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Review Article

World Health Organization Reporting System for Soft Tissue Cytopathology: A Concise Review with a Practical Diagnostic Approach

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Abstract

Background and objectives: Soft tissue cytopathology plays a vital role in the diagnosis and management of soft tissue neoplasms, necessitating a standardized classification system to improve diagnostic accuracy and guide clinical decision-making. This article provides a concise review of the World Health Organization (WHO) Reporting System for Soft Tissue Cytopathology and presents a practical diagnostic approach to soft tissue cytopathology. ***Methods:*** The WHO Reporting System is reviewed in conjunction with relevant literature. The reporting system employs a six-category framework: non-diagnostic, benign, atypical, soft tissue neoplasm of uncertain malignant potential, suspicious for malignancy, and malignant. Each category is associated with a corresponding risk of malignancy and recommended clinical management guidelines. This classification aligns with the WHO Classification of Soft Tissue and Bone Tumours (5th edition) and incorporates cytomorphologic features, ancillary studies, and clinical correlation to enhance diagnostic reproducibility and communication among pathologists and clinicians. ***Results:*** The system supports a probabilistic approach to risk stratification, enabling more consistent diagnostic and therapeutic strategies. ***Conclusions:*** As molecular diagnostics and immunocytochemistry continue to advance, this framework provides a robust foundation for the interpretation of soft tissue fine-needle aspiration biopsies and optimized patient care.

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Introduction

Cytopathology is a critical component of the diagnostic pathway for soft tissue neoplasms. Fine-needle aspiration biopsy (FNAB) has been widely adopted in clinical practice as a minimally invasive method for evaluating both primary and metastatic lesions, owing to its high diagnostic yield, cost-effectiveness, and ability to rapidly guide patient management. However, despite its utility, soft tissue FNAB has historically lacked a universally accepted standardized reporting system and consistent terminology. This has resulted in challenges related to interobserver variability and diagnostic interpretation. Reported interobserver variability rates of 20–30% prior to standardization highlight the need for a more consistent reporting framework and strongly justify its implementation.[1] Recognizing these issues, a group of experts—through the collaborative efforts of the International Academy of Cytology, the International Agency for Research on Cancer, and the World Health Organization (WHO)—recently developed the WHO Reporting System for Soft Tissue Cytopathology. This system aims to establish a structured diagnostic framework that enhances accuracy, reproducibility, and clinical relevance.[1–4] It is aligned with the 5th edition of the WHO Classification of Soft Tissue and Bone Tumours, providing enhanced contextual accuracy.[5]

The diagnosis of soft tissue tumors via FNAB presents unique challenges due to the broad morphological spectrum of mesenchymal neoplasms, frequent cytological overlap between benign and malignant lesions, and the inherent subjectivity of cytopathologic interpretation. Unlike epithelial tumors, which often display well-defined cytological features, many soft tissue tumors exhibit subtle cytomorphologic variations that demand careful interpretation. Additionally, the WHO Classification of Soft Tissue and Bone Tumours (5th edition) includes limited content on cytology,[5] further underscoring the need for a dedicated reporting system. In recent years, there has been a growing emphasis on risk stratification, similar to systems such as the Bethesda system for thyroid cytopathology, to guide clinical decision-making more effectively. The implementation of a standardized classification system offers a clear, reproducible method for categorizing FNAB results, thereby improving diagnostic precision and informing appropriate management strategies.

As a practicing bone and soft tissue pathologist, cytopathologist, and chapter contributor to this book, I had the privilege of reviewing the material prior to publication. This paper presents an overview of the WHO Reporting System

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Table 1. The WHO Reporting System for Soft Tissue Cytopathology – diagnostic categories, modified

Category	Definition	Common findings	Examples
Non-diagnostic	The sample lacks adequate material in quantity or quality for a meaningful or reliable diagnosis	Scant material, necrotic debris, obscuring blood, crushed cells, acellular, or poor preservation	Acellular aspirates, extensive necrosis, and blood-contaminated samples
Benign	FNAB findings indicate unequivocal benign or a benign soft tissue neoplasm	Inflammation, uniform spindle or adipocytic cells, no significant atypia, no mitotic activity, background matrix consistent with benign tissue	Inflammation, lipoma, ganglion cyst, fibromatosis, moositis ossificans, tenosynovial giant cell tumor
Atypical	FNAB reveals cytological features that are not clear to determine tumor or not, or they are mostly benign, minimally worrisome for malignancy, but not sufficient for suspicious for malignancy	Variable cellularity, variable nuclear features, mild atypia and possible low mitotic activity	Lipomatous tumor, low grade spindle cell proliferation, schwannoma with degenerative changes
Soft tissue neoplasm of uncertain malignant potential (STNUMP)	FNAB demonstrates features of a mesenchymal neoplasm but lacks conclusive criteria to classify it as benign or malignant	Variable cellularity, atypia, or mitotic figures, absence of necrosis or clear malignant features, possible myxoid or fibrotic background	Solitary fibrous tumor, myxoid soft tissue neoplasm, low-grade spindle cell tumor, smooth muscle tumor, dermatofibrosarcoma protuberans
Suspicious for malignancy	FNAB findings are highly worrisome for malignancy but not definitive	Variable cellularity, increased nuclear pleomorphism and mitotic activity, occasional necrosis, may be short of quantitative or qualitative features for a definitive diagnosis of malignancy	Atypical lipomatous tumor, low grade myxofibrosarcoma, gastrointestinal stromal tumor
Malignant	FNAB findings are diagnostic of a malignant soft tissue neoplasm	High cellularity, marked nuclear pleomorphism, high mitotic index, necrosis, abnormal architecture, and infiltrative growth pattern	Liposarcomas, leiomyosarcoma, synovial sarcoma, high-grade myxofibrosarcoma, epithelioid sarcoma, Ewing sarcoma

FNAB, fine-needle aspiration biopsy; WHO, World Health Organization.

for Soft Tissue Cytopathology, detailing each diagnostic category, its associated risk of malignancy (ROM), clinical relevance, and corresponding management strategies. By establishing a standardized lexicon and diagnostic approach, this system promotes accurate, reproducible, and clinically meaningful cytopathological interpretations, ultimately ensuring optimal patient care.

Standardization of reporting and practical diagnostic approach

To ensure clarity, consistency, and clinical applicability, the WHO Reporting System for Soft Tissue Cytopathology recommends that every soft tissue FNAB report follow a structured format with clearly defined diagnostic categories. Each report should begin with one of six primary diagnostic categories, followed by a detailed cytopathological description, risk assessment, and management recommendations. This structured approach enhances diagnostic accuracy, facilitates communication between cytopathologists and clinicians, and provides a probabilistic framework for risk stratification and patient care.

Primary diagnostic categories and associated ROM

A fundamental component of the reporting system is the primary diagnostic category, which assigns every FNAB interpretation to one of six standardized classifications: non-diagnostic, benign, atypical, soft tissue neoplasm of uncertain malignant potential (STNUMP), suspicious for malignancy, and malignant. These categories serve as a universal lexicon for reporting soft tissue FNAB results and ensure cytopathologists convey diagnostic findings in a standardized and reproducible manner (Table 1). The assigned category determines subsequent risk stratification, the need for further testing, and management recommendations.

In summary, every FNAB interpretation should be assigned to one of the following six primary diagnostic categories:

- Non-diagnostic/Insufficient/Inadequate;
- Benign;
- Atypical;
- STNUMP;
- Suspicious for malignancy;
- Malignant.

Each diagnostic category is associated with an estimated ROM, providing a probabilistic approach to malignancy risk. The ROM estimates are derived from multi-institutional validation studies to ensure transparency in risk assessment.[2] ROM estimates should be presented as follows:

- Non-diagnostic –29.9% (9-42%);
- Benign – 2.5% (0-4%);
- Atypical – 39.6% (46%);
- STNUMP – 51.4% (20-27%);
- Suspicious for malignancy – 68.2% (71-80%);
- Malignant – 97.7% (91-100%).

ROM assessments should be based on institutional data and published literature to ensure evidence-based risk stratification.

Cytopathological description

The cytopathological description in the report could provide a concise yet detailed summary of microscopic findings, including cellularity (low, moderate, or high), cell arrangement (cohesive clusters, dispersed single cells, three-dimensional aggregates), nuclear features (pleomorphism, chromatin pattern, nucleoli), cytoplasmic characteristics (spindle, epithelioid, vacuolated, clear, or oncocytic cells), and background elements (necrosis, myxoid stroma, inflammatory infiltrates, mucin, or extracellular matrix). Special attention should be given to the presence of mitotic activity, atypical mitoses, or necrotic debris, as these features may indicate higher-grade lesions. These cytopathological findings assist in categorizing lesions into their respective risk groups and guide decisions regarding ancillary testing.

In summary, key components of the description of cytomorphological features include:

- Cellularity (low, moderate, high);
- Cell arrangement (cohesive clusters, dispersed single cells, three-dimensional aggregates);
- Nuclear features (pleomorphism, chromatin pattern, nucleoli);
- Cytoplasmic characteristics (spindle, epithelioid, vacuolated, clear, or oncocytic cells);
- Background elements (necrosis, myxoid stroma, inflammatory infiltrates, mucin, or extracellular matrix);
- Mitotic activity and atypical mitoses, if present.

Ancillary testing

When FNAB alone is insufficient for a definitive diagnosis and the tissue cell block is adequate, ancillary studies should be incorporated to refine tumor classification.[6,7] Immunocytochemistry (ICC) can assist in distinguishing between different soft tissue neoplasms, particularly when differentiating mesenchymal, epithelial, and hematopoietic lesions.[6] Key markers include S100 and SOX10 for schwannomas and melanomas; CD34 and STAT6 for solitary fibrous tumors; and desmin, smooth muscle actin, and MyoD1 for smooth muscle and skeletal muscle differentiation. Additionally, fluorescence in situ hybridization (FISH) and next-generation sequencing (NGS) can provide molecular confirmation for certain tumors.[8] For example, murine double minute 2 (MDM2) amplification confirms liposarcoma, Ewing sarcoma breakpoint region 1 (EWSR1) rearrangement is seen in Ewing sarcoma and myxoid liposarcoma, and KIT mutations are associated with gastrointestinal stromal tumors. When ancillary testing is performed, its findings should be incorporated into the report to aid in accurate classification and prognostication.

In summary, ancillary studies may be performed to refine tumor classification. These include:

ICC:

- Helps identify lineage-specific markers, differentiating mesenchymal, epithelial, and hematopoietic neoplasms;
- Common markers include: S100, SOX10 (schwannoma, melanoma); CD34, STAT6 (solitary fibrous tumor); desmin, smooth muscle actin, MyoD1 (smooth and skeletal muscle differentiation).

FISH & NGS:

- Molecular testing identifies characteristic genetic alterations in soft tissue tumors;
- Examples: MDM2 amplification (liposarcoma), EWSR1 rearrangement (Ewing sarcoma, myxoid liposarcoma), KIT mutations (gastrointestinal stromal tumor).

Clinical and imaging correlation

Soft tissue FNAB findings must be interpreted within the context of clinical and imaging findings to optimize diagnostic accuracy. Tumor location, size, and depth (deep-seated vs. superficial, intramuscular vs. subcutaneous), along with radiologic characteristics (well-circumscribed vs. infiltrative, presence of necrosis or calcifications), provide essential clues in differentiating benign from malignant lesions. Magnetic resonance imaging (MRI), computed tomography (CT), and ultrasound findings should be correlated with cytological results to refine the diagnostic approach. For indeterminate cases, multidisciplinary discussions with radiologists, oncologists, and surgeons can enhance diagnostic certainty and guide further management.

In summary, the report should include the context of clinical history and imaging studies. These include:

- Tumor location, size, and depth (deep vs. superficial, intramuscular vs. subcutaneous);
- Radiologic features (MRI, CT, ultrasound): well-circumscribed vs. infiltrative margins, necrotic, myxoid, or calcified components;
- History of prior malignancies or metastatic disease.

Practical diagnostic approach

The practical step-by-step diagnostic approach for soft tissue cytology developed by the author is summarized in Figure 1 and detailed in Table 2.[7] Similar approaches have been advocated by other pathologists.[9]

In summary, the practical diagnostic approach includes the following steps:

Step 1: Initial morphological assessment (pattern-based analysis):

Cellular pattern recognition:

- Round cell tumors;
- Spindle cell tumors;
- Pleomorphic cell tumors;
- Epithelioid cell tumors;
- Myxoid tumors.

Cytological features:

- Nuclear atypia;
- Cellular cohesion;
- Background matrix (myxoid, chondroid, necrotic, etc.);
- Presence of lipoblasts, giant cells, or inflammation.

Step 2: Correlation with clinical and radiological features:

- Age, site, growth pattern;
- Imaging (MRI, CT, ultrasound);
- Presence of metastases.

Step 3: Ancillary testing (confirmatory studies):

- ICC (e.g., S100, MDM2, CDK4, desmin, myogenin);
- Flow cytometry (lymphoid vs. non-lymphoid);
- Molecular testing (FISH, NGS, polymerase chain reaction) (e.g., MDM2 amplification for liposarcomas, EWSR1 translocation for Ewing sarcoma);
- Cytogenetics (chromosomal rearrangements in sarcomas).

Step 4: Final categorization:

- Benign;
- Atypical;
- STNUMP;
- Suspicious for malignancy;
- Malignant.

Management recommendations

The final section of the report should include management recommendations tailored to the diagnostic category. After emphasizing that correlation with clinical and imaging findings is essential, the following are recommended:For non-diagnostic cases, repeat FNAB or core needle biopsy (CNB) is recommended, whereas benign lesions typically require only clinical follow-up. Atypical and STNUMP cases may re-

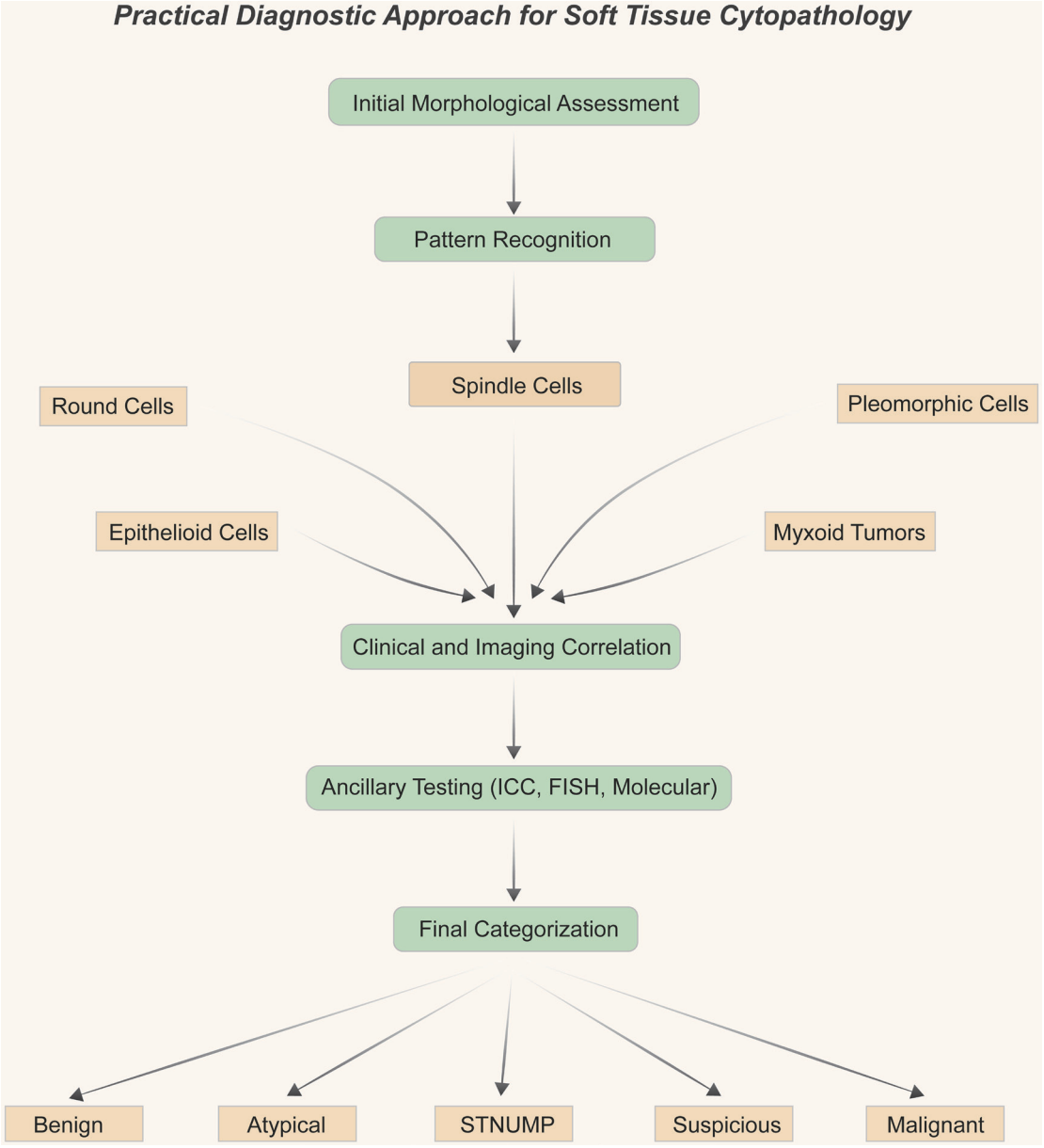

Fig. 1. Practical diagnostic approach for soft tissue cytopathology. This diagnostic algorithm was adapted from established protocols with modifications.[7] FISH, fluorescence in situ hybridization; ICC, immunocytochemistry; STNUMP, soft tissue neoplasm of uncertain malignant potential.

quire further workup with ancillary testing, biopsy, or excision. Suspicious for malignancy cases should be discussed in a multidisciplinary setting to determine the most appropriate next steps, including surgical biopsy or further molecular testing. Malignant diagnoses necessitate immediate referral for oncologic management, including additional staging, potential resection, and systemic therapy. The management plan should be tailored based on the diagnostic category, ROM, and clinical context to ensure the best possible patient outcome. Implied ROM and recommended clinical management are presented in Table 3.

In summary, each FNAB report should provide recommendations for further evaluation and treatment, which may include:

- Non-diagnostic: Repeat FNAB with rapid on site evaluation (ROSE) or consider core needle biopsy (CNB) if persistently inadequate; Clinical and radiological correlation is necessary;
- Benign: Clinical follow-up for benign lesions with imaging surveillance;
- Atypical: Clinical and radiologic correlation is recommended. Repeat FNAB with ROSE or proceed with CNB. Ancillary testing may help refine the diagnosis;
- STNUMP: Multidisciplinary discussion. Repeat FNAB or CNB. Excision may be warranted, particularly for deep-seated or enlarging lesions. Ancillary studies should be considered to further stratify risk;
- Malignant: Multidisciplinary team discussion for complex cases.

The management plan should be tailored based on the

Table 2. Summaries of differential diagnosis and ancillary testing based on morphology

Morphology category	Tumor type	Key features	Ancillary testing
Round cell tumors	Ewing sarcoma	Small blue round cells, EWSR1::FLI1 or EWSR1::ERG	FISH or NGS for rearrangement of EWSR1 or fusion of EWSR1::FLI1, or EWSR1::ERG; ICC CD99+, NKX2.2+, PKCBII+
	Rhabdomyosarcoma	Primitive round and spindle cells, rhabdomyoblasts, desmin+, myogenin+, MyoD1+	ICC Desmin+, myogenin+, MyoD1+
	Lymphoma	Lymphoid cells, CD45 (LCA)+	Flow cytometry for CD45 (LCA) and other CD markers
	Neuroblastoma	Primitive small round cells with neuroblastic component, NSE+, Synaptophysin+, NMYC amplification	FISH or NGS for amplification of NMYC; ICC NSE+, synaptophysin+
	Desmoplastic small round cell tumor	Nests of small round cells with desmoplasia, EWSR1::WT1, multilineage immunoreactivity	FISH or NGS for rearrangement of EWSR1 or fusion of EWSR1::WT1; ICC WT1 (c-terminus)+, cytokeratin+, desmin (dot-like)+
Spindle cell tumors	Leiomyosarcoma	Plump spindle cells with eosinophilic cytoplasm, cigar-shaped nuclei, fascicular pattern, showing nuclear pleomorphism	ICC Desmin+, SMA+, SMMS-1+, Caldesmon+
	Synovial sarcoma	Spindle cells, monophasic or biphasic pattern, SS18::SSX1/2/4	FISH or NGS for rearrangement or fusion of SS18::SSX1/2/4; ICC TLE1+, SS18-SSX fusion protein+, SSX protein (C-terminus)+
	Gastrointestinal stromal tumor (GIST)	Spindle cells, epithelioid, or mixed morphology, perinuclear vacuoles, KIT (CD117)+	(KIT) mutation for KIT and/or PDGFRA; ICC CD117+, DOG1+
	Fibrosarcoma	Herringbone pattern, uniform spindle cells	ICC Vimentin+, lacks specific markers
	Nodular fasciitis	Reactive proliferation, feathery spindle cells, myxoid stroma	FISH or NGS for USP6 rearrangement
Pleomorphic cell tumors	Undifferentiated pleomorphic sarcoma	Pleomorphic spindle and round cells, bizarre nuclei	ICC Vimentin+, no specific markers
	Dedifferentiated liposarcoma	Pleomorphic, spindle, or epithelioid cells, lipoblasts, lipogenic differentiation	FISH or NGS for MDM2 amplification; ICC MDM2+, CDK4+
	Pleomorphic liposarcoma	Pleomorphic, lipoblasts	No MDM2 or CDK4 amplification; ICC Vimentin+, lacks specific markers
	Pleomorphic rhabdomyosarcoma	Pleomorphic round cells, cross striations, desmin+	ICC Desmin,+ myogenin+, MyoD1+
	Malignant peripheral nerve sheath tumor (MPNST)	Spindle cells with wavy nuclei, S100 variably positive	ICC S100±, SOX10±, H3K27me3 loss
Epithelioid cell tumors	Epithelioid sarcoma	Epithelioid cells with central necrosis	ICC, Cytokeratin+, EMA+, INI1 loss
	Clear cell sarcoma	Epithelioid, melanoma-like cells, EWSR1::ATF1	FISH or NGS for fusion of EWSR1::ATF1;ICC S100+, SOX10+, HMB45+, Melan-A
	Epithelioid angiosarcoma	Epithelioid cells, vascular channels, ERG+	ICC CD31+, ERG+
	Alveolar soft part sarcoma	Nests of epithelioid cells, PAS+ crystalline inclusions, rich sinusoidal caplillaries	FISH for fusion of ASPSCR1::TFE3; PAS+ crystals; ICC TFE3+

(continued)

Table 2. *(continued)*

Morphology category	Tumor type	Key features	Ancillary testing
Myxoid tumors	Myxoid liposarcoma	Myxoid background, signet ring-like lipoblasts, plexiform vasculature	FISH or NGS for DDIT3 rearrangement or fusion of FUS::DIT3 or EWSR1::DDIT3; ICC DDIT3+
	Myxofibrosarcoma	Myxoid stroma, curvilinear vessels, spindle cells with variable pleomorphism	ICC Vimentin+, lacks specific markers
	Extraskeletal myxoid chondrosarcoma	Myxoid stroma, cords of bland cells with eosinophilic cytoplasm, NR4A3 rearrangement	FISH or NGS for rearmament of NR4A3 or fusion of EWSR1:: NR4A3
	Myxoinflammatory fibroblastic sarcoma	Myxoid stroma, inflammation, epithelioid or bizarre cells	ICC Vimentin+, lacks specific markers

ASPSCR1, alveolar soft part sarcoma chromosomal region candidate 1; ATF1, activating transcription factor 1 gene; CD117, c-KIT; CD45 (LCA), leukocyte common antigen; CD99, cluster of differentiation 99; CDK4, cyclin-dependent kinase 4; DDIT3, DNA damage inducible transcript 3; DOG1, discovered on GIST 1; EMA, epithelial membrane antigen; ERG, erythroblast transformation specific related gene; EWSR1, Ewing sarcoma breakpoint region 1; FISH, fluorescence in situ hybridization; FLI1, friend leukemia integration 1; FUS, fused in sarcoma; H3K27me3, trimethylation of lysine 27 on histone H3; HMB45, human melanoma black-45; ICC, immunocytochemistry; INI1, integrase interactor 1; KIT, proto-oncogene C-KIT encodes tyrosin-protein kinase KIT; MDM2, murine double minute 2; Melan-A, melanoma antigen; MyoD1, myogenic differentiation 1; NGS, next generation sequencing; NKX2.2, NK2 homeobox 2; NMYC, N-myc proto-oncogene; NR4A3, nuclear receptor subfamily 4 group A member 3; NSE, neuron-specific enolase; PAS, periodic acid-Schiff; PDGFRA, platelet-derived growth factor receptor; PKCBII, protein kinase C beta II; S100, protein's solubility in a saturated (100%) ammonium sulfate solutions in bovine brain; SMA, smooth muscle actin; SMMS-1, smooth muscle myosin heavy chain; SOX10, SRY-related HMG-box 10; TFE3, transcription factor E3; USP6, ubiquitin-specific protease 6 gene; WT1, Wilms' tumor protein 1.

diagnostic category, ROM, and clinical scenario.

Conclusions

This structured reporting system aligns with the WHO Classification of Soft Tissue and Bone Tumours (5th edition), ensuring that cytopathological findings are reproducible, clinically actionable, and globally applicable. The approach integrates cytomorphological features, ancillary testing, and clinical correlation, emphasizing a probabilistic framework for risk stratification and decision-making. By providing clear diagnostic criteria, this system enables pathologists to contribute effectively to multidisciplinary patient management. Furthermore, advancements in molecular diagnostics, ICC, and NGS are expected to enhance the accuracy and specificity of FNAB-based diagnoses, reinforcing the role of cytopathology in the evaluation of soft tissue tumors.

A limitation of this publication is that it applies primarily to FNAB and can be extended to CNB; however, its relevance to touch imprint of soft tissue remains unclear. Given the increasing trend of obtaining CNBs of soft tissue lesions with rapid on-site evaluation for cellularity via touch imprint cytology, it would be valuable to determine whether this approach is also applicable in this context. Additionally, it is important to assess whether the clinical team supports this reporting system, as they are the primary end users with whom communication is intended. It will be interesting to examine the broader impact of this reporting system and

Table 3. The WHO Reporting System for Soft Tissue Cytopathology – implied risk of malignancy (ROM) and recommended clinical management, modified

Diagnostic category	Risk of malignancy (ROM)	Recommended managements
Non-diagnostic	29.9% (9-42%)	Repeat FNAB with rapid on site evaluation (ROSE) or consider core needle biopsy (CNB) if persistently inadequate. Clinical and radiological correlation is necessary.
Benign	2.5% (0-4%)	Clinical follow-up based on imaging and clinical correlation.
Atypical	39.6% (46%)	Clinical and radiologic correlation is recommended. Repeat FNAB with ROSE or proceed with CNB. Ancillary testing may help refine the diagnosis.
Soft tissue neoplasm of uncertain malignant potential (STNUMP)	51.4% (20-27%)	Multidisciplinary discussion. Repeat FNAB or CNB. Excision may be warranted, particularly for deep-seated or enlarging lesions. Ancillary studies should be considered to further stratify risk
Suspicious for malignancy	68.2% (71-80%)	Ancillary molecular and immunocytochemical studies may help confirm malignancy and identify diagnostic, prognostic, and predictive biomarkers. Surgical biopsy or excision may be needed. Further imaging and clinical correlation with multidisciplinary discussion is recommended.
Malignant	97.7% (91-100%)	Immediate oncologic referral for staging and treatment. Management typically includes surgical resection, with consideration of radiation or systemic therapy based on tumor type and extent of disease. Biomarker information is important to guide patient management.

ICC, immunocytochemistry; WHO, World Health Organization.

explore its correlation with the upcoming 6th edition of the WHO Classification of Soft Tissue and Bone Tumours in the near future.

The hope is that by following this structured reporting format, the WHO Reporting System for Soft Tissue Cytopathology will ensure FNAB diagnoses are clear, reproducible, and clinically actionable. The integration of cytomorphological features, ROM assessment, ancillary testing, and clinical correlation will enhance the diagnostic accuracy of soft tissue FNAB and facilitate appropriate patient management. This standardized approach aligns with modern risk-based classification models and will improve communication among pathologists, radiologists, and oncologists, also ensure patient safety and high quality care.

It is important that the readers of this article refer to the exact wording and specific details related to the definition for each diagnostic category, risk of malignancy (ROM), and management recommendations as provided in the WHO Reporting System for Soft Tissue Cytopathology. The explanatory content in this review article has been adapted based on the author's interpretation of the forthcoming book.

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Conflict of interest

The author declares no conflict of interest related to this publication, except the author contributed as a co-author of some chapters of the WHO Reporting System for Soft Tissue Cytopathology.

Author contributions

MMB is the sole author of the manuscript.

References

[1] Layfield LJ, Dodd L, Esebua M. World Health Organization Reporting System for Soft Tissue Cytopathology: Risk of malignancy and reproducibility of categories among observers. Diagn Cytopathol 2024;52(9):480–484. doi:10.1002/dc.25340, PMID:38733149.

[2] Gajdzis P, Brisse HJ, Klijanienko J. Diagnostic performance of fine-needle aspiration in soft tissue tumors: Application of the World Health Organization System for Reporting Soft Tissue Cytopathology and risk of malignancy assessment. Cancer Cytopathol 2024;132(12):768–778. doi:10.1002/cncy.22897, PMID:39212584.

[3] International Academy of Cytology – International Agency for Research on Cancer – World Health Organization Joint Editorial Board. WHO Reporting System for Soft Tissue Cytopathology [Internet]. Lyon (France): International Agency for Research on Cancer; 2025 [cited June 20, 2025]. (IAC-IARC-WHO cytopathology reporting systems series, 1st ed; vol 4). Available from: https://tumourclassification.iarc.who.int/chapters/51.

[4] International Academy of Cytology – International Agency for Research on Cancer – World Health Organization Joint Editorial Board. WHO Reporting System for Soft Tissue Cytopathology. Lyon (France): International Agency for Research on Cancer; 2025. (IAC-IARC-WHO cytopathology reporting systems series, 1st ed; vol 4). https://publications.iarc.who.int/651.

[5] WHO Classification of Tumours Editorial Board. WHO Classification of Tumours: Soft Tissue and Bone Tumours. 5th ed. Lyon: International Agency for Research on Cancer; 2020.

[6] Wei S, Henderson-Jackson E, Qian X, Bui MM. Soft Tissue Tumor Immunohistochemistry Update: Illustrative Examples of Diagnostic Pearls to Avoid Pitfalls. Arch Pathol Lab Med 2017;141(8):1072–1091. doi:10.5858/arpa.2016-0417-RA, PMID:28745570.

[7] Wakefield C, Hornick JL. Update on immunohistochemistry in bone and soft tissue tumors: Cost-effectively replacing molecular testing with immunohistochemistry. Hum Pathol 2024;147:58–71. doi:10.1016/j.humpath.2023.12.002, PMID:38135060.

[8] Cordier F, Ferdinande L, Hoorens A, Van de Vijver K, Van Dorpe J, Creytens D. Soft Tissue and Bone Tumor Diagnostics: Harnessing the Power of Molecular Techniques. Genes (Basel) 2023;14(12):2229. doi:10.3390/genes14122229, PMID:38137051.

[9] Dodd L, Bui MM. Atlas of Soft Tissue and Bone Pathology: with histologic, cytologic and radiologic correlations. New York: Demos Medical Publishing; 2015.