Surgical Principles in Treatment of Sarcoma

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Introduction

- Tumors arising in the soft tissue form a diverse and complex group as they may display varying degrees of mesenchymal differentiation.
- Most soft tissue tumors are benign and can be cured with a simple surgical excision.
- Benign mesenchymal tumors are 100-fold more common than soft tissue sarcomas.

- Account for <1% of all malignant tumours but is life threatening. Approximately 40% of patients with newly diagnosed soft tissue sarcoma die of the disease.
- Rare 1% of all tumours in adults, 15% in paediatric population.

Etiology

Genetic syndromes associated with STS include

- Neurofibromatosis (MPNST)
- Retinoblastoma
- Li-Fraumeni syndrome. 80% of patients with this syndrome develop cancer by age 45, and the index tumors in 36% of patients are soft tissue or bone sarcomas of diverse histology
- Gardener's syndrome (familial adenomatous poliposis) associated with desmoid tumors

Other aetiological factors

- Radiation exposure (osteosarcoma, angiosarcoma)
- Chronic lymphoedema
- Trauma
- Chemical exposure eg. arsenic, polyvinyl chloride (hepatic angiosarcoma)
- Infections eg. Herpes Human Virus-8: causes Kaposi's Sarcoma in immunocompromised patients

Cytogenetic changes

Divided into 2 categories:

- One group has specific changes and relatively simple karyotypes eg. Fusion gene or point mutation
- Other group has non-specific changes and complex karyotypes

Site

Can occur at any site:

- Extermities 45% Lower Limb 30%
- Visceral 21%
- Retroperitoneal 17%
- Trunk/thoracic 10%
- Head and neck 5%

Classification

- Soft tissue and bone
- Viscera (gastrointestinal, genitourinary, and gynecologic organs)
- Non visceral soft tissues (muscle, tendon, adipose, pleura, and connective tissue)

By differentiation (usually with IHC staining)

- Adipocytic tumors
- Fibroblastic/myofibroblastic tumors
- Fibrohistiocytic tumors
- Smooth muscle tumors
- Pericytic (perivascular) tumors

- Primitive neuroectodermal tumors (PNETs)
- Skeletal muscle tumors
- Vascular tumors
- Neural Tumors
- Extraskeletal Chondro-Osseous Tumors
- Gastrointestinal Stromal Tumors
- Tumors of uncertain differentiation

Biologic Potential

- Benign Do not recur locally those that do recur usually are not locally invasive and can be cured with complete surgical excision.
- Intermediate (locally aggressive) These recur locally and are associated with a locally infiltrative growth pattern. Lesions in this category such as desmoids do not have any potential to metastasize but typically require wide excision with a margin of normal tissue for good local control.

- Intermediate (rarely metastasizing) locally aggressive and occasionally give rise to distant metastases. The risk of metastasis, usually to lymph nodes or lung is typically <2%.
- Malignant In addition to potential for local invasion and recurrence have a significant risk of distant metastasis ranging in most instances from 10% to 100% depending on histologic type and grade

Grading

- Grading based on morphologic features only evaluates the degree of malignancy and predicts outcomes mainly the probability of distant relapse. The pathologic features that define grade
- Mitotic index
- Necrosis
- Cellularity
- Pleomorphism
- Histologic type and subtype or differentiation

- Several grading systems are used
- Four-grade system (Broders)
- Three-grade systems such as the National Cancer Institute (NCI) grading system and Sarcoma Group of the French Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC)
- Two-grade system used at MSKCC

Presentation (extremity STS)

- Mostly asymptomatic mass
- Pain in 33% due to destruction of surrounding tissues
- Rarely paraneoplastic symptoms eg. Fever

The focus of the clinical evaluation is

- To determine the likelihood of a benign or malignant soft tissue tumor
- Involvement of muscular or neurovascular structures
- Ease with which biopsy or subsequent excision can be performed.

Imaging

- MRI
  - For extremity masses
  - Gives good delineation between muscle, tumor and blood vessels
- CT for abdominal and retroperitoneal masses
- PET
  - May help determine high vs. low grade
  - May be helpful in recurrences

Diagnosis

Core biopsies.

- Must be adequate and representative of the tumor tissue
- Must be well fixed and well stained.
- The biopsy incision or core track should be placed in a location that can be completely excised at the time of definitive resection with minimal sacrifice of overlying skin

- The most useful immunohistochemical markers are the intermediate filaments (e.g., vimentin, keratin, desmin), leukocyte common antigen, and S-100.
- Pathologist should be prepared to process tissue from selected cases for electron microscopy, cytogenetic studies or molecular analysis.

- Incision biopsies should not interfere with subsequent surgery,
- Therefore:
- over most superficial part of mass
- no raising of flaps
- meticulous haemostasis to prevent haematomas
- FNA limited value, mostly to diagnose recurrence

Staging

- • AJCC/UICC Staging System for Soft Tissue Sarcomas
- T1: <5cm
- T2: 5-10cm
- T3: 10-15cm
- T4: >15cm
- N1: Regional nodal involvement
- Grading
    - G1: Well-differentiated
    - G2: Moderately differentiated
    - G3: Poorly differentiated

- Stage IA G1 T1 N0 M0
- Stage IB G1 T2, T3, T4 N0 M0
- Stage II G2,3 T1 N0 M0
- Stage IIIA G2,3 T2 N0 M0
- Stage IIIB G2,3 T3 T4 N0 M0
- Stage IV Any G Any T N1 M1

Staging system predicts survival and risk of metastasis, but not local recurrence

Management

- Surgery is the principal therapeutic modality
- Controversy:
- – extent of surgery required
- – optimum combination of radio- and chemotherapy

Limb sparing surgery

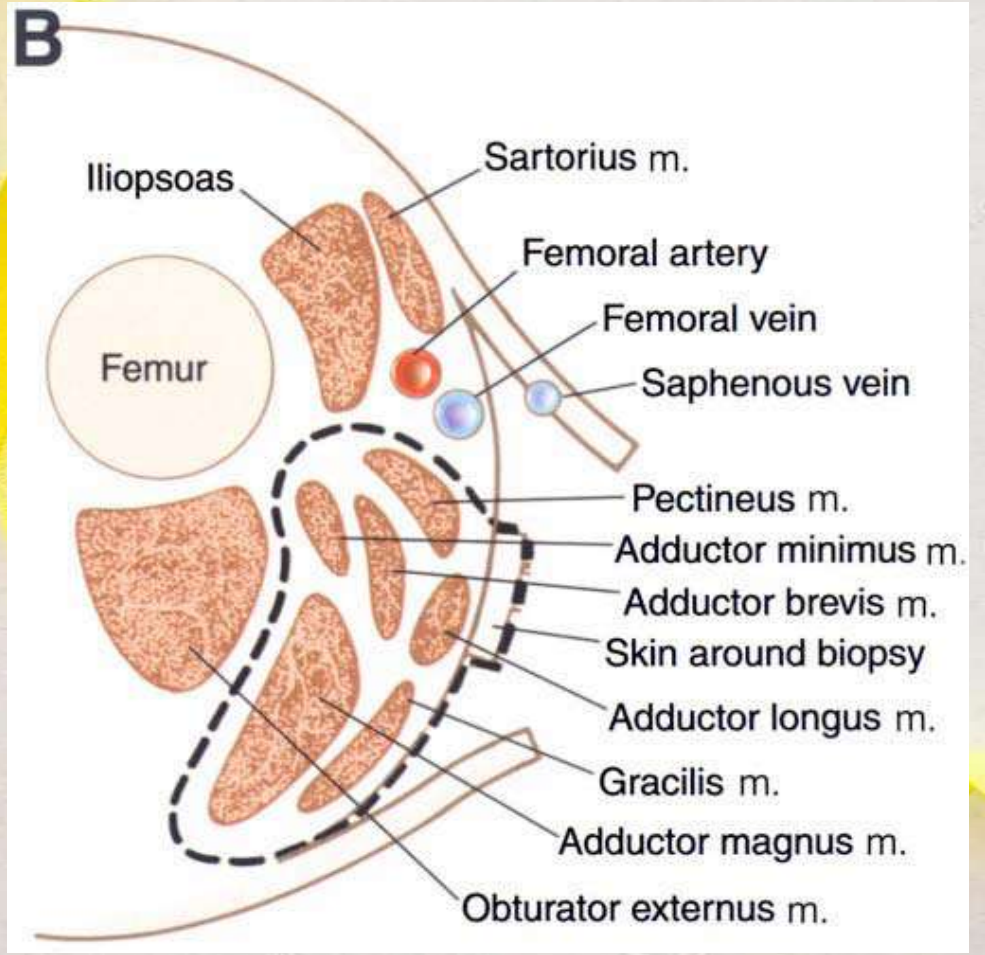
- Objective: complete removal of tumour with negative margins with maximum preservation of function
- Neurovascular structures can generally be preserved with meticulous dissection
- Bone also mostly preserved as invasion of bone is rare and periosteum provides a good fascial plane

- Amputations:
  - rarely required
  - reserved for patients with unresectable tumours, no metastasis and good propensity for rehabilitation
- Limb-sparing vs amputation
  - Comparison study with post-op radiation in limb sparing showed no difference in survival
- Amputation still may be indicated for neurovascular or bone involvement

Resection

- Historical attempts to resect all muscle bundles from origin to insertion have been supplanted by an encompassing resection aiming to obtain a 1-cm margin of uninvolved tissue in all directions.
- 2cm margins are employed for histologic subtypes with infiltrative borders (e.g., DFSP or myxofibrosarcoma).

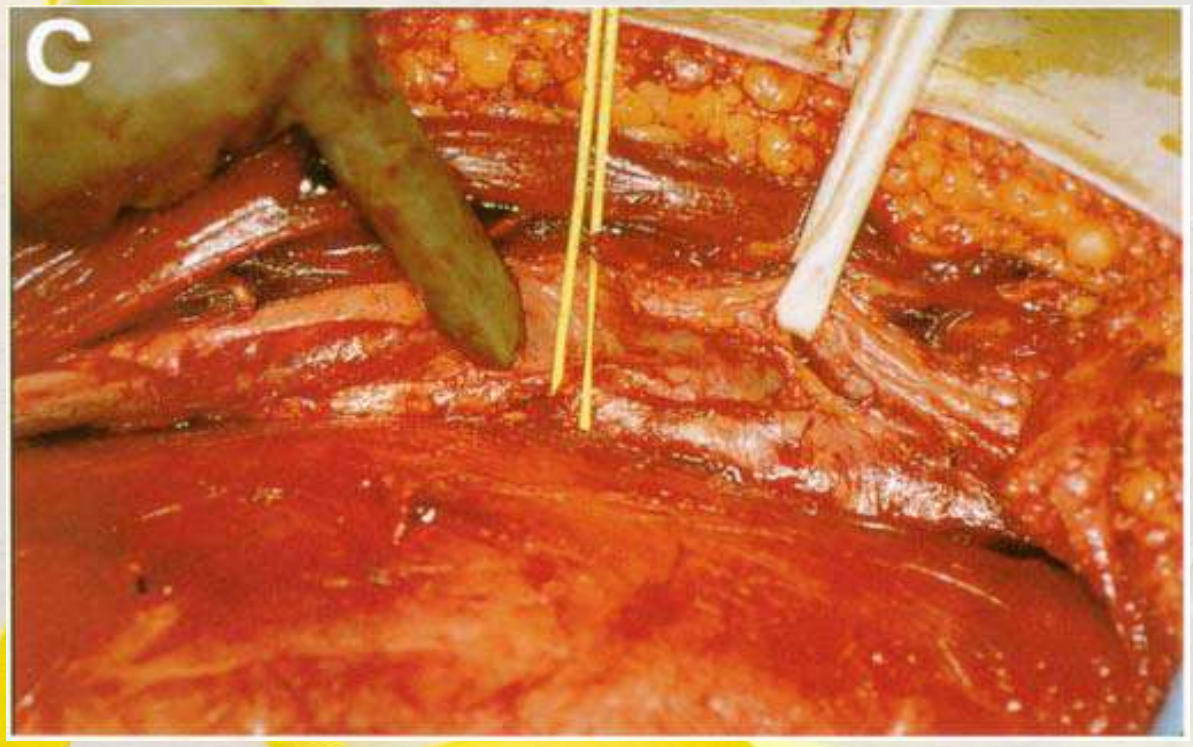
Case 1


B
Iliopsoas
Sartorius m.
Femoral artery
Femoral vein
Femur
Saphenous vein
Pectineus m.
Adductor minimus m.
Adductor brevis m.
Skin around biopsy
Adductor longus m.
Gracilis m.
Adductor magnus m.
Obturator externus m.

Large adductor tumor not involving the pelvic fossa or the hip joint showing significant hemorrhagic necrosis.

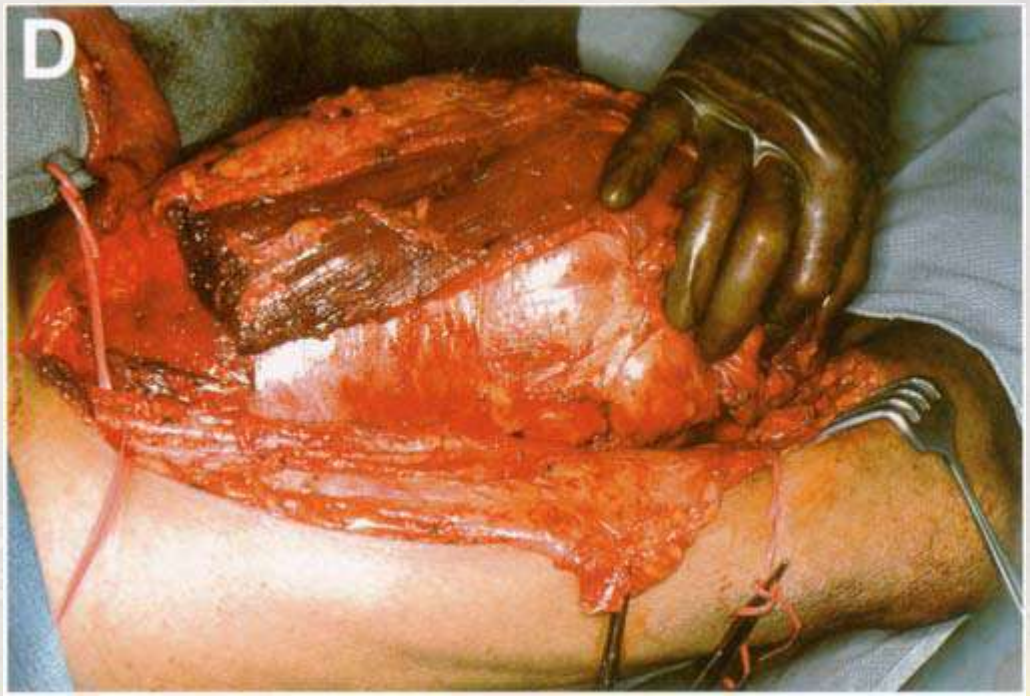
This occurred following induction chemotherapy.

T2 weighted MRI scan snowing no evidence of intrapelvic extension. The tumor is located proximally to the thigh with displacement of the superficial femoral artery



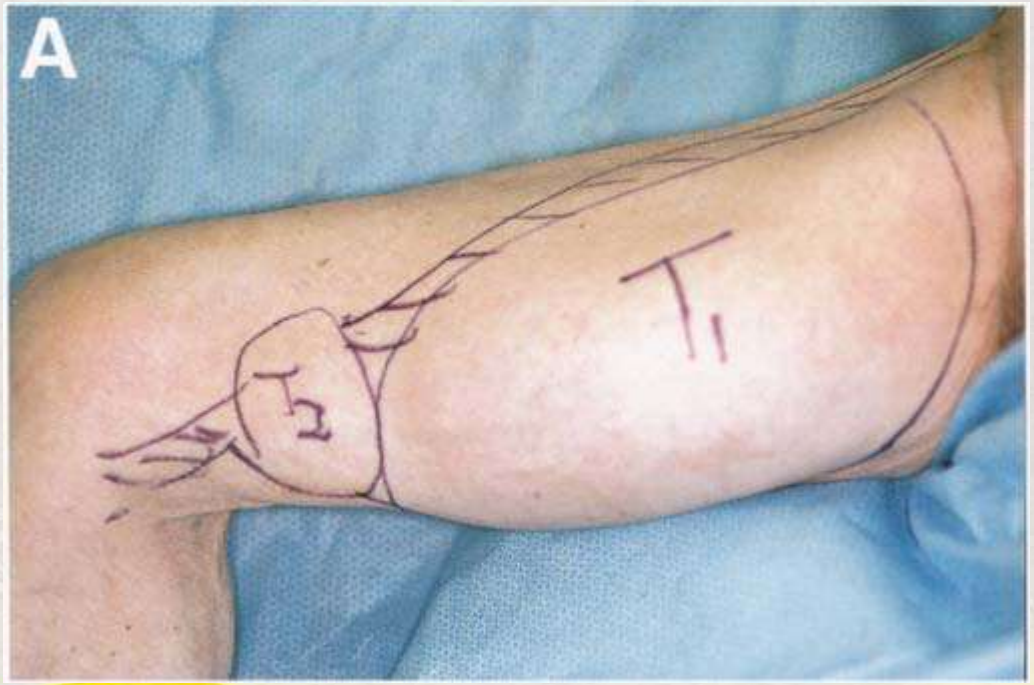
Intraoperative photograph demonstrating the exploration and dissection of the entire length of superficial femoral artery from the femoral triangle to the adductor hiatus.

Intraoperative photograph demonstrating the mobilization of the adductor tumor within the adductor muscle group covered by normal muscle

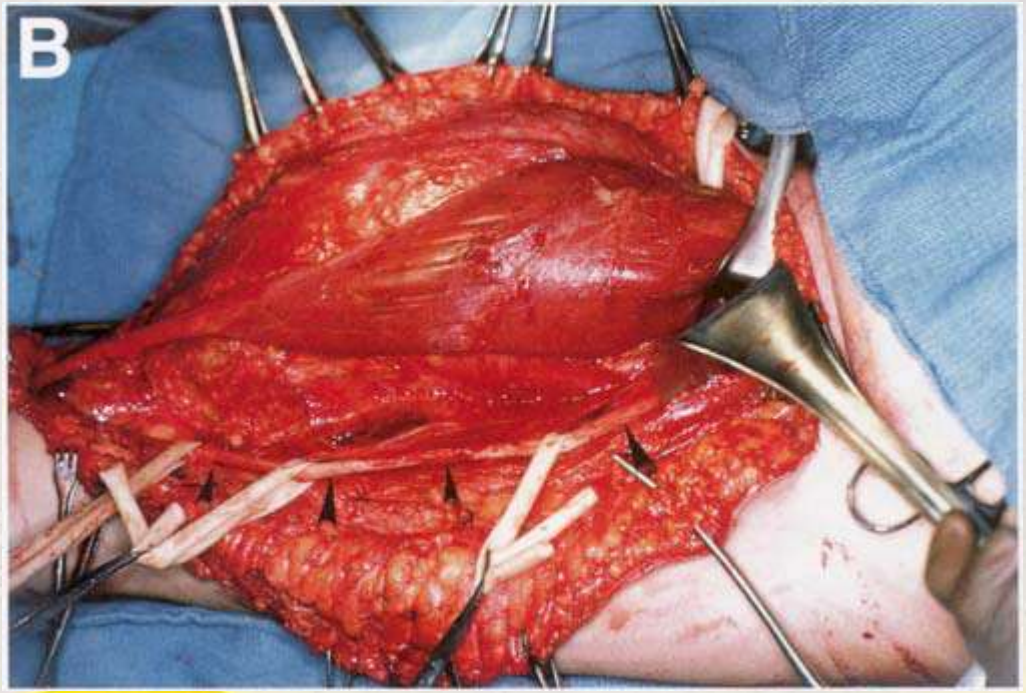


Case 2

Clinical photograph prior to incision showing the large size of the tumor involving the hamstrings with displacement of the adductor muscles. T1 and T2 represent two large palpable masses. Large posterior hamstring muscle tumors may invade adjacent structures and should involve exploration of the superficial femoral artery and popliteal space prior to resection.

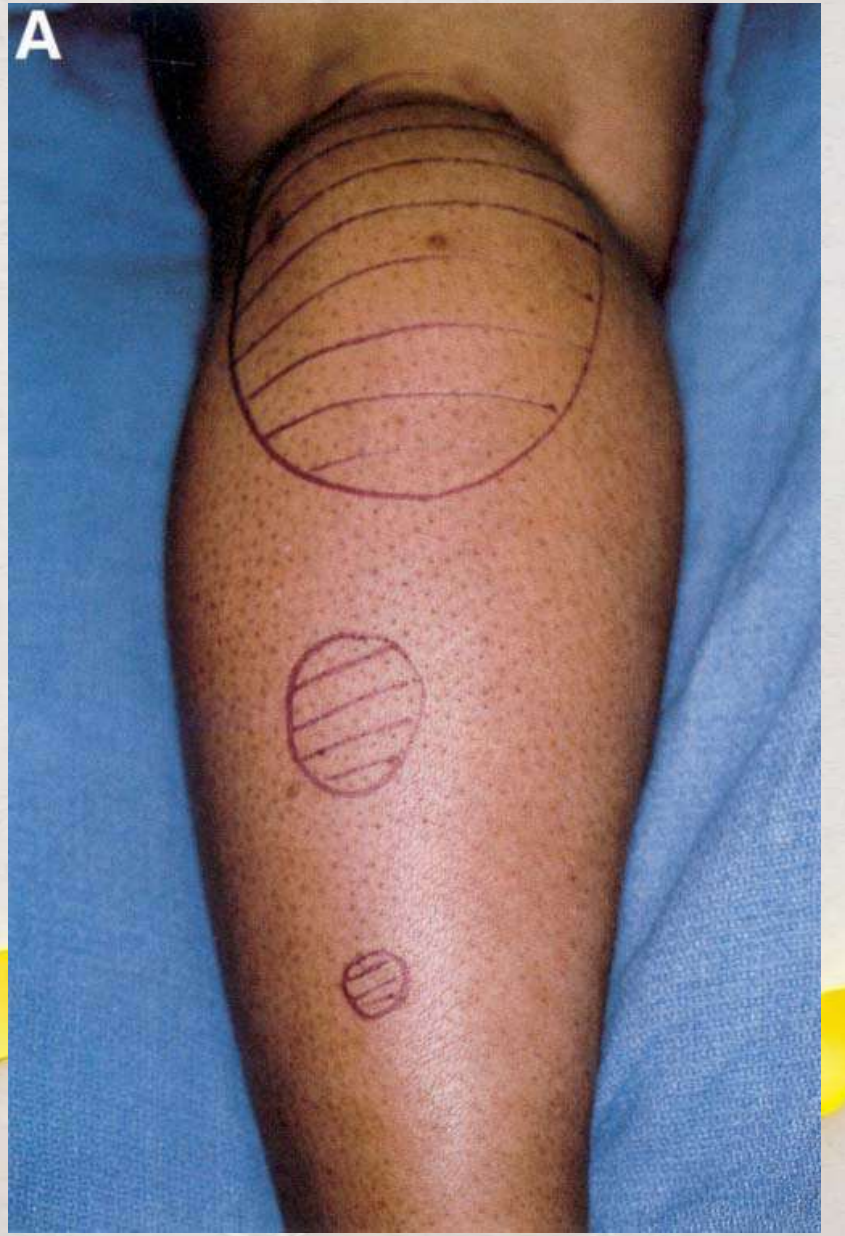


Intraoperative photograph demonstrating that the entire posterior compartment is being elevated, showing the tumor is located in the medial and lateral hamstrings. Note the sciatic nerve has been dissected completely free and appears not to be involved. The sciatic nerve must be exposed from the sciatic notch to the popliteal space. Functional results after posterior compartmental resection are excellent with minimal gait disturbance

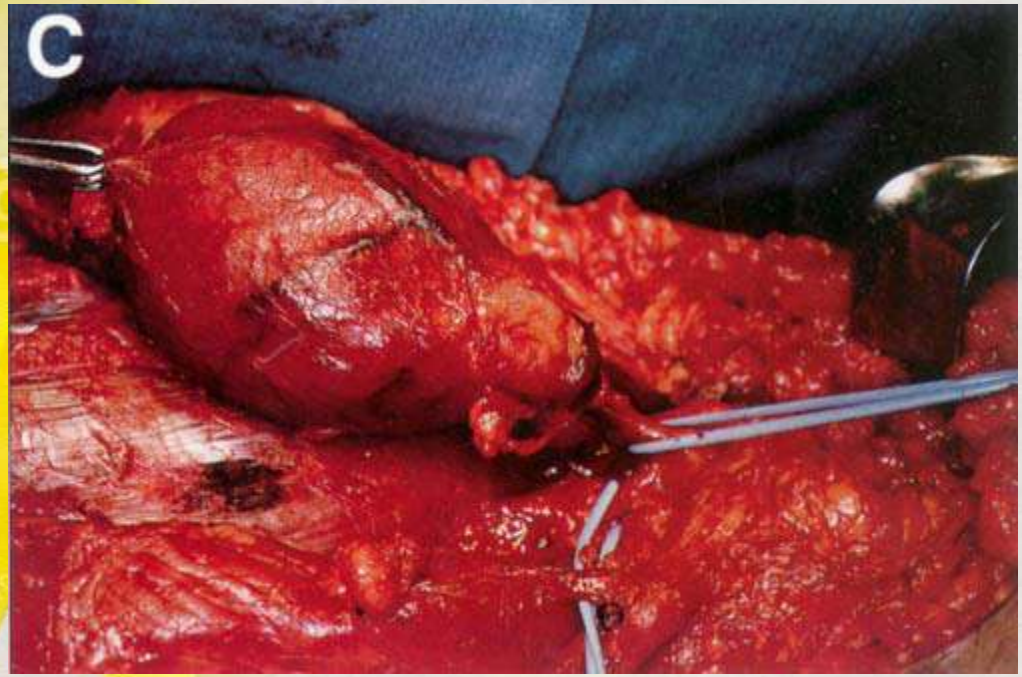


Case 3

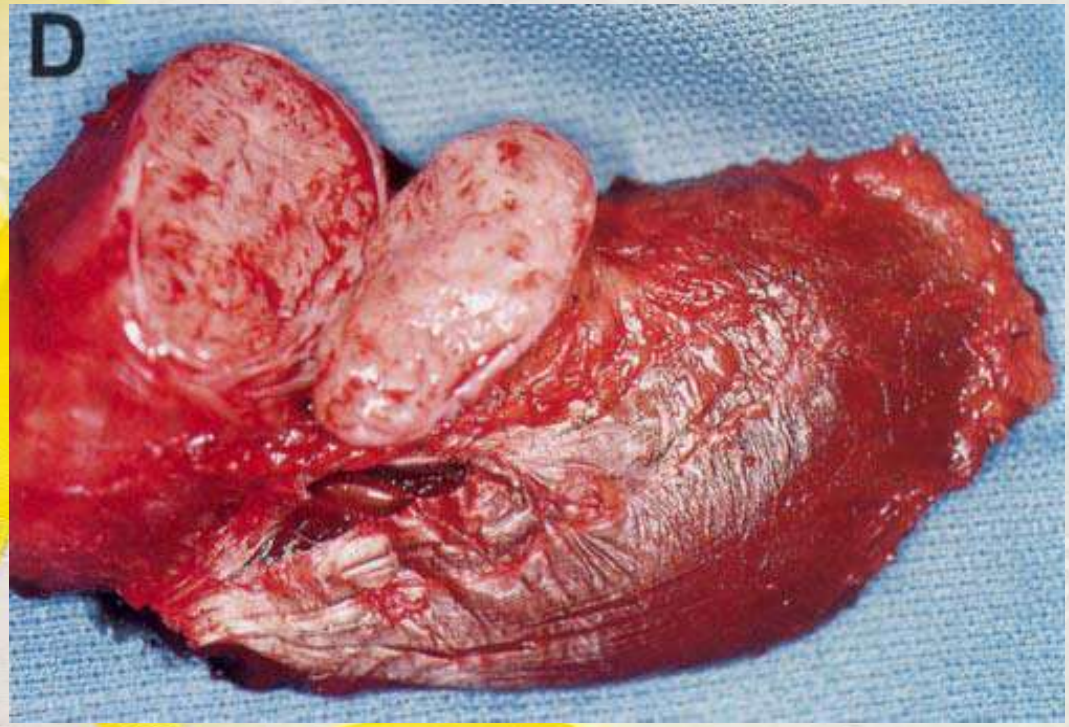
A 40-year-old woman presented with a rapidly enlarging mass in her calf. Core-needle biopsy revealed a high-grade leiomyosarcoma. Additional skin marks represent skip nodules within the substance of the soleus muscle.



Sagittal T1-weighted MRI of the superficial posterior compartment of the leg showing the tumor arising from the soleus muscle



The posterior leg was approached using the posterior utilitarian incision. The soleus muscle (tumor) has been completely mobilized. The primary pedicle (vessel loop) is now ligated and transected



Surgical specimen. The tumor was resected en-bloc with the underlying muscle.

- For low-grade histologic types even 1-cm margins are not required. Eg well-differentiated liposarcomas
- Skin surrounding the biopsy site tethered to the tumor or showing neovascularisation in association with an underlying lesion should be removed.
- Presence of positive margins increases local recurrence by 10-15%
- No need for lymph node dissection as only 2-3% have nodal metastasis

Recurrent and metastatic disease

- Lung most common site of metastasis but visceral mets often go to liver
- 50% recurrence of extremity STS is in the lung
- Local recurrence: mass or nodules in surgical scar
- Isolated local recurrence: resection
- All unresectable or extrapulmonary metastasis treated with chemotherapy

Treatment of Recurrence

- 20-30% of STS patients will recur
- More common in retroperitoneal and head & neck high grade tumors because hard to get clear margins
  - 38% for retroperitoneal
  - 42% for head and neck
  - 5-25% for extremity
- After re-resection recurrence is 32% for extremity and much higher for visceral

Prognosis

Factors that negatively impact prognosis:

- Age > 50 yrs
- Size > 8 cm
- Vascular invasion
- Local infiltration (vs. pushing)
- Tumour necrosis
- Deep location
- High grade tumours
- Recurrent disease
- Certain histological subtypes eg. non-liposarcoma histology

Surgical Management of Primary Localized Retroperitoneal Sarcoma

- The major issue in resection of visceral and retroperitoneal lesions is adequate exposure.
- Thoracoabdominal incisions, rectus-dividing incisions, and incisions extending through the inguinal ligament into the thigh may improve exposure and enhance the ability to achieve a complete resection.
- Only limited evidence that a more extensive resection of adjacent organs affects long-term survival

- Despite complete resection local recurrence developed in 40% to 50% of cases. There is a clear need for adjuvant local therapy. Of importance, local recurrence is a problem for both high-grade and low-grade lesions

Surgical Resection of Metastatic Disease

- Approximately 20% of patients with a soft tissue sarcoma of an extremity or the trunk develop pulmonary metastases and in the majority the lung remains the only clinically evident site of metastasis.

Criteria for surgical pulmonary metastasectomy

1) definitive control of the primary tumor has occurred (or is possible)
2) absence of (or ability to control) extrathoracic metastatic disease
3) the lung metastases are amenable to complete resection,
4) the patient can tolerate the planned procedure
5) there is no better treatment alternative.

Using these criteria long-term survival after metastatectomy remains uncommon reflecting the fact that in only a subset of patients does the resected disease represent the entirety of their metastatic burden.

Greatest management difficulty is differentiating patients that might benefit from surgical extirpation from those whose disease has already, or will soon, spread beyond the means of surgical control.

- Relation between lymph node metastasis and survival controversial
- Studies show improvement in survival if local lymphadenectomy if no distant metastasis
- However, only true if done with initial curative surgery and not if done after
- Median survival from development of metastatic disease is 8-12months

- Open Versus Minimally Invasive Surgery
- The comparison between these approaches is based on decreased pain, shorter hospital stay, and increased tolerability in patients with poor pulmonary function associated with VATS relative to improved detection of small metastases afforded by manual palpation of the lung, which is not possible with a minimally invasive approach.

Ablative Therapies

- Stereotactic body radiotherapy (SBRT) or stereotactic ablative body radiotherapy is highly precise and dose-intensive form of external beam radiation therapy.
- Percutaneous technologies include radiofrequency ablation (RFA) microwave ablation or cryoablation which uses heat or cold to create cellular destruction with necrosis.

Isolated Limb Perfusion

- ILP can be performed through various sites.
- For the lower limb it is done via the external iliac, common femoral or popliteal vessels; for the upper limb it is performed via the brachial, axillary or subclavian vessels.
- In the operating room the entire extremity is scrubbed.
- Four thermistor probes are inserted; two into the subcutaneous tissue and two into the muscles, in the distal and proximal parts of the extremity, respectively, to measure limb temperature during the procedure.

- A heating blanket is wrapped around the limb and sterile draping is applied on top of it. It is important that the limb can be manipulated and positioned during the procedure to permit the application and wrapping of the Esmark band on its root.

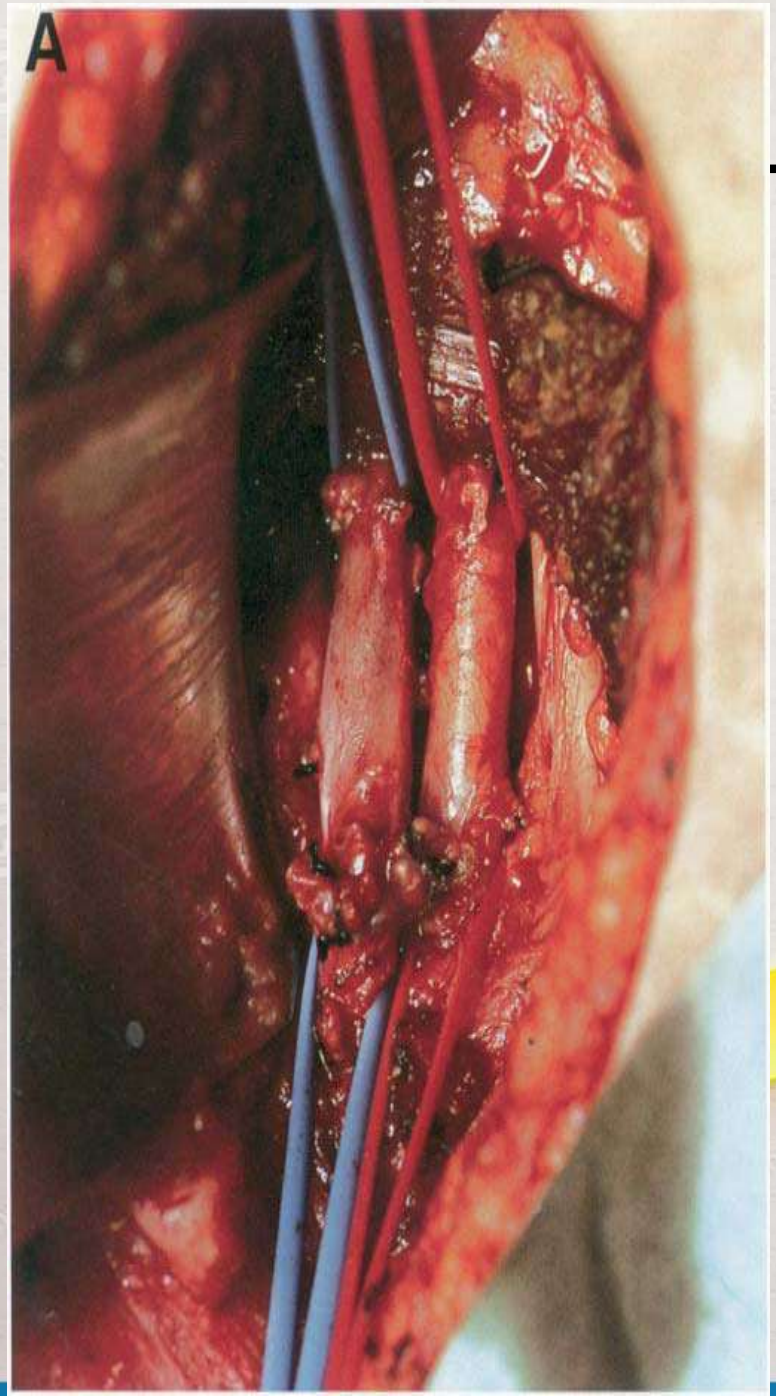
- After exposing the external iliac vessels from their origin to the inguinal ligament, the vessels are dissected circumferentially and all side branches, including collaterals situated behind the inguinal ligament (i.e. the epigastric, obturators, deep internal and external circumflex vessles), are ligated and sectioned.

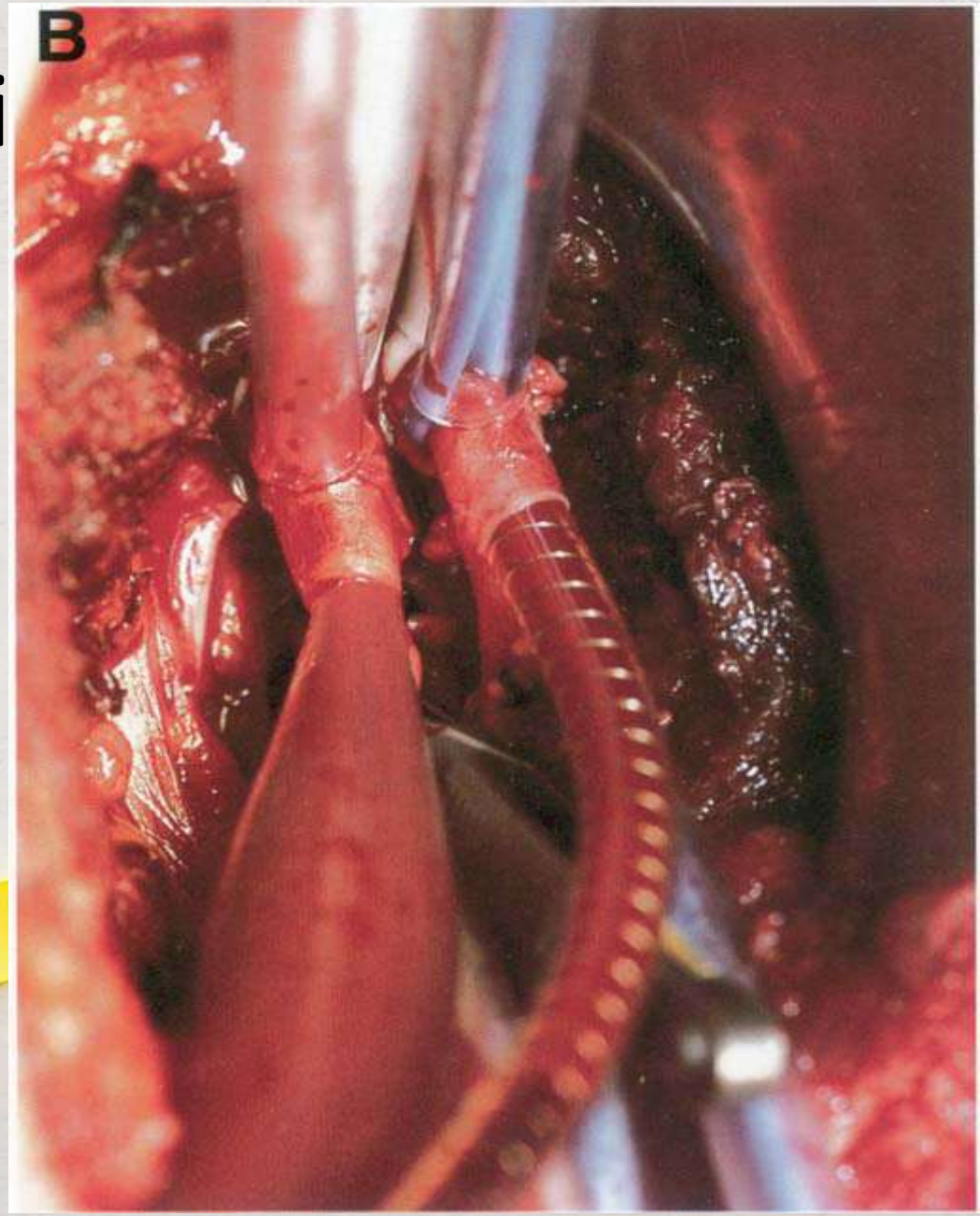
- All branches, especially from the posterior aspect of the external iliac vein, should be ligated.
- These deep collaterals are not affected by external Esmark banding, and their control is crucial for minimizing leakage during perfusion.

- The extracorporeal system consists of a roller-pump similar to that used for cardiopulmonary bypass surgery.
- A heat exchanger is required to warm the perfusate to 42°C.
- Mild hyperthermia (39–40°C) is used true hyperthermia (41–42°C) is rarely used because it produces severe limb toxicity

- The patient is continuously monitored to ensure that the perfusate does not leak into the circulatory system.
- After the drug administration and perfusion treatment periods (e.g. 30 min for TNF alone followed by 90 min of melphalan), the circuit is interrupted and the perfusate washed from the limb with 2 L of saline and 1 L of dextran polymer or blood.

- The pump is then turned off, the tourniquet cuff is deflated, and the cannulae are removed. The vein is repaired and thereafter the arteriotomy is sutured, re-establishing blood flow to the limb.


A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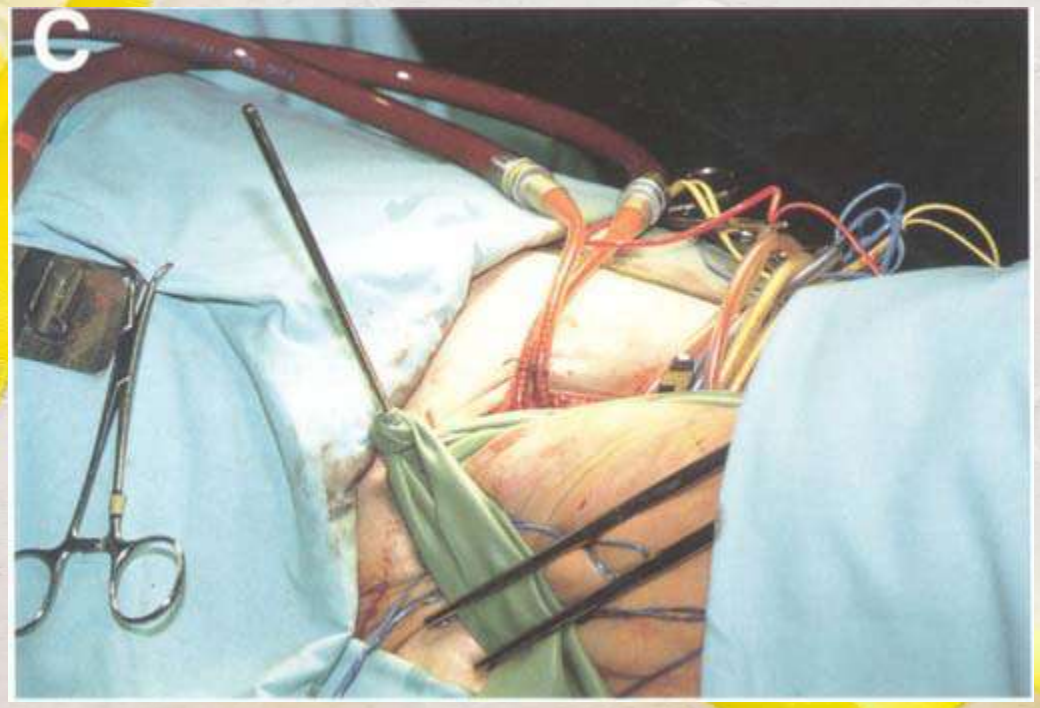
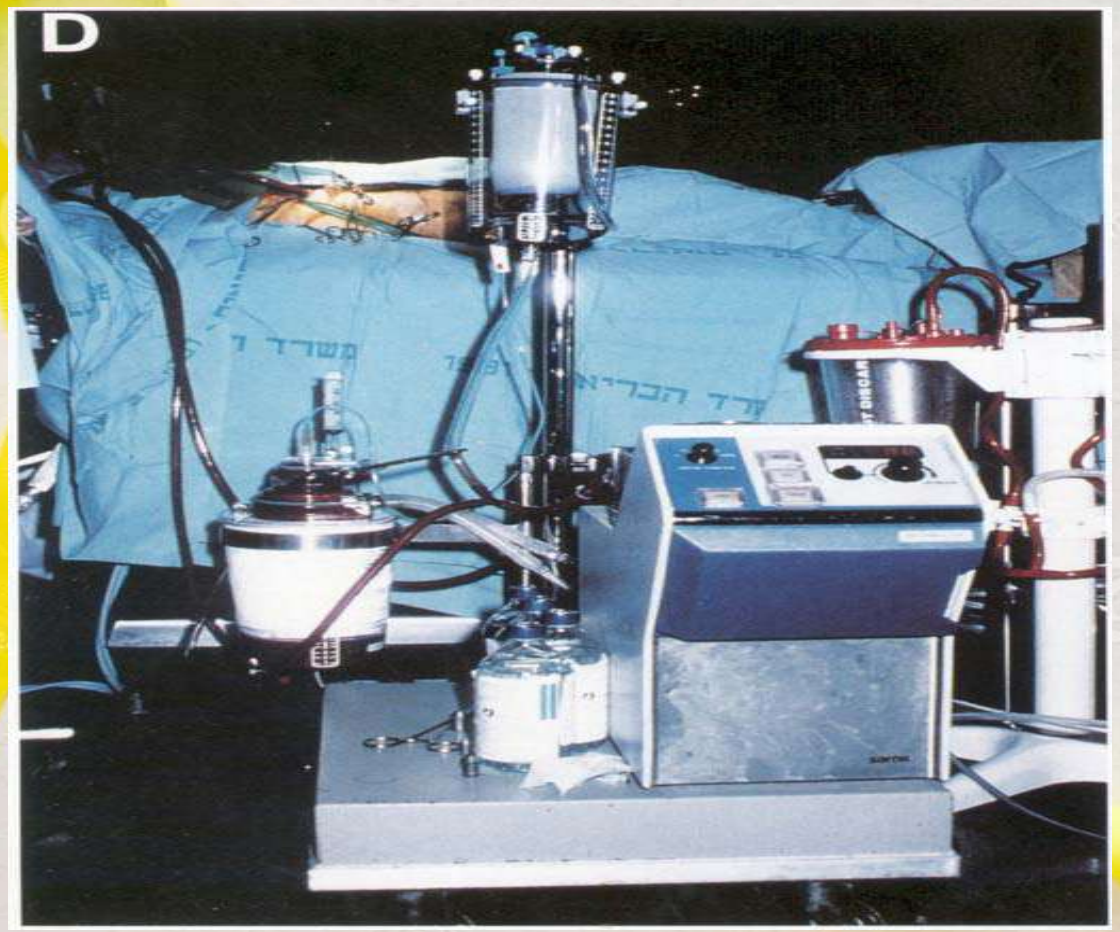
Isolated limb perfusion (ILP); stages of the procedure

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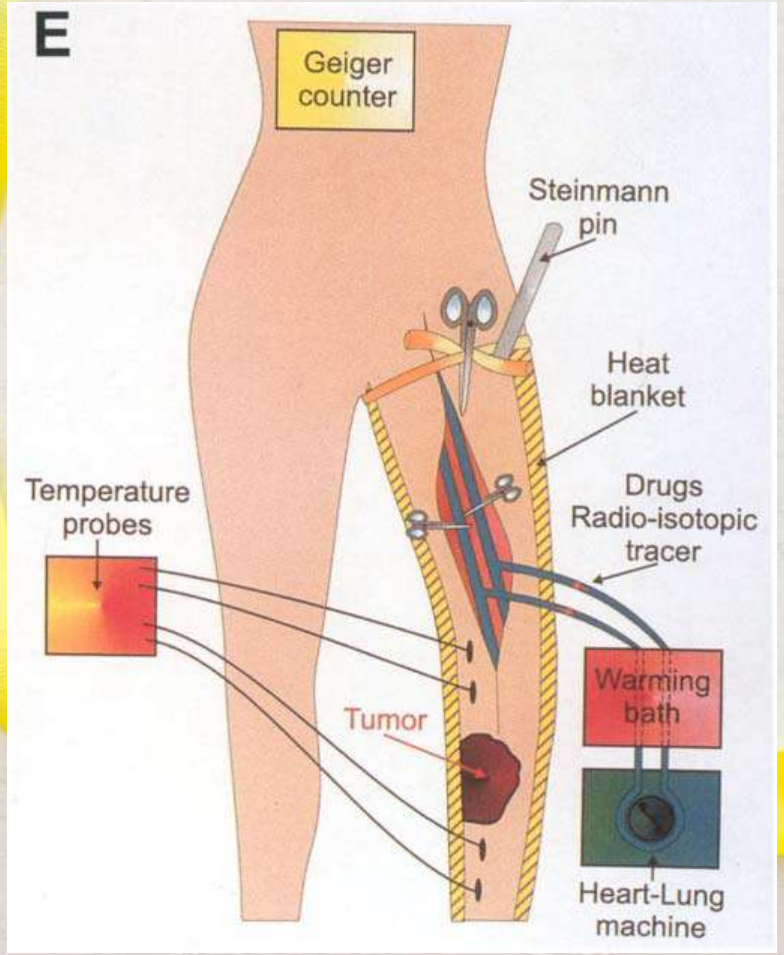
E
Geiger counter
Steinmann pin
Heat blanket
Temperature probes
Drugs Radio-isotopic tracer
Warming bath
Tumor
Heart-Lung machine

Thank You

MCQs

1. Which of the following statement is false?

A. Ratio of benign to malignant soft tissue tumors is 100 to 1.

B. Most common site for soft tissue sarcoma is lower limb.

C. Germline mutations of APC gene is associated with desmoid tumors.

D. Surgical removal of pulmonary metastasis from soft tissue sarcomas is not indicated.

Answer is D

2. Which of following is not a risk factor for development of soft tissue sarcoma?

A. Breast cancer surgery
B. Irradiation
C. Thorotrast
D. Chronic lymphedema

Answer is A

3. Which statement is not true?

A. Sarcomas always develop from mature differentiated tissues.

B. They have different biological aggressive potential depending on histology and grade.

C. Not responsive much to chemotherapy.

D. Have a great many histological subtypes.

Answer is A

4. Biopsy for soft tissue mass. Pick the false statement

A. Trucut biopsy should be done from the most representative area under image guidance.
B. Excisional biopsy can also be done in most cases.
C. Biopsy tract should always be excised at the definitive surgery.
D. Adequate tissue should be taken for IHC analysis.

Answer is B

5. Which is not a criteria for pulmonary metastatectomy?

A. Definitive control of the primary tumor has occurred (or is possible).

B. Absence of extrathoracic metastatic disease.

C. Lung metastases are amenable to complete resection.

D. Can only be done in a minimal invasive manner.

Answer is D

6. Which statement is false?

A. Staging system for soft tissue sarcoma includes grading.
B. Lymph node metastasis are uncommon in STS.
C. Compartmental resections are almost always indicated for all histological types.
D. Complete surgical resection with a margin of normal tissue is the mainstay of treatment.

Answer is C

Thank You