A Dissertation on

"COMPARATIVE STUDY OF SOFT TISSUE SARCOMA ON EXTREMITIES AND TRUNK''

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CERTIFICATE

Certified that this is the bonafide dissertation in **"COMPARATIVE STUDY OF SOFT TISSUE SARCOMA ON EXTREMITIES AND TRUNK''** was a work done by **Dr.M.SRIDHAR** and submitted in partial fulfilment of the requirements for the Degree of **M.S. GENERAL SURGERY, BRANCH I** of The Tamilnadu Dr. M.G.R Medical University, Chennai.

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DECLARATION

I Solemnly declare that the dissertation titled **"COMPARATIVE STUDY OF SOFT TISSUE SARCOMA ON EXTREMITIES AND TRUNK''** was done by me at Coimbatore Medical College and Government General Hospital during the academic year 2012-2015 under the guidance of **Prof. Dr. V. ELANGO M.S.** This dissertation is submitted to the TamilnaduDr.MGR Medical University towards the fulfilment of the requirement for the award of M.S. Degree in **GENERAL SURGERY (BRANCH I).**

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COMPARATIVE STUDY OF SOFT TISSUE SARCOMA ON EXTREMITIES AND TRUNK’

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INTRODUCTION

Soft tissue sarcomas (STS) are originating mainly from the embryonic mesoderm. STS are group of malignant tumour, anatomically and histologically diverse neoplasms that share a common embryonic origin arising primarily from mesenchymal tissue with notable exception of neurosarcoma, primitive neuro–ectodermal tumors and Ewing sarcoma, which are arise from neuro-ectodermal tissues. It is common in paediatric age group accounting for 6.5% of all childhood malignancy but rare in adult accounting for 1% of all adult malignancy and 2% of cancer death.

The incidence of STS is very less and may be 2-4 cases/ 100,000 per annum.

Mortality, is high; the mean five-year survival rate is about 60%. Because of multiple causes the STS occurs in multiple forms still etiology remains unknown.

The most common sites are limb about 40%-50% of these are lower extremities, 25% are upper extremities, and 15-20% are trunk. This study deals with STS arising from limb and trunk[7,9].

Hematogenic metastases decide the prognosis of poorly differentiated soft tissue sarcomas ,and but loco regional recurrence not decide much about prognosis. In the past three decades, the combined modality treatment of soft tissue sarcomas may be considerably. Although surgery is the cornerstone of the sarcoma treatment, there is definitive treatment by adjuvant radiotherapy after narrow surgical excision of the tumour. On the other hand, there is no definitive need for (neo) adjuvant chemotherapy after surgical treatment of soft tissue sarcomas, with the exception of rhabdomyosarcoma, extraosseous Ewing's sarcoma / primitive neuroectodermal tumor (PNET), and Extraosseous osteosarcoma.

Surgical resection with radiotherapy treatments have mainly involved to improved locoregional tumour control and only to a lesser degree to survival. Conversely, the 'aggressive' surgical approach in the treatment of metastasized tumours has contributed to improved disease-free and overall survival.

Surgery is the main corner stone in the multimodality treatment of the disease –which involves various methods including pathology, radiotherapy, medical oncology, rehabilitation medicine, genetics, and psychology.

Amputation was the treatment of choice for STS of extremity because of high rate of recurrence after local excision. With advent of combination treatment (surgery and radiotherapy (RT)), limb sparing surgery become treatment choice[7,5] .

Isolated limb perfusion[5,9] (ILP) treatment was the local administration of a cytostatic agent at the highest dosage without introducing systemic side effects. The extracorporeal circulation system used was similar to the one employed in open heart surgery. The technique was first applied to patients with in-transit metastases of melanoma of the lower extremities who refused amputation.Melphalan was the cytostatic agent of choice.

Oldhoff and Schraffordt Koops successfully operated the perfusion program of Groningen in the Algemeen Provinciaal Stads enAcademisch Ziekenhuis (APSAZ).

Hyperthermia was introduced in 1967 in the perfusion treatment by Cavalière. Recently, mild hyperthermia(39-40 °C) is widely used, because this causes less local toxicity than higher temperatures. As the search for the optimum perfusion technique, other cytostatics such as dacarbazine (DTIC), adriamycin and cisplatinum all are tried but melphalan become the most used and effective drug.

When Lejeune and colleagues added tumor Necrosis Factor alpha (TNFα) to melphalan as a perfusion agent in the isolated regional perfusion for locoregional advanced soft tissue sarcomas and melanomas. This resulted in a high local response rate with acceptable locoregional and systemic toxicity and a high percentage of limb salvage. Medical centers in Lausanne, Amsterdam, Rotterdam, Berlin, Brussels, Tel Aviv, and Groningen participated in this trial. They Used high dose of TNFα in combination with interferon and melphalan.

This technique useful for the salvage of the affected extremity in 84% of the cases. The perfused tumours were large size, around 20 cm on average. Resection was performed to many weeks after post perfusion. In 87% of the cases, Tumor response was well documented. It was then clear that ILP in combination with TNFα , interferon gamma and melphalan was safe and highly effective and constituted important treatment of locally advanced soft tissue sarcomas of the extremities.

Another important multimodality treatment was radiotherapy. Rosenberg was the first demonstrate the value of adjuvant radiotherapy in the limb-saving treatment of sarcomas. Yang and colleagues updated the study several years later, with a median follow up of about ten years.

They identified that maximum reduced in locoregional recurrence after radiation, without affecting patients survival rate.

Greater stiffness and increased edema of the involved extremity, are the complication of adjuvant radiation in combination with surgery.

AIM OF THE STUDY

1. To compare 6 months survival rate in extremities and trunk STS.

2. To compare metastasis free survival rate in extremities and trunk STS.

REVIEW OF THE LITERATURE

SOFT TISSUE SARCOMA

[15]Soft tissue sarcomas (STS) are a heterogeneous group of tumours arising mainly from the cells of the soft supporting tissues of the body (also known as mesenchyma): fat, muscles, nerves, fibrous tissues, blood and lymph vessels. The most commonly STS arises from extremities (30-52%), lower extremity (29-49%), upper extremity (12-21%), retroperitoneum (8-15%),head and neck (4-13%), abdomen (10-12%), pelvis (7-12%), and thorax (9-11).Soft tissue sarcomas are rare tumours, and globally account for less than 1% of all malignancies.

Soft tissue sarcomas are therefore a heterogeneous group of tumours. They currently include more than 50 different histological subtypes. The classification of these tumours is complex and review of the histopathologic specimen by experienced pathologists is generally recommended for clinical practice and for clinical research.

Progress in the understanding of sarcoma has frequently resulted in identification of new histological subtypes or reclassification of existing ones.

The development of immunochemistry, cytogenetic and molecular genetic has brought major progress in this field in the last 10 years. The World Health Organization classification of soft tissue tumours has been issued in 2002 .

Several histological grading systems have been proposed, with either 3 or 4classification levels. Most have been validated as prognosis level for metastases free and overall survival in untreated soft tissue sarcoma patient.

The two most widely used grading systems are the one of the us National Cancer Institute (3 levels, based on the histological subtype, and tumour necrosis level, mitotic index, cellularity rate and/or pleomorphism for some subtypes), and the one of the French “Fédération Nationale des Centres de Lutte Contre le Cancer” (3 levels, based on tumour necrosis, mitotic rate and tumour differentiation, giving an equal weight to these 3 factors). The French system has been shown to better predict outcome, but both systems are still used. The two systems do overlap in approximately 2/3 of the cases.

Soft tissue sarcomas are often diagnosed accidentally, because they generally develop without pain. Less than 1% of soft tissue tumours are malignant. Other soft tissue tumors are either benign or of intermediate malignancy (locally aggressive or rarely metastasizing), according to the last classification of soft tissue tumours [1]. The probability of malignancy of a newly diagnosed soft tissue tumour is related to size and depth, but, so far, malignancy cannot be accurately predicted by clinical examinations and imaging techniques. A tumour biopsy is needed to confirm the histology, and this should preferably be performed in a specialized sarcoma center to avoid compromising the results of the subsequent surgery.

ETIOLOGY[7,9,15]

Eventhough several factors are identified as causative factors no specific etiological factors can be identified. Bone and soft tissue sarcoma may be caused by previous radiation exposure. Cutaneous lymphangio sarcoma may caused by chronic lymphedema.

Chronic lymphedema after mastectomy surgery and radiotherapy may produce Angiosarcoma known as Stewart-Treves syndrome . Vinyl chloride, phenoxyacetic acid herbicides, and chlorophenols and their contaminants have been shown to increase the risk of sarcoma.

Certain genetic conditions such as neurofibromatosis1,caused by a mutation in 17q11, Aggressive malignant peripheral nerve sheath tumours (MPNST) may occur in 1-5% patient. Li-Fraumeni syndrome, mutation of p23,may be common relation with so many malignancies, including STS. Mutations in the retinoblastoma gene RB1, also increases risk of sarcoma.

Desmoids tumour is associated with phenotypical variant of familial adenomatous polyposis (FAP).Benign enchondromas, hemangiomas and lymphangiomas may undergone into their malignant sarcomatous changes in Maffucci syndrome.

Kaposi's sarcoma may be produced by human herpes virus 8 (HHV 8). Epstein-Barr virus (EBV) infection has been found to cause leiomyosarcoma during therapeutic immunosuppression treatment stage.

Even though no specific etiologic agent is identified in the overwhelming majority of patient with soft tissue sarcoma the risk factors of STS include the following:

1 . Previous radiation exposure

The risk of post radiotherapy saracomas arise more than 3 yrs after radiation therapy exposure and some decades later saracomas occurring after radiation exposure are most commonly malignant fibrous histiocytoma.

2. Environmental factors

Chemical exposure to phenoxy acetic acid found in herbicides, chlorophenol found in wood preservatives are associated with STS. Thorotrast, vinyl chloride, arsenic are associated with 'hepatic angiosaracoma".

3. Chronic lymphedema

Chronic lymphedema such as that experience after axillary dissection has been associated with lymphangio sarcoma (stewart-treves syndrome)

4. Chronic inflammatory process may a risk factor

Agents such as sharpnel, bullets, intra muscular iron injections and foreign body implants have been implicated.

5. Genetic predisposition

Specific inherited genetic alterations have been associated with an increased risk of STS. Patients with gardener's syndrome (familial polyposis) have a higher than normal incidence of desmoids.

Patients with germline mutations in the tumour suppressor gene p53(Li-fraumeni syndrome) have high incidence of sarcomas. Patients with von recklinhausen's disease who have abnormalities in the neurofibromatosis type I tend to develop neurofibrosarcoma.

Soft tissue sarcoma can occur in patients with hereditary retinoblastoma as a second malignancy.

6 . Chromosome rearrangements

A number of soft tissue tumours both benign and malignant have been found to have consistent chromosomal abnormalities which in many cases may be diagnostic. Chromosomal translocations are the most common cytogenetic abnormality in soft tissue tumours.

CLASSIFICATION AND HISTOPATHOLOGY[7,9,12]

Because of the rare variety and heterogeneity of STS tumours histology examination may be done by an experienced pathologist.

The World Health Organization Classification of STS Tumours into > 50 subtypes. Undifferentiated pleomorphic sarcoma (malignant fibrous histiocytoma (MFH)), is the most common type in adults, representing 28-39% of overall STS. Liposarcoma (14-22%), synovial sarcoma (11-12%), leiomyosarcoma (6-12%), fibrosarcoma (8-9%) and MPNST (6-7%), are also among the more common subtypes.

Rhabdomyosarcoma is the most commonly occur histologic finding in children, incidence occur > 50% of paediatric STS.

FIBROUS TUMOURS

Fibro Sarcoma

a) adult fibro sarcoma.

b) congenital or infantile fibro sarcoma intermediate tumours.

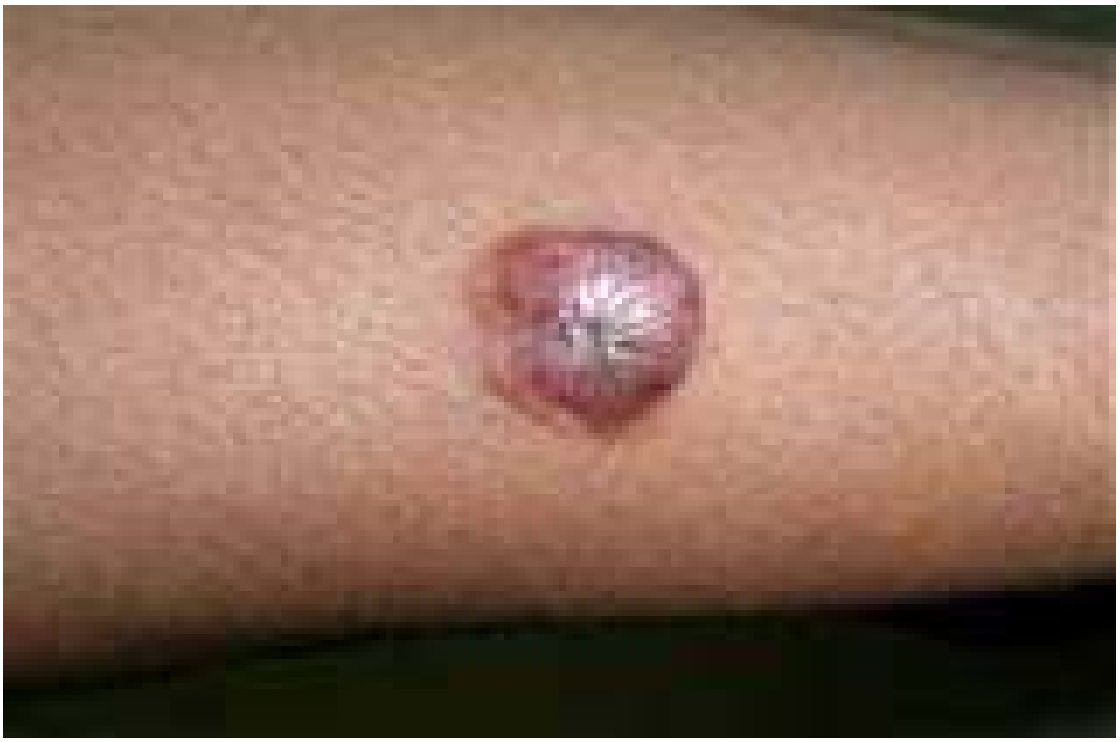
c) Inflammatory fibrosarcoma (inflammatory myofibroblastic tumour)

FIBROHISTIOCYTIC TUMOURS

1. Intermediatetumours

Dermato fibrosarcoma protuberans.

DERMATO FIBROSARCOMA PROTUBERANS



2. Malignant fibrous histiocytoma.

a. Storiform-plemorphic fibrous histiocytoma

b. Myxoid fibrous histiocytoma

c. Giant cell fibrous histiocytoma(malignant giant cell tumor of soft parts)

d. Xanthomatous(inflammatory type) fibrous histiocytoma.

LIPOMATOUS TUMOURS

Liposarcoma

a) well-differentiated liposarocoma
    i. lipoma-like liposarcoma
    ii. Sclerosingliposarocoma
    iii. Inflammatory liposarcoma

b) Myxoidliposarcoma

c) Round cell (poorly differentiated myxoid) liposarcoma

d) Pleomorphic liposarcoma

e) De-differentiated liposarcoma

SMOOTH MUSCLE TUMOURS

1. Rhabdomyosarcoma

a) Embryonal rhabdomyosarcoma

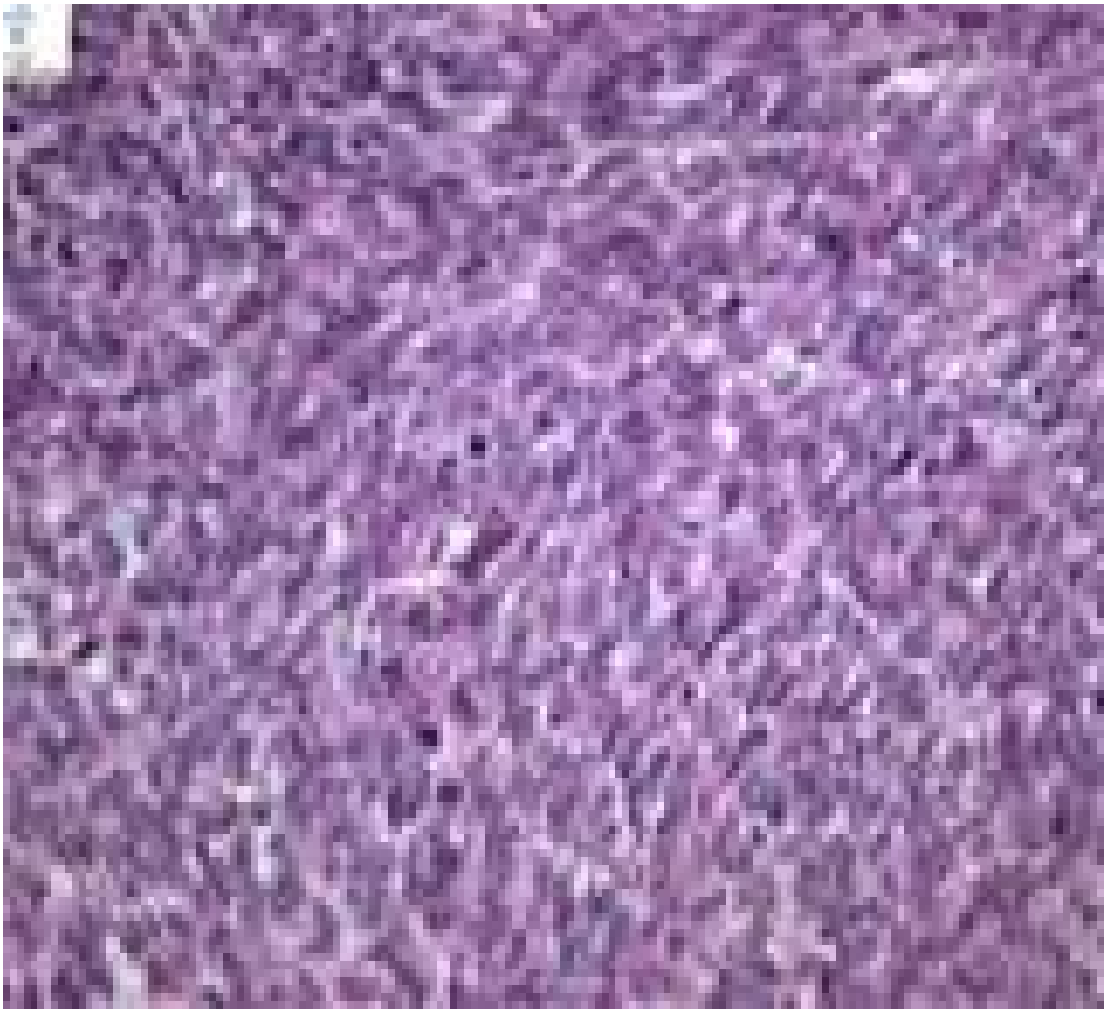
b) Botryoid rhabdomyosarcoma

c) Spindle cell rhabdomyosarcoma

d) Alveolar rhabdomyosarcoma

e) Plemorphic rhabdomyosarcoma

2. Rhabdomyosarcoma with ganglionic differentiation (etomesenchymoma)



LIPOSARCOMA HISTOLOGY SLIDE

TUMOURS OF BLOOD AND LYMPH VESSEL

1. Angiosaracoma and lymphangiosarcoma
2. Kaposi's saracoma
3. Follicular dendritic cell sarcoma

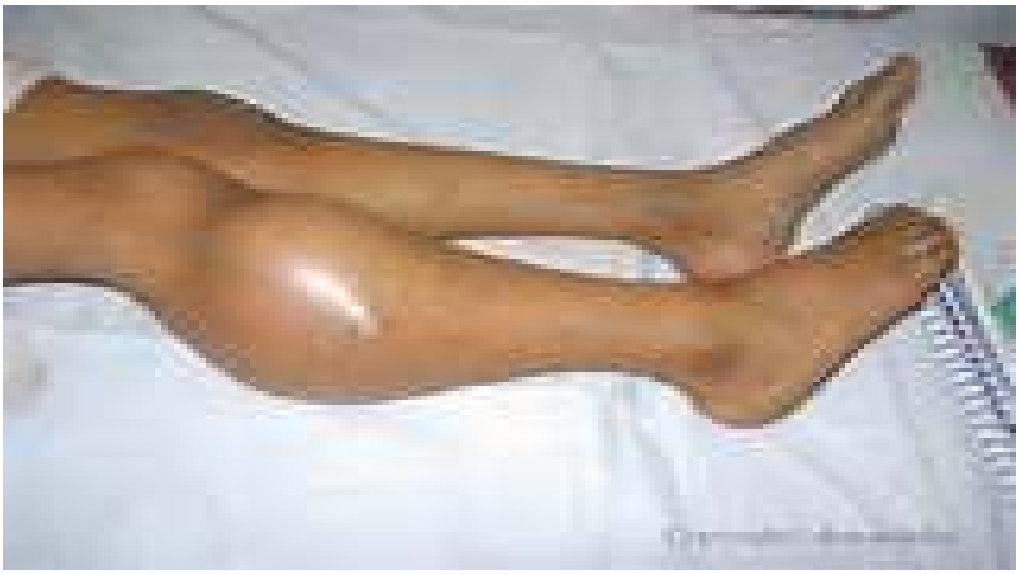
PERIVASCULAR TUMOURS

1. Malignant glomustumour
2. Malignant hemangio pericytoma

SYNOVAL TUMOURS

1. Synovial sarcoma
    a. Biphasic (fibrous and epithelial) synovial sarcoma
    b. Monophasic (fibrous or epithelial) synovial sarcoma
2. Malignant giant cell tumor of tendon schwannoma)

EXTREMITIES SYNOVIAL SARCOMA



MESOTHELIAL TUMOURS

1. Malignant solitary fibrous tumour pleura and peritoneum
2. Diffuse mesothelioma
    a. Epithelial
    b. Fibrous
    c. Diffuse

NEURAL TUMOURS

1. MPNST (malignant schwannoma , neurofibrosarcoma)
    a. Malignant Triton tumour (MPNST with rhabdomyosarcoma)
    b. Glandular MPNST (malignant glandular schwannoma)
    c. Epithelioid MPNST (malignant epithelioidschwannama)

2. Malignant granular cell tumour
3. Clear cell sarcoma(malignant melanoma of a soft parts)
4. Malignant melanocytic schwannoma
5. Gastrointestinal autonomous nerve tumour(plexosarcoma)
6. Primitive neuroectodermal tumour
    a. Neuroblastoma
    b. Ganglioneuroblastoma
    c. Neuroepithelioma
    d. Extraskeletal Ewing's sarcoma

PARAGANGLIONIC TUMOURS

Malignant Paraganglioma

EXTRASKELETAL CARTILAGINOUS AND OSSEOUS TUMOURS

1. Extraskeletalchondrosarcoma
    a) well differentiated
    b) myxoid
    c) mesenchymal

PLURIPOTENTIAL MESENCHYMAL TUMOURS

Malignant mesenchymoma

MISCELLANEOUS TUMOURS

1. Alveolar soft part sarcoma
2. Epitheloid sarcoma
3. Malignant extra rena rhaboidtumor
4. Desmoplastic small cell tumor

FIBROSARCOMA

The term fibrosarcoma conclude to its cells resemple normal fibroblast. The incidence and behaviour of this neoplasm greatly vary. Recently the incidence of fibrosarcoma is declining due to refinement of histopathological categorisation of sarcoma. The advent of immunohistochemistry, cytogenetics and molecular genetic techniques also contributing.

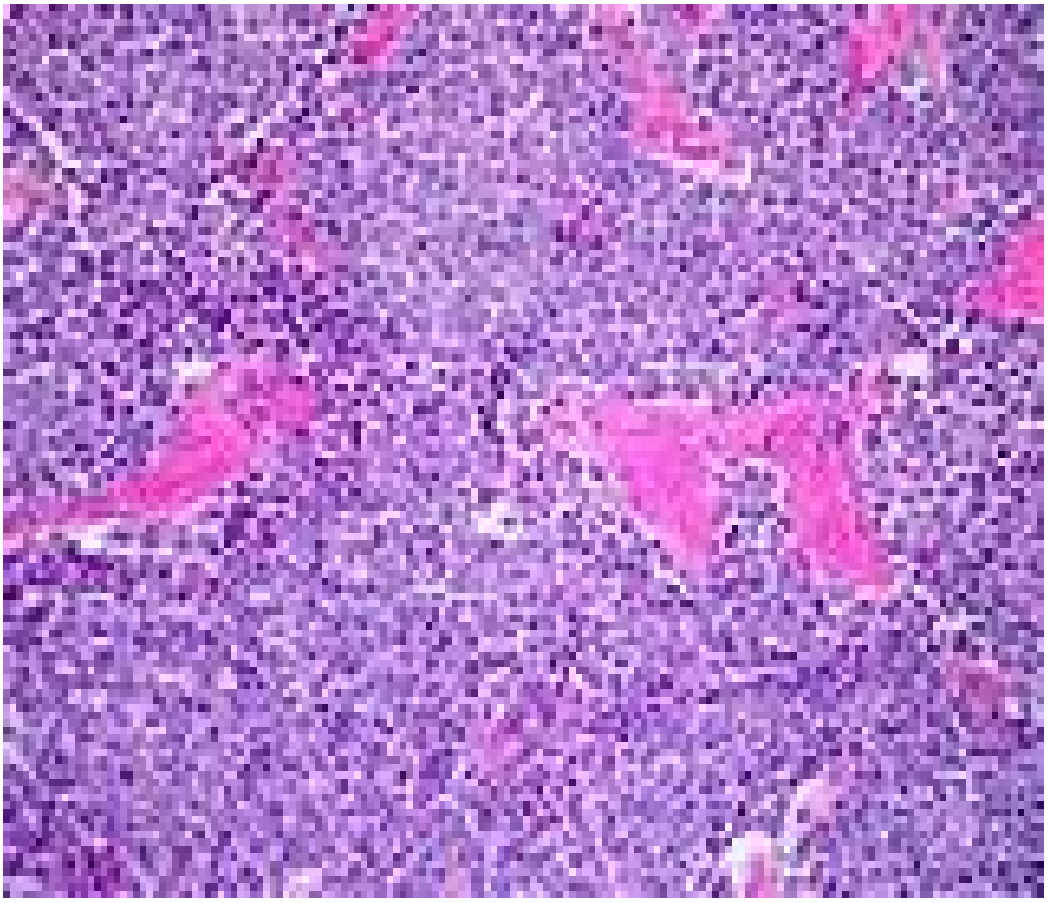
Classification of fibrosarcoma

Classified as adult type and juvenile/infantile type. Adult type further classified as classic, myxoid, fibromyxoid and sclerosing epitheloid. 45% occurs in lower extremities, 28% in upper

extremities,17% in trunk and 10% in head and neck. Commonly present as painless mass predominantly involve deep structure.

PATHOLOGY

The histologic picture is uniform fasciculated growth pattern consisting of fusiform or spindle- shaped cells. It is histologically graded as high grade fibrosarcoma and low grade fibrosarcoma by appearance and collagen content.It express vimentin which is used for immune histochemical identification. This tumour compossed of elongated fibroblastic cells with indented nuclei predominantly rough endoplasmic reticulum.



MALINGNANT FIBROUS HISTIOCYTOMA SLIDE

MALIGNANT FIBROUS HISTIOCYTOMA(PLEOMORPHIC UNDIFFERENTIATED SARCOMA)[5,7,9]:

It is common in late adult life range of 50 to 70 years. Has range of histological types as storiform pleomorphic, myxoid,giant cell and inflammatory. It is most common type soft tissue sarcoma, consisting mixure of pleomorphic and storiform areas. Frequently occur in lower extremity followed by upper extremity and retroperitoneum.But

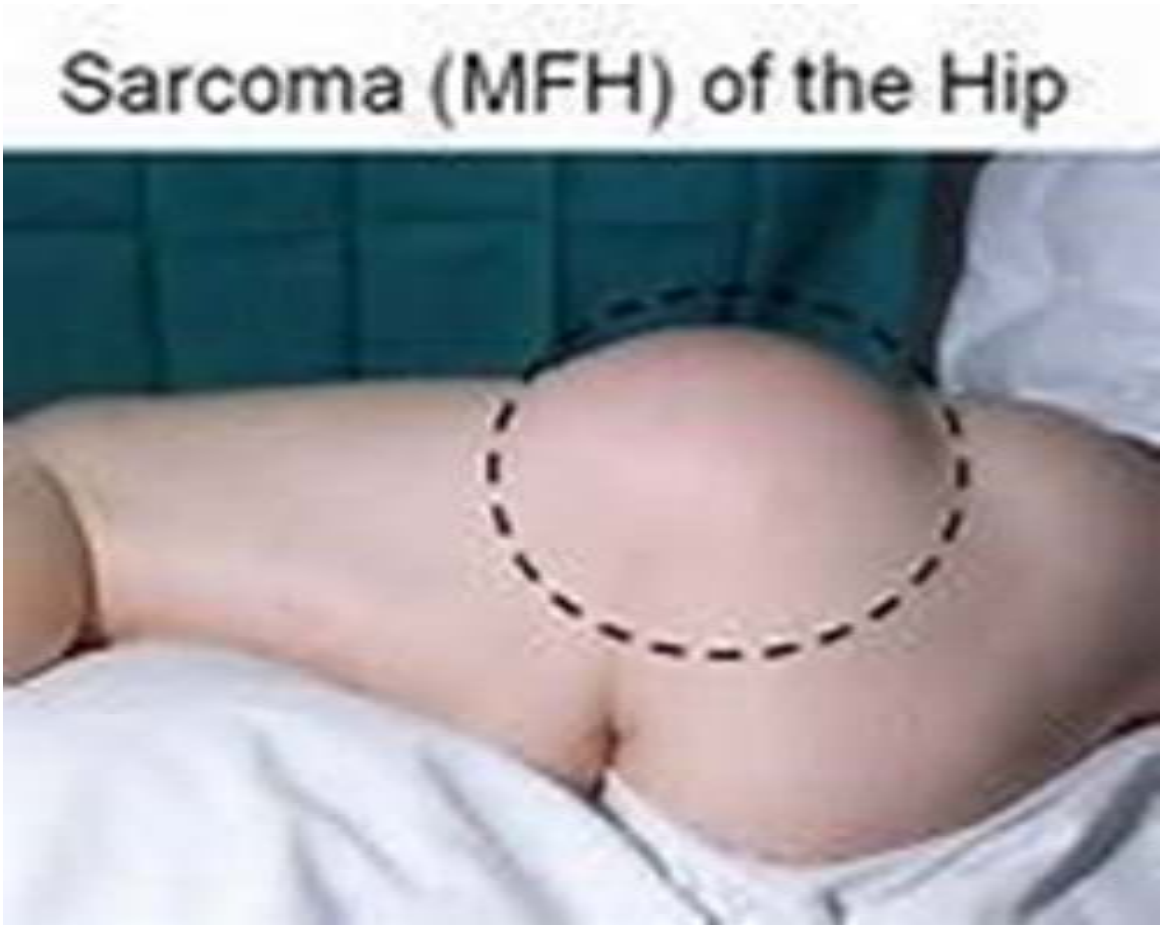
inflammatory fibrous histiocytoma frequently occurs in retroperitoneum.

Previous radiation is an important etiologic factor. Inflammatory fibrous histiocytoma may develop subsequently second neoplasm.

PATHOLOGY

The term sarcoma is Greek for “Fish flesh”,reffering tumour’s tendency to feel fleshy when palpated,Mesodermal cells give rise to the connective tissues distributed throughout the body including pericardium,pleura,blood vessel, endothelium, smooth and striated muscle, bone, cartilage and synovium are the cells from which all sarcomas orginate. Consequently sarcomas develop in a wide variety of anatomic sites.

Approximately one half of all STS occurs in extremities, most common histopathologies are malignant fibrous histiocytoma,followed by liposarcoma. Several histologic types of sarcoma have been characterized. This characterisation can be difficult and is aided by electron microscopy.



Vimentin , S-100, desmin , factor VIII, keratin , myoglobin and actin are the common immunohistochemical staining used for proteins. often facilitates reliable histo typing one of the pathologic hallmark of STS distinguishing it from carcinoma is the tendency of STS to spread by hematogenous means.

Metastases are uncommon in patients with low grade STS. Lymph node metastasis is rare,occurs in less than 3% of patients.

The histologic sub types with highest incidence of lymph node metastasis are:

a) Epitheloid sarcoma 16.7%

b) Embryonal rhabdomyosarcoma

c) Angiosarcoma

d) Malignant fibrous histiocytoma

e) Synovial sarcoma

Grading[5,9]

Broders identify the first grading system for STS when he analysis of squamous cell carcinoma. He demonstrate the 4-tiered system,That was based on mitotic rate, percentage of giant cells, and number of fibrous stroma in fibrosarcomas.

Low Grade tumours includes grade 1-2 (G1-G2) and High grade tumours includes grade 3-4 (G3-G4).The American Joint Committee on Cancer Union Against Cancer (AJCC/UICC) staging system utilize cellular differentiation as main base of 4tiered system.

Tumour necrosis, mitotic rate,and cellular differentiation are considered in the French Federation of Cancer Centers (FNCLCC) system,whereas the histologic variety, cellular differenciation, cellular pleomorphism, and mitotic activity are considered in 3-tiered National Cancer Institute (NCI) system .In both 3-tiered systems low grade is (G1) and high grade tumors are(G2-G3).

Staging[7,9]

Outcome not only based on histological grade.Staging systems uses other factors for prognosis.The Musculoskeletal Tumour Society(MSTS) staging system, called Surgical Staging System (SSS), That includes malignancy grade, atypical histology, and mitotic index, all three defined tumour may be grade Low (G1) or grade High (G2).Intracompartmental(T1) and extracompartmental (T2) difference also made.

Tumours which confined to a particular compartmental site is called as Intracompartmental tumours, other hand tumours which infiltrate into, or extend beyond the particular compartments is known as extracompartmental. The absence metastasis (M0) or presence of metastasis (M1) in last division.

TABLE 1.Surgical Staging System (SSS) of soft tissue sarcoma

Stage	Description	Grade	Site	Metastasis
Stage IA	LG,IC	G1	T1	M0
Stage IB	LC,EC	G1	T2	M0
Stage IIA	HG,IC	G2	T1	M0
Stage IIB	HG,EC	G2	T2	M0
Stage III	LG (or) HG with metastasis	G1-2	T1-2	M1

LG-Low grade, HG-High grade,

IC-Intracompartmental, EC-Extracompartmental,

The accurate prediction of STS prognosis is a problem. An attempt towards better result of outcome has been made in nomograms, which developed at MSKCC.

TABLE 2.AJCC TNM classification

Primary tumor (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor_ 5cm
T1a	Superficial tumor
T1b	Deep tumor
T2	Tumor> 5cm
T2a	Superficial tumor
T2b	Deep tumor
Regional lymph nodes (N)	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis
Distant metastasis (M)	
MX	Metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Histologic grade (G)	
GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Poorly differentiated or undifferentiated

TABLE 3.AJCC TNM classification

Stage	Tumor (T)	Node (N)	Metastasis (M)	Grade (G)	Description
StageI	T1a-T2b	N0	M0	G1-2	LG
StageII	T1a-T2a	N0	M0	G3-4	superficial HG
StageIII	T2(T2b)	N0	M0	G3-4	Large deep HG
StageIV	Any T Stage	N1	M0	Any grade	Lymph node Mets +
	Any T Stage	N0	M1	Any grade	Lung metastasis +

LG-Low grade, HG-High grade.

Surgical margins

Enneking reffered margins clearance of surgery based on depth and length of healthy tissue surrounding the resected tumour.Surgical clearance margins separated to radical, lenth, marginal.Intracompartmental tumours removal called as radical excision.Intracompartmental resection, with normal tissue excision surrounding the mass called as Wide margin clearance.The plane of dissection is within tumour zone or false capsule of the tumour called as marginal Resection.

Surgical margins classification is defined by the UICC, they are R0,R1,R2. R0 means no inresidual disease, R1 means microscopic disease,R2 means macroscopic disease.

It clearly demonstrated that positive surgical margins have negative prognosis.A recent gernals defined the clearence of 2-3 cm tumour margins is not possible, but it is followed in so many hospitals. so the need for ablative procedures when using a 2-3 cm margin instead of 1 cm. Enneking's compartmental surgery an intact fascia is enough clearance.

GENETIC ASPECTS OF SOFT TISSUE SARCOMAS (STSs)

Natural course and genetic features of STSs

The term sarcoma originates from the Greek language and means "fleshy growth".

[3,7]Sarcomas are malignant tumours of mesenchymal origin that can arise almost anywhere in the body. The most common location is in the extremities (the arms, legs, hands, or feet) where about 50% of the tumours are found. The trunk occurrence may be 40% (chest, back, hips, shoulders, and abdomen), and Head and neck occurrence may be 10%. The Sarcomas account for approximately 1% of all adult malignancies and 20% of pediatric malignancies.

One of the clinical features of sarcoma is that in the early stages they do not usually cause clinical symptoms. This is related to the fact that soft tissues are relatively elastic, and the tumours may grow large, pushing the normal tissue, before they are felt or cause any problems. Sarcomas generally are capable of invasive or destructive growth and the patients frequently develope recurrence and distant metastasis forming secondary tumours. Radical surgery is usually required to ensure total removal of these tumors.

The natural course of sarcomas is highly variable. For example, some sarcomas such as dermatofibrosarcoma protuberans rarely metastasise, while other types such as malignant fibrous histiocytoma (MFH) do so with alacrity. Because of the general aggressiveness of STSs and the frequent use of extensive surgery, development of prognostic and diagnostic markers is advocated. Until today, parameters such as tumour size, location, necrosis, intra-vascular invasion, histopathological malignancy grade, and the treatment of the tumour have been shown to have prognostic value.

The histopathological classification is a challenging task. More than 50 subtypes of proliferative soft tissue lesions are presently defined. Until today, the most common types of STS diagnosed have been malignant fibrous histiocytoma (MFH) and liposarcoma (LPS) that together account for 35% to 45% of all sarcomas.

The classification of STSs has not stayed constant over the years, but is regularly re-evaluated and re-formulated. For example, the MFH entity that was introduced forty-two years ago by Ozzello*etal* 51 has recently been challenged to its mere existence 16 by Fletcher and co-workers 52. Similarly, the gastrointestinal stromal tumor (GIST) entity was introduced by Stout 53 and Martin et al. in early 1960s and today

several abdominal STSs are classified as GIST that would have been diagnosed as e.g. leiomyosarcoma a few years earlier 55. Nevertheless, many of the tumours still lack clear-cut diagnostic foundation, especially when the tumours exhibit an undifferentiated morphology. Therefore, new specific molecular genetic markers are become very useful in the clinical evaluations of STSs.

STS tumours constitute a highly heterogenous group of tumours, for which genetic characterization is still limited. Therefore, the aims of this thesis has been to extend the knowledge of genetic and molecular alterations involved in the progression and metastasis formation of this tumour group.

2.2 Chromosomal events in STSs

The value of cytology and molecular genetics already well developed in pratical and clinical investigation of hematological malignancies, and specific gene dearrangement are used for diagnostic, prognostic and therapeutic purposes. Same method is presently applied for sarcomas, where so many chromosomal alterations, mostly reciprocal translocations, have been associated with distinct histopathological entities. In some status, different oncogenic fusion genes defect (or) mutation are associated with a single type of cancer.

Specific translocations result in fusion genes in STSs

On the genomic level fusion genes commonly result from breakage within introns of the two partner genes whereby exons with the same 5´-3órientation are joined in frame, enabling the translation of a functional new protein from the resulting fusion transcript. A series of specific translocations and fusion genes have already been reported and associated with certain STS subtypes (Figure 4). For example, a translocation t(12;16)(q13;p11) is found in more than 90% of myxoid LPS. Through this rearrangement the fusion gene *FUS-CHOP* is created and expressed specifically in the tumour cells. Although the same genes are involved in each case, variations on the base-pair level are frequently seen which are mainly attributed to varying 17 breakpoints in the FUS (TLS) gene (Figure 3) 56-59. Furthermore, myxoid LPS without a typical t(12;16)(q13;p11) may instead carry a *EWS-CHOP* fusion gene resulting from a t(12;22)(q13;q12). However, both these fusions lead to the same sarcoma subtype displaying indistinguishable histopathological features 60.

Altogether at least 25 fusion oncogenes have been described in STSs (Figure 4). Most recently, a novel fusion gene *FUS-BBF2H7* resulting from t(7;16)(q33;p11) was found in low grade fibromyxoid

sarcoma 61. Notably, it is common that the same partner gene is involved in different fusions, which can each be associated with different tumor phenotypes.

For example, the *EWS* gene has been found fused to one of nine partner genes, giving rise to five different types of STS (Figure 4) 62-70. Some of the *EWS*-fusions are associated with very aggressive clinical tumour progression, e.g. desmoplastic small round cell tumor 69. The *FUS* gene is reported to be involved in three different fusion genes 61, 71, 72, that are each associated with a different type of STS.

Obviously, these specific fusion genes and their phenotypes are tightly linked with each other, but the exact mechanism behind the specificity is still unclear. The expected pathogenic importance of the fusion genes is supported by the observations of chromosome translocations as the sole cytogenetic anomaly in a significant proportion of STSs (Figure 4). However, in several instances it still needs to be established whether STS fusion genes represent the first tumour initiating events or are proceded by other events not detectable on the chromosome level.

Amplicons are common findings in STSs

In addition to chromosome translocations, other recurrent aberrations are also found in STSs such as double minutes, ring chromosomes and giant rod chromosomes.

These alterations are non-randomly distributed and commonly involve amplifications and over-expression of genes in the target regions. Ring or giant rod marker chromosomes with amplification of 12q13-15, play a key role in lipomatous tumor development 73, 74. Well-differentiated LPS frequently involve several genes known to be amplified in human STSs, e.g. *MDM2*, *SAS*, *GLI*, *CHOP* and *CDK4* in the chromosomal region 12q13-15. Recently, Tallini et al. showed that the HMGA gene is commonly over-expressed in well-differentiated LPS with ring or rod chromosomes and amplification of 12q13-15.

The region 1q21-23 is also commonly involved in amplifications, and includes the *COAS2* gene as reported by Nilsson et al. By FISH, the most common localization of extra *COAS2* signals in lipomatous tumours was demonstrated to be in supernumerary ring and giant marker chromosomes.

In malignant fibrous histiocytoma (MFH), the *MASL1* gene has been suggested to be the oncogenic event driving the amplifications of the chromosome region 8p23.1 78.

Mutation of the C-KIT and PDGFRA genes in GIST

In addition to specific alterations that can be revealed at the cytogenetic level, STSs also demonstrate recurrent genetic alterations of more discrete types. A good example is provided by the gastrointestinal stromal tumours (GISTs) that show mutations and/or over-expression of the *C-KIT* and *PDGFRA* genes.

GISTs are the most common mesenchymal tumors of the gastrointestinal tract, representing approximately 20-30% of all STS in this location. The majority of GISTs exhibit mutations in *C-KIT* that cluster in four hot spot exons (9, 11, 13 and 17) and are especially frequent in exon 11. In GIST, the *C-KIT* mutations regularly alter or delete one or more amino acids, but are always in frame. This then leads to changes in the juxta membrane domain of the c-kit protein and tyrosine kinase activation without binding of the stem cell factor (SCF) ligand. The resulting constitutive expression of c-kit in turn results in altered cell proliferation and tumorigenesis . GISTs with *C-KIT* mutation are more likely to be of high malignancy grade, and are characterized by more

frequent recurrence and a higher mortality rate than tumours with wild-type *C-KIT* only.

GIST tumours with a *C-KIT* mutation are also responsive to treatment with Imatinib, a drug that inhibits the c-kit tyrosine kinase, and which is applied to patients with inoperable or metastatic disease. However, acquired resistance to Imatinib may develop after a period of treatment. Additional mutation of *C-KIT* is one possible explanation for the observed resistance. Most recently, Heinrich and co-workers found that approximately 35% of GISTs lacking C -*KIT* mutations carried activating mutations in the related receptor tyrosine kinase gene, platelet-derived growth factor receptor alpha (*PDGFRA*).

Tumours show*C-KIT* or *PDGFRA* oncoprotein spect to activation of were found to be indistinguishable with respect to activation of downstream signalling intermediates and cytogenetic changes associated with tumour progression. Therefore and *C-KIT,PDGFRA* mutations appear to be alternative and mutually exclusive oncogenic mechanisms in GISTs.

There are two hot spot exons for PDGFRA mutations, i.e. exons 12 and 18. Taken together both *C-KIT* and *PDGFRA* mutations contribute to more than 80% of GISTs.

PROGNOSTIC ASPECTS OF SOFT TISSUE SARCOMAS

Histopathological markers

Clinical and histopathological markers of documented prognostic value include e.g.malignancy grade (high grade III or IV), tumor size (>8 cm or >11 cm), tumor depth (deep location), tumor localization and surgical margin. Presence of necrosis and high mitotic count are similarly established markers.

As shown by us and others one of the best parameters is tumour size, which in turn is also related to the location of the tumour. For example, STSs located in the distal extremities are often small and superficial when diagnosed. On the other hand, the prognosis is usually better compared to the tumours located intra-abdominally, where the tumours are usually rather large already at the initial diagnosis.

The value of malignancy grade as prognostic variable for STSs has been reported. The features that define the grade are strongly linked with the degree of cellularity, differentiation,necrosis as well as the number of mitosis, that may also on their own be of prognostic value.

Immunohistochemical markers

Vascular invasion, metastasis and local recurrence are features of an aggressive tumour phenotype. Many immune hiostochemical markers studied are therefore chosen to reflect the three cornerstones of tumour growth, i.e. cell proliferation, apoptosis, and angiogenesis. For example, factor VIII measures vessel density, Ki-67 is a marker of proliferation, and the p53, p27 and Bcl2 proteins are all related to the regulation of the cell cycle and hence linked to apoptosis.

Increased expression of IGF1-R was seen in some malignancies in cases with metastatic disease ,while in high grade STS the IGF-1R expression was associated with favourable outcome.

Furthermore, expression of CD44 and ezrin are associated with cell adhesion, and related to the cell migration and metastasis. *Over-expression of ezrin is related to poor outcome.*

The tumour phenotypes that will usually lead to metastastic behaviour include the capacity of tumor cells to migrate within tissues, transmigrate through vessels and to adhere to the metastatic organs. Since metastasis are the main cause of death in cancer the identification of genes that regulate tumour cells migration may therefore lead to improved therapeutic strategies.

Recently, ezrin was identified as a key component in the metastasis of tumors as reported by several authour. In general, the role of ezrin in tumour metastasis was based on two of the major reasons: A) ezrin is best known to connect membrane proteins to the actin cytoskeleton, through the adhesion molecules that are known to depend on the ezrin-mediated linkage to actin, such as CD44, and are directly related to the invasion and metastasis of tumors B) The ability of ezrin to confer metastatic capabilities to tumors, which has been proved in experimental models, for example, mouse model of osteosarcoma and osteosarcoma in dogs.

The over-expression of ezrin in malignant tumours and its relation to poor outcome have been reported in carcinomas, such as, prostate cancer, glioma and melanoma. Concerning mesenchymal tumors, involvement of ezrin has been discussed for gastrointestinal stromal tumors, osteosarcoma and rhabdomyosarcoma . In this thesis the impact of ezrin expression as a prognostic marker in STS was further evaluated.

Genetic markers

Genetic markers represent a field of increasing importance in STS diagnostics and prognostics. In general, the oncogenes, which can induce malignant transformation and cell proliferation, have been implicated in the development of STSs. In the majority of cases, oncogene activation result from chromosomal rearrangements or gene amplifications. Changes of the microenvironment of the gene, for example following epigenetic modifications, must also be considered. Examples of oncogenes linked to STSs are *C-KIT* and *PDGFRA* mutations in GIST, and fusion oncogenes such as *SS18-SSX* in 90% of synovial sarcoma. In contrast, the tumour suppressor genes (TSG) play a critical role in cell growth and dictate the cell program to apoptosis. In contrast to oncogene activation, loss or change of the TSG function commonly result from deletions or discrete mutations. Two major TSGs that are relevant to STS are the *RB1* and the *TP53* genes.

Approximately 30%-60% of STS have been reported to harbour aberrations of the *TP53* gene, including a subset of patients with germ-line mutations i.e. the Li-Fraumeni syndrome.

Clinical Presentation

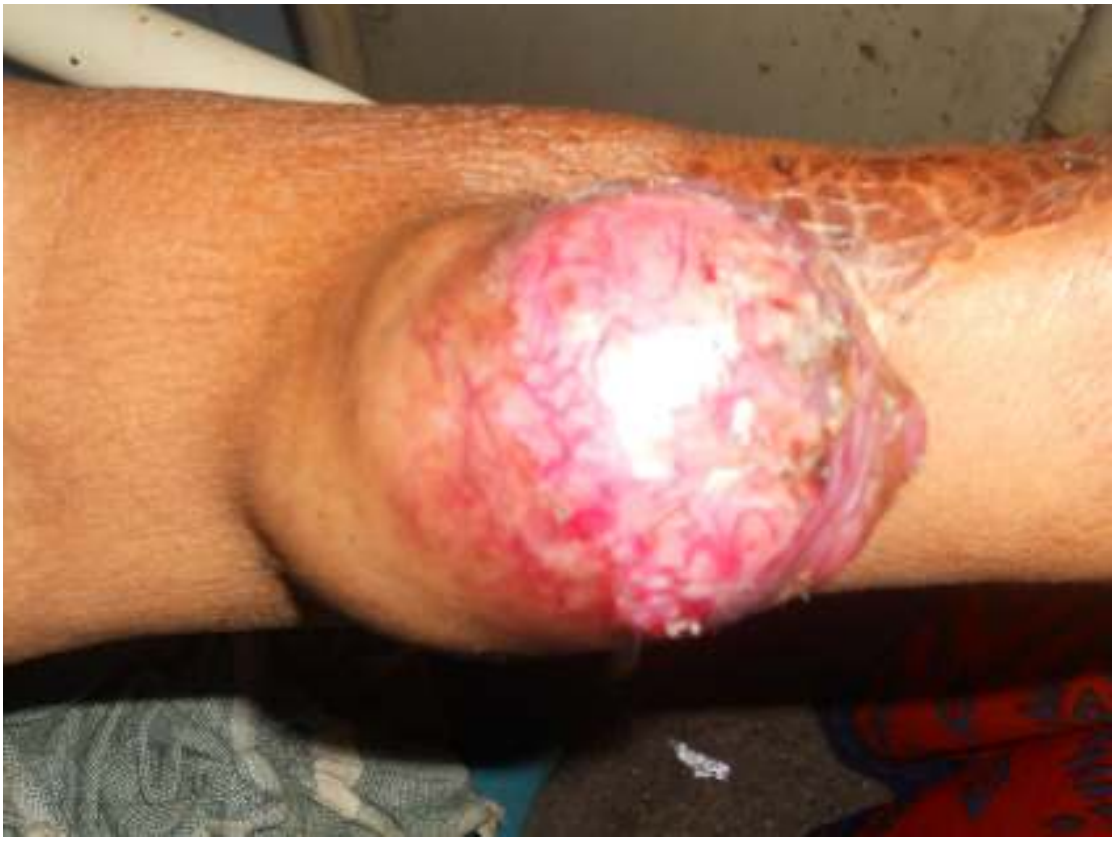
Most of the patient came with c/o painless mass, although the pain is noted half of the patient. No specific abdominal discomfort and GI symptoms in intra abdominal or retroperitoneal STS.

The most common differential diagnosis for extremities and trunk lesion being bleed collection or muscle mass leads to delay in diagnosis.

Diagnosis

Physical examination

Assess tumour size and movement of the mass, fascia intact or not,and near by neurovascular and bony infiltration present or not, and regional lymph node assessment.



FUNGATING MASS OVER THE LOWER EXTREMITIES

INVESTIGATIONS

1.**Biopsy**-The Primary thrust is to obtain adequate tissue for histopathologic examination, to assess the grade, and to define the prognostic factors that may help the patient for definitive treatment.

- Indications

Any soft tissue mass in an adult that is symptomatic or enlarging is greater than 5cm in size and any new soft tissue mass that persists beyond 4-6 weeks.

- Technique

Small superficial mass (<5cm) –excisional biopsy with clear margins in the preferred approach.

Large mass- incisional biopsy with a longitudinal incision (extremity lesions) to facilitate subsequent wide locall excision. Incision carried out by center of the mass with most superficial location.

Hemostasis should be adquate to prevent dissemination of tumour cells into other normal tissue planes.

Wide local resection of a previously biopsied sarcoma, the previous scar may be excised with the tumour. Biopsy specimens should be sent fresh, sterile and anatomical site orientation marked for pathologic studies..

FINE NEEDLE ASPIRATION CYTOLOGY

FNAC has been examined by a number of authors but is usually confirmed to the diagnosis of recurrence first, then for the primary diagnosis.

Imaging[9,15]

For appropriately assess the staging of STS,Radiological imaging are required and surgical approach as well as RT/CT treatment. Aim are to Identify anatomical site, tumour size, homo/hetrogeneity, and calcification present or not. Infiltration into, nearby vital structures present or not is essential for treatment approach.

X-ray is the first-line imaging method. Because of inexpensive and readily available, underlying bone involvement can be assessed. Also plain xray identify involvement of phleboliths of hemangiomas.

Extremity STS the main imaging modality are MRI.MRI have specific morphological images data, multiple-plane imaging, and no ionizing radiation load make the MRI for detection,delineation, differential diagnosis, and Treatment response monitoring, and also for postoperative follow-up. MRI used for guided needle-biopsy.fascial involvement presents or not and invasion of a tumour to adjacent structures have better idea for surgical planning.

CT is preferred imaging modality for the trunk and retroperitoneal STS, and also tumour bony invasion. CT is also the imaging of choice for patients not fit for MRI. Its available and cheap,so USG can sometimes

be used for solid and cystic masses. It's most useful in guided needle biopsy. vascular supply of tumors and vascular lesions Magnetic resonance angiography gives better information.

Positron emission tomography (PET) with ^{18}F-fluorodeoxyglucose (FDG) has advanced tool in STS imaging.Tissue glucose metabolism activity can be identified by FDG. Functional imaging PET scan used for STS tumour identification, differential diagnosis, imagine guided biopsy, for identify the difference between recurrences and therapy-related changes, and treatment responce monitoring.preoperative TNM-staging can be assessed by PET with CT.Assessment of tumor cell proliferation may be done using^{18}F-fluorothymidine (FLT), but only experimental use.

Plain chest radiographs essential of choice for all STS patients to ruleout mets,Most STS distant metastases are found in the lungs.Chest CTscan for all patients as the primary modality to R/O lung mets.with primary CT recommended for >5cm high grade lesions only. Plain chest radiographs diagnosis most lung mass and recommending chest radiographs for all patients, and primary CT only for patients with an abnormality in these. In addition, chest CT is recommended for patients

with large, deep, or grade 2 (or) 3 tumors, and other biologically aggressive histological subtypes.

CT SCAN

Provide information on the size of the lesion and its relationship to adjacent structure and organs.

MRI

- Examination of choice for imaging of soft tissue masses
- Enhances the contrasts b/w tumor and muscle, and b/w tumor mass and adjacent blood vessel.
- Provides superior 3 dimensional definition of fascial planes (These substantial advantages allow for improvement assessment of respectability with pre operative MRI evaluation)

NEWER INVESTIGATORY TECHNIQUES

Phosphorus magnetic resonance spectroscopy

- It is a form of noninvasive resonance spectroscopy that detects phosphorus containing metabolites.

- Employed to evaluate sarcoma inorganic-to-organic phosphate rations.
- In- vivo metabolic assessment of response to anti-neoplastic therapy.

Positron Emission Tomography (Pet Scan)

- By evaluating tumour metabolic activity PET scan may permit noninvasive assessment of tumour grade.

RadioNuclide Scintigraphy

- Thalium- 201 and gallium-67 in osseous sarcoma
- Gallium-67 in STS and in the assessment of patients with metastatic and recurrent STS.

RadioImmunoScanning

- I radioloabelled anti- sarcoma localizes foci of metastatic disease.

NATURAL HISTORY AND SURVIVAL

Painless mass is the characteric feature of STS, has a tendency to grow in anatomical compartment and along fascial planes take longer time for pseudocapsule around the tumour was created by growing mass

compresses the surrounding tissues. The tumour usually infiltrate into the surrending region beyond the falsecapsule, and simple “shellout” occur.

STS metastasis,Primarly occur in the Lung. with 17-20% of the patients developing pulmonary metastases . Median survivalis <12 months only after detection of lung metastases.

3-5% of STS only had Lymph node metastasis.Regional lymph nodes metastasis usually occur in rhabdomyosarcoma, epitheloid sarcoma, clear cell sarcoma, angiosarcoma, and possibly synovial sarcoma. Sentinel node biopsy for extremely rare sarcomas has been considered.

PROGNOSTIC FACTORS

1. A small disease-free peroid and inadquade pulmonary resection are important prognostic factors for survival of patients with pulmonary metastasis.
2. The presence of multiple metastatic pulmonary nodules (>3) is an adverse prognostic factor.
3. Tumor doubling time (TDT)
4. The most important prognostic factor is the possiblities to resect surgery all disease completely.

Table 4 MS-KCC sarcoma prognostic factors

	Favorable Factors	**Adverse Factors**
Size	<5 cm	>5cm
Site	Superficial	Deep
Histologic	Low	High

Prognostic markers in soft tissue sarcoma

- tumour size
- malignancy
- grade
- high mitotic rate
- tumour necrosis
- surgical margin
- tumour depth
- proliferation
- growth pattern
- vascular invasion
- metastasis
- local recurrence

TRETMENT[7,9]

Primary treatment consists of radical surgery, eventually associated to radiotherapy.Unfortunately, a large proportion of the patients will subsequently relapse locally or develop metastases. Adjuvant chemotherapy has not been proved to increase overall survival, but a meta-analysis or adjuvant trials has demonstrated a significant improvement of Disease free survival (10% at 5 years), both in terms of control of the local tumor (5% at 5 years) and of the metastatic spread (9% at 5 years) [3].

Advanced disease and clinical trials

Inoperable locally advanced or metastatic disease at presentation, inoperable locoregional relapse and development of metastases are generally called “advanced disease”.

Systemic therapy is used for patients with advanced disease. Although responses and prolongation of progression free survival have been observed, this therapeutic approach is generally considered as palliative.

Cytotoxic agents that have demonstrated activity against soft tissue sarcoma are limited to doxorubicin, ifosfamide and dacarbazine. Multiple

randomized clinical trials have been carried out to optimize the combination of these drugs as first treatment for advanced disease (generally called first line therapy). So far, no combination has been shown to significantly improve survival when compared to doxorubicin administered as a single agent at a dose of 75 or 80 mg/m^2 every 3 weeks.

Investigational new drugs are generally considered as therapeutic options after failure of the first line combination therapy. Most of the cytotoxic agents tested in the clinic against other malignancies have also been tested against soft tissue sarcoma in phase II trials, but none of them has showed any substantial activity in terms of objective response.

Targeted therapies have recently brought new expectations for the treatment of soft tissue sarcoma. Mechanisms of carcinogenesis and tumour growth have been extensively studied for sarcoma, making them ideal candidates for targeted therapies. These expectations have been substantiated by the documentation of the activity of imatinib mesylate for Gastro-Intestinal Stromal Tumors (GIST), a sarcoma entity that has been identified relatively recently and is known to be insensitive to chemotherapy. In a trial including 946 advanced GIST patients, the 2-years survival estimate is close to 70%, as compared to 20% with standard doxorubicin based chemotherapy [4]. The success of imatinib

therapy for GIST is an encouraging example of the possibilities that can be offered by targeted therapies.

Specific histological subtypes are, so far, rarely addressed in clinical trials, and are not even often used for stratification. The difficulty to conduct histology specific studies resides in the limited potential accrual (in a subgroup of a rare disease), associated to the complexity and constant evolution of the histopathological classification. Inclusion of this heterogeneous group of diseases in clinical trials may have restricted the discovery of new agents to "large spectrum" drugs active against most of the frequent histological subtypes. Additionally, the referral pattern of individual centers and even of clinical research groups may be largely affected by the quality of the collaboration between medical oncologists and organ specialists at the institutional level. This may lead to "selection biases" and irreproducible results in clinical trials.

As an example, trials conducted in uterine leiomyosarcoma have shown a promising activity of the combination of docetaxel and gemcitabine, two agents that had failed "mixed histology" phase II studies .

Objective response to therapy has been used to document activity of new drugs since there commendation of the WHO in 1979. "Response"

is defined as an objectively documented decrease in the size of cancer lesions (subsequent to the administration of the drug), which translates a biological activity of the drug. WHO response criteria may not have been an optimal screening tool for new drugs in sarcoma: they used a complex response evaluation algorithm that was often misunderstood or misinterpreted; they ignored modern imaging techniques like computerized tomographic scans and magnetic resonance imaging, both largely used for the staging of soft tissue sarcoma; more importantly, they are not appropriate to document the activity of cytostatic agents (expected to stop tumor growth) that do not necessarily result in an immediate decrease of the size of the lesions. A few active agents may have been missed because of the use of inappropriate criteria.

Long disease stabilizations have been observed in recent phase II trials with trabectedin [6] and brostallicin [7], despite a limited number of objective responses. Both agents that are currently awaiting confirmation of their activity in controlled clinical trials.

The Soft Tissue and Bone Sarcoma Group (STBSG) of the European Organization for Research and Treatment of Cancer (EORTC) has conducted multiple clinical trials in softtissue sarcoma, with a particular focus on patients with advanced disease. Those trials data have

all been managed at the EORTC Data Center, using similar data collection forms, and similar database formats. A central pathology review by a panel of experts is mandatory for all trials subjects. The group has consistently used the French grading system since its first publication. As results, the group has accumulated a database of over 2000 patients treated with first line therapy for advanced soft tissue sarcoma, 380 patients from phase II trials in second or third line therapy, and 946 advanced GIST patients treated with imatinib in the largest clinical trial conducted so far.

SURGERY- PRIMARY THERAPY AND RESULTS

For patients with localized diseases, surgical treatment is the corner stone of treatment. The surgical approach to sarcomas is predicted on one pathologic fact and its clinical correlate. STS used to expand and infiltrate tissue line, introduce a pseudo capsule composed of normal tissue inter locullated in filmbrise of tumour.

For patients with limb sparing option a multimodality approach proceed for limb-sparing surgery joint with adjuvant chemo or adjuvant radiotherapy produce local control and disease survival rates to amputation, while preserving a functional extremity.

SURGICAL APPROACH

Pre-operative imaging studies (CT scan/MRI) have enabled accurate prediction respectability. Wide resection should emcomposs the skin, subcutaneous tissue and soft tissues of tumour, including proir biopsy site and associated drain sites or wound complications.There are no data to support compartmental or large muscle group resections over wide local excision with negative margins.

Tumour should be excised with a 1-2 cm margin of normal surrounding tissue since there are good approaches to facilitate local control this ideal target margin is frequently compromised as opposed to attempting major vascular or bony section.

There is no role in regional lymph node biopsy. Therapeutic lymph node biopsy results in a 40% actual survival patients with regional lymph node involvement who has no evidence of extra nodal disease.

Amputation became the treatment of choice for extremity STS because local recurrence developed in 90% of patients after simple excision. Today extremity STS limb-sparing multidisciplinary treatment approach commonly used.

SURGICAL TREATMENT OF EXTREMITY SOFT TISSUE SARCOMA

Amputation vs. limb[7,9].

In limb-sparing surgery recurrence rate was high about 26% but amputation group its low about 4%. A recent study on osteosarcoma patients gives result as decreased outcome in amputees, but better results in limp sparing surgery.There was, no apparente difference in quality of life.

Age of limb-sparing treatment, amputation is reserved treatment modality for extremity STS. Amputation reserved with advanced reconstructive techniques combined with RT and/or chemotherapy,

patients with intractable pain, uncontrollable local bleeding, ulcerated skin, local infection, or neurovascular infiltration, surgery of choice is amputation.

Amputation and prosthetic reconstruction is the fastest and most reliable method to gave the result of acceptable functional results. This may suitable for lower leg, ankle and foot tumours,wide range of activities achived by modern below-knee prostheses permit. In other

anatomic sites, particularly hand, the situation is quite different, and follow limb-sparing protocols.

Reconstructive surgery[5,7,9]

Large soft tissue and bone defects,usually not affect the blood vessels, nerves, joints, or bone is the character of Extremity STS.

Normal tissue moved one place to a different site with a vessel pedicle or vascular rearrangment known as' graft'. "Flap" either regain its blood supply by flap pedicle (or) new vascularisation has blood supply reestablished at the recipient site.

Classification of Flaps can be done according (local, pedicle or free flap) their blood supply , The flap reconstruction may be unipedicled, bipedicled or both. Flaps may be includes of skin, fat, fascia ,or bone as well as nerve, intestine or omentum. Examples are fasciocutaneous, myocutaneous, osseous flap. Combinations of these, three flaps also used.

Traditionally, reconstructive ladder" have used the method of reconstruction,by reconstructive surgeons. Usually doing simplest and safest method in attempting(i.e. lower down the "ladder").The "Reconstructive ladder" more complex reconstructive methods are free

flap,pedicleflap,localflap,skin graft. The less complex reconstructive method is direct closure.

Because of well-vascularized tissue in myocutaneous flaps that with stands in RT and chemotherapy well,They promote wound healing very well after enbloc resection. There were fewer complication, more limb salvage rate, and hospitalization time less .

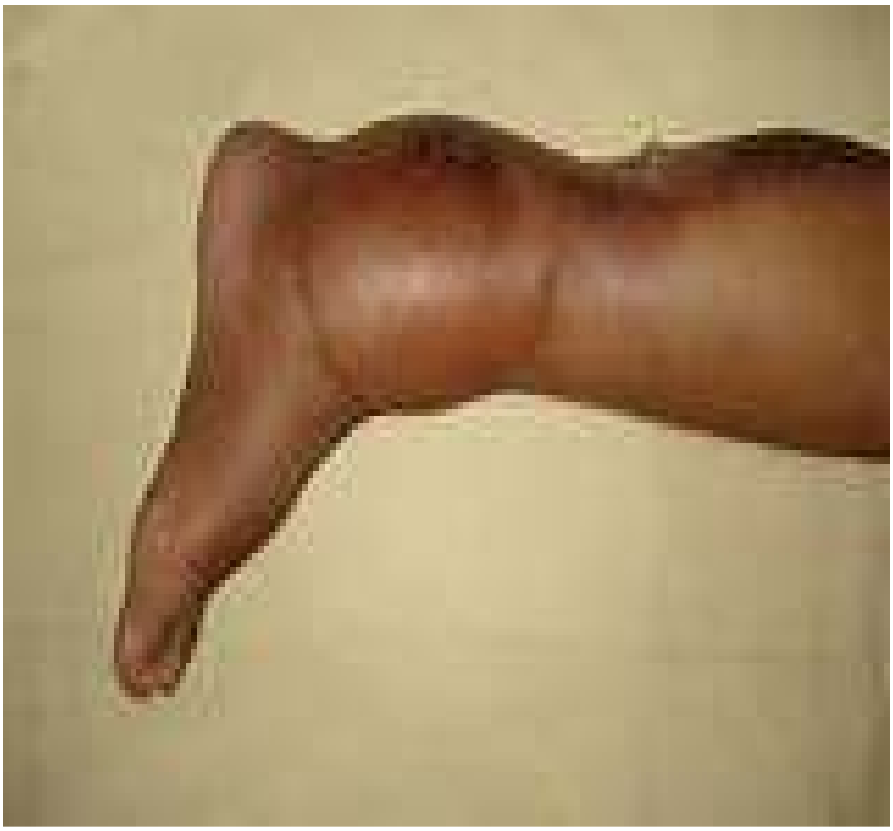
Microsurgical reconstruction in extremity soft tissue sarcoma

Pedicled vs. free flaps[7.9]

Pedicled flaps have advantages than free flaps are less procedure time, and less need of experence surgeon required .Blood and lymphatic flow disrupted by both local and pedicled flaps, pedicled flaps may be dearrange the remaining muscles in the affected limb, leading to further disrup of function. Excisions of large, deep seated STS,free flaps have been considered better suitable.

Free flaps have several advantages in extremity sarcoma resection and reconstruction.Free flap have without the limitations of rotational arcs and large soft tissue with un intrupted blood supply.

Skin, fascia, muscle, bone, and tendons, blood vessels, and nerves can be included in Composite flap and the well-vascularized tissue of free flaps is highly tolerable to wound complications, as well as to RT and chemotherapy.Chemotherapeutic agents delivery enhanced by high vascularity in the resection site.



FLAP RECONSTRUCTION IN EXTREMITYSTS

Choice of flap

After tumour resection factors influencing free flap choice mainly recipient site-dependent factors includes site, size, and depth,Which types of tissue requiring for functional reconstruction, and cosmetic

considerations. In addition to these, flap reliability and Previous surgery or RT, are the donor site-dependent factors and donor site morbidity all may be considered.

Upper extremity

Pedicle vessel LD or thoraco dorsal vessel perforator (TAP) flap commonly used for reconstruction of shoulder region and upper arm.Pedicled or free functional flap LD commonly used in the arm reconstruction surgery.

Pedicled radial forearm flap commonly recommented for elbow region. Repair of finger and wrist flexion or extension free gracilis muscle is well suited. Radial forearm, lateral arm, scapular, temporo parietal fascia flaps are Fascial or fasciocutaneous flaps, They are smaller and may be higher to muscle flaps. Fascial flaps produce well gliding surfaces for tendons.Finger reconstruction free toe transfer is a useful method.

Lower extremity

In the proximal thigh defects, pedicled rectus abdominis flaps can be used for reconstruction. Free flaps are commonly used for reconstruction of large defects of the distal thigh. Free LD flap needed

for large volumes defect.Pedicled gastrocnemius flaps used for defects covered around the knee. Middle lower leg defects may be covered with pedicled soleus flaps

In the distal third of the leg soft tissues are maintained and free flaps are used for coverage.

Reliable muscle or musculo cutaneous flaps are used for deep defects. The fascio cutaneous sural flap are used for small defects of the distal lower leg, ankle and proximal foot.ALT with the lateral femoral cutaneous nerve used for in sole of foot reconstruction.

Vascularised fibula derived from osteocutaneous or osteo musculocutaneous flap used for long bone defects of the extremities. Weight-bearing bones needed additional stability double-barrel configuration may be useful.

Functional outcome after free flap reconstruction, good functional outcome after extremity microvascular reconstruction can be achieved.

Pulmonary metastases

Recent guideline for pulmonary metastasectomy for STS of 27-39% good 5-year overall survival rates. In a resectable metastases and a controlled primary tumor patients.

Prosthetic considerations

After tumour resection, limb sparing surgery, free flap reconstruction ,Functional results are generally good. Below-knee prostheses are very functional and better normal activities. Upper limb prosthesis performance was poor because only one joint can be moved at a time.

Improved neural machine interfaces technology used in myoelectric prostheses, combined with targeted reinnervation surgery .

Radiotherapy

Radiotherapy is combined with surgery will results in good outcome. RT given either as external beam radiotherapy (EBRT), or brachytherapy. Placing catheters containing radioactive material into the site known as brachytherapy.

Adjuvant EBRT can be given by pre- or postoperatively, but thin doses of radiation and thinner surgical fields may be used when RT is given preoperatively (50 Gy), whereas postoperatively (60-66Gy). RT doses > 60 Gy have increased risk of fibrosis and impair functional outcome. But preoperative treatment may change the final histopathological examination.

Preoperatively RT treated patients had more acute wound complications, but postoperative treatment produce more late radiation-associated complications. Wound complications were more common in the extremity particularly lower extremities. No acute proper difference in outcome was made, but the postoperatively treated patients had significantly more pulmonary fibrosis, and more joint stiffness and edema.

Palliative radiotherapy may also be used in bone metastases or bleeding, compression symptoms or wound ulceration. Palliative radiotherapy decreasing spinal or mediastinal compression usually occur during metastatic disease.

RADIATION THERAPY- NEO-ADJUVANT AND ADJUVANT

Radiation therapy alone has been employed as primary treatment for STS for patients with locally advanced disease or for patients who present with stage IV metastatic disease.

Efforts to use RT as primary treatment have demonstrated that

1. High doses (>6500cGy) are required to achieve local control rates of 30% -60%
2. Local control rate is inversely proportional to tumour size.

In general, local control rates with RT alone are inferior to those following surgery.

Primary RT should therefore be reserved for patients.

i) Who are medically unfit

ii) Who have technically unresectable tumours

iii) Who refuse surgery as initial treatment

PRE-OPERATIVE RT HAS SEVERAL THEORETIC ADVANTAGES

1. The unmanipulated tumour allows for a smaller treatment field than postoperative radiation
2. Sterilization of tumour cells leads to reduced risk of intra vascular and would seeding with tumour cells at surgery
3. Reduction in tumour volume increases respectability rates (The adverse effects of preoperative radiation on wound healing balance these theoretic advantages)

Adjuvant external beams RT is designated to treat residual microscopic disease that extends beyond the primary tumour mass and the margin of resection.

Adjuvant RT has also been delivered using the brachytherapy technique.

- Involves either permanent placement of radioactive sources (gold-98 or iodine-131)
- Temporary placement of an interstitial implant with after loading catheters positioned in to the tumour bed at surgery (Usually iridium-192) on the 5^{th} or 7^{th} postoperative days to deliver 42 to 60 Gy over the following 4 to 6 days.

Chemotherapy

The favourable effect of chemotherapy obtained in Ewing sarcoma, osteosarcoma, and rhabdomyosarcoma. Chemotherapy useful in majority of paediatric sarcoma.

Adjuvant chemotherapy for STS is based on doxorubicin only or doxo with ifosfamide, or with mesna, ifosfamide and dacarbazine (MAID protocol). Chemotherapy results good for synovial and round cell sarcoma.

Down staging tumours prior to surgery, chemotherapy has been used preoperatively. Neo-adjuvant chemotherapy improve the recurrences

free and disease-free survival after treatment and local hyperthermia compared to chemotherapy alone.

The most commonly used chemotherapeutic agents are doxorubicin and ifosfamide, followed by taxanes and gemcitabine.

Molecularly targeted approaches

Gastrointestinal stromal tumours (GIST) have some new molecularly targeted treatment strategies like treatment with imatinib and similar drugs. Imatinib also shown effect in the treatment of DFSP.

SPECIFIC ANATOMIC SITES

SOFT TISSUE SARCOMA ON EXTREMITES

Extremities is the most common site for all STS. 2/3rd of STS arises from extremities. Out which ½ of STS arises from lower extremites, thigh is the most common site.

The most common histologic subtypes in adults are:

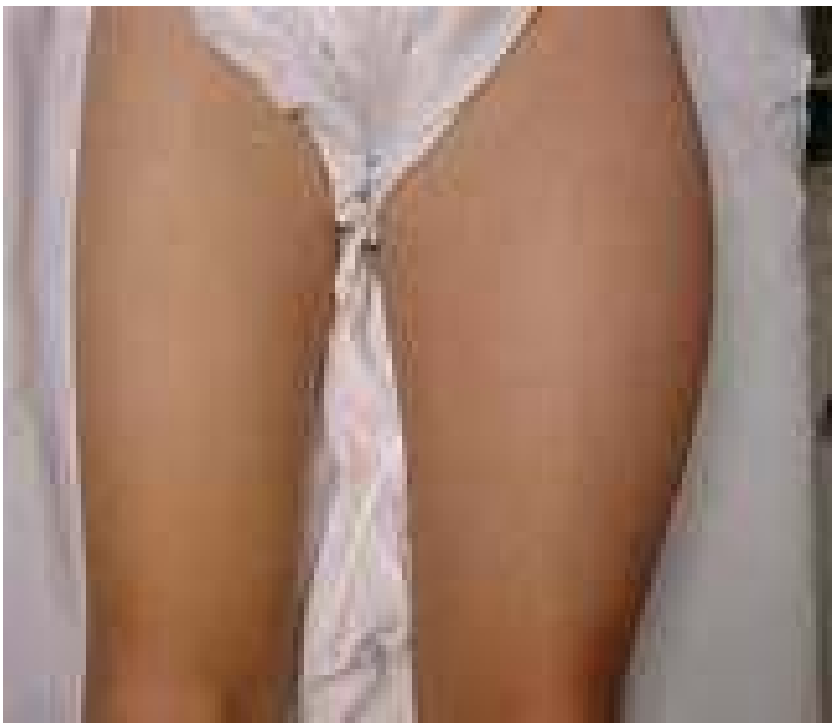
1. malignant fibrous histiocytoma
2. fibrosarcoma
3. liposarcoma

INVESTIGATION:

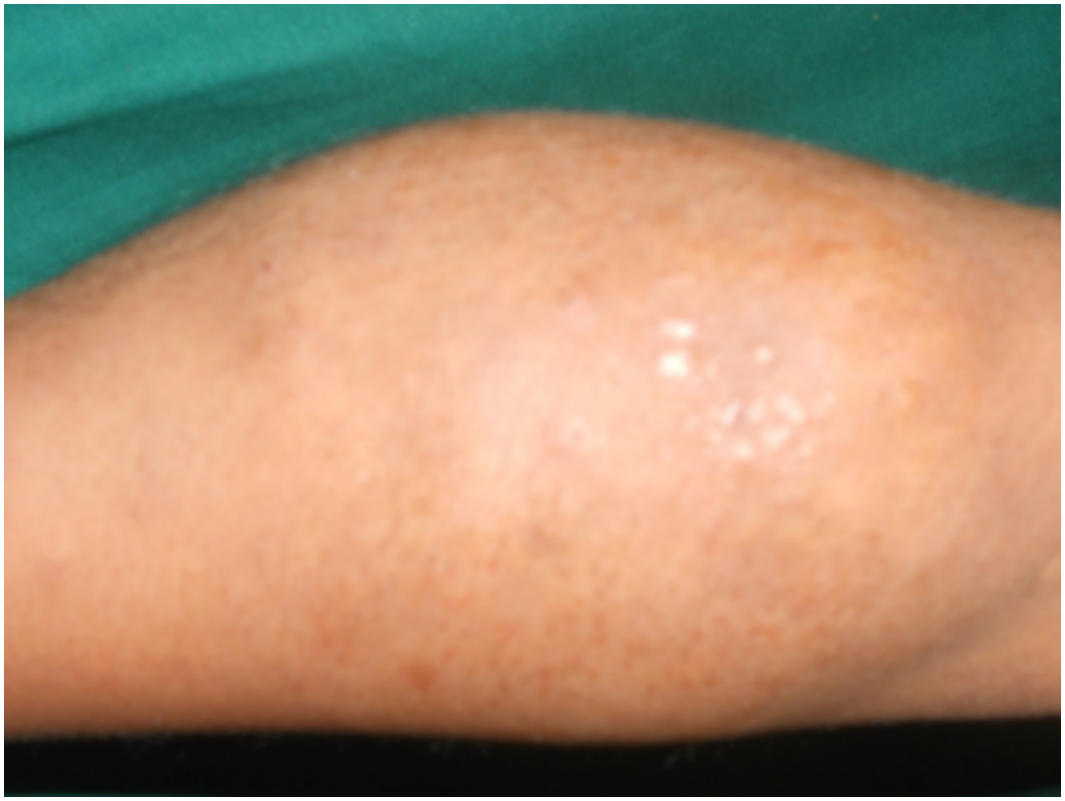
MRI is the choice for assessment extent of tumour. Core needle biopsy is the investigation of choice to conform STS.

TREATMENT

Previously ambutation was treatment of choice, now a days its followed very rarely. Limb salvage surgery is the choice. Micro surgery and isolated limb perfusion are achieved equal oncologial response.



LOWER LIMB EXTREMITIES STS



LOWER LIMB EXTREMITIES STS

SOFT TISSUE SARCOMA ON TRUNK:

Next to extremites ,trunk is the second most common site, painless mass is the most common clinical presentation. 1/3rd of STS arises from trunk.

The most common histologic subtypes in adults :

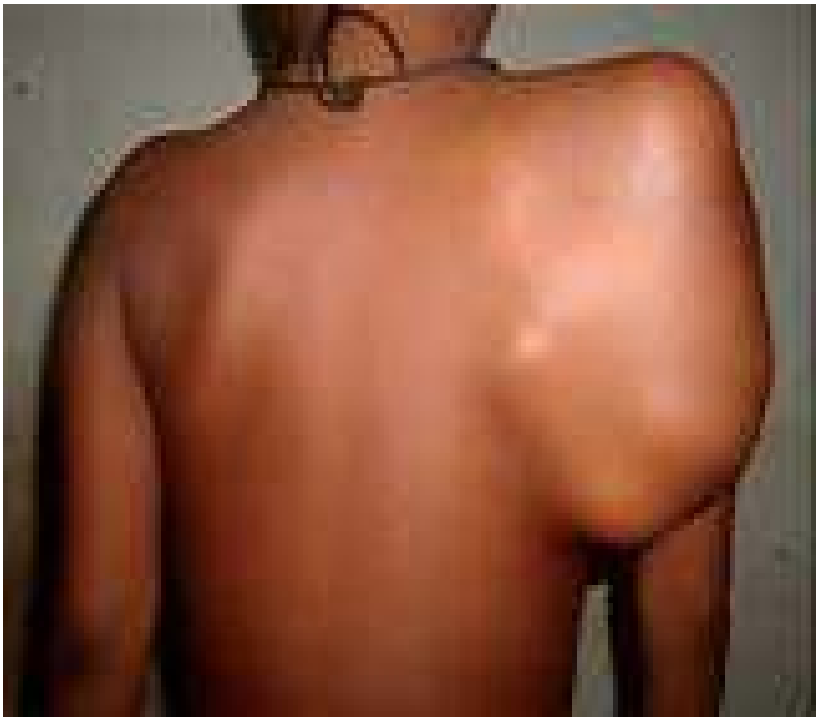
1. malignant fibrous histiocytoma
2. fibrosarcoma
3. liposarcoma

INVESTIGATION:

MRI is the image of choice, Core needle biopsy to conform STS

TREATMENT

Wide excision with adjuvant RT, in selected cases adjuvant chemotherapy.



SOFT TISSUE SARCOMA IN TRUNK

RETROPERITONEAL SARCOMAS

15% of all Sarcomas

Most common histologic subtypes are:

- Liposarcoma 42% of cases
- Leiomyosarcoma 26 % of cases
- Fibrosarcoma 6% of cases

PRESENTING SYMPTOMS AND SIGNS:

- Abdominal mass-80%
- Pain at presentation -50%
- Non-Specific gastrointestinal symptoms
- Neurologic symptoms (Primary Sensory)-27%
- Weight loss-7%

INVESTIGATIONS:

CT Scan and MRI

- Usefull to assess the consistency of the mass (cystic or solid) and to asses necrosis.
- Pinpoint the precise anatomic location and extent of any regional disease. Confirms the function of contralateral kidney**.**

DIFFERENTIAL DIAGNOSIS

Testicular neoplasm

Physical examination of testis, B-HCG and AFP, testicular ultrasound helps in differentiating.

Biopsy

In general, pre-operative needle biopsy should not be performed for most retroperitoneal tumours. For clearly unresectable lesions, or in cases in which physical examination or laboratory studies suggest lymphoma or germ cell tumor, a needle biopsy may facilitate the diagnosis.

Open biopsy or complete resection at exploratory laparotomy is the preferred to establish the diagnosis.

TREATMENT OF RETROPERITONEAL STS

The primary treatment is surgical resection with margins. With the possibility of en bloc multi organ resection to achieve negative margins (kidney, colon, or pancreas) the pre-operative bowel preparation and assessment of bilateral renal function is mandatory by CT scan.

Open biopsy or complete resection at exploratory laparotomy is the preferred means of establishing the diagnosis.

Treatment of retroperitoneal STS

Surgical resection with margins is the standard primary treatment. (With the possibility of en bloc multi organ resection to achieve negative margins (Kidney, colon, or pancreas), all patients should have pre-operative bowel preparation and assessment of bilateteral renal function by CT scan)

MOST COMMON REASONS FOR UNRESECTABILITY:

- Major vascular involvement (aorta, IVC), Peritoneal implants, or distant metastasis.

Partial resection/Debulking have been performed, but partial resection will not improves survival.

GASTROINTESTINAL SARCOMAS

Gastro intestinal sarcomas are uncommon, accouting for 4% of all sarcomas. The most common histologic subtype is leiomyosarcoma. With the exception of the oesophagus, which accounts for 5% of all GI sarcomas, the frequency of GI sarcoma declines as one moves distally along the gastrointestinal tract, with stomach, small bowel, and colorectal sarcomas accounting for 50,30 and 15% of GI sarcomas, respectively.

Presenting symptoms and signs of GI sarcomas are similar to those of carcinomas arising in the same segment of the gastrointestinal tract.

Diagnosis of GI sarcoma is often established pre operatively and is frequently made when the patient undergoes laparotomy for a mass in the small bowel or colon.

TREATMENT FOR GI SARCOMAS

The choice of appropriate surgical procedure for GI sarcomas is based on tumor size, anatomic site, and the fact that these sarcomas rarely spread to involve regional lymph nodes.

- Wedge resection is the procedure of choice for localized gastric lesions, with negative margins.
- For more extensive gastric lesions, total gastrectomy or en bloc resection of adjacent organs may required.
- Duodenal sarcomas like other duodenal malignancies may require pancreaticoduodenostomy to achieve negative resection margins.
- Segmental resection is the procedure of choice for small bowel and colon lesions.

- Extensive lymph node dissection or removal of grossly uninvolved mesentery is not required

- Results from recent limited series have shown no benefit to adjuvant chemotherapy or radiotherapy for patients with gastro intestinal sarcomas.

If feasible complete resection of isolated peritoneal or hepatic metastasis improves the survival.

HEAD AND NECK SARCOMAS

Sarcomas are uncommon in head and neck region, accounting for only 4% of all sarcomas and less than 1% of heas and neck malignancies in adults.

The most common histologic subtypes in adults are:

1. Fibrosarcoma 18%
2. Malignant fibrous histiocytoma 16%
3. Rhabdomyosarcoma 15%

Methods of diagnosis, imaging and biopsy for head and neck sarcomas do not differ substantially form those for other head and neck tumors.

Treatment for Head Neck Sarcomas

Wide surgical excision with negative margins is the therapeutic mainstay for head and neck sarcomas. Regional lymph node metastases are rare. In the absence of clinically positive lymph nodes routine lumpadenectomy is not required.

MATERIALS AND METHODOS

In this study 30 patients were selected from the surgery wards and out patient department of Coimbatore medical college hospital by simple random sampling.

STUDY DESIGN:

A prospective study

STUDY PERIOD:

Academic year 2013 – 2015

INSTITUTIONAL ETHICAL COMMITTEE APPROVAL:

Obtained

INCLUSION CRITERIA:

1. Patients with deep seated mass in trunk and extremity size>5 cm, and persisting for more than 4 weeks
2. Superficial mass in trunk and extremity which adherent to deep tissue.
3. Age 20-80 years.

EXCLUSION CRITERIA:

1. Pediatric age group
2. Pregnant women
3. Psychiatric patient

STUDY PROTOCOL:

In this study 58 patients with deep seated mass size>5 cm, and persisting for more than 4 weeks and superficial mass which adherent to deep tissue in trunk and extremity , attended surgical out patient department and admitted in surgical ward of Coimbatore medical college hospital by simple random sampling were selected for this study. After core needle biopsy and histopathological conformation 30 patients with soft tissue sarcoma were selected. 28 patients were excluded from this study because of non STS histopathological report. From day of admission patient were followed for 12months post treatment period to asses 6 months survival, recurrence, metastasis and complications.

HISTORY AND PHYSICAL EXAMINATION:

All the patients were evaluated with

1. Detailed history
2. Complete physical examination was done including vitals as per profoma
3. Lymph node assessment was done for all patients.

INVESTIGATIONS:

1. Core needle biopsy
2. MRI of swelling site
3. X-ray chest to assess metastasis.
4. Lymph node excision biopsy if node present
5. Routine blood investigations like RBS, Urea, Creatinine, Hb%,
6. Tumour excision biopsy after surgery for histopathological grading and typing.

OBSERVATION AND RESULTS

Statistical Analysis of STS

Group	6 Months Survival Rate		
	Mean	**Standard Deviation**	**No. of Patients**
Extremities	2.12	0.3	22
Trunk	1.14	0.25	4

T-Test for Equality of Means (6 Months Survival Rate)

t	Df	Prob	Sig.
15.5	60	.001	$p<0.01$

$P<0.01$ - Significant at 1% level

Statistical analysis of STS

Group	Metastasis free survival rate		
	Mean	**Standard Deviation**	**No. of Patients**
Extremities	1.94	0.37	20
Trunk	1.05	0.16	6

T-Test for Equality of Means(Metastasis free survival rate)

t	**Df**	**Prob**	**Sig.**
14	60	.001	p<0.01

P<0.01 - Significant at 1% level

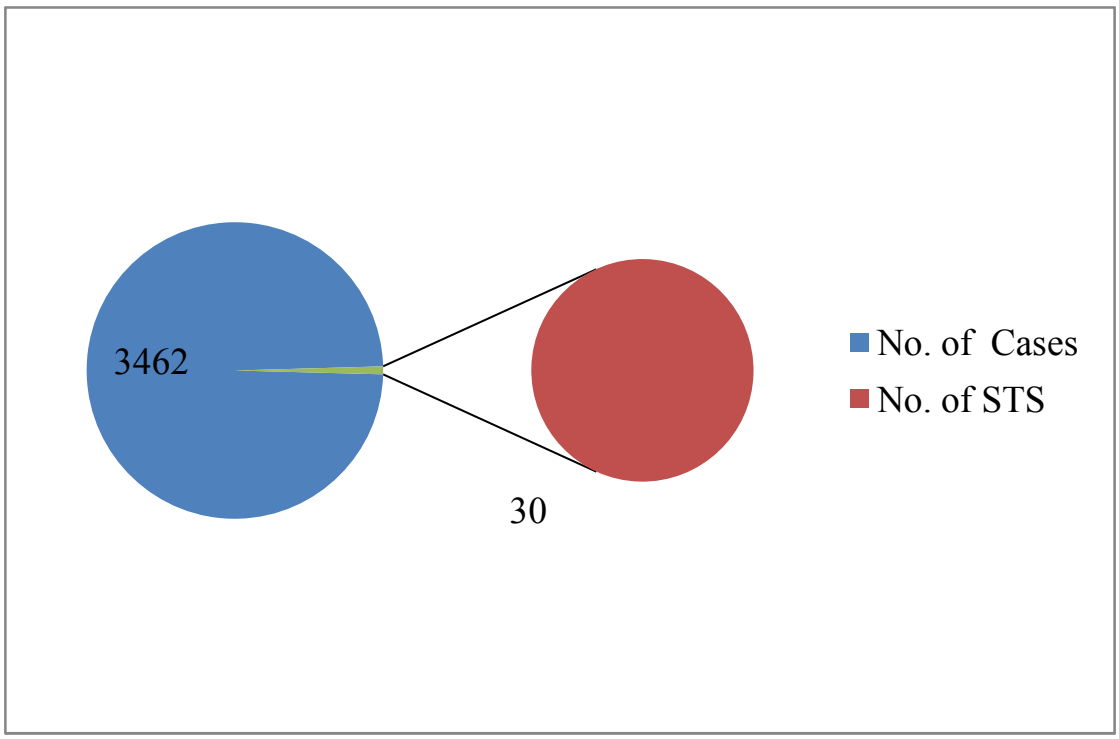
TABLE – 5

INCIDENCE OF STS IN OUR STUDY

No. of Cases	No. of STS	Percentage
3462	30	1.15

CHART – 1

INCIDENCE OF STS IN OUR STUDY



Incidence of soft tissue sarcoma in our study was 30cases out of 3462 cancer cases reported in Coimbatore medical college hospitals.

In percentage about 1.15%

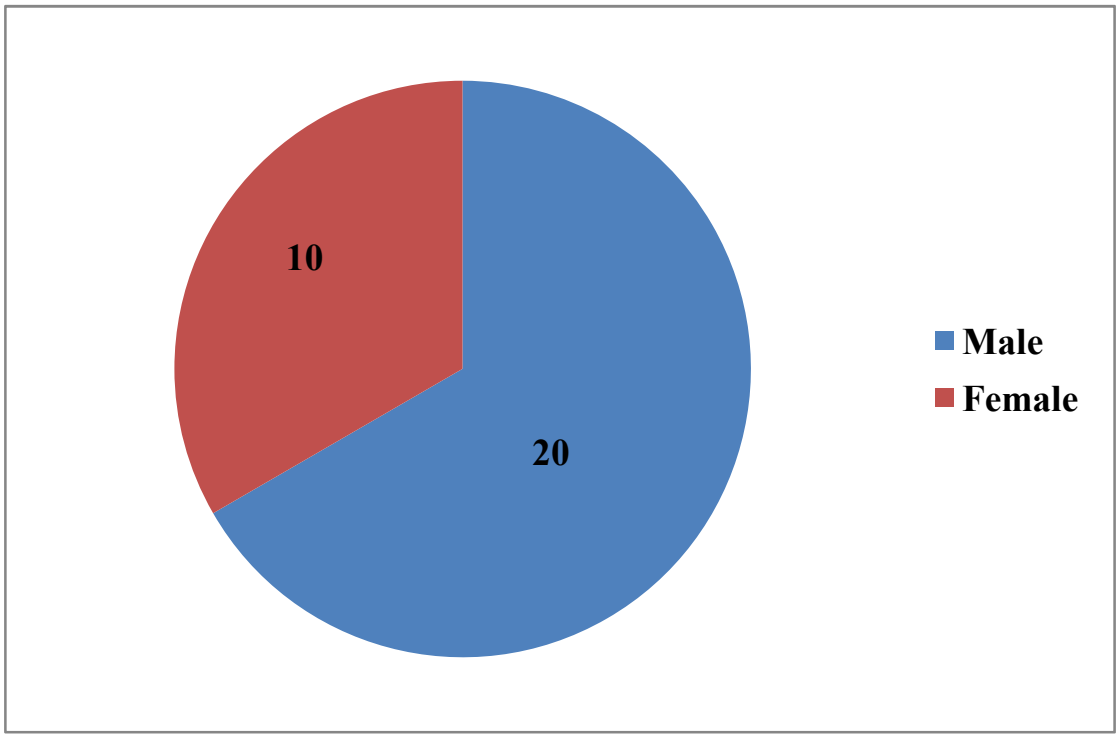
TABLE – 6

SEX DISTRIBUTION

Male	Female	Total
20	10	30

CHART – 2

SEX DISTRIBUTION



Sex Distribution in our study was 20 male and 10 femaleout of 30. Ratio about 2:1

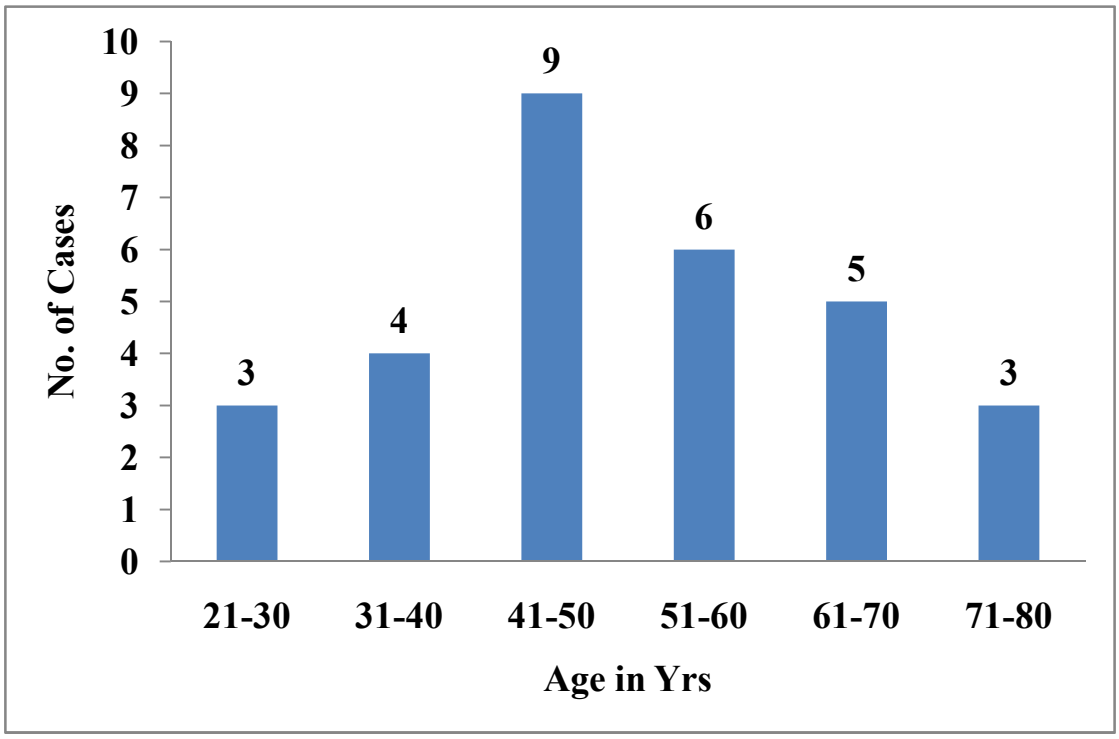
TABLE – 7

AGE DISTRIBUTION

Age in Yrs	No. of Case	Percentage
21-30	3	10%
31-40	4	14%
41-50	9	30%
51-60	6	20%
61-70	5	16%
71-80	3	10%

CHART – 3

AGE DISTRIBUTION



Age distribution in our study was maximum number of cases occurred in between theage of 41-50yrs.

Minimum age group of about 21-30yrs and Maximum age group of about 71-80

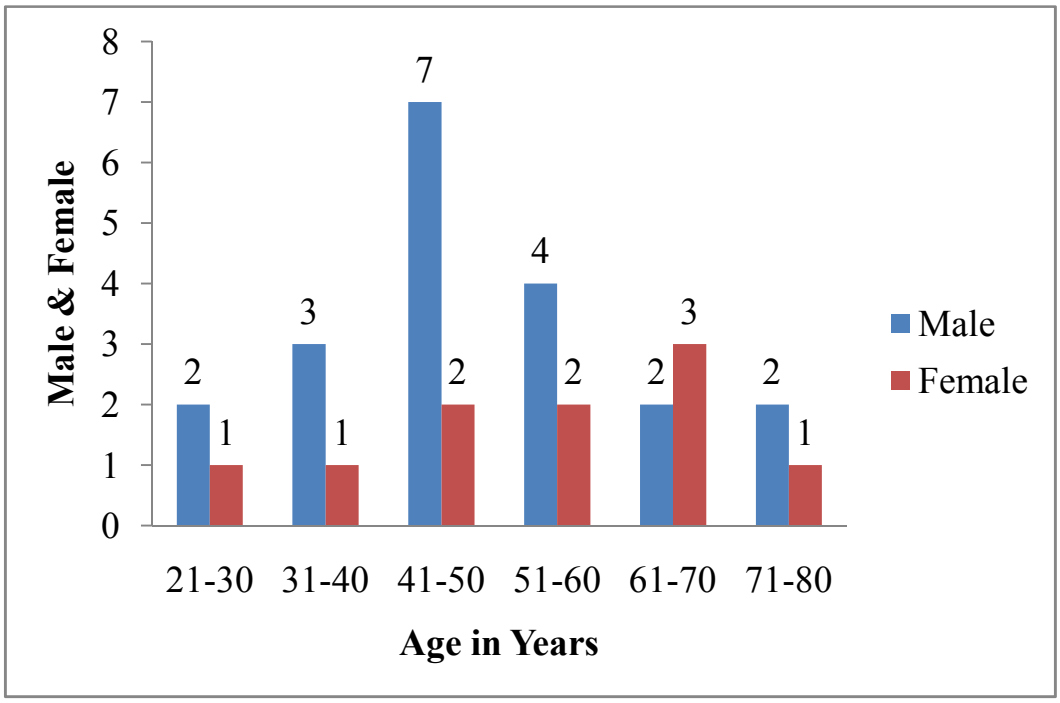
TABLE – 8

AGE & SEX DISTRIBUTION

Age in Yrs	Male	Female
21-30	2	1
31-40	3	1
41-50	7	2
51-60	4	2
61-70	2	3
71-80	2	1

CHART – 4

AGE & SEX DISTRIBUTION



Age and Sex distribution Maximum number of Male cases occur in about 41-50yrs and Maximum number of female cases occur in about 61-70yrs.

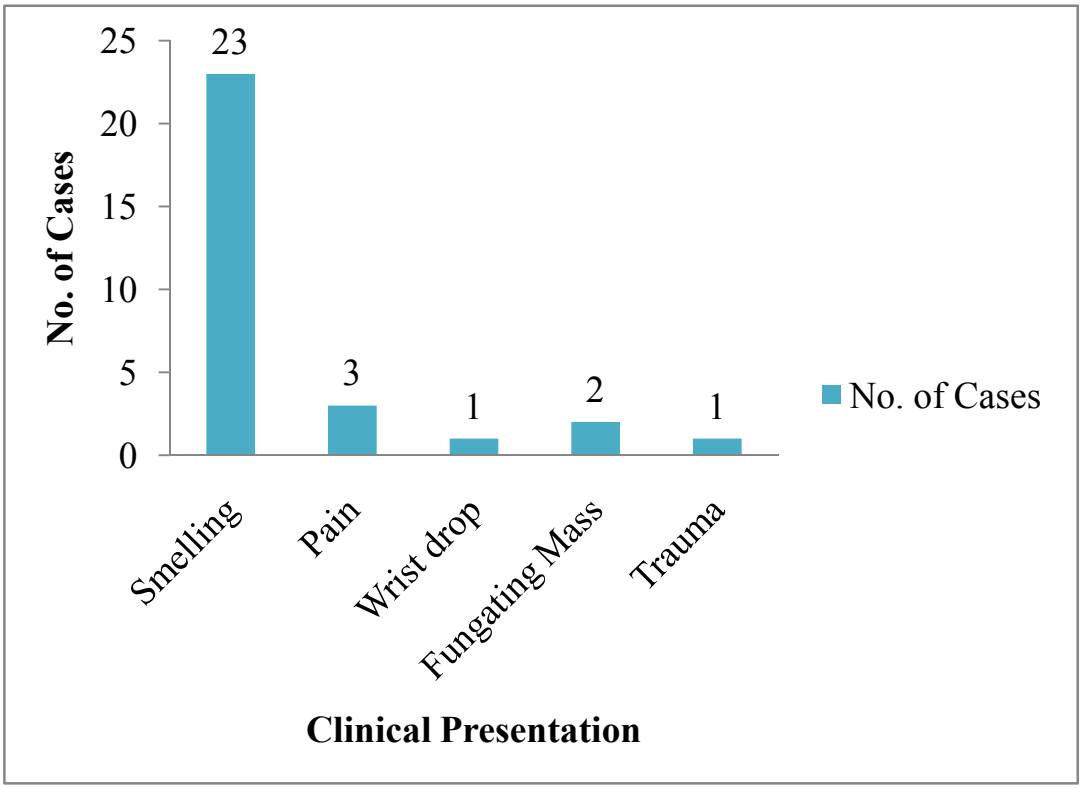
TABLE – 9

CLINICAL PRESENTATION

Clinical Presentation	No. of Cases	Percentage
Smelling	23	77%
Pain	3	11%
Wrist drop	1	3%
Fungating Mass	2	6%
Trauma	1	3%

CHART – 5

CLINICAL PRESENTATION



77% of patients presents with C/O Swelling. 3% (one) patient presents with C/O Wrist drop. 6% of patients presents with C/O Fungating mass. 3%(one) patient presents with C/O Trauma. 11% of patients presents with C/O Pain.

TABLE – 10

SITE DISTRIBUTION

Site	No. of Cases	Percentage
UL	9	30%
LL	14	47%
Trunk	7	23%

CHART – 6

SITE DISTRIBUTION

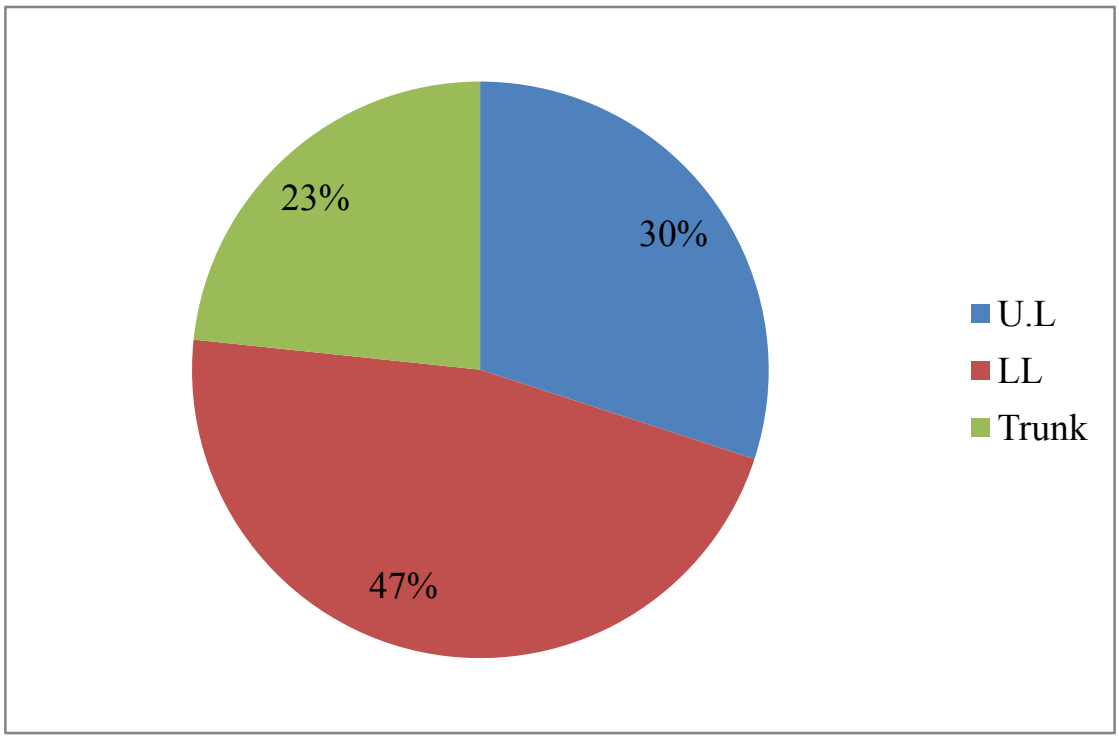


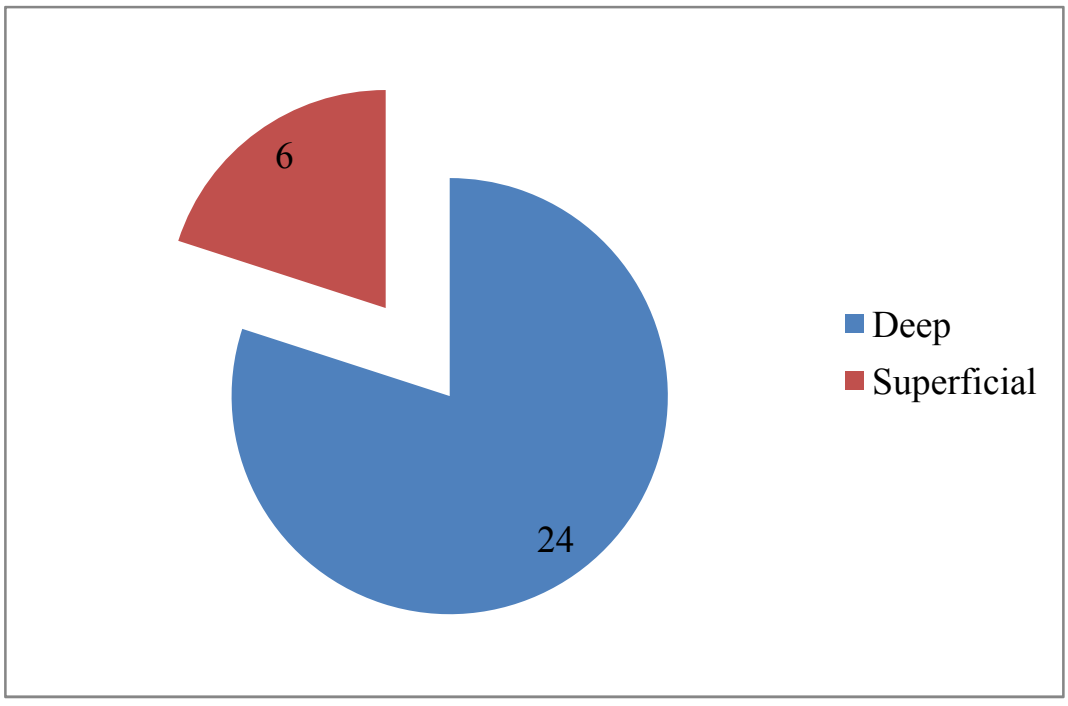
TABLE – 11

DEPTH OF TUMOUR

Depth	No. of Cases	Percentage
Deep	24	80%
Superficial	6	20%

CHART – 7

DEPTH OF TUMOUR



Most cases present as Deep mass around 80%.superficial mass only 20%.

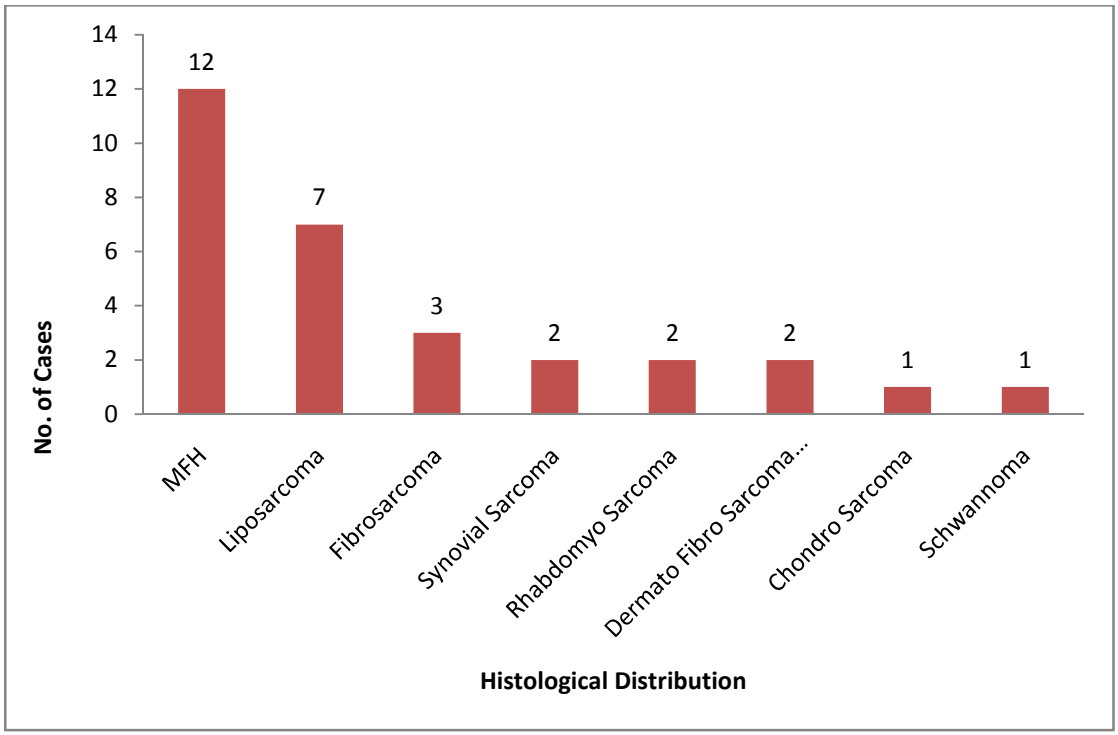
TABLE – 12

HISTOLOGICAL DISTRIBUTION

Histological Distribution	No. of Cases	Percentage
MFH	12	40%
Liposarcoma	7	23%
Fibrosarcoma	3	10%
Synovial Sarcoma	2	6%
Rhabdomyo Sarcoma	2	6%
Dermato Fibro Sarcoma Protuberance	2	6%
Chondro Sarcoma	1	3%
Schwannoma	1	3%

CHART – 8

HISTOLOGICAL DISTRIBUTION



Commenest histological type was (Malingnant Fibrous Histiocytoma) undifferentiated pleomorphic sarcoma around 40%.Liposarcoma was 2nd most common about 23%. Least was chondrosarcoma and schwannoma.

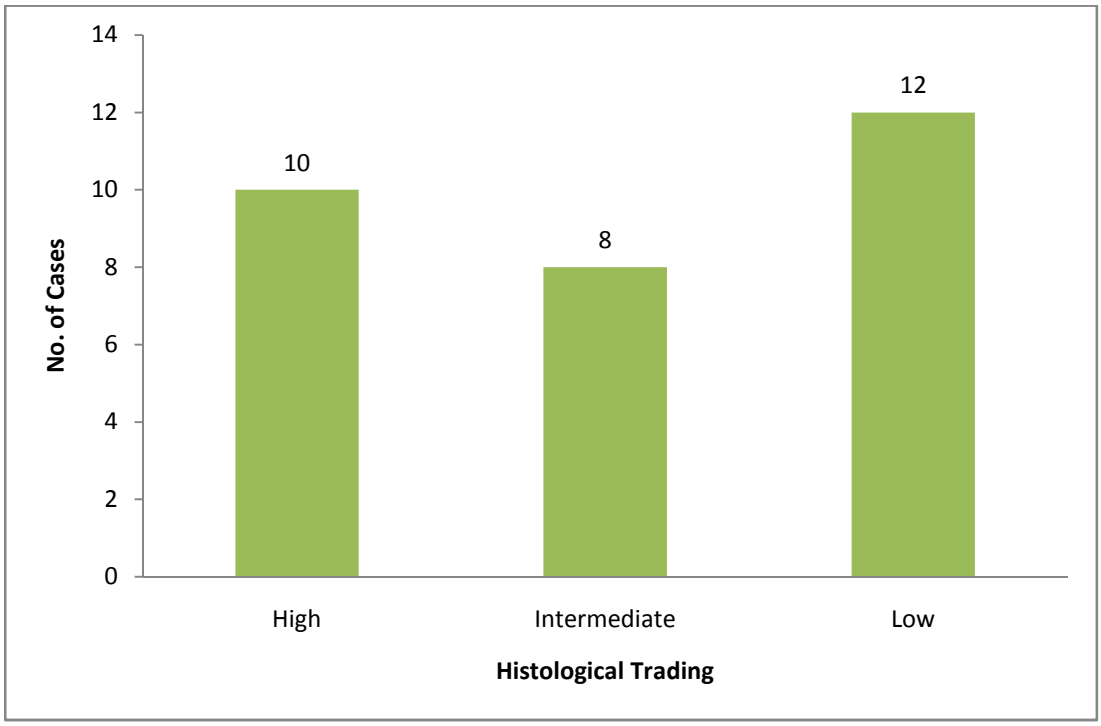
TABLE – 13

HISTOLOGICAL GRADING IN OUR STUDY

Histological Grading	No. of Cases	Percentage
High	10	34%
Intermediate	8	26%
Low	12	40%

CHART – 9

HISTOLOGICAL GRADING IN OUR STUDY



Most common Low Grade about 40%.Intermediate Grading about 26% and High Grade about 34%.

TABLE – 14

SURGICAL MANAGEMENT GIVEN TO OUR PATIENTS

Surgery	No. of Cases	Percentage
Wide Local Excision	18	60%
Amputation	2	6%
WLE with Flap reconstruction	6	20%
WLE with Flab reconstruction with ileoinguinal block dissection	2	6%
Palliative debulking	2	6%

CHART – 10

SURGICAL MANAGEMENT GIVEN TO OUR PATIENTS

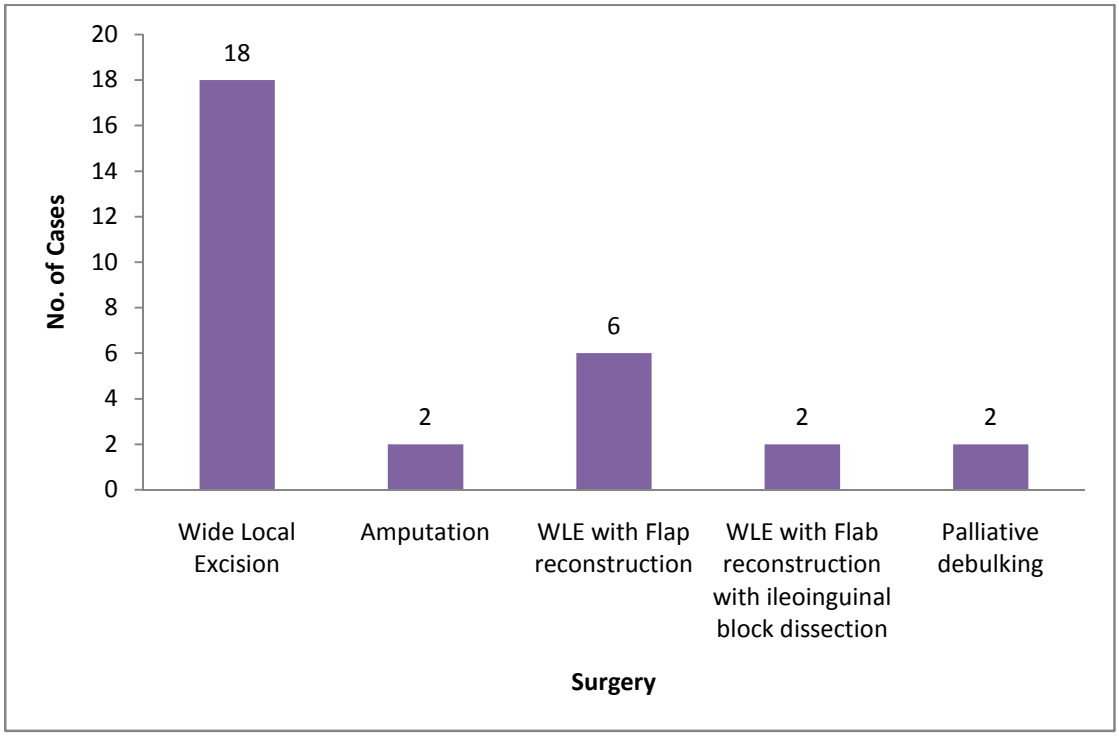


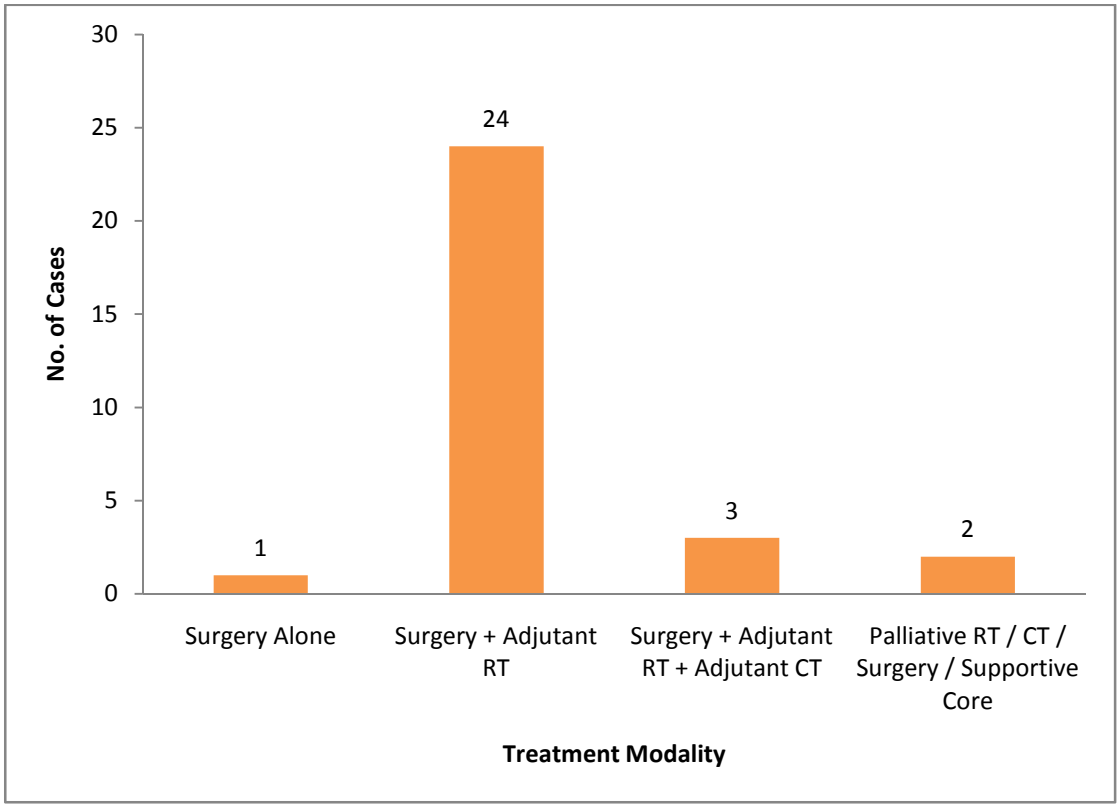
TABLE – 15

TREATMENT MODALITIES

Treatment Modality	No. of Cases	Percentage
Surgery Alone	1	4%
Surgery + Adjutant RT	24	80%
Surgery + Adjutant RT + Adjutant CT	3	10%
Palliative RT / CT / Surgery / Supportive Core	2	6%

CHART – 11

TREATMENT MODALITIES



80% of patient undergone surgery with Adjuvant RT.Surgery alone only 4%.10% patient undergone Surgery with Adjuvant RT/CT.

6% Undergone palliative care.

TABLE – 16

RECURRENCE

Site	No. of Cases	Percentage
Trunk	3	10%
Extremities	1	30%

CHART – 12

RECURRENCE

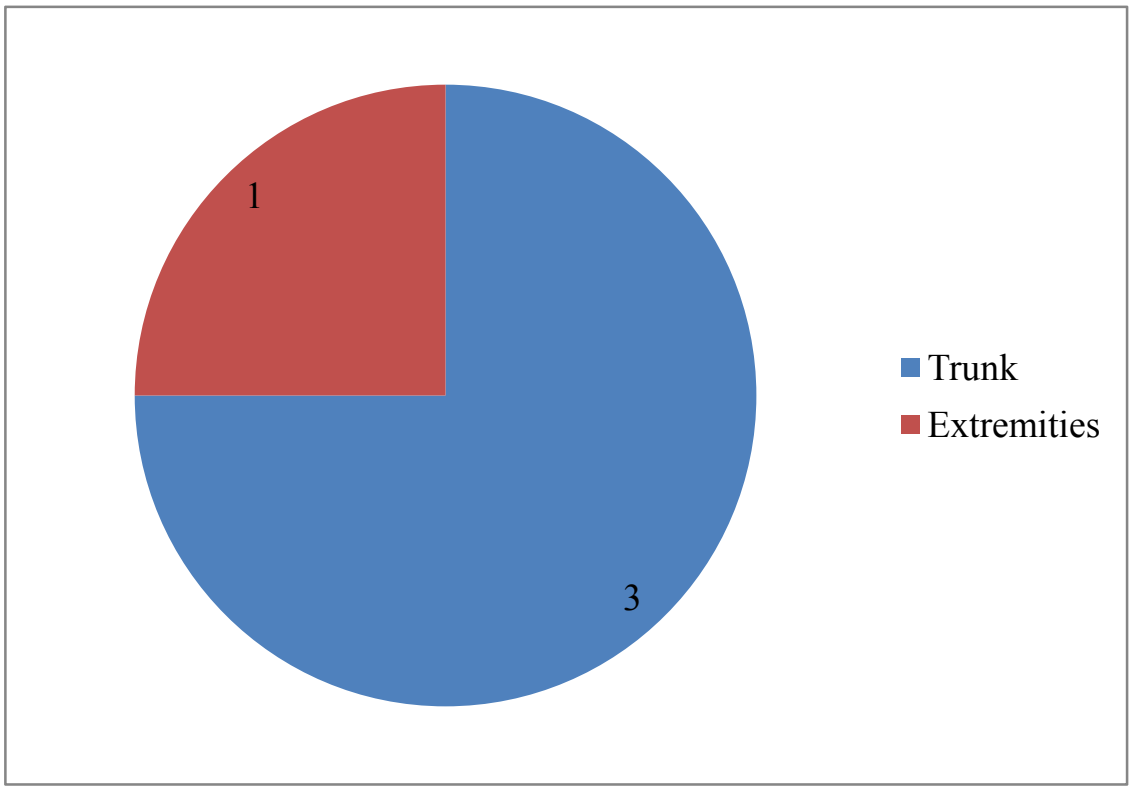


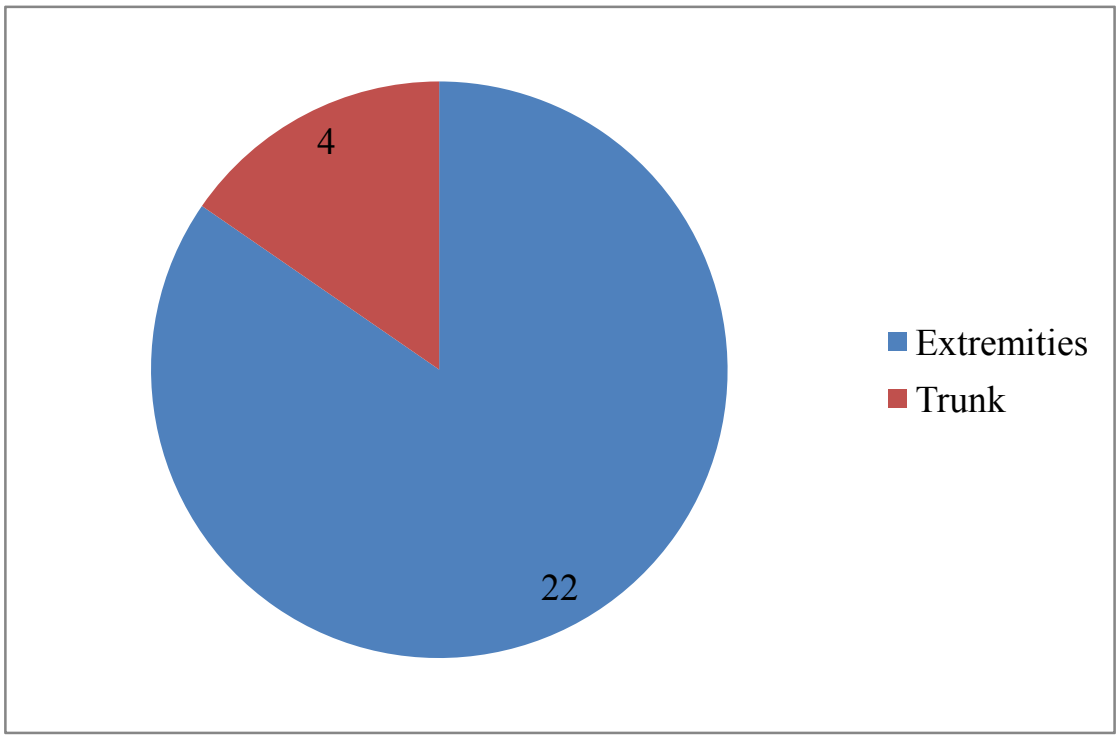
TABLE – 17

6 MONTHS SURVIVAL RATE

Site	No. of Cases	Percentage
Extremities	22	73%
Trunk	4	13%

CHART – 13

6 MONTHS SURVIVAL RATE



73% of Extremities STS have GoodSurvival.But Only 13% of Trunk STS have Good Survival.

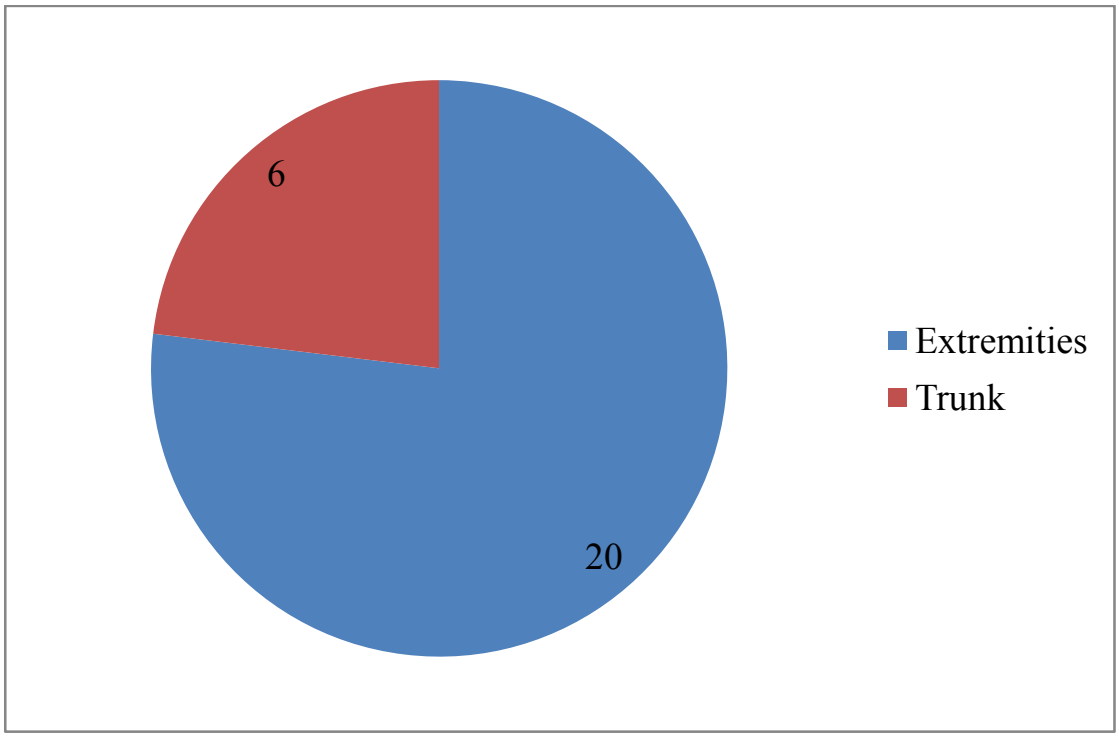
TABLE – 18

METS FREE SURVIVAL RATE

Site	No. of Cases	Percentage
Extremities	20	66%
Trunk	6	34%

CHART – 14

METS FREE SURVIVAL RATE



66% of Extremities STS have Mets Free Survival Rate. But only 34% of Trunk STS have Mets Free Survival Rate.

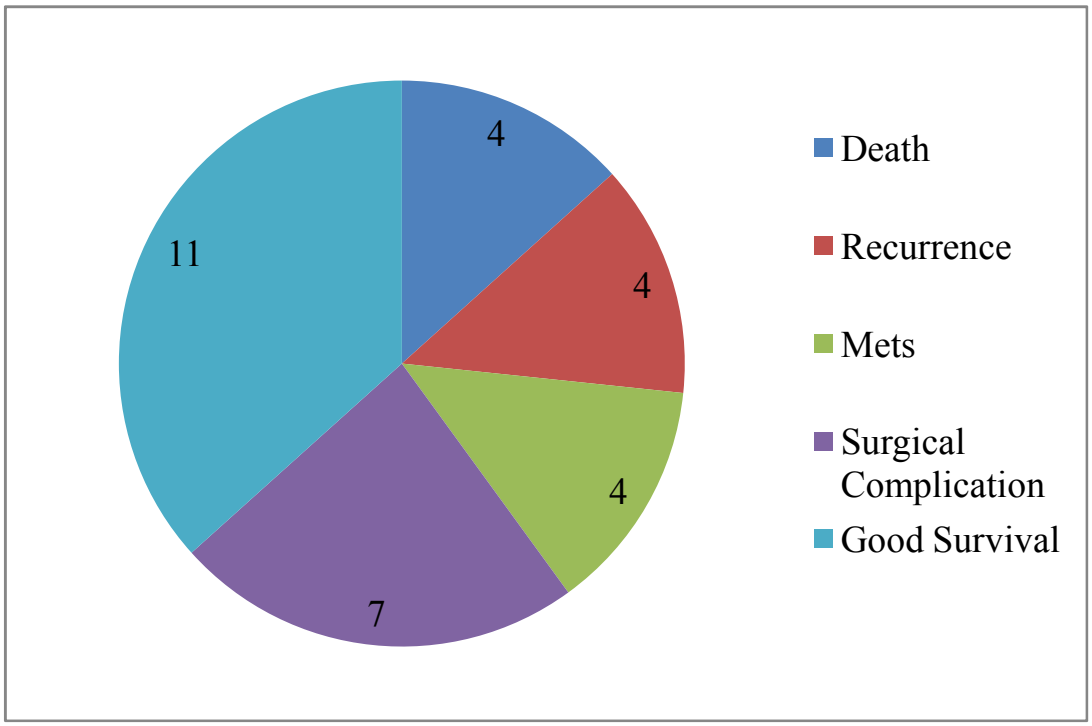
TABLE – 19

OUTCOME

	No. of Cases	Percentage
Death	4	13%
Recurrence	4	13%
Mets	4	13%
Surgical Complication	7	24%
Good Survival	11	37%

CHART – 15

OUTCOME



Our study outcome about 37%of STS Patients Have good survillence.13% Death And 13% Recurrence,13% Lung Mets,24% surgical complication occurred.

DISCUSSION

In our study total number of cancer cases admitted in Coimbatore medical college was about 3462 during the period of this study, out of 3462 cases only 30 cases were soft tissue sarcomas.The incidence of which was 1.15%,which was similar to that found in largest centres conducting Comparative study of soft tissue sarcoma in

- Incidence in Male was higher than female 2:1
- Soft tissue sarcoma was more common between the age group of 30 and 60yrs,about around 74% in our study.
- Most cases occur in 41-50yrs.
- The most common clinical presentation in our study was swelling around 77%.other symotoms are pain 11%,wrist drop 3%,fungating mass 2%,Trauma 3%.
- Duration maximum 24months and minimum 2months.
- Maximum size of tumour was 15cms and minimum size of tumour was 7cms.

- Largest tumour in our study was 15*12cms and out of 30 cases 9cases tumour size was >10cms.
- 7 patients had other medical conditions like SHT,COPD,DM.
- One patient had a history of trauma 6months back.
- One patient had a history of wrist drop.
- Most of the patients were Chronic smoker and alcoholics,some patient had h/o tobacco chewers,betel nut ,leaf chewers.

SITE DISTRIBUTION

The most common site of tumour occurrence in our study was Thigh.In general maximum number of cases occurrence in our study was Lower Extremities around 47%,next common site was Upper Extremities around 30%,others Trunk 23%.

DEPTH OF TUMOUR

Maximum number of patients tumour present as deep depth around 80%.Superficial presentation only 20%.

HISTOLOGICAL GRADING AND DISTRIBUTION

Most of cases present with LOW grading about 40% in our study.Most common histological type presentation was Malingnant Fibrous Histiocytoma about 40% in our study others are Liposarcoma 23%,Fibrosarcoma 10%,Synovial Sarcoma 6%,Rhabdomyosarcoma 6%,Dermatofibrosarcoma protuberance 6%,Chondrosarcoma 3%,Schwannoma 3%.

TREATMENT MODALITIES

The choice of appropriate treatment was based on tumour size,anatomic site,Histological varities and patient preference.

Surgery in the form of Wide Local Excision with Flap reconstruction,Ileoinguinalblock,dissection,Amputation,Palliative-

Debulking surgery.

1. Surgery Alone was done without Adjuvant Radio/Chemothrepy was one cases about 4% in our study.

2. Surgery With Adjuvant Radiotherapy(50-60Gy) was given for 24 cases around 80% of patient in our study.

3. Surgery with Adjuvant Radiotherpy with Adjuvant Chemotherapy(CTX,ADR,VCR-6 cycles) for 3cases about 10%.

4. Palliative Debulking/RT/CT given for 2cases about 6%.

All the patients were followed up at Monthly intervals during the course of the treatment with regular investigations Like CBC (HB%, TC, DC, Platelet Count),Blood, Urea, Sr.Creatinine, Sr.Billirubin, ECHO for cardiac evaluation while pt were on adjuvant CT/RT.

- After the treatment, patients were followed up at every monthly intervals.
- Maximum period of follow up in our study was 12 months.
- After 6 months survival and Mets free survival rate are about 37% in our study.
- Surgical complication about 27% of our study.
- Death, Recurrence rate, Metastasis are about 13% in our study result.
- Primary Metastasis site are lung about 13% of cases.

- Most common site of recurrence was chest wall in our study, may be due to insufficiency margin clearance and late presentation.

- Minimum duration for recurrence in our study was 3 months.

- Most common Histological type to recurrence in our study was Malignant fibrous histiocytoma about 10%.

- Metastasis free survival rate of extremities was 66%,where MFS rate for trunk was 34%.

- 6 months survival rate for extremities was 73%,where trunk was 13%.

Management of recurrent disease:

All the patients with recurrence were thoroughly investigated for metastatic work up.

1. One patient with extremities recurrence treated with amputation followed by radiotherapy.

2. Two patient with trunk recurrence treated with wide local excision followed by radiotherapy.

3. One patient with trunk recurrence treated with palliative chemotherapy.

4. Two trunk case recurred after 3 month, one extremities recurrence after 5 month, one trunk case recurred after 6month.

5. Recurrence cases followed up every month regularly.

P-Value

P<0.01 – Significant at 1% level indicate extremities Soft tissue Sarcomas have both 6 months survival and metastasis free survival rate are better than trunk.

SUMMARY

In any patient presenting with a soft tissue mass which is symotomatic or asymptomatic, is enlarging ,persisting beyond 4 to 6 weeks an early histological diagnosis, either by incision/excision biopsy should be made.

In case of soft tissue sarcoma,an early surgical intervention with adequate clearance,followed by adjuvant radiotherapy should be the practice,to be adopted to achieve better results in our set up and periodical follow up for the early detection of recurrence and metastasis.

CONCLUSION

1. The incidence of soft tissue sarcoma in Coimbatore medical college hospital was 1.15%.
2. In our study specific etiological factor is unknown.
3. Soft tissue sarcoma was common in 30-60yrs age group.
4. Most of the cases were found in the extremities particularly lower extremities.
5. Most common Histological type was (Malignant fibrous histiocytoma) undifferentiated pleomorphic sarcoma.
6. Uncommon type of soft tissue sarcomas like malignant schwannoma(one case) were noted.
7. Biopsy from either Incision or excision is mandatory for diagnosing as well as grading of soft tissue sarcoma.
8. FNAC may be helpful in case of recurrence and also lymph node metastasis.
9. Wide local excision with clear margins followed by adjuvant radiotherapy is the preferred treatment of choice.

10. Causes for recurrence may be Inadequate margin clearance,high grade tumours, presents with metastasis.

11. Monthly follow up for atleast 3yrs after the end of therapy is essential for the early identification of recurrence,metastasis.

12. Recurrent lesions were managed in the same manner as primary lesions.The outcome were as good nearly as non recurrent lesions.

13. In our study 6months survival rate is better for extremities(73%) than trunk(13%)

14. Metastasis free survival rate is better for extremities(66%) than trunk(34%).

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PROFORMA

Name	:	I.P No	:
Ward	:	Occupation	:
Age/Sex	:	Address	:
DOA	:		
DOS	:	Ph. No	:
DOD	:		

Presenting Complaint:

Swelling :

1.Onset

2.Duration

History of presenting illness:

1.Swelling

On set: Duration: Size: Character:

2.Pain

On set: Duration: Size: Character :

Radiation/Postural variation:

3.Any history of radiation exposure

4.Any history of trauma

5.H/O Chronic lymph odema

6.H/O Chronic chemical exposure

7.H/O Any viral infection

Bowel and bladder Habbits

Past history

Personal history

Menstrual history

GENERAL PHYSICAL EXAMINATION

1. Nutritional status:
2. Pallor:
3. Icterus:
4. Hydration:
5. Cyanosis/Clubbing/edema:
6. Generalised/regional Lymphadenopathy:

7. Pulse rate:

8. Blood pressure:

SYSTEMIC EXAMINATION:

SWELLING

Inspection

Site: Size: Shape: Extension:

PALPATION

Consistency: Margin: Warmth: Tenderness:

Cough impulse: Reducible/Not reducible:

PERCUSSION

AUSCULTATION

Any bruits present

CARDIOVASCULAR SYSTEM

RESPIRATORY SYSTEM

CENTRAL NERVOUS SYSTEM

INVESTIGATIONS:

BLOOD:	Urea:	Sugar:	CBC:
SERUM:	Creatine:	Electrolytes:	LDH:
URINE :	Albumin:	Sugar:	Deposits:

BLOOD GROUPING & TYPING

X ray Chest PA View

ECG

HIV

HBsAg

MRI of lesion

CT CHEST

TRUCUT BIOPSY

OTHERS

DIAGNOSIS

MANAGEMENT

SURGICAL MANAGEMENT

Date & time of surgery

Anaesthesia

Incision

Per operative findings

Procedure

Post op period

POST OF CHEMOTHERAPY

POST OF RADIOTHERAPY

COMPLICATIONS:

OUTCOME:

FOLLOW UP:

SUMMARY:

CONSENT FORM

It has been explained to me in my mother tongue and I completely understand my condition. Its related complications and the treatment going to be given.I have been explained in detail regarding this study- A comparative study on soft tissue sarcoma on extremities and trunk.I hereby give my consent for my treatment and to be a part of the above mentioned study.

Date:

Place:

Signature of the Relative withName

Signature of the Patient with Name

ஒப்புதல் படிவம்

பெயர் :

பாலினம் : வயது :

முகவரி :

அரசு கோவை மருத்துவக் கல்லூரியில் அறுவை சிகிச்சை மருத்துவ துறையில் பட்ட மேற்படிப்பு பயிலும் மாணவன் அவர்கள் மேற்கொள்ளும் **"கை, கால்கள் மற்றும் உடம்பு பகுதியல் உள்ள புற்றுநோய் பற்றி ஒப்பிட்டு ஆராய்தல்"** குறித்த ஆய்வில் செய்முறை மற்றும் அனைத்து விவரங்களையும் கேட்டுக் கொண்டு எனது சந்தேகங்களை தெளிவுப்படுத்திக் கொண்டேன் என்பதை தெரிவித்துக் கொள்கிறேன்.

நான் இந்த ஆய்வில் முழு சம்மதத்துடன், சுய சிந்தனையுடனும் கலந்து கொள்ள சம்மதிக்கிறேன்.

இந்த ஆய்வில் என்னுடைய அனைத்து விபரங்கள் பாதுகாக்கப்படுவதுடன் இதன் முடிவுகள் ஆய்விதழில் வெளியிடப்படுவதில் ஆட்சேபனை இல்லை என்பதை தெரிவித்துக் கொள்கிறேன். எந்த நேரத்தில் இந்த ஆய்விலிருந்து நான் விலகிக் கொள்ள எனக்கு உரிமை உண்டு என்பதையும் அறிவேன்.

இடம் : கையொப்பம் / ரேகை

நாள் :

KEY TO MASTER CHART

MFH	–	Malingnant fibrous histiocytoma.
DFSP	–	Dermatofibrosarcoma protuberance.
RMS	–	Rhabdomyosarcoma.
WLE	–	Wide local excision.
FLP	–	Flap reconstruction.
ILEO	–	Ileoinguinal block dissection.
STS	_	Soft tissue sarcoma.

MASTER CHART

S.no	Name	IP number / Age	Sex	Clinical presentation	Histopathologic	LN/MET	MRI	depth	SX	RT	CT	Recur	6 months survial	Outcome	Mets
				site	type	negative	size/cms							Complication	free surv
1	KAMATCHI CHETTIYAR	004/75	M	swelling over the left thigh	liposarcoma		7*8	super ficial	WLE	yes	no	no	yes	no complication	yes
2	GNANAMBIKA	671/62	F	Swelling over the left inguinal region	pleomorphic liposarcoma	negative	8*9	deep	WLE FLP	yes	no	no	yes	flap dehiscence	yes
3	SUGANTHI	007/46	F	Swelling over the left thigh	MFH	negative	9*9	deep	WLE	yes	no	no	yes	no complication	yes
4	LAKSHIMI	071/65	F	Swelling over the left gluteal region	liposarcoma	negative	9*7	deep	WLE FLP	yes	no	no	yes	no complication	yes
5	CHINNASAMY	319/63	M	Swelling over the left shoulder joint	MFH	negative	15*12	Super fical	WLE	yes	no	no	died	died	Lung mets
6	KRISHNAVENI	186/45	F	Swelling over the left thigh	Dermato fibro sarcoma protuberance	positive	7*7	deep	WLE ILEO* FLP	yes	no	no	yes	flap necrosis	yes
7	RAMU	371/47	M	pain left chest wall	MFH	negative	12*13	deep	debulky	yes	no	yes	died	recurrence died	
8	RANGANAYAKI	202/72	F	swelling left forearm	schwannoma	negative	7*7	deep	WLE FLP	yes	no	no	yes	wrist drop	yes
9	BADHRAKALI	107/32	M	fungating mass right leg	synovial sarcoma	negative	15*10	deep	AMP	yes	yes	no	yes	Amputation	lung mets
10	RAJU	567/42	M	right chest wall pain	MFH	negative	8*7	super ficial	WLE	yes	no	yes	yes	no complication	yes
11	SARAVANAN	202/36	M	Swelling over the left thigh	MFH	negative	9*6	deep	WLE	yes	no	no	yes	wound infection	yes
12	SANTHOSH	437/56	M	swelling right forearm	fibrosarcoma	negative	8*5	super ficial	WLE	yes	no	no	yes	no complication	yes
13	THULASIYAMMAL	558411/40	F	H/o trauma right thigh	liposarcoma	negative	9*5	deep	WLE	yes	no	no	yes	wound infection	yes
14	VARADHAN	23451/42	M	Swelling over the right chest wall	RMS	negative	10*6	deep	WLE	yes	no	yes	yes	recurrence	yes
15	ARUNPANDIAN	564382/23	F	Swelling over the right gluteal region	MFH	negative	7*8	deep	WLE FLP	yes	no	no	yes	flap dehicense	yes
16	ARUKAANI	432/59	F	Swelling over the back right side	high grade liposarcoma	negative	9*5	deep	WLE	yes	no	no	yes	wound infection	yes

17	PRATAP	188/21	M	Swelling over the right forearm	MFH	negative	7*5	super ficial	WLE	yes	no	no	yes	no complication	yes
18	RAMANAN	55432/45	M	Swelling over the back right side	MFH	negative	13*11	deep	WLE	yes	no	no	yes	no complication	yes
19	RAGURAM	52534/56	M	Swelling over the right forearm	RMS	negative	7*6	deep	WLE	yes	yes	no	yes	skin flap necrosis	yes
20	CHINNAN	741/76	M	Swelling over the right gluteal region	MFH	positive	9*8	deep	WLE ILEO* FLP	yes	no	no	died	recurrent growth died	lung mets
21	VALLIYAPAN	96/61	M	Swelling over the right forearm	Liposarcoma	negative	12*8	deep	WLE	yes	no	no	yes	no complication	yes
22	RAMACHANDRAN	23547/47	M	Swelling over the right thigh	MFH	negative	9*5	deep	WLE	yes	no	no	yes	no complication	yes
23	KOOTHAYEE	67342/67	F	Fungating lesion left forearm	MFH	negative	11*6	deep	WLE FLP	yes	no	no	yes	no complication	yes
24	PRATHAP	57750/25	M	Swelling over the left chest wall	dermato fibro sarcoma protuberance	negative	7*6	super ficial	WLE	yes	no	yes	yes	recurrence	yes
25	SHANTHARAM	12370/54	M	Swelling over the left knee joint	myxoid chondro sarcoma	negative	13*8	deep	AMP	yes	no	no	yes	Amputation	yes
26	AMBUSELVI	54367/47	M	Swelling over the right arm	fibrosarcoma	negative	12*12	deep	WLE FLP	yes	no	no	yes	no complication	yes
27	AMMASAI	23417/58	M	Swelling over the left back	MFH	negative	8*5	deep	debulky	yes	no	no	died	lung metastasis died	lung mets
28	ARUNKUMAR	100/47	M	Swelling over the left knee joint	synovial sarcoma	negative	8*7	deep	WLE	yes	yes	no	yes	no complication	yes
29	KUMAR	75634/40	M	pain right arm	fibrosarcoma	negative	9*6	deep	WLE	yes	no	no	yes	no complication	yes
30	RUCKMANI	15555/60	F	Swelling over the right thigh	liposarcoma	negative	7*7	deep	WLE	yes	no	no	yes	no complication	yes