

Soft Tissue Cytology

Brief Commentary

At least in my opinion, **formalin fixed paraffin-embedded tissue is usually necessary to definitively diagnose a new primary soft tissue tumor** (either in the form of a good cell block, core biopsy, or surgical specimen), which is often desirable for clinical management, as many diagnoses require immunohistochemistry and/or molecular testing

Pure cytology (i.e., just smears) is mainly useful only for **triaging** primary soft tissue tumors (i.e., is this sample lesional? Is it overtly high-grade?). However, cytology alone can often reasonably identify soft tissue *metastases* and *recurrences* of previously diagnosed tumors (with the history informing most of the diagnosis and cytology mostly establishing a compatible lesion).

As such, I'll refer you to my more comprehensive soft tissue notes for a detailed discussion of actual discrete diagnoses and concepts using FFPE. In this section I'll limit myself to the WHO system and what I think can be determined based on pure cytology.

WHO System

Diagnostic Group	Example of smear findings	Risk of Malignancy	Diagnostic management options
Insufficient/ Inadequate/ Non-diagnostic	Just blood or debris	~30%	CORRELATE. Repeat FNAB, preferably with ROSE.
Benign	Bland adipocytes	~2%	CORRELATE. If discrepancy, repeat FNAB and/or CNB. If correlation, review when appropriate.
Atypical	Spindled cells with mild atypia	~40%	CORRELATE. Discuss at MDTM. Repeat FNAB and/or CNB and/or surgical biopsy.
STNUMP	A known GIST	~50%	CORRELATE. Discuss at MDTM. Repeat FNAB and/or CNB and/or surgical biopsy.
Suspicious for malignancy	Discohesive epithelioid cells with moderate atypia.	~70%	CORRELATE. Discuss at MDTM. Consider repeat FNAB to gain material for ancillary testing, but will usually require CNB and/or surgical biopsy.
Malignant	Severely pleomorphic spindled cells with atypical mitoses	~98%	CORRELATE. Discuss at MDTM. Will usually require CNB and/or surgical biopsy.

Modified from: WHO Reporting System for Soft Tissue Cytopathology

You'll notice a couple of themes in the "management options" given by the WHO.

1) **Correlation is always essential** and cases should be discussed in a multidisciplinary team meeting (MDTM) and 2) **Fixed tissue is usually necessary for definitive diagnosis** and management (either cell block, core, or surgical biopsy) .

Insufficient/Inadequate/Non-diagnostic

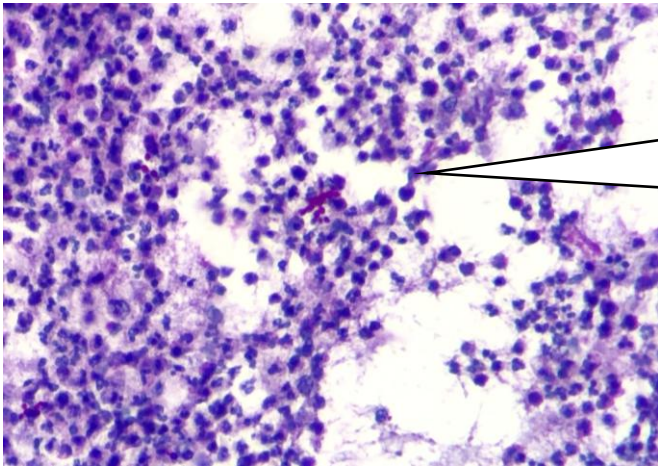
Insufficient or Inadequate are used for specimens where there is essentially no (interpretable) material present for evaluation. The specimen provided **no useful information** concerning the targeted lesion and additional sampling is necessary. The WHO says to pick one term to use at your institution, but both are acceptable.

Any specimen is regarded as adequate if it demonstrates a pathological process consistent with the clinical setting and imaging findings. If there are any atypical features in the cells or the background, even if there is suboptimal preparation or degenerative limitations, the case is categorized as “Atypical” rather than “Insufficient”.

For clinically suspicious cases with only normal (presumably not lesional) tissue present (e.g., skeletal muscle or fat), they say to either put this in the “**Benign**” category with the disclaimer that it “may not represent the lesion seen on imaging and further diagnostic workup is recommended” to explain that the discrepancy may relate to sampling error, or “**Non-diagnostic**” (although the book is not consistent, with some sections arguing against this second option)

Benign

Unequivocally benign cytologic findings which may or may not be diagnostic of a specific inflammatory process (e.g., abscess, granulomas) or benign neoplasm. Correlation of imaging and clinical findings with pathologic findings (the “triple test”) is essential.

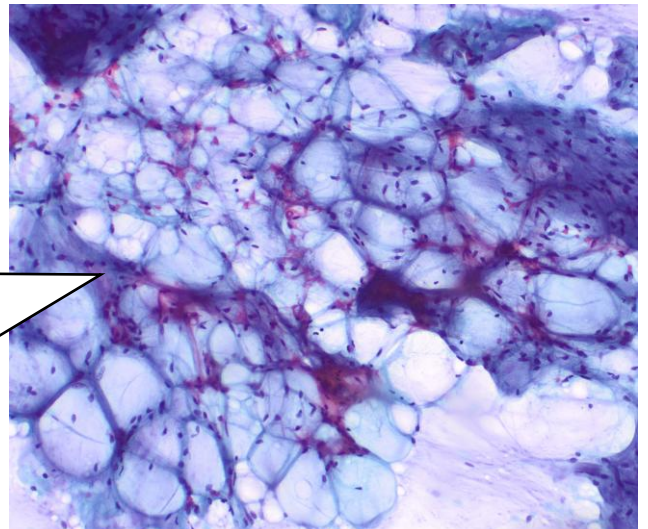


This smear is all neutrophils and fibrinous debris, consistent with an **abscess**.

If you see this during an on-site assessment, suggest sending cultures!

This smear consists of just mature-appearing adipocytes. If small and in a superficial location, these findings are compatible with a **lipoma**.

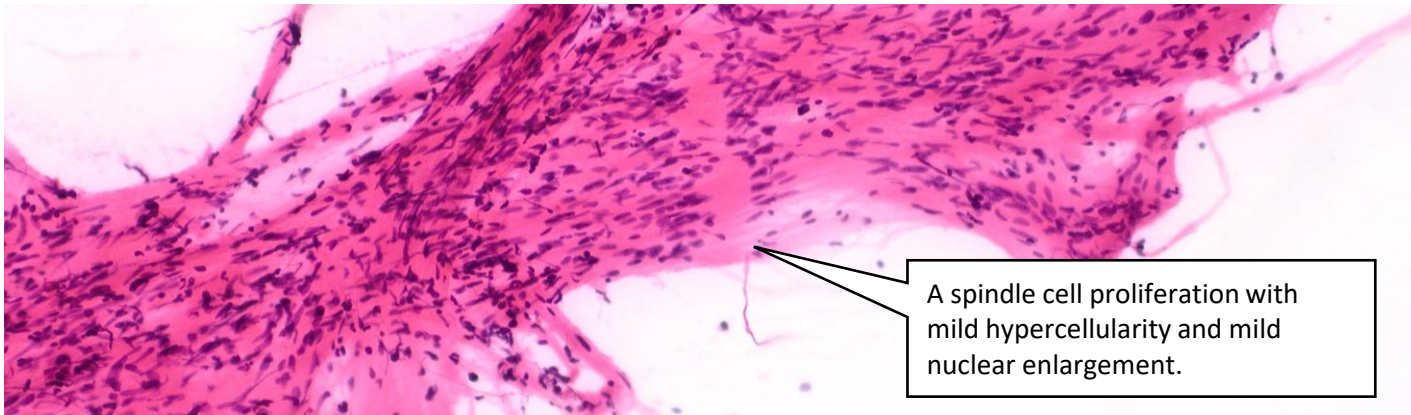
However, **clinical correlation is essential with soft tissue cases**. In the retroperitoneum, the most common fatty tumor is a well-differentiated liposarcoma, which can look almost identical!



Atypical

Demonstrates features seen predominantly in benign lesions and **minimal features that may raise the possibility of a malignant lesion**. These features are insufficient, either in number or in quality, to diagnose a benign or malignant process or lesion.

Often scant or poorly prepared cellular material. Most of the specimens in this category are likely to be from reactive, inflammatory, or reparative processes, but specific features sufficient for a definitive benign diagnosis are lacking.



Soft tissue neoplasm of uncertain malignant potential (STNUP)

Represents a diverse group of neoplasms whose **biological behavior cannot be predicted on an FNA**.

Two distinct groups:

- 1) The specific neoplasm or line of differentiation is known, but definitive criteria cannot be applied for risk stratification or assessment of malignancy. For example, both GIST and SFT risk stratification criteria are best applied to excision specimens.
- 2) The tumor type has an inherent but unpredictable risk of metastasis. This includes tumors with an “intermediate (locally aggressive)” or “intermediate (rarely metastasizing)” biological risk, such as inflammatory fibroblastic tumors, angiomatoid fibrous histiocytoma, etc...

Commentary: To me, a likely common scenario isn’t well-addressed in this system. What do you say when you have a lesion that is obviously from a tumor, but you don’t have enough info to say if it’s benign or malignant?

For example, it’s a bunch of spindled cells in myxoid stroma, but you can’t tell line of differentiation and a specific diagnosis. The DDX could include a cellular myxoma (benign) and a low-grade fibromyxoid sarcoma (low-grade malignant).

To me, this would fit best conceptually in a category like “STNUP” (since it’s definitely a tumor, but the behavior is uncertain), but the authors would probably have you put it in “Atypical,” and reserve STNUP for cases with a known diagnosis. To which, I would argue that if you know the diagnosis, just diagnose it then! Why bother with categories?! Just don’t risk stratify it. Essentially, what we need is a category like Milan Category 4 in the salivary gland.

This problem is admittedly a bit dogmatic and academic. **What really matters is that you communicate clearly to the clinical team** about your Dx or DDX—not the category. Most clinicians won’t know about these categories anyways. ;-)

Suspicious for Malignancy

Features **suggestive of malignancy**, but with features insufficient, in either number or quality, for an unequivocal diagnosis of malignancy.

Often scant, poorly smeared, or poorly prepared. Also, cases where there is considerable material, some of which appears malignant, but not all features of a particular malignancy are present or there may be discrepant features.

Malignant

Unequivocal features of malignancy without any discrepant findings.

No single cytopathological feature is diagnostic of malignancy, but the following are *suggestive*:

Round/oval cell proliferations (non-hematolymphoid): ***“Small round blue cell tumors”***

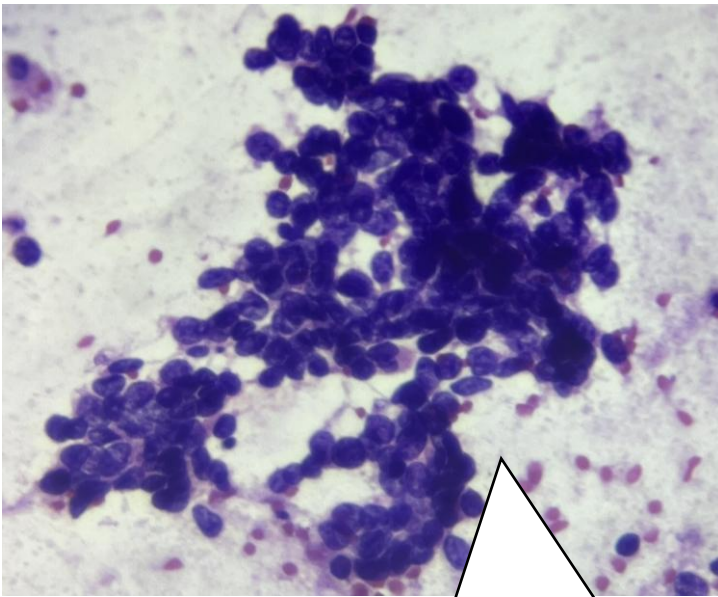
Pleomorphic cells with prominent atypia,

Marked abnormalities of N:C ratio,

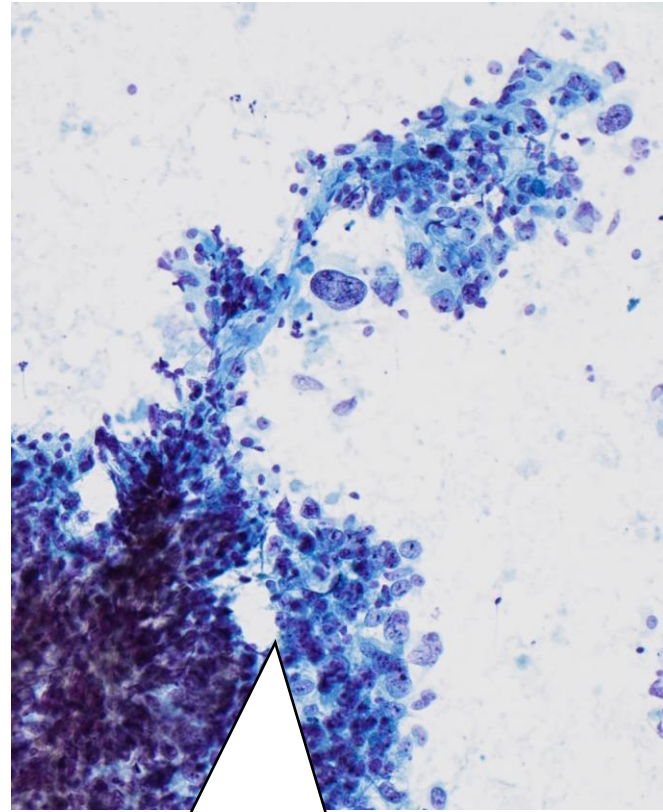
Atypical mitotic figures,

Necrosis, and

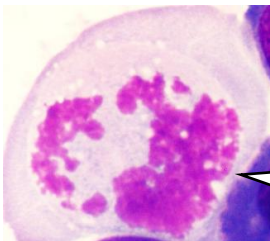
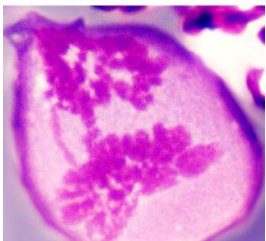
Hypercellularity



“Round Cell” lesions, with monotonous proliferations of high N:C ratio cells are often malignant, especially if they’re large lesions.



Pleomorphic cells with prominent anisonucleosis, nuclear contour irregularity, mitoses, and necrosis are often malignant.



Atypical mitoses are highly associated with malignancy, but are rare (good specificity, poor sensitivity).