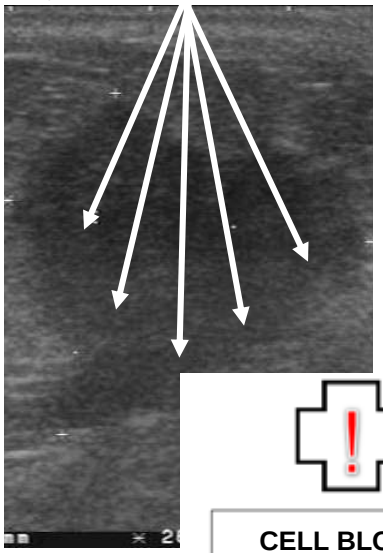
Core biopsy
Needle diameter
>1mm (18G)

Histology

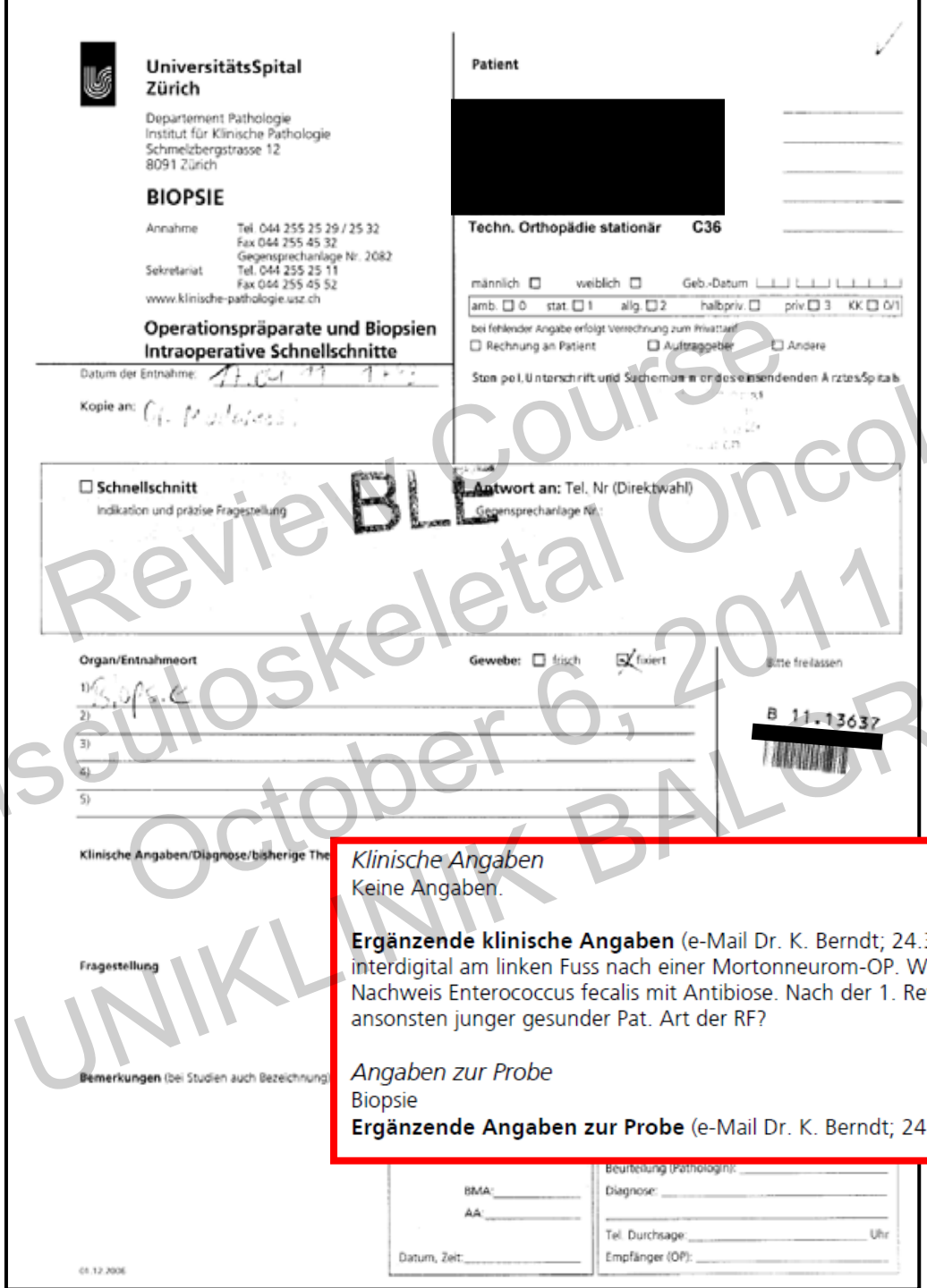


Fine needle biopsy
Needle diateter
<1mm (24G)

Cytology



CELL BLOCK



UniversitätsSpital Zürich

Departement Pathologie
Institut für Klinische Pathologie
Schmelzbergstrasse 12
8091 Zürich

BIOPSIE

Annahme Tel. 044 255 25 29 / 25 32
Fax 044 255 45 32
Gegensprechanlage Nr. 2082
Sekretariat Tel. 044 255 25 11
Fax 044 255 45 52
www.klinische-pathologie.usz.ch

Operationspräparate und Biopsien
Intraoperative Schnellschnitte

Datum der Entnahme:

Kopie an:

Patient

[redacted]

Techn. Orthopädie stationär C36

männlich ☐ weiblich ☐ Geb.-Datum

amb. ☐ 0 stat. ☐ 1 allg. ☐ 2 halbpriv. ☐ priv. ☐ 3 KK ☐ Ö/1

bei fehlender Angabe erfolgt Verrechnung zum Privattarif

☐ Rechnung an Patient ☐ Auftraggeber ☐ Andere

Stempel, Unterschrift und Sachgebiet des einsendenden Arztes/Spitals

☐ **Schnellschnitt**
Indikation und präzise Fragestellung

Antwort an: Tel. Nr (Direktwahl)
Gegensprechanlage Nr.:

BLE

Organ/Entnahmeort

1)
2)
3)
4)
5)

Gewebe: ☐ frisch ☒ fixiert ☐ ohne freilassen

B 11.13637

Klinische Angaben/Diagnose/bisherige The

Fragestellung

Bemerkungen (bei Studien auch Bezeichnung

BMA:
AA:
Datum, Zeit:

Beurteilung (Pathologin):
Diagnose:
Tel. Durchsage: Uhr
Empfänger (OP):

01.12.2006

Klinische Angaben
Keine Angaben.

Ergänzende klinische Angaben (e-Mail Dr. K. Berndt; 24.3.11): Chronischen Wunde interdigital am linken Fuss nach einer Mortonneurom-OP. Wundheilungsstörung mit Revision. Nachweis Enterococcus fecalis mit Antibiose. Nach der 1. Revision erneut keine Heilung. RF bei ansonsten junger gesunder Pat. Art der RF?

Angaben zur Probe
Biopsie
Ergänzende Angaben zur Probe (e-Mail Dr. K. Berndt; 24.3.11): interdigital Fuss links

OBLIGATORY DATA

Submission Form Biopsy

- **Primary diagnostics**
  - Age, gender
  - Topography (printouts of Rtx, CT or MRI scans)
  - Dynamics of the tumor growth
  - Known accompanying diseases (esp. malignant tumors!)
  - Any other relevant data (prior trauma? prior surgery? ect…)
- **Resection specimen**
  - Prior (neo-adjuvant) therapy (radiation, drugs / therap. substances)
  - Top. orientientation (thread mark, correlation with CT / MRI)
  - Relation / infiltration / distance to any critical, clinically relevant sites (resection margins, periosteum, ect)

TELL YOUR PATHOLOGIST

EVERYTHING (or almost) YOU KNOW ABOUT THE PATIENT

(in the interest of the patient and yourself)

Pathology is <u>not</u> about measuring concentrations

Pathology is an **<u>interpretation / consultation</u>**

Pathology is a very **<u>dynamic discipline</u>**

Pathologists ARE PHYSICIANS and want to help the patient (and you managing the patient)

Patient case

- 79 y, F
- Tumor, upper arm, several cm in diameter

- PathInst 1: Consult in Zurich

PI 1

Eingang 09.06.2011

Klinische Angaben: V. a. Sarkom Oberarm re.

Makroskopischer Befund AET/glu/ka

33086:

Ein halbiertes, 5,8 x 4,5 x 3cm messendes Exzisat. Dieses konfiguriert wie eine halbierte Hohlkugel, von welcher nur eine Hälfte eingesandt wurde. Die Aussenfläche von einer bräunlich glänzenden Kapsel bedeckt, die Innenseite gelblich-weisslich leicht höckerig, als Zyste konfiguriert. Auf Schnitt die Wandung der Zyste teils weisslich netzartig, teils gelblich imponierend.

PI 2

Eingang: 07.06.2011

Klinische Diagnose: Unklarer Tumor am rechten Oberarm.

Eingesandtes Material: Exzisat Oberarm rechts

Makroskopischer Befund: 13 g schweres flaches Präparat, angedeutet spindelförmig und einseitig teils glatt, 6,5 x 4,4 cm, maximal 1,4 cm dick. Die andere Seite ist teils stark zerklüftet. Das Gewebe ist beige-gelb und prall-elastisch. Auf lamellierenden Schnitten beiges solides Gewebe. (och/bl)

PI 3

Eingang : 08.06.2011

Klinische Diagnose: Verdacht auf Sarkom Oberarm rechts.

Makroskopischer Befund: Ein unregelmässig geformtes Weichteilexzisat, 7 x 5 x 3,5 cm. Fotodokumentation. Eine Seite konvex und von einer möglichen Faszie bedeckt, die andere Seite konkav und von gelb-weisslichen, tumorartigem Gewebe gebildet. Tuschemarkierung: Konvexe Seite schwarz, konkave Seite blau. Schnittfläche homogen beige-weisslich, leicht faserig. Angrenzend spärlich Fettgewebe (C). (eh/sba)

WHY?

Surgeon: Oncologists told me to do so.....

What about the resection margins?

Surgeon: I resected it with clear margins …..

PI 1

Pathologisch-anatomische Diagnose EMA/NW/ka
33086:
Oberarm rechts: Anteile eines hoch malignen pleomorphen Sarkoms.
G3 bei FNCLCC Score 6 (3, 1, 2) mit bis 13 Mitosen/10 HPF.

Kommentar

Zweifelsfrei handelt es sich um ein hochmalignes, pleomorphes Sarkom. Die zusätzliche Reaktion der Muskelmarker weist dabei jedoch auf einen myogenen Ursprung des Sarkoms hin.

PI 2

DIAGNOSE:
High grade Myxofibrosarkom im Exzisat aus Oberarm rechts.

Kommentar: *Das Präparat wird weitgehend durch den Tumor eingenommen. Das Tumorgewebe ist an der zerklüfteten Präparatseite randbildend.*
Tumorgrading nach FNCLCC-System: G3 (Score 6).

PI 3

Bern, 10.06.2011 vk/lr

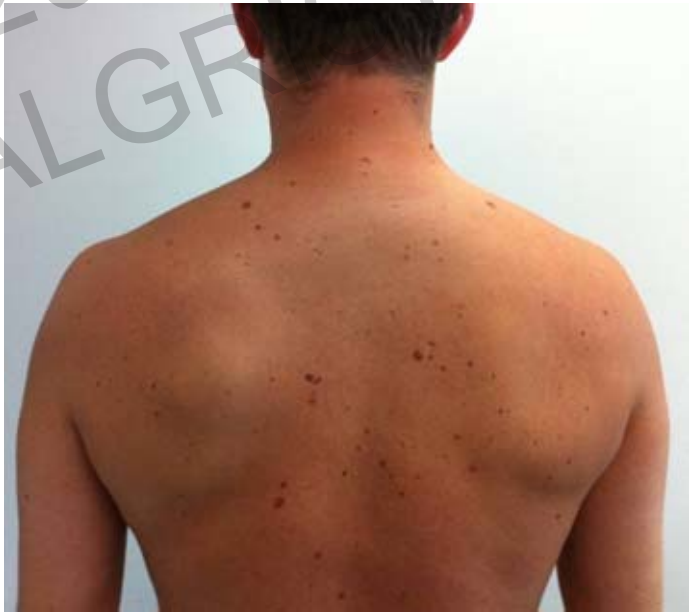
Diagnose:
Exzisat Oberarm rechts:
Sarkom (FNCLCC Score 4, Grad 2).

Kommentar:
Das Sarkom reicht breitflächig bis in einen tuschemarkierten Resektatrand.
Das Gewebe wird weiter immunhistochemisch untersucht. Sie erhalten einen Zweitbericht.

3rd report -> dedifferentiated liposarcoma, grade 3

- **NEVER split the biopsy or resection sample** sending only small fractions to different pathology labs (**malpractice**!!)
  - Tumor heterogeneity and variable experience of the histopathologist may lead to discrepant diagnoses – **and it is not the primary fault of the pathologists – it serves YOU right (pity on the patient)**
  - Problems in evaluating resection margins (if applicable)

- If you are not happy with the diagnosis (if you think it is not correct), **let the sample be send to other pathologists (any number you wish)** of your choice (usual practice among pathologists)



- **Work with a pathologist you know and trust – and communicate with him**

Sarcomas – epidemiology

USA 2007 (Gralow; JCO; 2008)

- 1 444 920 new diagnosed malignancies
- 9 220 soft tissue sarcomas (0.6%)
- 2 370 bone sarcomas (0.2%)
- 213 380 lung carcinomas
- 180 510 breast carcinomas
- 153 760 colon carcinomas
- 100 000 lymphome/leukaemia

Incidence of soft tissue sarcomas:
ca 25-30 new cases pro 1 000 000 / year:

Switzerland: ca 175-200 **Germany**: 2000 - 2500

Incidence of bone sarcoma:
ca 8 new cases pro 1 000 000 / year:

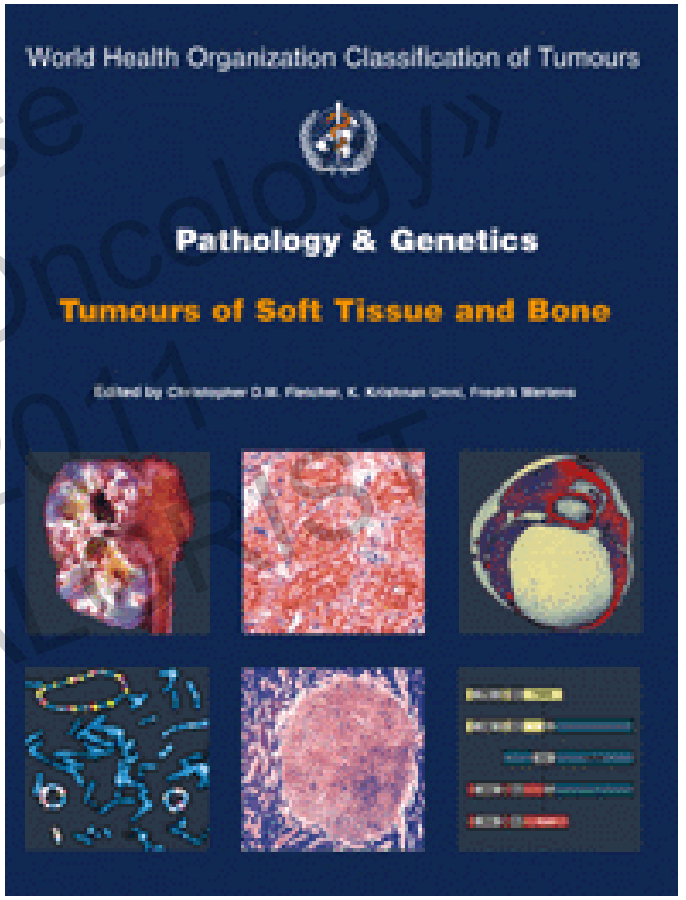
Schweiz ca 55-65, including ca 15 osteosarcomas **Germany:** 600-700

WHO 2002 **Classification**
Soft tissue and Bone Tumors

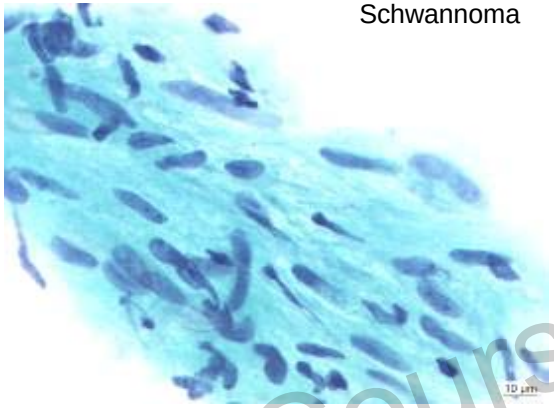
Clinical presentation
Histopathology

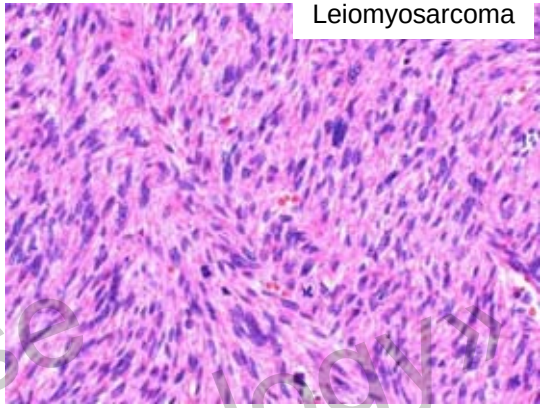
Immunhistochemistry

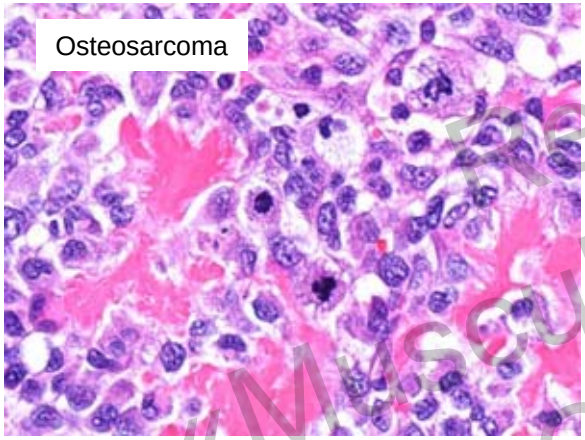
Molecular genetics

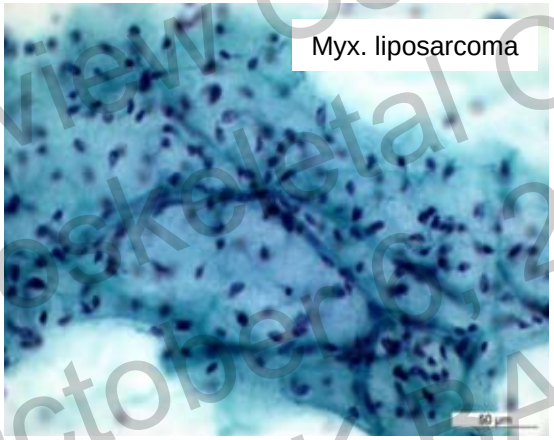


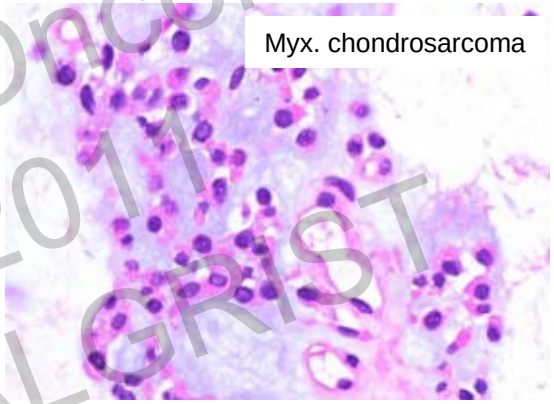
Heterogenity

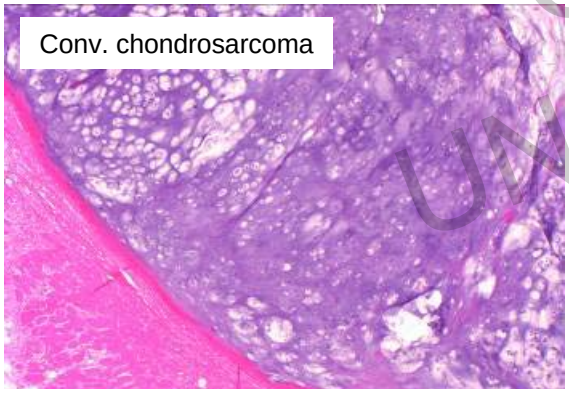


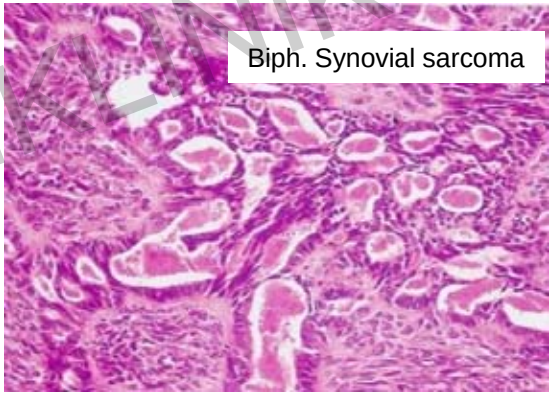


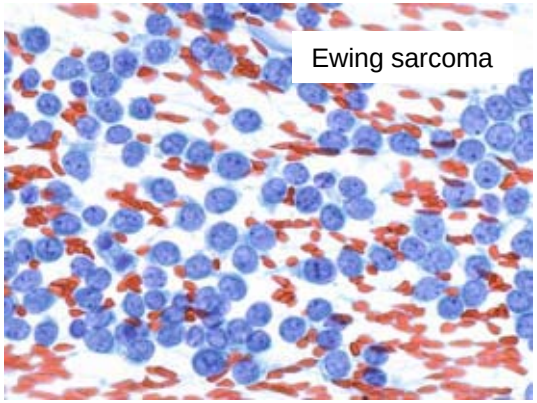






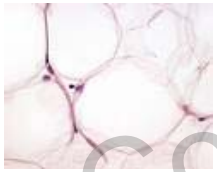






Nomenclature

Morphological similarity to mature tissue types

- lipomatous  lipoma, liposarcoma
- leiomyomatous  leiomyoma, Leiomyosarcoma
- fibroblastic  fibromatosis
- endothelial hemangioma, angiosarcoma
- etc ….

NOT the „cell of origin“
- eg. rhabdomyosarcoma
- eg. synovial sarcoma

IMMUNHISTOCHEMISTRY

line of differentiation

- myogenic differentiation
  - Actin, calponin,
  - Desmin caldesmone
  - Myogenin, MyoD1
- neurogenic differentiation (S100, NSE)
- endothelial differentiation (CD31, FVIII)

- epithelial markers (cytokeratins, EMA)
- lymphatic markers (CD45, CD20, CD3, CD68, CD30…..)
- melanocytic markers (S100, HMB45)

- CD34 (DFSP, Kaposi sarcoma, spindel cell lipom, endothel)
- CD99 (Ewing sa, synovial sa, SFT, mes. chondro sarcoma)

Line of differentiation uncertain

NOT similar to any body tissue

- Ewing sarcoma / PNET

- Myxomas
- Epitheloid sarcoma
- Alveolar soft part sarcoma
- Clear cell sarcoma

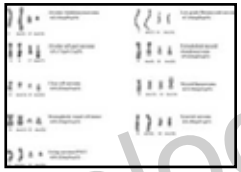
- Ossifying fibromyxoid tumor **(OFMT)**
- Desmoplastic small round cell tumor **(DSCRT)**
- Pleomorphic hyalinizing angiectatic tumor **(PHAT)**
- Myxo-inflammatory fibroblastic sarcoma **(MIFS)**
- Tumor with perivascular epitheloid differentiation **(PECom)**

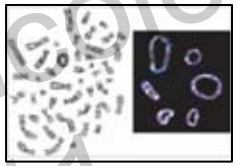
- Phosphaturic mesenchymal tumor (oncogenic osteomalacia)

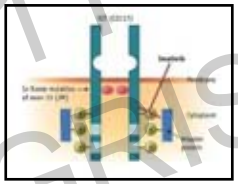
- ……

CYTOGENETICS & MOLECULAR BIOLOGY

Genetic event precursor (stem) cell







- Translocation (synovial sarcoma, DFSP,…)
- Amplification (atypical lipomatous tumor)
- Point mutation (GIST)
- Deletion (epitheloid sarcoma)
- etc…

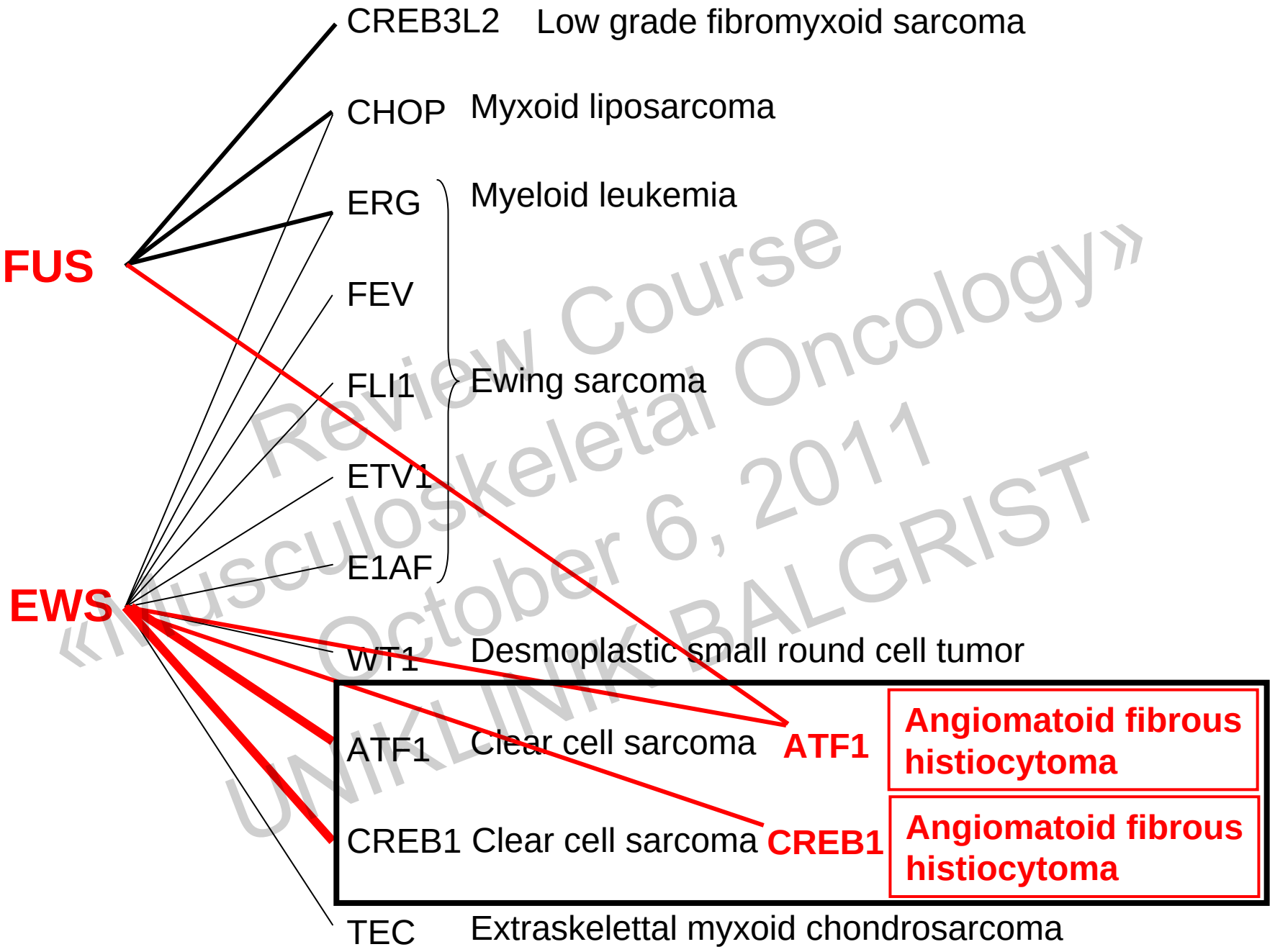
Specific: eg. *SYT-SSX* -> synovial sarcoma

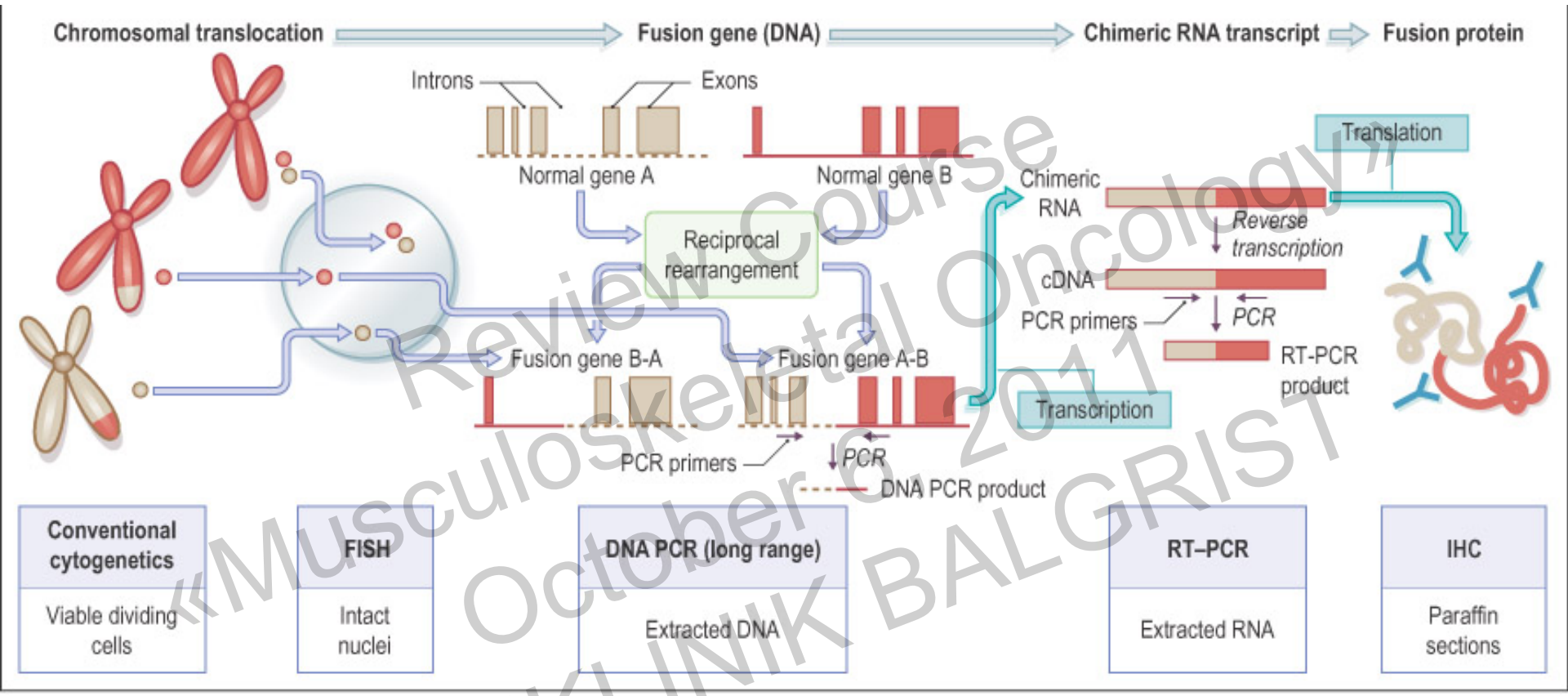
Exceptionally the same translocation in different tumor types

EWS-AFT1 or EWS-CREB1 in

- clear cell sarcoma (malignant melanoma of soft tissue)

- angiomatoid fibrous histiocytoma

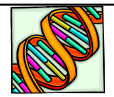




Frequency of soft tissue sarcoma types

Ca: 1960 – 1980
- Malignant fibrous histiocytoma (MFH)
- Liposarcoma
- Fibrosarcoma
- Leiomyosarcoma

Immunhistochemistry

Molecular genetics 

1990 - 2000
- Liposarcoma
- Myxofibrosarcoma
- Leiomyosarcoma
- Pleomorphic undifferentiated sarcoma

1: Am J Surg Pathol. 1992 Mar;16(3):213-28.

Comment in:
Am J Surg Pathol. 1992 Oct;16(10):1023-4.
Am J Surg Pathol. 1993 Apr;17(4):422-3.

Pleomorphic malignant fibrous histiocytoma: fact or fiction? A critical reappraisal based on 159 tumors diagnosed as pleomorphic sarcoma.

Fletcher CD.

Department of Histopathology, St. Thomas's Hos

Pleomorphic malignant fibrous histiocytoma (
adulthood, but no definable criteria exist for
specific differentiation. To determine the vali
sarcomas have been reassessed morpholog
these 97 cases (63%) proved to be specific
neoplasms, and 42 were unclassifiable (of w
these cases were eligible for consideration a
the other tumors studied, nor was this grou
true monocyte/macrophage differentiation. I
group of poorly differentiated neoplasms, a
sufficient effort, a specific line of differentiati
tumors; with advances in investigative techr
diminish further in the future.

- 97 (63%) other specific sarcoma types
- 20 non mesenchymal (NHL, Ca, melanoma)
- 42 non classified
  - 21 small or necrotic biopsies
  - 20 pleomorphic sarcoma NOS

Cytogenetic Analysis of 46 Pleomorphic Soft Tissue Sarcomas and Correlation With Morphologic and Clinica
A Report of the CHAMP

Fredrik Mertens,[1*] Christopher D. M. Fletcher,[7] F
Felix Mitelman,[1] Juan Rosai,[8] Anders Rydholm,[2] R
Roberta Vanni,[4,10] and Helena Willén[3]

[1]Department of Clinical Genetics, University Hospital, Lund,
[2]Department of Orthopedics, University Hospital, Lund, Swe
[3]Department of Pathology and Cytology, University Hospita
[4]Center for Human Genetics and Flanders Institute of Biotec
[5]Department of Oncologic Surgery, University of Leuven, Be
[6]Department of Pathology, University of Leuven, Belgium
[7]Department of Pathology, Brigham & Women's Hospital, H
[8]Department of Pathology, Memorial Sloan-Kettering Cance
Italy

GENES, CHROMOSOMES & CANCER 22:16–25 (1998)

- 8 lipogenic (4 pleo, 3 dediff, 1 combined)
- 19 myogenic (11 LMS, 1 rhabdo, 4 NOS)
- 8 myxofibrosarcoma
- 1 MPNST
- 1 extraskel osteosarcoma
- 1 mesenchymoma (dediff lipo?)
- 1 sarcoma resembling prolif fasciitis

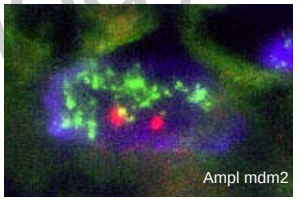
- 7 pleomorphic sarkoma NOS

Problem entitity (1963, Stout)

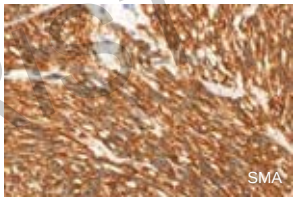
Malignant Fibrous Histiocytoma **(MFH)**

1. Myxoid
   Myxofibrosarcoma, …..

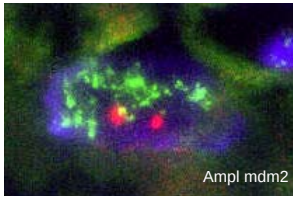
2. Pleomorphic-storiform
   Dedifferentiated liposarcoma, ….



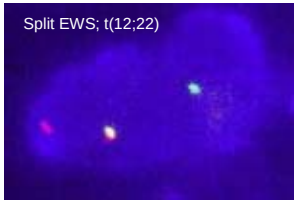
3. Giant cell
   Giant cell containing leiomyosarcoma, .



4. Inflammatoric
   Dedifferentiated liposarcoma, …..



5. Angiomatoid
   Specific, genetically def. entity



Liposarcoma

Low grade (G1) → High grade (G3)

1. Well differentiated (G1)
   Dedifferentiated (G2-3)

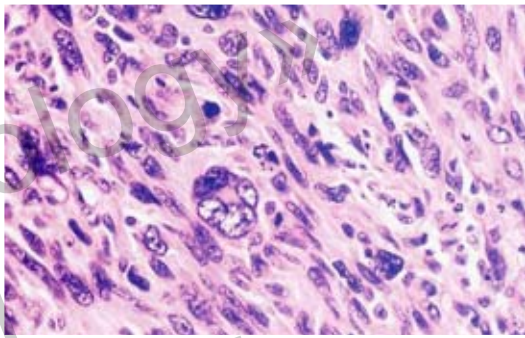
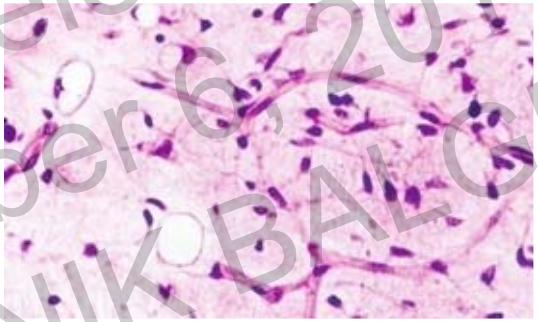
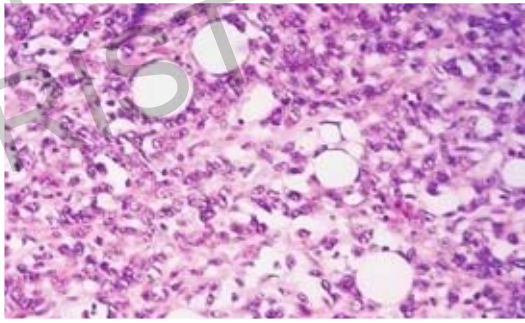
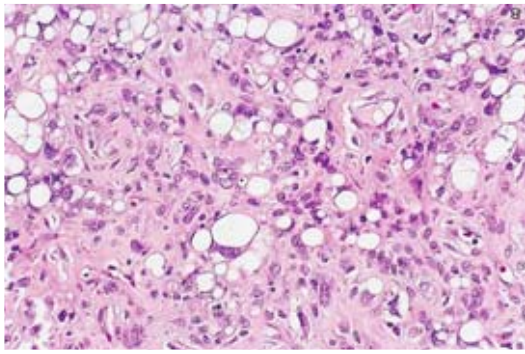
Ring or giant chromosomes 12q
Amplicon *mdm2/cdk4*

2. Myxoid (G1)
   Round cell (G2-3)

Translocation t (12;16)

3. Pleomorphic (G3)

Komplex karyotype

Two groups of sarcoma

with <u>simple</u> karyotypes and **<u>WITH</u>** typical translocations

- Synovial sarcoma
- Ewing sarcoma / PNET
- Myxoid liposarcoma
- ….

with <u>komplex</u> karyotypes **<u>WITHOUT</u>** typical translocations

- Leiomyosarcoma
- Myxofibrosarcoma
- Osteosarcoma
- …

Histology + Immunhistochemistry + **Molecular genetics (FISH+PCR)**

Histology +/- Immunhistochemistry

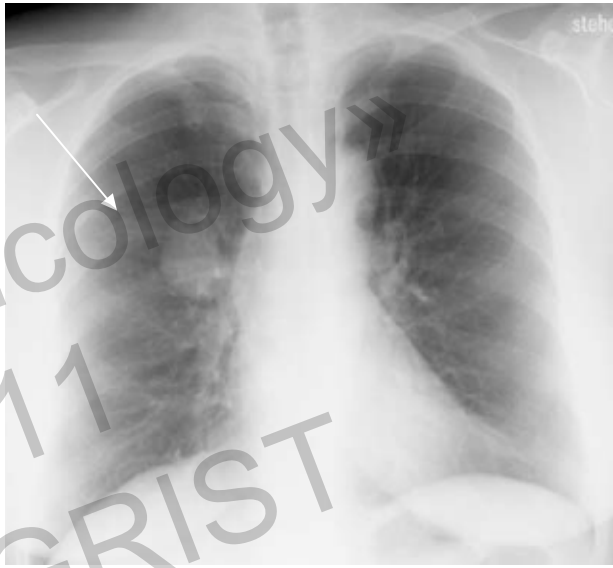
TABLE 4–1 **RECURRENT CHROMOSOMAL TRANSLOCATIONS IN BENIGN AND MALIGNANT SOFT TISSUE TUMORS**

Soft tissue tumor	Translocation	Gene fusion	Approximate prevalence[1]
Alveolar rhabdomyosarcoma	t(2;13)(q35;q14)	*PAX3-FKHR*	65%
	t(1;13)(p36;q14)	*PAX7-FKHR*	15%
Angiomatoid fibrous histiocytoma	t(2;22)(q33;q12)	*EWS-CREB1*	*
	t(12;22)(q13;q12)	*EWS-ATF1*	*
	t(12;16)(q13;p11)	*FUS-ATF1*	*
Alveolar soft part sarcoma	t(X;17)(p11;q25)[2]	*ASPL-TFE3*	>95%
Clear cell sarcoma	t(12;22)(q13;q12)	*EWS-ATF1*	>90%
	t(2;22)(q33;q12)	*EWS-CREB1*	*
Dermatofibrosarcoma protuberans/giant cell fibroblastoma	t(17;22)(q21;q13)[3]	*COL1A1-PDGFB*	>90%
Desmoplastic fibroblastoma	t(2;11)(q31;q12)	Unknown	*
Desmoplastic small round cell tumor	t(11;22)(p13;q12)	*EWS-WT1*	>95%
Epithelioid hemangioendothelioma	t(1;3)(p36.3;q25)	Unknown	*
Extraskeletal myxoid chondrosarcoma	t(9;22)(q22-q3;q12)	*EWS-NR4A3*	75%
	t(9;17)(q22;q11)	*TAF15-NR4A3*	25%
Ewing sarcoma/PNET	t(11;22)(q24;q12)	*EWS-FLI1*	90%
	t(21;22)(q22;q12)	*EWS-ERG*	5%
	t(7;22)(p22;q12)	*EWS-ETV1*	<1%
	t(2;22)(q33;q12)	*EWS-FEV*	<1%
	t(17;22)(q12;q12)	*EWS-E1AF*	<1%
	t(16;21)(p11;q22)	*FUS-ERG*	<1%
Fibromyxoid sarcoma (low-grade)	t(7;16)(q33;p11.2)	*FUS-CREB3L2*	>95%
	t(11;16)(p13;p11.2)	*FUS-CREB3L1*	<5%
Giant cell tumor of tendon sheath	t(1;2)(p13;q37)	*CSF1–COL6A3*	*
Infantile fibrosarcoma	t(12;15)(p13;q26)	*ETV6-NTRK3*	>95%
Inflammatory myofibroblastic tumor	t with 2p23	*ALK* fusions	>50%
Lipoblastoma	t with 8q12	*PLAG1* fusions	*
Lipoma, ordinary	t with 12q15	*HMGA2* fusions	*
	t with 6p21	*HMGA1* rearrangements[4]	*
Myxoid/round cell liposarcoma	t(12;16)(q13;p11)	*FUS-CHOP*	>95%
	t(12;22)(q13;q11)	*EWS-CHOP*	<5%
Pericytoma	t(7;12)(p2;q13)	*ACTB-GLI*	*
Synovial sarcoma	t(X;18)(p11.2;q11.2)	*SYT-SSX1*	65%
		SYT-SSX2	35%
		SYT-SSX4	<1%

80 y old woman

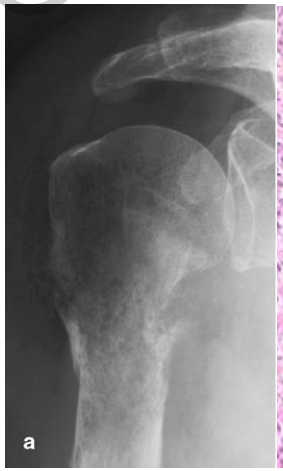
1989

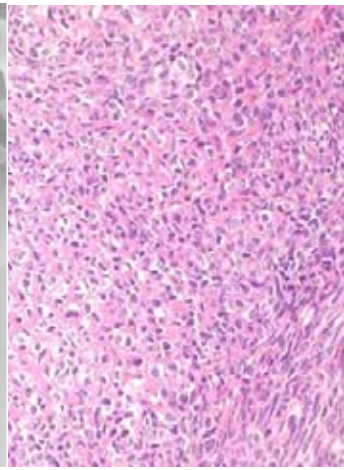
- Tumor of the lung
- diagnosis: **Atypical carcinoid**



2001

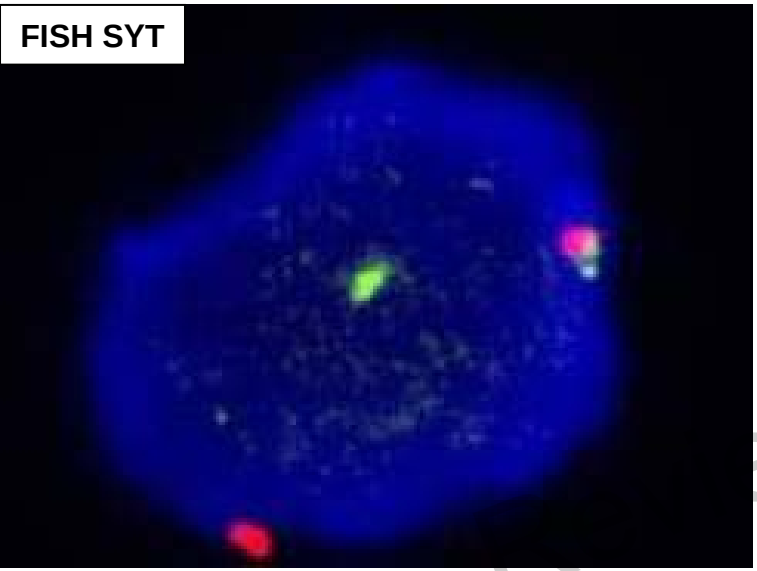
- Locally advanced, radiologically malignant humerus tumor
- Diagnosis: **Small cell osteosarcoma**

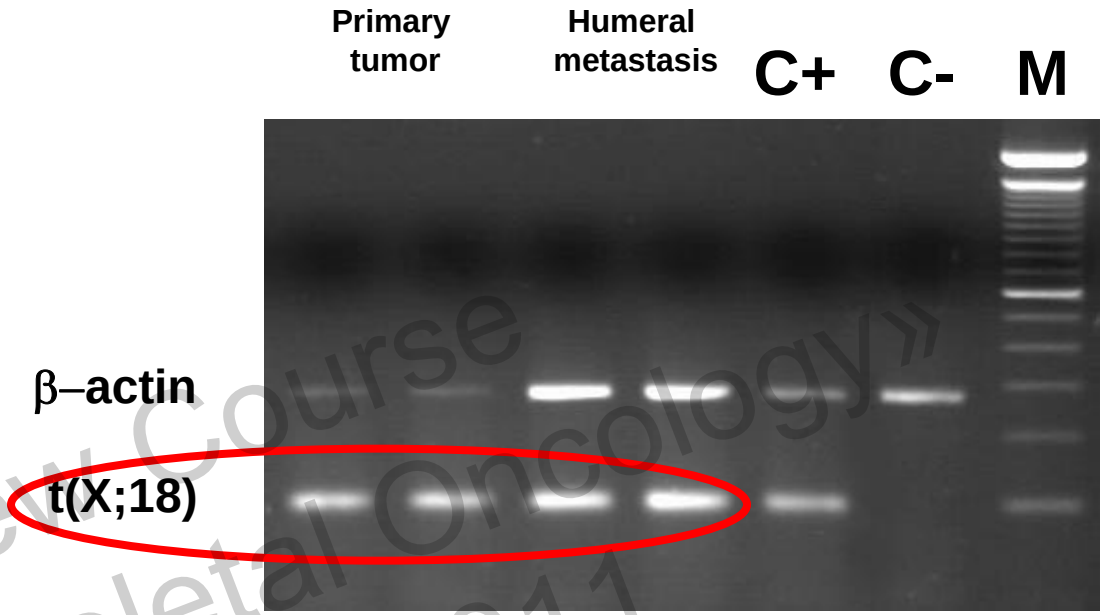




2003

- Local recurrence upper arm

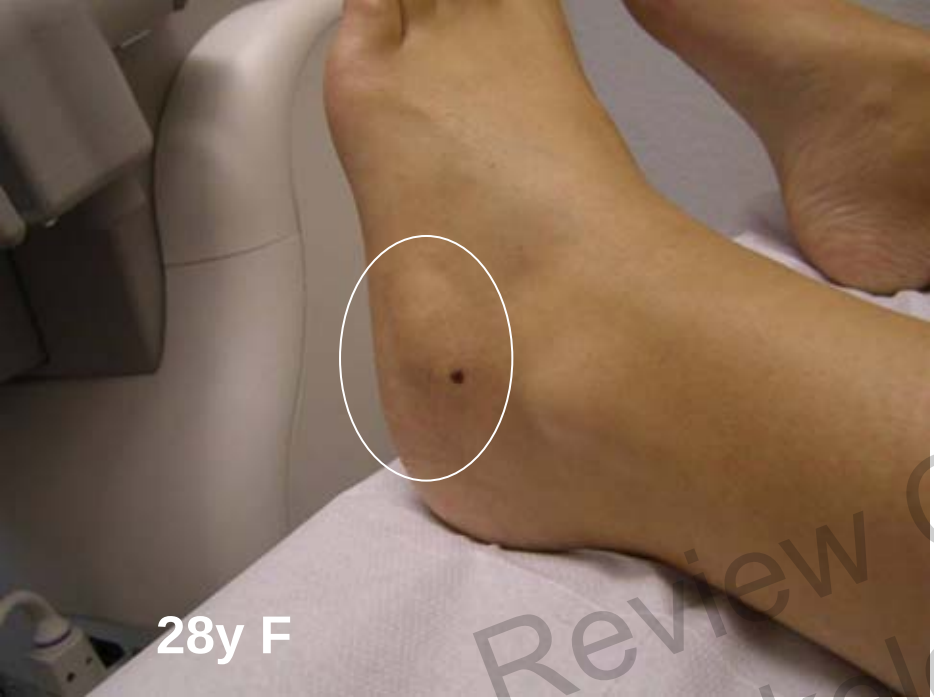


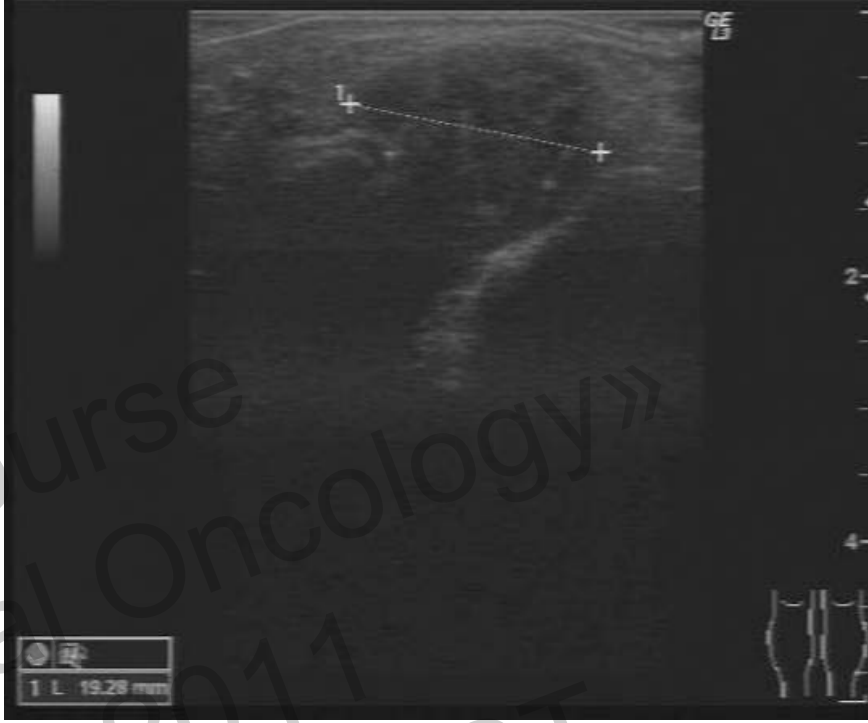


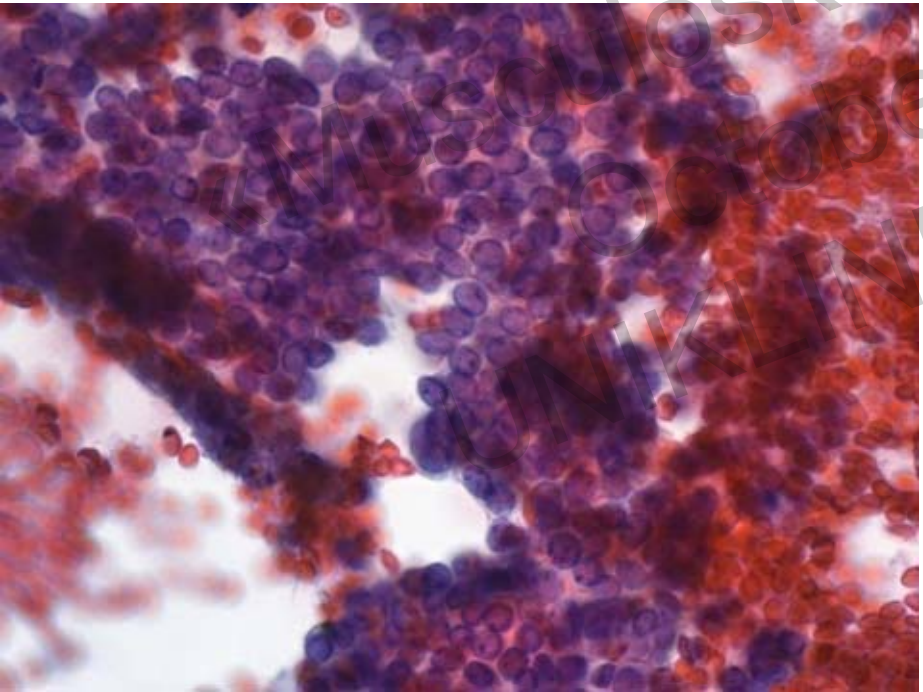
B. Bode-Lesniewska · J. Hodler · A. von Hochstetter · L. Guillou · U. Exner · R. Caduff

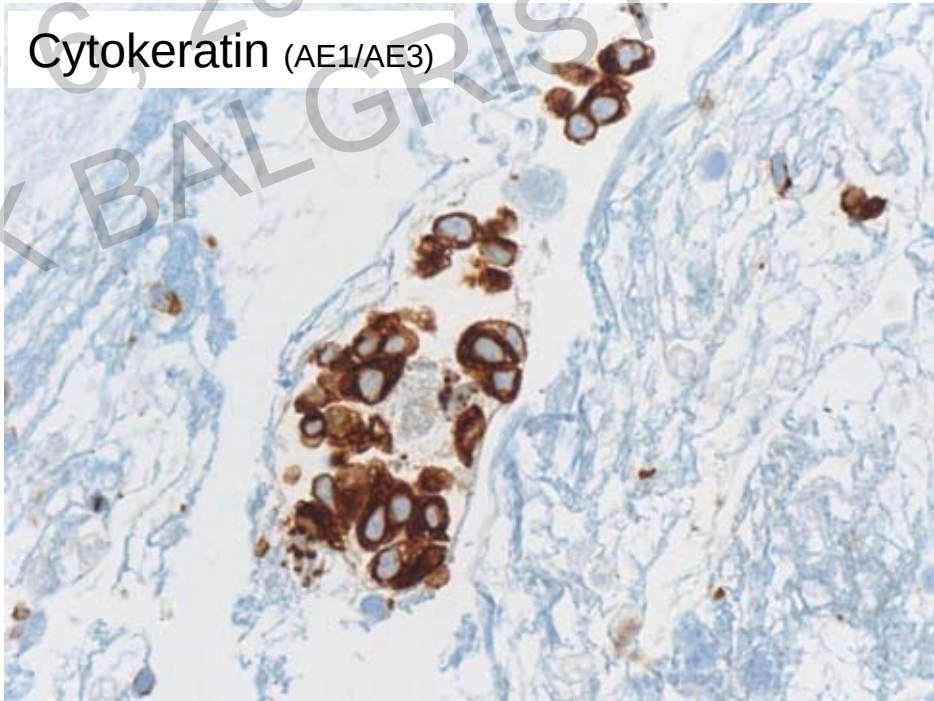
Virchows Arch (2005) 446: 310–315

Late solitary bone metastasis of a primary pulmonary synovial sarcoma with SYT-SSX1 translocation type: case report with a long follow-up

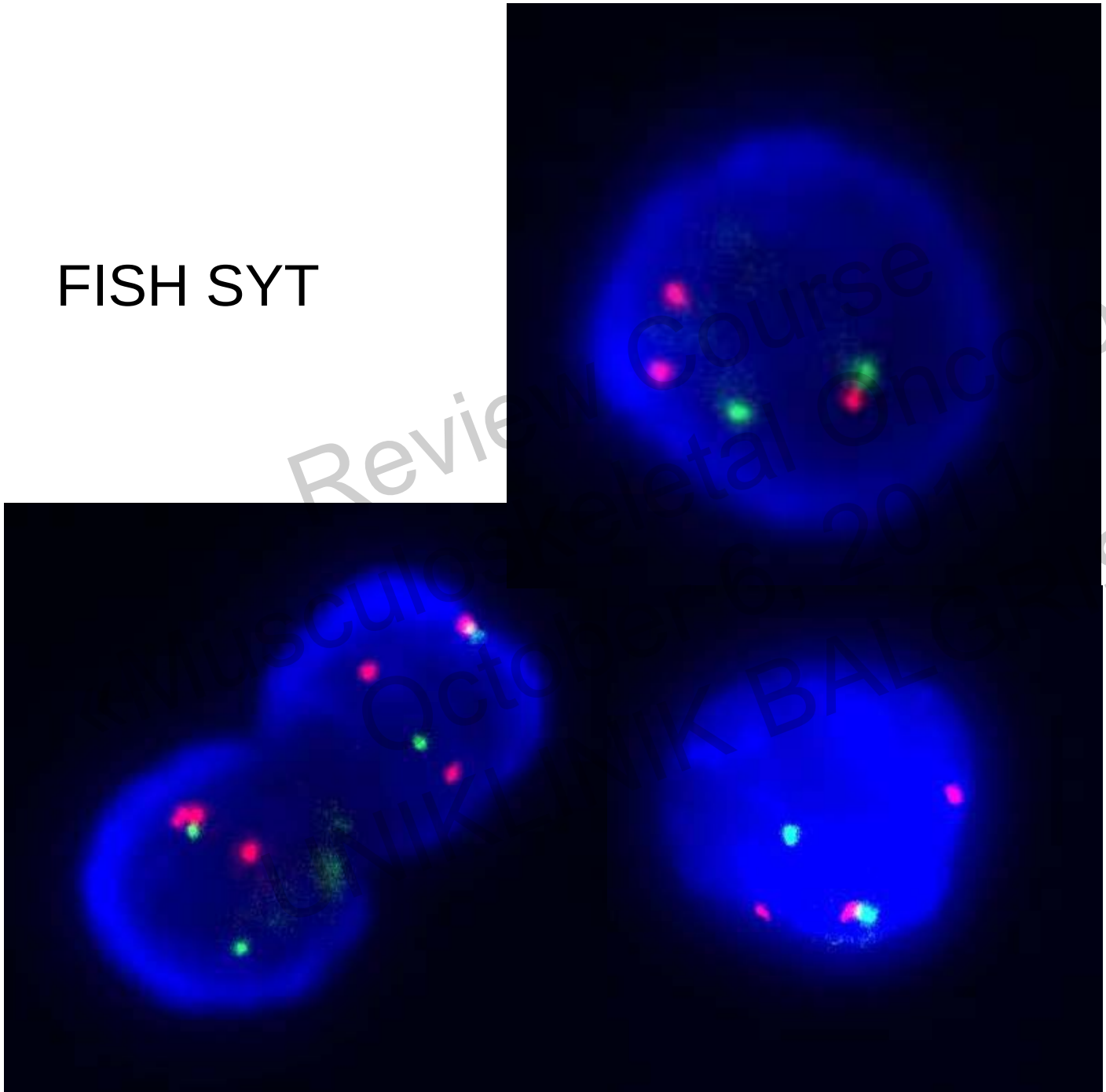




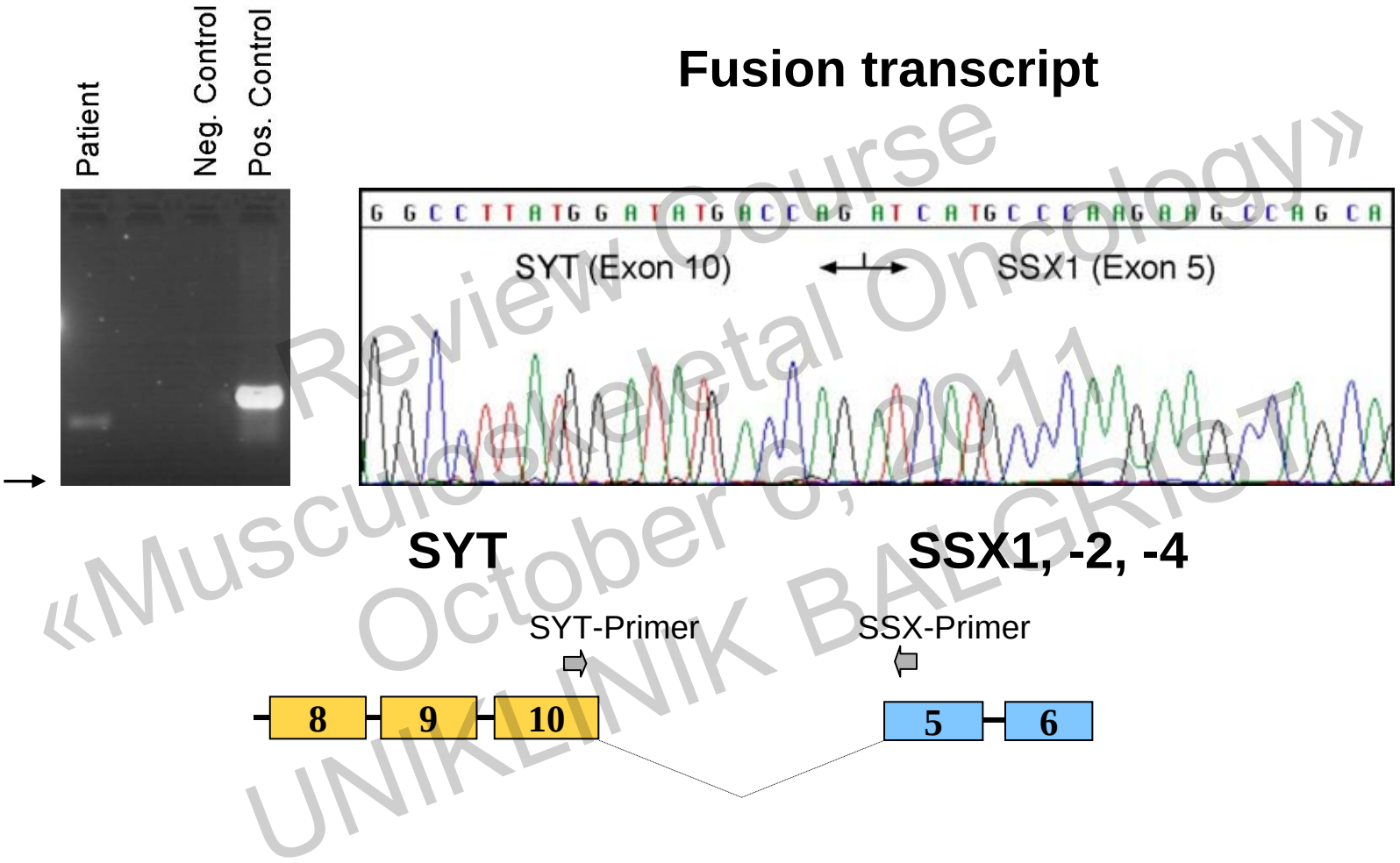




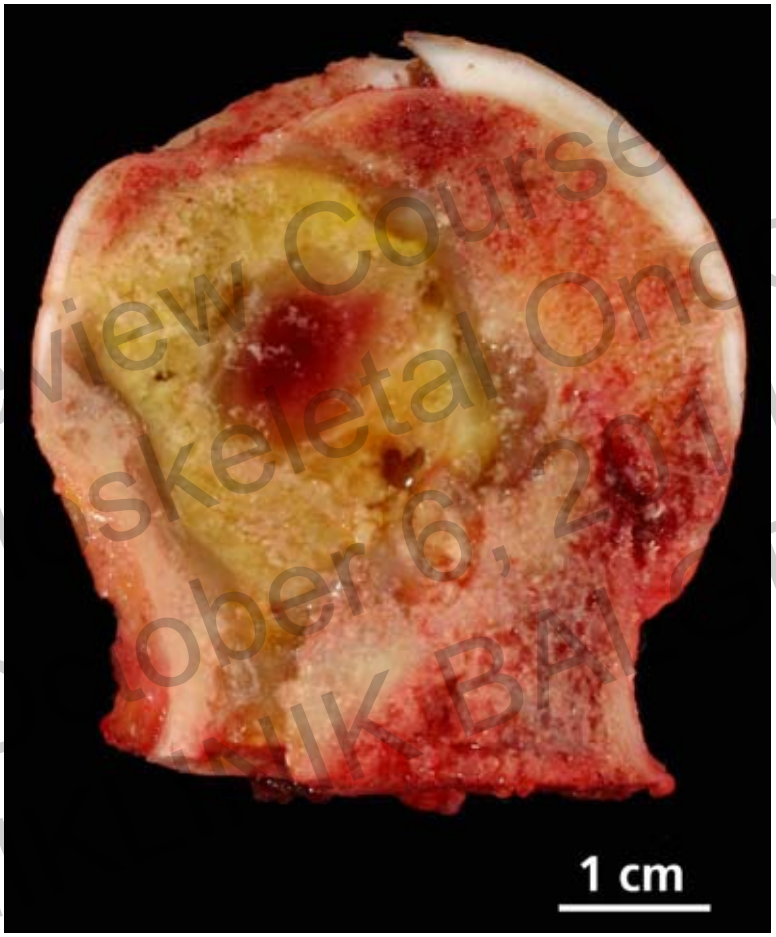
FISH SYT



t(X;18) RT-PCR / Sequencing



Biphasic synovial sarcoma



Metastasis: most frequent malignant tumor of the bone (especially in adults)

Bone is following lung and liver the 3rd most common target organ of metastases

Primary tumors:

- Breast
- Lung
- Prostate
- Kidney
- Thyroid

ca 95% of the cases

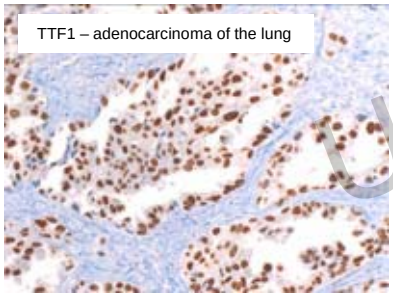
Metastasis as a **first manifestation** of a tumor

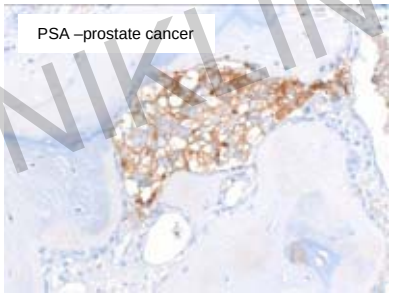
Solitary metastasis: DD primary bone tumor

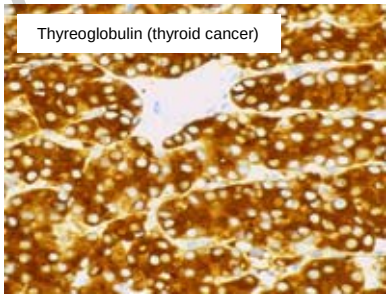
Two or more **different primary tumors**

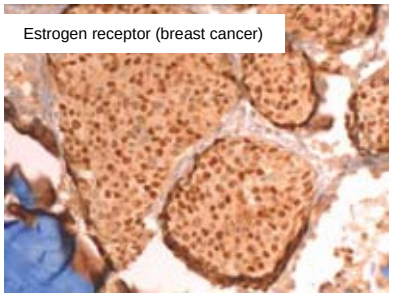
Biopsy (mostly with immunhistochemistry and/or mogecular studies)

- helpful in the **search of the primry tumor**
- analysis of the **predictive markers** (ER, PR, Her2, EGFR,….)









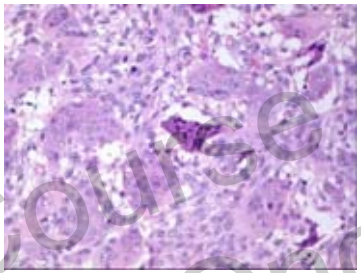
Primary Bone Tumors
WHO 2002

According to the type of the extracellular matrix

- **Osteogenic tumors**
  - -Osteoid osteoma
  - -Osteoblastoma
  - -**Osteosarcoma**
- **Chondrogenic tumors**
  - -Osteochondroma
  - -(En-)Chondroma
  - -Chondroblastoma
  - -Chondromyxoid fibroma
  - -**Chondrosarcomaa**
- **Fibrous / fibro-histiocytic tumors**
  - - Desmoplastic fibroma
  - - **Fibrosarcoma**
  - - Benign fibrous histiocytoma
  - - **Malignant fibrous histiocytoma**

- **Ewing sarcoma / PNET** (Peripheral NeuroEctodermal Tumor)

- **Giant cell tumor of bone**



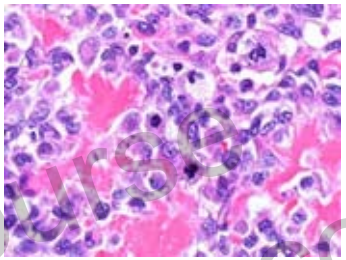
- Tumors/Lesions of **unclear origin / differentiation**

  - Simple bone cyst
  - Aneurysmatic bone cyst → typical translocation (USP6 17p13)
  - Fibrous dysplasia → Akt. mutation GNAS gene
  - Langerhans cell histiocytosis

- Metastases
- Hematopoietic tumors (plasmozytoma, lymphoma)
- Notochordal tumors (chordoma)
- Soft tissue tumores (angiosarcoma, leiomyosarcoma, …..)

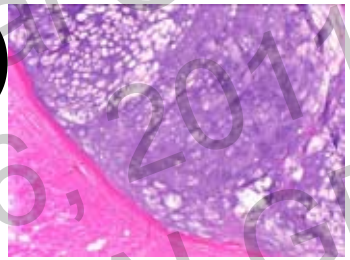
Frequency of the primary malignanr bone tumors

- **Osteosarcoma (35%)**



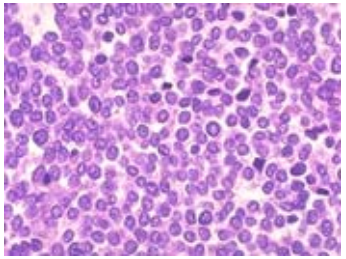
- Osteoblastic
- Chondroblastic
- Fibroblastic
- Small cell
- Teleangiectatic
- Parosteal
- Periosteal

- **Chondrosarcoma (25%)**



- Conventional
- Dedifferentiated
- Mesenchymal
- Myxoid
- Clear cell

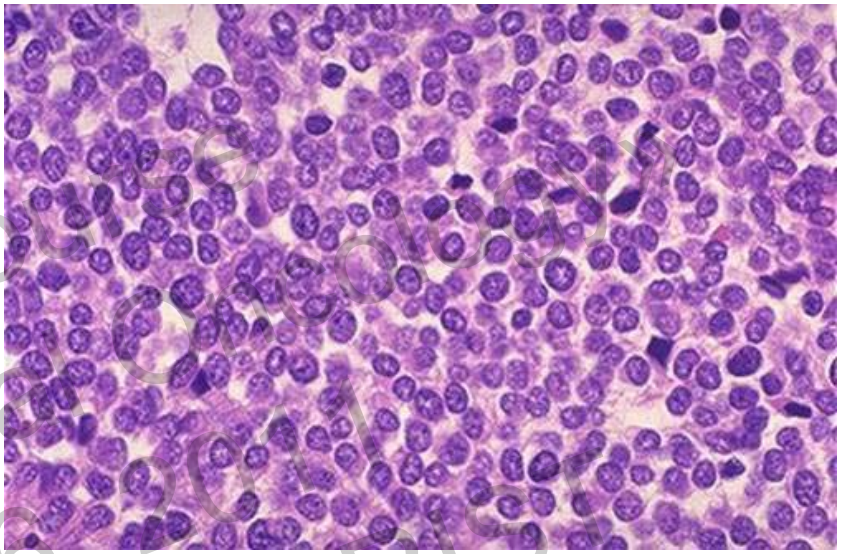
- **Ewing sarcoma (16%)**



- Chordoma (8%)
- MFH (malignant fibrous histiocytoma) (5%)

Small, blue and round cell tumors

Ewing sarcoma / PNET



Neuroblastoma
Rhabdomyosarcoma
Small cell osteosarcoma
Mesenchymal chondrosarcoma
Round cell liposarcoma
Poorly differentiated synovial sarcoma
Desmoplastic small and round cell tumor (DSRCT)

Lymphoma / leukemia
Small cell carcinoma

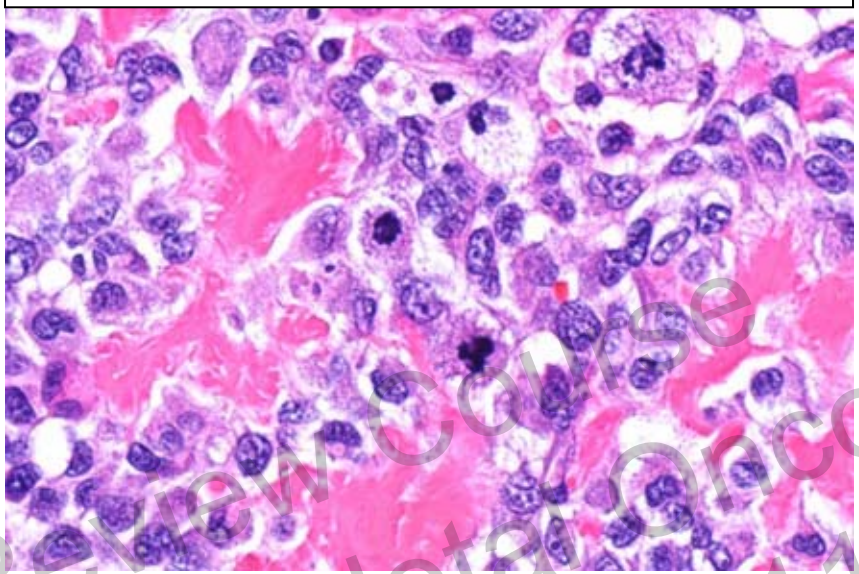
Immunhistochemistry + Molecular genetics

- Influence of the therapy
  - Chemotherapy (osteosarcoma, Ewing sarcoma)
  - Radiotherapy (soft tissue sarcomas)

- Resection margins
  - Extremity sparing resections

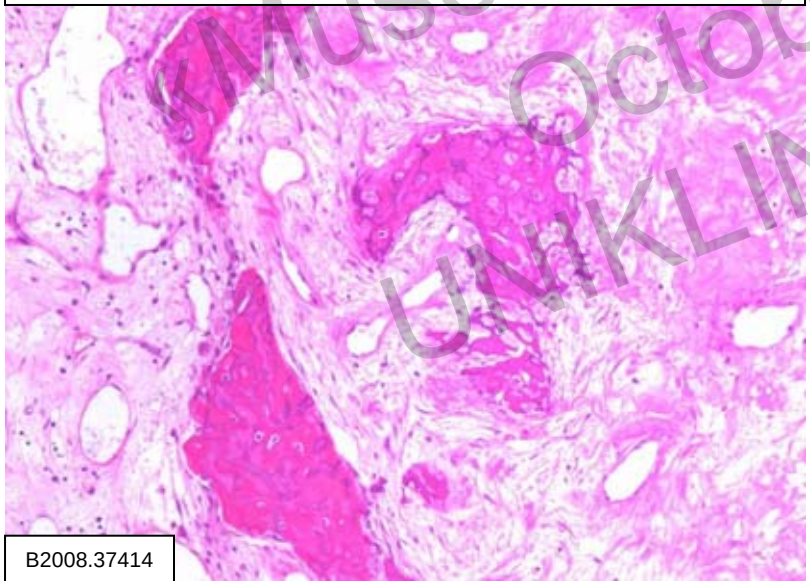
- Local recurrences
- Metastases

High grade osteoblastic osteosarcoma



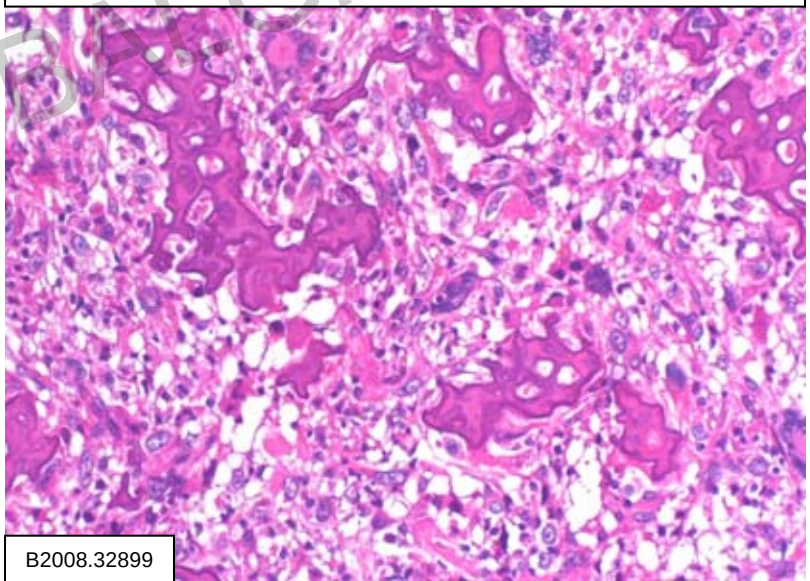
Neo-adjuvant chemotherapy

Completely devitalised tumor tissue

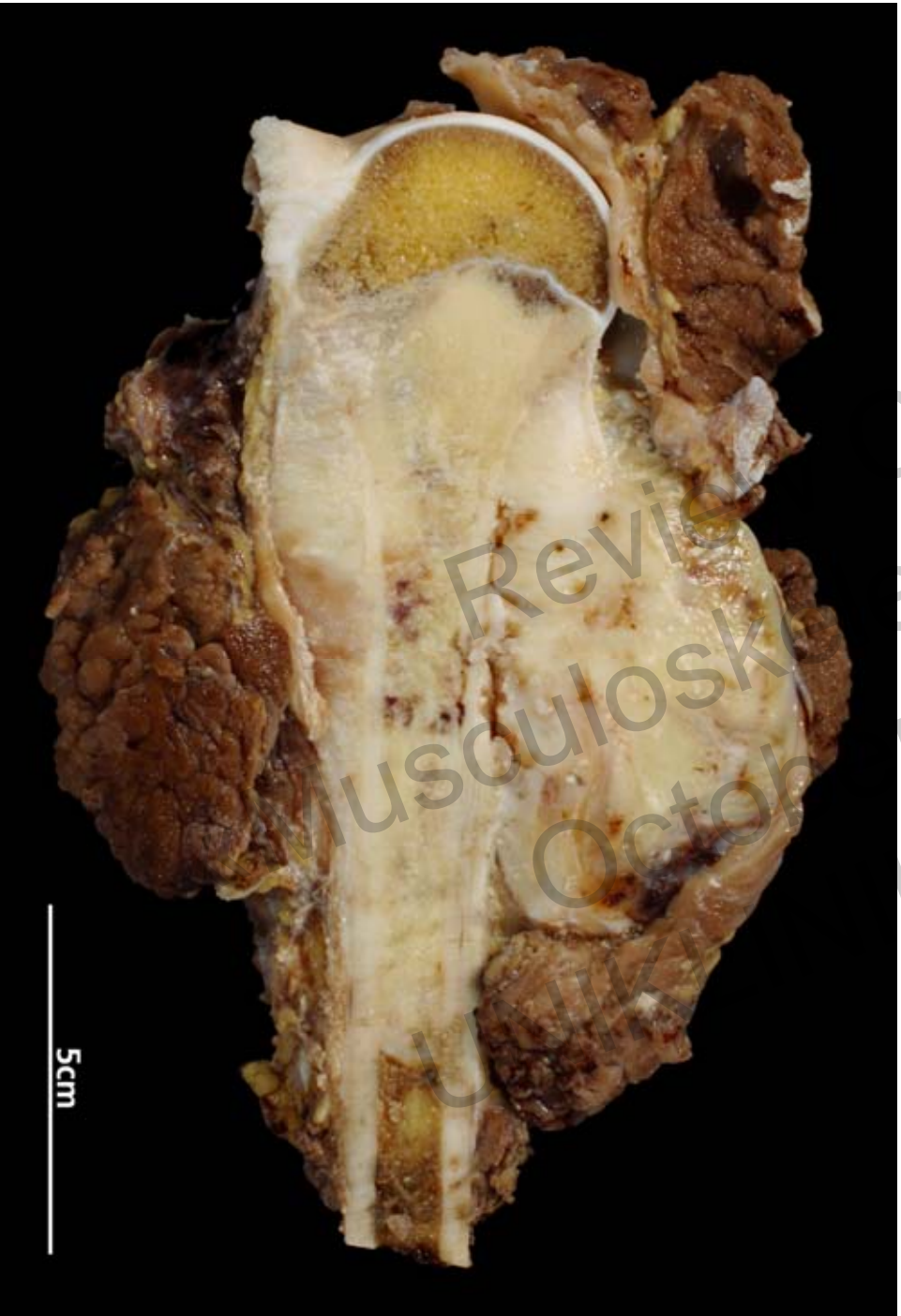


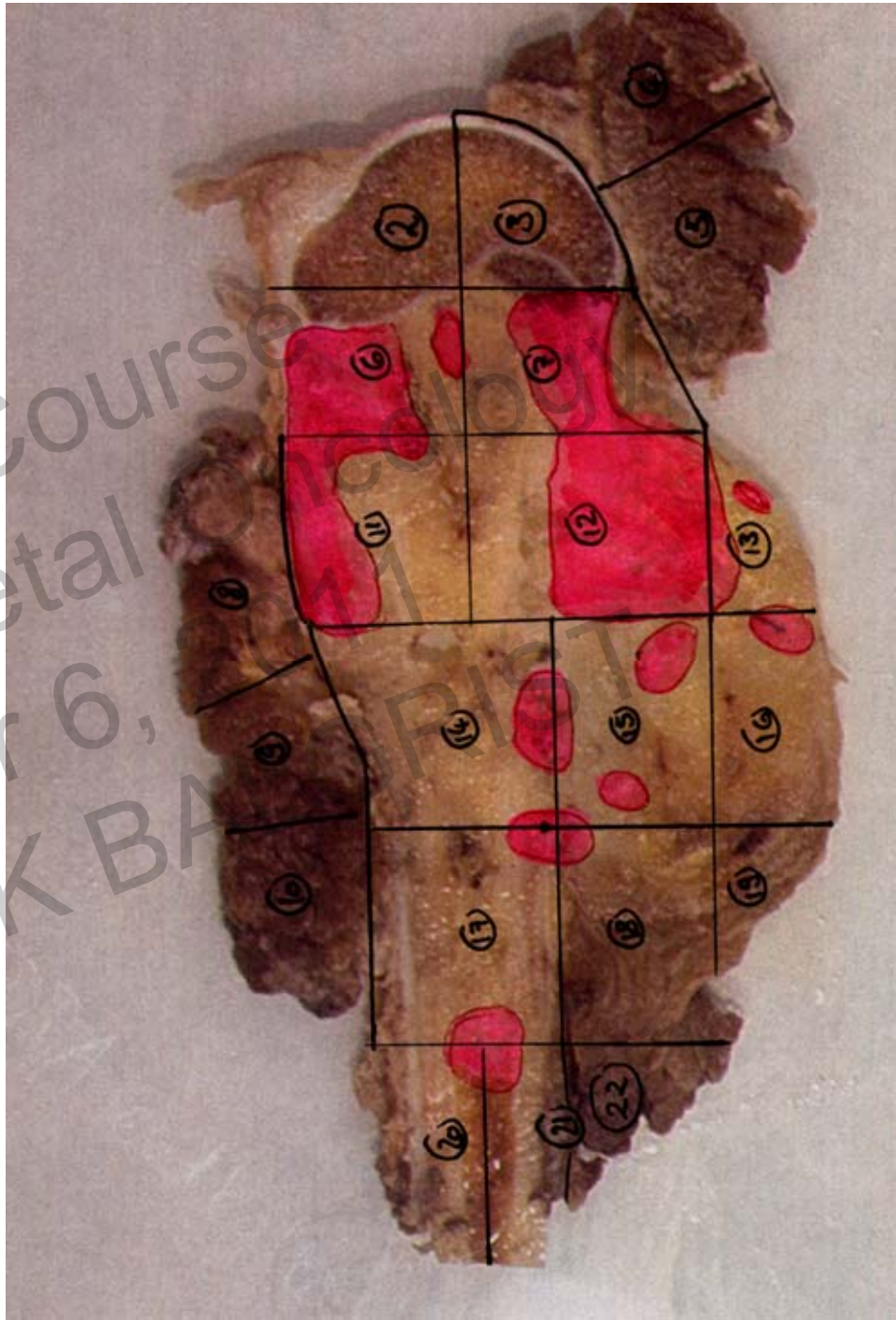
B2008.37414

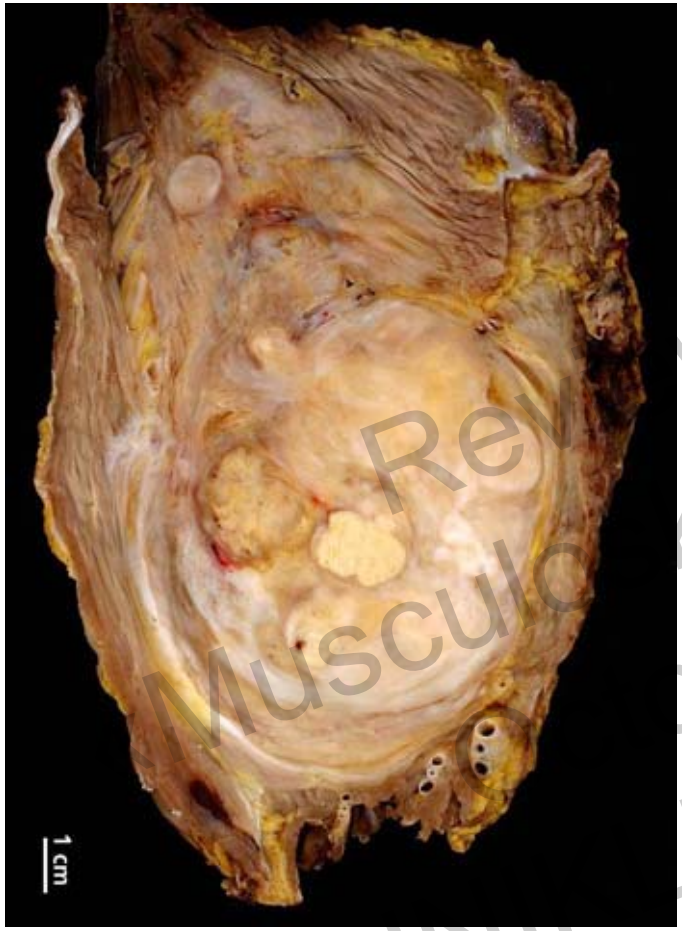
Vital tumor tissue



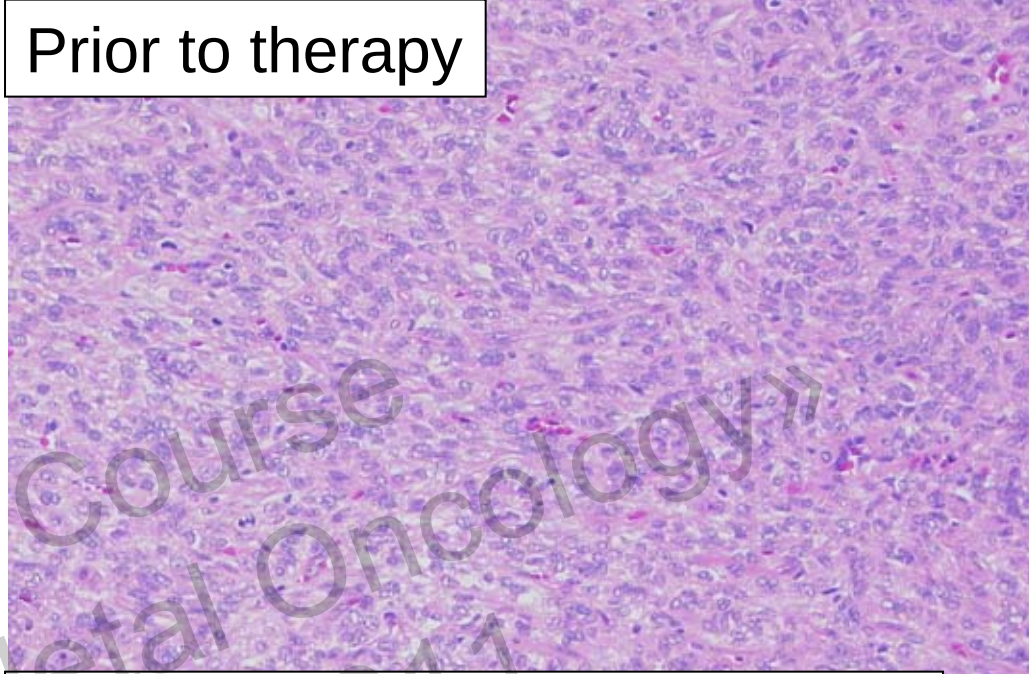
B2008.32899



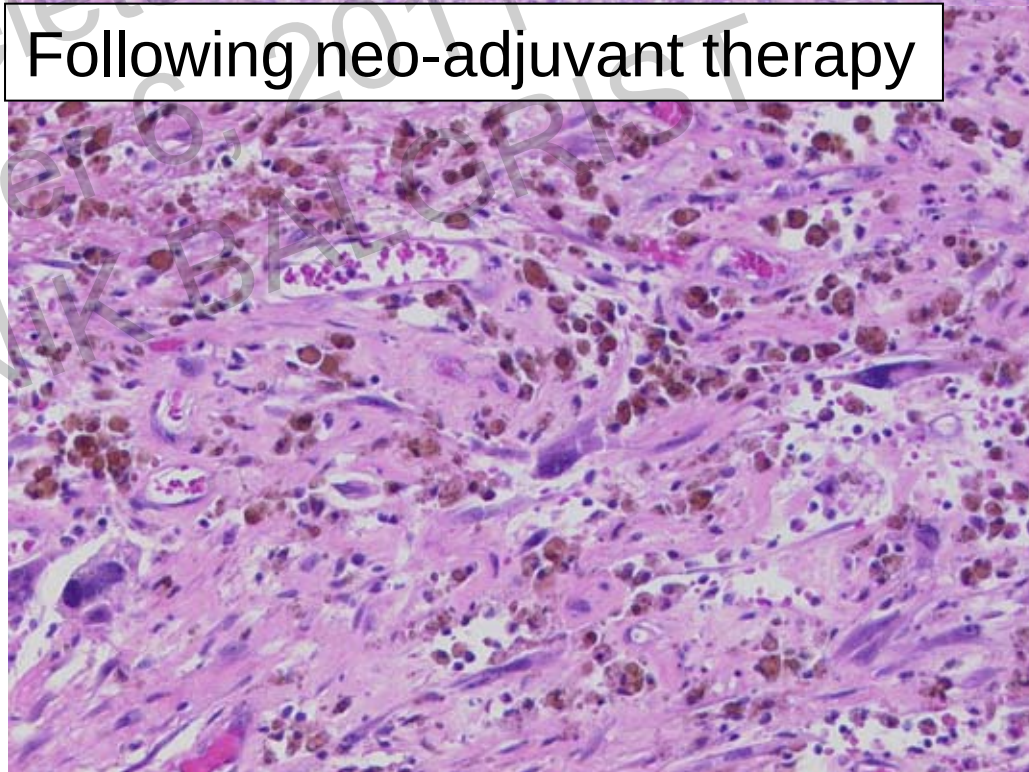




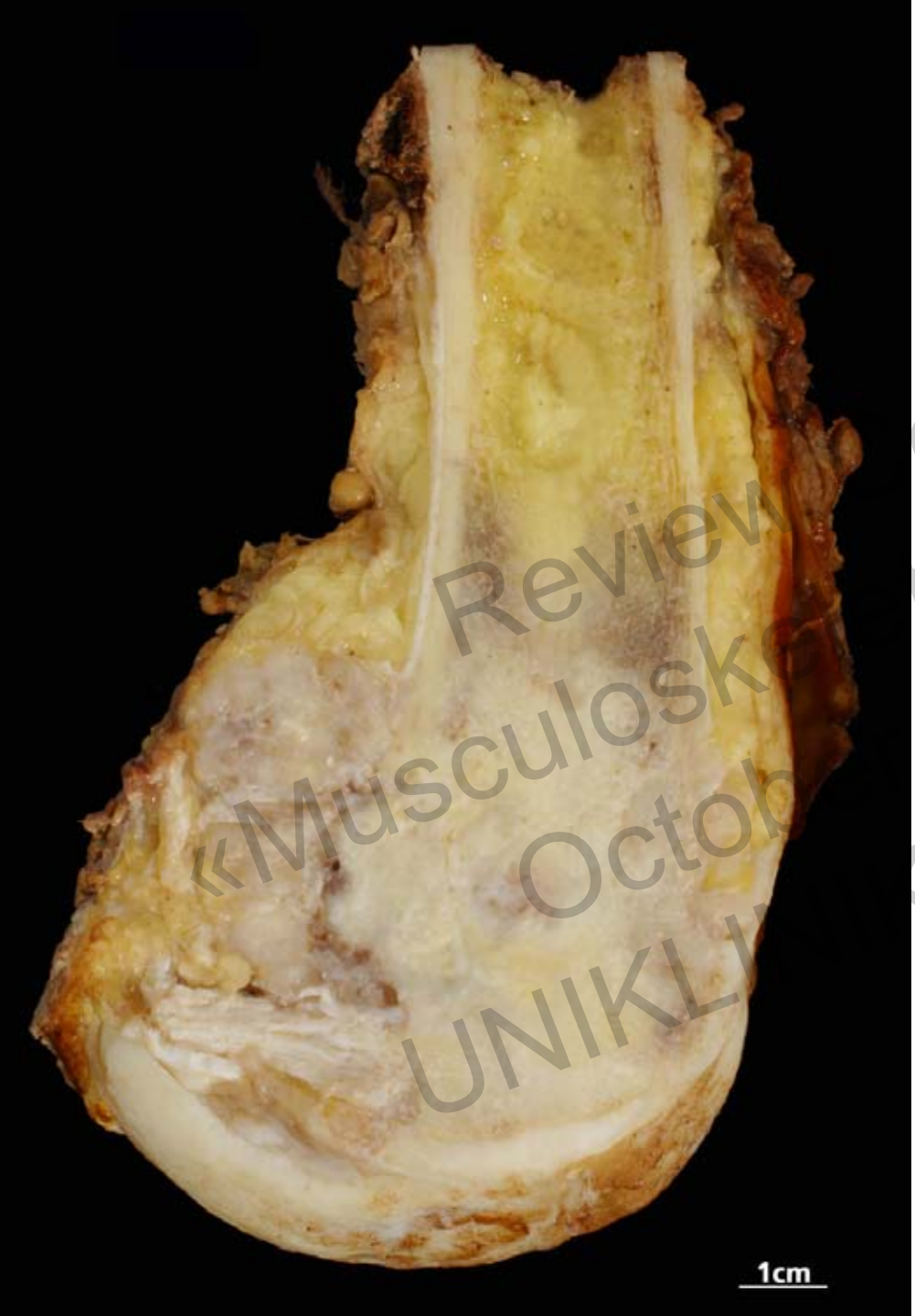
Prior to therapy

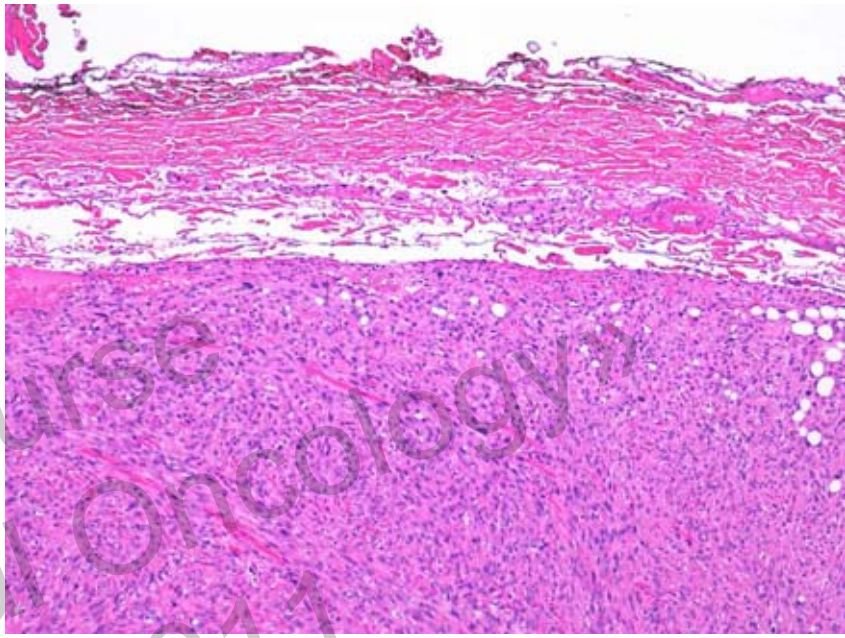


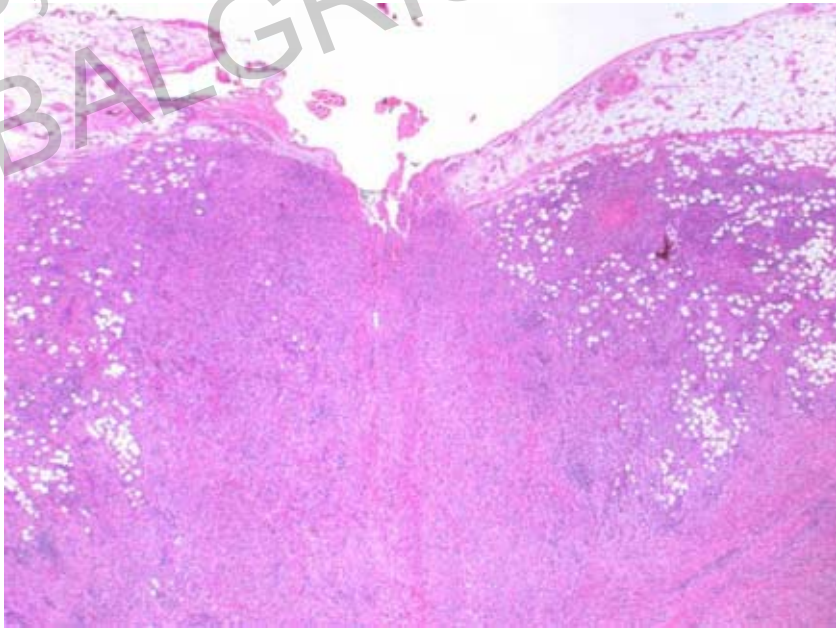
Following neo-adjuvant therapy



Resection margins







Pathology of Soft tissue and Bone Tumors
Summary

- Understanding of the **pathogenesis**
- Developement of **new concepts for diagnostics and treatment**

- **Diagnostics**
  - Despite the progress in radiological methods**, histopathology remains gold standard** in diagnosis of musculoskeletal tumors
  - Differential diagnosis is based **on clinical presentation**; **H&E, immunhistochemistry and advanced ancillary studies** (FISH, RT-PCR)
  - Minimally invasive histopathological diagnostics is only possible if **adequate clinical and radiological correlation** is available (multidisciplinary centers with a sufficient case load)

- **Therapy**
  - Precise histopathologic diagnosis is crucial for the planning of the therapy and postoperative management
  - Extend of the surgery
  - (Neo-) adjuvant chemotherapy