Review of Literature
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Soft tissue can be defined as non-epithelial extra skeletal tissue of the body exclusive of the reticuloendothelial system, glia and supporting tissue of the various parenchymal organs. It is represented by the voluntary muscles, fat, and fibrous tissue along with the vessels serving these tissues. By convention it also includes the peripheral nervous system because tumors arising from nerves present as soft tissue masses and pose similar problems in differential diagnosis and therapy. Embryologically, soft tissue is derived principally from mesoderm with some contribution from neuroectoderm.\textsuperscript{10}

Soft tissue tumors are highly heterogeneous group of tumors that are classified on a histogenetic basis according to the adult tissue they resemble. Lipomas and Liposarcomas, for example, are tumors that recapitulate to a varying degree normal fatty tissue; and hemangiomas and angiosarcomas contain cells resembling vascular endothelium. Within the various histogenetic categories, soft tissue tumors are usually divided into benign and malignant forms.\textsuperscript{10}

Benign tumors, which more closely resemble normal tissue, have a limited capacity for autonomous growth. They exhibit little tendency to invade locally and are attended by a low rate of local recurrence following conservative therapy.
Malignant tumors, or sarcomas, in contrast, are locally aggressive and are capable of invasive or destructive growth, recurrence, and distant metastasis. Radical surgery is required to ensure total removal of these tumors. Unfortunately, the term sarcoma does not indicate the likelihood or rapidity of metastasis. Some sarcomas, such as dermatofibrosarcoma protuberans, rarely metastasize, whereas others, such as malignant fibrous histiocytoma, do so with alacrity. For these reasons it is important to qualify the term sarcoma with a statement concerning the degree of dedifferentiation or the histologic grade. “Well differentiated” and “poorly differentiated” are qualitative, and hence subjective, terms used to indicate the relative maturity of the tumor with respect to normal adult tissue. Histologic grade is a means of quantititating the degree of differentiation by applying a set of histologic criteria. Usually well differentiated sarcomas are low grade lesions, whereas poorly differentiated sarcomas are high grade neoplasms. There are also borderline lesions for which it is difficult to determine the malignant potential, and there are benign neoplastic and nonneoplastic lesions that morphologically appear to be malignant but follow a benign clinical course (pseudo sarcomas).

Soft tissue sarcomas are a heterogeneous group of malignant neoplasms that can arise from mesenchymal elements anywhere in the body. Despite the fact that soft tissues and bone comprise almost two-thirds of the mass of the human body, sarcomas are uncommon tumors.
Benign neoplasms of the soft tissues, in contrast, are commonplace and rarely consequential. These facts explain a number of clinical observations about the management of soft tissue sarcomas. Because of the relative rarity of sarcomas compared to benign soft tissue tumors, both patients and clinicians frequently fail to appreciate the significance of an enlarging soft tissue mass, and a tissue diagnosis is commonly obtained only after a significant delay. Few Pathologists accumulate extensive experience with these rare tumors; hence, once biopsied, Pathologic classification may be incomplete or inaccurate. After the diagnosis is made, many Oncologists lack sufficient knowledge of the behavior specific soft tissue sarcomas to provide appropriate therapy.

**WHO (2002) CLASSIFICATION OF SOFT TISSUE TUMORS**

Soft tissue tumors are divided into the following four categories

1) **Benign:** These usually do not recur locally, and if they do, the recurrence is non-destructive and almost always readily curable by complete local excision. Morphologically benign lesions which are extremely rare, may give rise to distant metastases that cannot be predicted on the basis of routine histological evaluation. Cutaneous benign fibrous histiocytoma is the best example.

2) **Intermediate (locally aggressive):** These tumors show an infiltrative and locally destructive growth pattern; however, they
do not metastasize. The example in this category is Fibromatosis.

3) **Intermediate (rarely metastasizing):** These tumors are often locally aggressive but in some cases, they also have a tendency to produce distant metastasis (usually in a lymph node or lung). This risk is low (<2%). The classic examples are Plexiform fibrohistiocytic tumors and Angiomatoid fibrous histiocytoma.

4) **Malignant:** Soft tissue sarcomas are locally destructive with the potential to recur; the risk of distant metastasis is significant. Depending on the histological type and grade, the potential ranges from 20% to almost 100%.

**WHO CLASSIFICATION OF SOFT TISSUE TUMORS (2002)**

**ADIPOCYTIC TUMORS**

**Benign**

- Lipoma
- Lipomatosis
- Lipomatosis of nerve
- Lipoblastoma/Lipoblastomatosis
- Angiolipoma
- Myolipoma
• Chondroid lipoma

• Extrarenal angiomyolipoma

• Extraadrenal myelolipoma

• Spindle cell/Pleomorphic lipoma

• Hibernoma

**Intermediate (locally aggressive)**

• Atypical lipomatous tumor/ Well differentiated liposarcoma

**Malignant**

• Dedifferentiated liposarcoma

• Myxoid liposarcoma

• Round cell liposarcoma

• Pleomorphic liposarcoma

• Mixed type liposarcoma

• Liposarcoma, not otherwise specified

**FIBROBLASTIC/ MYOFIBROBLASTIC TUMORS**

**Benign**

• Nodular fasciitis

• Proliferative fasciitis
• Proliferative myositis

• Myositis ossificans fibro-osseous pseudotumor of digits

• Ischaemic fasciitis

• Elastofibroma

• Fibrous hamartoma of infancy

• Myofibroma/ Myofibromatosis

• Fibromatosis coli

• Juvenile hyaline fibromatosis

• Inclusion body fibromatosis

• Fibroma of tendon sheath

• Desmoplastic fibroblastoma

• Mammary type myofibroblastoma

• Calcifying aponeurotic fibroma

• Angiomyofibroblastoma

• Cellular angiofibroma

• Nuchal type fibroma

• Gardner fibroma
• Calcifying fibrous tumor

• Giant cell angiofibroma

**Intermediate (locally aggressive)**

• Superficial fibromatoses (palmar/plantar)

• Desmoid type fibromatoses

• Lipofibromatosis

**Intermediate (rarely metastasizing)**

• Solitary fibrous tumor and Haemangiopericytoma (incl. Lipomatous haemangiopericytoma)

• Inflammatory myofibroblastic tumor

• Low grade myofibroblastic sarcoma

• Myxoinflammatory fibroblastic sarcoma

• Infantile fibrosarcoma

**Malignant**

• Adult fibrosarcoma

• Myxofibrosarcoma

• Low grade fibromyxoid sarcoma hyalinizing spindle cell tumor
• Sclerosing epithelioid fibrosarcoma

SO-CALLED FIBROHISTIOCYTIC TUMORS

Benign

• Giant cell tumor of tendon sheath

• Diffuse type giant cell tumor

• Deep benign fibrous histiocytoma

Intermediate (rarely metastasizing)

• Plexiform fibrohistiocytic tumor

• Giant cell tumor of soft tissues

Malignant

• Pleomorphic ‘MFH’/ Undifferentiated pleomorphic sarcoma

• Giant cell ‘MFH’ / Undifferentiated pleomorphic sarcoma with giant cells

• Inflammatory ‘MFH’/ Undifferentiated pleomorphic sarcoma with prominent inflammation

SMOOTH MUSCLE TUMORS

• Angioleiomyoma

• Deep leiomyoma
• Genital leiomyoma

• Leiomyosarcoma (excluding skin)

**PERICYTIC (PERIVASCULAR) TUMORS**

• Glomus tumor (and variants)/ malignant glomus tumor

• Myopericytoma

**SKELETAL MUSCLE TUMORS**

**Benign**

• Rhabdomyoma
  
  adult type
  
  fetal type
  
  genital type

**Malignant**

• Embryonal rhabdomyosarcoma (includes spindle cell, botryoid, anaplastic)

• Alveolar rhabdomyosarcoma (incl. solid, anaplastic)

• Pleomorphic rhabdomyosarcomas
VASCULAR TUMOR

Benign

- Haemangioma of
  - Subcutaneous/ deep soft tissue
  - Capillary
  - Cavernous
  - Arteriovenous
  - Venous
  - Intramuscular
  - Synovial
- Epithelioid haemangioma
- Angiomatosis
- Lymphangioma

Intermediate (locally aggressive)
- Kaposiform haemangioendothelioma

Intermediate (rarely metastasizing)
- Retiform haemangioendothelioma
• Papillary intralymphatic angioendothelioma
• Composite haemangioendothelioma
• Kaposi sarcoma

**Malignant**

• Epithelioid haemangioendothelioma
• Angiosarcoma of soft tissue

**CHONDRO-OSSEOUS TUMOR**

• Soft tissue chondroma
• Mesenchymal chondrosarcoma
• Extraskeletal osteosarcoma

**TUMOR OF UNCERTAIN DIFFERENTIATION**

**Benign**

• Intramuscular myxoma (incl. cellular variant)
• Juxta- articular myxoma
• Deep ('aggressive') angiomyxoma
• Pleomorphic hyalinizing angiectatic tumor
• Ectopic hamatomatous thymoma

**Intermediate (rarely metastasizing)**

• Angiomatoid fibrous histiocytoma
• Ossifying fibromyxoid tumor (incl. atypical / malignant)
• Mixed tumor / Myoepithelioma/ Parachordoma
Malignant

- Synovial sarcoma
- Epithelioid sarcoma
- Alveolar soft part sarcoma
- Clear cell sarcoma of soft tissue
- Extraskeletal myxoid chondrosarcoma ("chordoid" type)
- PNET/Extraskeletal Ewing's tumor
  - PNET
  - Extraskeletal Ewing's tumor
- Desmoplastic small round tumor
- Extra-renal rhabdoid tumor
- Malignant mesenchymoma
- Neoplasms with perivascular epithelioid cell differentiation (PEComa)
- Clear cell myomelanocytic tumor
- Intimal Sarcoma

CYTOLOGICAL CLASSIFICATION

Soft tissue tumors are classified into five groups\textsuperscript{12} on the basis of their cytological features –

1) **Pleomorphic pattern**: The aspirate is richly cellular and there is marked variation in cell size and shape. Nuclear pleomorphism is
striking and some of the tumor cells show large nucleoli; bizarre tumor giant cells can be detected. Pleomorphic liposarcomas, pleomorphic undifferentiated sarcomas, and pleomorphic rhabdomyosarcomas belong to this group.

2) **Spindle cell pattern:** Spindle cells are shed as fascicles. A typical spindle cell has fusiform or ovoid nuclei; the cytoplasm is tapered, unipolar, or bipolar; mitotic figures are variable. Fibrosarcomas, leiomyosarcomas and nerve sheath tumors present with this pattern.

3) **Myxoid pattern:** Smears show myxoid background and the matrix stains blue or blue violet in May-Grunwald-Geimsa and faintly green in Papanicolau stain. The tumor cells could be round, spindle shaped, or pleomorphic. Myxofibrosarcomas and myxoid liposarcomas are two common tumors encountered in this group.

4) **Small round cell pattern:** Tumor cells are individually dispersed or appear as loose, cohesive clusters of small round cells. They have round to oval nuclei and scanty cytoplasm. Ewing’s sarcoma / PNET and neuroblastomas follow this pattern.

5) **Epithelioid (polygonal) cell pattern:** Tumor cells occur in groups, tight clusters, and or are dispersed as round to polygonal
cells with abundant cytoplasm. Epithelioid sarcomas and clear cell sarcomas show this pattern.

The location of a soft tissue sarcoma influences the treatment options; for instance, retroperitoneal tumors require an approach different from that of tumors in extremities. In virtually all series of adult soft tissue sarcomas the extremities represent the predominant site of origin. Approximately 45% of soft tissue sarcomas occur in the extremity, 15% in the upper extremity, 15% in the retroperitoneum, and 10% in the head and neck region, and nearly all the rest in the abdominal and chest walls. Visceral sarcomas, which arise from the connective tissue stroma found in all organs, account for a small number of cases. Although their overall behavior may be similar to that of sarcomas found elsewhere, treatment of a visceral sarcoma is highly dependent on the organ in which it is located.

Fine needle aspiration biopsies (FNABs) have become an established tool in the diagnostic armamentarium of many clinical practices. The initial diagnosis of many lesions in both superficial (e.g., breast and thyroid) and deep (e.g. lung and pancreas) body sites can often be readily and safely assessed by FNAB. One of the few remaining frontiers for FNAB is evaluation of primary soft tissue tumors. Several important challenges are inherent to the FNAB evaluation of soft tissue neoplasms. First, many of these lesions, especially the sarcomas, are rare. Accordingly, most practicing
Pathologists do not encounter them on a routine basis and may not be familiar with their morphologic, clinical, and radiographic features. Another reason pathologists may be reluctant to evaluate soft tissue tumors is that they have overlapping histopathologic and cytomorphicologic attributes that are further compounded by the morphologic heterogeneity present in some of these mass lesions. The increasing recognition of borderline tumors or neoplasms of intermediate malignancy make the interpretation of FNAB of soft tissue masses even more problematic. For these reasons, some Pathologists and Surgeons, particularly those from Scandinavia, have advocated that the diagnosis and treatment of many soft tissue lesions, especially sarcomas, take place in centralized medical facilities.14

The FNAB has a number of distinct, well recognized advantages that require consideration for its application to skeletal neoplasm.13 Aspiration biopsy, compared to other techniques, is a rapid out-patient procedure that can provide an immediate diagnosis. It permits the Surgeon to discuss potential additional diagnostic procedures and therapy with the patient during the initial visit. It also facilitates further processing or triaging of the patient by the Surgeon. Patients suffer relatively little pain or discomfort from the aspiration procedure, and in most circumstances local anesthesia is not necessary. A major advantage of FNAB over core-needle biopsies is the much greater sampling of a mass lesion. By altering the direction of the needle during
a single puncture, multiple portions of the mass can be aspirated. If necessary, multiple separate needle punctures can be performed during a single patient visit. Cellular material may be obtained during the same biopsy setting for cell blocks. Cell blocks are preferred to direct smears for immunocytochemical studies that assist in determining the histogenesis of a neoplasm. Material may also be obtained by FNAB for electron microscopy, cytogenetics, and molecular biologic analysis.

The FNAB has a low rate of significant clinical complications, and in most patients there are none. Others may suffer bleeding, edema, or tenderness at biopsy site. The procedure does not disrupt tissue planes or contaminate the subsequent surgical site. Thus “no bridges are burned”, and if not diagnostic the FNAB can be followed by another biopsy procedure. There has not been any documented instance of needle tracking of sarcomatous tumor cells by a fine needle. Finally, compared to all other biopsy techniques, FNAB is relatively inexpensive and viewed as cost-effective in our current medical economical milieu.

Unfortunately, however, FNAC has several disadvantages, some of which are relatively specific for orthopedic lesions. FNAC always results in relatively small samples of a tumor. There is dispersion of individual cells inherent in the aspiration technique and at least partial loss of recognizable diagnostic tissue patterns. These limitations inevitably can result in less specific diagnosis with regard to histologic type and subtype of tumors. Thus, even if the neoplasm can be identified as
sarcomatous, the Cytopathologist may not be able to define more specifically the exact type of malignant mesenchymal tumor. It may also be difficult to distinguish among benign cellular lesions, borderline tumors, and low grade sarcomas. Accurate grading of many sarcomas is impossible when utilizing current histopathologic classification schemes. As with other types of tumors, in densely collagenised or sclerotic masses or highly vascular lesions. FNAC may provide only sparse cellularity on the smear, making a benign versus malignant distinction impossible.

It is important to emphasize that diagnosis of a soft tissue tumor by aspiration biopsy always requires the intimate cooperation and interaction of surgeons, radiologists, and pathologists. This is absolutely necessary to optimize the integration of all clinically relevant information to achieve the best cytological diagnosis. Whenever possible, an on-site evaluation of the aspirate by the Pathologist is preferred. It provides the opportunity for the Pathologist to provide an on-site evaluation of adequacy and to review important imaging studies, discuss the mass lesion with the Surgeon, and possibly examine the patient.13

Walaas et al (1985)15 correlated cytologic and histologic study of 12 benign lipomatous tumors and 15 liposarcomas (well differentiated, myxoid, round cell, and pleomorphic). In two cases the fine needle aspiration material was embedded in Epon for light and electron microscopic examination. Good correlation was found between the histologic and cytologic findings in the fine needle aspiration material.
Pitfalls in the cytologic diagnosis of regressively changed lipoma, intramuscular lipoma, angiolipoma, hibernoma, and lipoblastoma lead to an erroneous diagnosis of liposarcoma. The cytologic appearance of the Liposarcoma varied with histologic type, although in all of these tumors the main criteria was the presence of atypical multivacuolated lipoblasts with characteristically scalloped nuclei. Staining of the aspirated material with Alcian blue at varying pH levels for characterization of the glycosaminoglycan content helped in the distinction of myxoid liposarcomas from myxoid chondromatous tumors and chordomas. May-Grunwald-Giemsa staining was considered the most useful staining method, while fat staining is considered of limited or no value in the cytologic diagnosis of lipomatous tumors. Epon embedding of fine needle aspirates for light and electron microscopic examination seemed to be a useful diagnostic technique.

Miralles et al (1986) reviewed the use of fine needle aspiration cytology in 117 cases of soft tissue lesions: 23 non-neoplastic lesions, 34 benign mesenchymal tumors and 60 histologically proven soft tissue sarcomas. The soft tissue sarcoma aspirates were classified according to their cytomorphology into five groups of possible histologic diagnosis. Difficulties were experienced in the correct assessment of aspirates from low grade malignancies. On the other hand, in high grade malignant sarcomas and in recurrent or metastatic soft tissue sarcoma, FNA cytology was useful in both the initial diagnosis of new lesions (22
patients) and in the confirmation or exclusion of a suspected treatment failure (38 patients with recurrence or metastases). In the latter, FNA cytology supported the clinical data and reduced the number of repeat open biopsies. However they concluded that the final diagnosis of soft tissue sarcomas should be based upon the histopathologic study of tissue sections.

Layfield et al (1986) obtained one hundred seventy-six soft tissue aspirates as an initial diagnostic procedure. Forty cases were excluded because of inadequate clinical and histologic follow-up. The remaining 136 cases formed the basis of their study. Patients ranged in age from 10 months to 83 years, with the majority of malignant soft tissue lesions found in patients 40 to 65 years of age. Superficial soft tissue lesions were aspirated by palpation guidance; computed tomography was used for nonpalpable lesions. Cytologic diagnoses were classified into following general categories: specific diagnosis, atypical cells present, benign cells present (including inflammatory cells), and nonspecific or unsatisfactory aspirates. Fine needle aspirates and histopathologic findings were correlated, with the definitive diagnosis being that provided by the surgical specimen. When histopathologic material was unavailable, clinical follow-up was obtained to determine the nature of the lesion. Histologic correlation was available in 104 of the 176 soft-tissue aspirates and adequate clinical information was obtained in an additional 32 cases. Fine-needle aspiration showed high diagnostic
sensitivity (95%) and specificity (95%) for the determination of malignancy, approaching that obtained with frozen-section interpretation.

Oland et al (1986)\textsuperscript{18} reported their experience with 196 patients, including children, who underwent FNAC of a soft tissue mass. Altogether, patients had a benign cytologic diagnosis (tumor or inflammation) and were followed medically. Another 16 patients were diagnosed with metastatic carcinoma, without subsequent surgery. A total of 48 patients underwent histologic examination of their masses following the FNAC, and all 25 FNAC diagnoses of frank sarcoma were confirmed; thus there were no false-positive interpretations. Of the 17 benign soft tissue tumors diagnosed by cytology, one was a false-negative interpretation. A diagnosis of Fibroma was rendered in an individual who was proven to have a fibrosarcoma. The final six patients had an FNAC diagnosis that did not commit between benign and malignant; their subsequent histologic evaluations proved to be benign.

Wakely et al (1990)\textsuperscript{19} described a series of 28 fine needle aspiration biopsies (FNAB) of soft tissue from 22 patients. Four patients had two separate FNABs, and one had three aspiration procedures. The patient population was limited to children and young adults (age range, 2 months to 29 yrs, mean 16 yrs) who were known to have diverse forms of cancer, and who subsequently developed a mass in the peripheral soft tissues. All the FNAB diagnoses were confirmed by subsequent surgical
open biopsy or clinical follow up greater than 1 year. Twenty two aspirates were diagnosed as Cytologically malignant, one as suspicious of malignancy. Seven were considered benign. None were unsatisfactory. One false positive and no false negative cytologic diagnosis were obtained. The overall accuracy of FNAB diagnoses was 96%, while sensitivity was 100% and specificity 88%. Sites of aspiration included soft tissues of head and neck (seven cases), trunk (eight cases), breast (four cases), and extremities (nine cases). Malignant cytologic diagnoses included sarcoma (thirteen), seminoma (two), lymphoma/leukaemia (two), melanoma (one), undifferentiated neoplasm (one), and neuroblastoma (one). Electron microscopy of aspirated cells was used to confirm the diagnosis in two cases. Fine needle aspiration biopsy of soft tissue masses from children and young adults with cancer demonstrated a high diagnostic accuracy, and its use was justified in this population.

**Barth et al (1992)** prospectively sampled 38 large soft tissue masses in 37 patients with both core needle biopsy (CNBX) and fine needle aspiration (FNA) to determine the diagnostic utility of these biopsy methods. In 27 cases the histologic diagnosis made from the resected specimen was compared with the diagnosis based on the biopsy. CNBX correctly identified 16 of 16 malignant sarcomas and 10 of 11 benign masses (one was indeterminate). There were no false malignant or false benign core needle biopsy diagnoses. FNA correctly classified 12 of 14 malignant sarcomas and 4 of 11 benign lesions. Diagnoses based on FNA
were limited by a high proportion of samples, especially from benign lesions, that were inadequate for definitive diagnosis and by an inability to grade many malignant sarcomas. There were no significant complications resulting from the biopsies. They concluded that core needle biopsy is a highly accurate, easily performed method for the diagnosis of large soft tissue masses that can be accomplished with minimal morbidity.

Campora et al (1992)\textsuperscript{21} reviewed 98 cases of fine needle aspiration of soft tissue tumors with histologic confirmation performed during an eight year period and proposed a working morphologic classification based on the most prominent cytologic features. Six main tumor groups were recognized: myxoid, round cells, spindle cells, pleomorphic cells, polygonal cells and well differentiated. They believed that this classification allows recognition of the most common soft tissue tumors while helping with the differential diagnosis of other neoplasia, primary or secondary, with similar morphology and a similar presentation.

Bennert et al (1994)\textsuperscript{22} performed one hundred seventeen FNACs for soft tissue lesions (1980-1992). The mean age of the patients was 52.7 years (range, 4-89). Of these, 59 patients (51\%) had both an FNA and needle core biopsy performed either concomitantly or sequentially as part of the initial diagnostic workup. The distribution of the soft tissue lesions was as follows: extremities, 36(61\%), and retroperitoneum, 23(39\%). The FNACs were divided into three categories: diagnostic 53
(45%) (37 sarcoma, 16 benign); unsatisfactory, 44 (37%); normal/inflammatory cells present, 20(18%). Of these, 59 had concomitant needle core biopsies (NCB): 37 on patients with sarcoma on FNA, 22 on unsatisfactory FNA and none on those with normal/inflammatory cells (followed clinically). There was 100% correlation between FNA and needle core biopsy when sarcoma was diagnosed. In 7 of these cases, the NCB further specified the type of sarcoma. No NCB's were employed to confirm the diagnosis of benign tumor on FNA; excisional biopsies showed a total correlation. The 22 needle core biopsies for unsatisfactory FNA yielded 15 sarcomas, 2 fibromatosis and 5 benign lesions. Seventeen patients with unsatisfactory FNA had surgical biopsies (3 sarcoma, 14 benign), and 5 were lost to follow-up. In their experience, diagnostic FNA gave a yield identical to that of NCB, and the latter did not contribute to patient management. Core biopsies may have the advantage of sub typing selected sarcomas diagnosed by FNA. Unsatisfactory FNA should be evaluated further by a repeat aspirate or NCB. Performance of FNA by Cytopathologist can reduce the number of unsatisfactory specimens and allow repeat aspiration. In their study most of the unsatisfactory FNACs were from retroperitoneal and pelvic lesions were performed under radiographic guidance and could have been minimized by immediate cytologic assessment.

**Brosjo et al (1994)** evaluated 342 patients with a relatively equal distribution between benign and malignant soft tissue tumors. The FNAB
diagnosis was conclusive in 300 of these patients (88%). There was a 5% false-negative rate among the 153 benign cytologic diagnoses, and a 2% false-positive rate resulted among the 147 malignant cytologic diagnoses. Accordingly a correct diagnosis was rendered in 97% of this population.

Costa et al (1996)24 included 52 FNABs of 46 soft tissue and 6 bone neoplasms. Among the biopsies, 43 were for a primary diagnosis, and 9 were for clinically suspected recurrence. They reported a 7% false-negative rate and an 8% false-positive diagnostic rate; most of the latter occurred during evaluation of potential recurrent tumors. They suggested that some Pathologists may be more comfortable rendering a malignant interpretation in patients with a previous histologic diagnosis of sarcoma.

Liu et al (1998)25 systematically examined a series of 89 aspirates that included samples derived from 20 benign and 69 malignant masses including 11 metastatic malignant melanomas. Among the aspirates, 69 were from soft tissue lesions. Each FNAC was independently evaluated by four pathologists who differed in their experience in performing and interpreting aspiration biopsies. Each Pathologist evaluated these specimens in two settings: without and then with the clinical history. In each of these two scenarios, each Pathologist provided a precise cytopathologic diagnosis for the aspiration smears and classified the smears into one of four categories: benign, probably benign, probably malignant, or definitely malignant. These data were then utilized to create receiver operator characteristic (ROC) curves. Without benefit of
the clinical history, the proportion of precise correct diagnoses ranged from 0.19 to 0.44. With addition of the clinical history, the proportions of precise interpretations improved to a range of 0.48-0.66. The proportion of correct diagnoses improved for all four Cytopathologist. These results strongly support contention that one must integrate relevant clinical data and radiographic interpretations whenever evaluating aspiration biopsies of soft tissue lesions. Without addition of the clinical history, the proportion of correct classifications (as measured by the area under the ROC curve) ranged from 0.81 to 0.90. The range of correct classification improved to 0.89-0.90 with addition of the clinical history. Difficulty was especially noted for benign spindle cell tumors, including haemangiomas and nerve sheath neoplasms. Integration of the clinical history with the cytomorphology proved to be most useful for evaluating Lipomatous neoplasms and particularly for diagnosing Liposarcomas definitely malignant. Interestingly, the clinical information was, in some cases misleading in that the proportion of correct classifications declined for both haemangiomas and myositis ossificans. In the diagnostic exercises, the more experienced Cytopathologist fared better when designating a precise diagnosis and determining the correct benign/ malignant ratio. Overall, knowledge of the clinical history provided greater assistance for the less experienced Pathologists. This reiterates the crucial premise that FNAC of soft tissue lesions should be interpretated in conjunction with
the clinical and radiographic information pertaining to that specific mass.

**Akerman and Willen (1998)** from Sweden have described the largest series of FNAC of soft tissue lesions. Over a 20-year period these investigators evaluated 517 patients with an aspirate for a primary diagnosis of a soft tissue neoplasm; of these, 315 were benign and 202 were sarcomas. These authors were able to distinguish benign from malignant in 94% of the patients as proven by clinical follow up, resection or both. These errors were equally divided between 14 false-negative interpretations and 14 false-positive diagnoses. Among the latter, two patients underwent excessive surgical therapy. In their experience, the area of greatest difficulty for morphologic interpretation is the spindle cell neoplasms followed by lipomatous tumors.

**Kilpatrick et al (1999)** retrospectively reviewed 73 consecutive aspirates from 67 patients, none of whom had a previously established sarcoma diagnosis. Sarcoma cases were subgrouped according to predominant cytomorphologic features: pleomorphic cell-19, small round cell-18, spindle cell-18, myxoid-10, epithelioid/polygonal cell-7, one case of well differentiated liposarcoma was analyzed separately. Ancillary studies were used for 25 cases. Among adequate specimens, 61 tumors were recognized as sarcoma. A specific and accurate histologic subtype was determined in 34 cases. Ancillary studies were most useful for histologic subtyping of small round cell and spindle cell sarcomas.
Myxoid sarcomas were subtyped easily based solely on histomorphologic features. Pleomorphic cell and epitheloid / polygonal cell sarcomas were recognized easily as malignant but difficult to subtype by FNAB. With the exception of small round cell sarcomas, histologic subtyping of a sarcoma usually did not directly influence therapy. With meticulous attention to clinicopathologic features and ancillary techniques, many sarcomas, especially small round cell, spindle cell, and myxoid type, may be subtyped successfully by FNAC, within limitations.

Wakely et al (1999)\textsuperscript{26} reviewed the results of cytopathologic diagnoses obtained by fine needle aspiration biopsy over a consecutive 11- month period in patients that presented primarily with a palpable soft tissue mass. A few patients with deep non-palpable soft tissue masses also were evaluated by radiologically guided FNA. Eighty two aspirates were performed without complications from 77 patients ranging from 12-88 years of age (mean=50 years) with men outnumbering women (1.5:1). Soft tissue masses were most common in the extremities (41 cases), followed by the trunk (34 cases), retroperitoneum (5 cases), and head and neck (2 cases). Fine needle aspirates were diagnosed as malignant in 42(51%), benign in 32(39%), nondiagnostic in 6(7%), and atypical in 2(2%) cases. Malignant aspirates were comprised of 24 sarcomas (57%), 9 carcinomas (21%), 6 malignant lymphomas (14%), and 3 melanomas (7%). Twenty-two aspirates (52%) had an initial diagnosis of malignancy; where as 18(43%) represented metastatic and
2(5%) recurrent neoplasms. Confirmation of the cytopathologic diagnosis was by concurrent or subsequent tissue examination in 57%, flow cytometry in 5%, clinical outcome in 34%, and repeat aspiration in 4%. One false negative and no false positive diagnoses were made with a sensitivity and specificity of 100% and 97% respectively. Of the malignant aspirates, 83% could be subtyped whereas 72% of benign aspirates were correctly subtyped. For primary soft tissue sarcomas, 12 of 19 (63%) were accurately subtyped. In 48% of cases a concurrent cell block was obtained and found diagnostically useful in 54% of them.

Bezabih M (2001) determined the patterns of soft tissue tumor and tried to assess the utility of fine needle aspiration cytology (FNAC) in diagnosing soft tissue tumor. Of 15,361 patients who visited the cytology diagnostic service of the Pathology Department, Medical faculty, Addis Ababa University, 623 (4.1%) cases with a diagnosis of soft tissue tumor were retrieved from the department’s records for the years 1991-96. Fifty-three soft tissue tumors (25 benign and 28 malignant tumors) with combined FNAC and surgical biopsy results were traced for cyto-histological correlations. Twenty-two out of 25 benign soft tissue tumor were correctly diagnosed, with three false cytologic diagnoses where one mesenchymal neoplasm, one haemangioma, and one haemorrhagic lesion were identified; and out of 28 malignant soft tissue, 23 were correctly diagnosed, however the five false cytological diagnoses were one soft tissue sarcoma, one dermatofibrosarcoma, one malignant
mesenchymal neoplasm, one spindle cell neoplasm and one mesenchymal neoplasm. Thus in their study, a sensitivity and specificity of 88.5% and 81.5% respectively for the diagnosis of soft tissue tumor was reported. They concluded that FNAC of soft tissue tumor is a fast, effective and reliable diagnostic tool that may help in categorising soft tissue tumor into benign and malignant groups for clinical management.

**Kilpatrick et al (2001)** reviewed the clinicopathologic features of 145 consecutive fine needle aspiration biopsy (FNAB) specimens from 140 patients without a previous diagnosis of sarcoma. Among 138 adequate specimens, 42 bone sarcomas and 80 soft tissue sarcomas were recognized as sarcomas; histologic subtyping was easier in bone than in soft tissue sarcomas and in pediatric than in adult cases. There was no correlation in accuracy of subtype (in low vs. high-grade sarcomas). FNAB was most accurate for subtyping of skeletal osteosarcoma, pediatric small round cell bone/soft tissue sarcomas, synovial sarcoma, skeletal chondrosarcoma, and adult myxoid soft tissue sarcomas. Although almost always recognized as sarcoma, subtyping of adult pleomorphic soft tissue sarcomas generally was not possible but did not influence therapy; all were considered high grade sarcomas for treatment purposes. There were 4 misinterpretations of subtype in soft tissue sarcomas; none resulted in a change in therapy. Among bone and soft tissue sarcomas, FNAB was sufficient for initiation for definitive therapy in 87% and 83% of patients, respectively. Most FNAB specimens
from bone and soft tissue sarcomas are recognized easily as sarcoma, but subtyping seems more accurate in bone sarcomas. Although histologic subtyping of adult soft tissue sarcomas is often impossible, no influence on initial therapy is usually observed. In contrast, subtyping of pediatric sarcomas by FNAB seemed highly accurate and was necessary for appropriate therapy.

Cardillo et al (2001)\textsuperscript{29} analyzed the cytologic features of nine histologically confirmed epithelioid sarcomas. The criteria included cell size and shape, cell borders, cluster organization, cytoplasmic characteristics, nuclear and nucleolar features, and background characteristics. In most cases, single, dispersed cells represented the predominant pattern, with only a few clusters present. The cells were mostly round with interspersed spindle cells and mild to moderate pleomorphism. The nuclei were large and eccentrically located, with a plasmacytoid appearance. A pale zone in the perinuclear area was evident in three of nine cases. Well defined cell borders with intercellular spaces between malignant cells were observed in eight cases. In three cases, a granuloma-like structure was identified. In two cases, the cells were mostly spindle and showed greater cellular pleomorphism.

Palmer et al (2001)\textsuperscript{30} retrospectively reviewed all histologically confirmed soft tissue sarcomas in adult patients evaluated with FNAB during a 10-year period. They conducted a blind review of 84 FNAB specimens from 77 malignant and 7 benign soft-tissue lesions. Smears
were reviewed separately by two cytopathologists without knowledge of the histopathological diagnosis. Cytomorphologic groups included 31 spindle cell, 24 pleomorphic, 11 myxoid, 7 epithelioid/polygonal, 3 small round cell, and 8 nondiagnostic cases. Malignancies included one lymphoma, 41 primary, 15 recurrent, and 20 metastatic soft-tissue sarcomas. Adequacy was defined as a majority of slides with at least 5 clusters of 10 unobscured cells. Five originally false-negative cases were considered non-diagnostic on review. Sarcoma was recognized in 59 of 64 adequate cases (92%) with available histology; however, the specific histopathologic subtype was identifiable in only 9 cases (14%). The assigned cytologic grade by them accurately reflected the histologic grade in 90% of sarcomas when segregated into high and low grades.

Nagira et al (2002) retrospectively reviewed fine needle aspiration biopsy (FNAB) specimens of 301 soft tissue lesions of the extremities and trunk. Final diagnosis was 137 benign and 86 malignant neoplasms and 78 nonneoplastic lesions. Of the 301 FNAB samples, 279 (93%) were adequate for cytologic diagnosis. The adequate FNAB specimens were initially grouped into three broad categories: benign (197 cases), malignant (57 cases), and suspicious for malignancy (25 cases). Sensitivity and specificity for diagnosis of a malignant lesion were 92% and 97%, respectively. The specimens were cytomorphologically classified into categories: small round (14 cases), spindle cell (77 cases), epithelioid/ polygonal (16 cases), pleomorphic (29 cases), myxoid (19
cases), lipomatous (37 cases), epithelial (23 cases), inflammatory lesions (28 cases), and others (36 cases). Specific FNAB diagnoses were correct in 151 of 279 cases (54%) in combination with clinical and radiologic findings. They concluded FNAB as a valuable technique for the primary diagnosis of soft tissue lesions.

Klijanienko et al (2002) studied cytomorphological patterns of malignant peripheral nerve sheath tumor (MPNST). Cytological and histological specimens in 24 tumors in 17 patients were correlated. The review of the original cytology reports showed that four (16.6%) tumors were correctly diagnosed, eight (33.3%) were diagnosed as sarcoma not otherwise specified, four (16.7%) as fibrosarcoma, three (12.5%) as synovial sarcoma, three (12.5%) as lipomyosarcoma, and one (4.2%) case each as malignant fibrous histiocytoma and rhabdomyosarcoma. At review, tumors were histologically reclassified as well-differentiated MPNST in 11 (45.9%) cases, anaplastic MPNST in 11 (45.9%) cases, epithelioid MPNST and malignant Triton tumor in one (4.2%) case each. Cytologically, well-differentiated MPNST was composed of polymorphous oval to round cells, small spindle-shaped cells with wavy and comma-like naked nuclei, and a fibrillary, delicate stroma. Anaplastic MPNST, moreover, were composed of anaplastic giant and polymorphous cells. The malignant Triton tumor was composed of oval to round rhabdomyoblastic cells with eccentric nuclei and the epithelioid MPNST of polymorphous and round, epithelial like cells. The cytological
diagnosis of MPNST may be difficult, especially in anaplastic tumors. The correlation between the cytological features and the clinical information-origin of the tumor from a nerve trunk, a preexisting neurofibroma, and patients with known history of neurofibromatosis-1 could be indicative of an MPNST diagnosis.

Klijianenko et al (2002)\textsuperscript{32} reviewed the cytologic and the corresponding histologic material of 56 synovial sarcoma (SS) from 36 patients. Synovial sarcoma (SS) is a high-grade malignant soft tissue tumor that manifests different phenotypic subtypes that may render their cytological evaluation challenging. Classical patterns defined as dispersed or small clusters of cells with bland chromatin, inconspicuous nucleoli, oval to spindle-shaped cytoplasm and branching tumor tissue fragments, vessels stalks, acinar structures in scant mucin background were seen in all 53 (94.7\%) cellular cases. Epithelial, squamous, round cells, mast cells, necrosis, comma-like nuclei, marked nuclear atypia, secretory mucin, and rosette-like structures were also occasionally observed. Comparing the histological subtype they noted that epithelial cells and secretory mucin were restricted to biphasic synovial sarcoma, round cells to poorly differentiated synovial sarcoma, and comma-like nuclei to monophasic fibrous synovial sarcoma. They concluded that the classical pattern is highly suggestive of synovial sarcoma of all three monophasic, biphasic, or poorly differentiated subtypes. These
characteristics, along with molecular genetic studies, may improve the cytologic diagnosis of synovial sarcoma.

Sapi et al (2002)\textsuperscript{33} examined ninety-four FNA cytologic specimens and compared them with the corresponding histology. Ordinary lipomas were excluded. Morphologic evaluation was supplemented by ancillary techniques such as fluorescence in situ hybridisation (FISH), DNA cytometry, and immunocytochemistry. From a practical clinicopathological point of view, the cases were grouped in the following categories:

1) tumors with definite diagnosis
   a. high grade malignant neoplasms (high grade sarcomas, metastatic carcinomas, lymphoma)
   b. tumors with precise histogenetic origin by cytogenetics
   c. benign tumors.

2) tumors of questionable nature.

In the first group there were 74 tumors: 22 high grade sarcomas, six metastatic metastatic carcinomas, one malignant lymphoma, 16 malignant tumors in which the precise histogenetic origin could be established by cytogenetic studies, and 29 benign soft tissue tumors other than lipomas. In the second group there were 20 tumors comprising of benign and malignant soft tissue tumors of low grade,
wherein the precise nature of the neoplasm could not be established with confidence on cytologic study, even using ancillary techniques. FNAC of soft tissue tumors combined with ancillary techniques should be considered a viable diagnostic technique for therapeutic protocols. Although the second group was fairly large, they have reliable, well circumscribed categories which provided them great freedom for preoperative and surgical treatment, thus providing the best chance for healing.

**Mathur et al (2003)**[^34] evaluated the applicability and accuracy of grading spindle cell sarcomas on fine needle aspiration cytology (FNAC) smears, 54 cases of histologically documented spindle cell sarcomas, consisting of synovial sarcomas (20 cases), neurofibrosarcomas (12 cases), leiomyosarcomas (9 cases), dermatofibrosarcoma protuberans (DFSP: 6 cases), fibrosarcoma (3 cases), hemangiopericytomas (2 case), and spindle cell sarcomas, unclassified (2 cases), were graded according to a three-tier system proposed earlier for FNAC smears, while the histological sections were graded using the French Federation of National Cancer center (FNCLCC) grading system. The cytological grading was correlated with the histological grade. There was an overall cytologic and histologic concordance in 40/54 (74%) cases, and concordance in 9/13 (69%) grade I, 19/25 (76%) grade II, and 12/16 (75%) grade III cases. Analysis of grading of individual sarcomas revealed a concordance in 92% of neurofibrosarcomas, 78% of leiomyosarcomas, 70% of synovial...
sarcoma, 67% of dermatofibrosarcoma protuberans, 67% of fibrosarcomas, 50% of hemangiopericytomases, and 50% of cases of malignant mesenchymal tumors, spindle-cell type unclassified. Minor non-correlation was seen in 4/54 (7.4%) cases. Thus it was possible to accurately predict the grade in 74% of cases of spindle cell sarcomas. The cytological and histological concordance was better (75%) in high grade (grades II and III) as compared to grade I sarcomas (69%). Sampling errors due to morphologic heterogeneity in sarcomas may have caused non-correlation in a few cases.

Roy et al (2003) observed that out of a total of 21,391 cases aspirated during a period of 12 years, 556 were soft tissue lesions, of which 116(20.86%) were malignant and the 440(79.14%) benign. Lipoma, vascular hamartoma, neural tumors and fibrohistiocytic tumors form the main chunk of the benign lesions, accounting for 47.27%, 32.85%, 13.87% and 2.95% respectively. Malignant lesions were mainly rhabdomyosarcoma, undifferentiated round cell sarcoma, synovial sarcoma and pleomorphic sarcomas, having an incidence of 39.65%, 18.96%, 14.65% and 6.89% respectively. Non-specific diagnosis of spindle cell sarcoma was given in 14.65% cases. In 75% of the cases histological correlation was available. Errors in cytodiagnosis were found in 2 (0.5%) cases of benign and 10 (8.6%) cases of malignant tumors respectively. They regarded FNAC as a quick and safe preliminary tool for diagnosis of soft tissue lesions.
Kitagawa et al (2003)\textsuperscript{35} studied the usefulness of fine needle aspiration cytology for the preoperative diagnosis of soft tissue tumor of the hand. Fine needle aspiration cytology was performed on 93 soft tissue tumors of the hand which were classified as malignant, benign or unclassified based on cytological findings. They also attempted to make specific diagnosis by cytology. The cytological diagnosis was then compared with the postoperative histopathological diagnosis. The cytological differentiation between benign and malignant tumors showed neither false-positive nor false-negative results. Of the 47 lesions with sufficient material for cytology and that were postoperatively diagnosed histologically, 35 (including one recurrent lesion) were correctly diagnosed by fine needle aspiration cytology. No complications were encountered. They concluded that fine needle aspiration cytology has a high degree of diagnostic accuracy and safety for soft tissue tumors of the hand.

Klijianenko et al (2004)\textsuperscript{36} reviewed cytopathology files from The Institute Curie between 1954 and June 2003. They retrieved 2,378 soft tissue tumors, of which 86 were Liposarcomas (55 patients). Patients were 27 males and 23 females. Age ranged from 15 to 90 yr (mean: 51.8, median: 47 Yr). Twenty-four tumors (27.9\%, equal number of patients) had FNA for the initial pretherapeutic diagnosis. Thirty-four tumors (39.5\%, 25 patients) were recurrent from known primary; 28 (32.6\%, 19 patients) were secondary from a previously known primary. Tumors were
localized in the head and neck area in 5 (5.8%) cases, in the supradiaphragmatic trunk in 16 (18.6%) cases, in the infra-diaphragmatic trunk in 16 (18.6%) cases, and in the extremities in 49 (57%) cases. The liposarcomas were well differentiated in 14 cases (9 pure, 2 dedifferentiated, 3 sclerosing), 64 myxoid, and 8 pleomorphic. Aspirate samples of 12 recent tumors were analyzed by cytogenetics and molecular biology. Flow cytometric DNA analyses from the aspirates were analyzed in 5 tumors (in each one example of pure well-differentiated, sclerosing, round cell myxoid, pure myxoid, and pleomorphic liposarcoma.

Dey et al (2004) evaluated the usefulness of fine needle aspiration cytology (FNAC) in the diagnosis of soft tissue tumor. They also assessed the various pitfalls of FNAC of soft tissue tumor. This was a retrospective study and analyzed 82 histopathology proven cases of FNAC of soft tissue tumor diagnosed in a five and a half year period. On histopathological examination, 55 of these cases were malignant and 27 were benign. There were a total of 15 recurrences and histopathology was available prior to FNAC in only eight of these cases. Therefore, excluding these eight cases, malignant tumors were primarily diagnosed by FNAC in 47 cases. The sensitivity, specificity and positive predictive value of FNAC in diagnosis of soft tissue tumor were 91.5%, 92.5% and 95.5% respectively. Only 22 of 47 cases (46.8%) were correctly categorized. There were two false positive and four false negative cases. One case
each of fibromatosis and schwannoma were reported as sarcoma. False
negative cases were fibrosarcoma (1), malignant nerve sheath tumor (2)
and haemangiopericytoma (1). FNAC was very useful in distinguishing
benign from malignant soft tissue tumor. However, it was not so effective
in exact categorization of tumor.

Klijanienko et al (2006)\textsuperscript{38} reviewed cytology aspirates in
corresponding histological sections from 34 schwannoma diagnosed at
The Institute Curie. Histologically, 24 cases were classic, 5 were
“ancient”, 4 were cellular, and 1 was epithelioid schwannoma. No
example of melanotic schwannoma was recorded. Original cytological
diagnosis was schwannoma in 13 (38.2%) cases, benign soft tissue tumor
in 11(32.4%), pleomorphic adenoma in 2 (6%) cases, angioma in 1 (2.9%)
case, nodular fasciitis in 1(2.9%) case, suspicious in 3(8.8%) cases and
not satisfactory in 3 (8.8%) cases. There were no major differences
between classical, “ancient”, cellular, and epithelioid variants on cytology
smears. Myxoid stroma, mast cells, and intranuclear inclusions were
limited to classical subtype. Similarly, cytonuclear atypia was more
frequent in classical subtype than in other subtypes.

Rekhi et al (2007)\textsuperscript{39} aimed at evaluating scope of FNAC in
diagnosing 127 cases of soft tissue tumors. Immunocytochemistry (ICC)
was performed in 15 cases. Histopathological details were available in
115 cases. 50% cases were referred for a primary diagnosis, while 26.8%
and 22.8% cases were evaluated for recurrent and metastatic lesions
respectively. Extremities were the commonest sites. On FNAC, 101 cases (79.5%) were labeled as malignant, whereas 10 cases (7.9%) were labeled as benign. The remaining 16 cases (11%) were not categorized and were labeled as unsure/not specified. Histopathological confirmation in 115 cases, gave a diagnostic accuracy of 98% with a positive predictive value in malignant cases and a negative predictive value of 100% in benign cases. Two cases were false positive. Among the various cytological categories, 60 cases (47.2%) were of spindle cell type, followed by 32 (25.2%) of round cell type and 14 cases (11%) of lipomatous type. Other 12 cases (9.4%) were of pleomorphic type; 7(5.5%) cases of epithelioid type and remaining 2 cases were of myxoid type. All the round cell, pleomorphic and myxoid type of tumors were sarcomas, whereas 73.3% cases of spindle cell type were labeled as malignant. Exact cytological subtyping was offered in 58 cases, with rhabdomyosarcoma (RMS) as the most frequently sub typed tumor. The two false positive malignant cases were of fibromatosis and a pigmented schwannoma, on biopsy. Out of 28 metastatic lesions, lymph node was the commonest site for metastasis, with epithelioid tumors that formed highest percentage of metastatic cases. They concluded that FNAC is fairly specific and sensitive in soft tissue tumor diagnoses for primary, recurrent and metastatic lesions. The cytological types, especially round cell and pleomorphic sarcomas, can be quickly identified.
Roy S et al (2007) studied 105 cases of soft tissue tumors by fine needle aspiration cytology (FNAC). Aspiration was carried out using a 21 gauge disposable needle and a 20 cc disposable syringe capable of producing good suction. 65 (61.9%) were benign, 33 (31.4%) were malignant and 7 (6.7%) cases were inconclusive. All the cases were corroborated by histopathological examination. Leishman-Giemsa (LG) and Papanicolaou (Pap) stains were used for the aspiration smears while hematoxylin-eosin (H&E) was used for the histopathological study supported in some cases by Periodic acid schiff (PAS) and reticulin stains. On histopathological examination, accuracy rate of benign tumors was found to be 90.6% and that of malignant tumors was 91.3%. The overall accuracy rate was 90.8%. So they considered FNAC as a useful cost-effective procedure for the diagnosis of soft tissue tumors.