Soft Tissue Sarcoma

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Disclosures

- National Comprehensive Cancer Centers (NCCN) bone and soft tissue sarcoma panels
- Musculoskeletal Transplant Foundation (MTF) medical board of trustees

Soft Tissue Sarcomas – Intro

- Soft tissue includes skeletal muscle, fat, fibrous tissue, and the vessels supplying these tissues.
- Tumors of the soft tissue include those that occur within or are derived from those tissues
- Tumors of the peripheral and autonomic nervous system are grouped with these as well, because of similar anatomic location, histology and treatment

Embryology

- Soft tissues derive primarily from mesoderm
- Inclusion of peripheral and autonomic nervous system implies a portion comes from neuroectoderm

Classification

- Soft tissue tumors are classified according to their theorized histogenetic origin, typically based on the adult tissue that they most resemble
- Benign – limited capacity for autonomous growth and little tendency for local invasion
- Malignant – (sarcomas) locally aggressive and capable of distant metastatic spread

WHO (2002) Classification of Soft Tissue Tumors

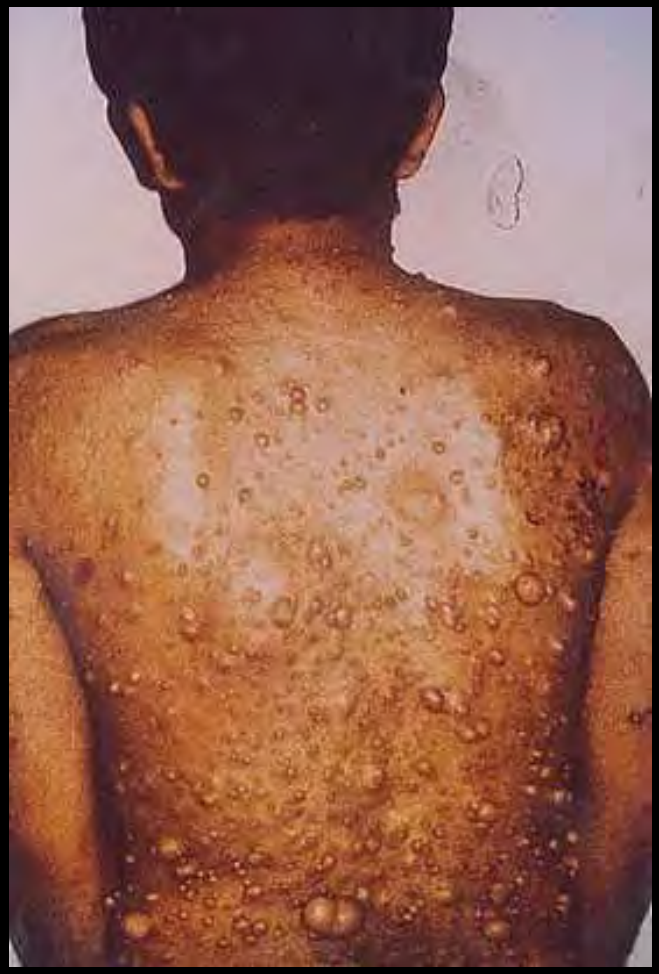
- Adipocytic tumors
  - Benign - Lipoma
  - Malignant – Liposarcoma
- Fibroblastic tumors
  - Benign – Fibroma
  - Malignant – Fibrosarcoma
- Fibrohistiocytic tumors
  - Benign – Benign fibrous histiocytoma
  - Malignant – Malignant fibrous histiocytoma
- Smooth muscle tumors
  - Benign – Leiomyoma
  - Malignant – Leiomyosarcoma
- Skeletal muscle tumors
  - Benign – Rhabdomyoma
  - Malignant – Rhabdomyosarcoma
- Vascular tumors
  - Benign – Hemangioma
  - Malignant – Angiosarcoma
- Chondro-osseous tumors
  - Benign – Soft tissue chondroma
  - Malignant
    - Mesenchymal chondrosarcoma
    - Extraskeletal osteosarcoma
- Tumors of uncertain differentiation
  - Benign – Myxoma
  - Malignant
    - Synovial sarcoma
    - Epithelioid sarcoma
    - Alveolar soft-part sarcoma
    - Clear cell sarcoma of soft tissue
    - Primitive neuroectodermal tumor (PNET)/extraskeletal Ewing tumor

Epidemiology

- In 2007, about 9,220 new soft tissue sarcomas will be diagnosed in the United States (about 50-60% occur in the extremities)
- During 2007, 3,560 Americans are expected to die of soft tissue sarcomas
- Slight male to female predominance
- Benign to malignant – 100 to 1

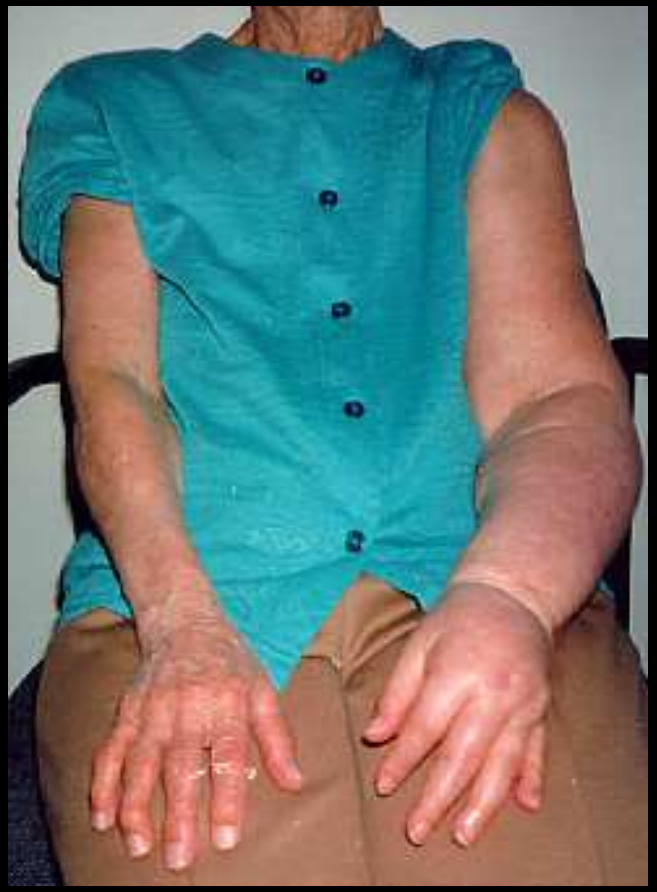
Etiology – Genetic Predisposition

- Li-Fraumeni syndrome (mutation in p53 tumor suppressor)
  - Increased risk of osteosarcoma and liposarcoma
- Neurofibromatosis
  - Lifetime risk for development of malignant schwannoma is 2-5%



Etiology

- Chronic lymphedematous extremity
  - Lymphangiosarcoma
- Patients treated with mastectomy and/or radiation for breast cancer
- Chronic filarial infection



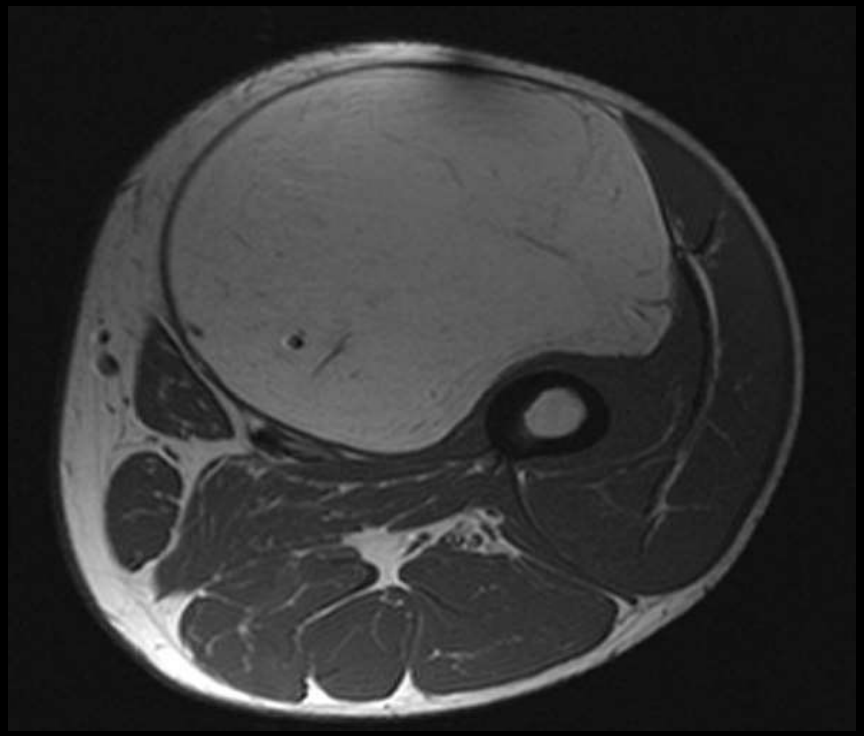
Etiology – Environmental Carcinogens

- Anecdotal evidence
  - Urethane
  - Phenoxyacids in herbicides
  - Ethylene derivatives
  - Agent orange

Etiology – Post-traumatic

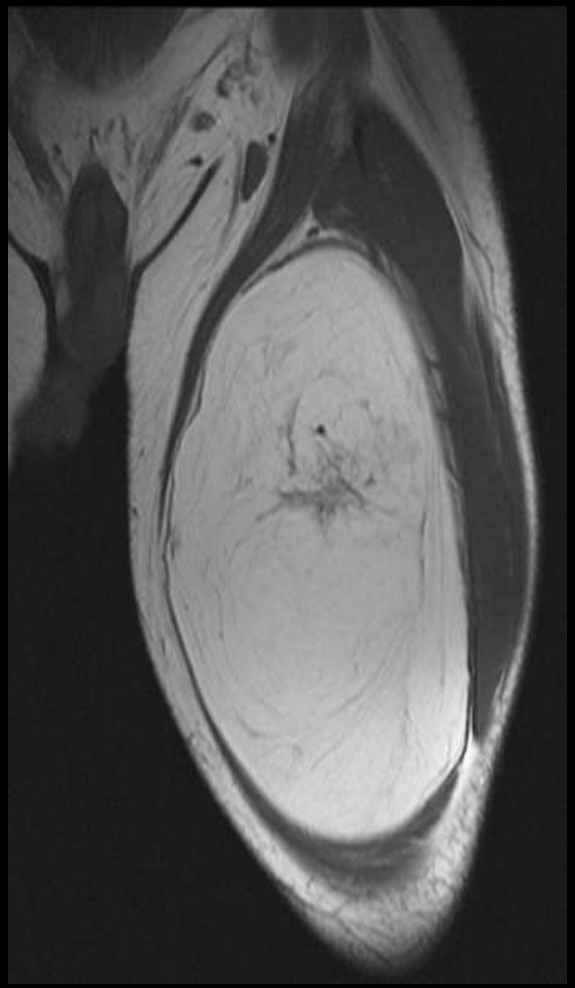
- Previously thought that the trauma merely drew attention to a previously present tumor
- Some now think that pluri-potent stem cells involved in the reparative process post-trauma may go awry and lead to tumor formation

Growth Characteristics



- Centripetal growth until it reaches the axial borders of the compartment then longitudinal growth
- Usually respects fascial planes
- Usually displaces neurovascular structures rather than invading them

Growth Characteristics



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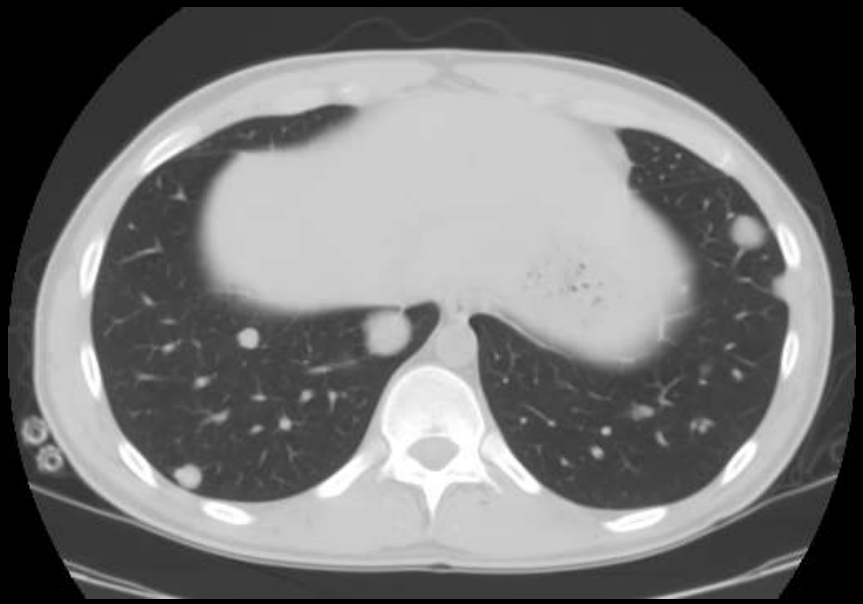
Growth Characteristics

- At periphery of tumor a “pseudocapsule” forms
  - Not a true capsule
  - Layer of compressed atrophic cells resulting from rapid tumor growth
- Reactive zone
  - Edematous, neo-vascularized layer
  - May contain satellite lesions of tumor

Prognostic Factors

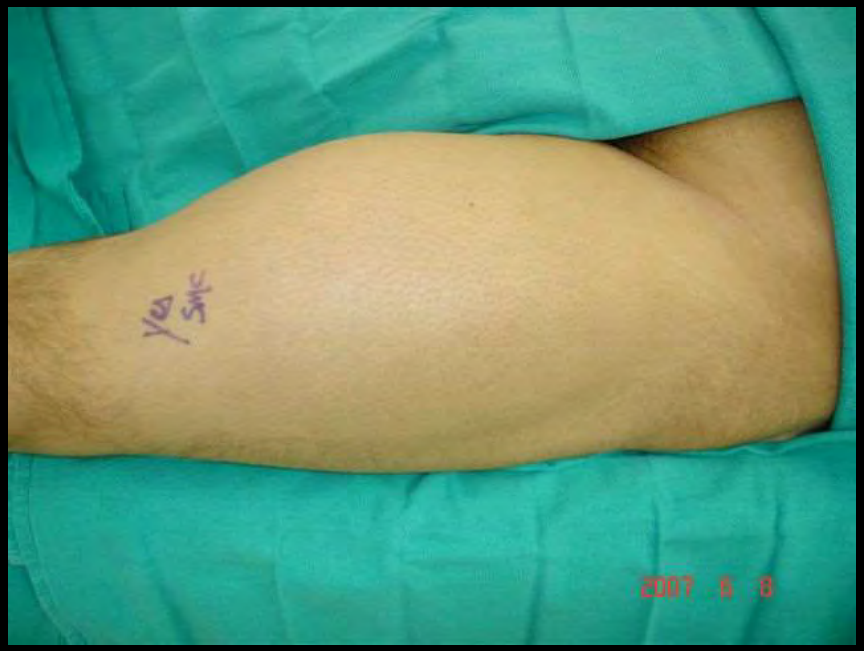
- Histologic grade
- +/- Metastases
- Deep vs. superficial (to the fascia)
- Proximal vs. distal
- Size </> 5 cm

Metastases



- Hematogenous vs. lymphatic spread (exc. synovial sarcoma, epithelioid sarcoma, clear cell sarcoma, and angiosarcoma)
- Most common site of metastases is lungs
- If it is metastatic to other places is usually is present in the lungs as well

History and Presentation



- Most patients present with history of a painless mass
- Sometimes give history of minor trauma
- Predisposing conditions should be sought

Physical Exam

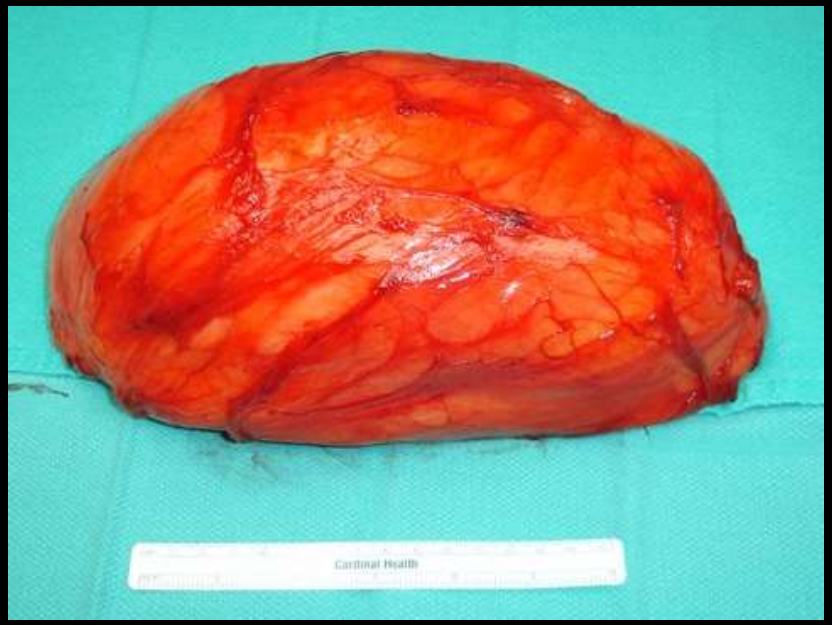
- Size
- Location (superficial or deep to fascia)
- Overlying skin changes
- Thorough neurovascular examination in the distal extremity

Laboratory Evaluation

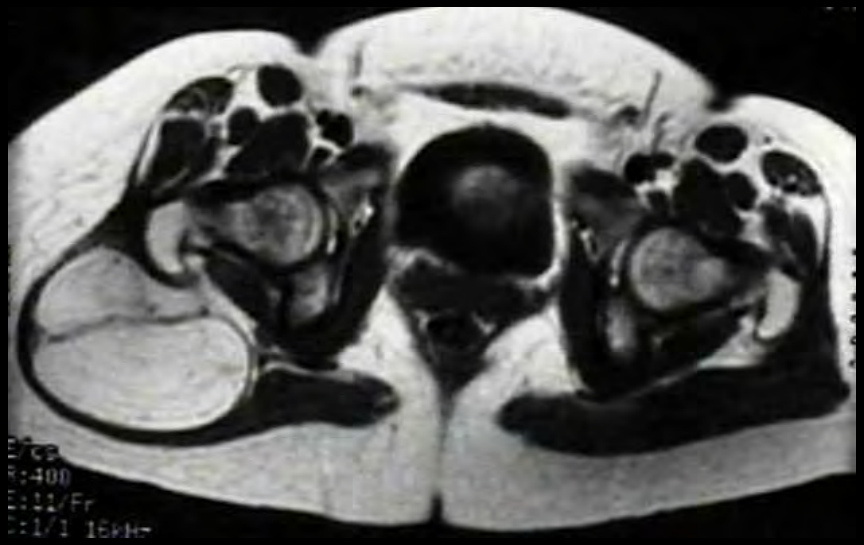
- Not particularly helpful

Imaging

- Plain radiographs of the lesion
  - Synovial sarcoma
  - Extraskeletal chondrosarcoma or osteosarcoma
- MRI of the lesion
- CT scan of the chest (to rule out metastatic disease)

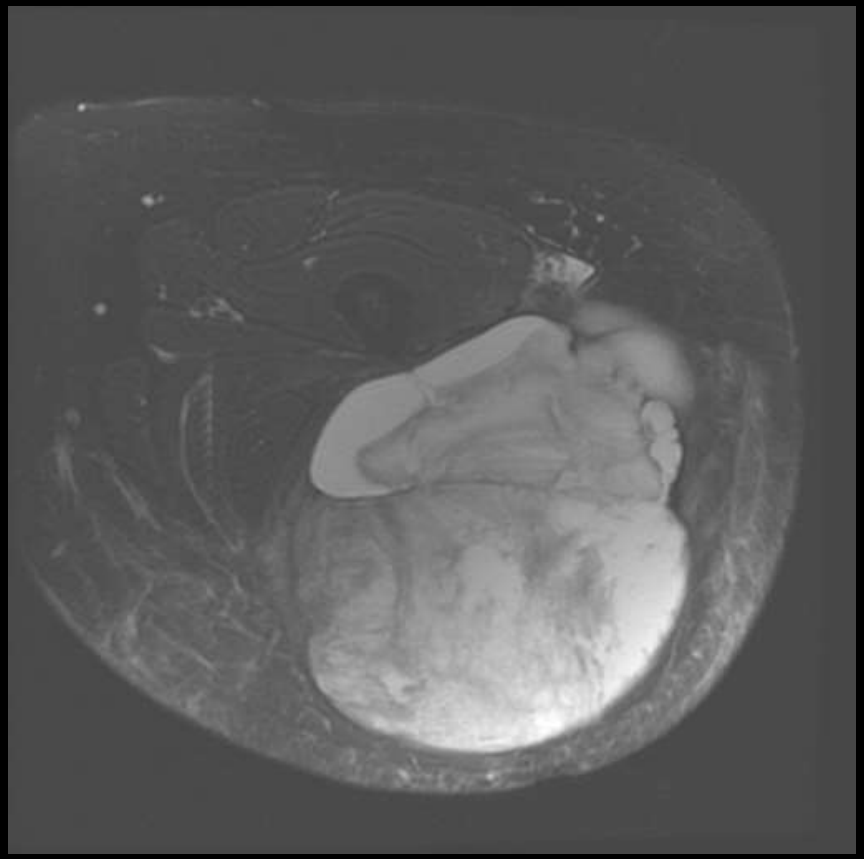


MRI



- Only able to make a diagnosis about 25% of the time based on MRI findings usually benign lesions
  - Lipomas
  - PVNS (Pigmented villonodular synovitis)
  - Hemangiomas

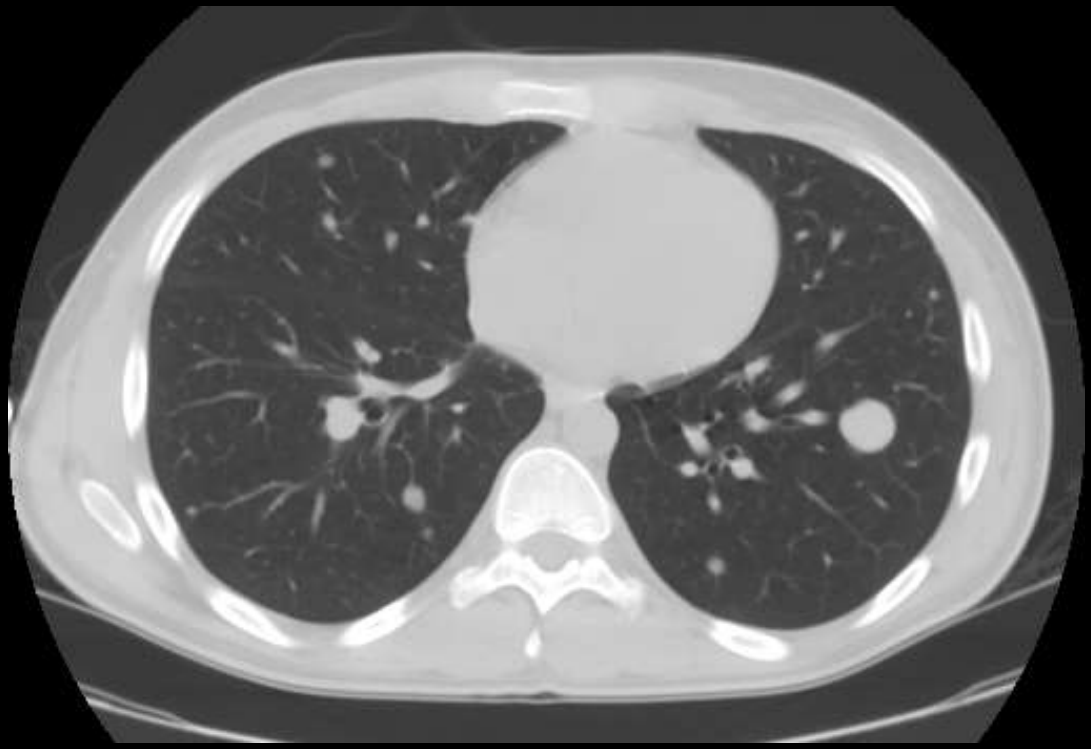
MRI



- Almost never able to make a specific histological diagnosis in malignant lesions

CT

- If sarcoma is suspected a CT scan of the chest should be done to rule out metastatic disease



Biopsy – General Considerations

- Poorly performed biopsies, poorly placed incisions, and biopsy complications can considerably compromise the subsequent local management of bone and soft tissue tumors
- Biopsy should be performed by the person who will provide the definitive care of the patient

Biopsy – General Considerations

- Soft tissue sarcomas seed wounds
- Biopsy tracts must be excised with the tumor
- Appropriate location of the biopsy site is crucial to subsequent treatment

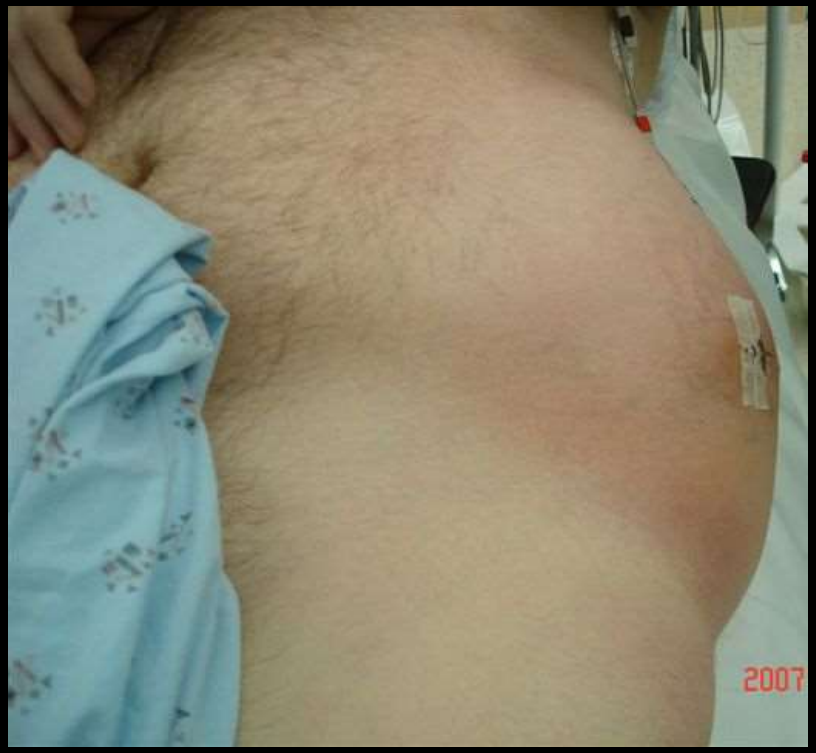
Biopsy Placement

- Longitudinal incisions should be made
- Major neurovascular bundles should be avoided
- Biopsy tracts should not traverse muscle compartments or joints to get to tumor in another compartment
- Standard surgical approaches are often inappropriate

Closed Biopsy – Core Needle Bx

- Advantages
  - Percutaneous
  - Clinic-based procedure
- Disadvantages
  - Sampling error
  - Amount of tissue

Open Biopsy



- Incisional
  - Diagnostic
- Excisional
  - Diagnostic and therapeutic
  - Typically only for small (< 5cm) subcutaneous lesions and lesions felt to be benign lipoma

Pre-operative Planning for Biopsy

- Requires communication between pathologist, radiologist and surgeon for determination of a differential diagnosis
- Frozen section confirms the presence of diagnostic tissue

Treatment

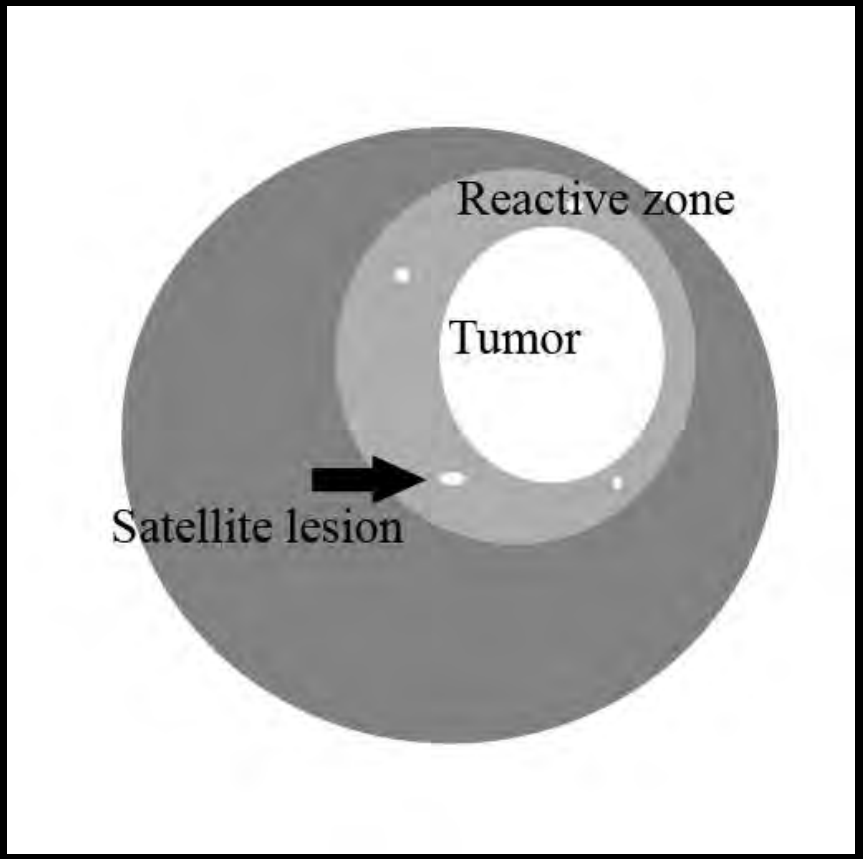
- Once diagnosis (either radiographic or biopsy proven) is made treatment can proceed
- Often presumed benign lesions are diagnosed and treated with the same procedure (excisional biopsy)
- Treatment of benign soft tissue tumors is straightforward
  - Symptomatic → remove
  - Asymptomatic → observe

Treatment

- Treatment of soft tissue sarcomas requires wide surgical margins and radiation therapy (pre vs. post-operative)
- Although evolving, historically chemotherapy has not played a large role in the treatment of patients with soft tissue sarcomas

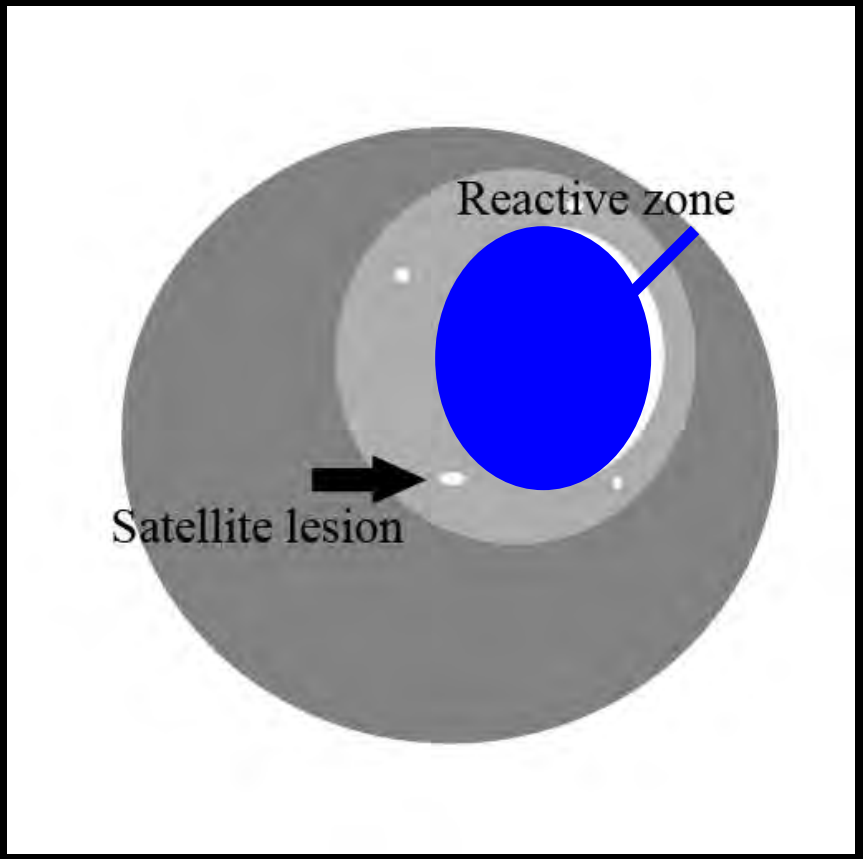
Surgical Margins

- Intralesional
- Marginal
- Wide
- Radical



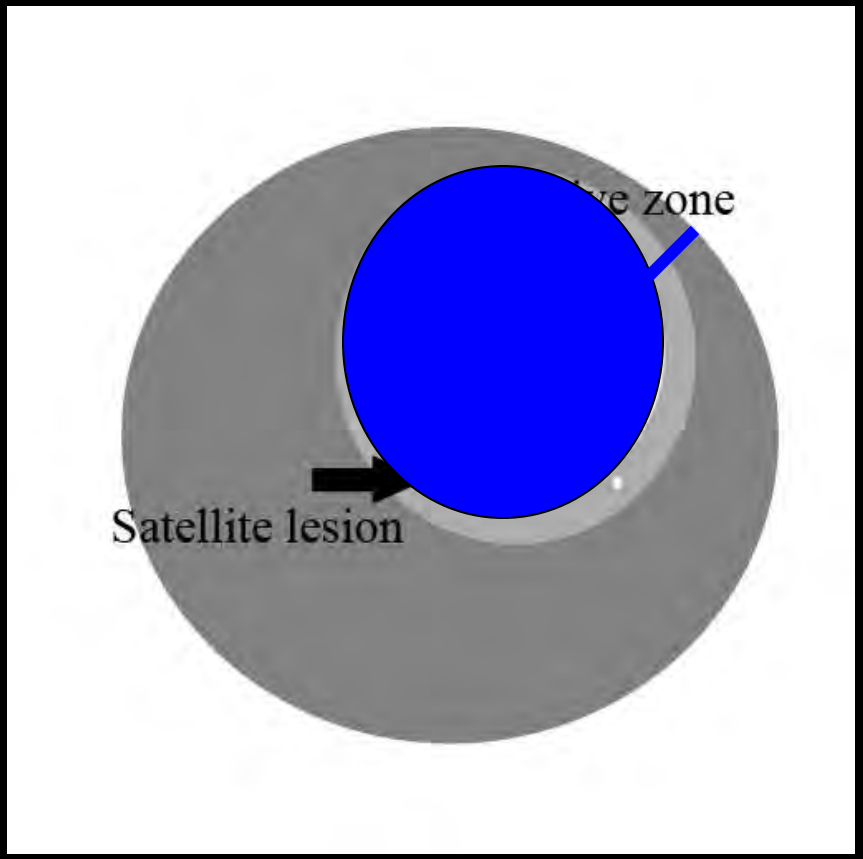
Margins – Intralesional

- Intralesional – into the tumor potentially leaving some tumor behind
- Used for benign lesions, low risk of recurrence, minimize the damage to normal adjacent tissue



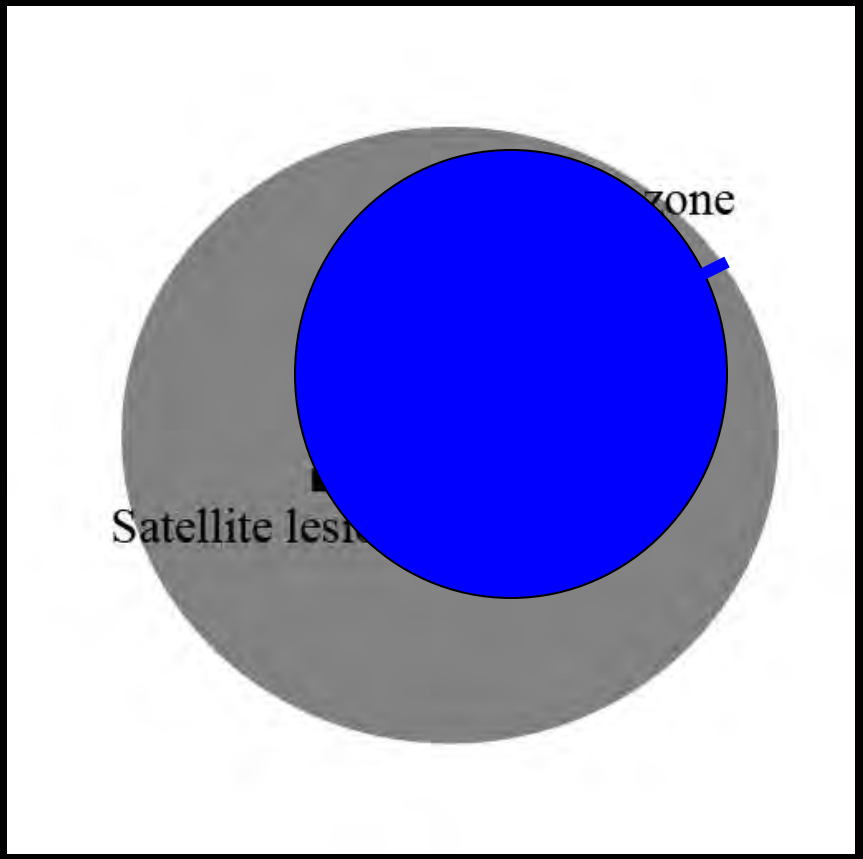
Margins – Marginal

- Marginal – resection of tumor and most of the reactive zone
- Potential to leave behind a satellite lesion
- Can be appropriate for sarcoma with adjuvant radiation therapy



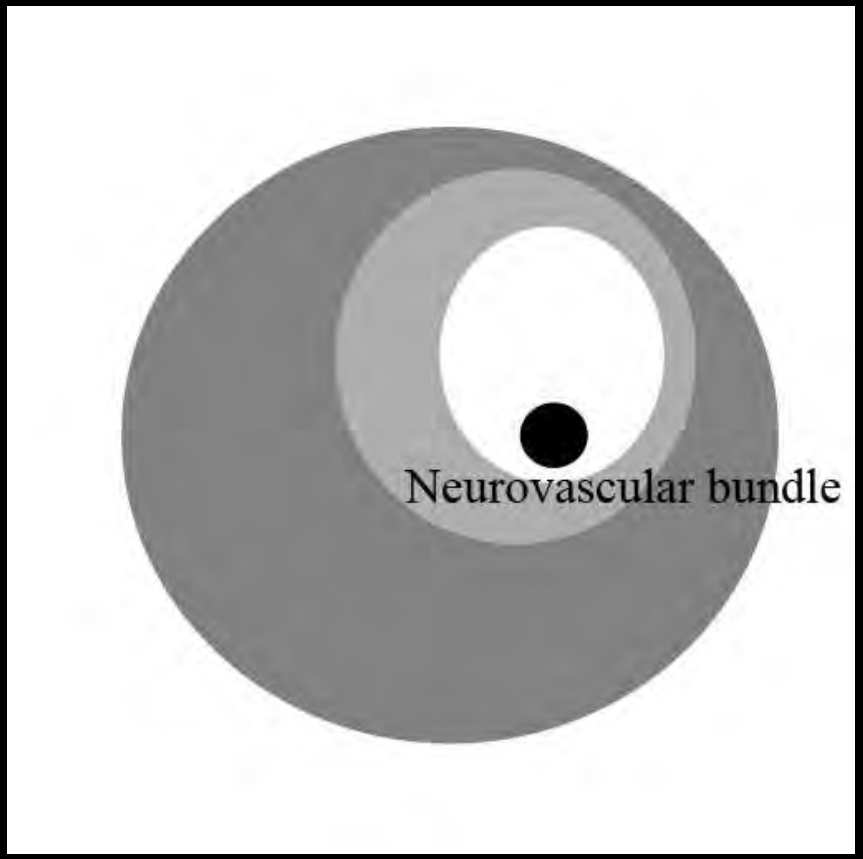
Margins – Wide

- Wide – resected margin includes all of the reactive zone and some normal tissue
- Appropriate for treatment of sarcoma when it can be done



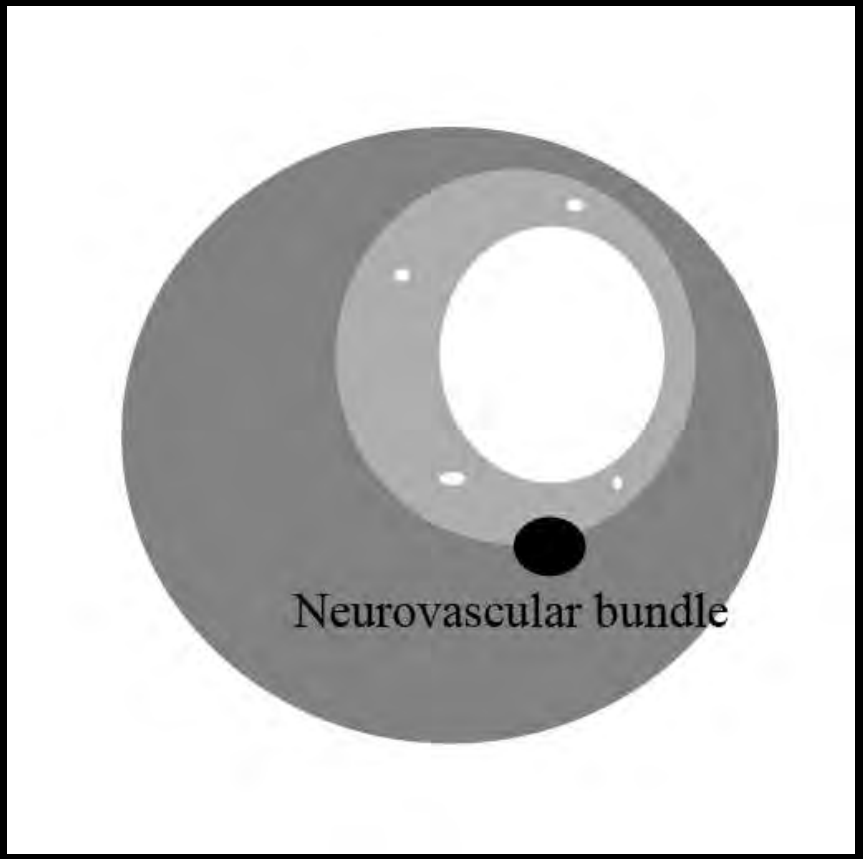
Margins – Radical

- Radical excision involves removal of the entire involved muscle compartment – usually means amputation
- Is sometimes appropriate if the neurovascular bundle cannot be saved



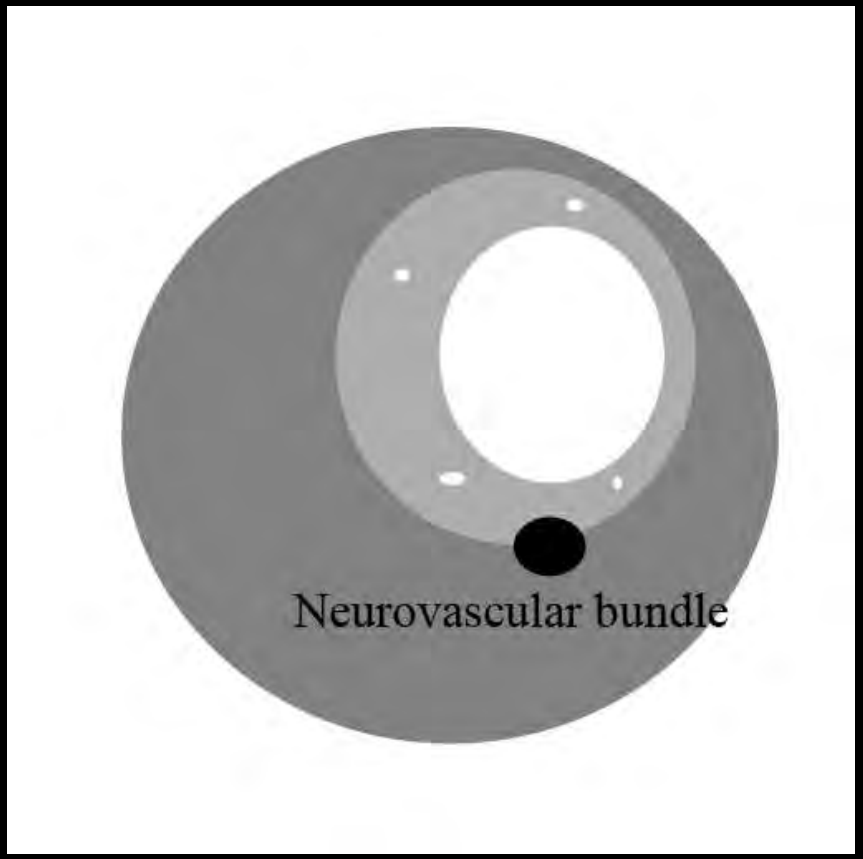
Role of Radiation Therapy

- Oftentimes the neurovascular bundle will lie within the reactive zone
- This necessitates marginal resection at the NV bundle to perform limb salvage surgery



Role of Radiation Therapy

- Radiation can sterilize the reactive zone
- Thus leaving behind no tumor and allowing limb sparing surgery to be performed



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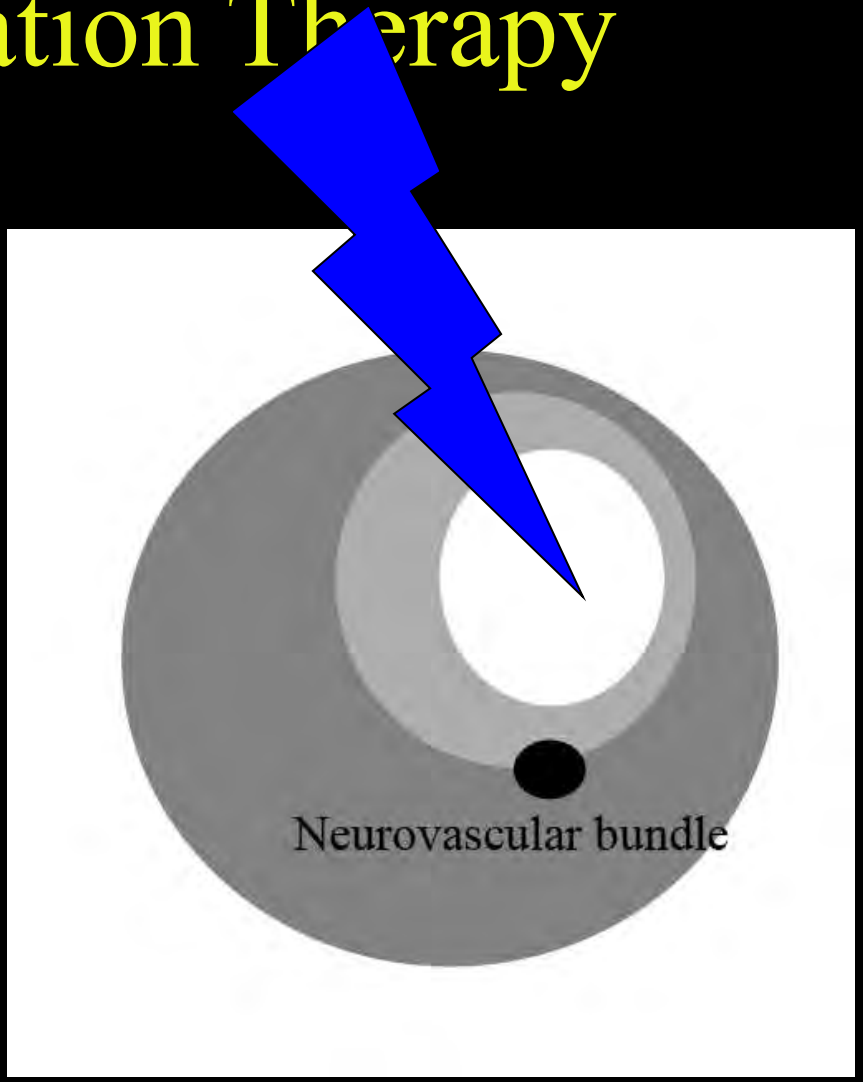

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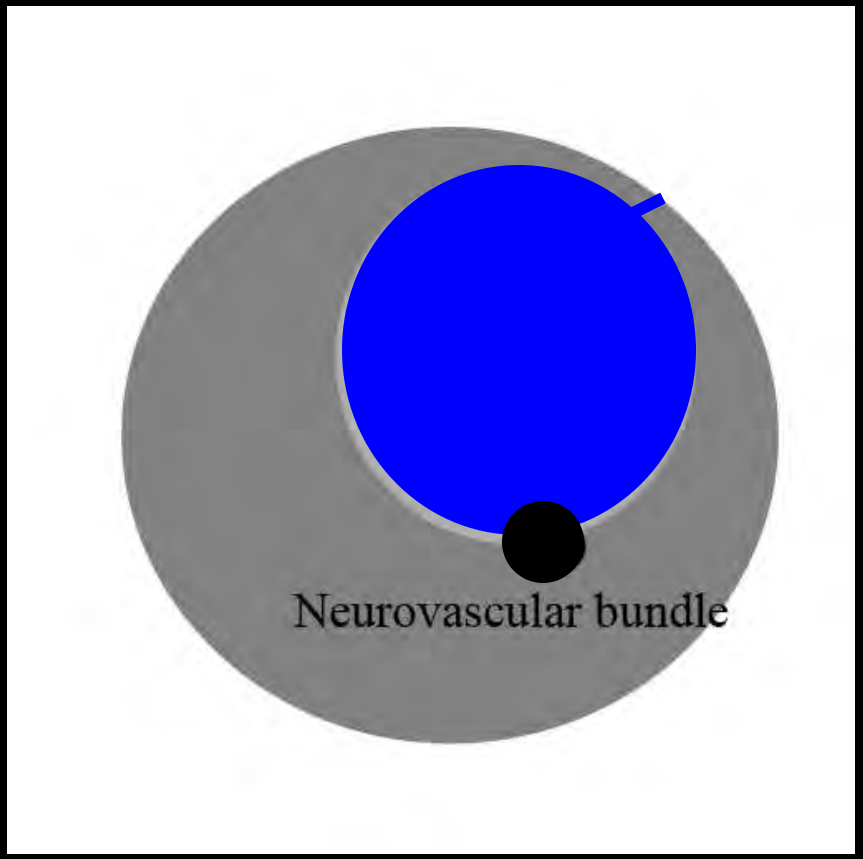

Pre vs. Post-Operative Radiation Therapy

- Pre-operative radiation therapy
  - Pro's – allows smaller radiation field
  - Con's – higher incidence of wound problems post-operatively

Pre vs. Post-Operative Radiation Therapy

- Post-operative radiation therapy
  - Pro's – lower incidence of wound complications
  - Con's – larger radiation field

Chemotherapy and Soft Tissue Sarcoma

- In general for localized disease chemotherapy is not used in the treatment of soft tissue sarcoma
- Rhabdomyosarcoma of childhood is a notable exception
- In general this is an older population with multiple comorbidities which poorly tolerates chemotherapy

Chemotherapy and Soft Tissue Sarcoma

- Sometimes chemotherapy is used as palliative or salvage treatment for patients with widely disseminated disease
- Drugs used as single agent or in combination with one another include:
  - Doxorubicin
  - Ifosfamide
  - Methotrexate
  - Carboplatin/cisplatin

Chemotherapy and Soft Tissue Sarcoma

- No consistent benefit in overall survival has been shown with any published reports of single agent or combination chemotherapy
- Combined with high toxicity in older patients with multiple comorbidities, chemotherapy is not usually used in the treatment of soft tissue sarcoma
- However, many younger patients are being enrolled in protocols as long as they can tolerate the side effects

Objectives