Leiomyosarcoma (LMS) Patient Education Symposium
Saturday, July 14, 2018
Geffen Auditorium – Gonda Building
Mayo Clinic
**Presentations to be 20-25 minutes with 5 minutes for Q&A*

8:00 – 9:00 a.m.	***Registration, Continental Breakfast***
9:00 – 9:15 a.m.	Welcome and Introduction *Scott H. Okuno, M.D.*
9:15 – 9:45 a.m.	Understanding Pathology Reports *Karen Fritchie, M.D., Department of Lab Medicine and Pathology*
9:45 – 10:15 a.m.	Diagnosis and Treatment *Steven I. Robinson, M.B.B.S., Medical Oncology*
10:15 – 10:30 a.m.	***Refreshment Break***
10:30 – 11:00 a.m.	Extremity Soft Tissue Sarcoma *Matthew T. Houdek, M.D., Orthopedic Oncology*
11:00 – 11:30 a.m.	Intraabdominal Surgery *Travis E. Grotz, M.D., Surgical Oncology*
11:30 a.m. – 12:00 p.m.	Treatment and Clinical Trials *Brittany Siontis, M.D., Medical Oncology*
12:00 – 12:45 p.m.	***Lunch***
12:45 – 1:15 p.m.	Radiation *Safia K. Ahmed, M.D., Department of Radiation Oncology*
1:15 – 1:45 p.m.	What's New, What's True in Nutrition for Cancer Survivors? *Jacalyn A. See, M.S., RDN, LD,* Dietitian
1:45 – 2:15 p.m.	Voices of A Patient's Journey
2:15 – 2:30 p.m.	***Refreshment Break***
2:30 – 3:00 p.m.	Panel Discussion / Q&A (Med Onc, Rad Onc, Surgical Onc, Ortho Onc) *Safia K. Ahmed, M.D., Travis E. Grotz, M.D., Matthew T. Houdek, M.D., Steven I. Robinson, M.B.B.S., and Brittany Siontis, M.D.*
3:00 – 4:00 p.m.	Optional Tour of Proton Beam Center
4:00 p.m.	***Adjourn***

Understanding Pathology Reports

Karen Fritchie, MD
Associate Professor of Laboratory Medicine and Pathology
Mayo Clinic, Rochester, Minnesota
Fritchie.karen@mayo.edu

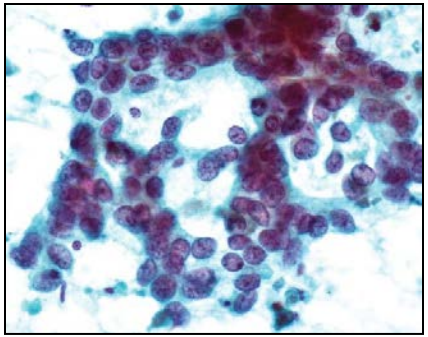
Outline

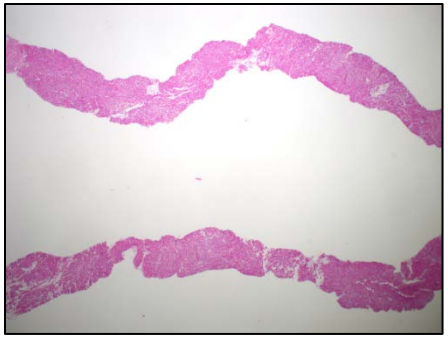
- What does a pathologist do?
- What is sarcoma?
- The value and impact of ancillary testing
- How to read a pathology report

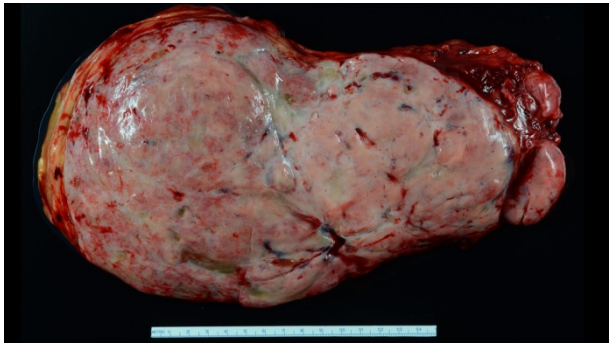
1. What does a pathologist do?

1. What does a pathologist do?

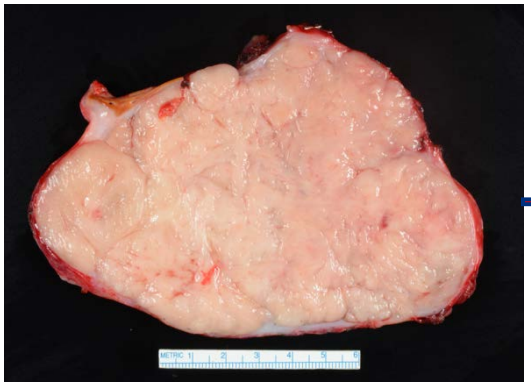
- Examines tissue specimens for diagnostic purposes
  - Fine needle aspirations
  - Biopsies
  - Resections

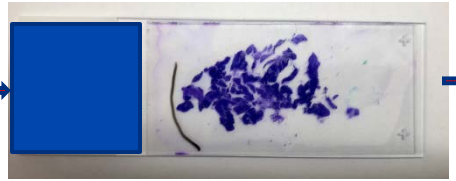






What a pathologist does





2. What is sarcoma?

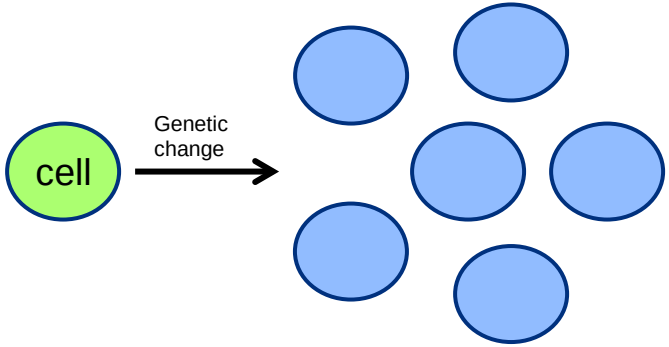
What is neoplasia? (aka ‘tumor’)

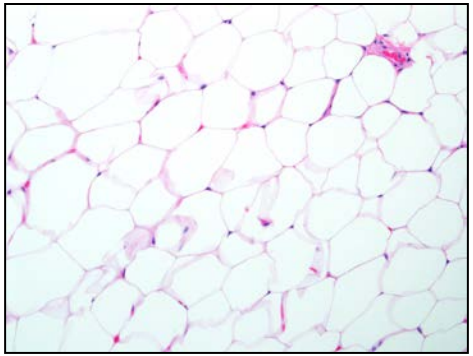
- “New growth”
- “An abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissue and persists in the same excessive manner after cessation of the stimuli which evoked the change.” Willis (oncologist)
- The persistence of tumors results from heritable genetic changes which allow excessive and unregulated proliferation/growth that becomes autonomous

Benign vs. Malignant

- Benign tumor → local growth
- Malignant tumor → capable of spreading to other sites (metastasis)

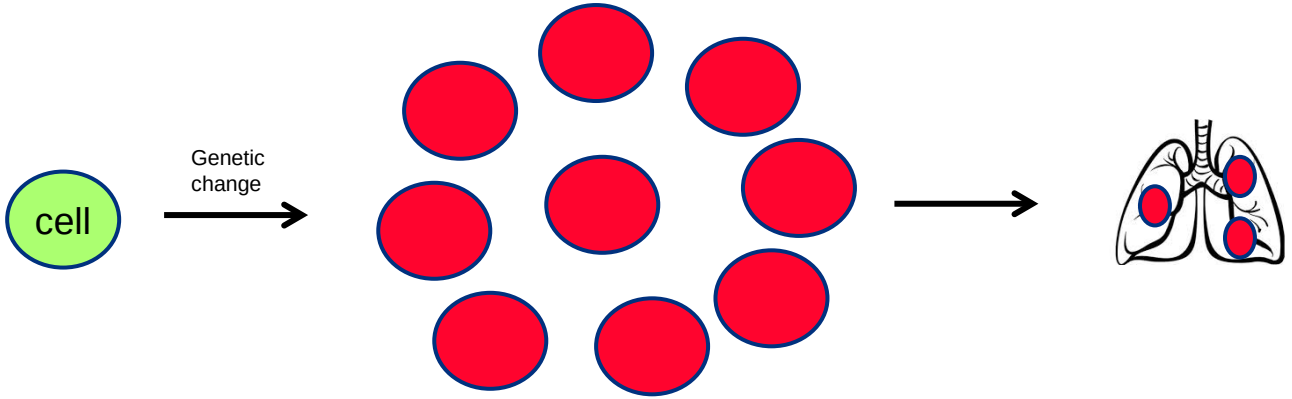
Neoplasia: benign tumor

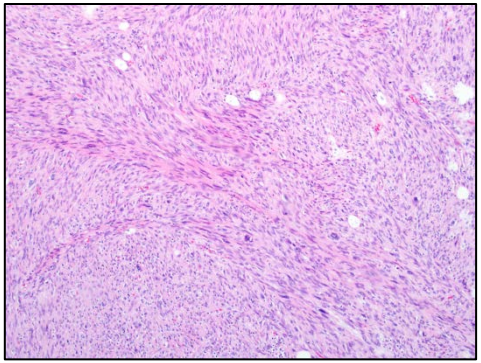




lipoma

Neoplasia: malignant tumor

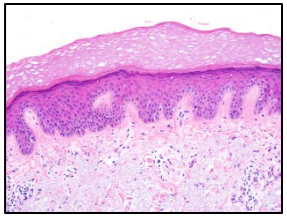
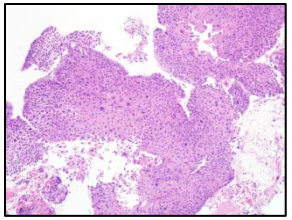


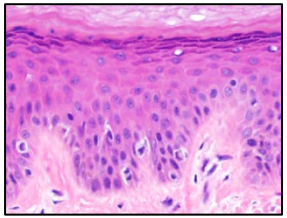
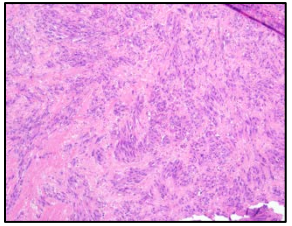


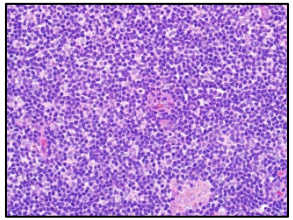
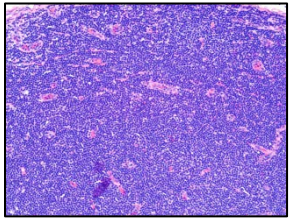
sarcoma

What is sarcoma?

Different cell types in the body

Epithelial cells →  → Carcinoma → 

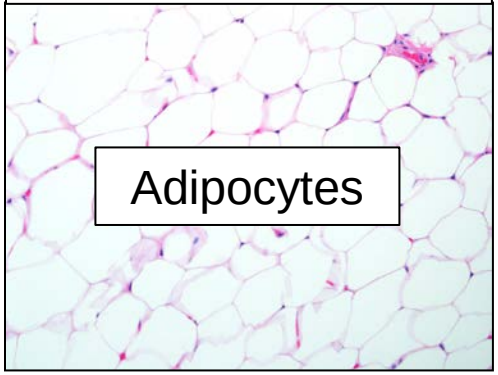
Melanocytes →  → Melanoma → 

Hematolymphoid →  → Lymphoma → 

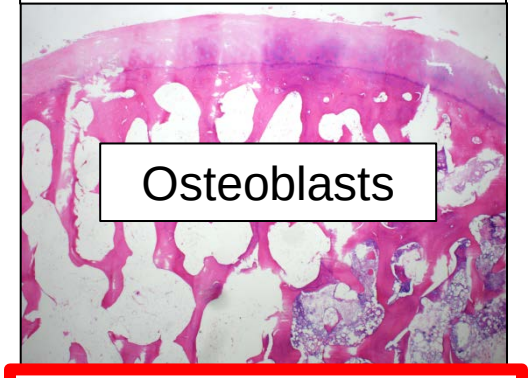
Connective tissue →

What is connective tissue?

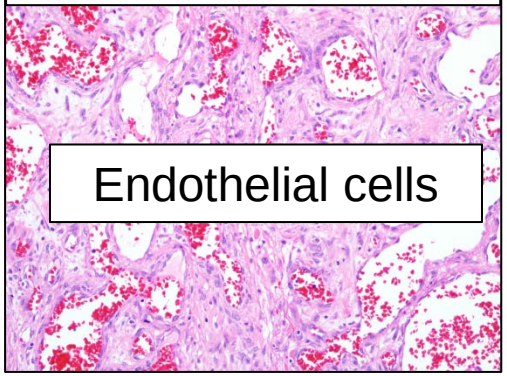
FAT

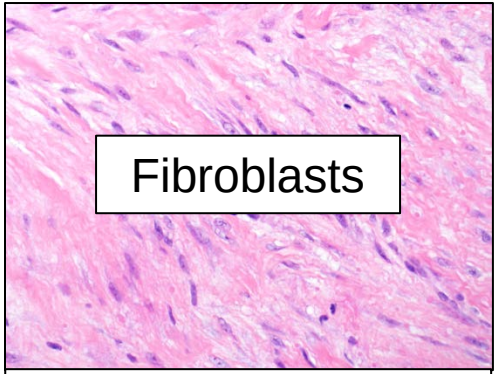


BONE

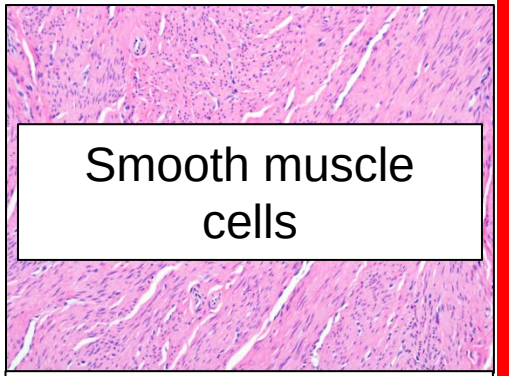


BLOOD VESSELS

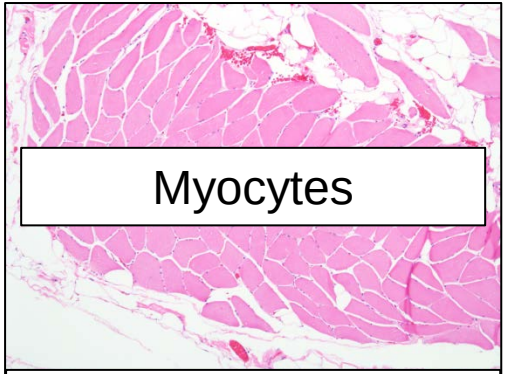




FIBROUS TISSUE



SMOOTH MUSCLE



SKELETAL MUSCLE

Smooth muscle

- Cardiovascular system: regulates blood pressure, blood flow
- Respiratory system: contraction and relaxation of airways
- GI system: helps move food
- Renal system: regulates blood flow and glomerular filtration
- Reproductive system: present within the wall of the uterus

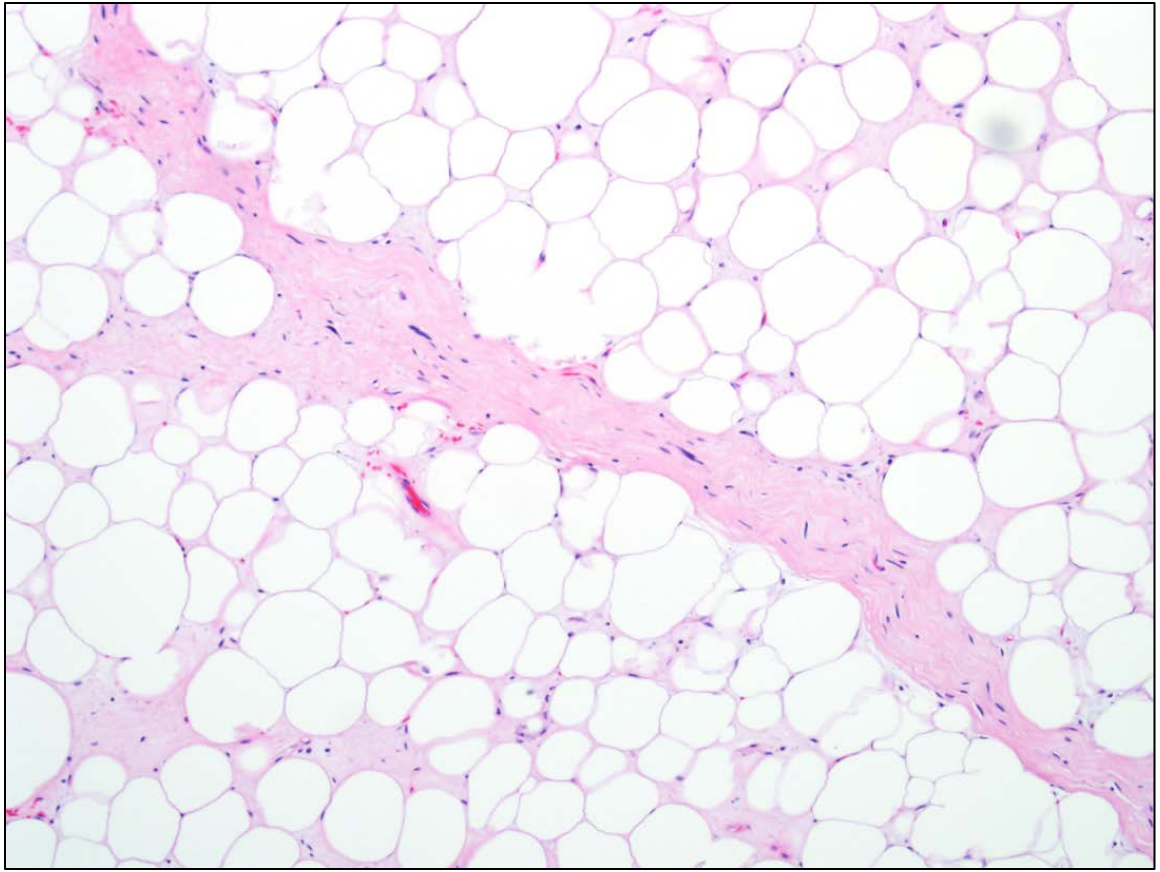
	Benign tumor
Fat	Lipoma
Smooth muscle	Leiomyoma
Skeletal muscle	Rhabdomyoma
Blood vessels	Hemangioma
Bone	Osteoid osteoma Osteoblastoma

	Benign tumor	Malignant tumor
Fat	Lipoma	Liposarcoma
Smooth muscle	Leiomyoma	Leiomyosarcoma
Skeletal muscle	Rhabdomyoma	Rhabdomyosarcoma
Blood vessels	Hemangioma	Angiosarcoma
Bone	Osteoid osteoma Osteoblastoma	Osteosarcoma

What is sarcoma?

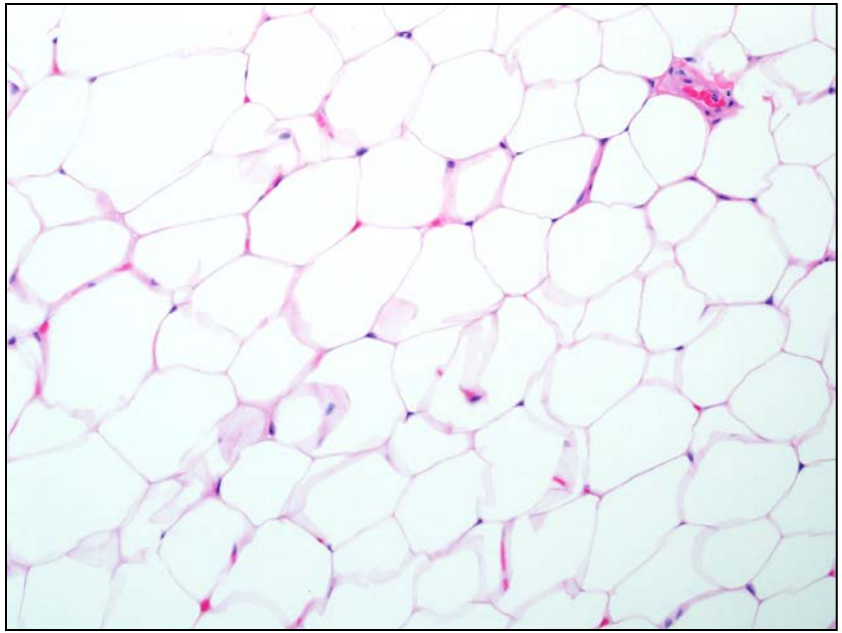
Malignant tumor that arises from connective tissue

What is this?

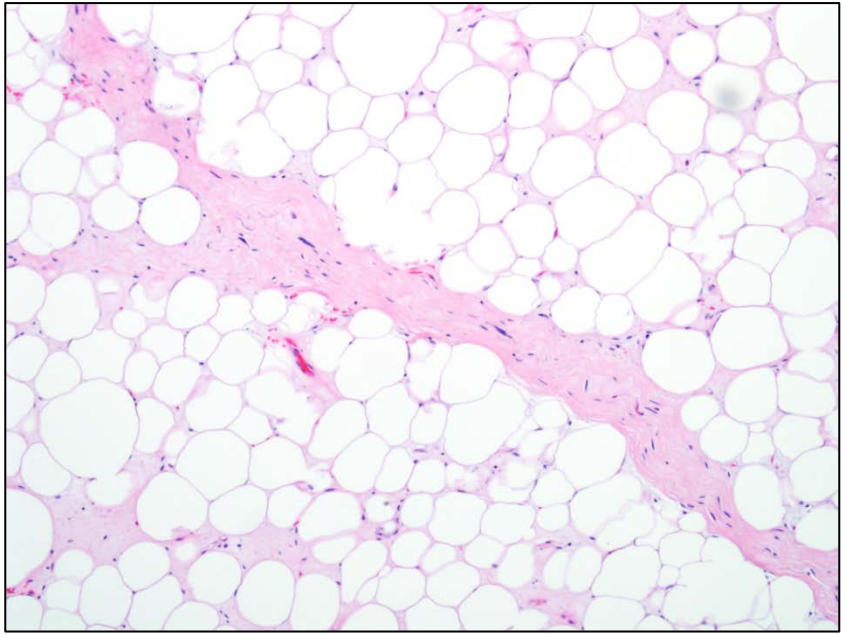


What is this?

FAT



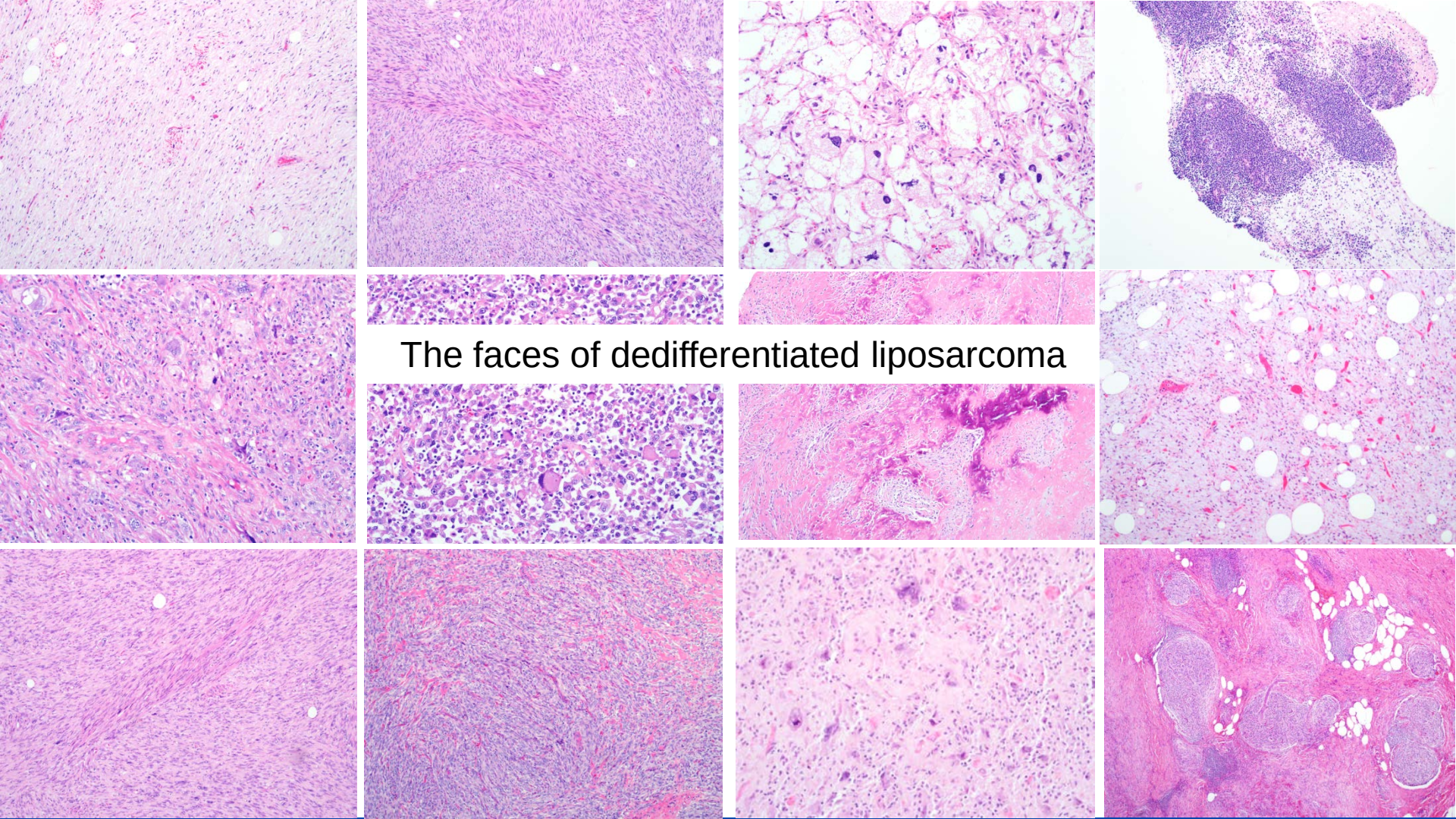
Liposarcoma



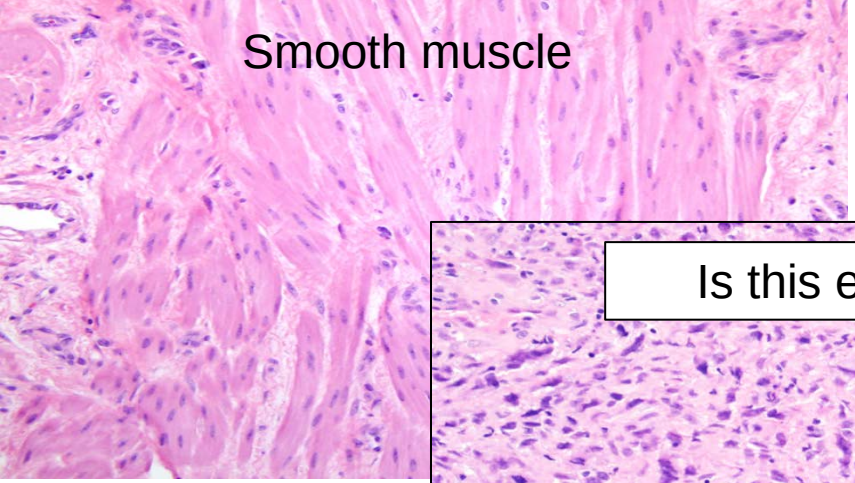
So, pathology is pretty straight-forward, right?

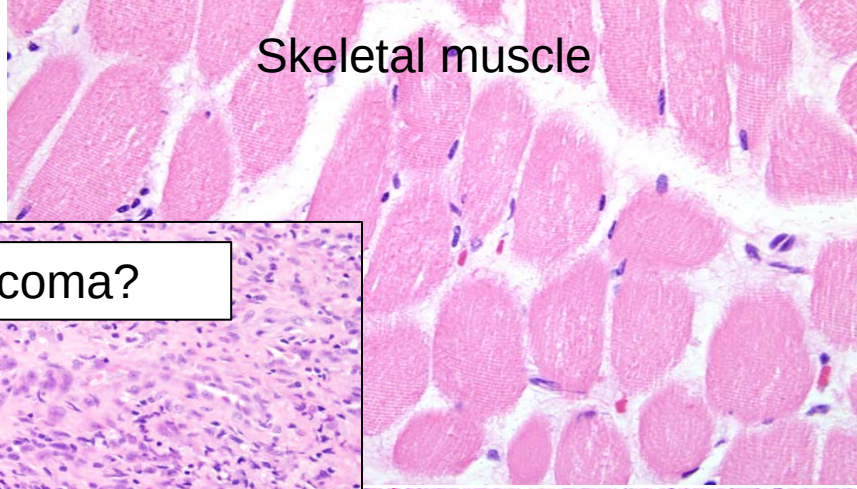
Why pathology is not always straight-forward

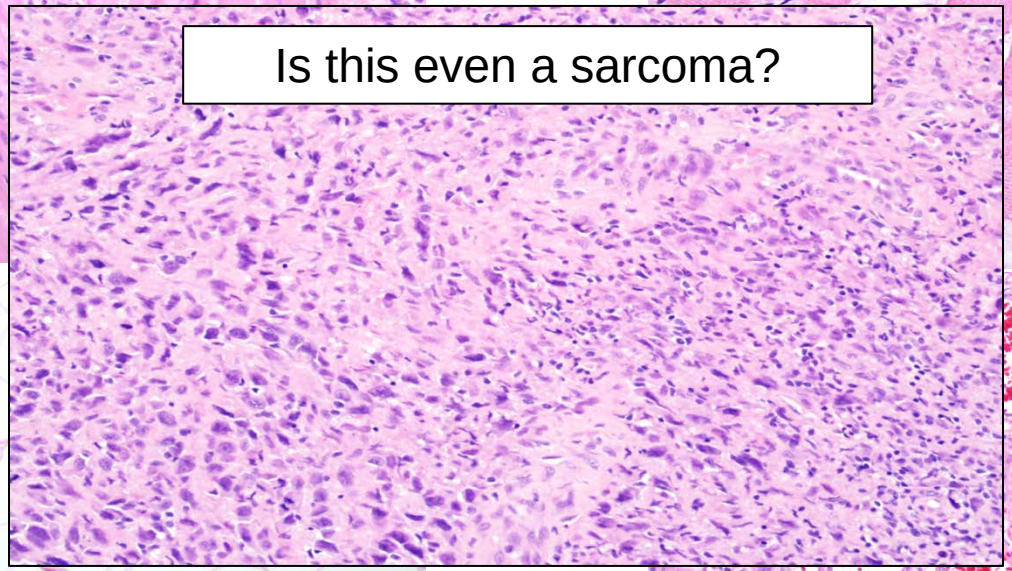
- Tumors can have variable appearances
  - From tumor to tumor
  - Even within the same tumor
- Different tumors can look the same
  - Most common with high grade/poorly differentiated tumors

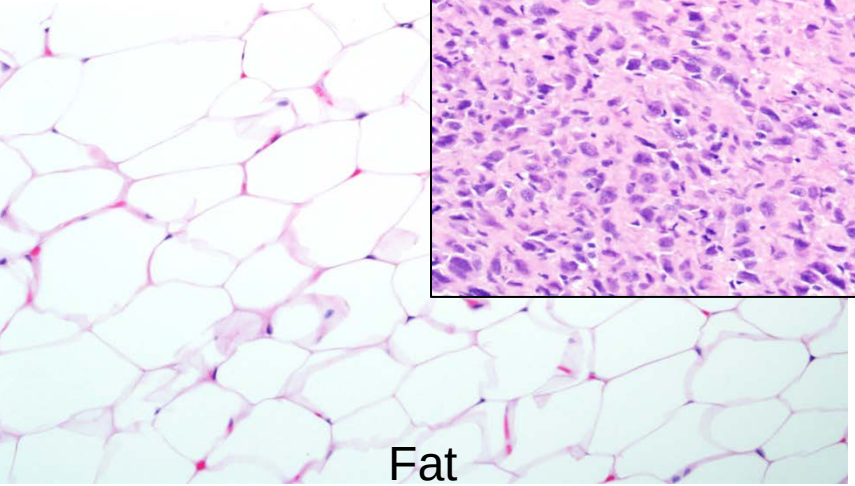

The faces of dedifferentiated liposarcoma

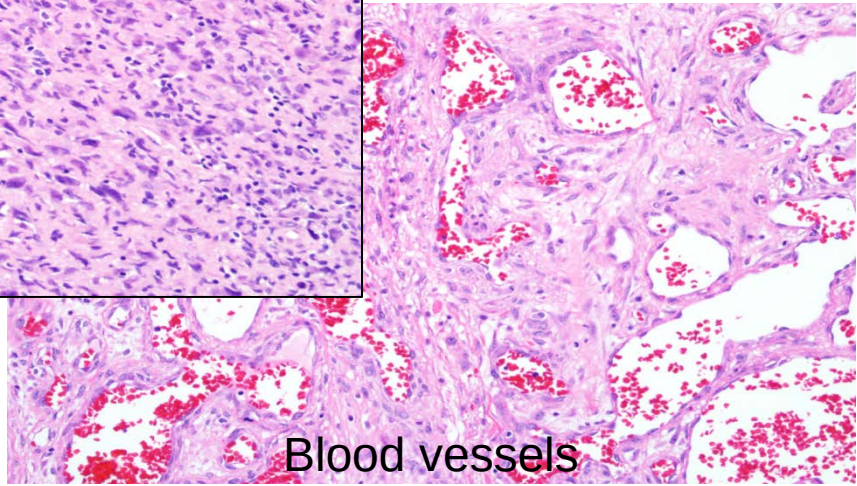

And, what is this????







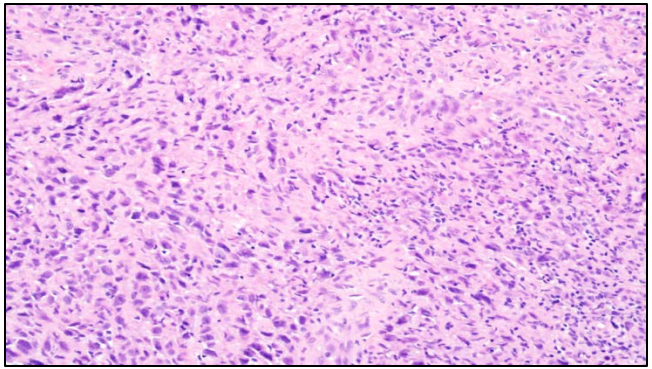




How can we tell these tumors apart?

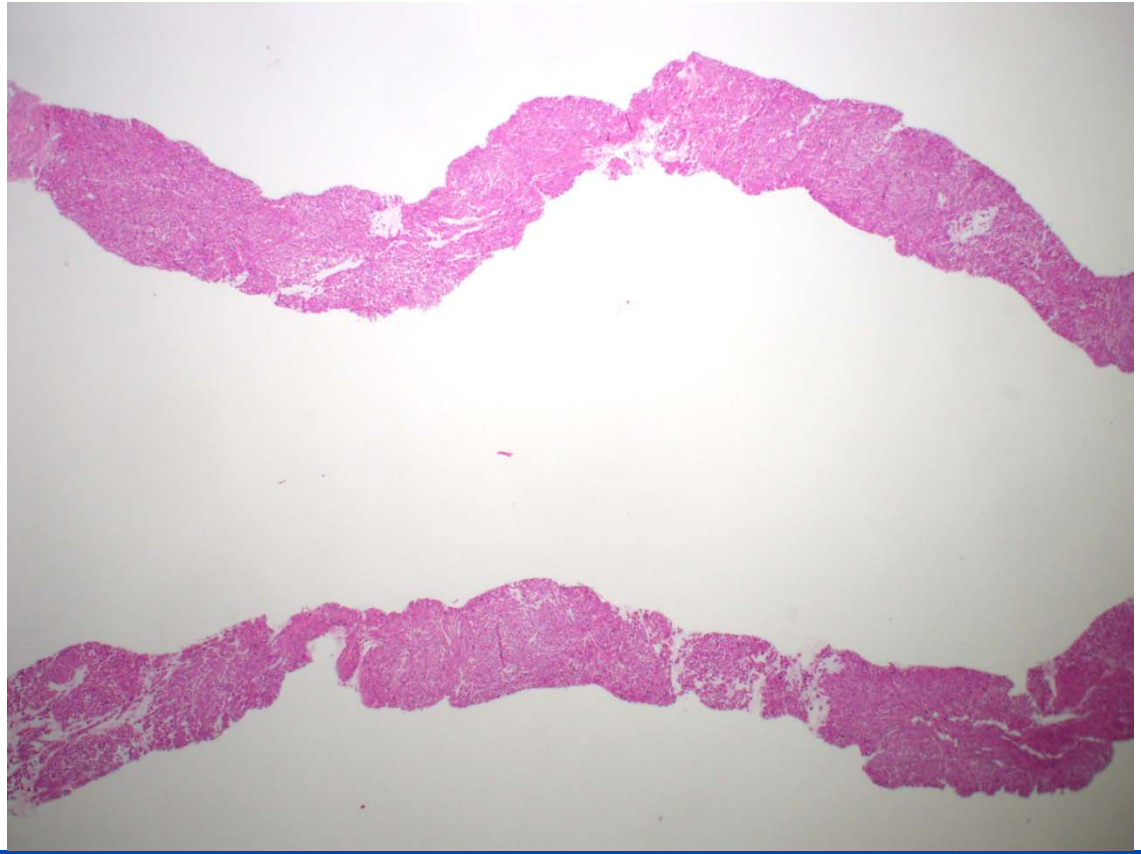
- What the tumor looks like (morphology)
- Immunohistochemical stains
- Molecular testing
  - Fluorescence in situ hybridization
  - RT-PCR
  - Larger molecular panels

3. The value and impact of ancillary testing

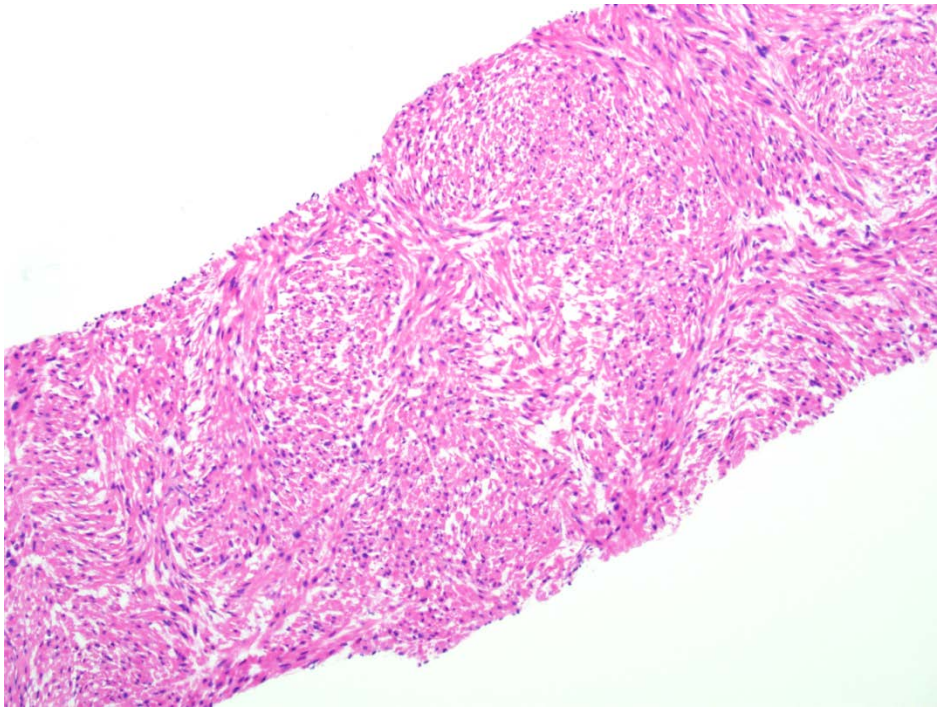


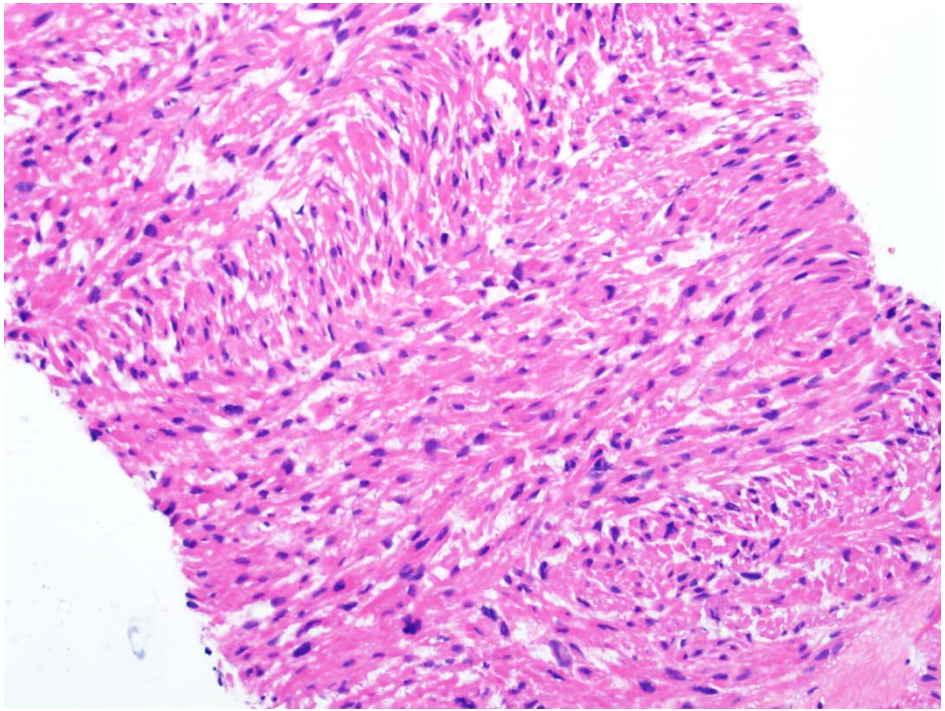
Connective tissue	Immunohistochemistry Aka: “stains”
Smooth muscle	Actin, desmin
Skeletal muscle	Desmin, myogenin
Blood vessels	CD31, FLI-1, ERG
GIST	KIT, DOG1

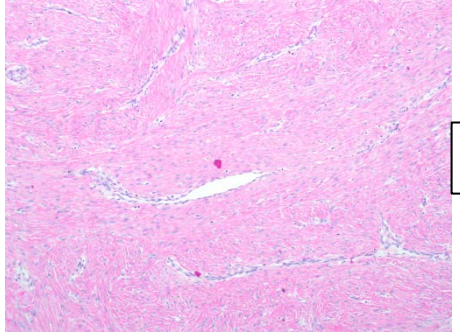
60 year old with an abdominal mass



Abdominal mass

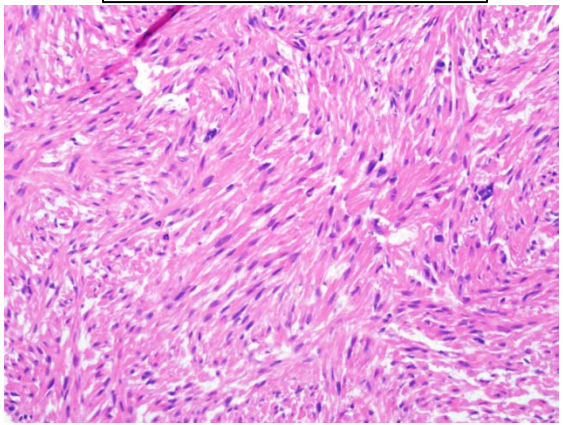


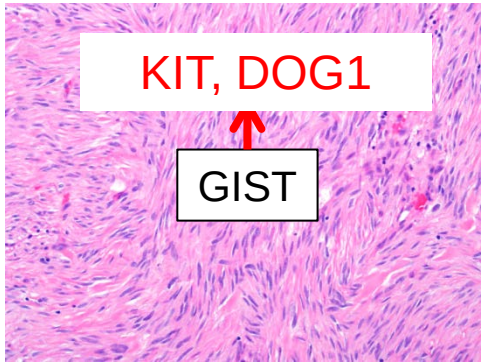




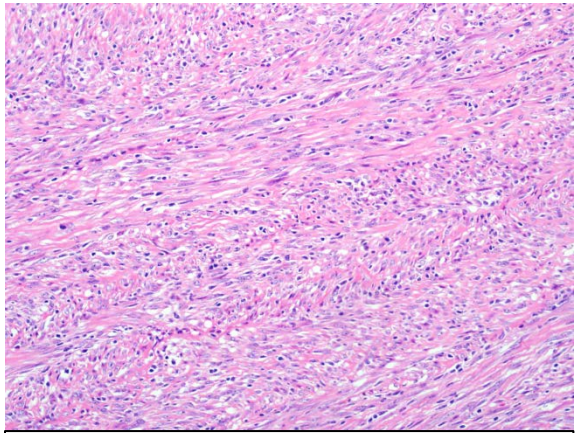
Desmoid → b-catenin

SMA, desmin ← Leiomyosarcoma

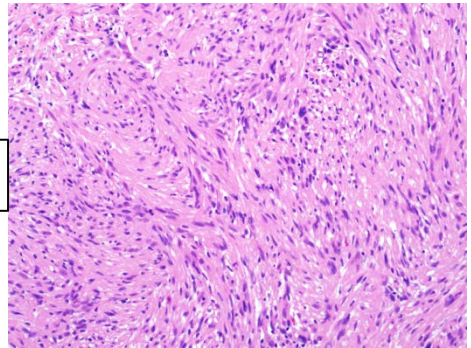




KIT, DOG1 ← GIST



Inflammatory myofibroblastic tumor → ALK

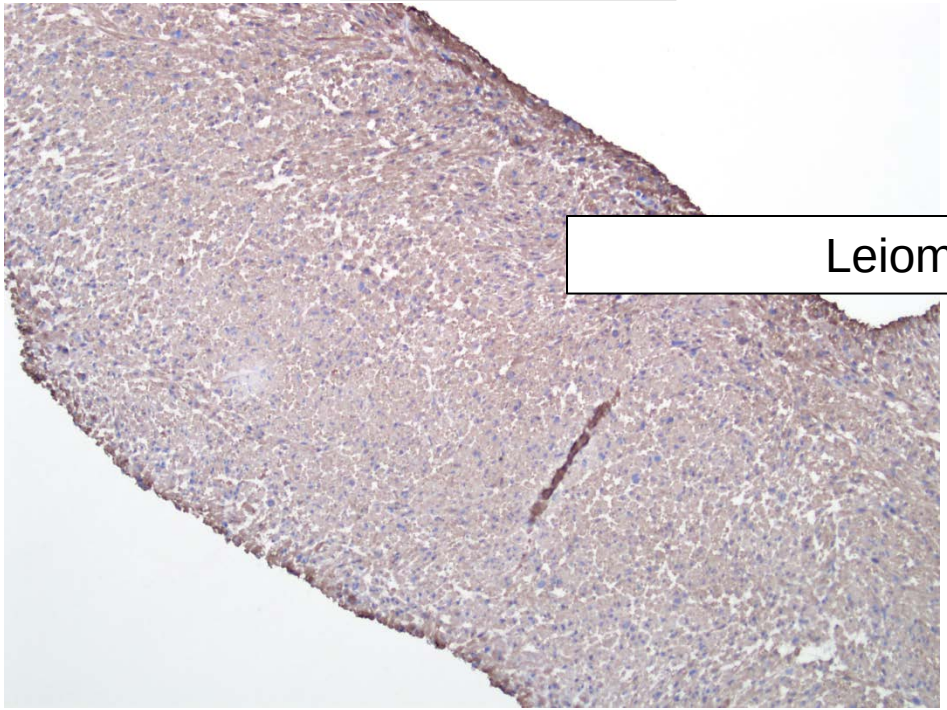


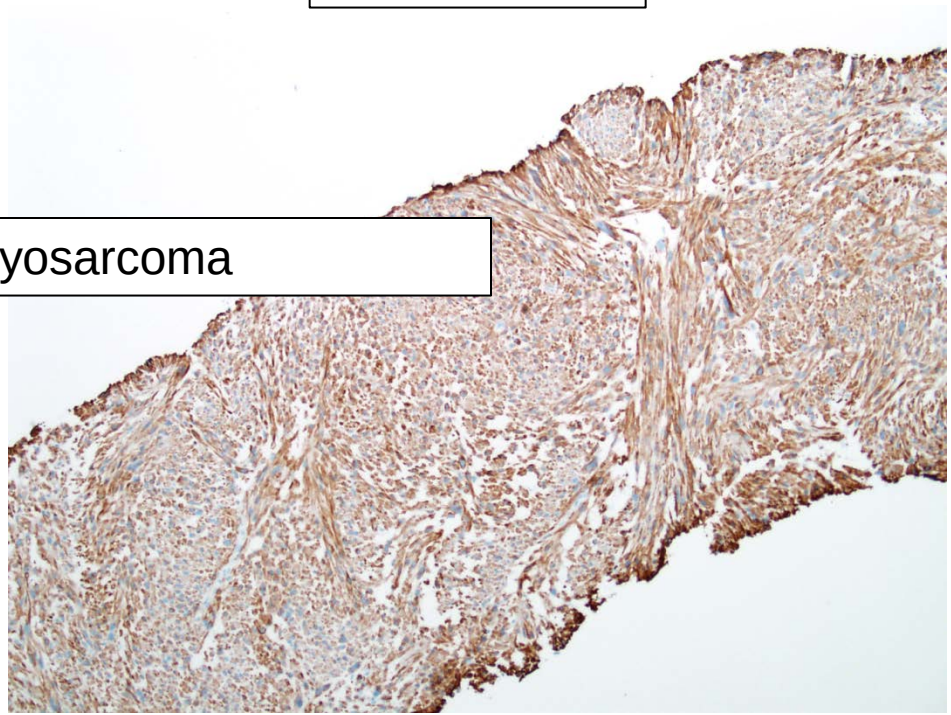
S100 ← Schwannoma

Retroperitoneal mass

SMA

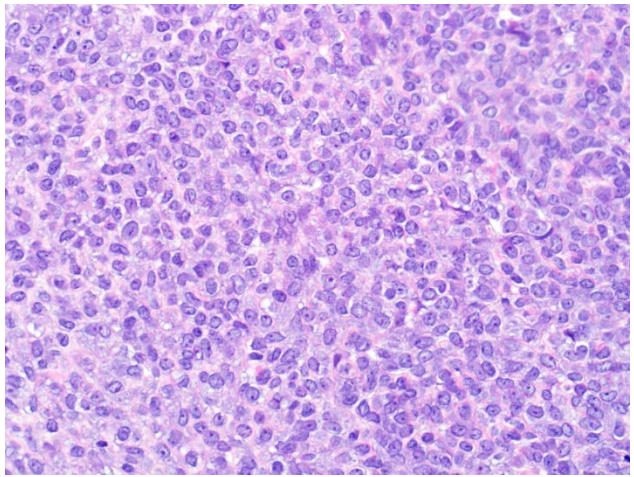
Desmin

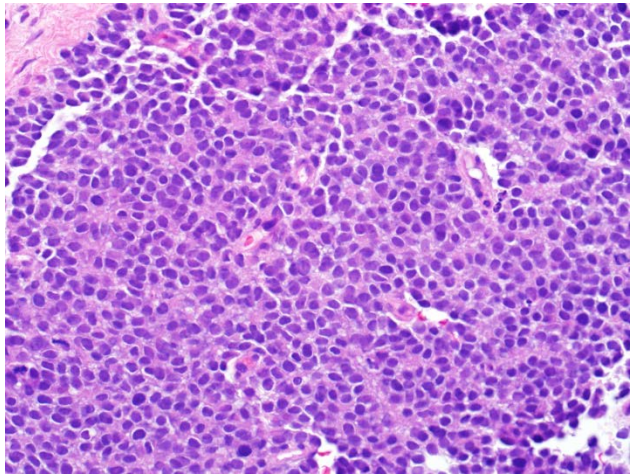


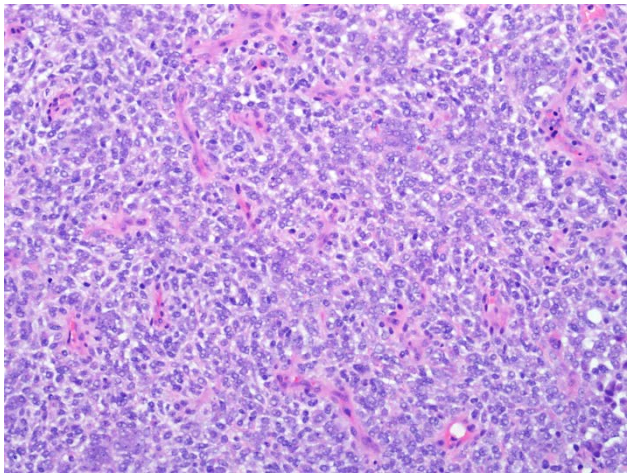


Leiomyosarcoma

Round cell sarcomas: value of molecular testing







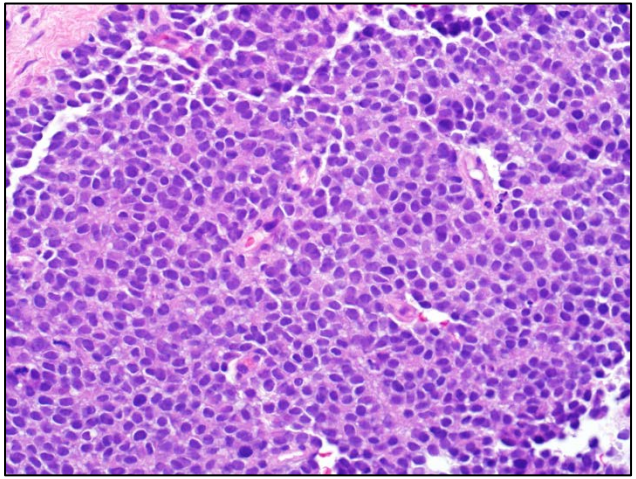
CIC — *DUX4*

EWSR1 — *FLI-1*

BCOR — *CCNB3*

Fluorescence in situ hybridization
RT-PCR

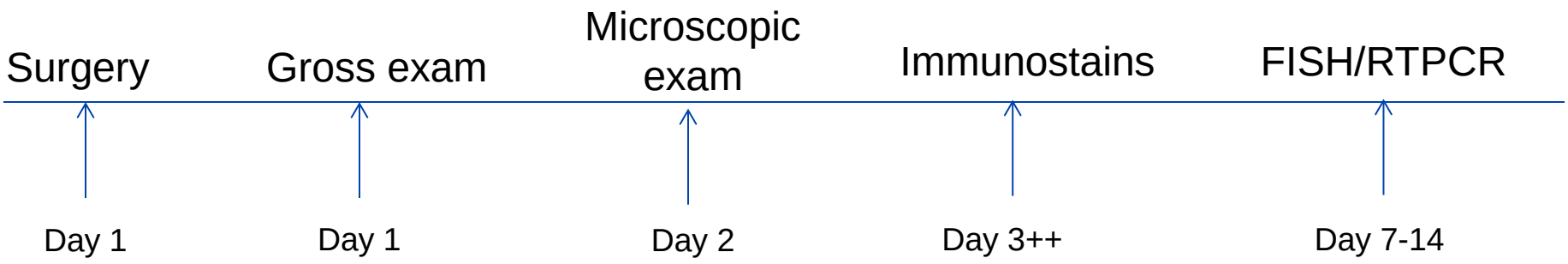
20 year old with bone tumor….



EWSR1 — *FLI-1*

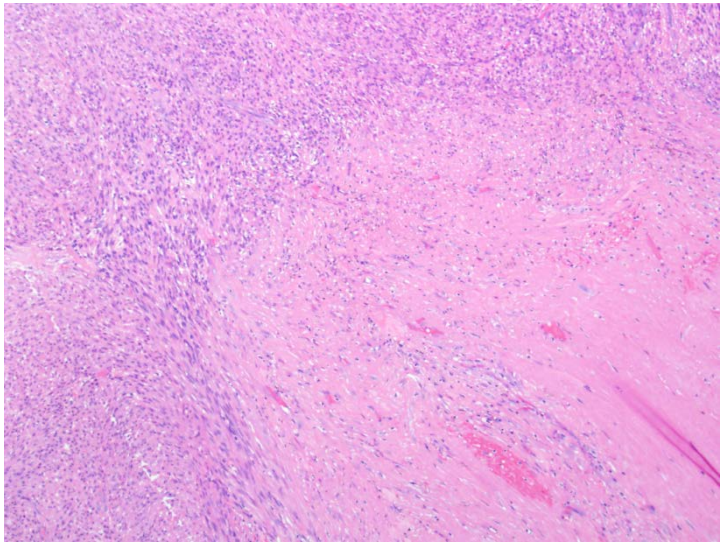
Diagnosis: Ewing sarcoma

Timeline

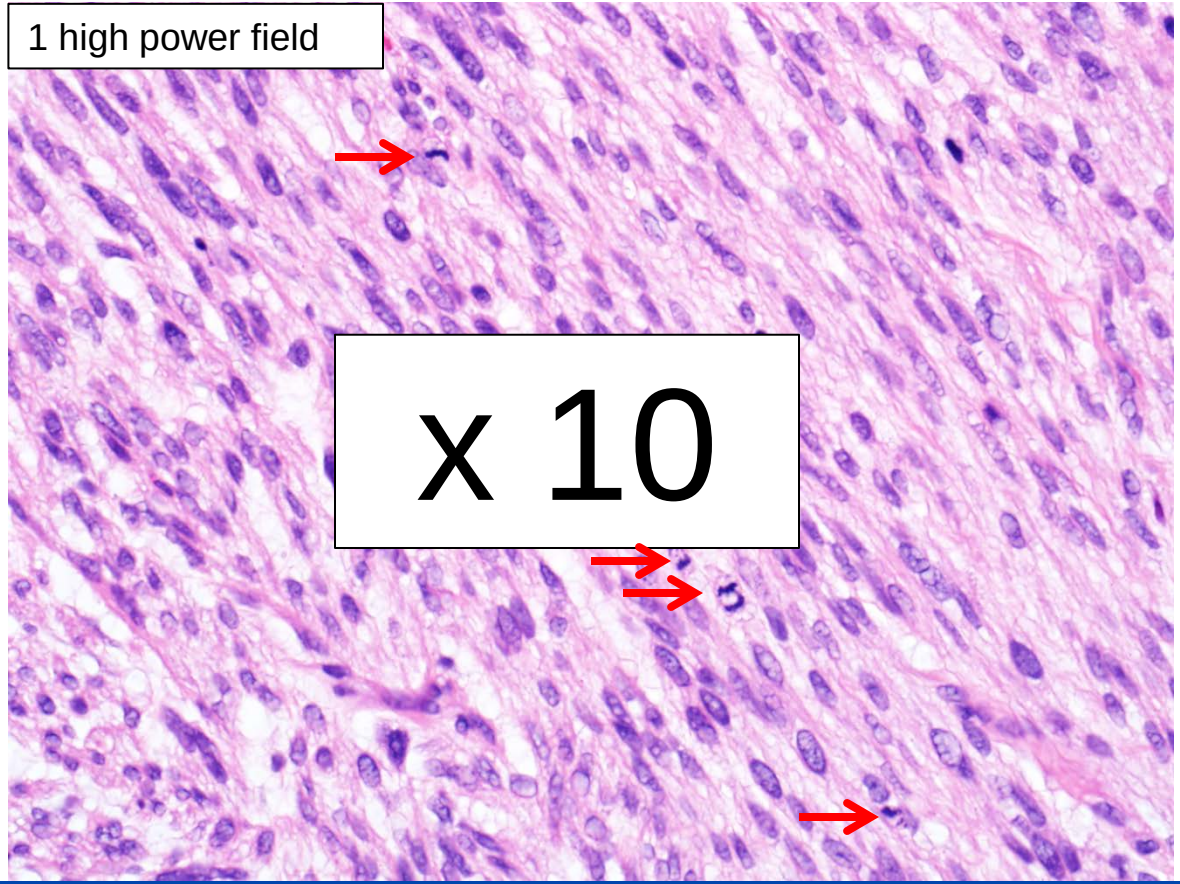


Now we've made a diagnosis…what else do we need to do….

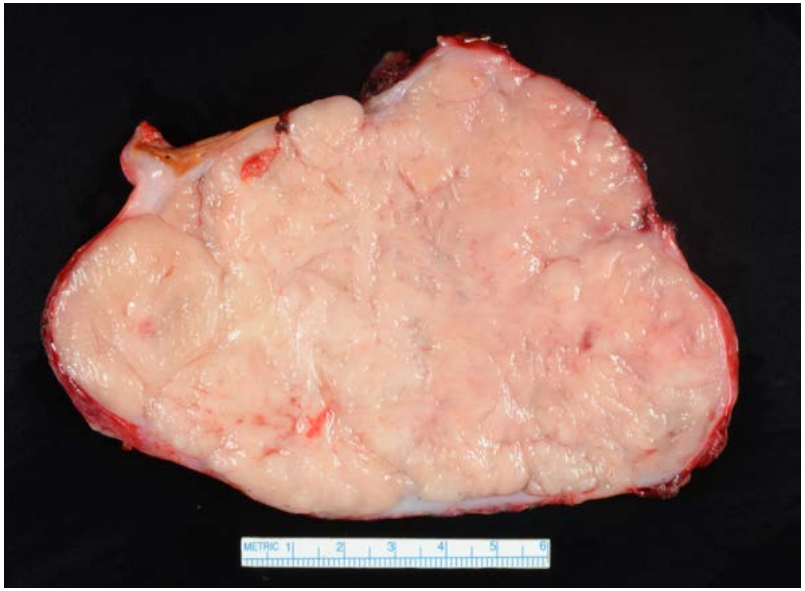
- Tumor grade
- Many sarcomas are graded using the FNCLCC scheme (grades 1-3):
  - Tumor differentiation
  - Necrosis
  - Mitotic rate



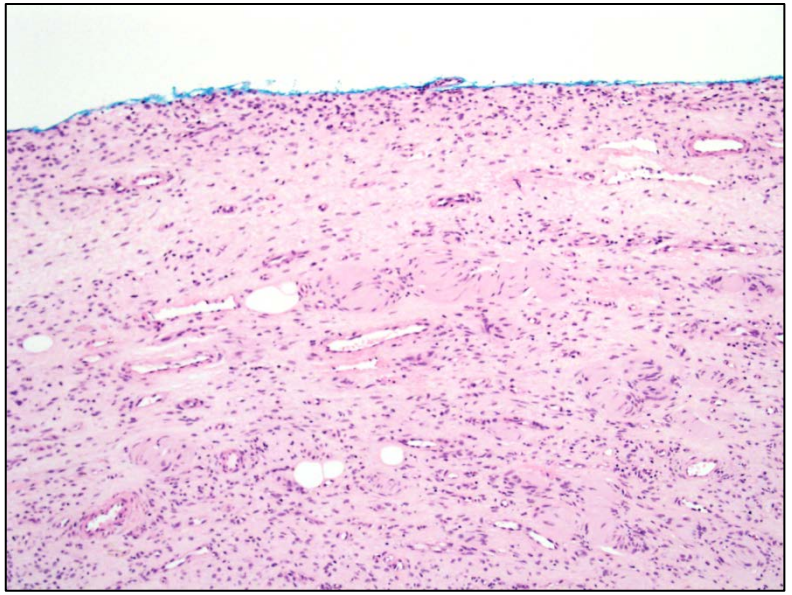
Mitotic rate



Margin status



Gross examination



Microscopic examination

4. How to read a pathology report

INTERPRETATION

FINAL DIAGNOSIS

A. Soft tissue mass and adrenal gland, right, excision and adrenalectomy: Leiomyosarcoma, low-grade (FNCLCC grade 1 of 3), forming a 5.3 x 3.5 x 3.2 cm mass. The surgical margins are negative for tumor. Unremarkable adrenal gland. See synoptic report.

Immunoperoxidase studies were performed on paraffin sections (block A1) using antibodies directed against the following antigens: SMA, Desmin, c-kit, S100 and DOG1. The tumor cells are positive for SMA and Desmin, and are negative for c-kit, S100 and DOG1.

COMMENT

Although the mitotic rate is low and there is no tumor necrosis, given presence of diffuse mild cytologic atypia in conjunction with the anatomic location, this tumor is best classified as low grade leiomyosarcoma.

SYNOPTIC REPORT

Procedure: Marginal resection
Tumor Site: Retroperitoneum
Tumor Size: 5.3 x 3.5 x 3.2 cm
Histologic Type: Leiomyosarcoma
Mitotic Rate: Less than 1/10 high-power fields
Necrosis: Absent
Histologic Grade: FNCLCC grade 1 of 3
Margins: Negative for tumor
Regional Lymph Nodes
    Number of Lymph Nodes Involved: Not applicable
    Number of Lymph Nodes Examined: 0
Pathologic Staging (AJCC, 8th edition)
    TNM Descriptors: not applicable
    Primary Tumor: pT2
    Regional lymph nodes: pNx
    Distant Metastasis: not applicable
Ancillary Studies
    Immunohistochemistry: The tumor cells are positive for SMA and Desmin, and are negative for c-kit, S100 and DOG1.
    Cytogenetics: cytogenetic results will be reported separately
    Molecular Pathology: not performed

Questions & Discussion

The Diagnosis and Treatment of Leiomyosarcoma: A “Simplified” View

Steven Robinson, MBBS
Assistant Professor of Oncology
Mayo Clinic
July 14, 2018

Disclosures

- No relevant disclosures

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Goals

- **Define leiomyosarcoma**
- **Appreciate the differences between the "types" of leiomyosarcoma**
  - Presentation
  - Prognosis
- **Role of chemotherapy**
  - Localized disease
  - Metastatic disease (disease has spread or recurred)

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Sarcomas

- 1,734,350 new cases of cancer expected in 2018
- 16,490 cases of sarcoma (~1%)
  - 6,760 deaths from sarcoma predicted
- Average age ~58 yrs.

TABLE 14. Five-Year Relative Survival Rate (%) for the Most Common Childhood and Adolescent Cancers, United States, 2007 to 2013

	BIRTH TO 14	15 TO 19
All ICCC groups combined	83.0	84.2
Lymphoid leukemia	90.5	74.2
Acute myeloid leukemia	65.1	61.5
Hodgkin lymphoma	97.6	96.1
Non-Hodgkin lymphoma	90.6	87.1
Central nervous system neoplasms	72.5	78.9
Neuroblastoma & other peripheral nervous cell tumors	79.0	62.8*
Retinoblasoma	95.2	†
Renal tumors	91.8	72.7*
Hepatic tumors	79.0	50.9*
Osteosarcoma	69.8	65.5
Ewing tumor & related bone sarcomas	77.7	61.5
Soft tissue and other extraosseous sarcomas	74.6	68.2
Rhabdomyosarcoma	69.8	45.9
Germ cell and gonadal tumors	92.4	92.0
Thyroid carcinoma	99.4	99.5
Malignant melanoma	93.3	94.0

Siegel et al. Ca cancer J. 2018.

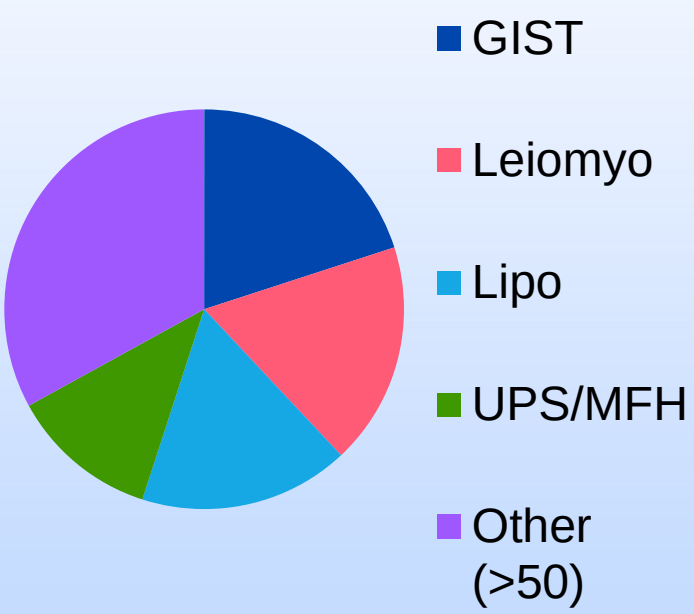
Sarcomas

- Comprise a group of neoplasms of mesenchymal origin
- Heterogeneous, >70 subtypes
- Requires experienced bone and soft tissue pathologist
  - ~40% cases read by general pathologist modified by expert BST pathologist

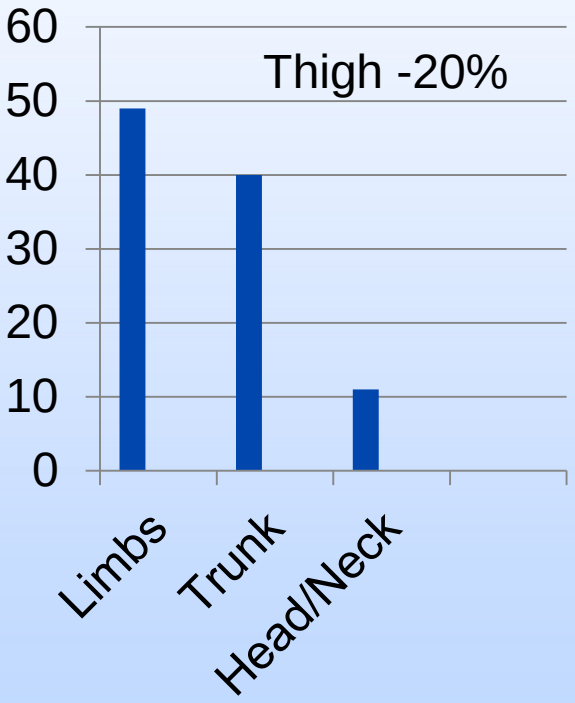
Ray-Coquard. Ann Oncol. 2011

Soft Tissue Sarcomas

Frequency of subtypes



Non-GIST Soft Tissue Sarcomas



Ducimetiere Plos ONE 2011
Ray-Coquard. Ann Oncol. 2011

What is Leiomyosarcoma?

- “A malignant neoplasm showing pure smooth muscle differentiation”
- Smooth muscle
  - Found in the walls of our hollow organs and glands
  - Involuntary control
  - E.g. blood vessels, stomach, bladder, uterus, sweat glands, sphincter muscles in our pupils (eyes)…..

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Fletcher et al. WHO Class of Tumors of Soft Tissue and Bone. 2013

Clinical Features of Leiomyosarcoma

- Comprise 10-20% of Soft Tissue Sarcomas
  - ~1300-2600 new cases in US in 2018
- Most common 5th to 7th decades of life
- Extremities
  - Pain or growing lump
- Abdomen & Pelvis
  - Most common location and can present late
    - Pain
    - Symptoms due to mechanical effects

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Siegel et al. Ca cancer J. 2018.
Fletcher et al. WHO Class of Tumors of Soft Tissue and Bone. 2013

Leiomyosarcoma groups by site of origin

Cutaneous (skin)

- Arises in the muscles attached to hair follicles
- Small at presentation ~2 cm
- Most are low grade, easily excised with good prognosis
- Present as skin lump, discoloration or ulceration

Extremity soft tissue

- Muscle layer of small vessels in muscle or subcutaneous tissue
- Usually lower extremity
- M=F
- 4-6 cm at presentation as enlarging lump or pain
- 64-84% 5 year survival rates

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Enziger and Weiss's Soft Tissue Tumors. Saunders. 2014

Leiomyosarcoma groups by site of origin

Retroperitoneum/abdomen & pelvis

- F>>M, in 7th decade
- Large at presentation
  - At least 5 cm, most > 10 cm
- Involve nearby structures, and present with poor appetite, abdominal mass or pain, nausea, vomiting, jaundice
- 20-50% 5-yr survival rates

Inferior vena cava

- F >>>>M, ~50 yrs
- Symptoms
  - Jaundice or ascites
  - Nausea, vomiting, lower extremity swelling
- Often present late
- 23-55% 5-yr survival rates

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Enziger and Weiss's Soft Tissue Tumors. Saunders. 2014

Diagnosis of Cancer

- What is the mass?
  - **Core biopsy** preferred for sarcoma
- Imaging: what is the **extent of the disease**?
  - Localized?
  - Has the disease spread?
    - Sites most commonly involved
- Leiomyosarcoma
  - Lungs, Liver (commonest)
  - Bone, lymph nodes (less commonly)
  - Skin, brain (rare)

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Leiomyosarcoma Initial Imaging

Primary tumor

- Extremity
  - MRI is preferred
- Abdomen & pelvis
  - CT
    - (MRI if allergic to contrast)

Metastatic (Spread)

- Chest CT without contrast
  - Or X-ray
- CT abdomen/pelvis with contrast

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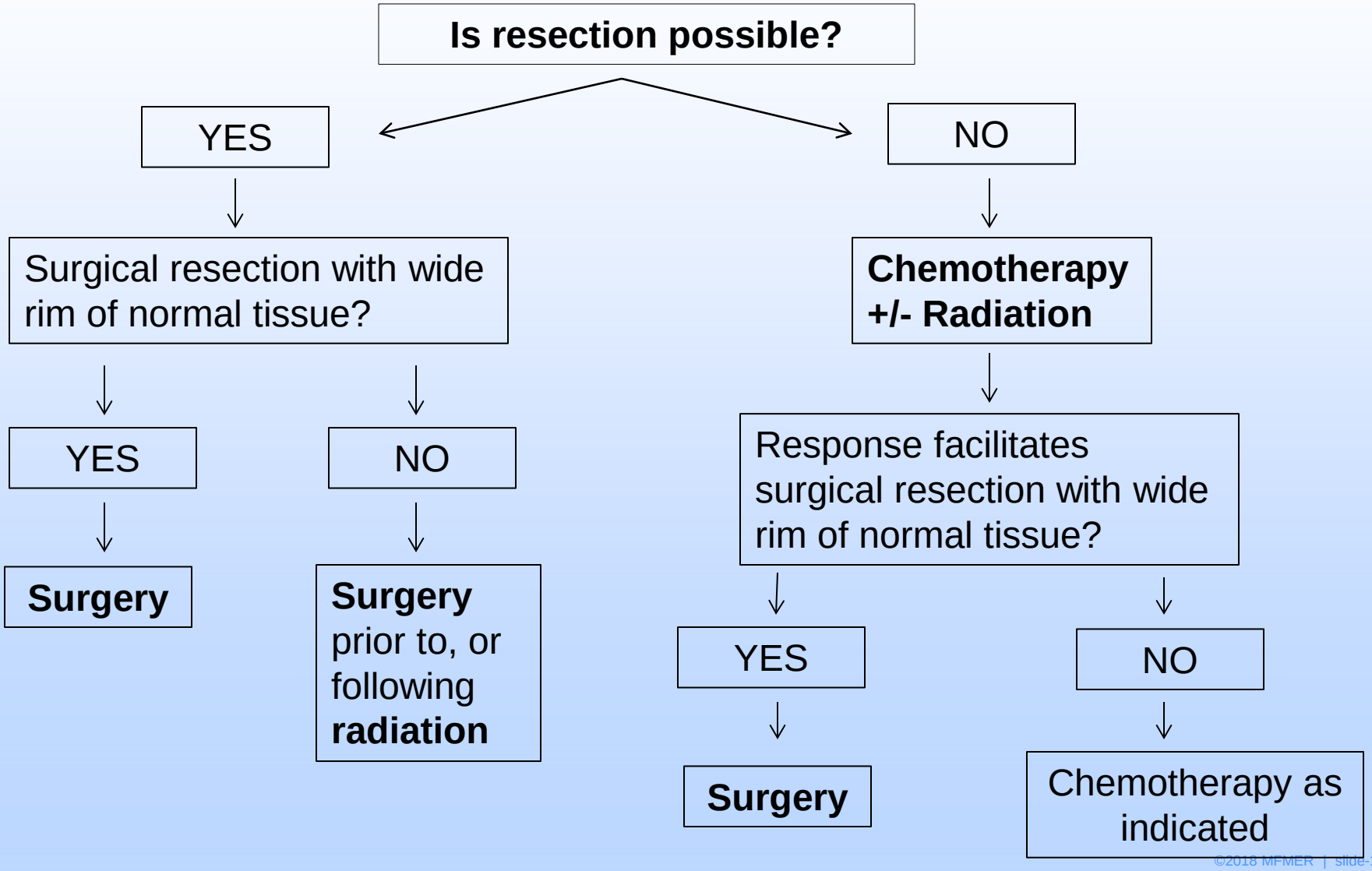
NCCN Guidelines Version 2.2018

Localized disease



Prognostic factors

- Likelihood of relapse and survival
- Localized disease
  - 73-76% at 5 years
  - 62% at 25 years
- Poor risk factors
  - Size > 5cm
  - High grade
  - Deep location
- Leiomyosarcoma: **location**

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Pisters et al. JCO. 2018.
Zagars et al. Cancer. 2003

Chemotherapy for overall survival benefit in localized disease?

- EURACAN 2018
  - “Adjuvant chemotherapy is not standard”
  - “Can be proposed as an option to high risk patients for **shared decision making**”
- NCCN 2018
  - “Limited data regarding benefit…category 2B recommendation”
    - 2B: lower level evidence with no consensus that the intervention is appropriate

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NCCN Guidelines Version 2.2018
ESMO-EURACAN guidelines. Annal Oncol. 2018

Chemotherapy for overall survival benefit in localized disease?

SMAC 1997

- 1568 patients in 14 trials
  - 1973-1990
- Sites: 12 extremity, 10 trunk, 7 head/neck, 5 retroperitoneum, 1 uterus
- Improved relapse free survival
- NO benefit to overall survival

Meta-Analysis 2008

- 1953 patients in 18 trials
  - 1973-1996
- 5 anthracycline + ifosfamide containing trials
- Absolute risk reduction in death of 11% at 10 yrs.
  - Doxorubicin+ ifosfamide
- **included multiple types of sarcoma

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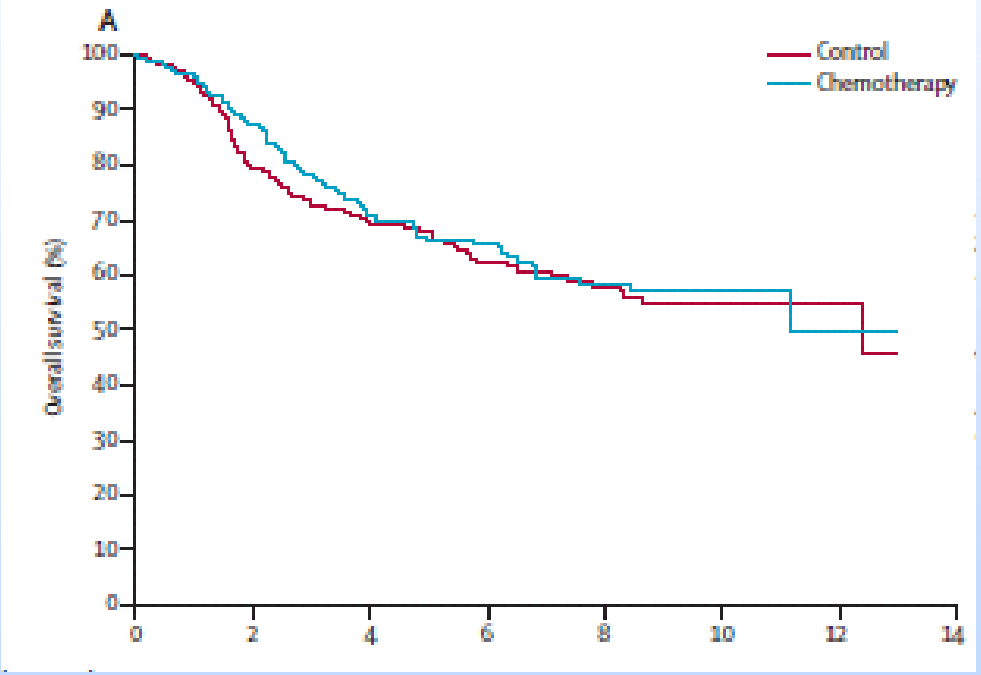
SMAC. Lancet. 1997
Pervaiz et al. Cancer. 2008

Chemotherapy for overall survival benefit in localized disease?

EORTC 62931

- 1995-2003, 351 patients
- Doxorubicin 75mg/m^2 + ifosfamide 5 g/m^2
- No benefit in OS or RFS
- Criticized
  - dose of ifosfamide
  - Inclusion of pts with small or lower grade tumors



Woll et al. Lancet Oncol. 2012

Chemotherapy for overall survival benefit in localized disease?

Histotype-tailored neoadjuvant chemotherapy versus standard chemotherapy in patients with high-risk soft-tissue sarcomas (ISG-STS 1001): an international, open-label, randomised, controlled, phase 3, multicentre trial

Alessandro Gronchi, Stefano Ferrari, Vittorio Quagliuolo, Javier Martin Broto, Antonio Lopez Pousa, Giovanni Grignani, Umberto Basso, Jean-Yves Blay, Oscar Tendero, Robert Diaz Beveridge, Virginia Ferraresi, Iwona Lugowska, Domenico Franco Merlo, Valeria Fontana, Emanuela Marchesi, Davide Maria Donati, Elena Palassini, Emanuela Palmerini, Rita De Sanctis, Carlo Morosi, Silvia Stacchiotti, Silvia Bagué, Jean Michelle Coindre, Angelo Paolo Dei Tos, Piero Picci, Paolo Bruzzi, Paolo Giovanni Casali

Gronchi et al. Lancet Oncol. 2017

ISG-STS-101

High Risk STS

-Localized
->5 cm
-High grade
-Deep seated

32 hospitals
287 patients
Italy, Spain, France, Poland

Ifosfamide and epirubicin

Subtype	Histo specific Chemo
Undiff pleomorphic	Gemcitabine & doxetaxel
Synovial sarcoma	High dose ifosfamide
MPNST	Ifosfamide & etoposide
LMS	**Gemcitabine & Dacarbazine**
High risk Myxoid LPS	Trabectedin

Gronchi et al. Lancet Oncol 2017

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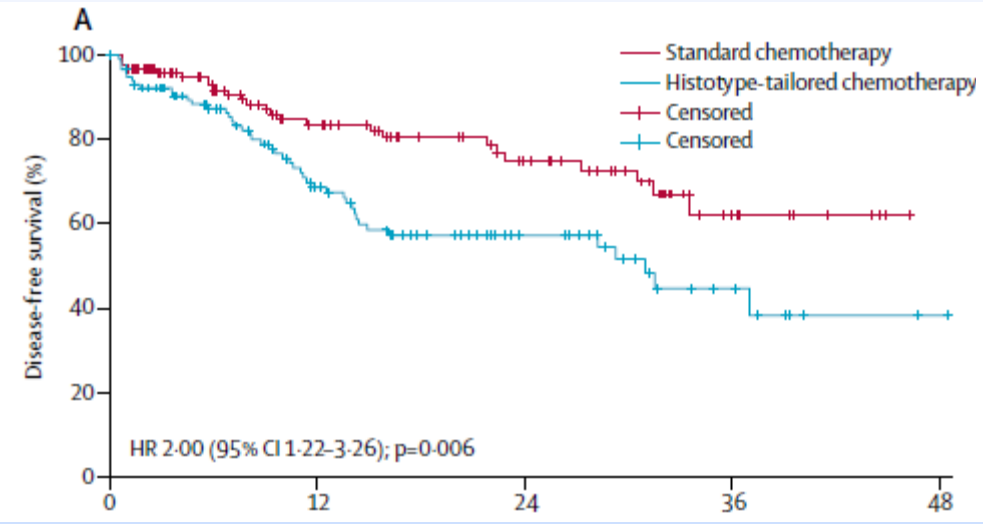
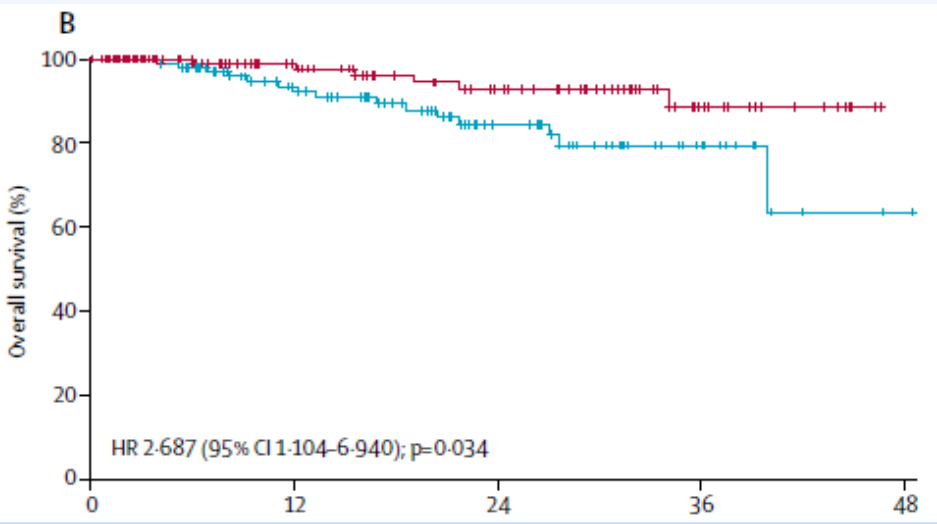
ISG-STS-101

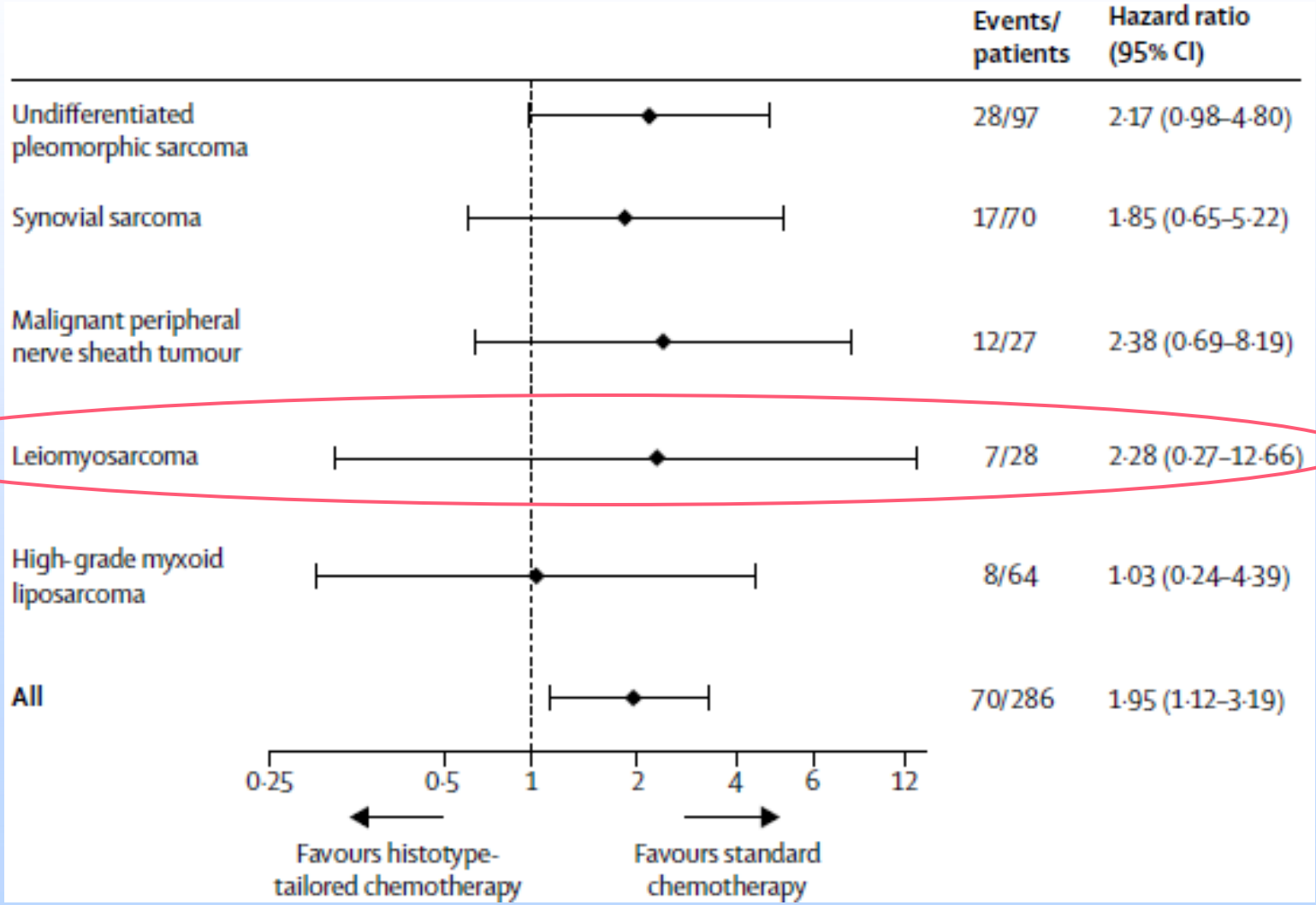




Disease Free (HR 2.00) and Overall Survival (HR 2.687) favored standard chemotherapy

Gronchi et al. Lancet Oncol 2017

ISG-STS-101



Gronchi et al. Lancet Oncol 2017

ISG-STS-101

- Criticisms
  - Small number for each subtype
  - Choice of chemotherapy
    - LMS Doxorubicin & Dacarbazine?
  - Halted early (DSMB review)
  - Short follow up
  - **Did not include “no chemotherapy” arm**

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Uterine Leiomyosarcoma?

- Peak in 40-50 yr, ~50% of women suffer relapse
- SARC005
  - Uterus limited high grade LMS
  - 4 cycles of gemcitabine/docetaxel followed by 4 cycles of doxorubicin
  - 57% progression free at 3 yrs
- GOG 277 (Randomized phase 3)
  - Slow accrual (38 of 216)
  - No benefit to chemo (worse survival)

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Chemotherapy for overall survival benefit in localized disease?

- EURACAN 2018
  - “Adjuvant chemotherapy is not standard”
  - “Can be proposed as an option to high risk patients for **shared decision making**”
- NCCN 2018
  - “Limited data regarding benefit…category 2B recommendation”
    - 2B: lower level evidence with no consensus that the intervention is appropriate

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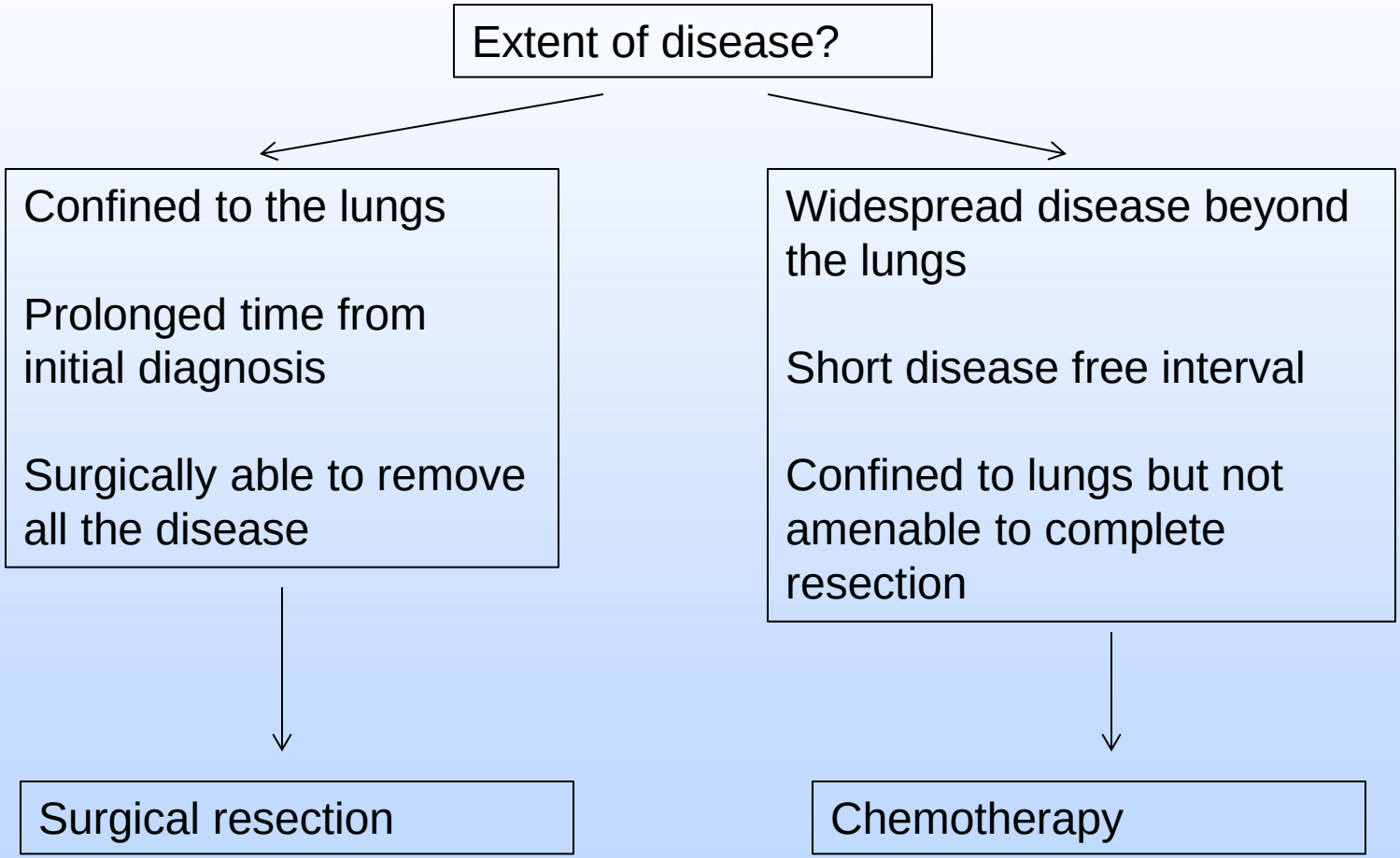
NCCN Guidelines Version 2.2018
ESMO-EURACAN guidelines. Annal Oncol. 2018

Recurrent or advanced disease



Systemic therapy with benefit in LMS

Single Agent

- Doxorubicin
- Liposomal doxorubicin
- Gemcitabine
- Trabectedin
- Pazopanib
- Dacarbazine

Combinations

- Doxorubicin with olaratumab
- Doxorubicin + ifosfamide
- Gemcitabine + docetaxel
- Gemcitabine + Dacarbazine

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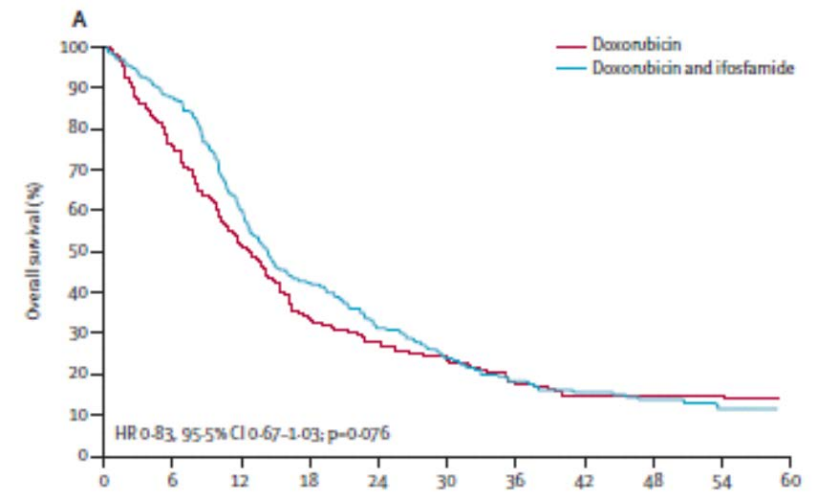
Doxorubicin in advanced STS

Year	Control Arm	Experimental Arm	RR (%)	Median PFS (Mo)	Median OS (Mo)
2014	Doxorubicin	Doxorubicin + Ifosfamide	14 vs 26	4.6 vs 7.4, p=0.003	12.8 vs 14.6, p=0.076
2016	Doxorubicin	Doxorubicin + Olaratumab	11.9 vs 18.2	4.1 vs 6.6, p=0.0615	**14.7 vs 26.5**, p= 0.0003

Judson et al. 2014
Tap et al. Lancet. 2016

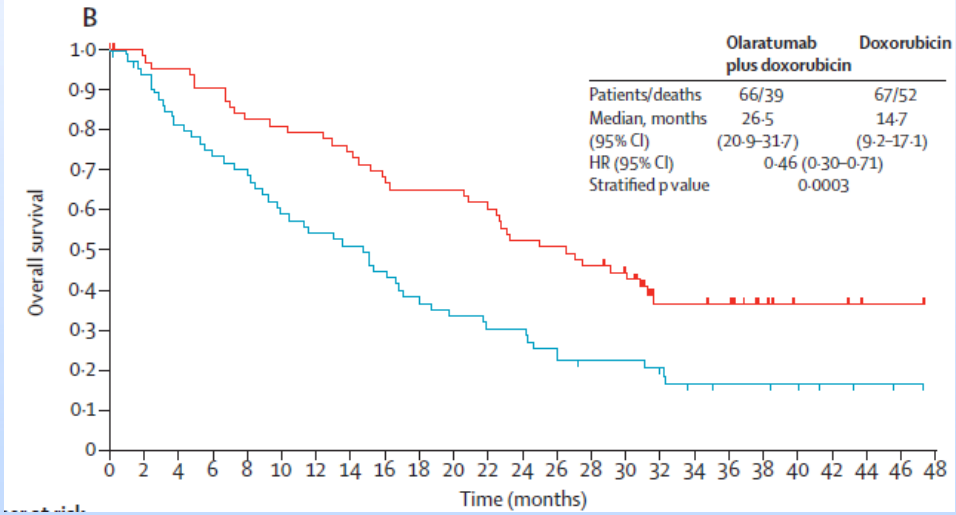
Doxorubicin in advanced STS

Doxorubicin Ifosfamide



RP3 study, 455 patients
LMS = 23% patients

Doxorubicin + Olaratumab*



*RP2 study, 133 patients
LMS = 38% patients

Judson et al. 2014
Tap et al. Lancet. 2016

Conclusions

- Presentation and prognosis of leiomyosarcoma varies by site of origin
- Localized disease
  - Surgery with or without radiation is the mainstay of treatment
  - Role of chemotherapy determined on case by case basis
- Advanced/metastatic disease
  - The addition of olaratumab to doxorubicin dramatically improved overall survival

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Conclusions

- Pressing need to understand tumor biology to guide emerging therapeutic options
- Participation in **collaborative histology specific clinical trials** will strengthen our availability and confidence in emerging treatment options

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Questions?

Extremity Soft Tissue Sarcoma

Matthew T. Houdek MD

Mayo Clinic Department of Orthopedic Surgery – Rochester, Minnesota

Disclosures

- None related to this presentation

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SOFT TISSUE SARCOMAS

- Rare
- 1,688,780 cancer cases in 2017
  - 255,180 (15%) cases of breast
  - 243,170 (15%) cases of lung
  - 12,390 (0.73%) cases of soft tissue sarcomas

Siegel RL, Miller KD, Jemal A (2015) Cancer statistics, 2017.CA Cancer J Clin 65(1), 5–29.

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Too Often :

- Arrive Late
  - Wrong diagnosis
  - Wrong treatment
  - Wrong operation

- *Difficult to Salvage*

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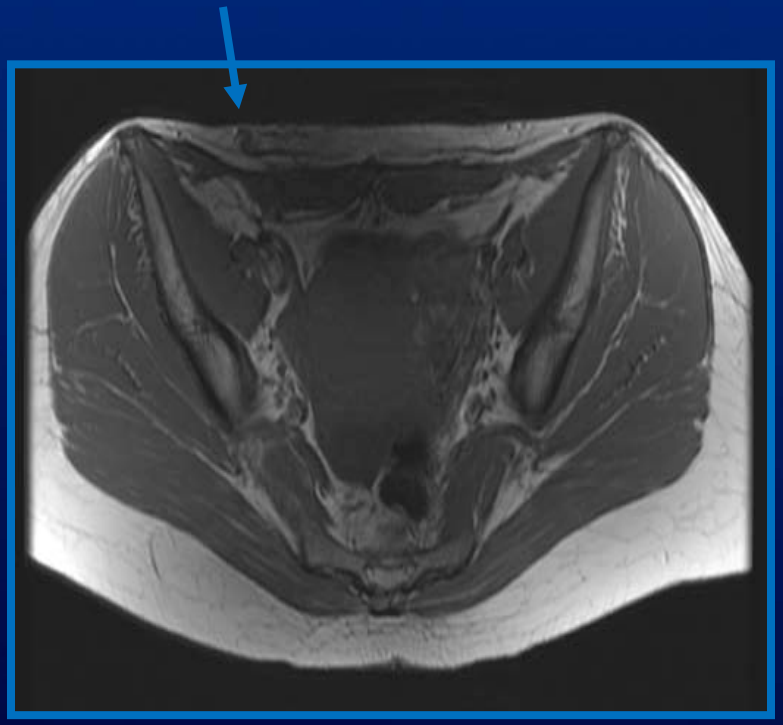
Scope of the Problem
Wide Variability in Presentation



30 F

55 M

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CURRENT MANAGEMENT

- Clinical pathologic correlation
- Clinical staging
- Improved surgical concepts
- Surgical adjuvant treatment regimens

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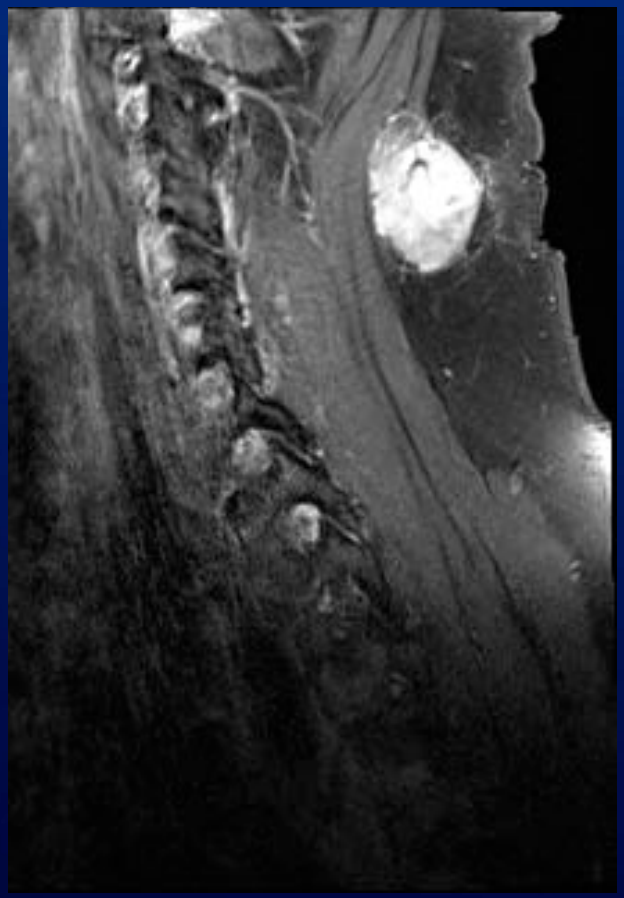
EVALUATION OF MASSES



- Lumps and bumps are common
- Soft tissue sarcomas are rare
  - Benign 300 / 100,000
  - Malignant 2 / 100,000
- Most masses are benign
- MR very useful imaging modality

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EVALUATION OF MASSES

- All masses are abnormal
  - 2 myths : Sarcomas are painful
    Patients will look ill

Resolve

- "Pulled muscle" – how often does this present as a discrete mass?
- Hematoma – how often do spontaneous hematomas arise absent coagulopathy?
  - Dependent echymosis, bruising
  - Not encapsulated

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Failure of Recognition

“It’s just a simple hematoma…”

“It felt like a lipoma…”

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EVALUATION OF MASSES

- What masses are most worrisome?
  - Enlarging
  - Large (> 5 cm)
  - Deep to fascia
- But…
  - 1/3rd of soft tissue sarcomas are superficial
  - Malignant tumors may be small

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EVALUATION OF MASSES

- Clinical Examination
  - Ganglion cyst
    - Transilluminate
  - Hemangiomas
    - Skin findings
    - Size fluctuates with activity
    - Compressible
  - Abscess
    - Fluctuant, tender, erythematous

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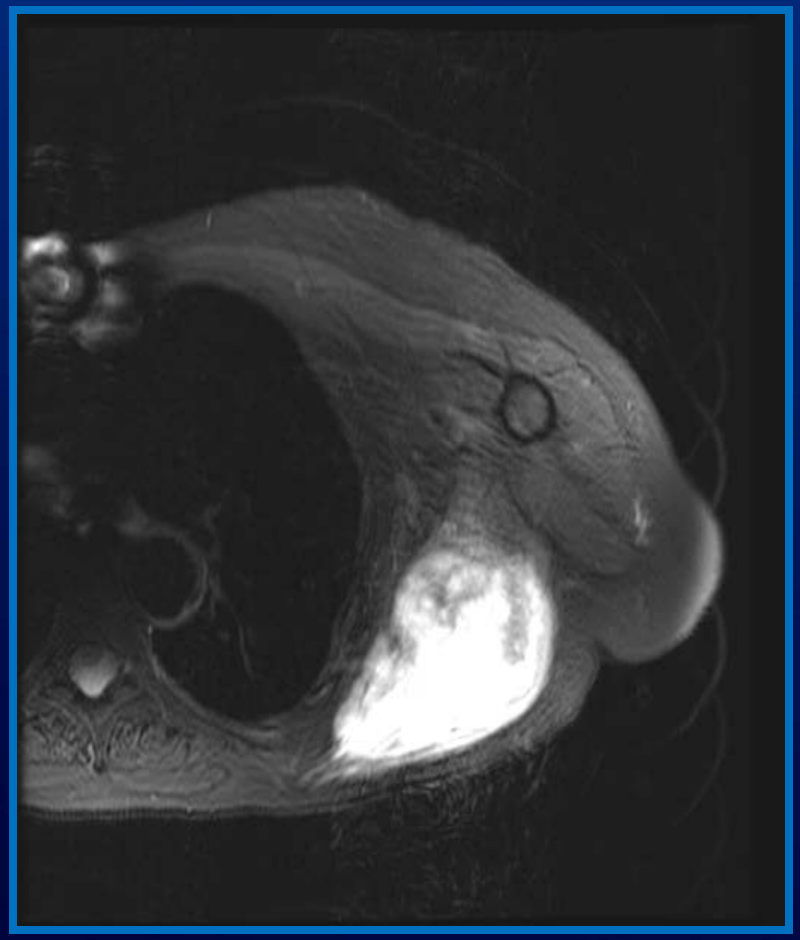
EVALUATION OF MASSES



- Who needs imaging?
  - Masses that cannot be clinically diagnosed as benign
- MR is the most sensitive and specific imaging modality
- If MR indeterminate → **well planned biopsy**

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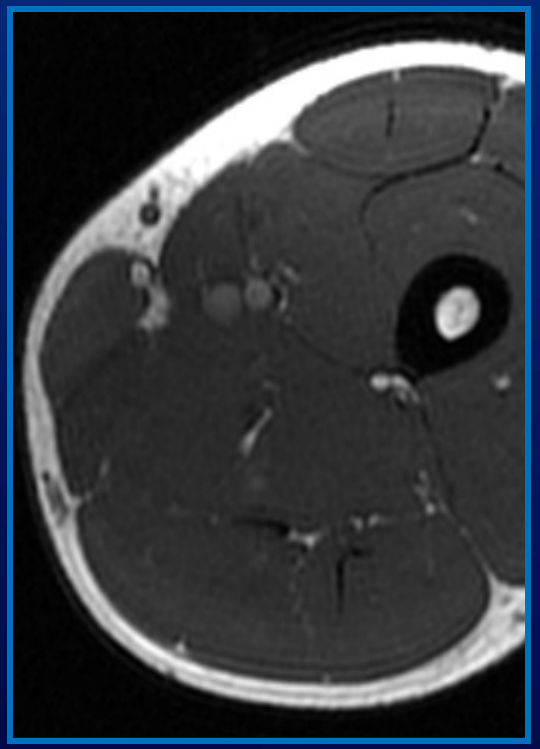
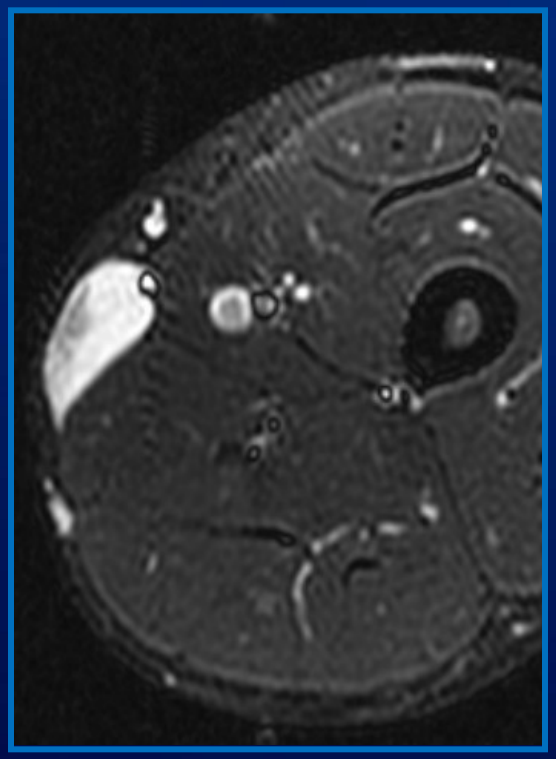
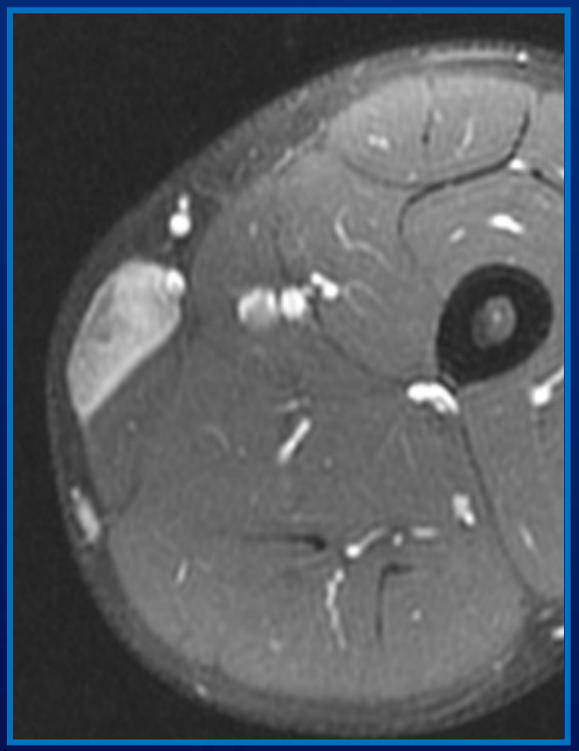
If MRI indeterminate→well planned biopsy



T1



T2



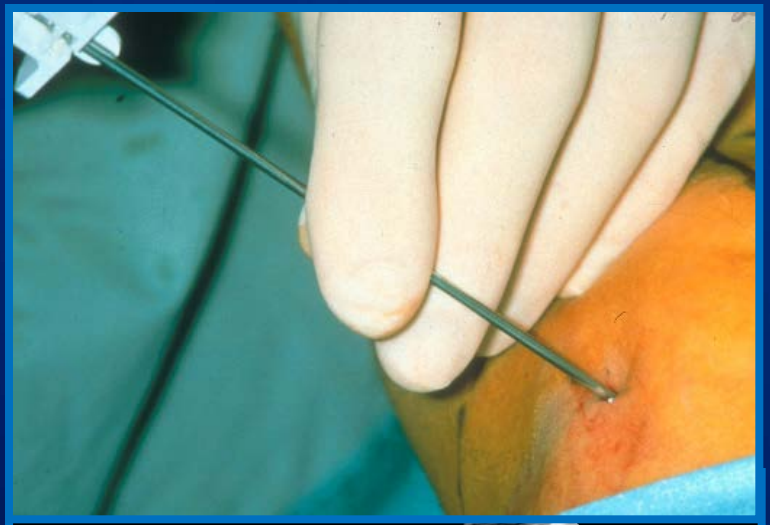
Post gad

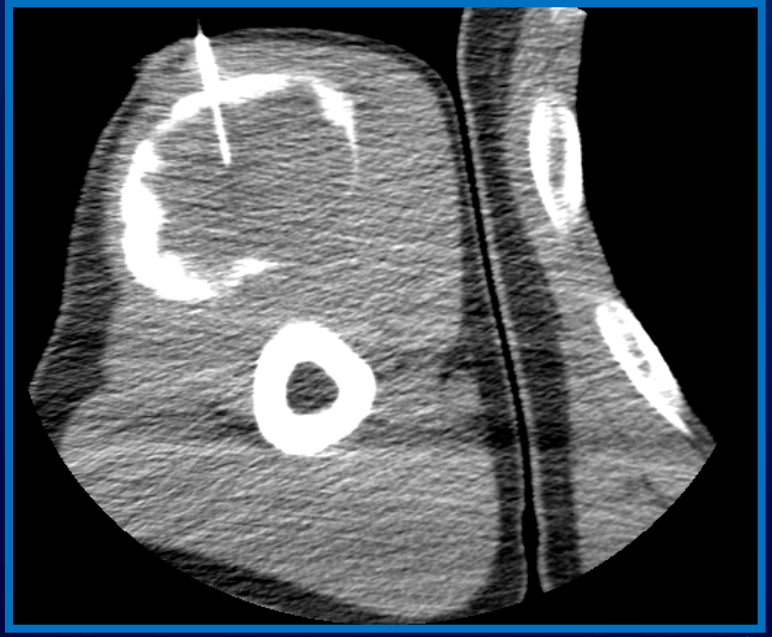
Although small, well marginated and relatively homogeneous, the mass has nonspecific signal characteristics and is therefore, indeterminate.

Biopsy revealed low grade myxoid liposarcoma

BIOPSY

- Needle
  - FNA or core
  - Image guided
- Open incisional
- Open excisional
- Wide Resection





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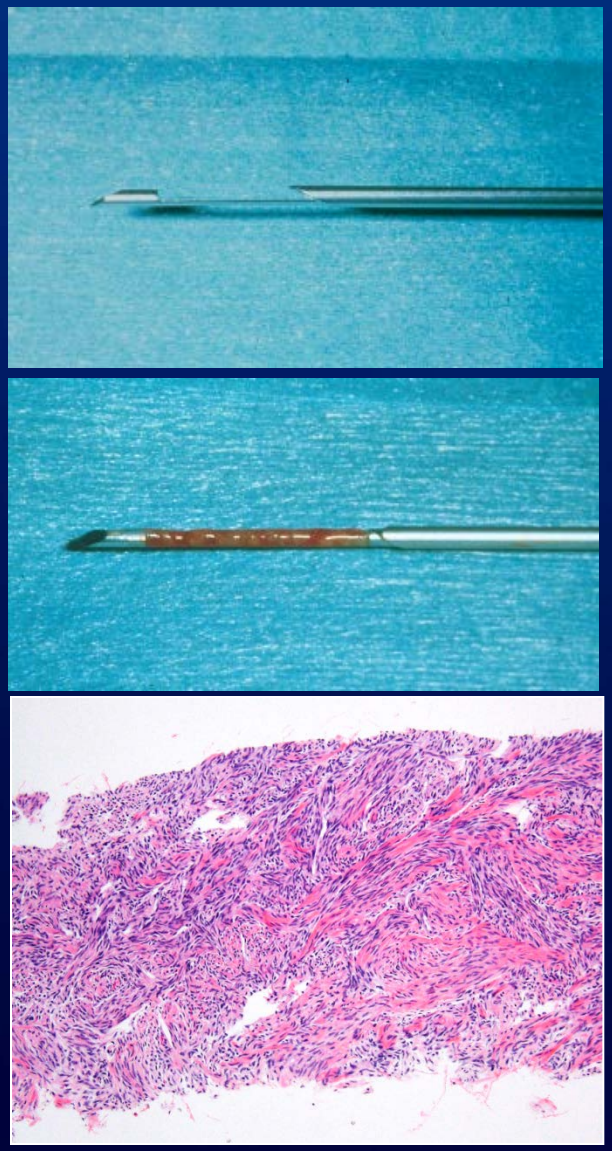
Percutaneous Needle Biopsy



- Safe
- 85-90% accurate
- Effective
- Good reliability
- Cost effective

Beauchamp et al. AAOS, 1989.

Skzinski et al. JBJS(Am), 1996.

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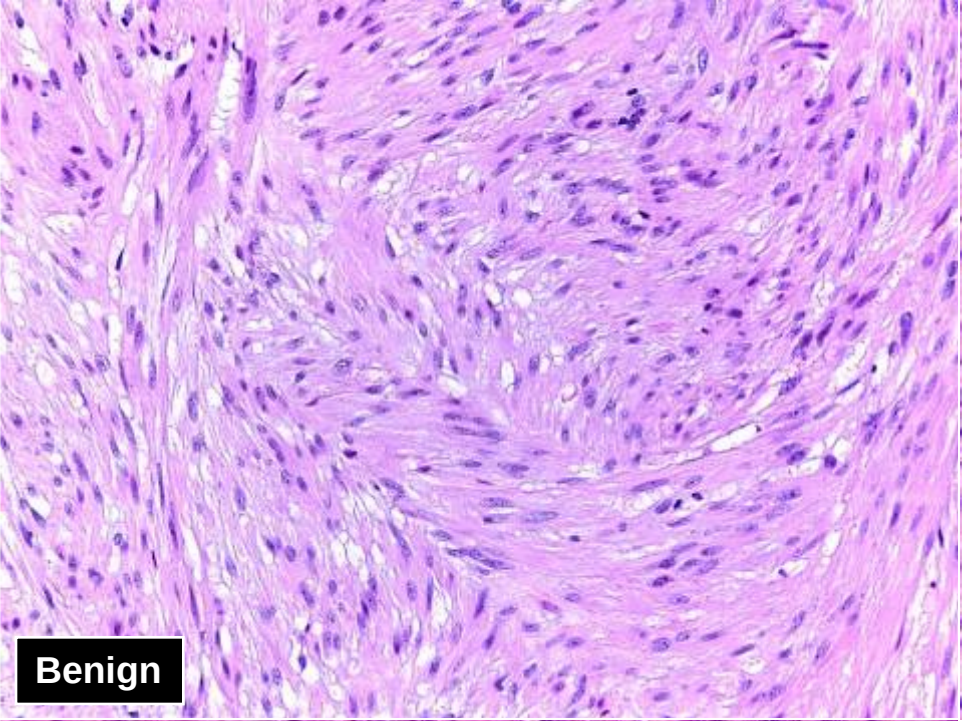
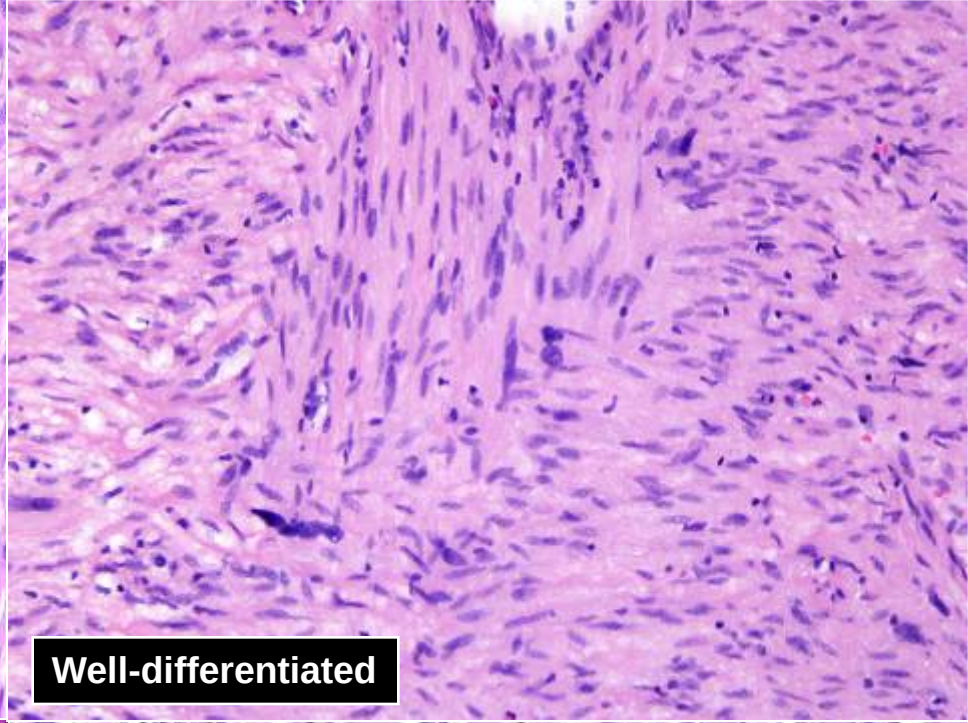
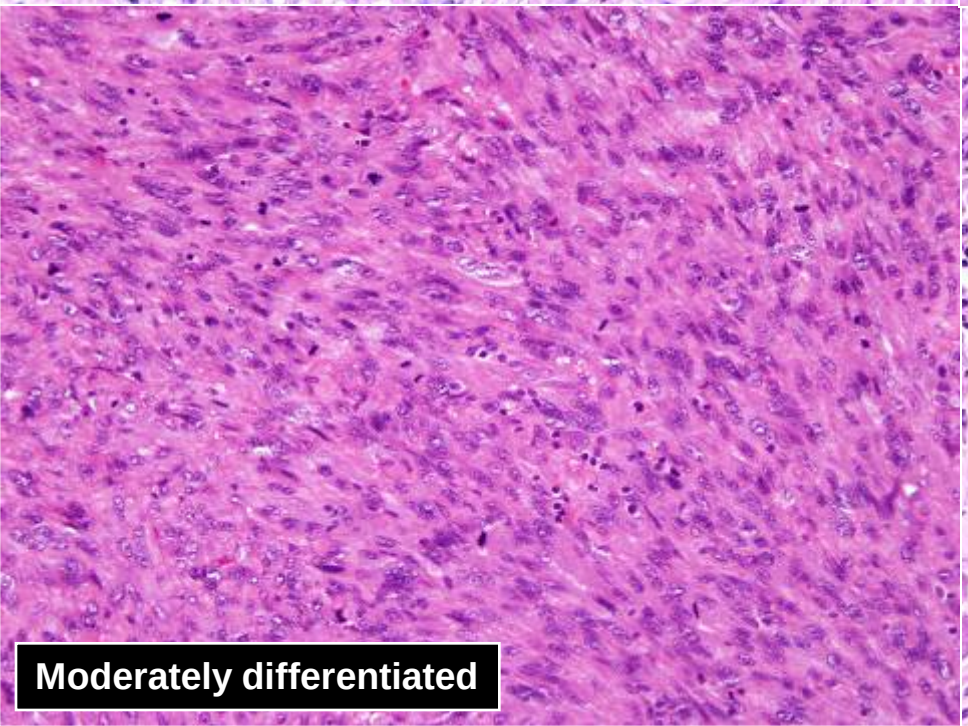
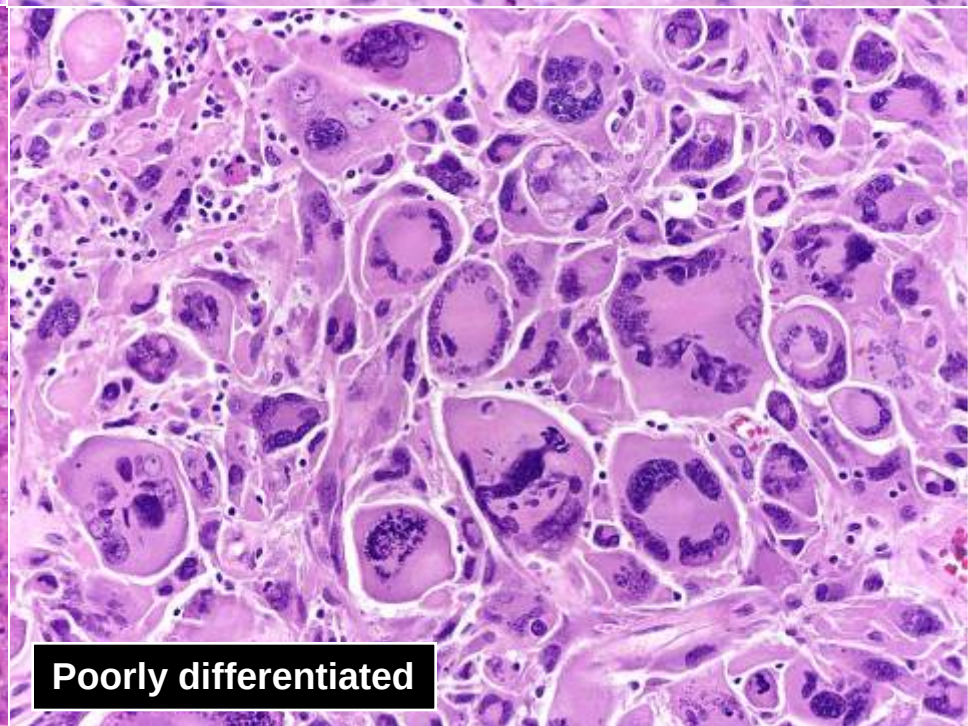

Benign

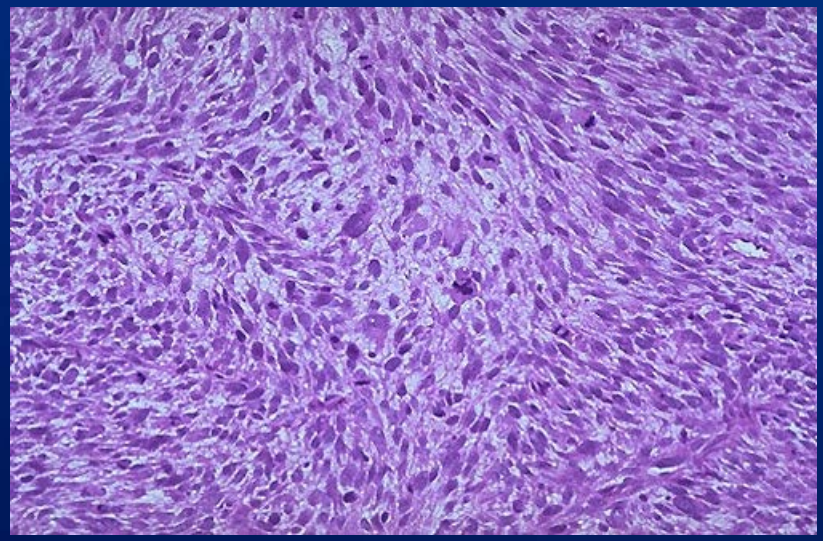

Well-differentiated


Moderately differentiated


Poorly differentiated

LEIOMYOSARCOMA

- Arises from smooth muscle
- Relatively common form of STS
- Poor Prognostic Factors
  - Large Tumors
  - Deep Tumors
  - High Grade



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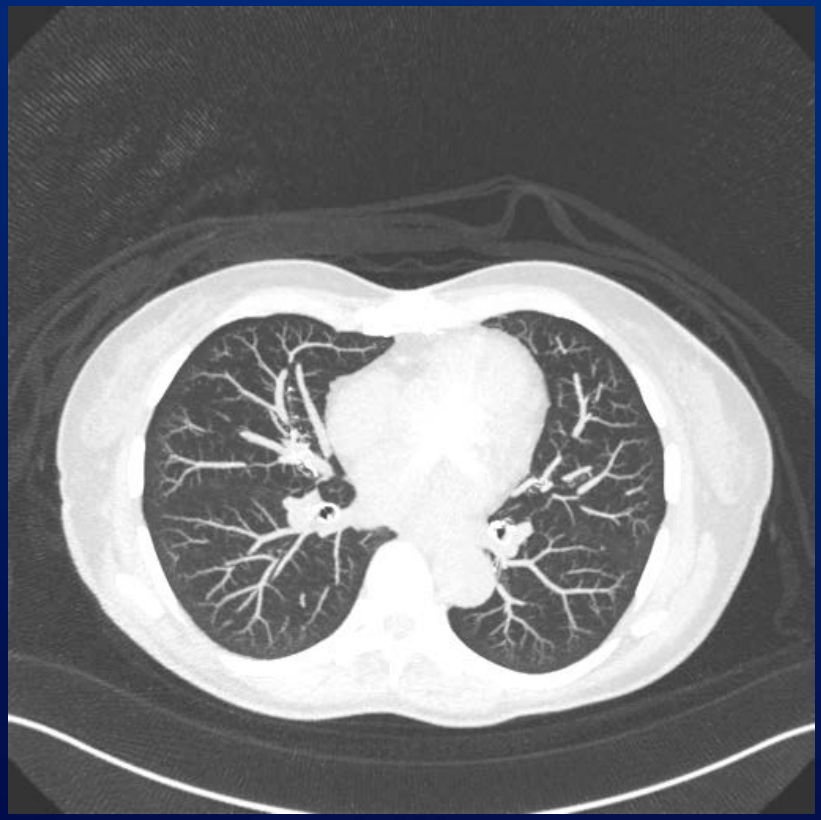
STAGING

- Evaluation for metastatic disease
- CT Chest
- Special cases
  - Total body MRI
    - Myxoid Liposarcoma



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PREOPERATIVE RADIOTHEAPY

- One of the biggest advances in soft-tissue sarcoma surgery
  - Bony resection
  - Major nerve
  - Vascular resection
- Soft tissue reconstruction
  - Flaps

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CHEMOTHERAPY

- Response to chemotherapy variable

Benefit	No Benefit
Rosenberg 1983	Edmonson 1988 (Mayo Study)
Brennan 2007	Alvegard 1989
Milan study 1986	EORTC 2012
Gherlinzoni 1986	

- Meta-analysis: 4-12 % survival benefit

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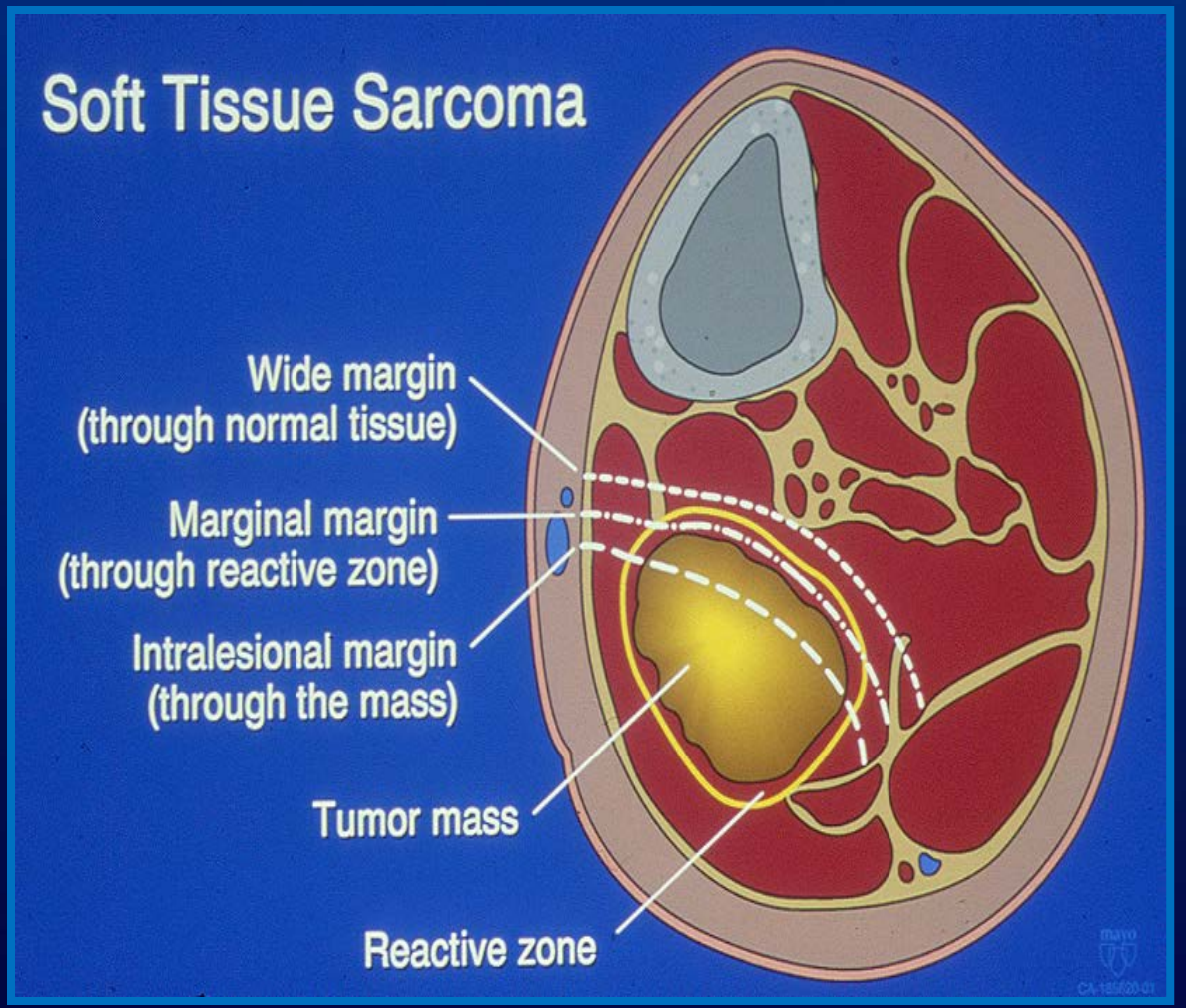
LOCAL RESECTION

- Surgical Margins
  - Intra-lesional
  - Marginal
  - Wide
  - Radical



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Challenges – Morbidity of treatment

- Chemotherapy
- Radiotherapy
- Surgery

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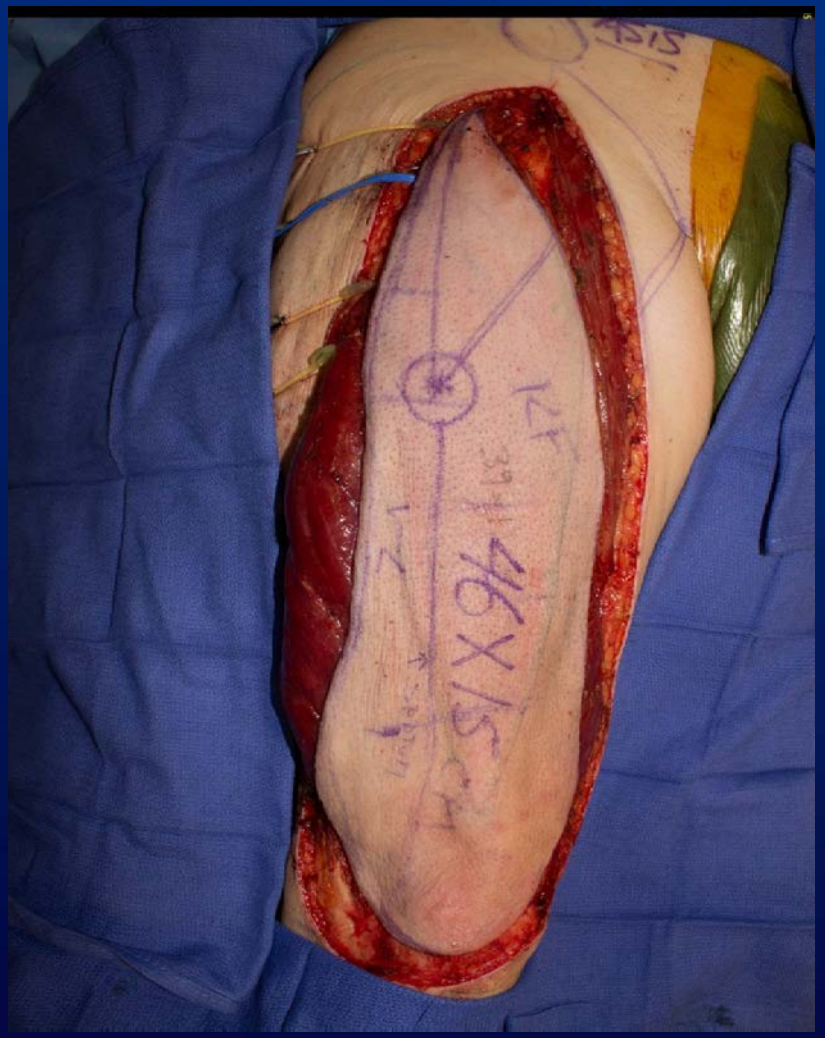
Wound Complications

- High rate of complications following extremity surgery
- Related to preoperative radiotherapy and tumor location
- Preoperative Radiation Therapy
  - 2/18 (11%) with vascularized flaps
  - 16/56 (30%) primary wound closure



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LOCAL RECURRENCE

- Local adjuvant Rx improves local control but no difference in overall survival in randomized groups
  - Rosenberg 1982
  - Brennan 2007
- Prevention of LR in high grade tumors did not prevent metastatic disease
  - Yang 1998
  - Tanabe et al 1994
  - Ueda 1997
  - Trovik 2000

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LOCAL RECURRENCE

- Local recurrence in extremity STS placed patient at increased risk for re-rec, distant metatasis, and tumor-related mortality

  Pisters, JCO 1986

- Strong effect of recurrence on systemic spread

  Bell, JBJS 1989
  Dickinson 2006
  Stajadinok /Brennan 2002
  Novais (Mayo Study) 2010

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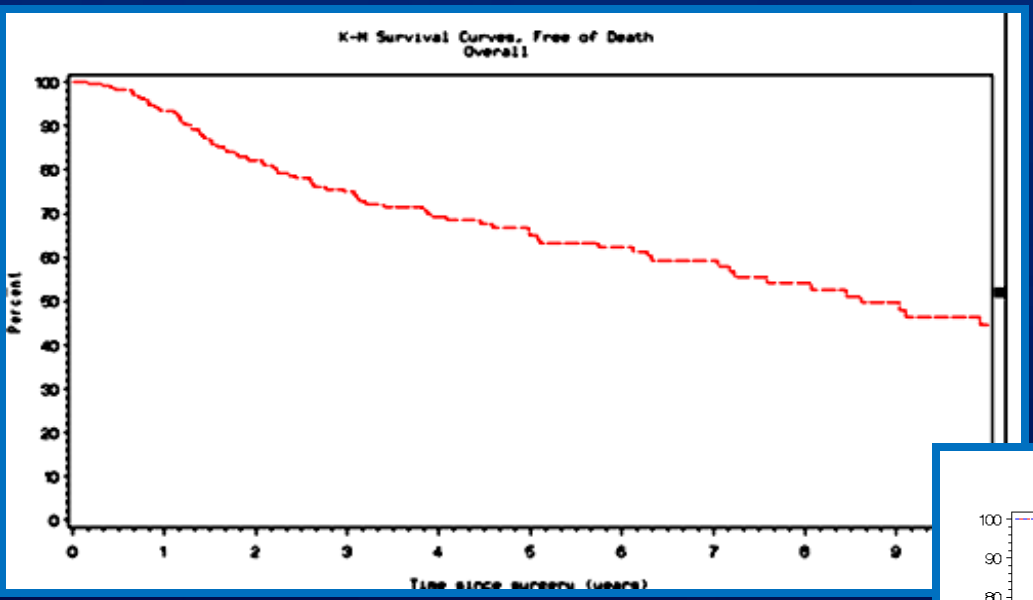
Do Surgical Margin and Local Recurrence Influence Survival in Soft Tissue Sarcomas?

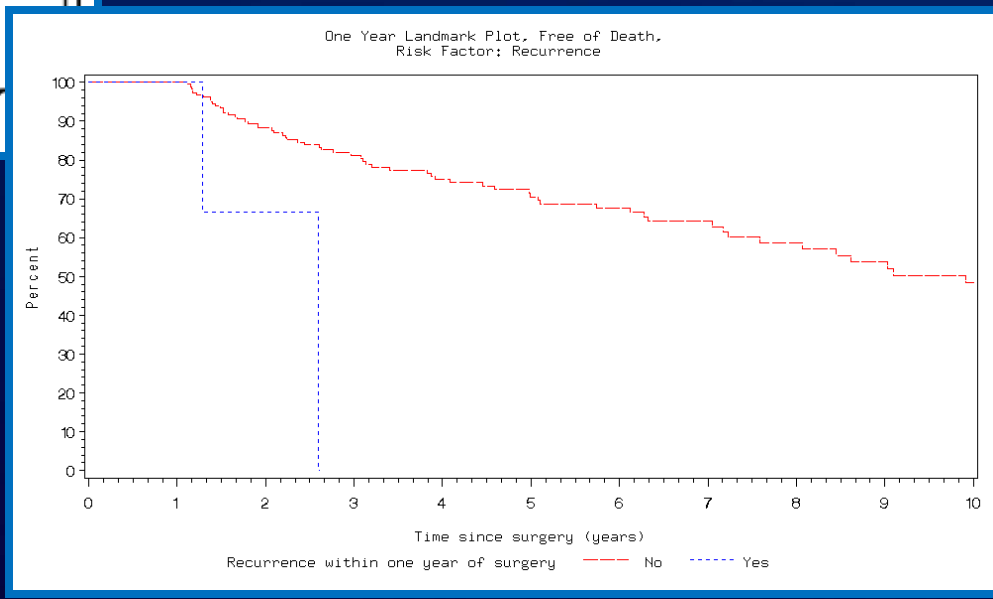


Overall Survival

Overall survival 5 yrs 65%

Mayo Study (248 pts)

Effect of Local Recurrence (1st Yr)



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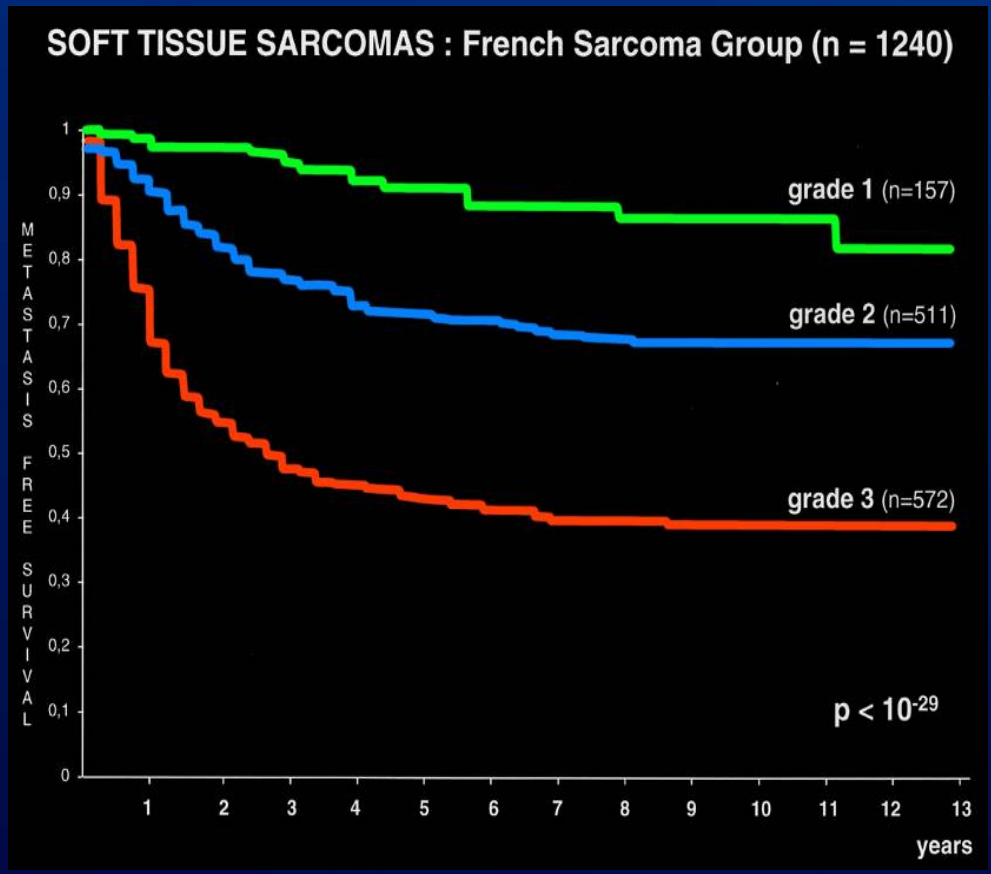
CORR 2010

SOFT TISSUE SARCOMAS

- Even with surgery remains high rate of mortality
- Pulmonary Metastasis
  - 50% high grade lesion
- Emphasize need for effective chemotherapy



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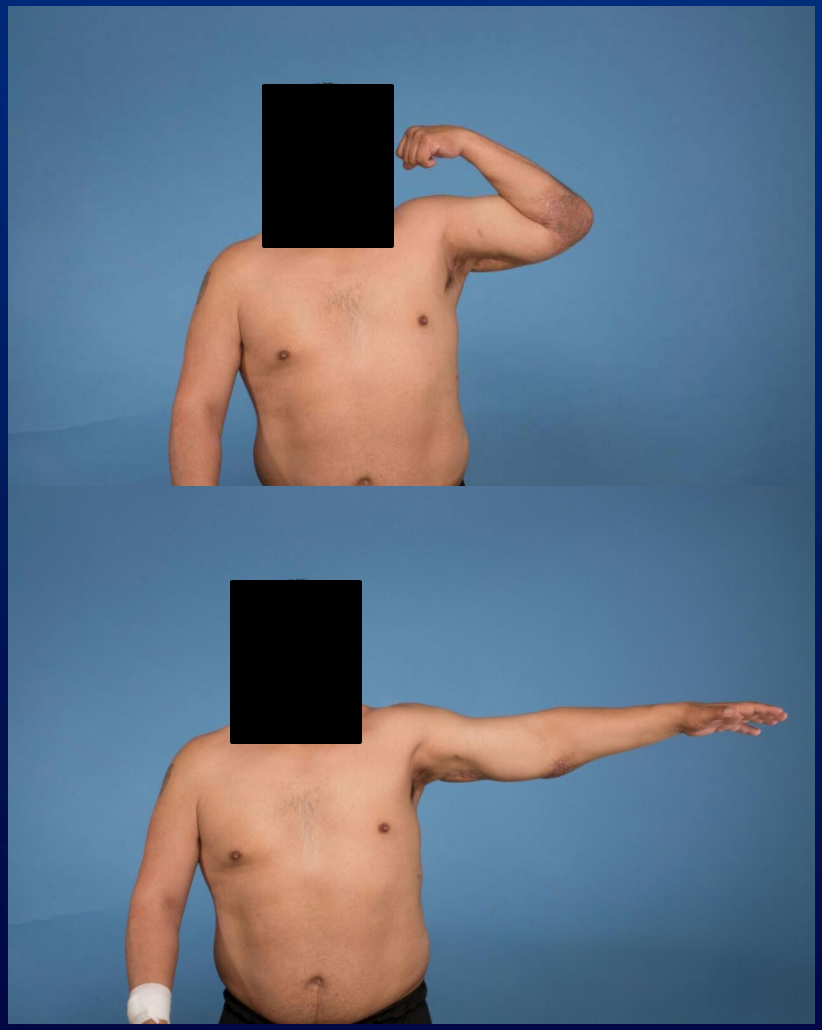
FUNCTIONAL OUTCOME

- Majority of patients will have a functional extremity following limb salvage
- Continued improvement for 2 yrs
  - Stiffness/fatigue
    - Plateaus at 3 mo
  - Pain
    - Plateaus at 3 mo
      - Decreases



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FUTURE OF PATIENT CARE

- Identify which patients are at risk for metastases
- Develop effective therapies for distant disease
  - traditional, anti-angiogenesis, immunologic, molecular

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MODERN MANAGEMENT

- Surgery is critical
- Adjuvant therapy
  - Chemotherapy for osteosarcoma and Ewing sarcoma
  - Chemotherapy ineffective for some STS
  - Radiotherapy for STS
- Advanced disease
  - Chemotherapy is less effective
  - Low response rate
  - Toxic
- Targeted therapies
    - Molecular rationale

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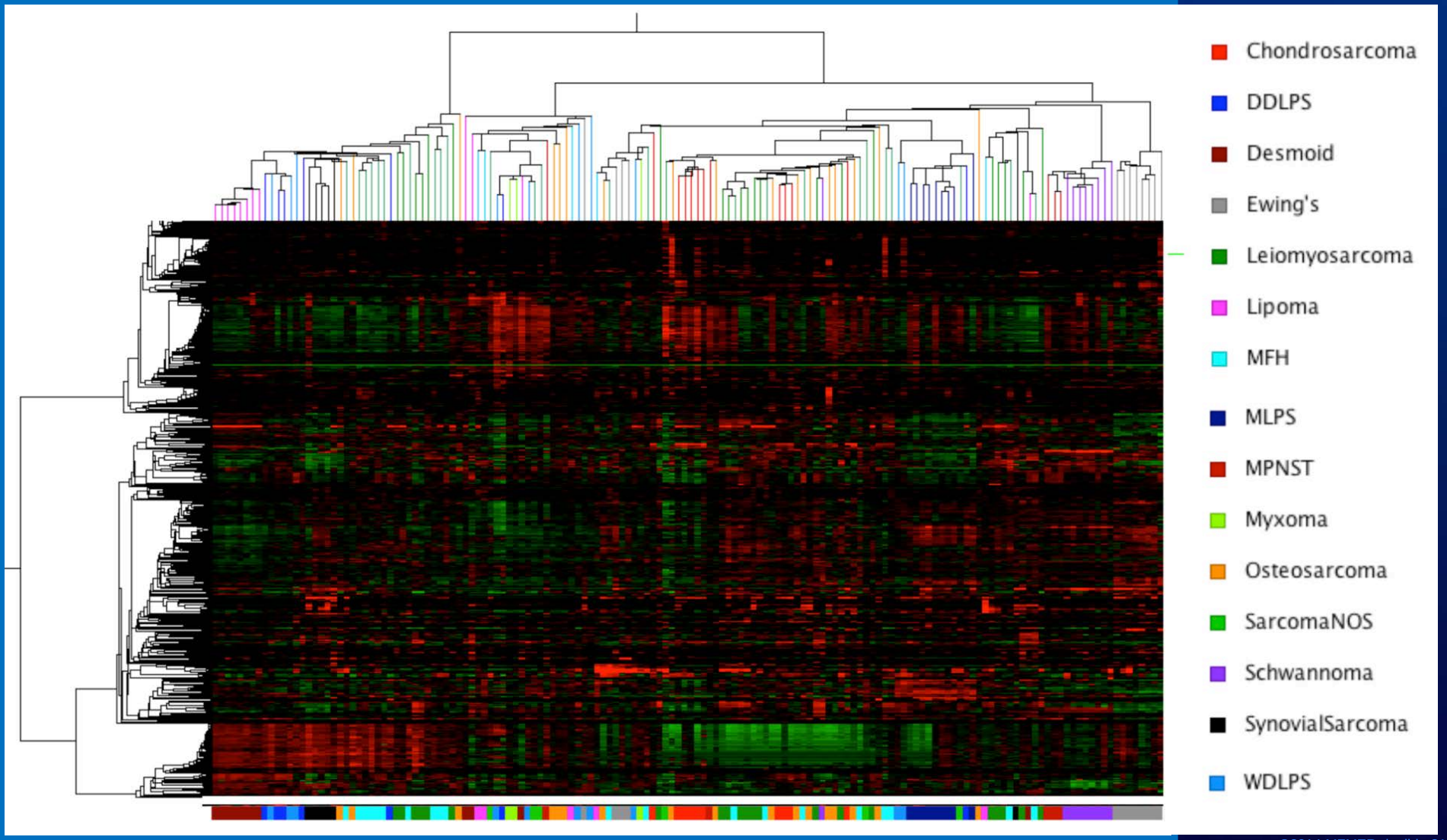
MOLECULAR CLASSIFICATION



MOLECULAR PATHOGENESIS

Phenotype Apparent heterogeneity		Genotype Molecular signature
Sarcoma	→	Target present in 90+%
GIST	→	KIT mutations
DFSP	→	PDGF translocation
GCT bone	→	RANKL expression
WDLPS	→	MDM2/CDK4 amplification

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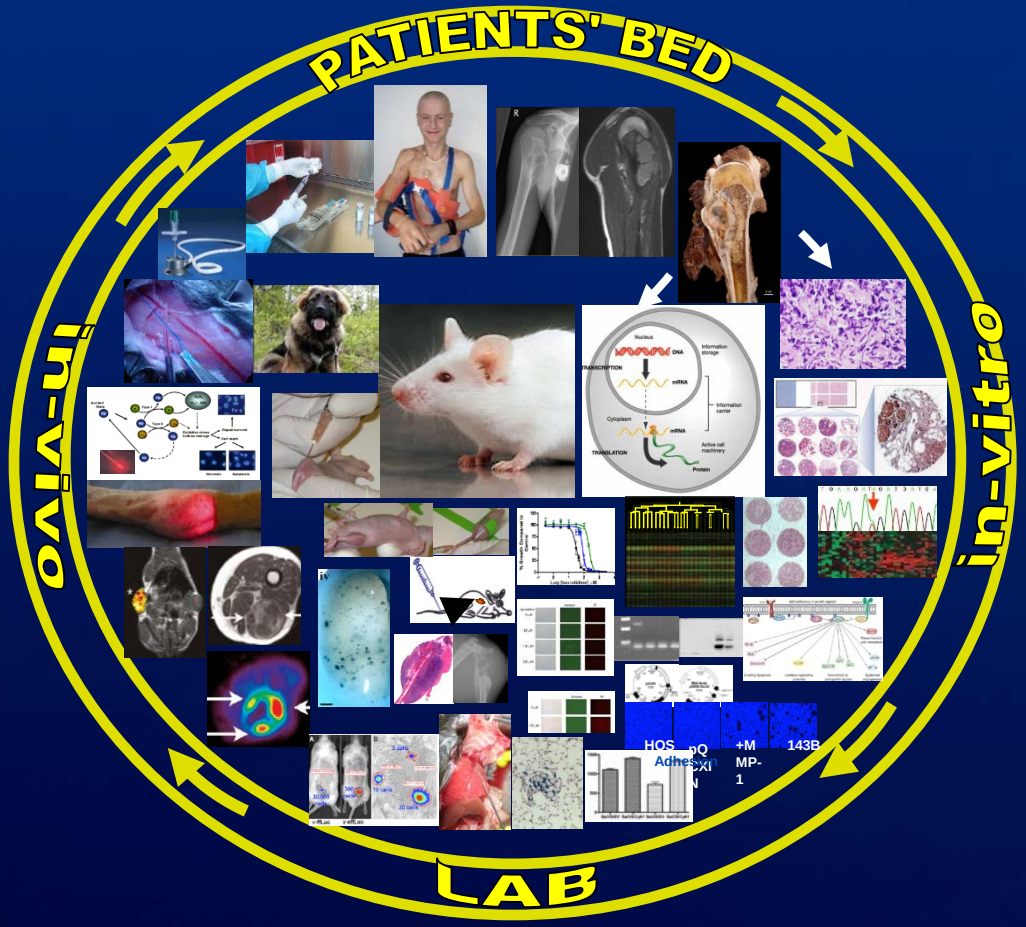
INDIVIDULIZED MEDICINE



Diagnostic markers

Improved imaging

Individualized therapy

→ Prognosis ⬆

Molecular characterization of sarcoma subtypes represents the navel for improved prognosis

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Dermatofibrosarcoma protuberans (DFSP)

- Translocation between Col1α1 and PDGFβ
- Upregulation of PDGFβ activity
- Tyrosine kinase inhibitor (imatinib, glivec) inhibits c-kit, abl and PDGFr

NOV 06

June 07

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Care of Extremity Soft-Tissue Sarcomas at Mayo Clinic

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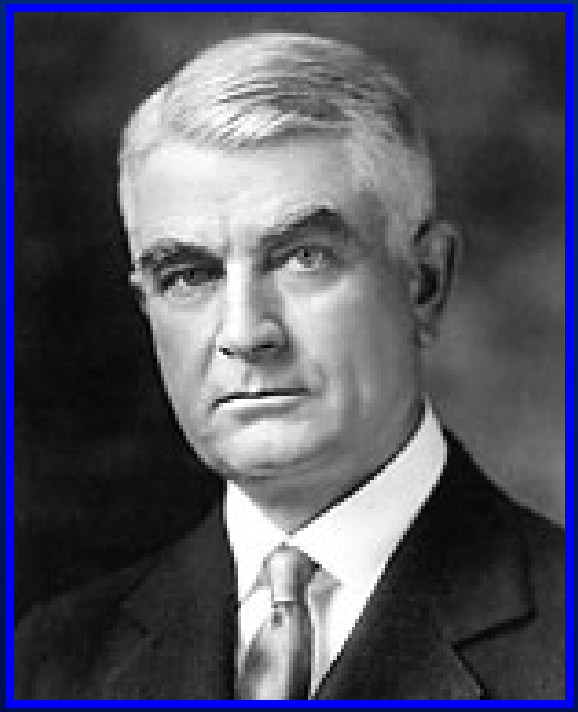
TEAMWORK

"As we grow in learning, we more justly appreciate our dependence upon each other..... and in order that the sick may benefit of advancing knowledge, **union of forces is necessary**."



William Mayo

1910

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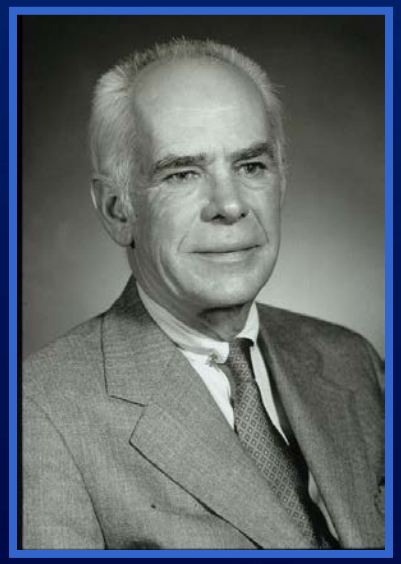
MENTORSHIP



Dr. Ivins

Dr. Sim

Dr. Dahlin

Dr. Unni

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Multidisciplinary Approach

- Surgical
- Medical
- Radiation

} Oncologist

- Imaging Specialist
- Pathologist
- Geneticists
- Molecular Biologist




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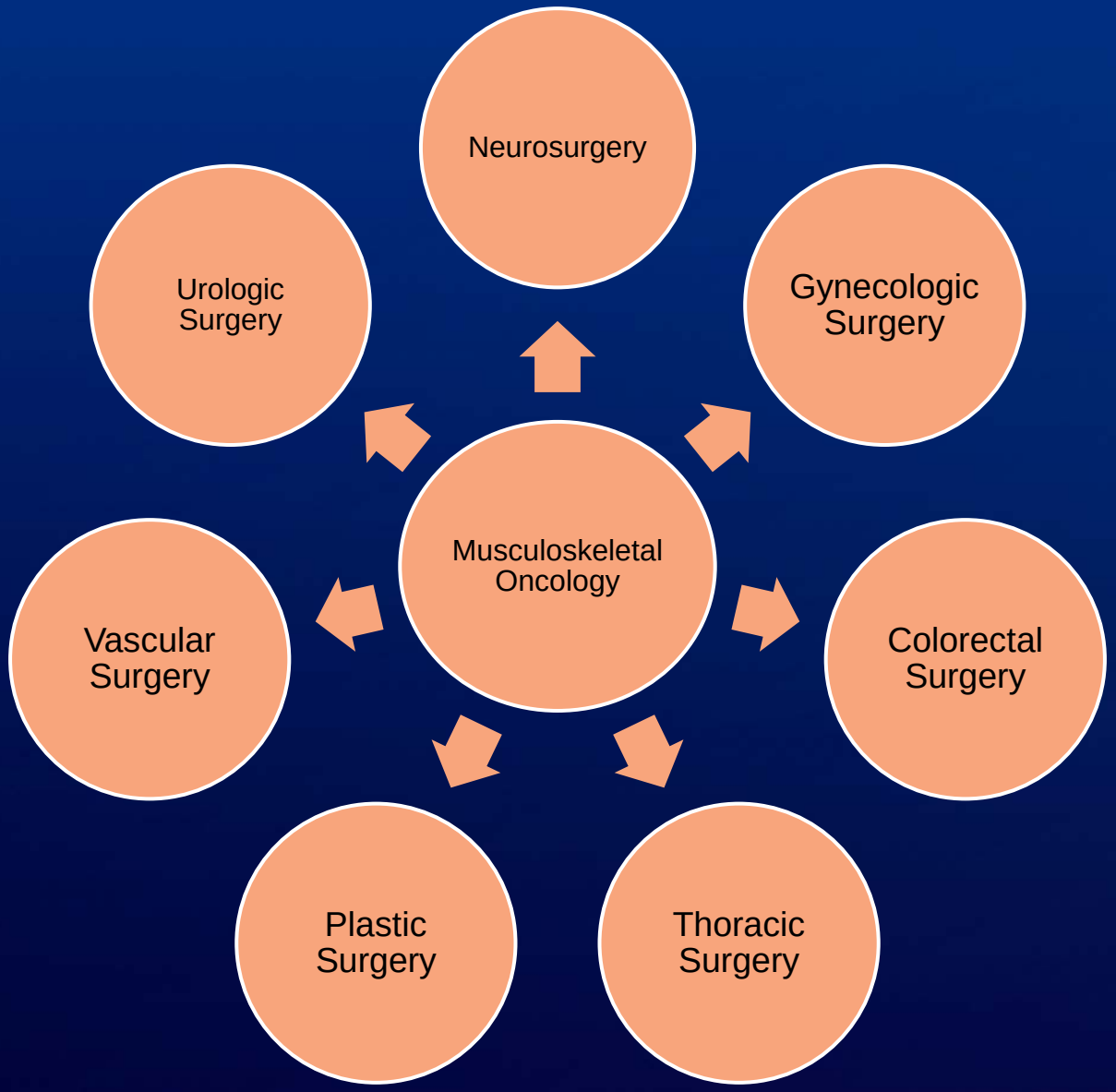
“TEAM MAYO”

Orthopedics | Pathology | Radiology | Medical and Radiation Oncology | Plastics

Teamwork in Musculoskeletal Oncology



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CONCLUSION

- Care for soft-tissue sarcomas has improved
- Able to provide a high rate of local control
  - Metastatic disease remains a problem
  - Molecular targeted “individualized” approaches hold promise
- Care for soft-tissue sarcoma requires a team

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THANK YOU

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Intra-abdominal Surgery for Sarcoma

Travis E. Grotz, M.D.
Surgical Oncologist
Division of Hepatobiliary and Pancreas Surgery
Mayo Clinic

Disclosures

- None

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Intra-abdominal Surgery for Sarcoma

- Trunk and Retroperitoneal Sarcoma
  - Background
  - Presentation
  - Diagnostic Workup
  - Classification, Staging and Grading
  - Treatment
  - Prognosis and Outcomes

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Intra-abdominal Surgery for Sarcoma

- Trunk and Retroperitoneal Sarcoma
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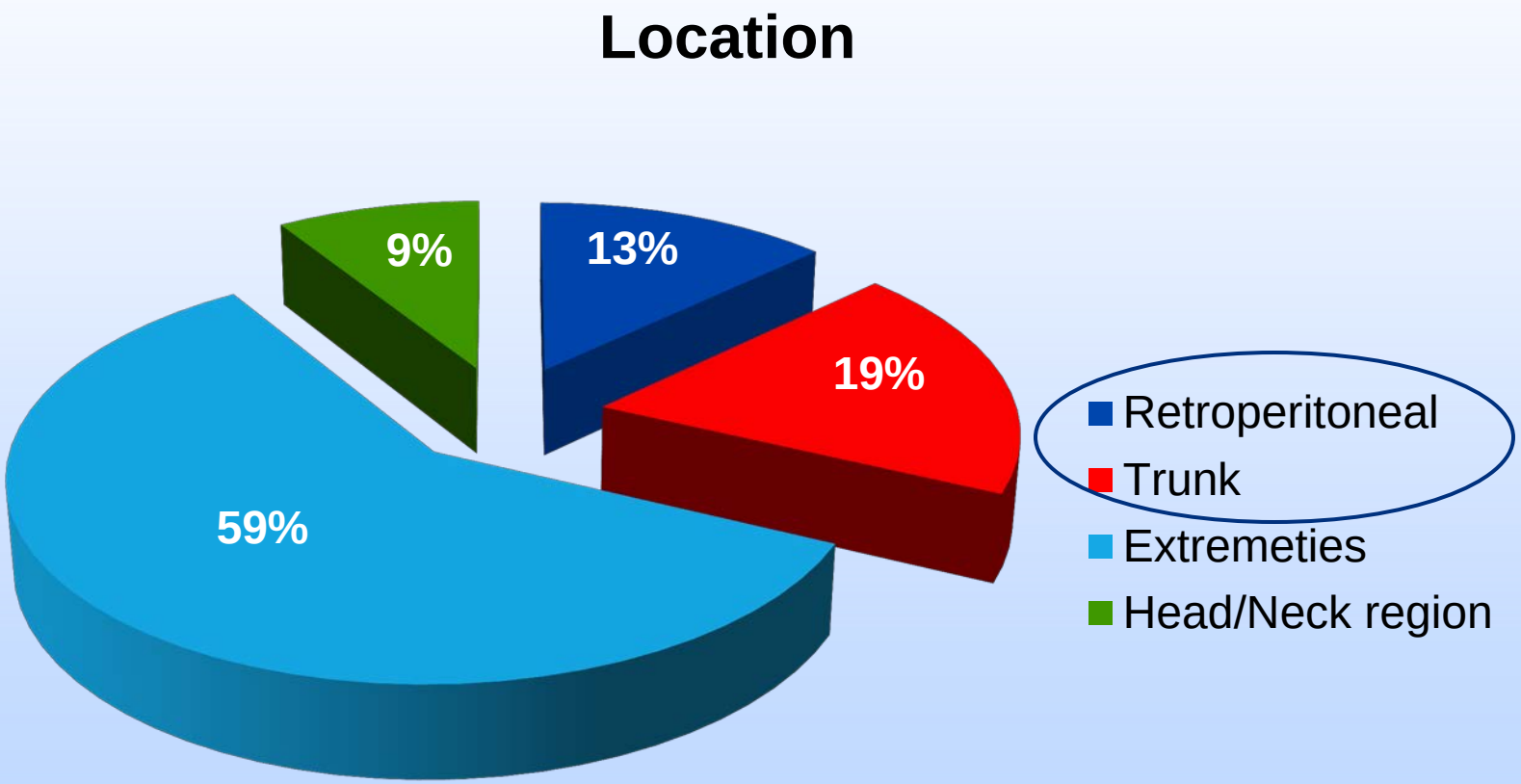
Background



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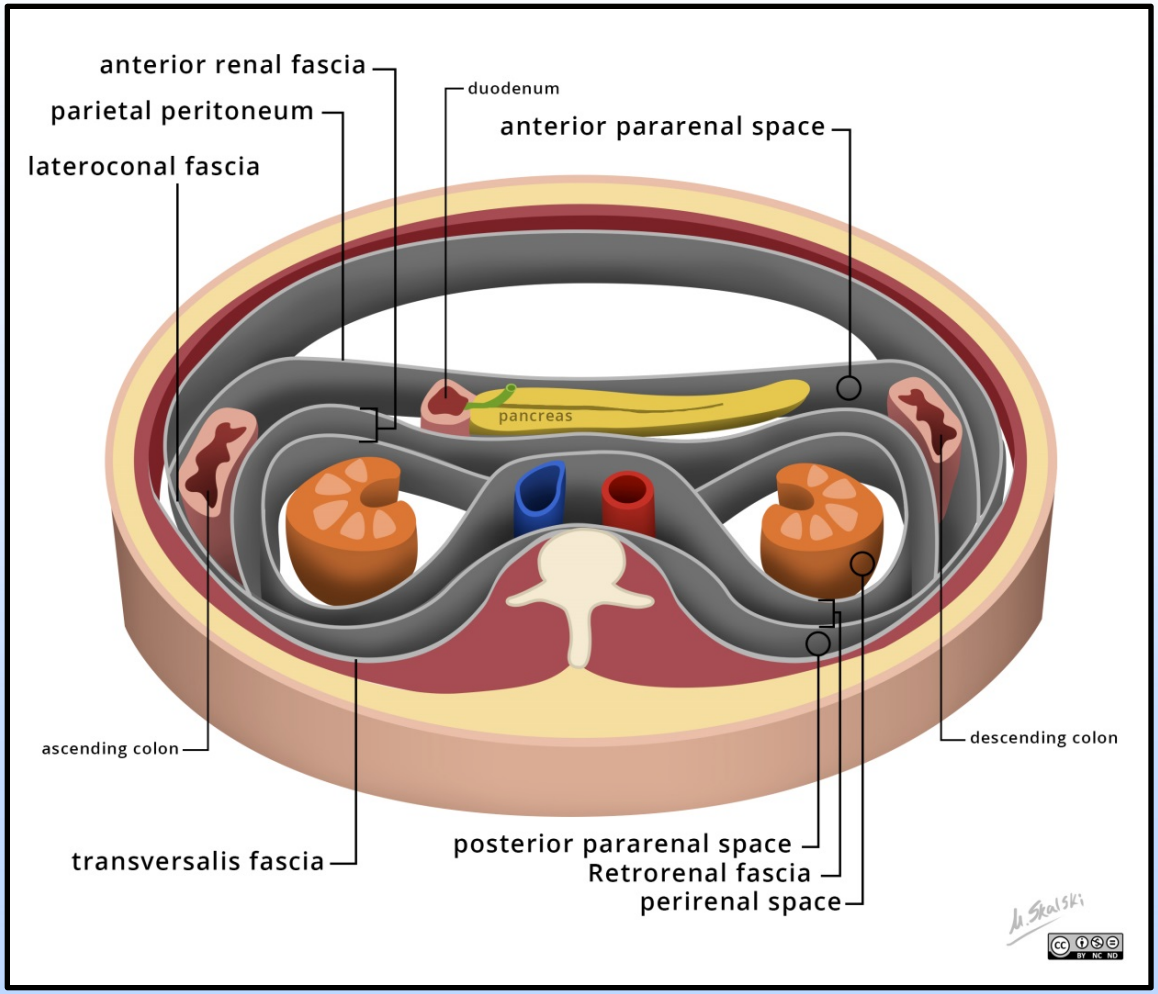
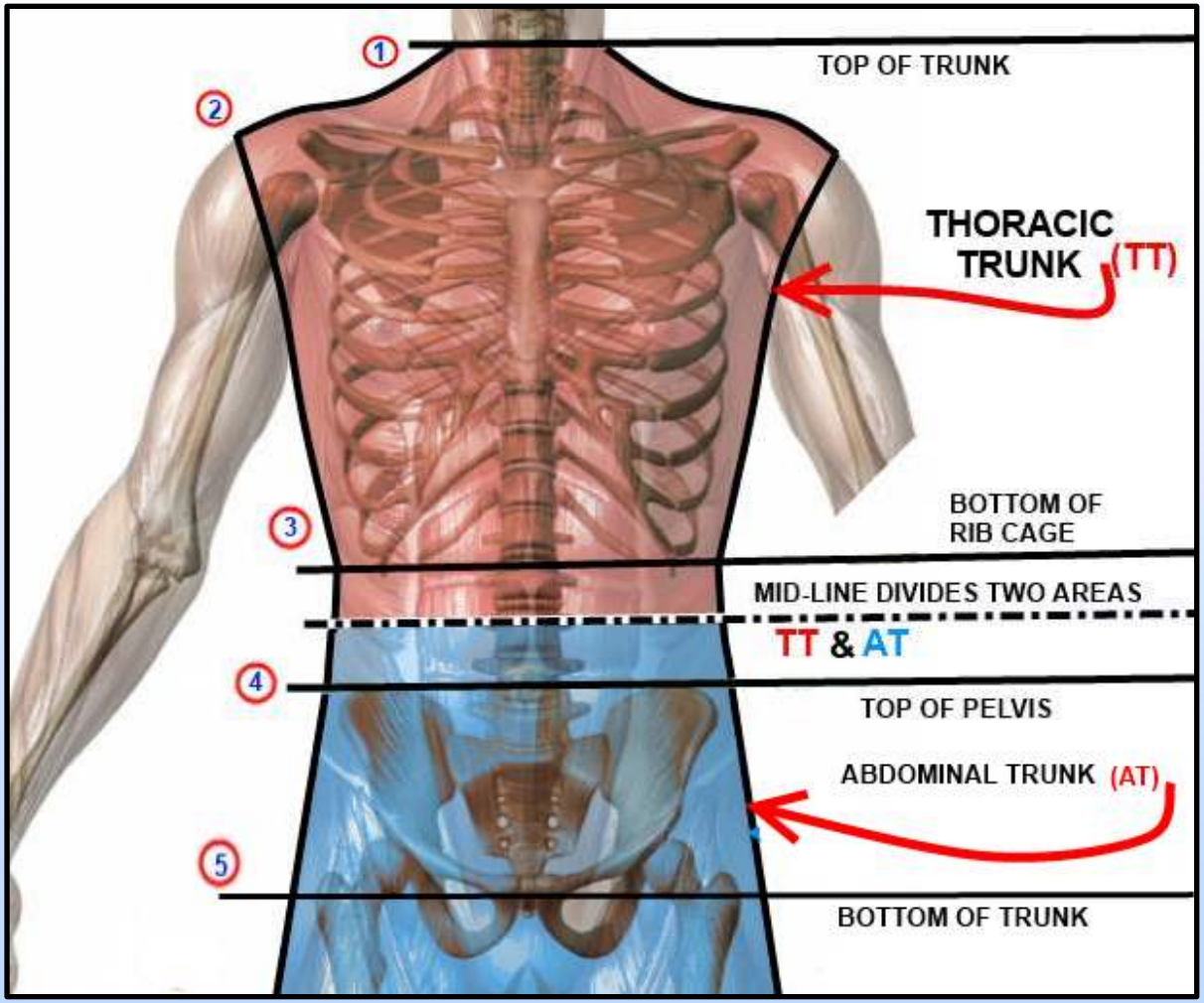
Background

- Retroperitoneum
  - Large potential space



Background

- Trunk:
  - Chest
  - Abdomen
  - pelvis



Background

- RPS are the largest tumors in the human body with 25-50% of RPS tumors exceeding 20 cm.

- Because of their large size and the limited space in the rest of the abdomen, these tumors often touch, compress, displace or outright invade major organs and blood vessels.

- RPS are challenging cancers to treat and often require long operations with multiple different types of surgeons to remove

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Intra-abdominal Surgery for Sarcoma

- Trunk and Retroperitoneal Sarcoma
  - Background
  - **Presentation**
  - Diagnostic Workup
  - Classification, Staging and Grading
  - Treatment
  - Prognosis and Outcomes

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Presentation

- No screening tests
- Patients typically present later due to lack of symptoms
  - Pain, fullness, distention
- Or found incidentally during imaging for an unrelated reason

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Intra-abdominal Surgery for Sarcoma

- Trunk and Retroperitoneal Sarcoma
  - Background
  - Presentation
  - **Diagnostic Workup**
  - Classification, Staging and Grading
  - Treatment
  - Prognosis and Outcomes

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Diagnostic Workup

- Diagnostic test of choice to evaluate truncal or RPS is a contrast-enhanced CT scan or MRI of the abdomen and pelvis
- Radiographic imaging is often diagnostic
- Pre-treatment needle biopsy should be done to obtain diagnosis

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Intra-abdominal Surgery for Sarcoma

- Trunk and Retroperitoneal Sarcoma
  - Background
  - Presentation
  - Diagnostic Workup
  - **Classification, Staging and Grading**
  - Treatment
  - Prognosis and Outcomes

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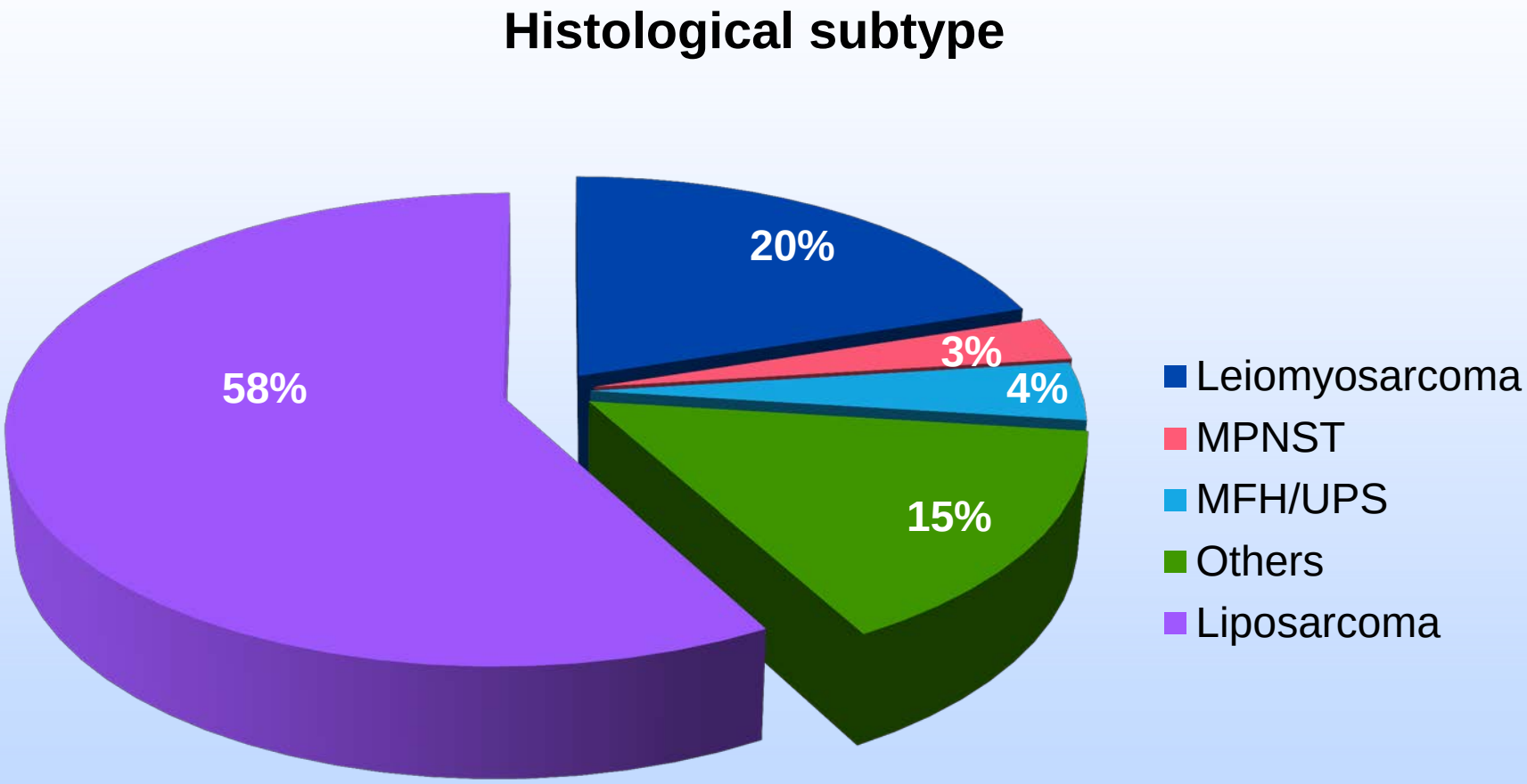
Classification, Staging and Grading



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Classification, Staging and Grading

- Staging imaging consists of either a CT scan of the chest or a PET scan
- Despite their large size most RPS rarely metastasize
  - ≈10% of RPS are found to have metastatic disease at presentation
  - ≈20-25% will develop distant metastasis, typically to the lungs or liver.
  - 3 out of 4 deaths due to RPS is from local recurrence

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Classification, Staging and Grading

TNM staging of soft tissue sarcoma in the abdomen

Definitions of TMN

Primary Tumor (T)	
TX	Primary tumor cannot be assessed
T1	Organ confined
T2	Tumor extension into tissue beyond organ
T2a	Invades serosa or visceral peritoneum
T2b	Extension beyond serosa (mesentery)
T3	Invades another organ
T4	Multifocal involvement
T4a	Multifocal (two sites)
T4b	Multifocal (three to five sites)
T4c	Multifocal (>5 sites)

Regional Lymph Nodes (N)	
N0	No regional lymph node metastasis or unknown lymph node status
N1	Regional lymph node metastasis

Distant Metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis

- Staging is not useful/meaningful as there are no recommended prognostic stage groupings.

AJCC Cancer Staging Manual, Eighth edition (2017) published by Springer Science and Business Media.

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Classification, Staging and Grading

- **Histology** - the specific type of cancer cell in a given sarcoma.
- **Necrosis** - the amount of dead tissue within a tissue sample.
- **Cellularity** - the number and types of cancer cells in a given tissue sample.

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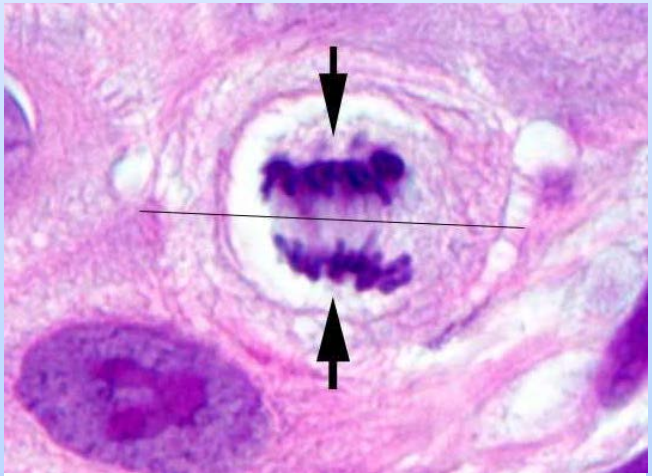
Classification, Staging and Grading

- **Differentiation** - how the cancer cells look compared to normal cells.
- **Pleomorphism** - the degree of variation in size and shape of cancer cells.
- **Mitotic index** - the rate at which cancer cells are dividing.



Mitosis = cells rapidly dividing

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Intra-abdominal Surgery for Sarcoma

- Trunk and Retroperitoneal Sarcoma
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  - **Treatment**
  - Prognosis and Outcomes

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Treatment

- Chemotherapy – non-curative/downstaging
- Radiation – local control/palliation
- Surgery – only known cure, most important
- Optimal survival = all 3 modalities – Team Approach
- For patients with local disease (85%) survival outcomes are directly linked to quality of the cancer operation (neg. margins/ low complications) that is determined by the experience, training, and skillset of the sarcoma surgeon

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Treatment

- In contrast to extremity sarcoma, removal of the entire tumor with a rim of normal tissue (wide margins) is usually not possible in RPS (due to adjacent large vessels, nerves, or bony structures)
- As a consequence, local recurrence is common
- Pre-operative radiation can reduce but not eliminate the risk of recurrence
- Surgical Oncologist's advocate liberal compartmental, en-bloc resection of adjacent organs in order to reduce the risk of local relapse
- Despite aggressive radiation and surgery, three out of every four deaths due to RPS is secondary to local recurrence

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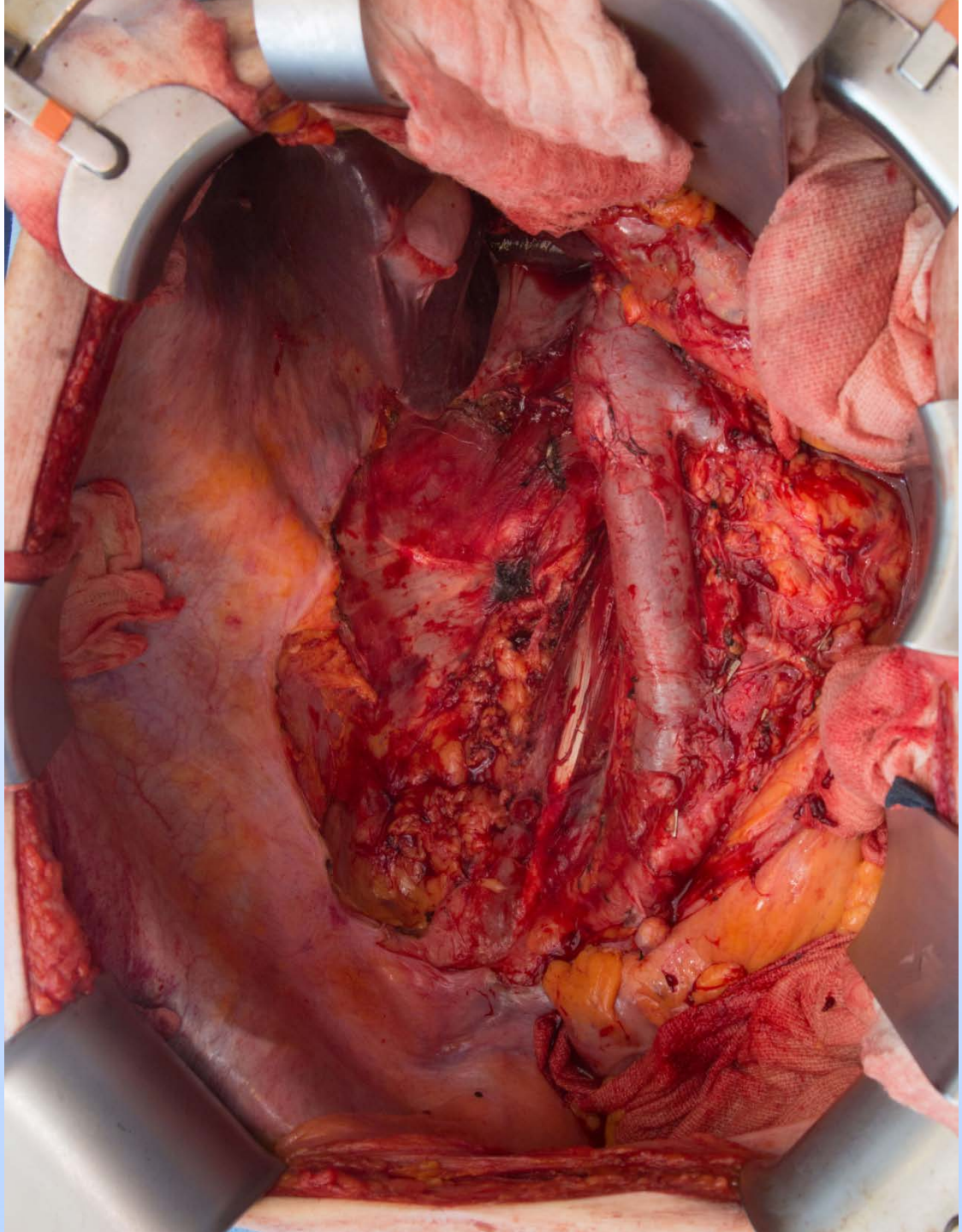

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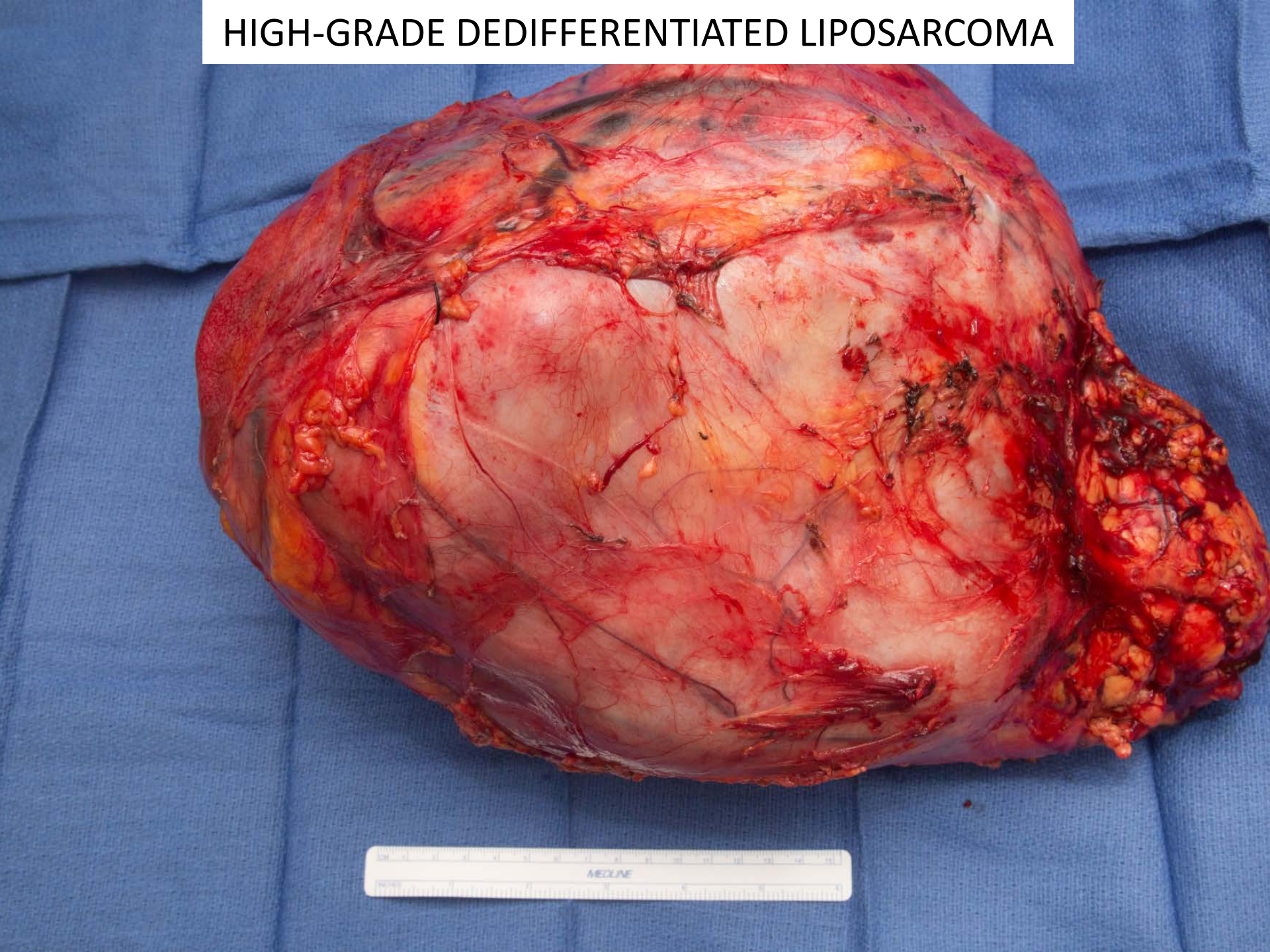
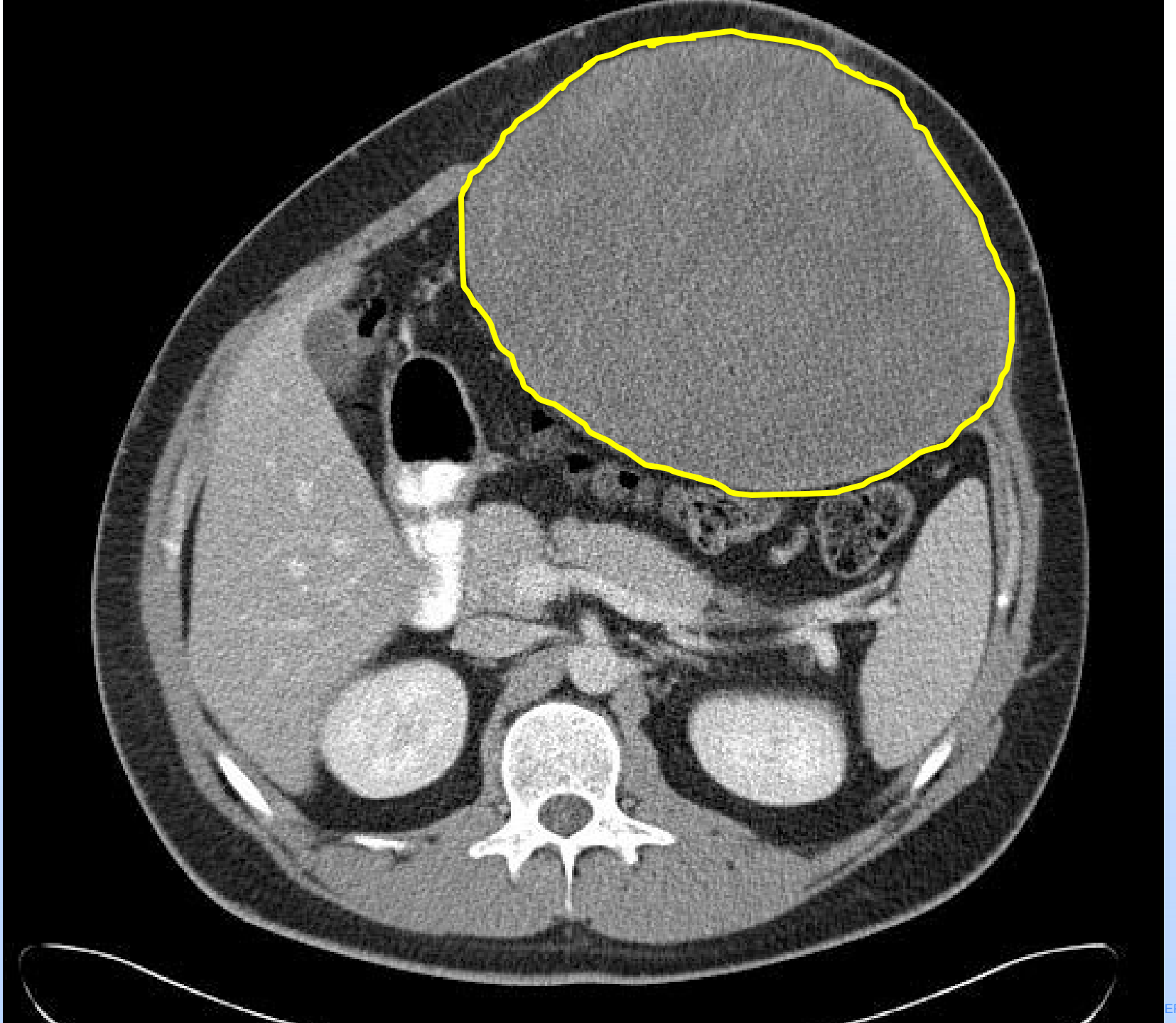
HIGH-GRADE DEDIFFERENTIATED LIPOSARCOMA





HIGH-GRADE RECTUS SYNOVIAL SARCOMA

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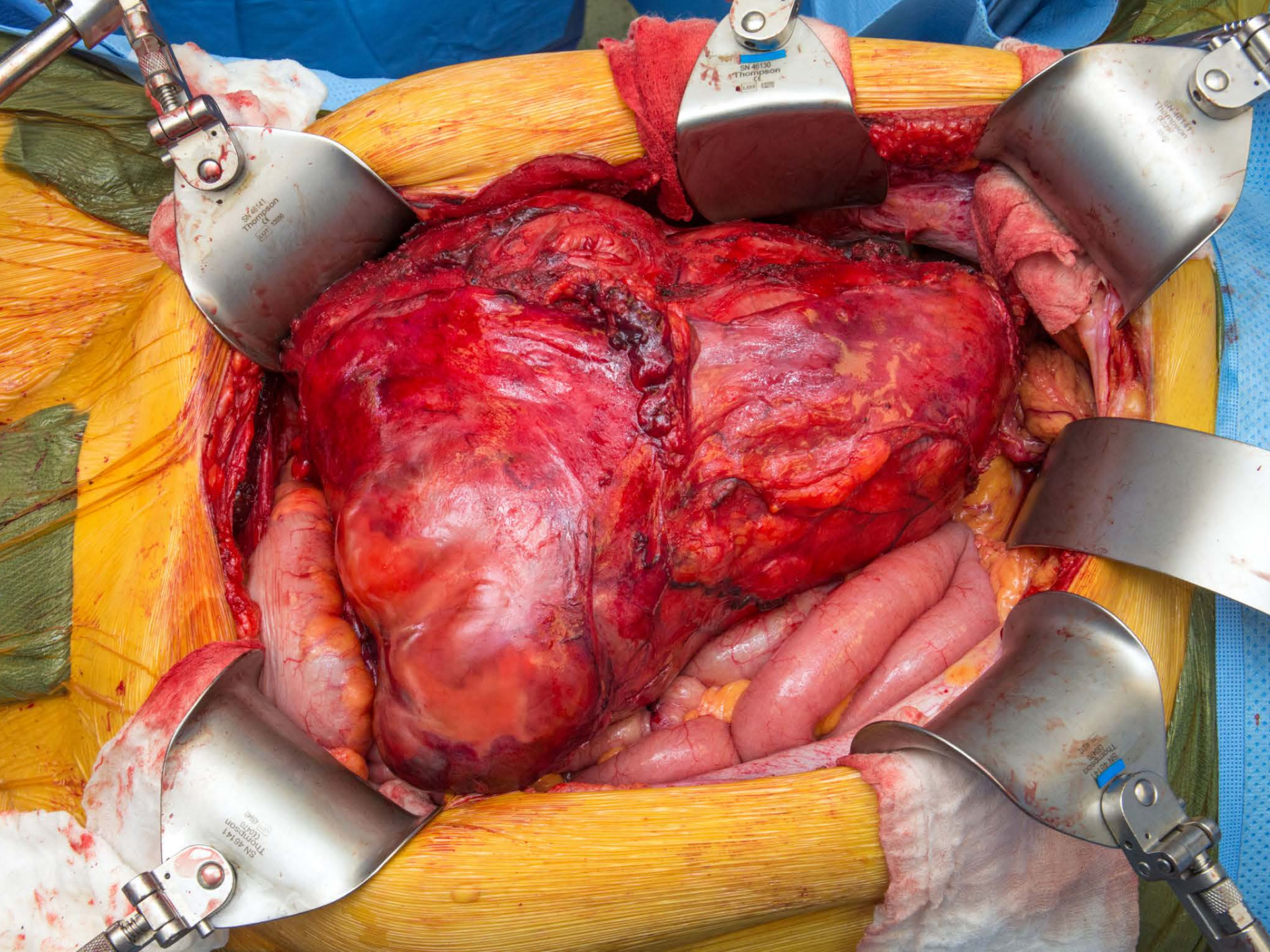
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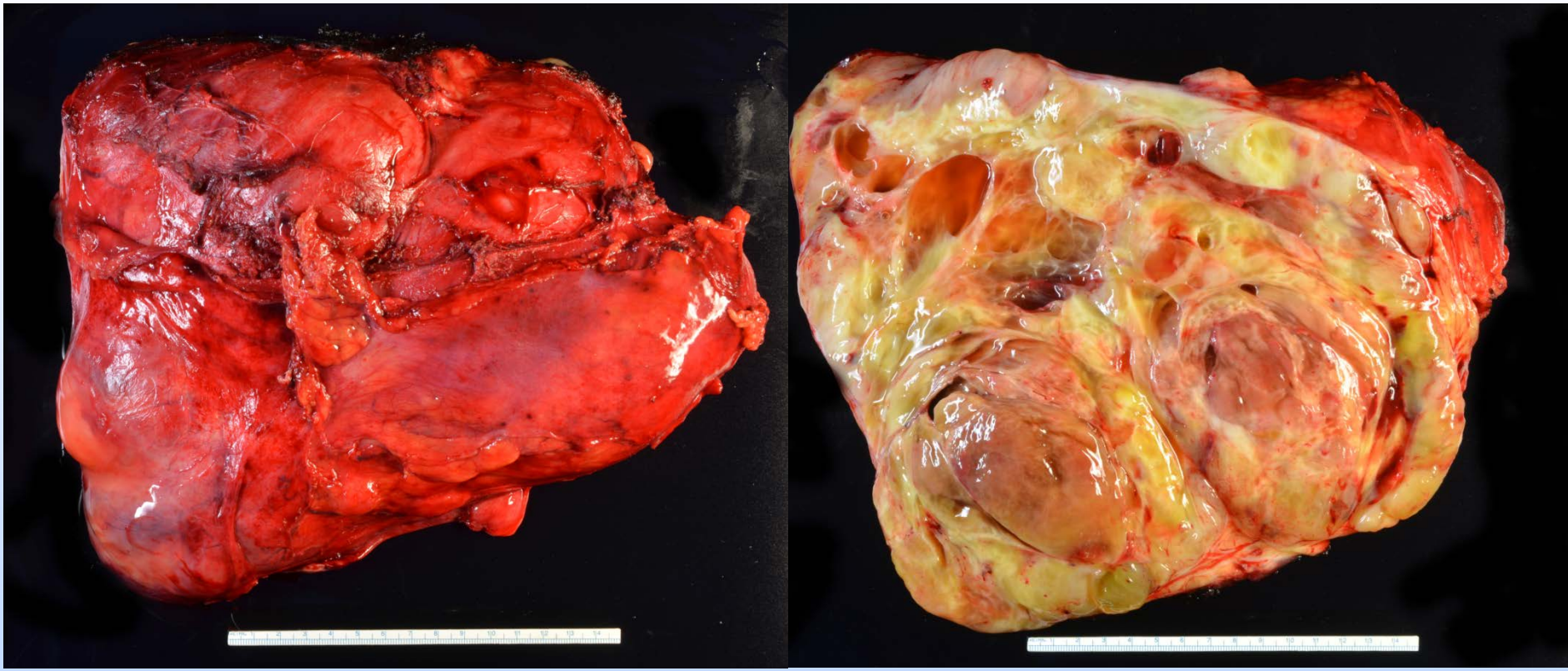
HIGH-GRADE LEIOMYOSARCOMA



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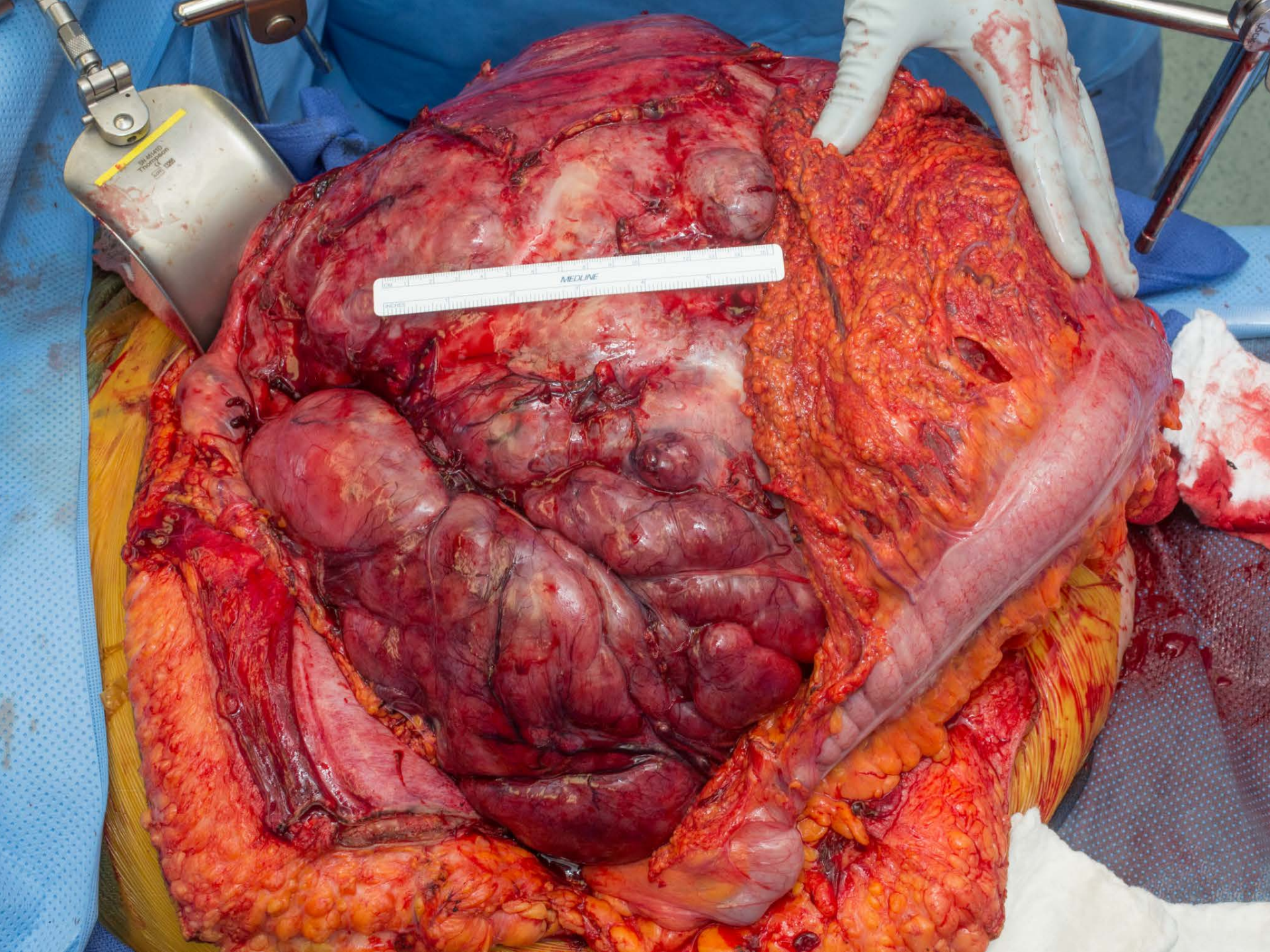
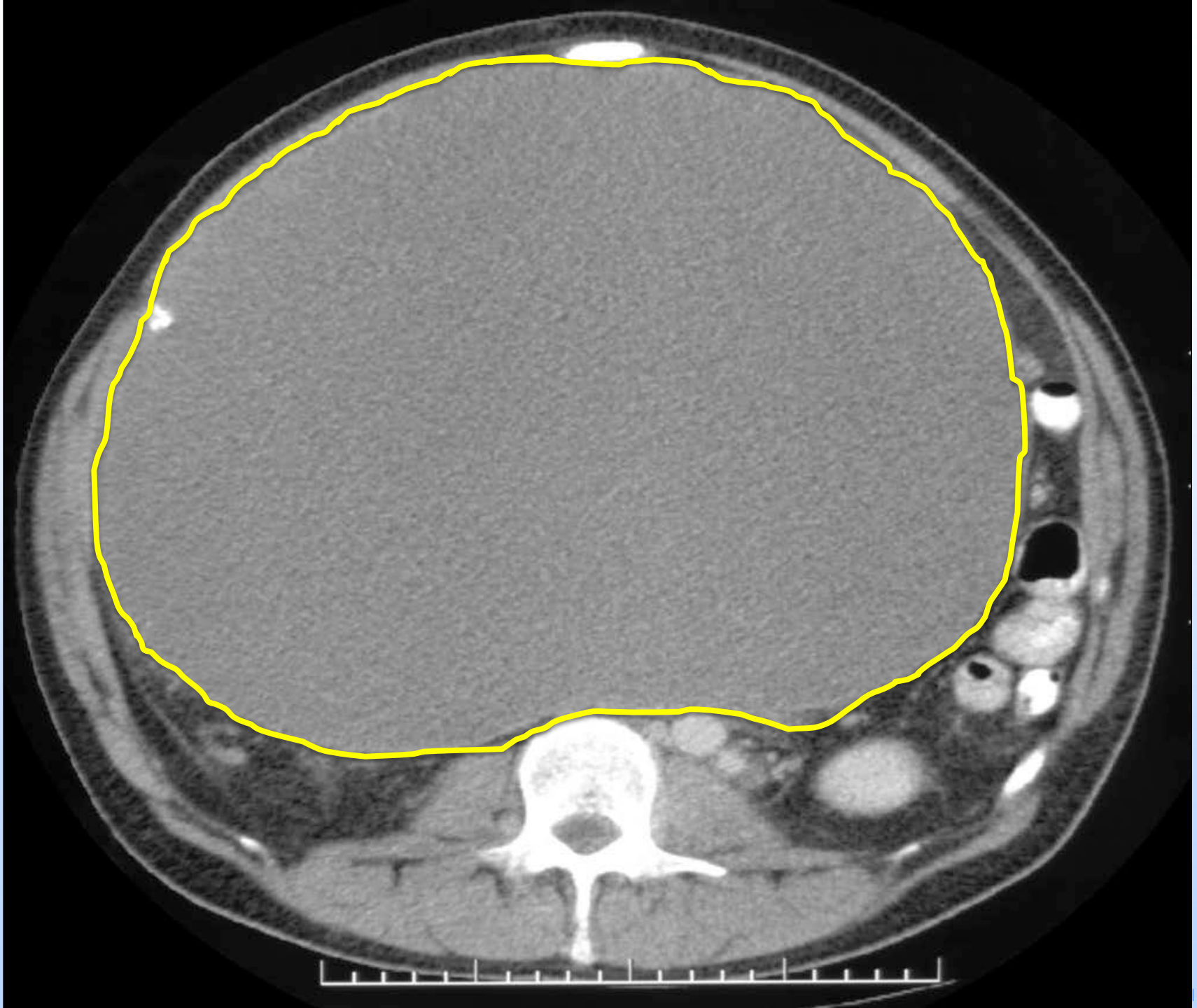
Ioban™ 2
3M


MEDLINE

HIGH-GRADE PLEOMORPHIC SARCOMA



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HIGH-GRADE DEDIFFERENTIATED LIPOSARCOMA

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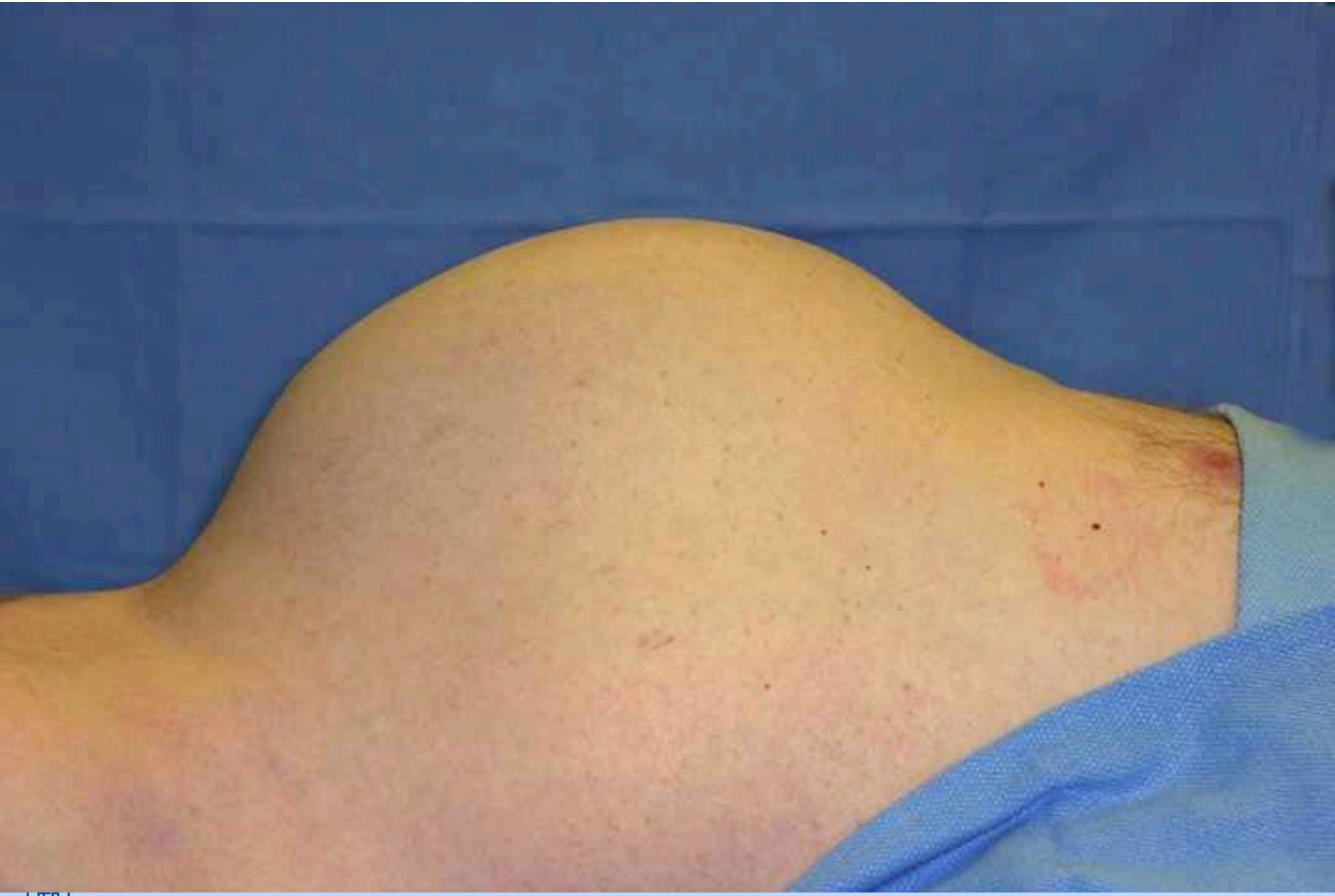

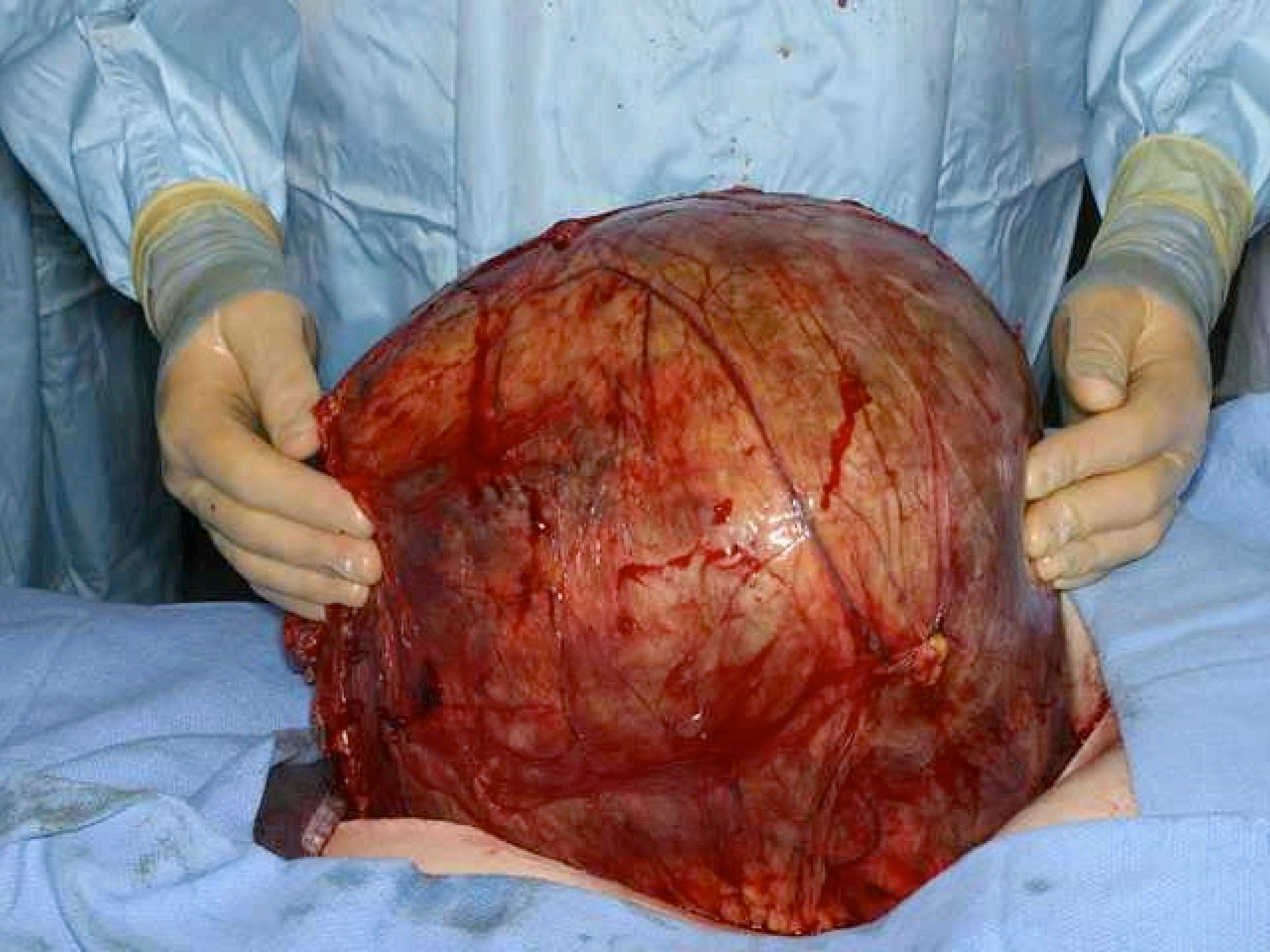

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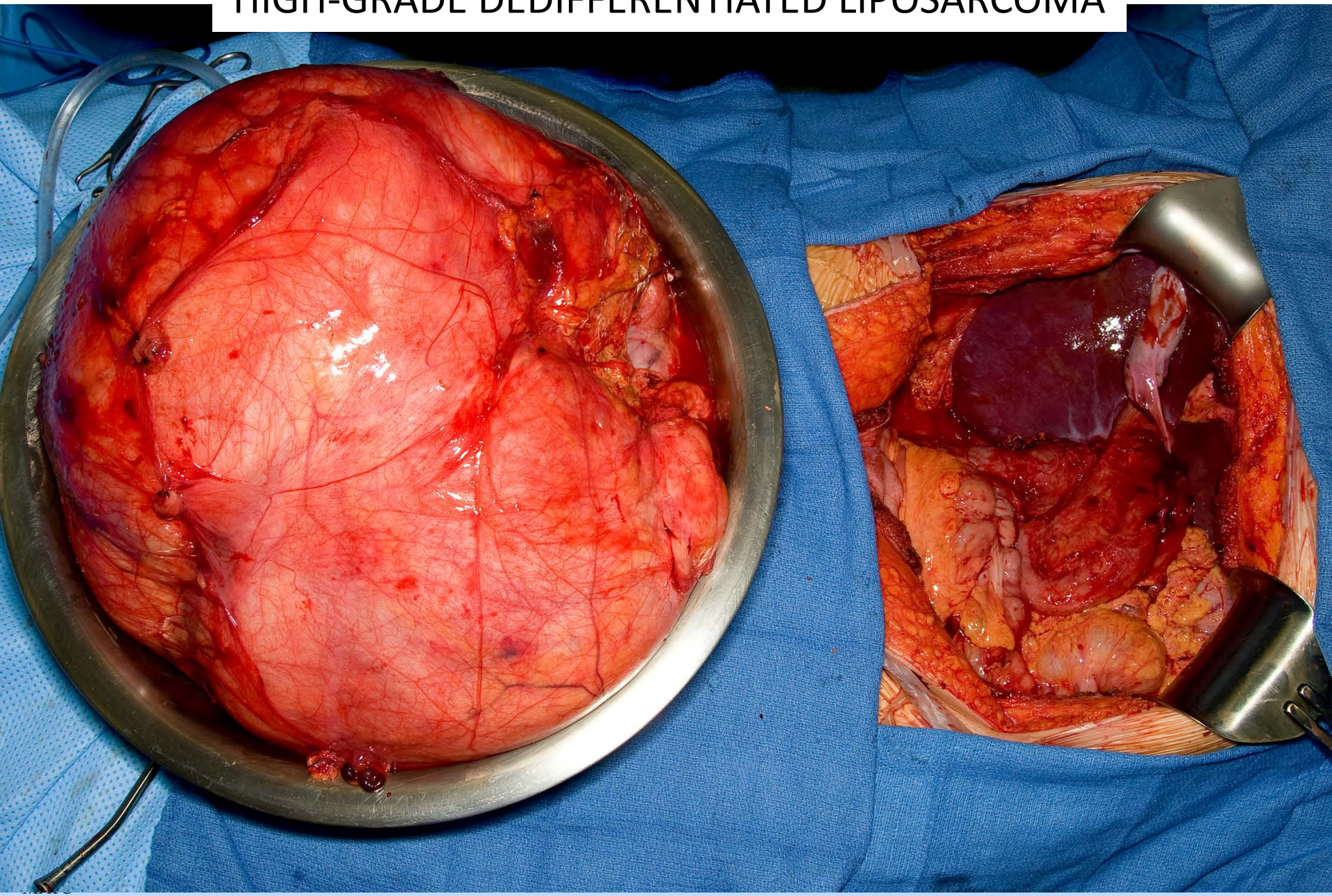
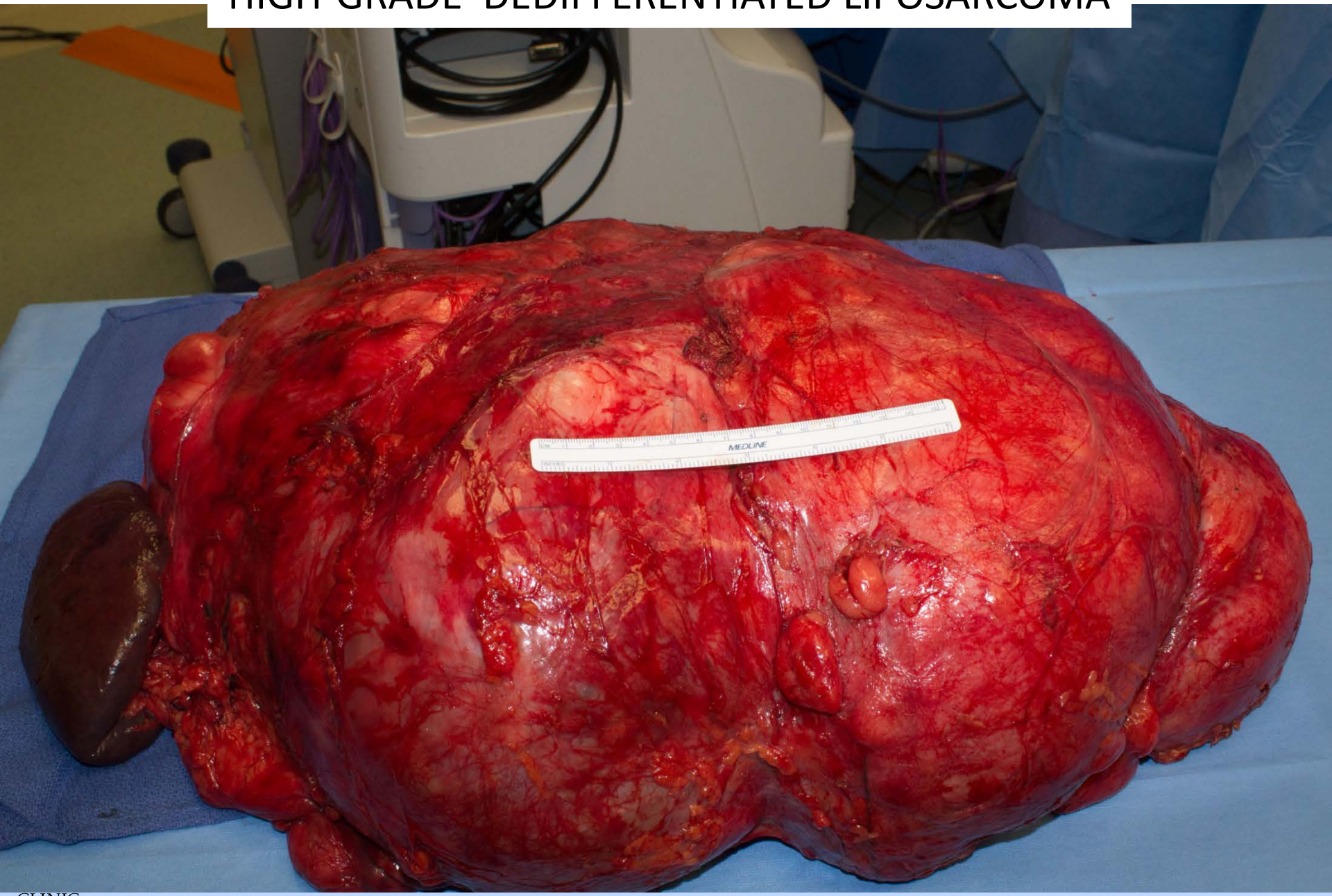



Count Process
Count IN
Tucked Items
Count OUT
Pause Before Closure
Final Count
THE LIVER
Valleylab

HIGH-GRADE DEDIFFERENTIATED LIPOSARCOMA



IVC leiomyosarcoma

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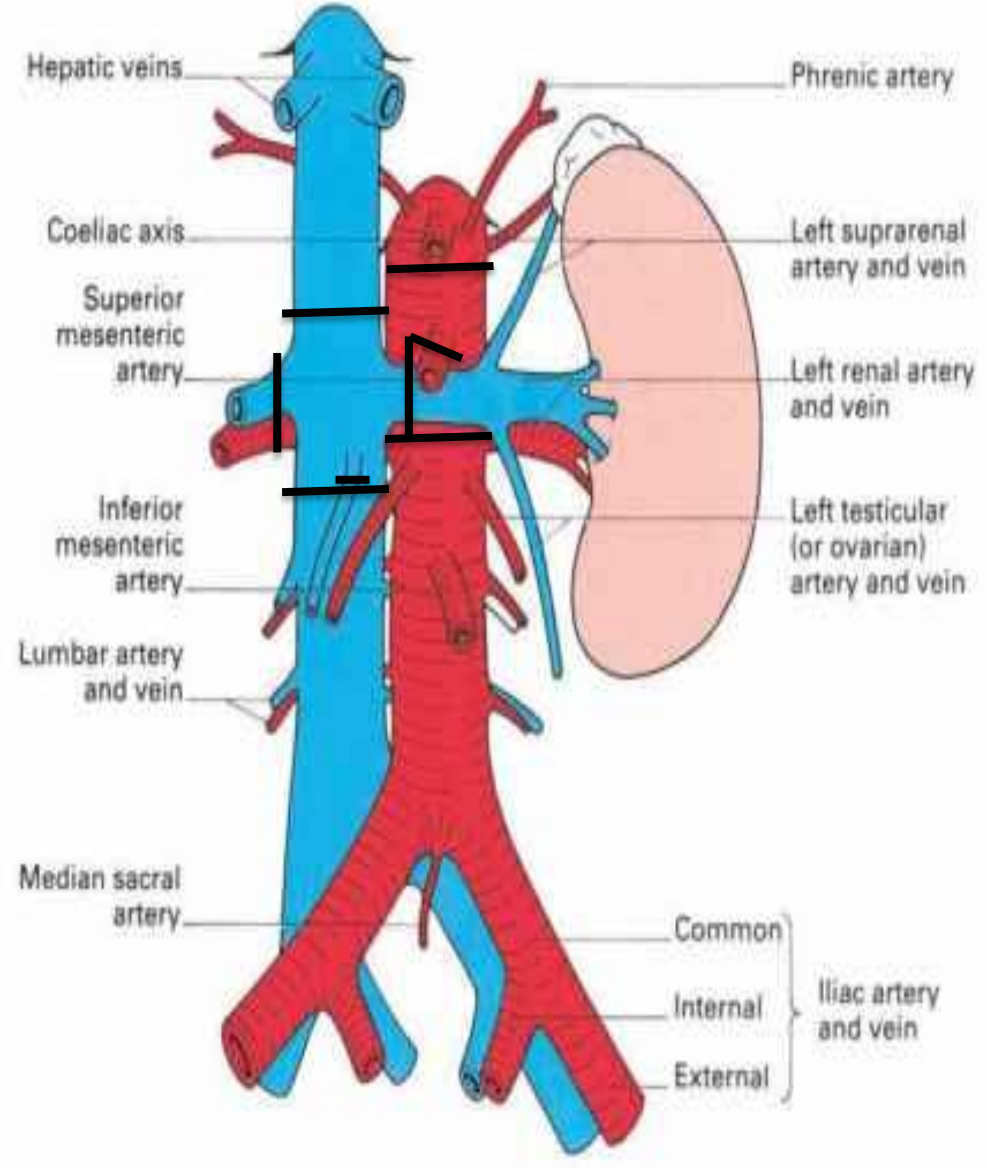
DIAGNOSIS AND EVALUATION

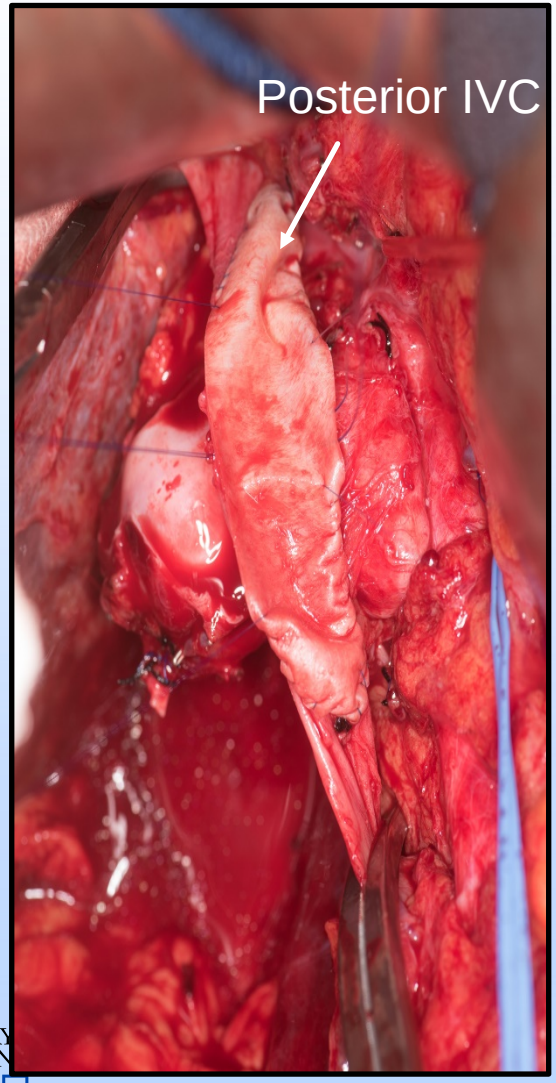
SMA

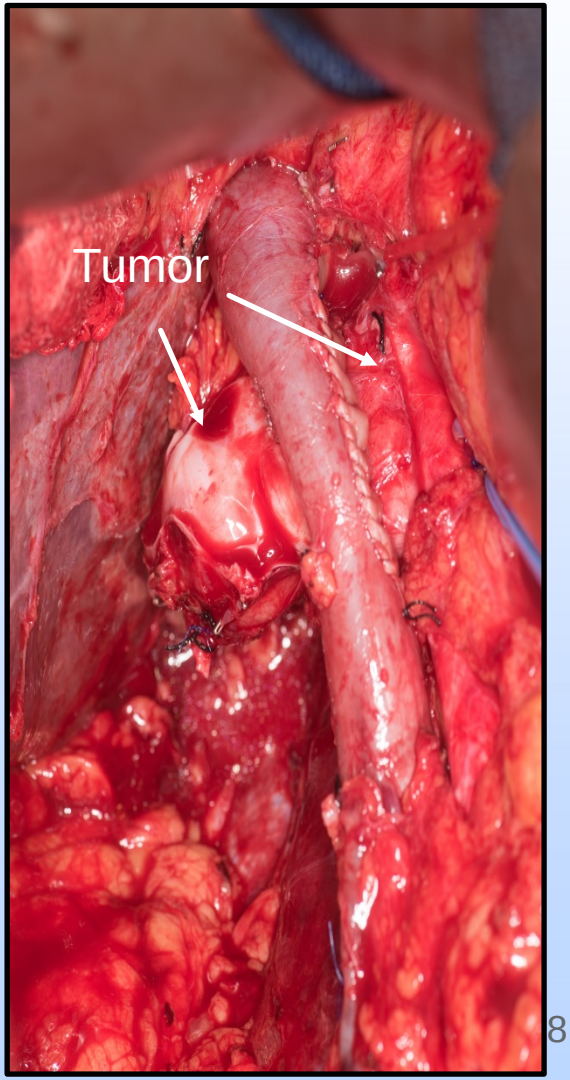
Left renal vein

OPERATIVE CONSIDERATIONS

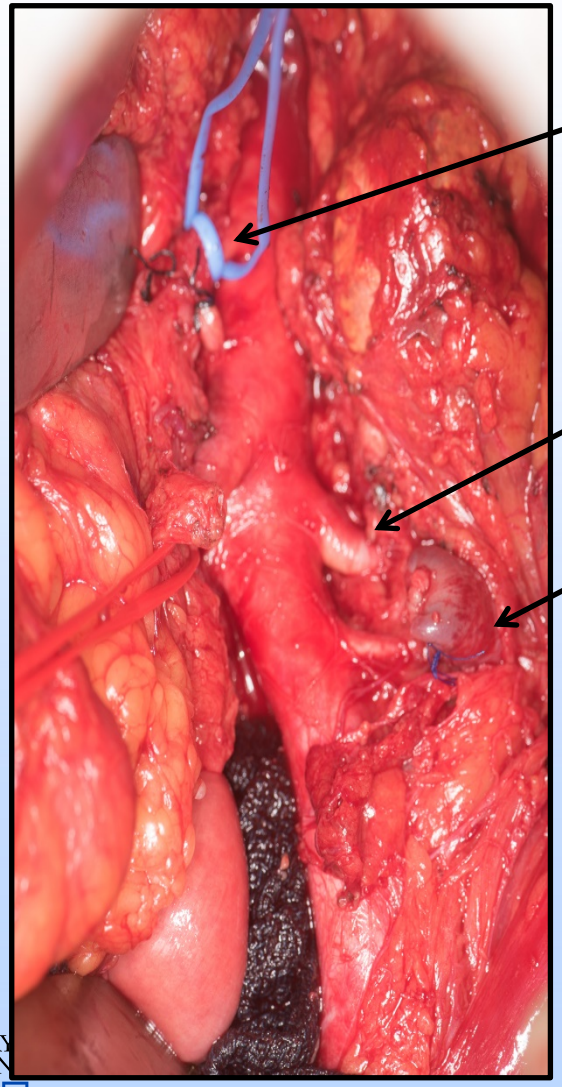


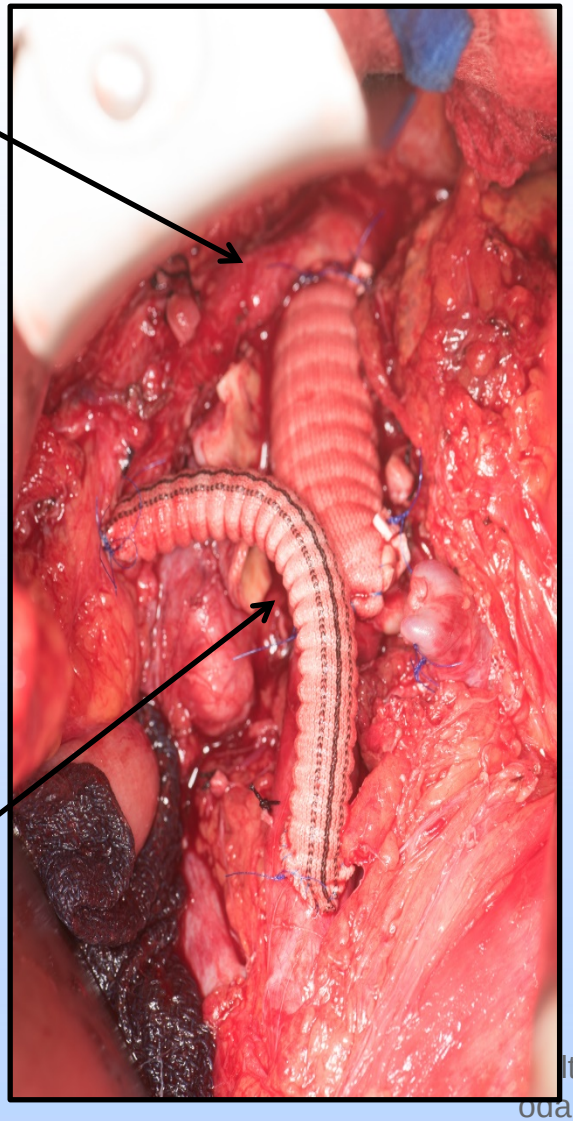
OPERATIVE CONSIDERATIONS





OPERATIVE CONSIDERATIONS





High grade Leiomyosarcoma

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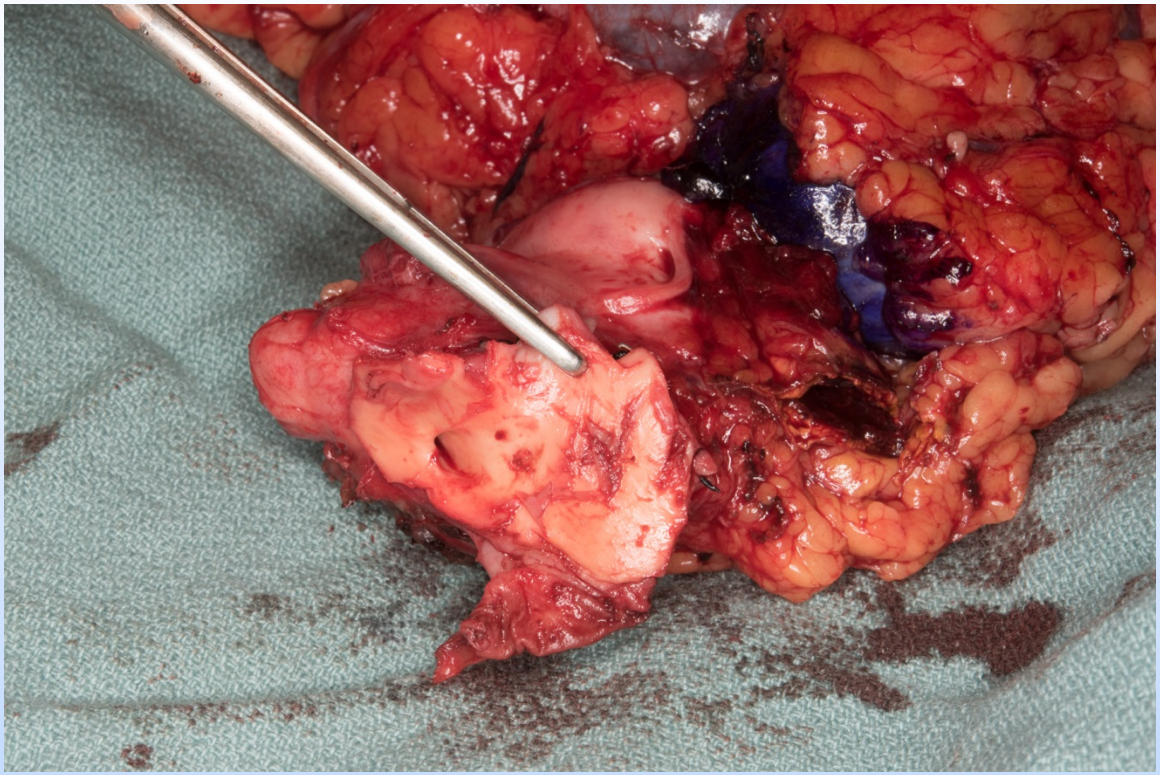
Wall of the IVC where the sarcoma arose from



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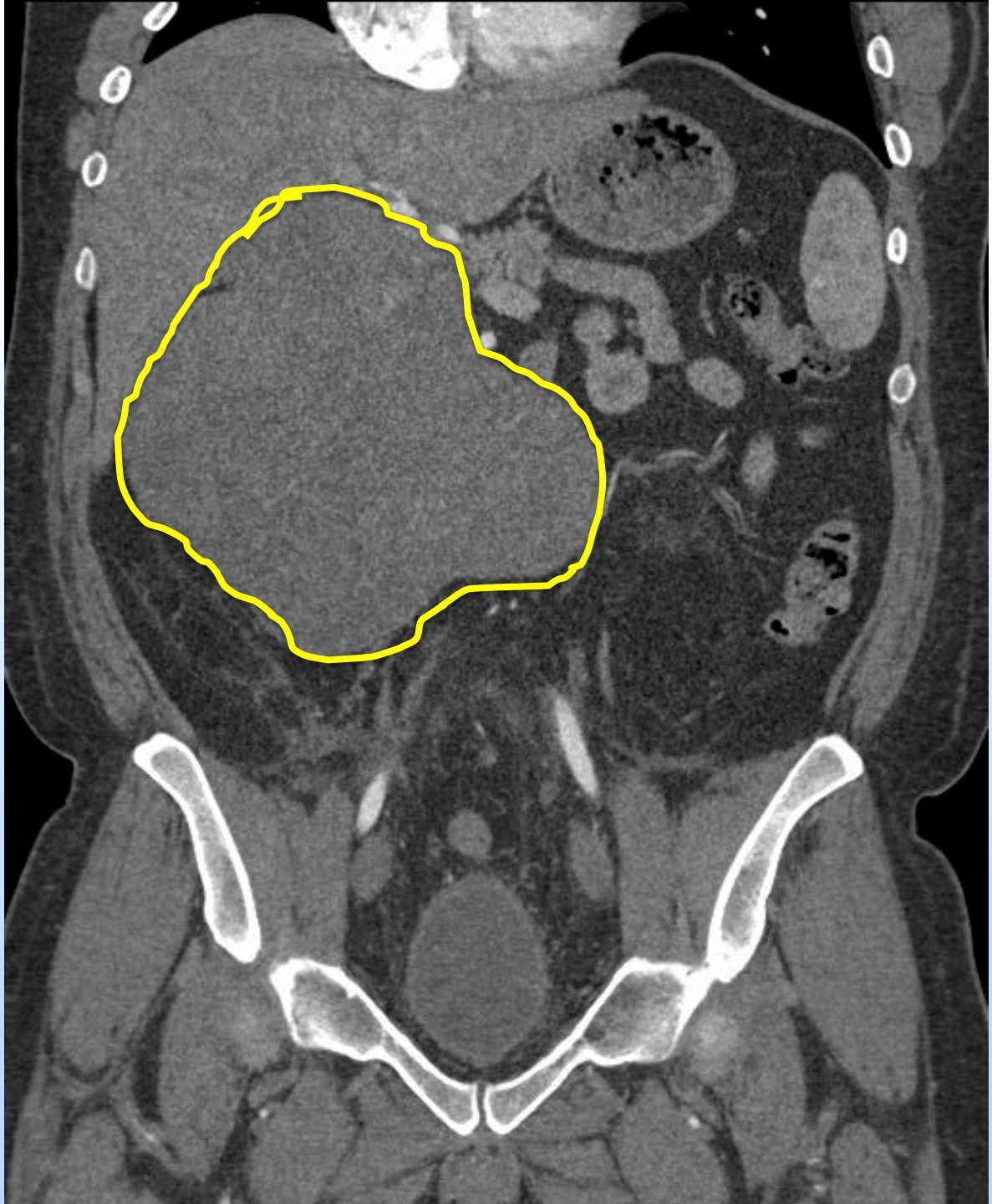

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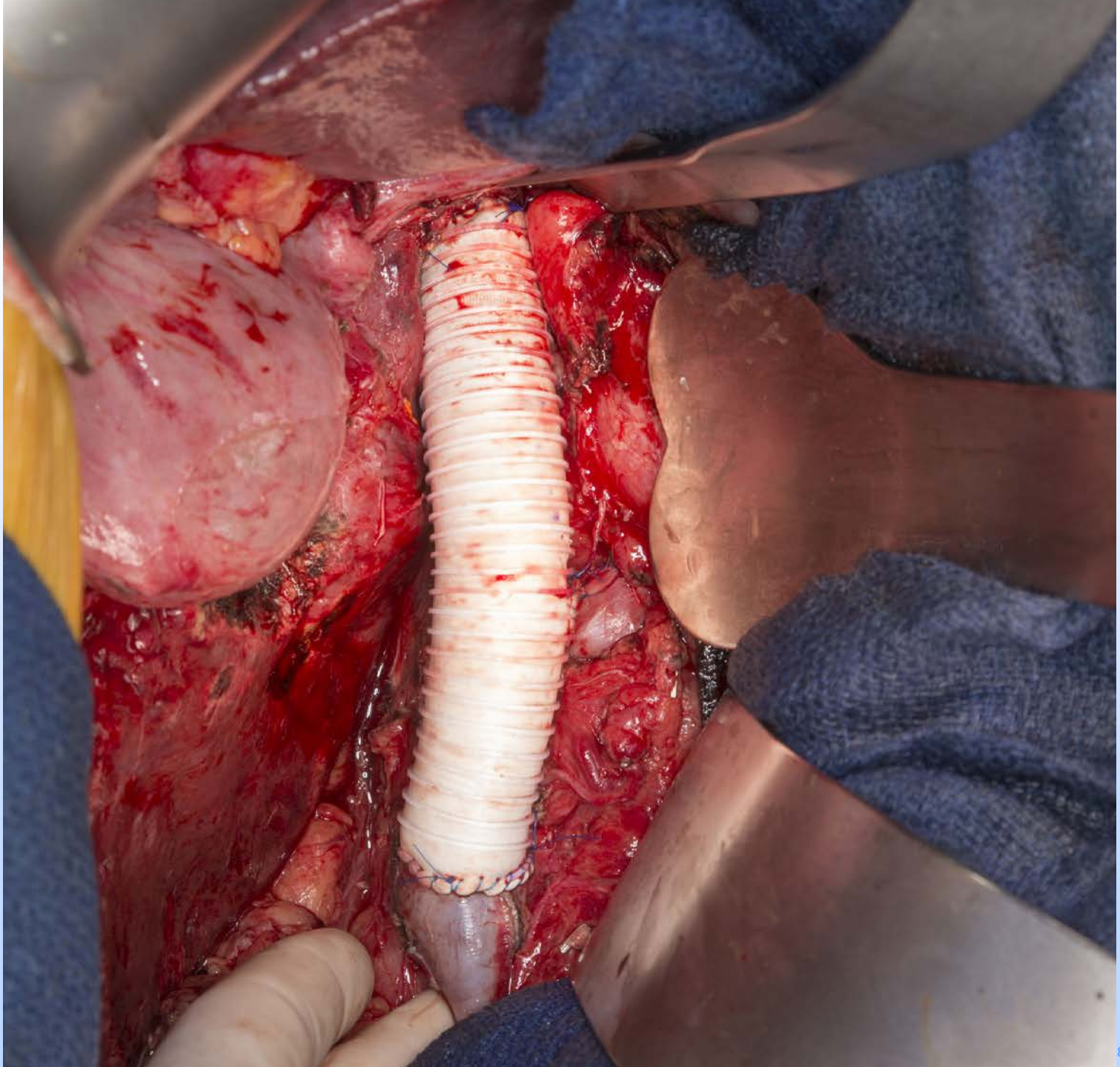
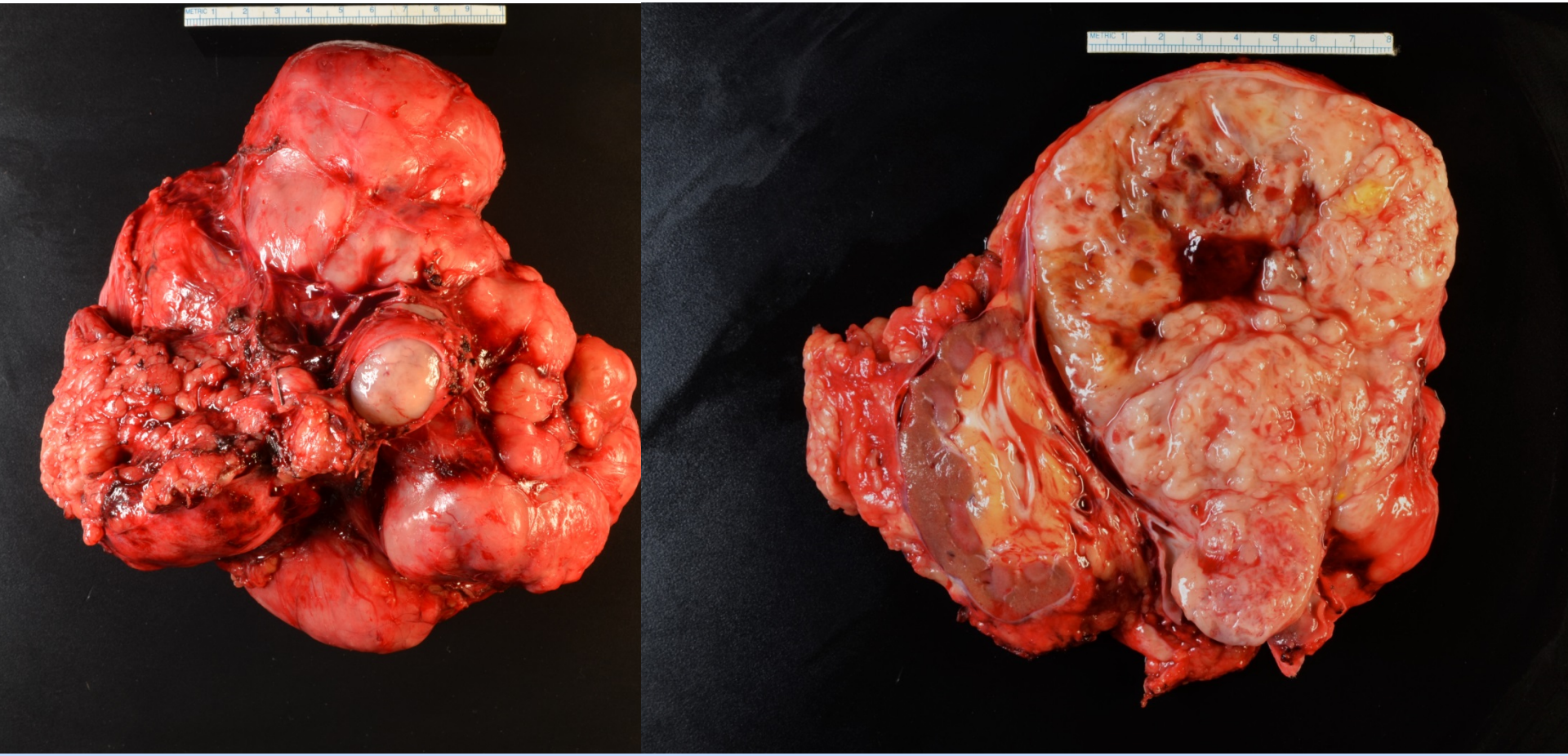


HIGH-GRADE IVC LEIOMYOSARCOMA



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Recovery

- Often require 3-6 days in the hospital depending on extent of resection
- 15-30% complication rate depending on extent of surgery
- Most common complications are GI anastomotic leak (5.2%), infection (4%), and bleeding (2.4%).
- <5% risk of returning to the operating room
- <2% risk of death

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Long-term effects

- Long term risk of kidney failure- following nephrectomy
- Neuropathy- resection of the psoas muscle
- Fatigue, insomnia, pain, sexual dysfunction and urinary symptoms.
- Overall good QOL scores

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Intraabdominal Surgery for Sarcoma

- Trunk and Retroperitoneal Sarcoma
  - Background
  - Presentation
  - Diagnostic Workup
  - Classification, Staging and Grading
  - Treatment
  - **Prognosis and Outcomes**

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PREDICTORS OF POOR SURVIVAL AFTER SARCOMA SURGERY

- Older Age
- Male Sex
- Positive Surgical Margins
- Multi-organ Invasion
- Aggressive Histologic Subtypes
- Increased Tumor Size
- Higher Tumor Grade

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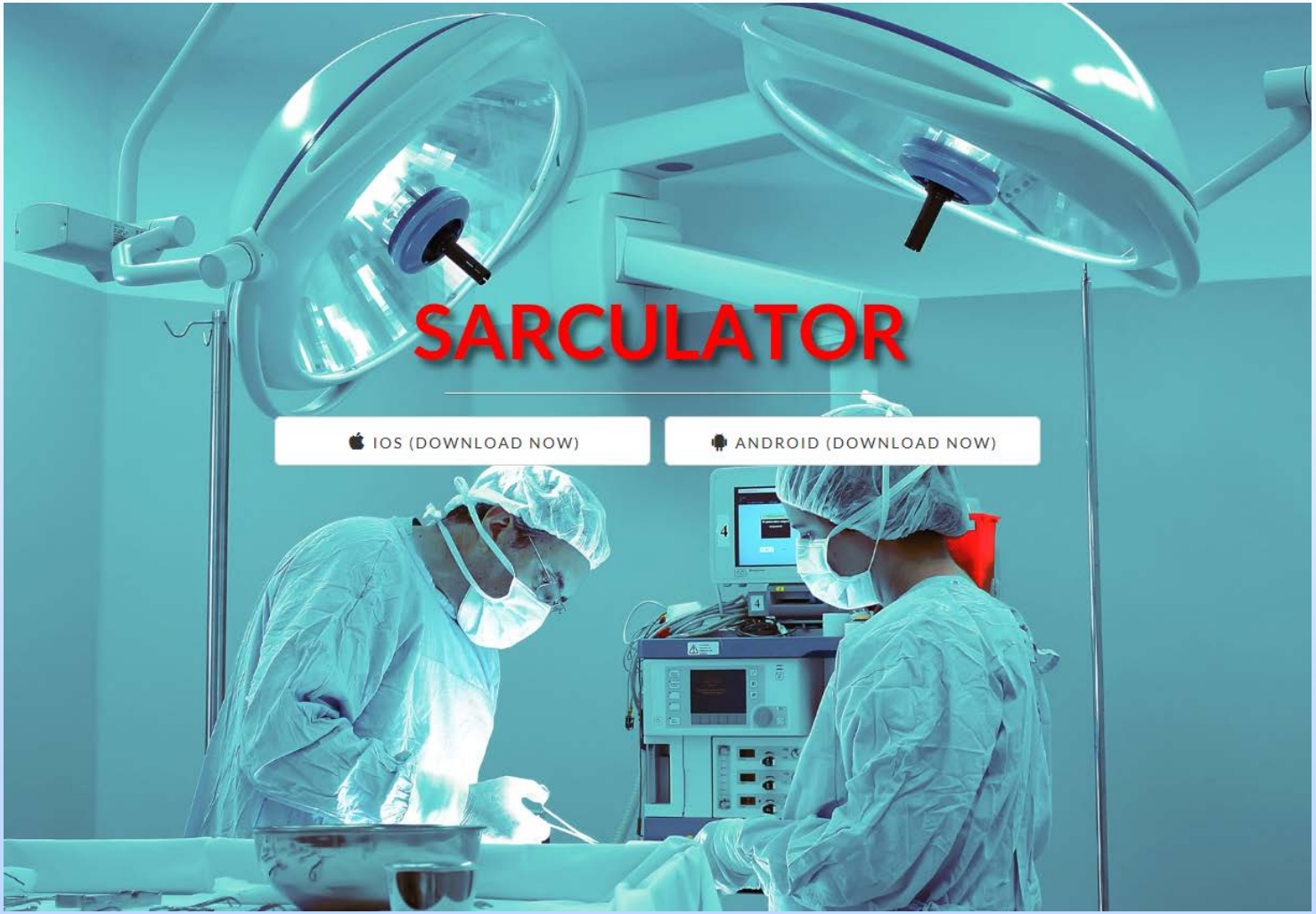

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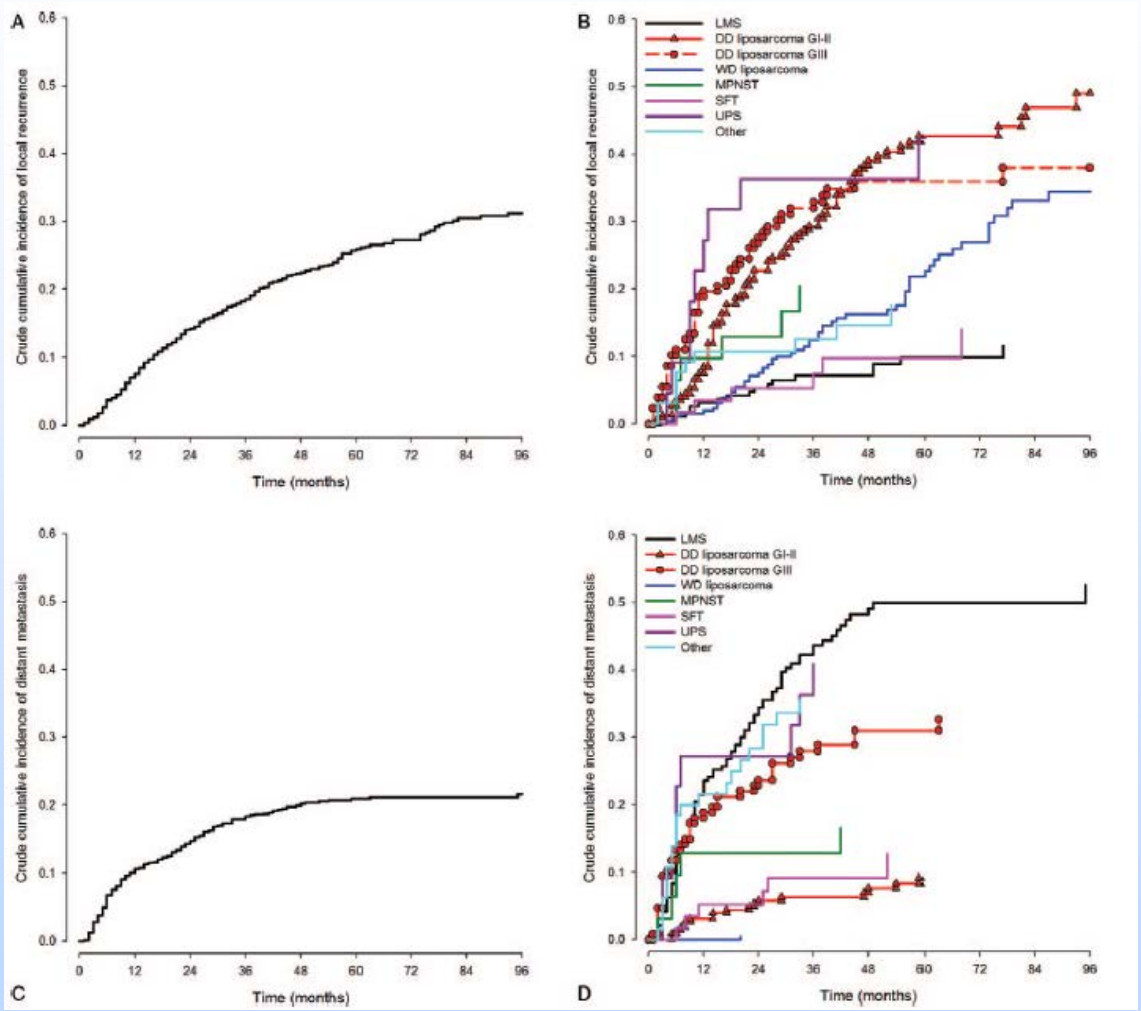
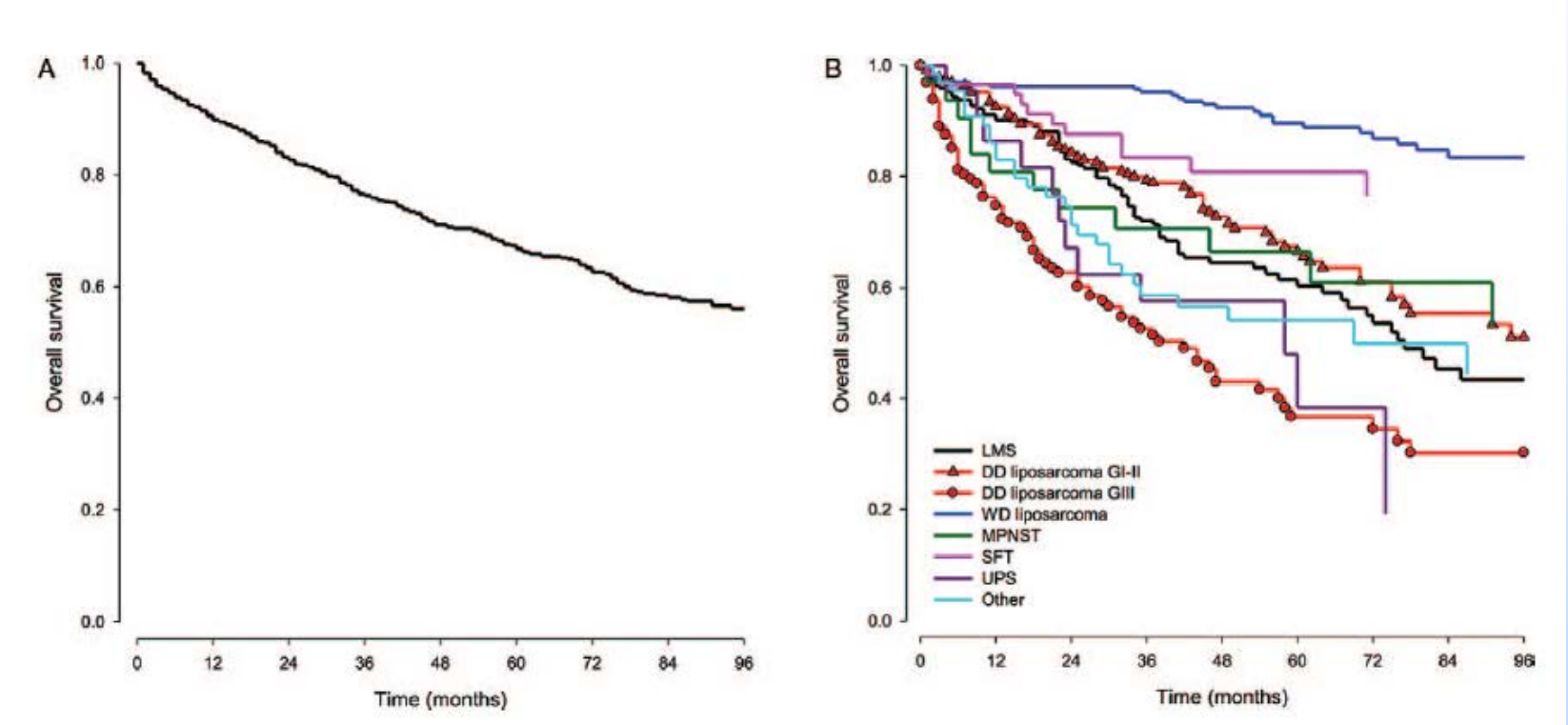
Pattern of Recurrence



Survival


A
1.0
0.8
0.6
0.4
0.2
0.0
Overall survival
0
12
24
36
48
60
72
84
96
Time (months)
B
1.0
0.8
0.6
0.4
0.2
0.0
Overall survival
LMS
DD liposarcoma GI-II
DD liposarcoma GIII
WD liposarcoma
MPNST
SFT
UPS
Other
0
12
24
36
48
60
72
84
96
Time (months)

Summary

- Sarcomas are a rare type of tumor and sarcomas involving the trunk and retroperitoneum are even less common
- RPS often grow to enormous size and can be challenging to resect
- Multidisciplinary coordinated oncologic care is critical to optimizing outcomes.

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Questions?

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Treatment and Clinical Trials in Leiomyosarcoma

Brittany L. Siontis, MD

July 14, 2018

Outline

- Clinical Trials 101
  - What are they?
  - Why are they important?
- Molecular Considerations and Emerging Targets
- Current Clinical Trials

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Clinical Trials 101

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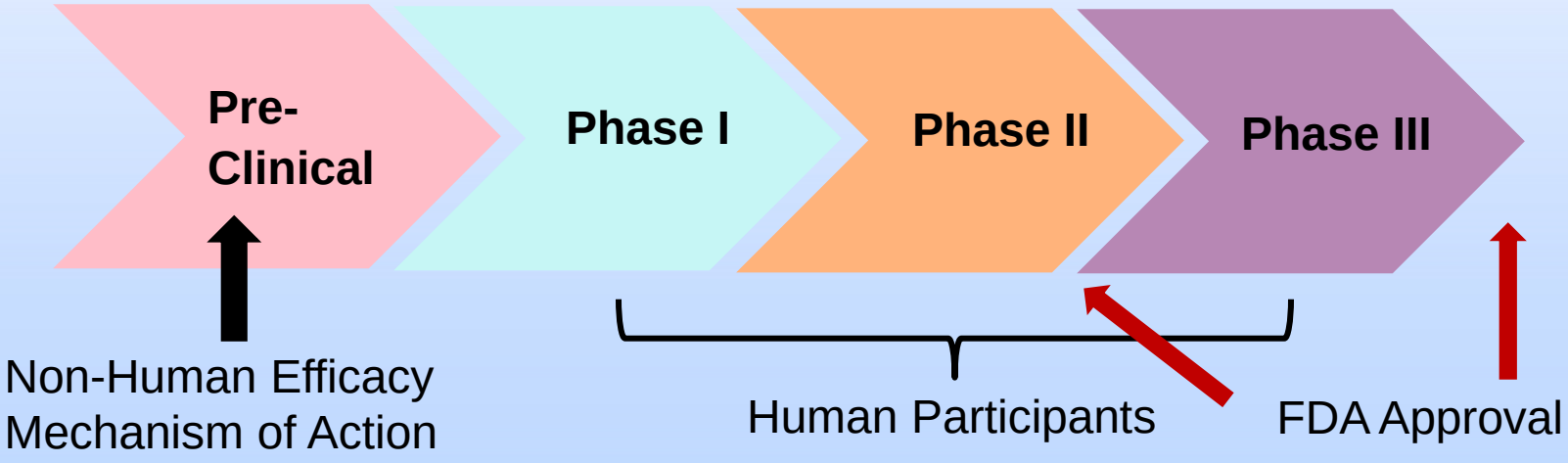
Clinical Trials 101 – What are they?

- A research study prospectively evaluating new, cutting edge therapies in cancer
- Conducted in phases, each with a specific endpoint



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Clinical Trials 101 – Definitions/Concepts

- Randomized:
  - Algorithm randomly assigns patient to specific treatment group
- Blinded:
  - Patient/investigator unaware of which treatment is being administered
- Dose-Limiting Toxicity (DLT):
  - Side effect of drug such that dose cannot be increased
- Maximum Tolerated Dose (MTD):
  - Highest dose of drug tolerated without unacceptable toxicity
- Progression-Free Survival (PFS):
  - Time from start of therapy to disease progression
- Overall Survival (OS):
  - Time from start of therapy to death

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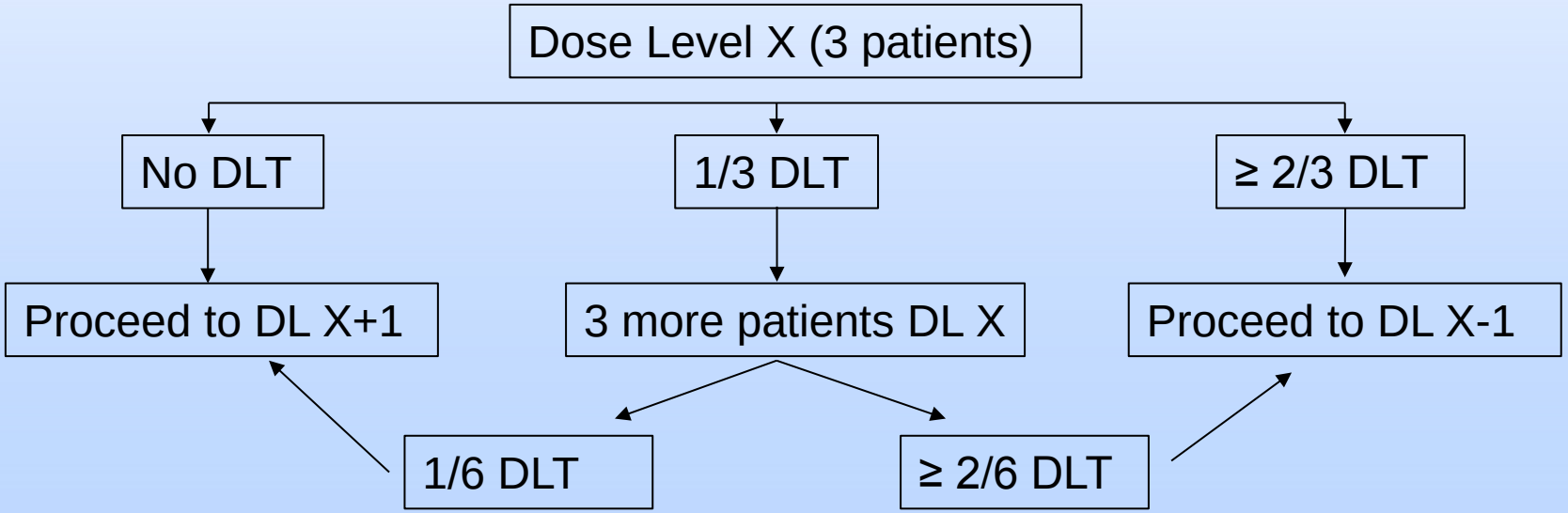
Clinical Trials 101

Phase I

- Overall Goal: Safety of study drug in humans
  - Small number of study subjects with variety of diseases
- Multiple doses of drug evaluated to identify MTD
  - MTD used for phase II and III clinical trials



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Clinical Trials 101

Phase I

- Other Endpoints:
  - Pharmacodynamics (PD): Effect of drug on body
  - Pharmacokinetics (PK): Effect of body on drug
- Results may give insight into efficacy and desired target population
  - **NOT** an endpoint of phase I studies

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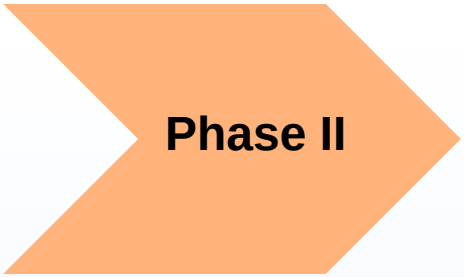
Clinical Trials 101



- Overall Goal: Efficacy and Safety
  - Larger number of subjects limited to specific disease(s)
- Common endpoints:
  - Response Rate
  - Progression-Free Survival (PFS) and Overall Survival (OS)
  - Safety: side effects monitored and recorded in standard fashion
- Exploratory endpoints are common
  - May include extra biopsies or blood tests to evaluate effect of drug on body/tumor

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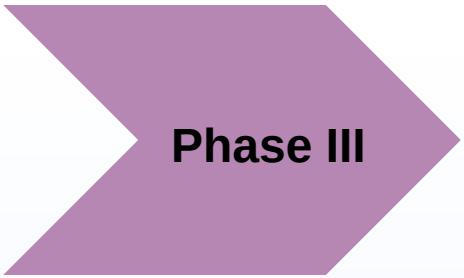
Clinical Trials 101



- Overall Goal: Efficacy and Safety
  - Larger sample size with specific disease(s)
- Compares efficacy to standard therapy or placebo
  - Patients randomized, blinded
  - Some allow cross-over: if progress on one treatment, can transition to other treatment arm
- Most common primary endpoint is OS
- Safety remains important outcome
  - Compare toxicity between treatment groups
- Results used for FDA Approval

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Clinical Trials 101: Why are they important?

- Improve knowledge
  - Allow for ongoing development of cancer therapeutics
  - Advances understanding of diseases
- Give patients access to promising new therapies
  - Continues to develop ‘evidence-based’ medicine
  - Patients on clinical trials often receive better care
- Particularly important in sarcoma
  - Rare disease
  - Limited efficacy to currently available treatments

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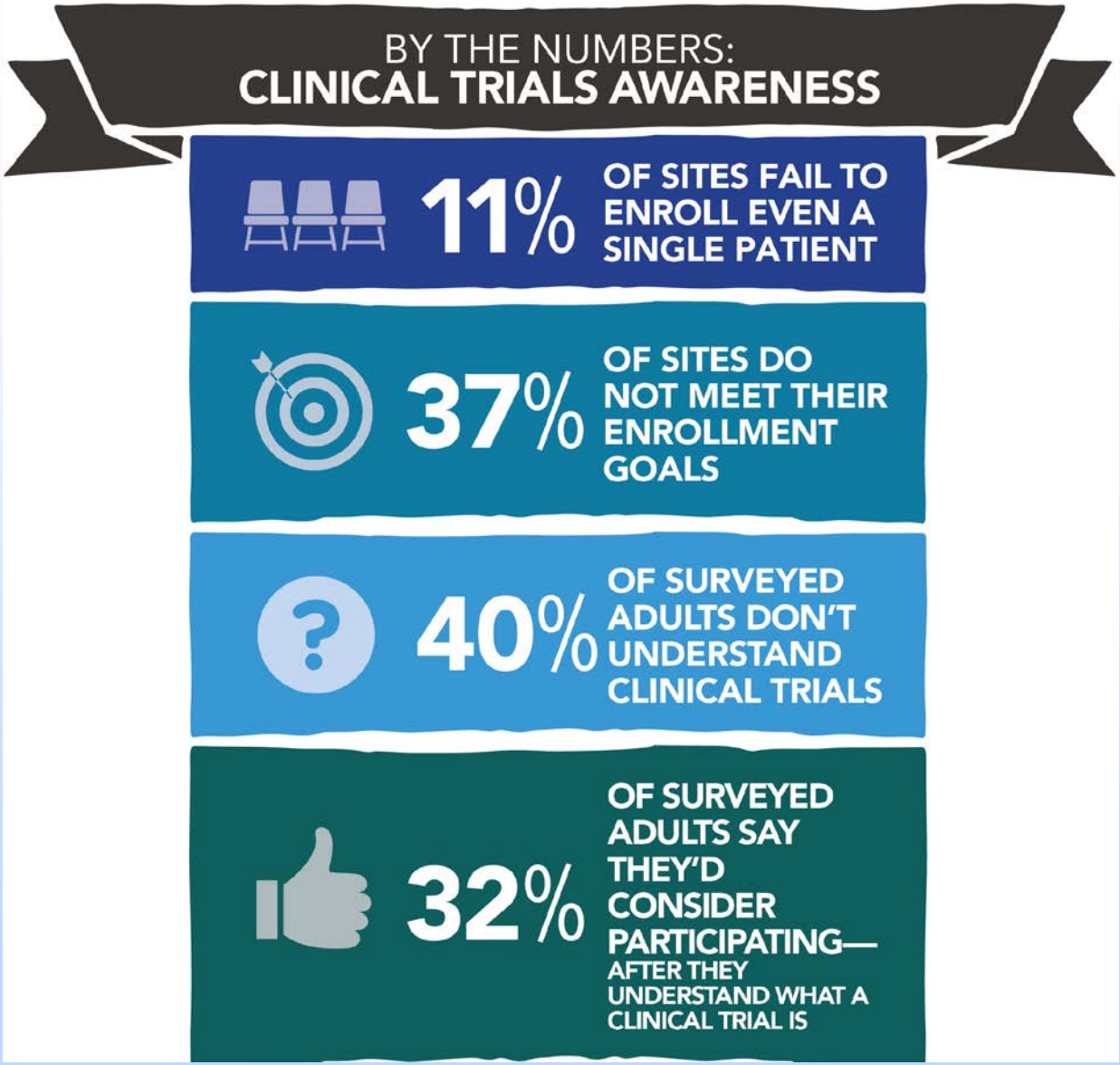
Clinical Trials 101: Why are they important?



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http://cctawareness.org

Clinical Trials – Things to Remember

- Not all trials are available at each cancer center
- Each trial has specific criteria for enrollment
  - Not every patient is eligible for every clinical trial
  - Disease type, prior therapies, other health conditions can impact consideration for each trial
- Additional testing might be asked of you
  - You are NOT responsible for paying for these tests
- Treatment on trial must be administered at the trial center

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Molecular Considerations and Emerging Targets

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Definitions

- Genomic sequencing/Molecular profiling:
  - Evaluates for mutations or alterations that play a role in cancer development
- Mutation:
  - Change in DNA that has potential to cause cancer
- Actionable mutation:
  - Mutation/alteration in DNA that is the target of a drug

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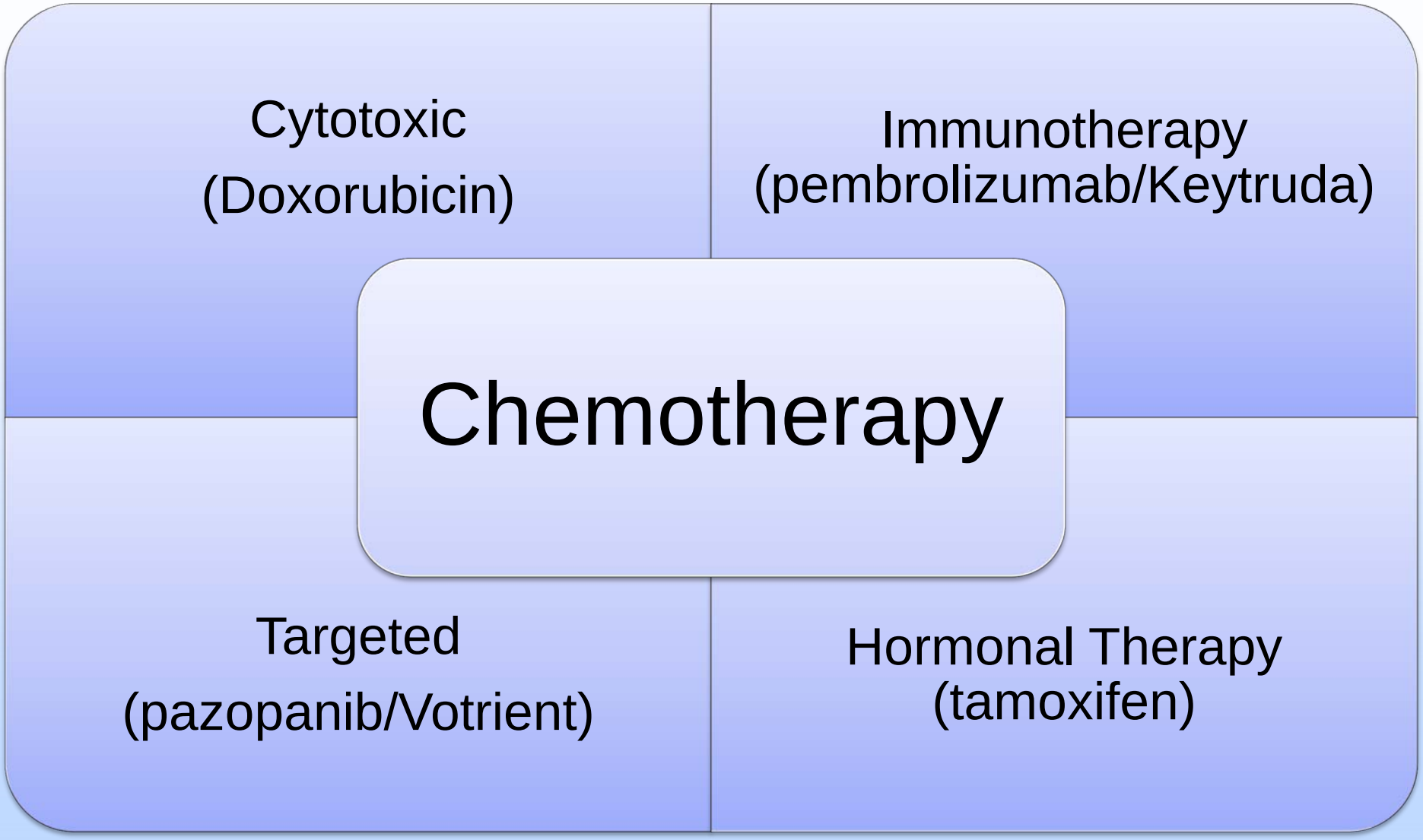
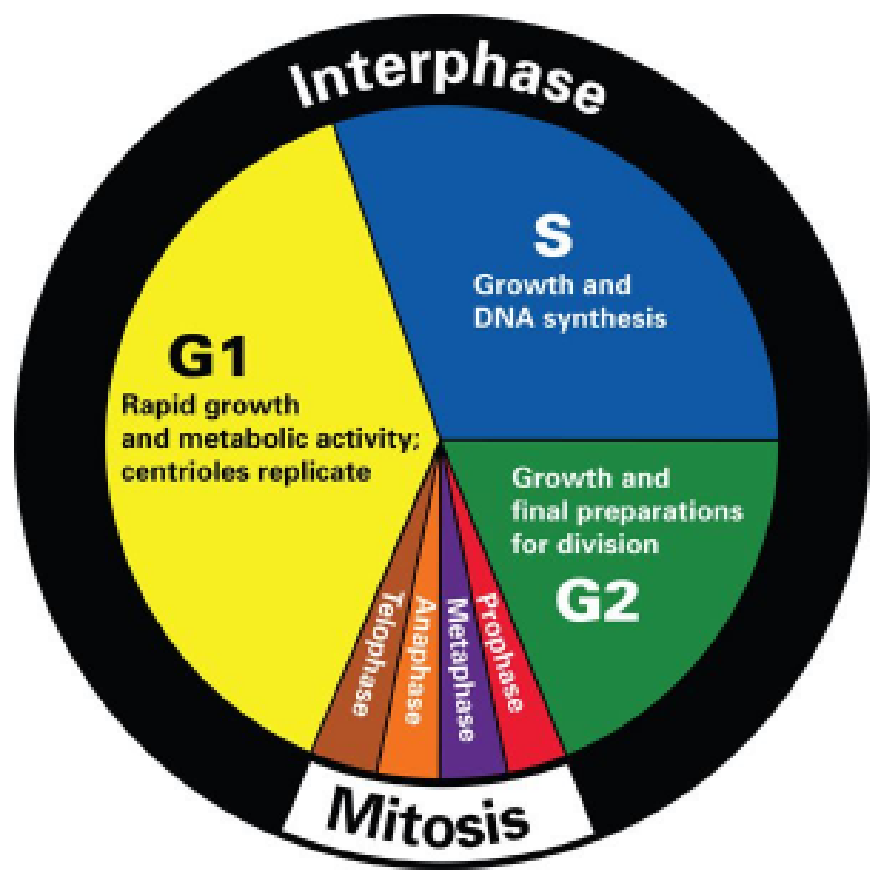
Chemotherapy



Cytotoxic Chemotherapy

- All cells grow and divide in the same manner
- Cytotoxic chemotherapy (doxorubicin, gemcitabine, docetaxel) target one or more steps normal cell cycle
- Targets rapidly dividing cells, NOT specific to cancer cells
  - Results in cell death and toxicity to normal cells



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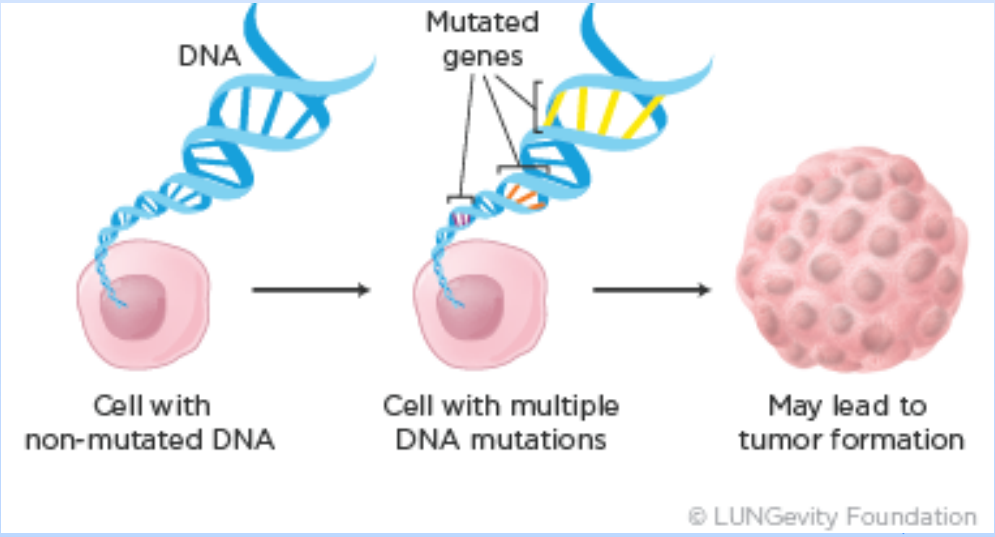
Targeted Therapy

- More specific targets within cells
- May only have activity when certain mutations (DNA changes) present in cancer cells
  - Molecular profiling of tumors important
- Most are oral
- More specific action against cancer cells
- Different side effect profile

Genomic Sequencing/Molecular Profiling

- Goal: identify genetic changes in cancer cells for which there are available therapies
  - Gene mutations can alter the function of signaling pathways that drive the cell cycle
  - Various drugs are available that target aberrant signaling
- Results allow for individualized treatment
- Multiple commercially available platforms
  - Foundation One
  - CARIS
  - Tempus



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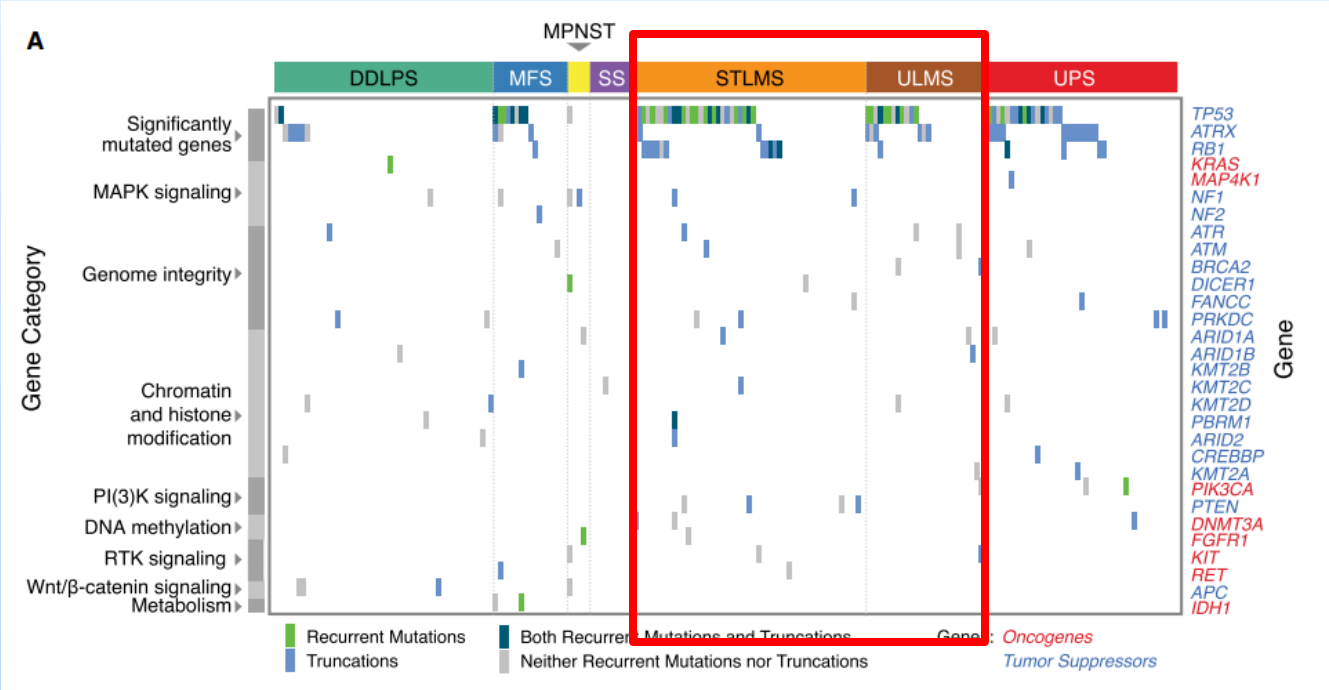
Molecular Considerations in Sarcoma

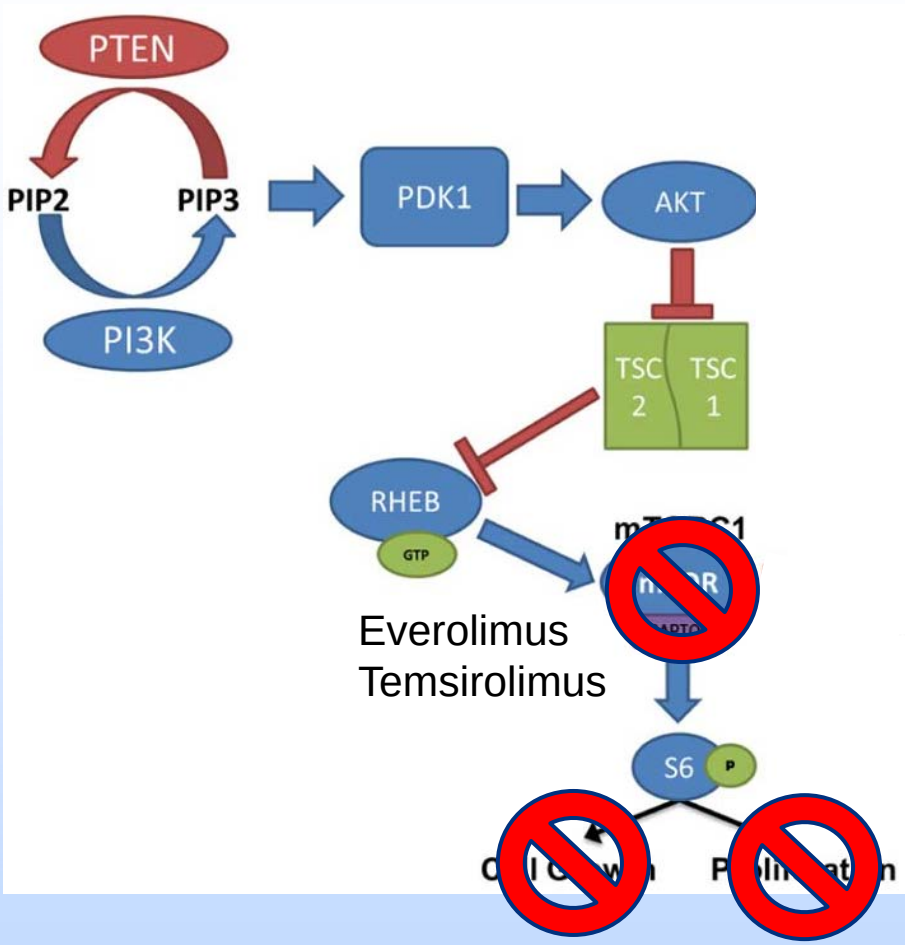
- The Cancer Genome Atlas (TCGA)
  - 206 sarcomas including 53 soft tissue LMS and 27 uterine LMS
  - Soft-tissue and uterine LMS more similar to each other than other sarcomas
  - Genetically complex but with overall low tumor burden



TCGA Research Network. Cell 2017

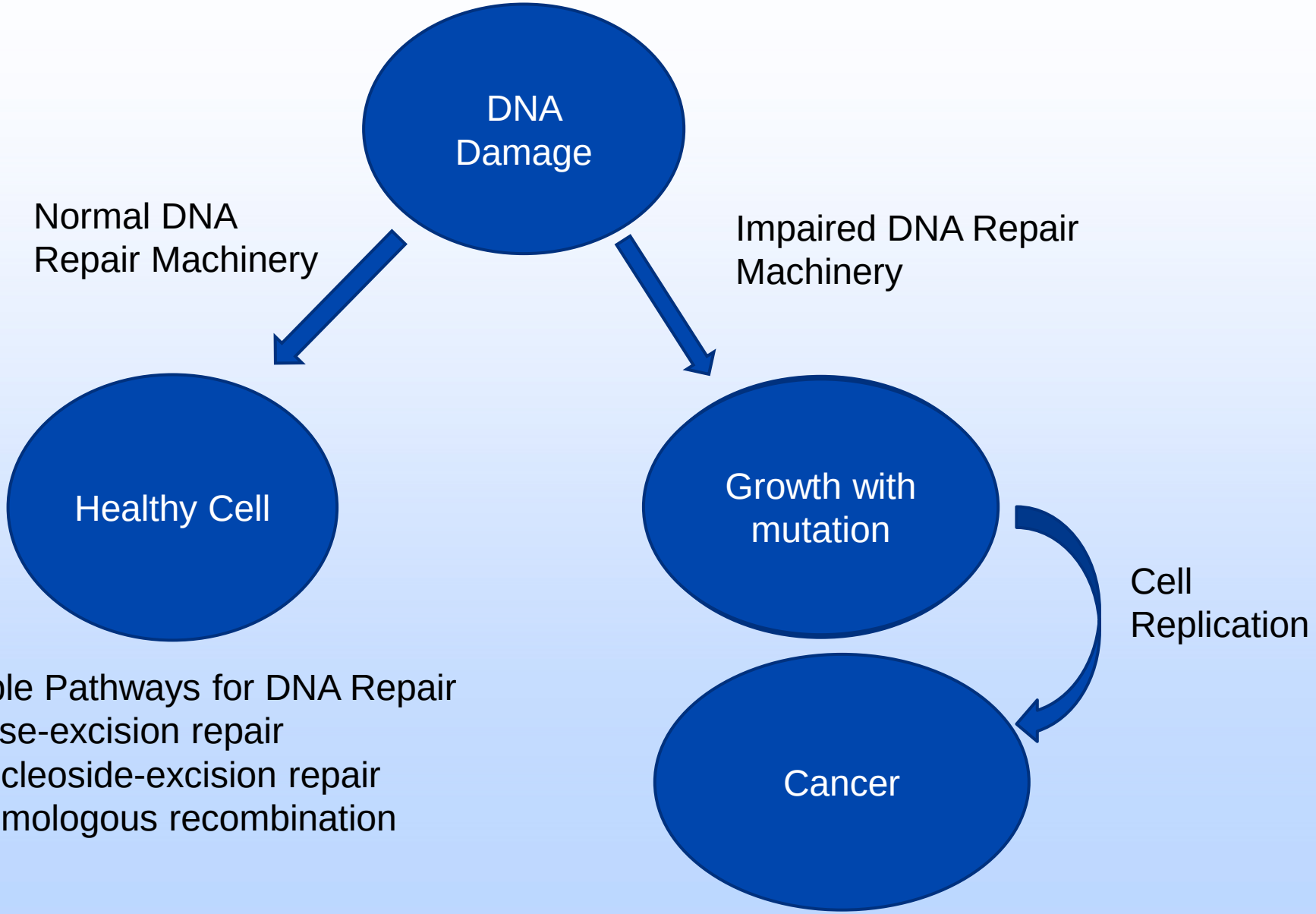
Emerging Targets in LMS: mTOR inhibitors

- LMS has aberrant PI3K/AKT/mTOR signaling
  - Everolimus and temsirolimus have shown some activity in small clinical trials
- Ongoing studies underway in soft tissue sarcoma including LMS
  - Combination with therapies



Adapted from LaSarge et al. Front Mol Neurosci 2014

Emerging Target: DNA Repair



Multiple Pathways for DNA Repair

- Base-excision repair
- Nucleoside-excision repair
- Homologous recombination

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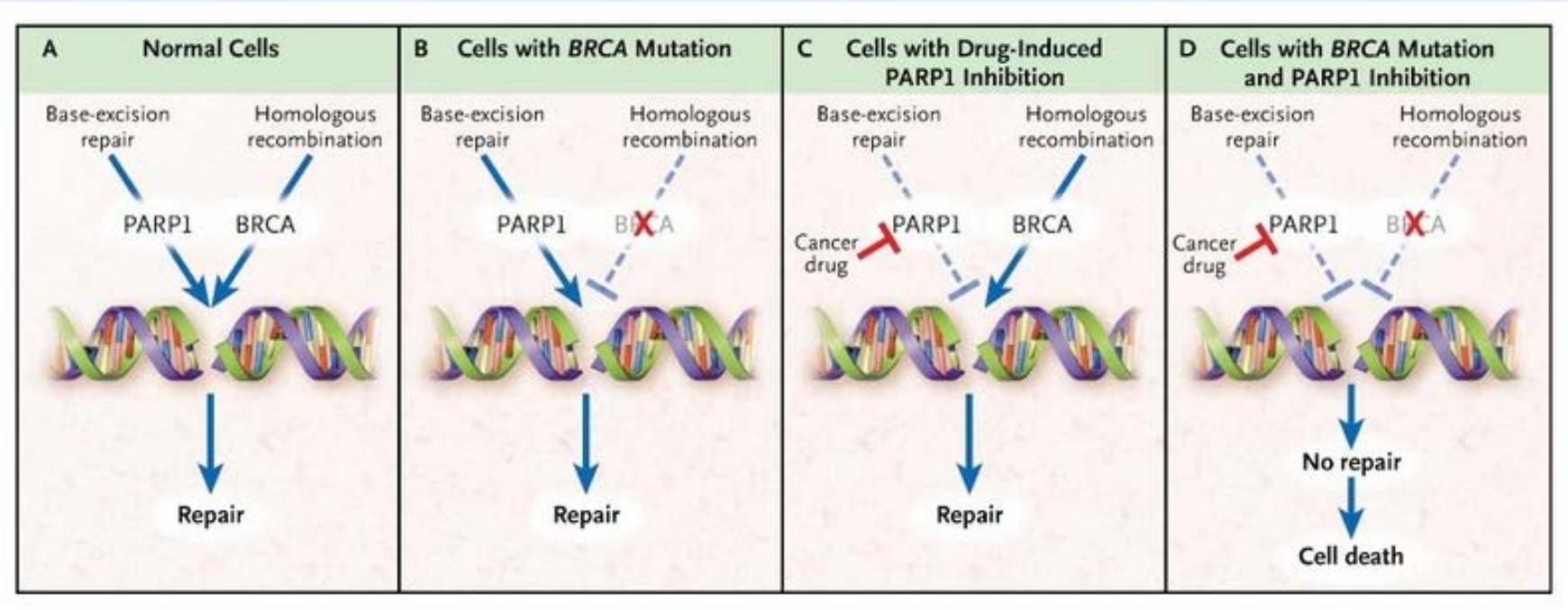
Emerging Target: DNA Repair Defects

- Recurrent mutations in DNA repair machinery
  - LMS 'BRCA-ness': impaired homologous recombination pathway
  - Increased susceptibility to PARP inhibitors
- Synthetic Lethality



Iglehart et al. NEJM 2009

Emerging Targets: Immunotherapy

- Immunotherapy takes the breaks **off** the immune system
  - Allows the immune system to attack cancer cells
  - Prevents cancer cells from putting the breaks on immune cells
- Effective therapy that has changed outcomes for many cancers
  - Lung, melanoma, kidney/bladder
- Role in sarcoma currently under investigation

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Potential Role of Immunotherapy in LMS

- Evaluation of T cell infiltration and PD1/PDL1 in sarcoma:
  - 4 subtypes evaluated
  - LMS and undifferentiated pleomorphic sarcoma found to have higher PD1/PDL1 expression
  - Suggests potential efficacy of immunotherapy
- SARC028: Pembrolizumab in sarcoma
  - 0/10 partial responses in LMS group
  - Ongoing clinical trials in sarcoma as single-agent and combination therapy

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Pollack et al. Cancer 2017; Tawbi et al. Lancet 2017

Current Clinical Trials in Leiomyosarcoma

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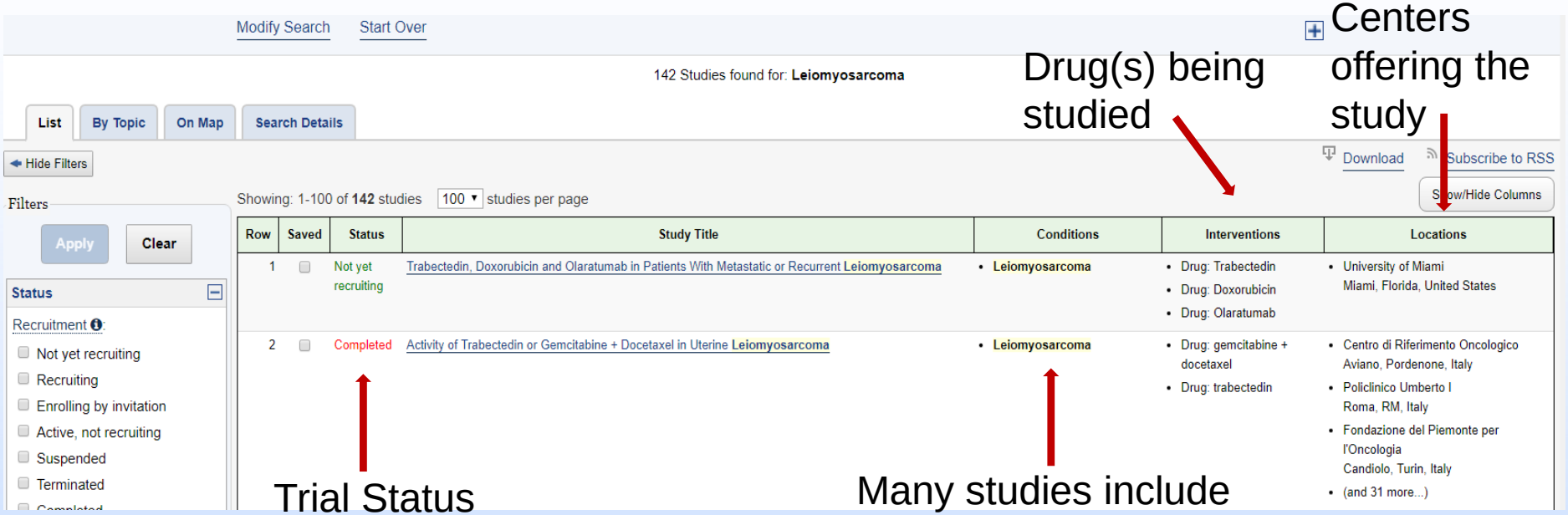
Clinicaltrials.gov



- Each trial will list further details regarding study design and criteria for enrollment

Current Clinical Trials

- Many studies involve combination therapy
  - Improve upon what we already know has activity
  - Drugs with different mechanisms can work together and enhance anti-cancer activity
- Most sarcoma studies evaluating targeted therapies alone or in combination with chemotherapy
- Given rarity of sarcoma, most studies include multiple subtypes
  - Each histology may be separate cohort (group) within the study

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Current Clinical Trials - TAPUR

- Targeted Agent and Profiling Utilization Registry
- Includes all solid tumors
- Allows access to targeted drugs based on molecular profiling of patient's tumor

Intervention/treatment
Drug: Axitinib
Drug: Bosutinib
Drug: Crizotinib
Drug: Palbociclib
Drug: Sunitinib
Drug: Temsirolimus
Drug: Trastuzumab and Pertuzumab
Drug: Vemurafenib and Cobimetinib
Drug: Cetuximab
Drug: Dasatinib
Drug: Regorafenib
Drug: Olaparib
Drug: Pembrolizumab
Drug: Nivolumab and Ipilimumab

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Clinicaltrials.gov NCT02693535

Conclusions

- Clinical trials are conducted in phases, each with a specific overall goal
- Leiomyosarcoma is genetically complex and heterogeneous
  - We continue to work to obtain a better understanding
  - Some potential targets (mTOR, immune system, PARP) have emerged
- Many clinical trials in leiomyosarcoma are ongoing
  - Specific criteria must be met for enrollment
  - Not all studies are available at all sites
  - Special studies may be molecularly based and tissue agnostic

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Thank You

siontis.brittany@mayo.edu

REIN IN SARCOMA

LMS
NATIONAL
LeioMyoSarcoma
FOUNDATION
Moving Forward in the Quest for the Cure

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Radiation Therapy

Safia K. Ahmed, MD

Leiomyosarcoma Patient Education Symposium

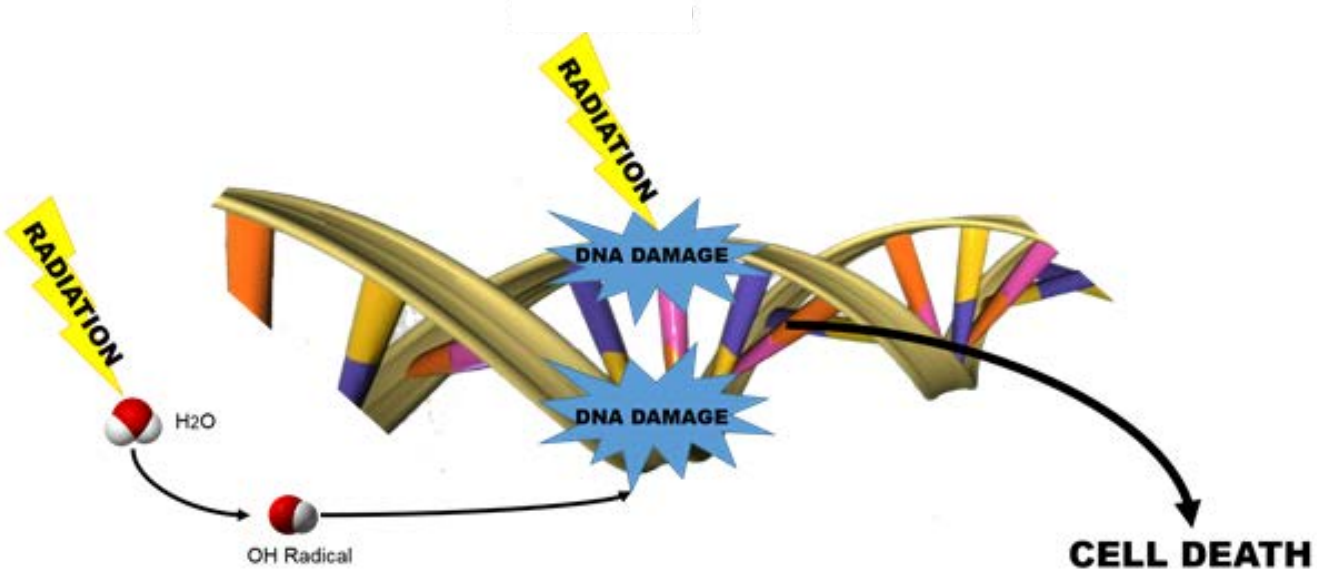
July 14, 2018

Outline

- What is radiation therapy
- Types of radiation therapy
- Radiation therapy for leiomyosarcoma (LMS)
- Radiation therapy logistics and side effects
- Ongoing research studies
- Conclusions

What is Radiation Therapy?

- Type of cancer treatment that uses intense energy to kill cancer cells

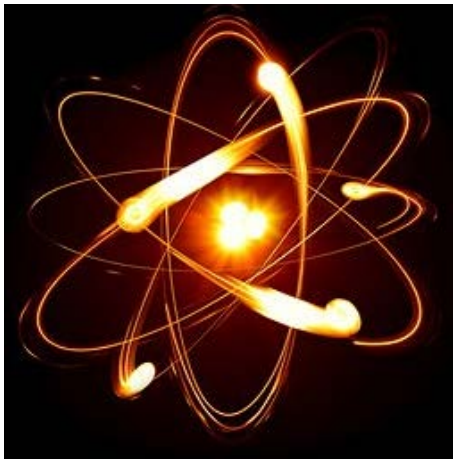


H_2O = water

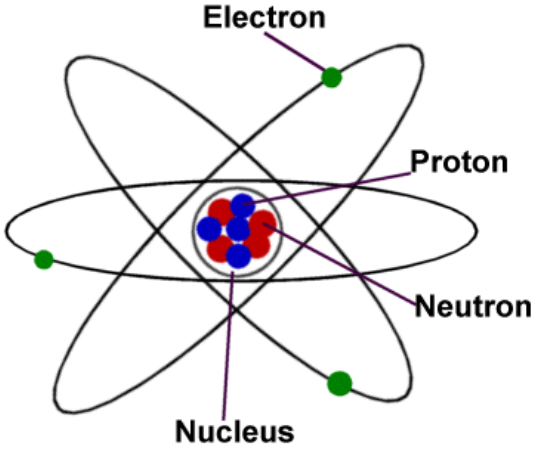
Types of Radiation Therapy
Based on Energy Source

- X ray

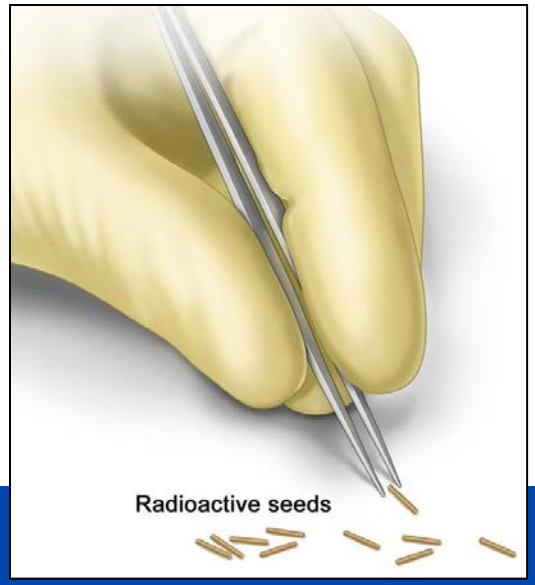
- Electron



- Proton

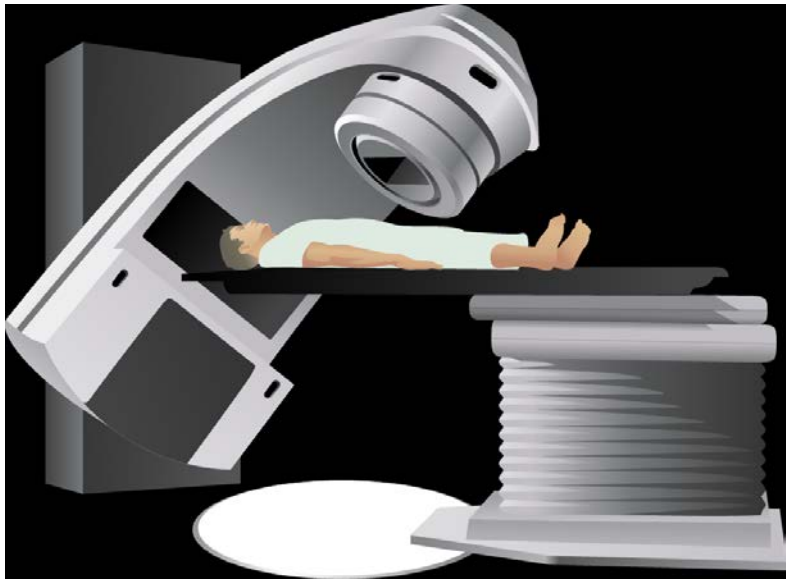


- Radioactive sources

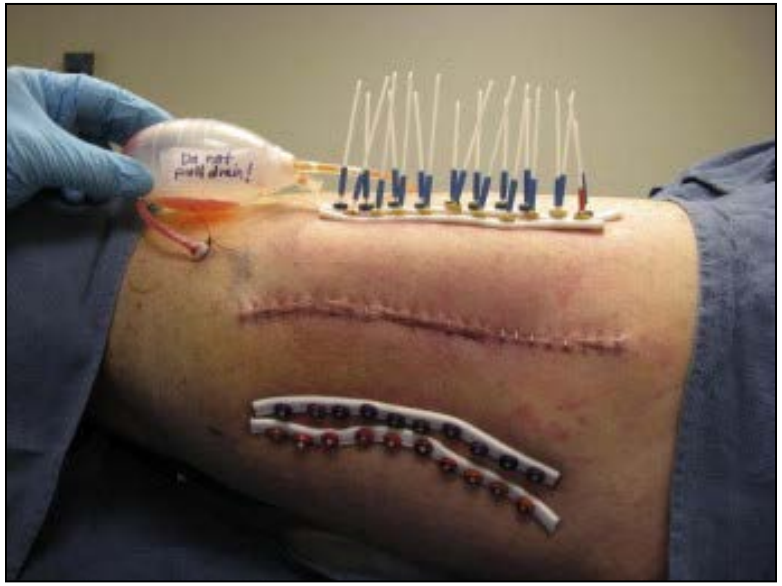


Types of Radiation Therapy
Based on Treatment Delivery Method

- External Beam



- Brachytherapy



Types of Radiation Therapy

- External Beam
  - X ray
  - Proton
  - Electron
- Brachytherapy
  - Radioactive sources

Radiation Therapy for LMS

- Local tumor treatment
- Used in combination with surgery
- Or, used by itself

Radiation Therapy + Surgery

- Radiation helps decrease the chances of LMS returning locally once it is removed

- Given before surgery or after surgery

Radiation Therapy + Surgery

- We favor preoperative radiation therapy for most situations
  - Better visualized and smaller treatment target
  - Lower radiation dose delivered to normal tissues
  - Fewer irreversible long-term side effects

Radiation Therapy + Surgery

- Preoperative / postoperative radiation sometimes combined with intraoperative radiation therapy or brachytherapy

- Used for tumors that are difficult to remove during surgery and there is concern microscopic amounts of cancer may remain

Radiation Therapy Only

- For cases in which surgery is not a good option

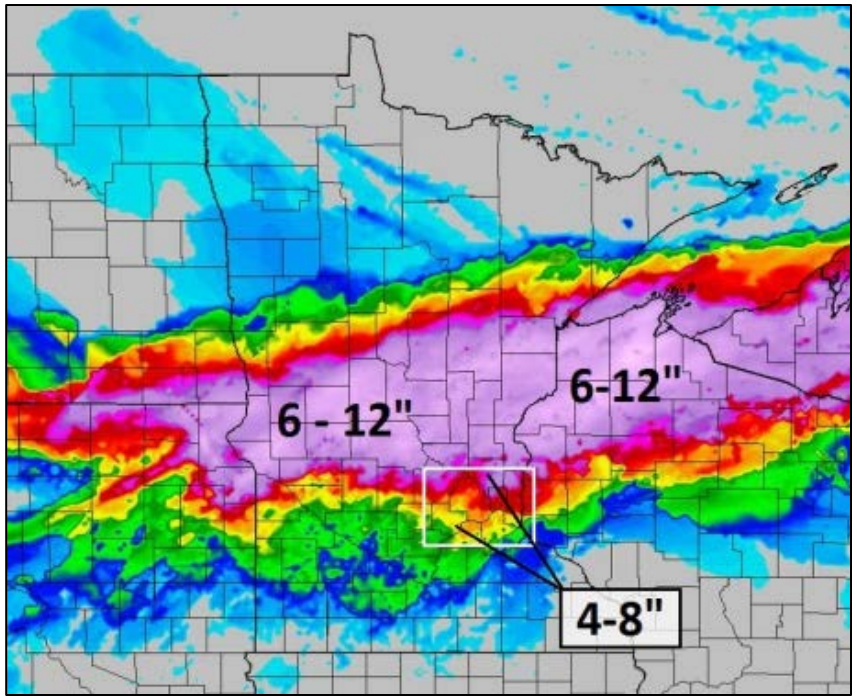
- For metastatic tumors causing symptoms
  - Muscle/bone pain
  - Breathing difficulty

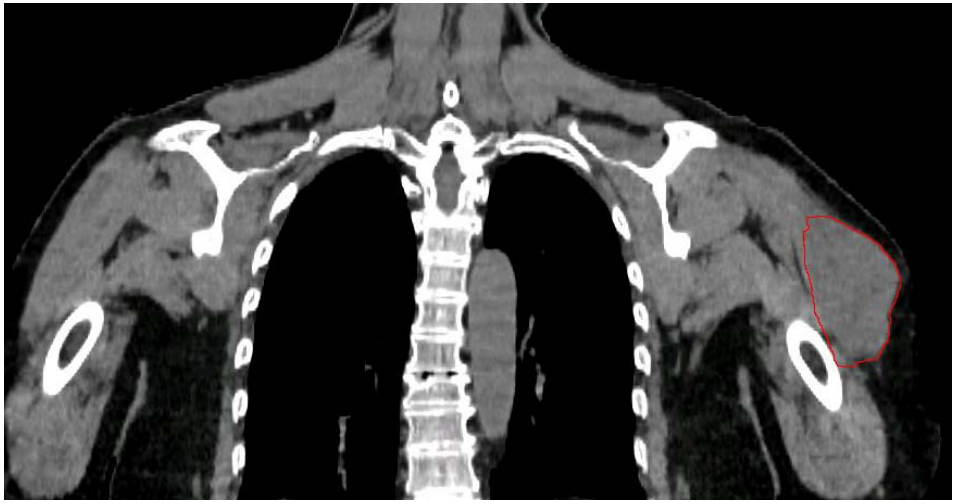
"Palliative Radiation"

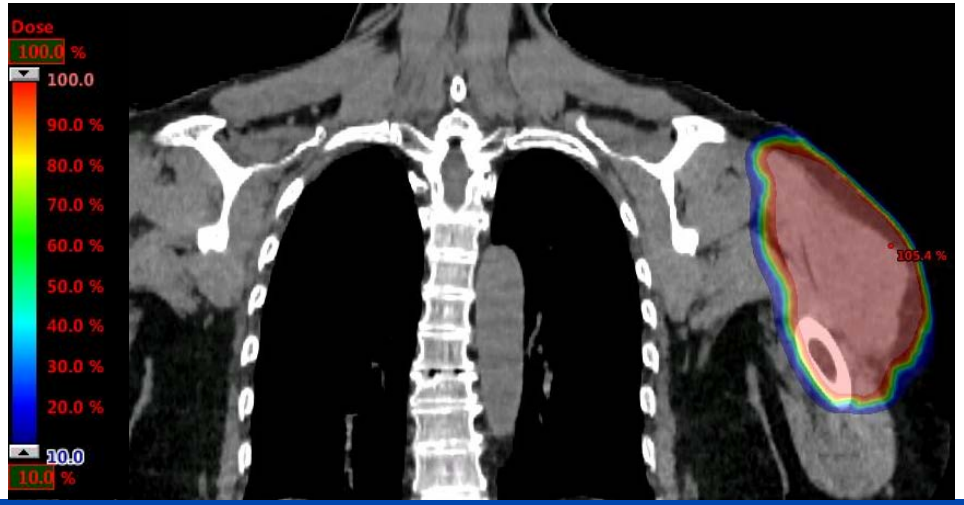
Measuring Radiation

- Units: Gray (Gy)
- Give one fraction (or treatment) a day
  - Often 2 Gy per fraction
- Treat 5 fractions a week, every week, until you reach the desired total dose of radiation
- Standard treatments:
  - Preoperative: 50 Gy in 25 fractions
    - 5 weeks
  - Postoperative and radiation only: 60-70 Gy in 30-35 fractions
    - 6-7 weeks
  - Palliative: 1, 5, or 10 fractions

Visualizing Radiation Dose





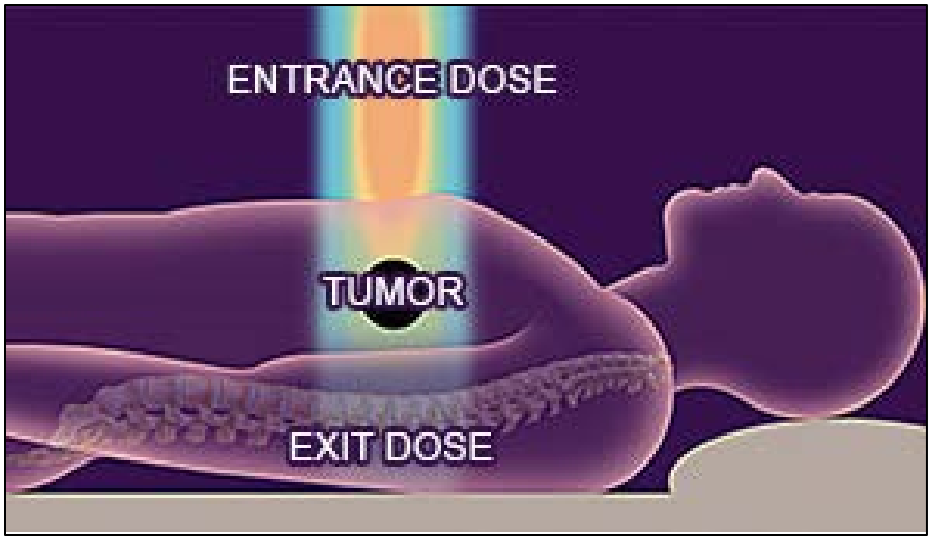


X Ray & Proton Therapy

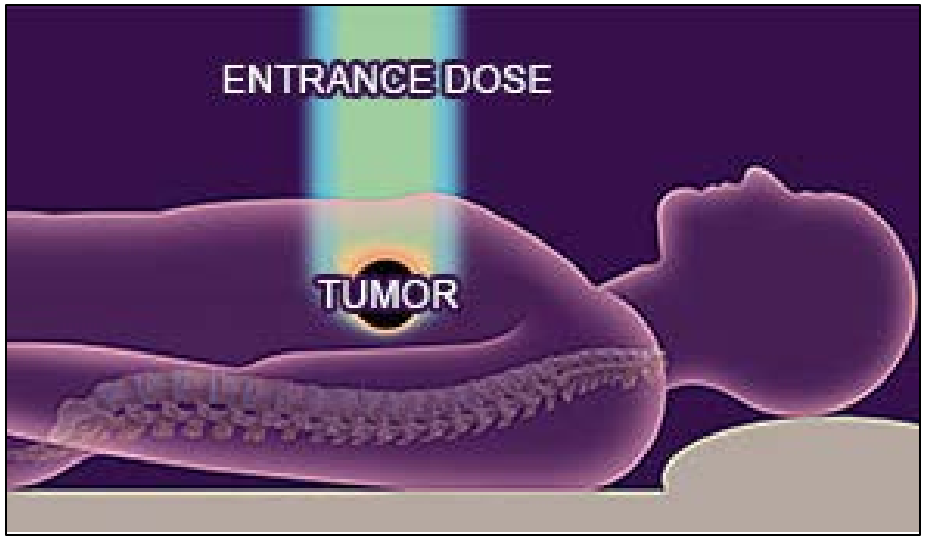
Linear Accelerator

Gantry

X Ray versus Proton Therapy

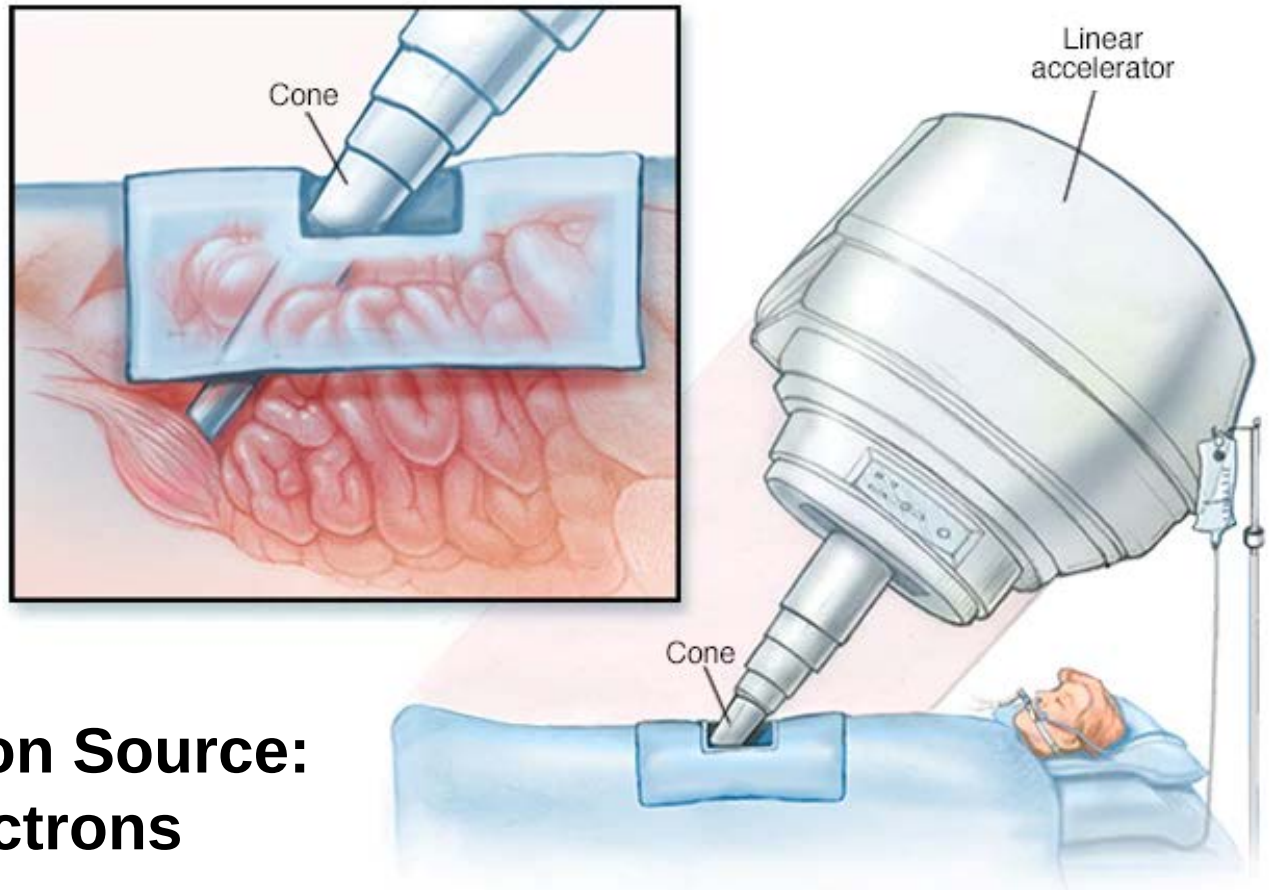


X Ray



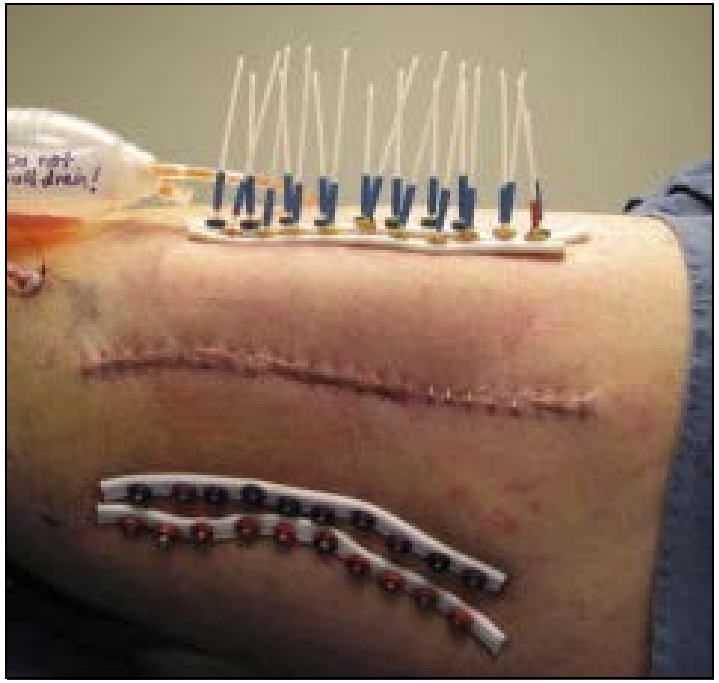
Proton

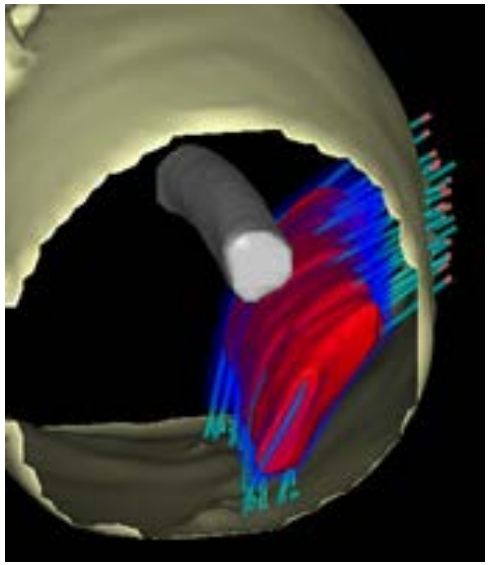
Intraoperative Radiation Therapy



Radiation Source: Electrons

Brachytherapy





2 fractions a day
for 2-3 days

Radiation Therapy Work Flow

Consultation
- Determine role of radiation, duration, & modality
- Discuss treatment logistics & side effects

Simulation
-Determine treatment position
-Obtain CT & MRI

Treatment planning
-Define treatment target and normal tissues
-Dosimetry and physics teams help generate plan

Daily treatments
-Delivered by radiation therapists
-Meet with care team & physician once weekly

Follow up
-Regular imaging & in office visit
-Intraoperative radiation 4-6 weeks later (if applicable)

Debunking Radiation Therapy Myths

Radiation therapy is painful

Debunking Radiation Therapy Myths

Radiation therapy causes you to be radioactive

Debunking Radiation Therapy Myths

Radiation therapy burns your skin

Debunking Radiation Therapy Myths

Radiation therapy causes you to lose your hair

Debunking Radiation Therapy Myths

Radiation therapy affects your immune system

Debunking Radiation Therapy Myths

Radiation therapy causes more cancer

Debunking Radiation Therapy Myths

Radiation therapy is a one time treatment

Radiation Therapy Side Effects
During Treatment

- Fatigue
- Skin changes
- Local swelling
- Nausea, vomiting, diarrhea
  - From radiation to abdomen or pelvis
- Pain with swallowing
  - From radiation to head, neck, or chest

Radiation Therapy Side Effects
After Treatment

- Skin discoloration
- Soft tissue stiffness & swelling
- Wound complications
- Bone weakness
- Lung & heart damage
  - From radiation to chest
- Bowel damage
  - From radiation to abdomen or pelvis
- Second cancer

Ongoing Research Studies

- Use of perfusion MRI and MR Elastography for surgical planning, radiation therapy target delineation, and treatment response in sarcomas

Ongoing Research Studies

- Use of IMPT with “boost” to high risk margin for retroperitoneal sarcomas

Conclusions

- Radiation therapy is a common and critical component of LMS treatment
- Radiation therapy dose, duration, treatment modality, and treatment target are individualized for each patient and situation
- Our department is committed to furthering sarcoma radiation therapy research and improving radiation therapy practices

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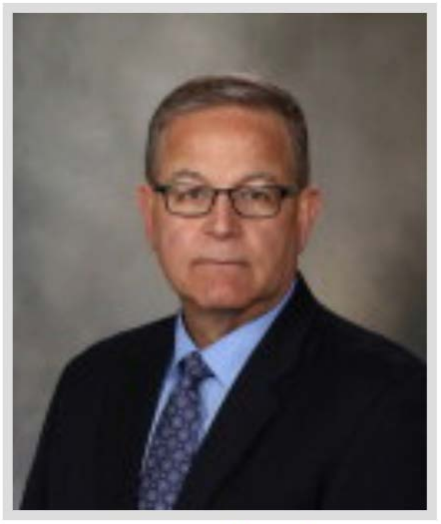
Ivy A. Petersen, M.D.

Safia K. Ahmed, M.D.



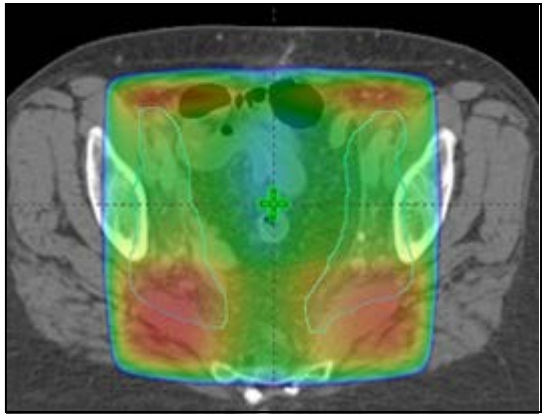
Scott L. Stafford, M.D.

Michael G. Haddock, M.D.

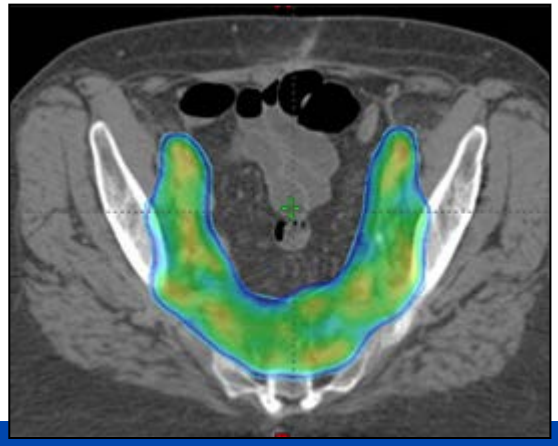
Rochester Sarcoma Radiation Oncology Specialists

X Ray Therapy

3D Conformal Therapy



Intensity Modulated Radiation Therapy (IMRT)



What's New, What's True in Nutrition for Cancer Survivors

Jacalyn See, MS, RDN, LD
Assistant Professor of Nutrition
Mayo Clinic

Nutrition and Exercise Guidelines for Survivors

- Be at a healthy weight.
- Be physically active.
- Eat a diet high in vegetables, fruits and whole grains.

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Nutritional Goals Vary

- Treatment/Recovery
- After recovery
- Advanced cancer
- Adequate calories, protein; manage side effects
- Prevention
- Comfort, pleasure

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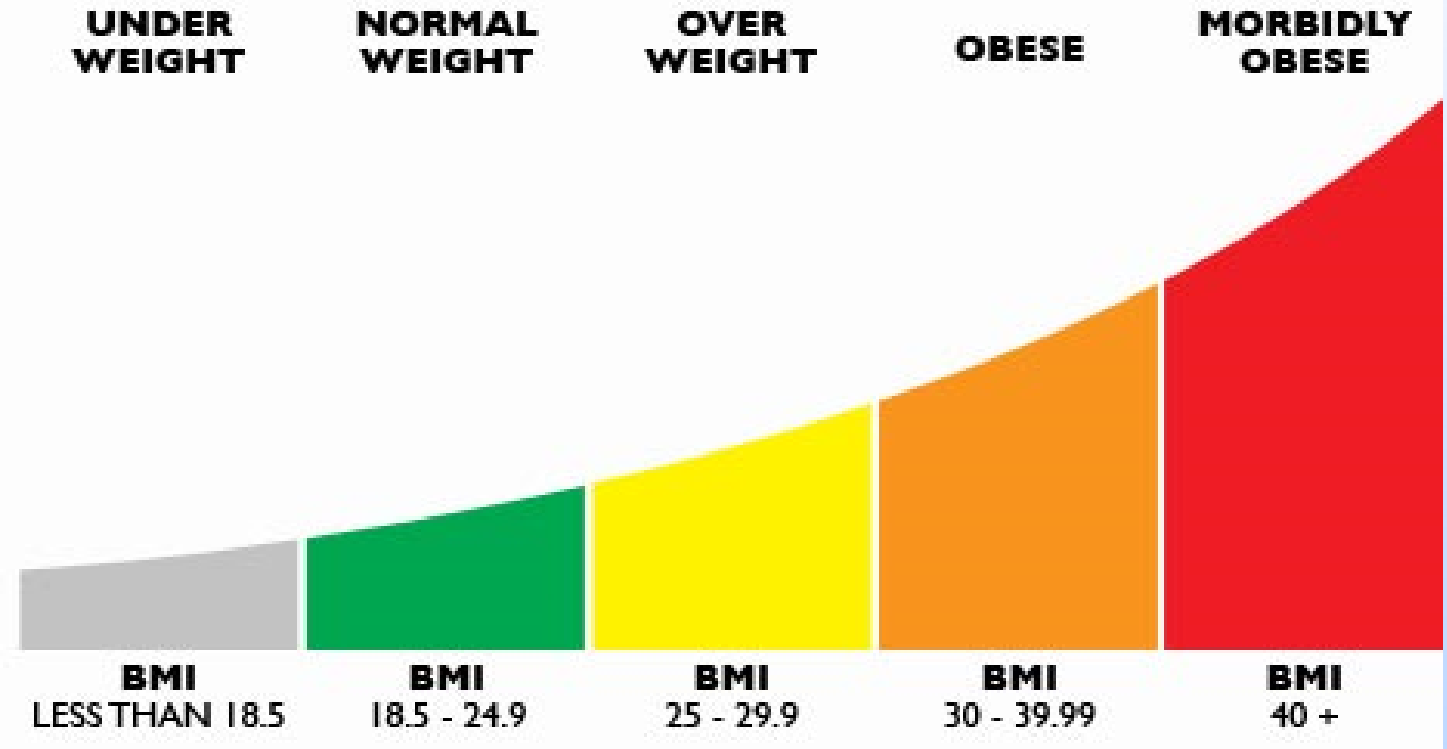
Be a Healthy Weight



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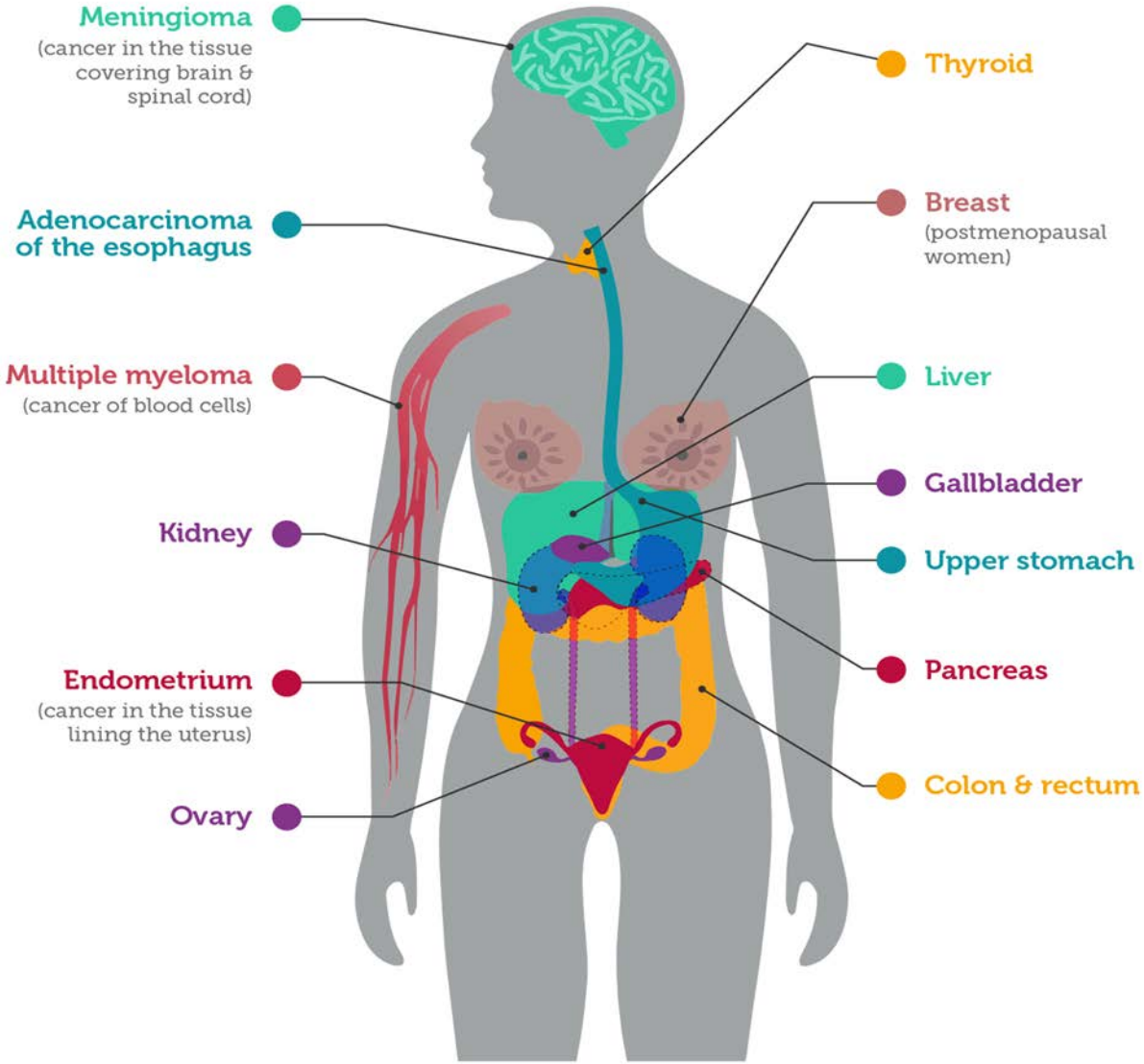
NATIONAL CANCER INSTITUTE

Cancers Associated with Overweight & Obesity



cancer.gov/obesity-fact-sheet

Adapted from Centers for Disease Control & Prevention

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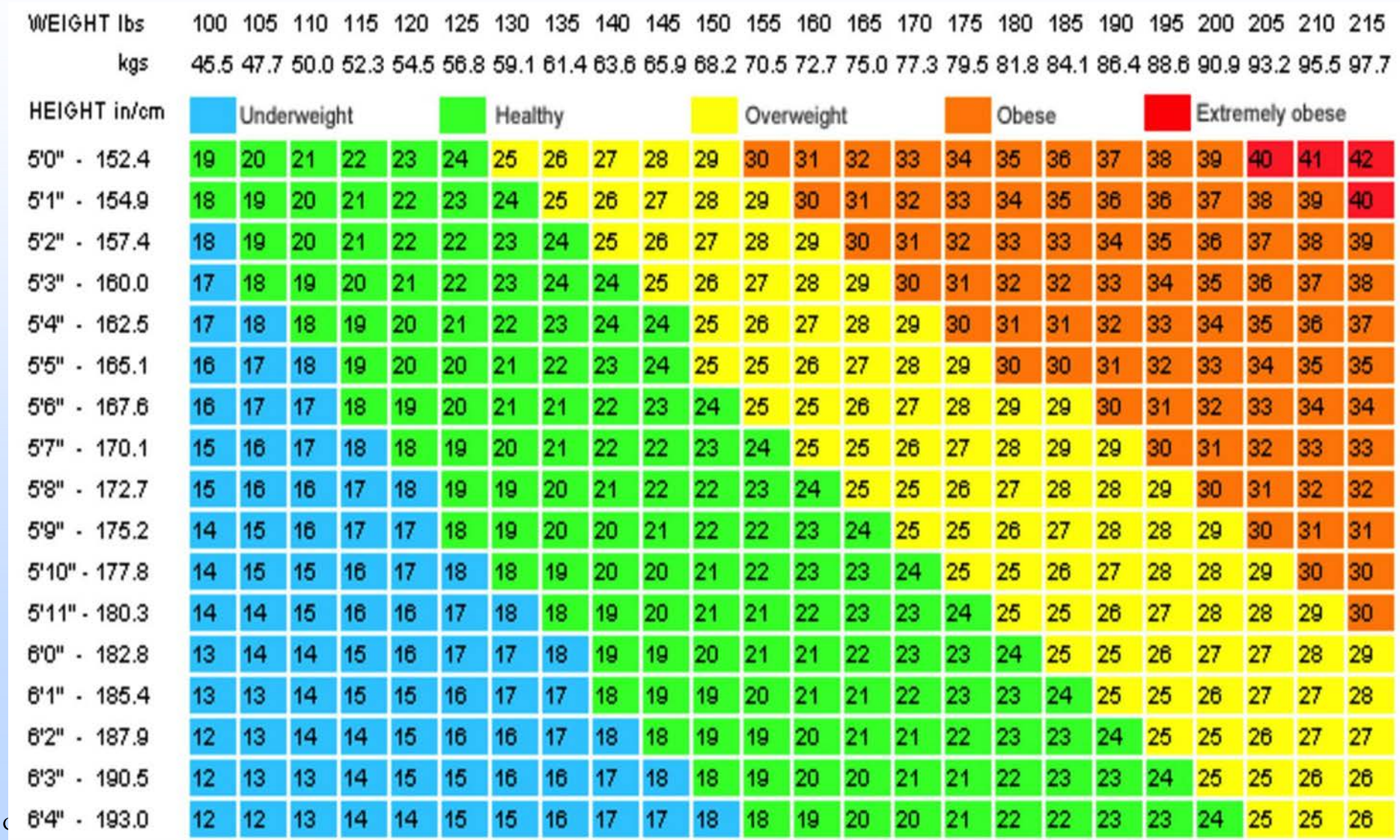
Are You at a Healthy Weight?



WEIGHT lbs	100	105	110	115	120	125	130	135	140	145	150	155	160	165	170	175	180	185	190	195	200	205	210	215
kgs	45.5	47.7	50.0	52.3	54.5	56.8	59.1	61.4	63.6	65.9	68.2	70.5	72.7	75.0	77.3	79.5	81.8	84.1	86.4	88.6	90.9	93.2	95.5	97.7
HEIGHT in/cm	Underweight					Healthy						Overweight				Obese				Extremely obese				
5'0" - 152.4	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
5'1" - 154.9	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	36	37	38	39	40
5'2" - 157.4	18	19	20	21	22	22	23	24	25	26	27	28	29	30	31	32	33	33	34	35	36	37	38	39
5'3" - 160.0	17	18	19	20	21	22	23	24	24	25	26	27	28	29	30	31	32	32	33	34	35	36	37	38
5'4" - 162.5	17	18	18	19	20	21	22	23	24	24	25	26	27	28	29	30	31	31	32	33	34	35	36	37
5'5" - 165.1	16	17	18	19	20	20	21	22	23	24	25	25	26	27	28	29	30	30	31	32	33	34	35	35
5'6" - 167.6	16	17	17	18	19	20	21	21	22	23	24	25	25	26	27	28	29	29	30	31	32	33	34	34
5'7" - 170.1	15	16	17	18	18	19	20	21	22	22	23	24	25	25	26	27	28	29	29	30	31	32	33	33
5'8" - 172.7	15	16	16	17	18	19	19	20	21	22	22	23	24	25	25	26	27	28	28	29	30	31	32	32
5'9" - 175.2	14	15	16	17	17	18	19	20	20	21	22	22	23	24	25	25	26	27	28	28	29	30	31	31
5'10" - 177.8	14	15	15	16	17	18	18	19	20	20	21	22	23	23	24	25	25	26	27	28	28	29	30	30
5'11" - 180.3	14	14	15	16	16	17	18	18	19	20	21	21	22	23	23	24	25	25	26	27	28	28	29	30
6'0" - 182.8	13	14	14	15	16	17	17	18	19	19	20	21	21	22	23	23	24	25	25	26	27	27	28	29
6'1" - 185.4	13	13	14	15	15	16	17	17	18	19	19	20	21	21	22	23	23	24	25	25	26	27	27	28
6'2" - 187.9	12	13	14	14	15	16	16	17	18	18	19	19	20	21	21	22	23	23	24	25	25	26	27	27
6'3" - 190.5	12	13	13	14	15	15	16	16	17	18	18	19	20	20	21	21	22	23	23	24	25	25	26	26
6'4" - 193.0	12	12	13	14	14	15	15	16	17	17	18	18	19	20	20	21	22	22	23	23	24	25	25	26

How Excess Weight May Lead to Cancer

- Increases hormone levels
- Increases insulin levels
- Promotes inflammation
- Affects microbiome

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Be Physically Active

150 minutes a week

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How May Exercise Reduce Risk of Recurrence?

- Aids in weight control
- Reduces estrogen levels
- Reduces insulin levels
- Boosts immune system
- Reduces colon transit time

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NEAT (nonexercise activity thermogenesis)

- Walk in the house
- Pace while talking on the phone
- Wear a pedometer
- Do housework
- Do yard work
- Get up from sitting every hour

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Avoid foods and beverages high in fat and/or sugar.

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Eat mostly plant foods.

- Vegetables
- Fruits
- Whole grains
- Legumes

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Protective Nutrients in Plants

- Fiber
- Antioxidants
- Other vitamins/minerals
- Phytochemicals

Bonus: Minimal fat, no cholesterol, low in calories

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Potential Benefits of Fiber

- Decreases colonic transit
- Prebiotics
- Low in calories
- Replaces meat
- Other protective nutrients

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Antioxidants

- Carotenoids - green and orange vegetables, tomatoes
- Vitamin C - citrus, strawberries, melons
- Vitamin E - whole grains, nuts, oils
- Selenium - whole grains, nuts

Antioxidants block damaging reactions.

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Phytochemicals (Plant Chemicals)

- Flavonoids - berries, citrus fruits, tea
- Lignins - whole grains, flax
- Isoflavones - soy foods
- Isothiocyanates - cruciferous vegetables

Go For Color

Pigments give nutrients to fruits and vegetables.

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Pesticides

-No convincing evidence of risk.

-No difference in nutrients.

-The benefits of eating fruits and vegetables far outweigh any risk.

-The American food supply is among the safest in the world.

Tips for Reducing Pesticide Residues

- Select produce without cuts, mold, decay.
- Scrub under running water.
- Discard outer leaves.
- Trim fat from meat, poultry, and fish.
- Eat a variety of foods.

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Grain Products

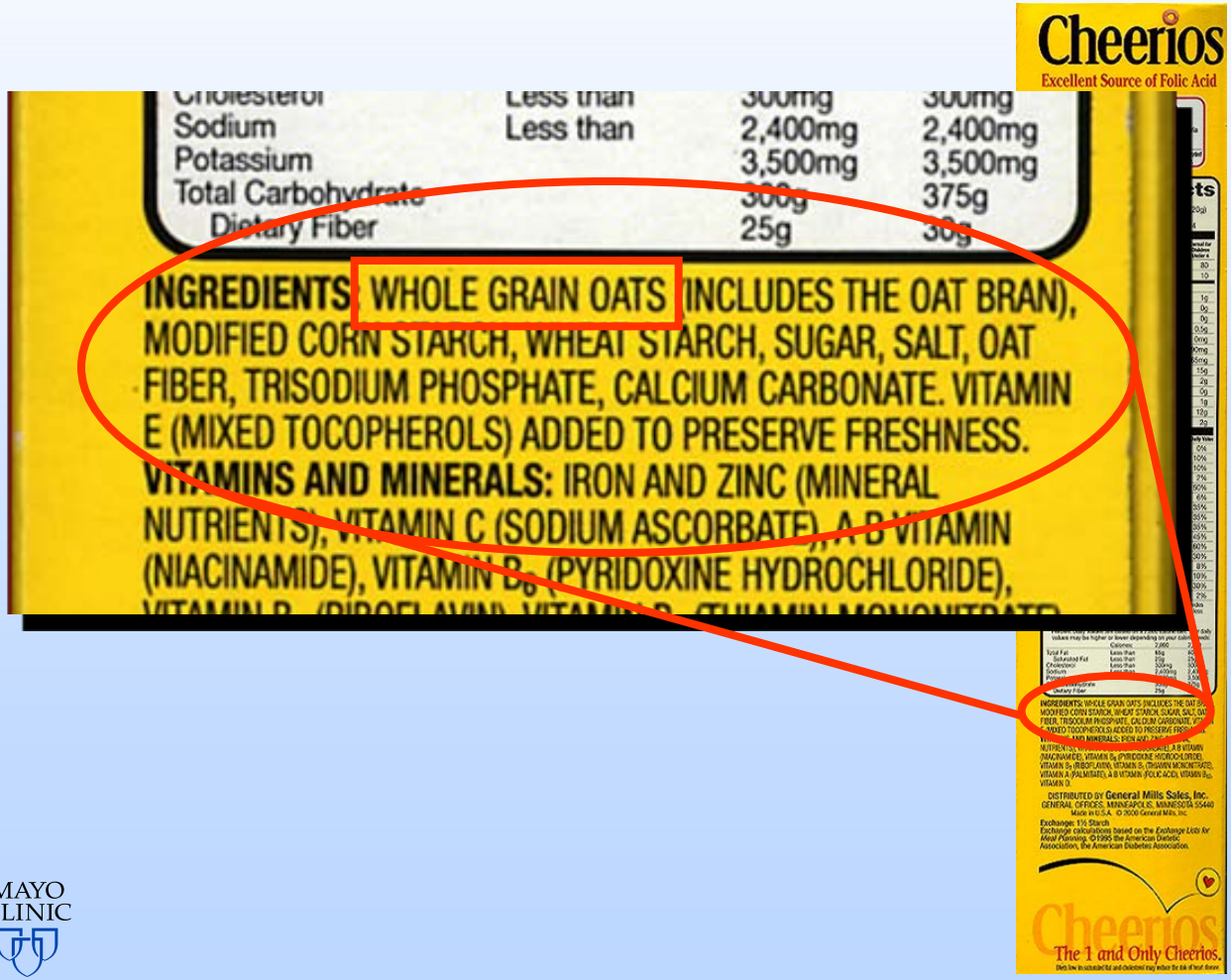
Whole Grains

- Oatmeal
- Branflakes
- Whole wheat bread
- Brown rice
- Whole wheat pasta
- Popcorn

Refined Grains

- Cream of wheat
- Cornflakes
- White bread
- White rice
- White pasta
- Pretzels

Label Reading for Whole Grains



Look for "Whole Grain" as a leading ingredient

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Legumes

- Kidney beans
- Navy beans
- Pinto beans
- Soy beans
- Peanuts
- Split peas
- Lentils
- Garbanzo beans
- Baked beans
- Black-eyed peas

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Legumes vs Meat

Nutrient	1 cup beans	3 oz lean meat
Protein (g)	16	21
Fat (g)	1	12
Cholesterol (mg)	0	75
Calories	200	200
Fiber (g)	6.6	0
Iron (mg)	4.5	2.5

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Limit red meat and avoid processed meats.

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Tips for Reducing Red Meat

- Eat more poultry, fish, shellfish
- Have legumes for a vegetarian meal
- Limit red meat to 3 oz portion, lean
- Use meat in stews, stir-fry or casseroles to make it go farther

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Grilling to Reduce Cancer Risk

- Use medium heat
- Precook meat
- Avoid flare-ups
- Marinate
- Grill veggies and fruits

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Limit Alcohol Consumption

For cancer prevention it's best not to drink.

IF you choose to drink, limit to 1 drink/day for women and 2 for men.

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Do not rely on supplements to protect against cancer.

- Lack synergy
- Safety unknown
- Studies have been disappointing

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Use Supplements Cautiously

- Choose food first
- Use to supplement poor intake
- Use to correct a deficiency
- Check with your physician

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In a Nutshell

- Choose mostly plant foods.
- Be physically active.
- Be a healthy weight

Additional Resources

American Cancer Society

www.cancer.org

1-800-ACS-2345

American Institute for Cancer Research

www.aicr.org

1-800-843-8114

Oncology Nutrition Dietitians

www.oncologynutrition.org

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QUESTIONS

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