Cancer Association of South Africa (CANSA)

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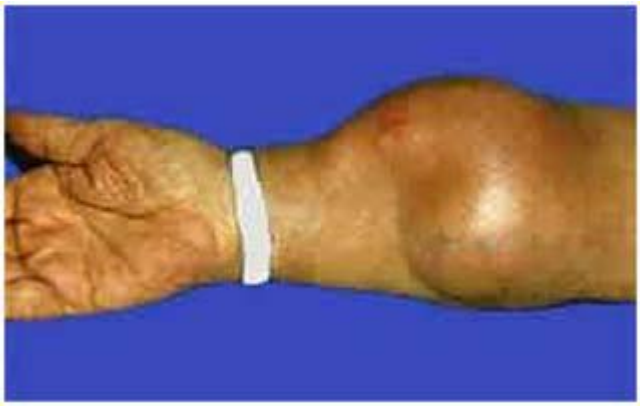
Fact Sheet On
Cancer of Connective Tissue

Introduction

Connective tissue, also referred to as soft tissue, is the name given to all the supporting tissues in the body, which includes the bones. This includes fat, muscle, nerves, deep skin tissue, blood vessels and the tissue that surrounds joints (synovial tissue). These tissues support and connect all the organs and structures of the body.

A connective tissue (soft tissue) sarcoma is a rare type of cancer that forms usually as a painless lump (tumour) in any one of these soft tissues. It most commonly develops in the thigh, shoulder and pelvis. Sometimes it can also grow in the abdomen or chest (trunk).



[Picture Credit: Connective Tissue Sarcoma]

There are over seventy (70) types of connective tissue cancers. It is named after the abnormal cells that make up the sarcoma.

Types of connective tissue sarcomas include:

- malignant fibrous histiocytoma (MFH) – the most common type from abnormal spindle-shaped cells
- liposarcoma - the next most common type of soft tissue sarcoma from abnormal fat cells
- leiomyosarcoma – from muscle tissues
- rhabdomyosarcoma - from muscle tissues
- angiosarcoma - from blood vessels
- Ewing's sarcoma – from bone tissue, mainly in children
- primitive neuroectodermal tumour (PNET)
- malignant peripheral nerve sheath tumour (MPNST or PNST)
- gastrointestinal stromal sarcoma (GIST)
- stromal sarcoma - from supporting tissues
- kaposi sarcoma of the skin
- synovial sarcoma – from synovial tissues

(Cancer Council Victoria)

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Incidence of Connective Tissue Cancer in South Africa

According to the National Cancer Registry (2012) the following number of cancer of connective tissue cases was histologically diagnosed in South Africa during 2012:

Group - Males 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	285	1:674	0,77%
Asian males	12	1:828	1,38%
Black males	155	1:914	1,33%
Coloured males	36	1:367	0,83%
White males	83	1:419	0,41%

Group - Females 2012	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	285	1:838	0,76%
Asian females	12	1:680	1,07%
Black females	185	1:907	1,12%
Coloured females	33	1:633	0,78%
White females	56	1:627	0,35%

The frequency of histologically diagnosed cases of cancer of connective tissue in South Africa for 2012 was as follows (National Cancer Registry, 2012):

Group - Males 2012	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	33	15	26	46	56	47	40	14
Asian males	1	1	0	2	3	1	3	1
Black males	24	7	19	23	30	22	9	6
Coloured males	3	2	2	7	5	9	5	1
White males	3	1	4	11	16	14	19	7

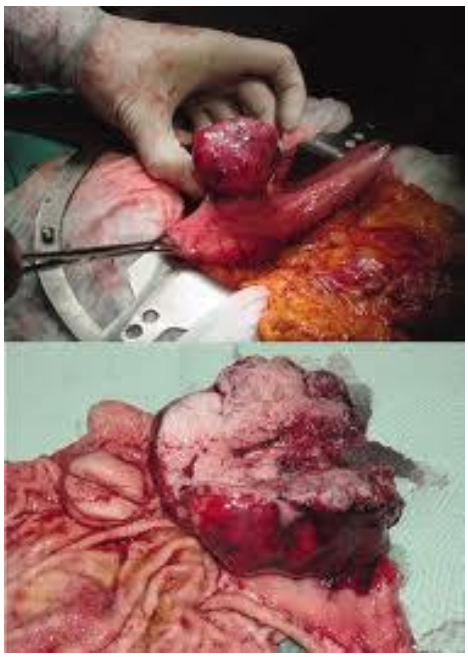
Group - Females 2012	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	44	22	27	33	59	44	35	16
Asian females	1	0	0	2	6	1	1	0
Black females	28	15	20	21	37	25	20	6
Coloured females	5	3	2	6	2	5	5	3
White females	8	3	4	2	11	11	7	7

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

Malignant Fibrous Histiocytoma

Malignant fibrous histiocytoma (MFH), a type of sarcoma, is a malignant neoplasm of uncertain origin that arises both in soft tissue and bone. It was first introduced in 1961 by Kauffman and Stout and controversy has plagued it since. It was described as a tumour rich in histiocytes with a storiform growth pattern. By 1977, it was considered the most common soft tissue sarcoma of adult life. Despite the frequency of diagnosis, MFH has remained an enigma. No true cell of origin has ever been identified. In 2002, the World Health Organization (WHO) declassified MFH as a formal diagnostic entity and renamed it as an undifferentiated pleomorphic sarcoma not otherwise specified (NOS).

This new terminology has been supported by a compelling body of evidence over the last decade to suggest that MFH represents a final common pathway in tumours that undergo progression towards undifferentiation. While it remains unclear how to most accurately organise these tumours, the term malignant fibrous histiocytoma represents the diagnosis for thousands of patients and is still commonly used by both patients and physicians.



[Picture Credit: Malignant Histiocytoma]

MFH manifests a broad range of histologic appearances with four sub-types:

- Storiform-pleomorphic
- Myxoid
- Giant cell
- Inflammatory

(The Liddy Shiver Sarcoma Initiative).

Typically, MFHs occur in adults (range 32-80; mean 59 years) with a slight male predilection with a M:F ratio of 1.2:1). Presentation is usually with a painless, enlarging palpable mass. Although MFH can occur almost anywhere in the body, it has a predilection for the retroperitoneum and proximal extremities. It is usually confined to the soft tissues, but occasionally may arise in or from bone (1-5%).

It is the most frequent soft tissue sarcoma to occur as a result of radiotherapy and is also seen on a background of Paget disease.

Pathology

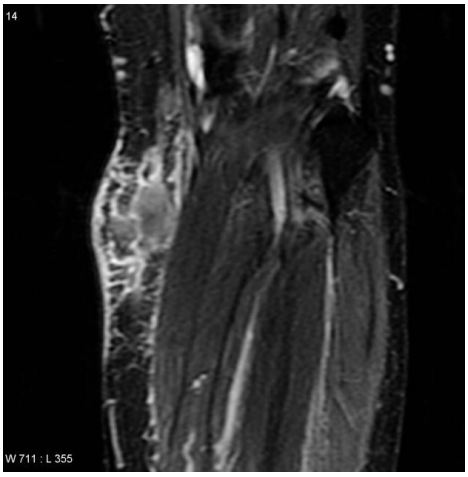
MFH are aggressive tumours which account for 25-40% of all adult soft tissue sarcomas, making it the most common type. However, the classification system is becoming more restrictive, with many tumours being re-classified as variants of myogenic sarcomas. Macroscopically (looking at it with the naked eye), these tumours are typically large (5 - 20 cm) well circumscribed but unencapsulated with a grey firm heterogeneous cut surface sometimes with areas of necrosis (tissue death).

Microscopically (looking at it under a microscope) these tumours are heterogeneous fibroblastic made up of poorly differentiated fibroblasts, myofibroblasts, histiocyte-like cells with significant cellular pleomorphism, storiform architecture and also demonstrate bizarre multi-nucleated giant cells. It is sometimes difficult to distinguish from other high grade sarcomas. A number of histological sub-types have been described including:

- storiform-pleomorphic : most common 50-60%
- myxoid : 25% : myxofibrosarcoma
- inflammatory : 5-10%
- giant cell : 5 - 10%
- angiomatoid
    - relatively non-aggressive
    - metastases uncommon
    - usually occurs in young adults / adolescents

Radiographic features

Plain x-rays will demonstrate a soft tissue mass and if arising from bone, then an aggressive destructive bony lesion. In some cases, curvilinear or punctate regions of calcification may be demonstrated.



[Picture Credit: MFH]

The density of MFH is typically similar to adjacent muscle, with heterogeneous lower density areas if haemorrhage, necrosis or myxoid material is abundant. The soft tissue component enhances. In up to 15-20% of cases some mineralisation is present.

MRI is the modality of choice for assessing soft tissue sarcomas, as it is best able to locally stage the tumour. These tumours are typically relatively well circumscribed, located within or adjacent to muscle, exerting positive mass effect on surrounding structures due to their (usual) large size at presentation.

Grading of MFH

Grading is as follows:

T1 - intermediate (to low) signal intensity, similar to adjacent muscle
heterogeneity if haemorrhage, calcification, necrosis, myxoid material present
prominent enhancement of solid components

T2 - intermediate to high signal intensity
heterogeneity if haemorrhage, calcification, necrosis, myxoid material present

Treatment and Prognosis

Most MFH are of high grade (3 and 4) and are aggressive in its biological behaviour. It frequently metastasises (30-50% at diagnosis) and locally recur despite aggressive treatment. The overall 5 year survival is between 25-70%.

Prognostic factors include :

- tumour size : smaller being better
- location
  - superficial is better
  - distal is better
- histological grade

Treatment usually consists of aggressive *en bloc* resection with a wide margin. Supplementary neoadjuvant chemotherapy and radiotherapy is especially useful in reducing the local recurrence rate. Limb-sparing surgery is usually possible.

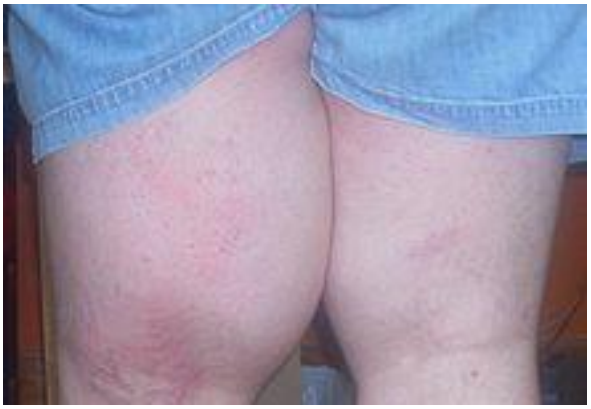
Differential Diagnosis

General imaging differential considerations include:

- other sarcomas and soft tissue tumours
  - synovial sarcoma
  - aggressive fibromatosis

- benign fibrous tumours
  - soft tissue metastases
  - myositis ossificans

(Radiopaedia.Org).



Liposarcoma

[Picture Credit: Liposarcoma]

Liposarcoma, a type of soft tissue sarcoma, is a cancerous (malignant) tumour that develops from fat cells. Liposarcoma tumours can develop anywhere, but typically appear in the deep fat tissues of the limbs or abdomen in people aged 50 to 65. Although liposarcoma is rare, It is the most common form of soft tissue sarcoma that occurs in adults.
(Mayo Clinic).

Causes of Liposarcoma

The exact cause of liposarcoma is not known, but it may be caused by damaged genes. Liposarcomas more commonly occur in an area of the body that has been injured. One may be at a higher risk if one has received radiation treatment in the past.

Different Types of Liposarcoma

Liposarcoma may be a low-grade or a high-grade tumour. A low-grade tumour is usually slow growing and does not spread to other areas of the body. A high-grade tumour is usually larger and often spreads to other areas in the body. The type of liposarcoma depends on the kind of cells that make up the tumour.

It may be any of the following:

- Well-differentiated - this is the most common type of liposarcoma and usually does not spread to other areas. It is most often found in the deep tissue of the legs and thighs. It may also be found in the back, abdomen, or arms
- Myxoid - this is the second most common type of liposarcoma. Myxoid liposarcomas are often low grade and are commonly found in the leg muscles. Myxoid tumours may spread to the tissue that covers the lungs and heart. Round cell liposarcoma is a type of myxoid liposarcoma that is high grade and more likely to spread to other areas of the body
- Dedifferentiated - this kind of liposarcoma is made up of both a fatty tumour and a non-fatty tumour. These are normally found in the back or abdomen This type of liposarcoma may spread to other areas such as the lungs, liver or bones
- Pleomorphic - this is a rare type of liposarcoma. It has very little or no fat in it and it is a high-grade tumour. It is commonly found in the leg muscles. Pleomorphic tumours often spread to the lungs, liver, brain and bone
- Mixed - this tumour is made up of more than one type of liposarcoma. It most often grows in the abdomen

Signs and Symptoms of Liposarcoma

Liposarcomas are usually painless and slow growing. One can often see or feel it under the skin. The patient may have pain if the tumour grows and presses on nerves and blood vessels. Depending on where the tumour is, one may have any of the following:

- Decreased movement in the limb that has the tumour
- Pain and swelling in the area of the tumour
- Chest pain
- Abdominal pain, constipation, diarrhoea or bloody bowel movements
- Trouble urinating or pain while urinating
- Trouble swallowing or weight loss
- Coughing or trouble speaking and breathing

Diagnosis of Liposarcomas

Diagnosis includes a general medical examination. One may also need one or more of the following tests:

- X-ray - this is used to take an image of the tumour and the area around it. These images may show if the tumour has damaged the bones. The doctor may also take an x-ray of the lungs to check if the cancer has spread.
- CT scan - this test is also called a CAT scan. An x-ray machine uses a computer to take images of the tumour and check for other problems. Images of the lungs and other organs may be taken to check if the cancer has spread. One may be given a dye before the images are taken to help caregivers see the images better.
- MRI - this scan uses powerful magnets and a computer to take images of the tumour and the area around it. An MRI may be used to look at the organs, blood vessels, nerves and bones around the tumour. It may also help the doctor identify what type of tumour the patient has. A dye may be administered to help the images show up better. Patients should inform the staff if they have any metal in or on their body
- Positron emission tomography scan - this is also called a PET scan. It may be used to see if there is cancer and if it has spread. A dye is injected into a vein (blood vessel). This dye helps show up the cells and tissue more clearly.
- Biopsy - during this procedure, a small amount of tissue is removed from the tumour. A needle or other small instrument is used to remove the tissue sample. If a large sample is needed, the doctor may need to make an incision. The sample will be sent to a laboratory for tests. The laboratory test will show if the tumour is a liposarcoma and what type it is.

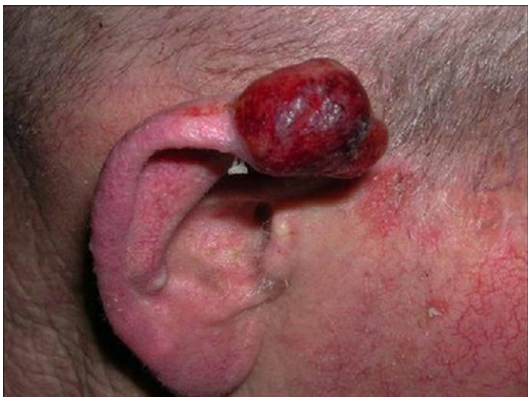
Treatment of Liposarcoma

- Chemotherapy - -these medicines work by killing cancer cells. The doctor may use chemotherapy to make the tumour smaller before surgery. He/she may also give chemotherapy after surgery to kill any cancer cells that remain
- Radiation - radiation kills cancer cells and prevents the cancer from spreading. Radiation may also help stop the cancer from coming back after surgery. Some patients may need radiation before, during or after surgery
- Surgery – some patients need surgery to remove the tumour and some of the tissue around it. A graft may be used to replace bone or tissue that has been removed. A graft is a piece of tissue from another area of the body or from a donor. In some cases it may be necessary to amputate (remove) a limb to completely remove the tumour

(Drugs.Com).

Leiomyosarcoma

Leiomyosarcoma belongs to a group of cancers called soft tissue sarcomas. Sarcomas are cancers that develop in the supporting or connective tissues of the body, such as muscle, fat, nerves, blood vessels, bone, and cartilage. Soft tissue sarcomas are rare. Approximately 1% of all cancers are soft tissue sarcomas. Most people with leiomyosarcoma are over the age of 50.



[Picture Credit: Leiomyosarcoma]

Leiomyosarcomas are one of the more common types of sarcoma to develop in adults. It starts from cells in a type of muscle tissue called smooth muscle. Smooth muscles are involuntary muscles that over which man has no control. It is found in the walls of muscular organs like the heart and stomach, as well as in the walls of blood vessels throughout the body. This means that leiomyosarcomas can start anywhere in the body. Common places are the walls of the womb (uterus), the limbs and the digestive system - particularly the stomach.

The exact causes of leiomyosarcoma are not known, and research is ongoing to try to find out as much as possible about it. Very rarely, soft tissue sarcomas may occur in an area that has previously been treated with radiotherapy for another type of cancer. The sarcoma will usually not develop until about 10 years after the radiotherapy treatment.

Exposure to some types of chemicals may also increase the risk of developing some sarcomas. The chemicals include vinyl chloride (used for making plastics), some types of herbicides (weedkillers) and dioxins.

People with early leiomyosarcoma often don't have any symptoms. Most leiomyosarcomas are diagnosed after a person develops symptoms which may include:

- a lump or swelling
- abdominal discomfort or bloatedness
- swelling or pain in any area of the body
- bleeding from the vagina in women who have reached menopause, or a change in periods for women who have not yet reached menopause

If any of the above symptoms are noticed, a medical practitioner should be consulted. It must, however, be noted that these symptoms can also be caused by many other things. (MacMillan Cancer Support).

<u>Classification of Leiomyosarcoma</u>

Histologically, soft tissue leiomyosarcomas that arise in different anatomic locations are similar. However, based on the location of the tumour, prognosis and possible treatments differ. For this reason leiomyosarcoma of soft tissues is divided into four groups. Furthermore there are sporadic case reports of primary leiomyosarcoma of bone, a clinically distinct entity.

- Leiomyosarcoma of Soft Tissue Retroperitoneal Somatic soft tissue – immuno-histochemical analysis suggests that the cell line of origin of leiomyosarcoma is the smooth muscle cell. The most common site of leiomyosarcoma of soft tissue is the

retroperitoneum, accounting for 50% of all cases. Smooth muscle sarcomas arising from the abdominal viscera or uterus are considered to be distinct disease entities. Other sites of involvement include the deep soft tissues of the extremities and are referred to as leiomyosarcoma of somatic soft tissue. Soft tissue leiomyosarcoma was at one time believed to arise from leiomyomas, however, this is now thought to be an extremely rare occurrence. Most malignant leiomyosarcomas arise independently, and are not associated with benign tumours. Histologic studies of somatic soft tissue leiomyosarcomas have shown that many, if not all, of these tumours arise directly from the smooth muscle cells lining small blood vessels.

When the retroperitoneum is involved, presenting symptoms are usually vague abdominal discomfort, an abdominal mass and weight loss. Peripherally located masses present as an enlarging mass, often painless, with few constitutional signs. Due to the deep inaccessible location and large volume of the abdominal cavity, leiomyosarcomas of the retroperitoneum tend to be significantly larger than those of the extremities at presentation. Retroperitoneal leiomyosarcoma is an aggressive disease that is often not amenable to complete surgical resection.

- Leiomyosarcoma of Cutaneous Origin – leiomyosarcoma can arise within the dermis. When this occurs it is referred to as cutaneous leiomyosarcoma. Unlike other forms of leiomyosarcoma, men are affected more than women at a ratio of 2:1. These lesions are typically small when first diagnosed (1-2 cm), and prognosis is generally good. When leiomyosarcoma develops within the dermis itself it is thought to be derived from the *pilar erecti* (tiny muscles in the skin that make the hair stand erect). Tumours that develop within subcutaneous tissue arise from small or microscopic vessels and should be considered leiomyosarcoma of somatic soft tissue. The behavior of these tumours is more consistent with that of deeper tumours than intradermal tumours.

  When the lesion is confined to the dermis, metastasis typically does not occur. Deeper lesions can metastasise in up to 30-40% of cases, usually haematogenously to the lungs. Treatment consists of wide resection, and is often curative when the lesion is initially confined to the dermis, regardless of histologic grade.

- Leiomyosarcoma of Vascular Origin (large vessel) - leiomyosarcoma rarely arises directly from major blood vessels, however, when it does, it is termed leiomyosarcoma of vascular origin.

  If the tumour develops in the inferior vena cava in the supra-hepatic segment, Budd-Chiari syndrome develops: hepatomegaly, jaundice, and ascites. These tumours are usually not surgically resectable. Tumours that arise in the inferior vena cava below the liver present with lower extremity oedema and vague abdominal pain. Symptoms are defined by the anatomic location of the lesion, and the local vascular physiology and drainage patterns.

  Arterial leiomyosarcoma usually affects the pulmonary artery. Patients will typically complain of dyspnoea (difficult breathing) and chest discomfort, relating to the arterial obstruction. Symptoms are related to the vascular distribution of the affected artery and the presence or absence of collateral blood flow.

- Leiomyosarcoma in the Immunocompromised Host - since the 1970s there have been a number of cases of leiomyosarcoma reported in immunocompromised patients having undergone transplantation and treated with immunosuppressive regimens.

  More recently, there have been further case reports involving people infected with the HIV/AIDS virus. There appears to be a relationship between these immunocompromised patients and super-infection with Epstein-Barr virus (EBV). Case reports of synchronous multiple leiomyosarcoma have been published where clonal analysis have shown that the individual tumours arose independently from each other. It is not known what interaction exists between immuno-incompentence and EBV infection that predisposes to leiomyosarcoma.

- Leiomyosarcoma of Bone - primary leiomyosarcoma of bone is extremely rare. There have been approximately 90 cases reported since initially described in 1965. Many cases that are thought to represent primary disease of bone, after further investigation, actually represent metastatic disease from another site or bony invasion from a neighbouring soft tissue lesion.

  Most cases of leiomyosarcoma of bone reported so far have been in the metaphysis of long bones. These lesions are thought to arise from the smooth muscle cells lining the intra-osseous vessels or from pluripotent mesenchymal cells. The histology is the same as leiomyosarcoma of soft tissue. These tumours have an equal or slightly male-predominant gender distribution. The radiographic appearance of these tumours is typically a radiolucent lesion in the metaphysis of a long bone, although the tumour has been described in other locations as well. A permeative appearance is characteristic. There are no specific radiographic features that can diagnose leiomyosarcoma by radiography alone.

Leiomyosarcoma Staging

Staging of leiomyosarcoma is important both in guiding treatment and in providing prognostic information. While many staging systems exist for soft tissue sarcoma, the most commonly used system is the AJCC system. This system classifies the tumour based upon histologic grade, the tumour size, location as superficial or deep, and the presence or absence of metastatic disease.

The Surgical Staging System of the Musculoskeletal Tumour Society (MSTS) is also used. It is utilised for staging bone and soft tissue sarcomas, including leiomyosarcoma. This staging system classifies tumours as Ia, Ib, IIa, IIb, or III based upon the histologic grade of the tumour, its local extent and the presence or absences of macroscopic distant metastatic disease. If the tumour is localised to a single anatomic compartment, it is said to be confined. If it has spread locally beyond its initial compartment, then it is said to be unconfined.

AJCC staging system

Stage	Histological Grade	Size	Location (Relative to fascia)	Systemic / Metastatic Disease Present
IA	Low	< 5cm	Superficial or Deep	No
IB	Low	≥ 5cm	Superficial	No
IIA	Low	≥ 5cm	Deep	No
IIB	High	< 5cm	Superficial or Deep	No
IIC	High	≥ 5cm	Superficial	No
III	High	≥ 5cm	Deep	No
IV	Any	Any	Any	Yes

MSTS Staging system

Stage	Histological Grade	Local Extent of Disease	Systemic / Metastatic Disease Present
Ia	Low	Confined	No
Ib	Low	Unconfined	No
Ia	High	Confined	No
Ib	High	Unconfined	No
III	Any	Any	Yes

Leiomyosarcoma Treatment

Due to the rarity of these tumours, and the need for a multi-specialty treatment team, treatment is best carried out in a specialised centre with expertise in sarcoma care. Treatment planning begins with a multi-disciplinary review of the patient's history, all available radiographic imaging, and the pathologic results from biopsy. A treatment plan is then formulated based upon the input from orthopaedic and general surgeons, musculoskeletal radiologists, pathologists, medical oncologists, and radiation oncologists.

- Surgery - Local control of soft tissue sarcomas is usually achieved with surgical resection. Pre-operative planning based upon radiographic and pathologic information is important to ensure adequate surgical margins. Achieving wide surgical margins is important in preventing local recurrence.

- Radiation Therapy - Many tumours involve or are directly adjacent to vital structures. In these cases achieving a wide surgical margin is impossible. Radiation therapy is an important additional treatment for improving rates of local control when surgical margins are close, especially in high-grade sarcomas. Radiation therapy can be delivered either pre-operatively (neoadjuvant) or post-operatively (adjuvant).

Radiation therapy can also be utilised as a means of palliative local control in cases where extensive metastasis has already occurred.

- Chemotherapy – the primary role of chemotherapy is in the treatment of metastatic disease. While not curative, it may slow the progression of systemic disease. Agents that are used in some sarcoma centres include: doxorubicin and ifosfamide, gemciabine and taxotere (docetaxewl), dacarbazine and ecteinascidin. There are currently investigational studies underway to identify other agents that may prove useful in the treatment of leiomyosarcoma.

  Chemotherapy is sometimes used as an adjuvant in the treatment of localised sarcomas. No clear survival benefit has been demonstrated in retroperitoneal leiomyosarcomas. However, pre-operative chemotherapy may help to shrink a tumour away from vital structures, and improve the ability of surgeons to successfully remove a large tumour. In localised leiomyosarcoma of the extremities, there may be a survival benefit for adjuvant chemotherapy using doxorubicin-based regimens. Both retrospective and prospective studies have shown a benefit for neoadjuvant doxorubicin and ifosfamide based regimens in patients with large (>8cm) high-grade sarcomas.

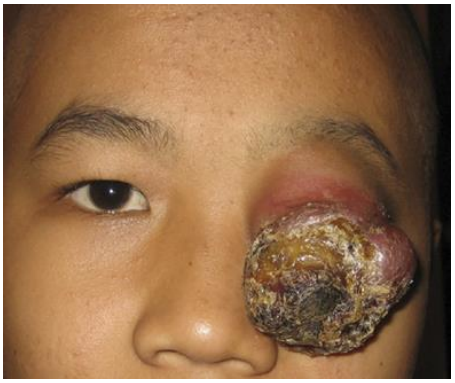
(The Liddy Shriver Sarcoma Initiative).

Rhabdomyosarcoma

Rhabdomyosarcoma is a cancerous (malignant) tumour of the muscles that are attached to bones. It can occur in many places in the body. The most common sites are the structures of the head and neck, the urogenital tract and the arms or legs.

Rhabdomyosarcoma is the most common soft tissue tumour in children.

The cause of rhabdomyosarcoma is unknown. It is a rare tumour. Some children with certain birth defects are at an increased risk and some families have a gene mutation that elevates risk. However, the great majority of children with rhabdomyosarcoma do not have any known risk factors.



[Picture Credit: Rhabdomyosarcoma]

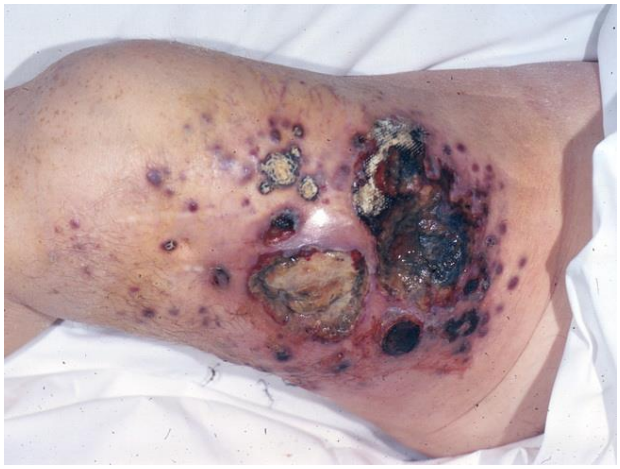
The most common symptom is a mass that may or may not be painful. Other symptoms vary depending on location of the tumour:

- Tumours in the nose or throat may cause bleeding, congestion, swallowing problems or neurological problems if they extend into the brain
- Tumours around the eyes may cause bulging of the eye, problems with vision, swelling around the eye or pain
- Tumours in the ears may cause pain, hearing loss or swelling
- Bladder and vaginal tumours may lead to trouble starting to urinate or having a bowel movement or poor control of urine
- Muscle tumours may lead to a painful lump and are often thought to be because of an injury.

(MedlinePlus).

Angiosarcoma

An angiosarcoma (AS) is an uncommon malignant neoplasms characterised by rapidly proliferating, extensively infiltrating anaplastic cells derived from blood vessels and lining irregular blood-filled spaces. Doctors apply the term angiosarcoma to a wide range of malignant endothelial vascular neoplasms that affect a variety of sites.



[Picture Credit: Angiosarcoma]

Angiosarcomas are aggressive and tend to recur locally, spread widely and have a high rate of spreading through lymph nodes to the rest of the body (systemic metastases). The rate of tumour-related death is high .
(Medscape.com).

Ewing's Sarcoma

Ewing's sarcoma is a primary bone cancer that affects mainly children and adolescents. It is one of a group of cancers known collectively as the Ewing sarcoma family of tumors (ESFT). It is the second most common bone cancer in children, but is also relatively uncommon. It accounts for only 1% of all childhood cancers. Although it can occur at any age, it very rarely occurs in adults over the age of 30.

[Picture Credit: Ewing's Sarcoma]

Because many illnesses can cause the same symptoms as Ewing's sarcoma, it is sometimes missed in its early stages. Early diagnosis and treatment is important. If found early enough, before it spreads to multiple organs (metastisises), Ewing's sarcoma can be treated successfully in 50 to 75% of cases.
(WebMD).

Primitive Neuroectodermal Tumour

Primitive Neuroectodermal tumours (PNET) are a group tumours that look similar under a microscope. PNETs develop from cells that are left over from the earliest stages of a baby's development in the womb. Normally these cells are harmless but occasionally they turn into a cancer. These cancers are more common in children than adults.

[Picture Credit: PNET]

Doctors use the term PNET to classify the tumour. They are divided into two main groups:

- PNETs of the brain and central nervous system. Primitive neuroectodermal tumours that occur in the brain and spinal cord (the central nervous system or CNS) include
  - Medulloblastoma, which develops in the back part of the brain – the hindbrain
  - Pineoblastoma which develops in the pineal region of the brain
  - Non pineal supratententorial PNET, which develops in the upper part of the brain

  Medulloblastoma is the most common of these. You can find information about treating primitive neuroectodermal tumours in the treating brain tumours section.

- Peripheral PNETs (outside the brain and nervous system). Doctors used to use the term peripheral PNET to describe these tumours when they occur in the soft tissues of the body. The tumours have the same genetic change as Ewing's sarcoma of the bone and so they are now called soft tissue Ewing's sarcoma.

(Cancer Research UK).

Nerve Tumours

Nerve tumours can form in the peripheral nerve network anywhere in the body. These tumours often affect the function of the nerve, causing pain and disability. A large majority of peripheral nerve tumours are benign (not cancerous). Some are caused by neurofibromatosis, or schwannomatosis (genetic disorders of the nervous system).

There are three major categories of nerve tumours. They are:

- Neurofibroma. Most commonly found within the genetic disorder of neurofibromatosis
- Schwannoma. These are nerve sheath tumours and can occur in isolation. Less commonly these tumours can occur in patients suffering from neurofibromatosis or schwannomatosis
- Malignant Peripheral Nerve Sheath Tumour. These very aggressive tumours are cancerous nerve sheath tumours and should be managed by a multi-disciplinary team. They can occur in association with neurofibromatosis Type 1

<u>Schwannomas</u>

Schwannomas are tumours that grow along the peripheral nervous system in the body. A common cause of schwannomas is schwannomatosis. For many patients, the tumours are watched over time, as they can grow very slowly. These tumours need to be removed when patients feel pain or the tumours are observed to be growing quickly .

[Picture Credit: Schwannoma]

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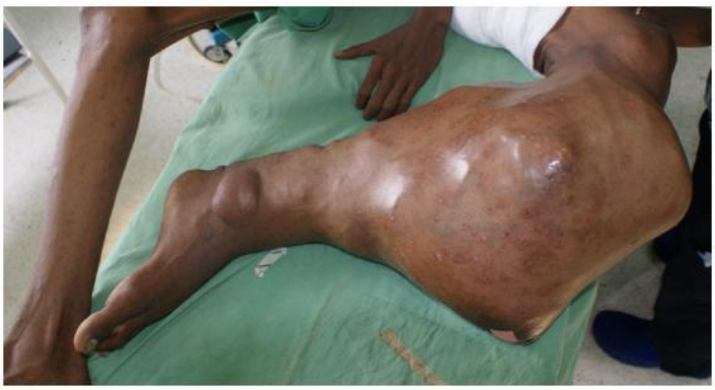
<u>Neurofibromas</u>

Neurofibromas are benign (non-cancerous) tumours which grow on nerves in the body. A common cause of neurofibromas is neurofibromatosis. Patients with neurofibromatosis often have numerous tumours throughout their body. If a tumour begins to cause pain or is associated with loss of neurological function, compresses a nearby structure, or shows rapid growth on imaging, surgical excision (removal) may be considered. If there is a question of the tumour being malignant

(cancerous), sophisticated imaging using a PET/CT scan and image-guided stereotactic biopsy can resolve if the tumour is cancerous.

Malignant Nerve Sheath Tumours



Also called neurofibrosarcoma, nerve sheath tumours are malignant (cancerous) tumours that grow in the cells surrounding peripheral nerves. A common cause of nerve sheath tumours is neurofibromatosis type 1 (NF1).

[Picture Credit: Neurofibromasarcoma]

These tumours should be removed to prevent local recurrence of malignancy and to halt growth and possible spreading of the cancer (metastasis) throughout the body. These are aggressive tumours that may require aggressive medical therapy (chemotherapy) or radiation therapy in addition to surgery.

The symptoms caused by these tumours can vary. Some patients are asymptomatic, meaning they have no symptoms. Possible symptoms may include:

- Pain
- A mass, or thickening in the muscle fibres
- Numbness, burning, or 'pins and needles'
- Weakness in the affected muscles
- Dizziness/loss of balance

Diagnosis of a nerve tumour

The doctor will do a thorough examination and may order several imaging studies including:

- MRI Neurography
- CT
- EMG (electrodiagnostic study to examine electrical pathways in the nerves)

Treatment options for nerve tumours

Nonsurgical treatment options - for many patients non-operative care is the most appropriate treatment. The tumours are often slow growing and can remain asymptomatic for a long period of time. Following patients with serial examinations and imaging studies can provide a guide to if, and or when, a patient may require surgery.

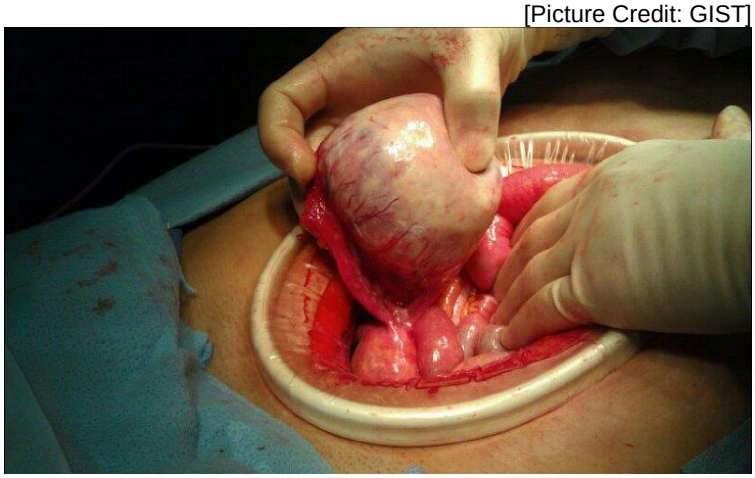
Surgical treatment options - there are several factors in deciding to surgically remove these tumours. Some, like schwannomas are slow-growing and can be watched using imaging studies over time. Others, like malignant nerve sheath tumours need to be removed immediately, as they are very aggressive.
(Johns Hopkins Medicine).

Gastrointestinal Stromal Sarcoma

Gastrointestinal stromal sarcoma (GIST) is a rare type of sarcoma found in the digestive system, most often in the wall of the stomach. Some GISTS are not cancerous (they are benign.) But they can become cancerous if not treated. Generally speaking, the larger the GIST, the more likely it is to be cancerous. 'Gastrointestinal' means they start in the digestive system (the gastrointestinal tract). 'Stromal' means they develop from tissues that support the connective tissues controlling the movements of the gut. 'Tumour' means a lump or growth in the body.

About 60% of these tumours start in the stomach. But they can begin anywhere in the digestive system, for example in the bowel or food pipe (oesophagus). Very rarely, they develop outside the gastrointestinal tract. GIST are most common in people between 50 and 70 years old. It is generally not what causes GIST but it is know that individuals who have the genetic condition called neurofibromatosis (NF) has an increased risk of developing GIST. Rarely, GIST can develop in children.

[Picture Credit: GIST]



People with early stage GIST often do not have any symptoms. So early stage GIST may be found when people are having tests for other medical conditions. Most GISTs are diagnosed in later stages of the disease. The symptoms of advanced GIST are likely to include:

- Pain or discomfort in the tummy (abdomen)
- A feeling of fullness
- Being sick (nausea with or without vomiting)
- Blood in stools or vomit
- Feeling very tired
- A low red blood cell count (anaemia)

Other medical conditions apart from GIST can cause these symptoms. If one has any of these symptoms one should see a doctor. GIST is rare so it is more likely to be caused by something less serious, but it is always best to have it checked.
(Cancer Research UK).

<u>Diagnosis of GIST</u>

Diagnosis starts with a thorough physical examination followed by various laboratory tests which may include:

Ultrasound scan - an ultrasound scan uses sound waves to produce an image of the inside of the body – this instance the abdomen. A gel is spread onto the abdomen after which a small device that looks much like a microphone is then moved over the area. The scan is painless and takes about 15-20 minutes.

Endoscopy - the doctor passes a thin, flexible tube called an endoscope into the mouth, down the gullet and into the stomach and small bowel. The endoscope has a light and

camera at the end, which allows the doctor to see any abnormalities. Some biopsies (tissue samples) may also be taken. These are sent to a laboratory to be tested.

An endoscopy can be uncomfortable but is usually not painful. Some people have a sore throat after an endoscopy. This gets better after a couple of days.

Endoscopic ultrasound - an endoscopic ultrasound may be used to show the size and position of a GIST. It produces an image of the stomach and surrounding structures. It is done using an endoscope with an ultrasound probe at the end.

Biopsy - the patient may have samples of tissue (biopsies) taken from the tumour which will be examined under a microscope.

A special test is done on the biopsy to look for a protein called KIT (CD117). Most GIST cells have this protein.

CT (computerised tomography) scan - a CT scan takes a series of x-rays that build up a three-dimensional picture of the inside of the body. The scan is painless and takes 10-30 minutes. CT scans use small amounts of radiation. The patient is requested not to eat or drink for at least four hours before the scan.

The patient may be given a drink or injection of a dye that allows particular areas to be seen more clearly. This may make the paerson feel hot all over for a few minutes. If the patient has allergies to iodine or has asthma, it is important to let the doctor know beforehand.

MRI (magnetic resonance imaging) scan - this test is similar to a CT scan but uses magnetism instead of X-rays to build up a detailed picture of areas of the body. Before the scan, the patient may be asked to complete and sign a checklist. This is to make sure it is safe for him/her to have an MRI scan.

Before having the scan, the patient will be asked to remove any metal belongings, including jewellery. Some people are given an injection of dye into a vein in the arm. This is called a contrast medium and can help the images from the scan show up more clearly.

During the test, the patient will be asked to lie very still on a couch inside a long cylinder (tube) for about 30 minutes. It is painless but can be slightly uncomfortable, and some people feel a bit claustrophobic during the scan. It is also noisy, but the patient is usually given earplugs or headphones. The patient can also hear and speak to the person operating the scanner.

PET (positron emission tomography) scan - a PET scan uses low-dose radioactive sugar to measure the activity of cells in different parts of the body. A very small amount of a mildly radioactive substance is injected into a vein, usually in the arm. A scan is taken a few hours later. Areas of cancer are usually more active than surrounding tissue and show up on the scan.

Staging of GISTs

The stage of a cancer is a term used to describe its size and whether it has spread beyond its original site. Knowing the particular type and the stage of the cancer helps the doctors decide on the most appropriate treatment. Generally, sarcomas are divided into four stages, from 'small and localised' (stage 1) to 'spread into surrounding structures' (stages 2 or 3) or

'spread to other parts of the body' (stage 4). If the cancer has spread to distant parts of the body this is known as secondary or metastatic cancer.

The stage of the cancer is an important factor in helping doctors plan the best treatment. They also consider other factors. These include: where the cancer started, how fast the cells are dividing and if there are genetic changes (mutations) in the cells.

If a cancer comes back after initial treatment, it is known as recurrent cancer. It may come back in the tissues where it first started (local recurrence) or it may come back in another part of the body (metastasis).

Treatment of GISTs

The treatment for GIST depends on a number of factors, including general health and the size and position of the tumour. The results of the tests will help the doctors decide on the best treatment.

Because GISTs are rare cancers, one should be referred for treatment at a specialist unit.

The most common treatment for GIST is surgery to remove the tumour. Drugs known as growth inhibitors are used to treat GISTs that cannot be removed with surgery.

Chemotherapy and radiotherapy do not work well for this type of cancer and so are not used.

Surgery - surgery is usually the first choice of treatment for GIST. The surgeon removes the tumour along with some surrounding healthy tissue. If the tumour has begun to grow into other tissues close by, these are also removed. The aim is to make sure that all the GIST cells have been taken away. If the GIST has begun to spread, it is sometimes possible to remove the secondary tumours. Surgery may also be used to treat GISTs that come back after treatment.

If the GIST is in the small bowel, the patient may have an operation to remove part of the small bowel. This does not usually have any long lasting side effects. If the GIST is in the stomach, part or most of the stomach is removed. This may mean making changes to one's diet, particularly the size and frequency of meals. Specialist registered dietitians can give advice and support.

Growth inhibitors - growth inhibitors are drug treatments that are taken as tablets. It works by blocking signals within the cancer cells that make them grow and divide.

In about 85% of people with a GIST, the tumour cells have a change (mutation) in a protein called KIT. This change means the GIST cells constantly get signals telling it to grow and multiply.

Treatment with growth inhibitors can block these signals. This may make the cancer shrink or stop it from growing. Growth inhibitors may be used to treat GISTs that cannot be completely removed with an operation. There are two growth inhibitors that can be used to treat a GIST. These are imatinib (Glivec®) and sunitinib (Sutent®).

The side effects of imatinib are usually mild or moderate. Some of the common side effects include tiredness, feeling sick (nausea), diarrhoea, swollen ankles and puffy eyes, and an itchy rash. Common side effects of sunitinib include a skin rash and soreness, tiredness,

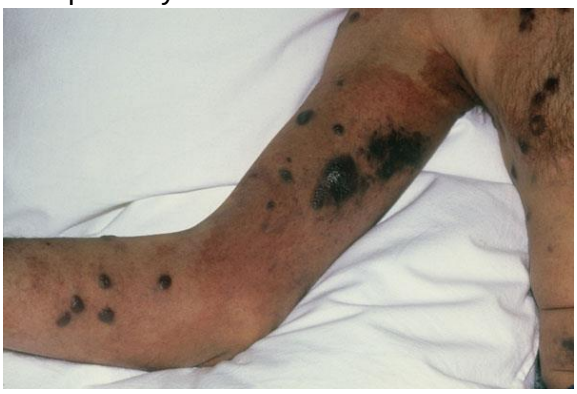
mouth ulcers and high blood pressure. These side effects can usually be well controlled with medicines.

Imatinib may sometimes be given to people who have had surgery to completely remove a GIST but who also have a high risk of the cancer coming back. Treatment that is given to reduce the risk of cancer returning is called adjuvant therapy.
(MacMillan Cancer Support).

Kaposi Sarcoma of the Skin
Kaposi sarcoma (KS) is a cancer that develops from the cells that line lymph or blood vessels. It usually appears as tumours on the skin or on mucosal surfaces such as inside the mouth, but tumours can also develop in other parts of the body, such as in the lymph nodes (bean-sized collections of immune cells throughout the body) or digestive tract.

The abnormal cells of KS form purple, red, or brown blotches or tumours on the skin. These affected areas are called *lesions*. The skin lesions of KS most often appear on the legs or face. They may look bad, but they usually cause no symptoms. Some lesions on the legs or in the groin area may cause the legs and feet to swell painfully.

KS can cause serious problems or even become life threatening when the lesions are in the lungs, liver, or digestive tract. KS in the digestive tract, for example, can cause bleeding, while tumours in the lungs may cause trouble breathing (American Cancer Society).



[Picture Credit: Kaposi Sarcoma]

Please visit CANSA's Fact Sheet on Kaposi Sarcoma for more information.

Synovial Sarcoma
Synovial sarcoma is a type of soft-tissue sarcoma. It is a rare cancer. Only about 1 to 3 individuals in a million people are diagnosed with this disease each year. It can occur at any age, but it is more common among teenagers and young adults. Synovial sarcoma seems to have a slight preference for males, with 12 male patients for every 10 female patients.

Despite its name, synovial sarcoma is not related to the synovial tissues that are a part of the joints. The disease starts most commonly in the legs or arms, but it can appear in any part of the body. On a pathology report, synovial sarcoma may be classified in different subtypes depending on what it looks like under the microscope or what specific gene mutation is involved. Synovial sarcoma is a high grade tumor. It spreads to distant sites in up to 50% of cases.

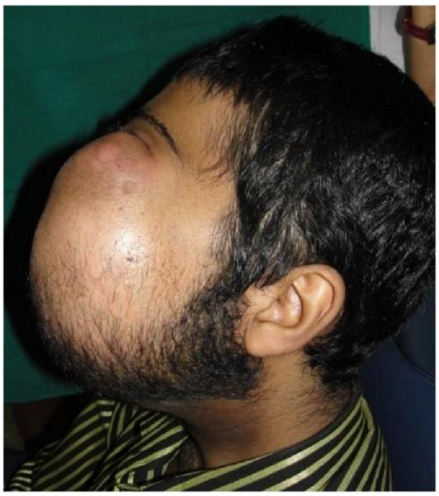
<u>Causes of Synovial Sarcoma</u>
There are no well-established risk factors for synovial sarcoma, but the disease is associated with the chromosomal translocation t(X;18) (p11;q11). This means that parts of

chromosome 18 and chromosome X have switched places in synovial sarcoma tumor cells. It is not known whether this mutation occurs randomly or follows a specific chain of events. Because of this translocation, synovial sarcoma cells contain a mutant gene. This mutant gene is thought to contribute to the development of the disease.

Symptoms of synovial sarcoma

Symptoms vary based on tumor location, and the following symptoms may arise:

- The mass may hinder a bodily function. For example, in the head and neck region, it may cause difficulties swallowing and breathing or it may alter the voice.
- The mass may be painful, in particular if nerves are involved.



[Picture Credit: Synovial Sarcoma]

A slow-growing painless mass is common and may give the false impression that it is harmless. When a tumor is painless and deep-seated within the body, it may go unnoticed for a long time. Because tumors can go unnoticed, follow-up guidelines generally involve regular imaging (such as CT scans) after treatment is completed. These tests can detect recurrences at the site of the original tumor or elsewhere in the body. If the cancer occurs elsewhere in the body, it is called metastasis.

Less than 10% of patients have detectable metastases at the time of diagnosis. In such cases, synovial sarcoma tumor cells are believed to have moved from one site (origin) to the second site (metastatic). The lungs are the most common location for metastases.

Treatment and Prognosis

Treatment involves a combination of surgery and usually adjuvant radiotherapy +/- chemotherapy. Radiotherapy is particularly useful in treating tumours where an adequate clear margin cannot be achieved, and ideally radiotherapy is administered pre-operatively.

Good prognostic variables include:

- small size
- located in extremity
- younger age < 20 years of age
- solid homogenous mass
- presence of calcification
- biphasic histology (controversial)

Poor prognostic variables include:

- large size (> 5cm) - most important factor
- located in the trunk or head and neck
- older patients
- cystic / haemorrhagic components
- marked heterogeneity
- histology
    - poorly differentiated histology
    - rhabdoid cells

- extensive tumor necrosis
- high nuclear grade
- p53 mutations
- high mitotic rate (> 10 mitoses/10 high-power field)

Overall 5 year survival is between 36-76% with both local recurrence (30-50%) and distant metastases (40%) being common.

Differential Diagnosis

General imaging differential considerations include:

- malignant fibrous histiocytoma (MFH)
- other sarcomas
    - osteosarcoma
    - chondrosarcoma
    - liposarcoma
    - fibrosarcoma
- metastatic carcinoma (Radiopaedia.Org).

About Clinical Trials

Clinical trials are research studies that involve people. These studies test new ways to prevent, detect, diagnose, or treat diseases. People who take part in cancer clinical trials have an opportunity to contribute to scientists' knowledge about cancer and to help in the development of improved cancer treatments. They also receive state-of-the-art care from cancer experts.

Types of Clinical Trials

Cancer clinical trials differ according to their primary purpose. They include the following types:

Treatment - these trials test the effectiveness of new treatments or new ways of using current treatments in people who have cancer. The treatments tested may include new drugs or new combinations of currently used drugs, new surgery or radiation therapy techniques, and vaccines or other treatments that stimulate a person's immune system to fight cancer. Combinations of different treatment types may also be tested in these trials.

Prevention - these trials test new interventions that may lower the risk of developing certain types of cancer. Most cancer prevention trials involve healthy people who have not had cancer; however, they often only include people who have a higher than average risk of developing a specific type of cancer. Some cancer prevention trials involve people who have had cancer in the past; these trials test interventions that may help prevent the return (recurrence) of the original cancer or reduce the chance of developing a new type of cancer.

Screening - these trials test new ways of finding cancer early. When cancer is found early, it may be easier to treat and there may be a better chance of long-term survival. Cancer screening trials usually involve people who do not have any signs or symptoms of cancer. However, participation in these trials is often limited to people who have a higher than average risk of developing a certain type of cancer because they have a family history of that type of cancer or they have a history of exposure to cancer-causing substances (e.g., cigarette smoke).

Diagnostic - these trials study new tests or procedures that may help identify, or diagnose, cancer more accurately. Diagnostic trials usually involve people who have some signs or symptoms of cancer.

Quality of life or supportive care - these trials focus on the comfort and quality of life of cancer patients and cancer survivors. New ways to decrease the number or severity of side effects of cancer or its treatment are often studied in these trials. How a specific type of cancer or its treatment affects a person's everyday life may also be studied.

Where Clinical Trials are Conducted

Cancer clinical trials take place in cities and towns in doctors' offices, cancer centres and other medical centres, community hospitals and clinics. A single trial may take place at one or two specialised medical centres only or at hundreds of offices, hospitals, and centres.

Each clinical trial is managed by a research team that can include doctors, nurses, research assistants, data analysts, and other specialists. The research team works closely with other health professionals, including other doctors and nurses, laboratory technicians, pharmacists, dieticians, and social workers, to provide medical and supportive care to people who take part in a clinical trial.

Research Team

The research team closely monitors the health of people taking part in the clinical trial and gives them specific instructions when necessary. To ensure the reliability of the trial's results, it is important for the participants to follow the research team's instructions. The instructions may include keeping logs or answering questionnaires. The research team may also seek to contact the participants regularly after the trial ends to get updates on their health.

Clinical Trial Protocol

Every clinical trial has a protocol, or action plan, that describes what will be done in the trial, how the trial will be conducted, and why each part of the trial is necessary. The protocol also includes guidelines for who can and cannot participate in the trial. These guidelines, called eligibility criteria, describe the characteristics that all interested people must have before they can take part in the trial. Eligibility criteria can include age, sex, medical history, and current health status. Eligibility criteria for cancer treatment trials often include the type and stage of cancer, as well as the type(s) of cancer treatment already received.

Enrolling people who have similar characteristics helps ensure that the outcome of a trial is due to the intervention being tested and not to other factors. In this way, eligibility criteria help researchers obtain the most accurate and meaningful results possible.

National and International Regulations

National and international regulations and policies have been developed to help ensure that research involving people is conducted according to strict scientific and ethical principles. In these regulations and policies, people who participate in research are usually referred to as "human subjects."

Informed Consent

Informed consent is a process through which people learn the important facts about a clinical trial to help them decide whether or not to take part in it, and continue to learn new information about the trial that helps them decide whether or not to continue participating in it.

During the first part of the informed consent process, people are given detailed information about a trial, including information about the purpose of the trial, the tests and other procedures that will be required, and the possible benefits and harms of taking part in the trial. Besides talking with a doctor or nurse, potential trial participants are given a form, called an informed consent form, that provides information about the trial in writing. People who agree to take part in the trial are asked to sign the form. However, signing this form does not mean that a person must remain in the trial. Anyone can choose to leave a trial at any time—either before it starts or at any time during the trial or during the follow-up period. It is important for people who decide to leave a trial to get information from the research team about how to leave the trial safely.

The informed consent process continues throughout a trial. If new benefits, risks, or side effects are discovered during the course of a trial, the researchers must inform the participants so they can decide whether or not they want to continue to take part in the trial. In some cases, participants who want to continue to take part in a trial may be asked to sign a new informed consent form.

New interventions are often studied in a stepwise fashion, with each step representing a different “phase” in the clinical research process. The following phases are used for cancer treatment trials:

Phases of a Clinical Trial

Phase 0. These trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer. Phase 0 trials are also called micro-dosing studies, exploratory Investigational New Drug (IND) trials, or early phase I trials. The people who take part in these trials usually have advanced disease, and no known, effective treatment options are available to them.

Phase I (also called phase 1). These trials are conducted mainly to evaluate the safety of chemical or biologic agents or other types of interventions (e.g., a new radiation therapy technique). They help determine the maximum dose that can be given safely (also known as the maximum tolerated dose) and whether an intervention causes harmful side effects. Phase I trials enrol small numbers of people (20 or more) who have advanced cancer that cannot be treated effectively with standard (usual) treatments or for which no standard treatment exists. Although evaluating the effectiveness of interventions is not a primary goal of these trials, doctors do look for evidence that the interventions might be useful as treatments.

Phase II (also called phase 2). These trials test the effectiveness of interventions in people who have a specific type of cancer or related cancers. They also continue to look at the safety of interventions. Phase II trials usually enrol fewer than 100 people but may include as

many as 300. The people who participate in phase II trials may or may not have been treated previously with standard therapy for their type of cancer. If a person has been treated previously, their eligibility to participate in a specific trial may depend on the type and amount of prior treatment they received. Although phase II trials can give some indication of whether or not an intervention works, they are almost never designed to show whether an intervention is better than standard therapy.

Phase III (also called phase 3). These trials compare the effectiveness of a new intervention, or new use of an existing intervention, with the current standard of care (usual treatment) for a particular type of cancer. Phase III trials also examine how the side effects of the new intervention compare with those of the usual treatment. If the new intervention is more effective than the usual treatment and/or is easier to tolerate, it may become the new standard of care.

Phase III trials usually involve large groups of people (100 to several thousand), who are randomly assigned to one of two treatment groups, or "trial arms": (1) a control group, in which everyone in the group receives usual treatment for their type of cancer, or 2) an investigational or experimental group, in which everyone in the group receives the new intervention or new use of an existing intervention. The trial participants are assigned to their individual groups by random assignment, or randomisation. Randomisation helps ensure that the groups have similar characteristics. This balance is necessary so the researchers can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups.

Randomisation is usually done by a computer program to ensure that human choices do not influence the assignment to groups. The trial participants cannot request to be in a particular group, and the researchers cannot influence how people are assigned to the groups. Usually, neither the participants nor their doctors know what treatment the participants are receiving.

People who participate in phase III trials may or may not have been treated previously. If they have been treated previously, their eligibility to participate in a specific trial may depend on the type and the amount of prior treatment they received.

In most cases, an intervention will move into phase III testing only after it has shown promise in phase I and phase II trials.

Phase IV (also called phase 4). These trials further evaluate the effectiveness and long-term safety of drugs or other interventions. They usually take place after a drug or intervention has been approved by the medicine regulatory office for standard use. Several hundred to several thousand people may take part in a phase IV trial. These trials are also known as post-marketing surveillance trials. They are generally sponsored by drug companies.

Sometimes clinical trial phases may be combined (e.g., phase I/II or phase II/III trials) to minimize the risks to participants and/or to allow faster development of a new intervention.

Although treatment trials are always assigned a phase, other clinical trials (e.g., screening, prevention, diagnostic, and quality-of-life trials) may not be labelled this way.

Use of Placebos

The use of placebos as comparison or “control” interventions in cancer treatment trials is rare. If a placebo is used by itself, it is because no standard treatment exists. In this case, a trial would compare the effects of a new treatment with the effects of a placebo. More often, however, placebos are given along with a standard treatment. For example, a trial might compare the effects of a standard treatment plus a new treatment with the effects of the same standard treatment plus a placebo.

Possible benefits of taking part in a clinical trial

The benefits of participating in a clinical trial include the following:

- Trial participants have access to promising new interventions that are generally not available outside of a clinical trial.
- The intervention being studied may be more effective than standard therapy. If it is more effective, trial participants may be the first to benefit from it.
- Trial participants receive regular and careful medical attention from a research team that includes doctors, nurses, and other health professionals.
- The results of the trial may help other people who need cancer treatment in the future.
- Trial participants are helping scientists learn more about cancer (e.g., how it grows, how it acts, and what influences its growth and spread).

Potential harms associated with taking part in a clinical trial

The potential harms of participating in a clinical trial include the following:

- The new intervention being studied may not be better than standard therapy, or it may have harmful side effects that doctors do not expect or that are worse than those associated with standard therapy.
- Trial participants may be required to make more visits to the doctor than they would if they were not in a clinical trial and/or may need to travel farther for those visits.

Correlative research studies, and how they are related to clinical trials

In addition to answering questions about the effectiveness of new interventions, clinical trials provide the opportunity for additional research. These additional research studies, called correlative or ancillary studies, may use blood, tumour, or other tissue specimens (also known as ‘biospecimens’) obtained from trial participants before, during, or after treatment. For example, the molecular characteristics of tumour specimens collected during a trial might be analysed to see if there is a relationship between the presence of a certain gene mutation or the amount of a specific protein and how trial participants responded to the treatment they received. Information obtained from these types of studies could lead to more accurate predictions about how individual patients will respond to certain cancer treatments, improved ways of finding cancer earlier, new methods of identifying people who have an increased risk of cancer, and new approaches to try to prevent cancer.

Clinical trial participants must give their permission before biospecimens obtained from them can be used for research purposes.

When a clinical trial is over

After a clinical trial is completed, the researchers look carefully at the data collected during the trial to understand the meaning of the findings and to plan further research. After a phase I or phase II trial, the researchers decide whether or not to move on to the next phase or stop testing the intervention because it was not safe or effective. When a phase III trial is completed, the researchers analyse the data to determine whether the results have medical importance and, if so, whether the tested intervention could become the new standard of care.

The results of clinical trials are often published in peer-reviewed scientific journals. Peer review is a process by which cancer research experts not associated with a trial review the study report before it is published to make sure that the data are sound, the data analysis was performed correctly, and the conclusions are appropriate. If the results are particularly important, they may be reported by the media and discussed at a scientific meeting and by patient advocacy groups before they are published in a journal. Once a new intervention has proven safe and effective in a clinical trial, it may become a new standard of care.
(National Cancer Institute).

Medical Disclaimer

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Connective Tissue Sarcoma
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