Fine Needle Aspiration for Clinical Triage of Extremity Soft Tissue Masses

Vincent Y. Ng MD, Kristen Thomas MD,
Martha Crist RN, Paul E. Wakely Jr. MD,
Joel Mayerson MD

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Abstract

Background Fine needle aspiration cytology (FNAC) is a rapid and low-morbid alternative to open biopsy or needle core biopsy for soft tissue masses. Numerous reports describe its use with metastatic or recurrent lesions, but FNAC is less accepted for primary lesions.

Questions/Purposes We wished (1) to estimate the sensitivity, specificity, and positive and negative predictive values of FNAC for diagnosing malignancy; (2) to estimate the accuracy of subtyping and grading.

Methods We retrospectively examined the diagnostic accuracy and clinical effectiveness of office-based FNAC performed by a trained pathologist on 213 females and 219 males (mean age, 51.8 years) who presented with a palpable soft tissue mass to one musculoskeletal oncology clinic between 2002 and 2008.

Results The FNAC was reported as benign in 62.0%, indeterminate in 8.1%, and malignant in 29.9%. A second

technique, such as needle core biopsy or open biopsy, was performed for 24.8% of lesions before a definitive treatment plan was rendered. Final tissue confirmation by open biopsy or resection was available for 52.2% of benign FNAC and 78.3% of malignant FNAC. Sensitivity, specificity, and positive and negative predictive values for detecting malignancy with either histopathologic confirmation or clinical followup were 89.2%, 89.8%, 96.1%, and 98.1%. There were seven sampling and nine interpretation FNAC errors in determining the nature of the lesion. Subtyping and grading for malignant lesions were 77.2% and 95.2% accurate, respectively.

Conclusions FNAC is effective for initial triage and treatment selection at tertiary referral centers with close collaboration among the surgeon, pathologist, and radiologist.

Level of Evidence Level II, diagnostic study. See the Guidelines for Authors for a complete description of levels of evidence.

Each author certifies that he or she has no commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

Each author certifies that his or her institution has approved the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.

V. Y. Ng (✉), K. Thomas, M. Crist, J. Mayerson
Department of Orthopaedics, Ohio State University Medical Center, 1050 Doan Hall, 410 West 10th Avenue, Columbus, OH 43210, USA
e-mail: Vincent.Ng@osumc.edu; vincent_y_ng@yahoo.com

P. E. Wakely Jr.
Department of Pathology, Ohio State University Medical Center, Columbus, OH, USA

Introduction

Soft tissue sarcomas comprise 1% or less of all adult malignancies [5, 7]. In 2008, an estimated 10,000 Americans were diagnosed with a soft tissue sarcoma and approximately 3500 will die from it [12]. Orthopaedic oncology is a highly specialized field and improper management of these patients can result in unnecessary amputations and mortality [31]. Long-standing recommendations have been in place to refer all patients with suspicious musculoskeletal lesions to a high-volume tertiary care center for biopsy and definitive treatment [18]. Although traditional open incisional biopsies remain the diagnostic gold standard, less invasive methods such as

needle core biopsy (NCB) and, more recently, fine needle aspiration (FNA) have emerged [35].

FNAC has been an integral part of the highly centralized care for patients with sarcoma in Scandinavian countries for many years [1, 3, 7, 8, 33, 34, 38]. Although FNAC generally is accepted at musculoskeletal oncology centers in the United States for documentation of metastases and local recurrences, especially if prior samples are available for comparison, its role in the evaluation of primary soft tissue sarcomas remains controversial and limited [29, 37, 39]. Rubin et al. suggested FNAC can be a valuable and cost-effective tool in expediting the care of patients with breast cancer without incurring the risks or delay of an open surgical procedure [27]. Performed bedside, it provides results within 30 minutes and can facilitate additional staging or treatment decisions during the initial clinic visit. Although FNAC reliably distinguishes mesenchymal from metastatic tumors, malignant from benign lesions, and high- from low-grade sarcomas, it has been criticized for its inability to precisely subtype sarcomas [9]. FNAC is not without potential pitfalls such as sampling error, failure of ancillary techniques, and low cellular yield [10, 24]. Nevertheless, because treatment decisions for sarcomas usually are based on size, location, and grade, some authors support FNAC as a primary modality to provide the necessary information to proceed with care [15, 29]. Benign characteristics on FNAC, in addition to a nonaggressive clinical presentation and benign radiographic features, can provide clinicians the confidence to observe such lesions. If malignancy is detected on cytology, chemotherapy, surgical excision, or additional staging studies can be planned without the need for additional biopsy.

Successful FNAC is contingent on two main factors: an experienced cytopathologist and close collaboration between the orthopaedic oncologist and the pathologist [11, 17]. For the past 8 years we have had such a situation, allowing for collection of a large database. A previous report from our institution suggested high reliability of FNAC, but included bone lesions and was limited to high-grade sarcomas [9]. We presumed FNAC would be an effective diagnostic tool for triaging patients presenting with a palpable soft tissue mass.

The purpose of the current study therefore was (1) to estimate the sensitivity, specificity, and positive and negative predictive values of FNAC for diagnosing malignancy; (2) to estimate the accuracy of subtyping and grading; (3) to determine the number of patients definitively treated based on FNAC and the clinicoradiographic presentation without additional diagnostic biopsy; and (4) to determine whether the cases in which a false-positive or false-negative error occurred were a result of interpretive error by the pathologist or sampling error by the FNA.

Patients and Methods

We retrospectively searched the medical records of all patients seen by the primary musculoskeletal oncologist (JM) at the adult office of the Arthur G. James Comprehensive Cancer Center at The Ohio State University between September 2002 and April 2008 to identify patients who received a FNA. The study group included only patients with soft tissue masses that were palpable on physical examination and that did not require radiographic guidance for FNA. Results of all FNAC specimens were interpreted by the head cytopathologist (PEW) or another experienced musculoskeletal pathologist (CM). Pathology reports from open biopsies and mass resections were accepted from all attending physicians in the pathology department. We believe FNAC plays a different role in the management of pediatric soft tissue sarcomas, and we therefore excluded patients seen in the pediatric office. Because of the specific chemotherapeutic protocols for Ewing sarcoma, rhabdomyosarcoma, and osteosarcoma, histologic subtyping is necessary for appropriate selection of therapy. FNAC is more accurate in pediatric sarcomas in this regard [15]. We identified 459 cases of FNA. Twenty of these (4%) were excluded because the FNAC had been interpreted by a nonmusculoskeletal pathologist. Seven were excluded because the patient did not have definitive tissue verification of their FNA, did not return for followup, and could not be reached by telephone. The final study group consisted of 432 FNAs performed on 213 male and 219 female patients (Fig. 1). The mean age of the patients at the time of FNA was 51.8 years (range, 13–91 years). The most common locations were the thigh (107), leg (57), knee (37), arm (34), hand and fingers (28), forearm (24), foot and ankle (40), shoulder (23), and back (11). The FNAC diagnosis was benign in 268 of 432 (62.0%) cases, malignant in 129 (29.9%), and nondiagnostic or indeterminate in 35 (8.1%) (Fig. 1). The mean ages in each group were 48.7 years, 58.3 years, and 51.4 years, respectively. Proceedings were in accordance with the approved Ohio State University Institutional Review Board, application 2003C0058.

In all cases, a pathologist discussed clinicoradiographic findings with the surgeon, examined the patient, and performed a percutaneous FNA. One-, 1.5-, or 2-inch long 21- or 22-gauge needles connected to a 20-mL syringe was inserted without local anesthesia at the apex of the lesion or at a location specified by the orthopaedic oncologist to optimize future resection. Using firm suction and short, rapid strokes, an average of three separate passes was made. With each pass, the needle was angled in a different direction to sample as much of the mass as possible. Aspirated material was expelled onto glass slides and a second glass slide was used to make conventional smears.

Fig. 1 The study design is shown in this flow chart. Bx = biopsy; prn = as needed.

The needle was rinsed in a balanced salt solution after each pass for additional study: flow cytometry, paraffin-embedded cell block, or fluorescent in situ hybridization. For initial assessment, several slides were air-dried and stained with a Romanowsky stain. The remainder subsequently was rehydrated and stained using a modified Papanicolaou method. Within 20 minutes, a preliminary reading was rendered.

All pathology reports for tissue specimens acquired from open biopsies or resections were compared with the initial FNAC findings. Because the reliability of NCB compared with FNAC is controversial, NCB was not used for definitive verification of FNAC for the purposes of this study [4, 8]. Subtyping and cytomorphic groupings were based on the recommendations of Kilpatrick et al. [14, 15] and Singh et al. [29] and Fletcher et al. for the Association of Directors of Anatomic and Surgical Pathology (ADASP) [10] (Table 1).

All decisions to proceed with definitive treatment or to perform a secondary biopsy were made by the primary musculoskeletal oncologist (JM) based on clinical judgment, radiologic findings, and cytologic findings. Rarely was a repeat FNA performed if the initial FNAC was nondiagnostic.

For patients who did not have histopathologic followup of a benign FNAC, attempts were made for this study to contact them or their primary physician by telephone to detect any potential misdiagnoses. For the cases in which the FNAC report was discrepant from the final pathology report, the head musculoskeletal pathologist (PEW) reviewed the cytology slides and compared them with the definitive tissue sample. Error was classified as sampling error if the FNAC slide did not contain material indicative of the actual pathology. Otherwise, it was deemed an interpretive error.

In the benign FNAC group (Table 2), 123 of 268 (46%) patients had surgical removal of their soft tissue mass. The other 145 were managed nonoperatively and were instructed either to follow up on an as-needed basis or to return for repeat imaging and serial examination. For patients told to follow up as needed, successful telephone contact was made at an average of 3.2 years.

In the indeterminate FNAC group, 19 of the 35 patients had surgical removal of their mass; 16 received nonoperative management. Of these, 25 were benign (70.6%), four were high-grade malignant (11.8%), three were low-grade malignant (8.8%), and three were nongraded malignant (8.8%).

Table 1. Grading of soft tissue sarcomas based on subtype/cytomorphologic grouping on fine needle aspiration cytology*

Low grade (by definition)	High grade (by definition)	Varying behavior [†]	No grading parameters established
Well-differentiated liposarcoma	Small round cell tumors	Leiomyosarcoma	Synovial sarcoma
Myxoid liposarcoma	Rhabdomyosarcoma	Gastrointestinal stromal tumor	Myxoid chondrosarcoma
Extraskeletal myxoid chondrosarcoma	Ewing sarcoma	Malignant peripheral nerve sheath tumor	
Epithelioid hemangioendothelioma	Mesenchymal chondrosarcoma	Myxofibrosarcoma	
Infantile fibrosarcoma	Desmoplastic small round cell tumor	Conventional fibrosarcoma	
Kaposi sarcoma	Adult pleomorphic sarcoma	Hemangiopericytoma	
	Pleomorphic high-grade sarcoma	Malignant granular cell tumor	
	Pleomorphic rhabdomyosarcoma		
	Pleomorphic leiomyosarcoma		
	Pleomorphic liposarcoma		
	Extraskeletal osteosarcoma		
	Round cell liposarcoma		
	Epithelioid sarcoma		
	Clear cell sarcoma		
	Alveolar soft parts sarcoma		
	Angiosarcoma		

* Based on Kilpatrick et al. [15] and ADASP [10]; [†]potentially low or high grade. (Adapted from Singh HK, Kilpatrick SE, Silverman JF. Fine needle aspiration biopsy of soft tissue sarcomas: utility and diagnostic challenges. *Adv Anat Pathol*. 2004;11:24–37. Reprinted with permission from Wolters Kluwer Health.)

Table 2. Summary of the benign FNAC diagnoses

FNAC diagnosis	Number of cases	FNAC diagnosis	Number of cases
Benign material (adipose tissue, skeletal muscle)	84	Hemangioma	7
Lipoma	25	Schwannoma	7
Myxoma	24	Abscess	6
Hematoma	18	Ganglion cyst	6
Fibromatosis	13	Epidermal inclusion cyst	6
Giant cell tumor of tendon sheath	12	Fat necrosis	5
Spindle cell lesion	8	Other	47

In the malignant FNAC group of 129 patients, there were 59 high-grade sarcomas, three and nine of which were metastases and local recurrences. There were 14 low-grade primary sarcomas and four low-grade recurrent sarcomas (Table 3). A subtype or cytomorphologic group and grade were rendered in 88 of 108 (81.5%) and 77 of 108 (71.3%) sarcomas, respectively.

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for all patients who had FNAC (including those with indeterminate reports). These values were reported for patients with

histopathologic confirmation and patients with either histopathologic confirmation or clinical followup. The accuracy of grading and subtyping malignant lesions was calculated based on cases with a FNA diagnosis and histopathologic confirmation. The number of patients treated after FNA without additional biopsy and the number of nondiagnostic FNAs were reported as percentages of the total FNA cases.

Results

For patients with definitive tissue verification, the sensitivity and specificity for detecting malignancy with FNAC were 88.9% and 84.4%, respectively. The PPV was 95.1% and the NPV was 96.4%. If the cases without definitive tissue verification (ie, the benign FNAC cases managed nonoperatively and the malignant FNAC cases referred to oncology or hospice) are accepted as benign and malignant, the sensitivity, specificity, PPV and NPV improved to 89.2%, 89.8%, 96.1%, and 98.1% (Table 4). One hundred forty of the 268 (52.2%) patients with a benign lesion had a subsequent definitive tissue diagnosis after the initial benign FNA through open incisional biopsy, irrigation and débridement, or resection. Of these, 134 of the 140 masses (96%) were confirmed as benign and six were malignant neoplasms (Fig. 1). Of the 101 FNAC cases diagnosed as

Table 3. Summary of malignant FNAC diagnoses

FNAC diagnosis	Number of cases	FNAC diagnosis	Number of cases
Adenocarcinoma	2	MPNST	5
Adenoid cystic carcinoma	1	Melanoma	1
Chondrosarcoma	4	Myxofibrosarcoma	4
Chordoma	2	Myxoid liposarcoma	6
Epithelioid angiosarcoma	1	Myxoid sarcoma, NOS	3
Epithelioid HGS	5	Osteosarcoma, high grade	3
Epithelioid malignancy, NOS	1	Osteosarcoma, parosteal	1
Ewing sarcoma	3	Pleomorphic HGS	29
EMC	3	RCC	1
Fibromyxoid sarcoma	1	Sarcoma, NOS	1
Leiomyosarcoma	3	Small round cell HGS	4
Liposarcoma, NOS	6	Spindle cell sarcoma, NOS	2
Liposarcoma, WDL	3	Suspicious for sarcoma	6
Lymphoma*	15	Synovial sarcoma	2
Malignancy, nonsmall cell	1		

* Includes nonHodgkin's lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, and lymphoma NOS; HGS = high-grade sarcoma; NOS = not otherwise specified; WDL = well-differentiated liposarcoma; MPNST = malignant peripheral nerve sheath tumor; EMC = extraskeletal myxoid chondrosarcoma; RCC = renal cell carcinoma.

Table 4. Summary of FNAC and final diagnoses

FNAC diagnosis	Final diagnosis	
	Malignant	Benign
Malignant	124	5
Benign	5	263
Indeterminate	10	25

malignant with tissue verification, 96 (95%) were identified correctly as malignant. There were five false-positives for malignancy, two instances of overgrading, two sarcomas mistaken for lymphoma, and one rare spindle cell neoplasm reported as melanoma. Eleven of the 19 cases diagnosed with FNAC as locally recurrent sarcoma were after radiation in addition to prior surgical removal. There were no false positives, false negatives, or indeterminate FNACs for recurrent sarcoma.

For patients who had subsequent open biopsy or eventual resection, the subtyping and grading of malignant lesions, when provided by FNAC, were 77.2% and 95.2% accurate, respectively. For the 77 cases in which a sarcoma grade was provided by the FNAC, 60 were correct, three were incorrect, and 14 did not have final tissue verification. For the 88 cases in which a subtype was given, 61 were correct, 18 were incorrect, and nine were unverified.

Overall, 24.8% of patients required a secondary biopsy before pursuing a definitive treatment plan (Table 5). The nature of the lesion was indeterminate or the FNAC was inadequate in 8.1% of the cases. Among the 268 cases of

Table 5. Number and type of secondary biopsies performed after initial FNAC

Secondary biopsy	Benign FNAC	Indeterminate FNAC	Malignant FNAC
Repeat bedside FNA	0	0	1
CT-guided biopsy	1	0	1
Needle core biopsy	12	8	22
Intraoperative frozen section	18	2	5
Open incisional biopsy	20	12	10
Patients with more than one secondary biopsy	1	2	2

benign FNAC, definitive treatment was rendered in 218 (81.3%) based on the FNAC alone. An open biopsy, NCB, or intraoperative frozen section was performed in the remaining 50 (18.6%) patients. No malignant degeneration or questionable change in the mass was reported by any patient or outside physician on telephone followup. In the indeterminate FNAC group, the definite treatment plan was based in the FNAC in 15 of the 35 patients (42.9%), while 20 of 35 (57.1%) required an additional open biopsy, NCB, or intraoperative frozen section. In 27 of 35 (77.1%) cases, final tissue verification was available from either open incisional biopsy or definitive resection. Thirty-two of 129 (24.8%) patients with initially malignant FNAC required a separate open biopsy, NCB, repeat FNA, or CT-guided biopsy before definitive treatment could ensue. Intraoperative biopsy during surgical resection was performed in an additional five patients. One hundred one of 129 (78.3%)

Table 6. Summary of cases with major FNA discrepancies

Case	FNA diagnosis	Secondary biopsy diagnosis	Final histopathology diagnosis	Type of error
1	Fibroadipose tissue, benign skeletal muscle	NCB—fibroadipose tissue; open bx—spindle cell sarcoma, intermediate to high grade	Dedifferentiated WDL	SE
2	Suspicious for lymphoma	NCB—high-grade leiomyosarcoma	Not performed	SE
3	Hematoma	Open bx—spindle cell sarcoma, high grade	Sarcoma with chondrosarcomatous dedifferentiation	SE
4	Lipoma	NCB—minute fragment of malignant cells; open bx—synovial sarcoma, high grade	Synovial sarcoma, high grade	SE
5	Adipose tissue, skeletal muscle	NCB—focal dystrophic calcification, fibroadipose tissue	WDL with extensive fat necrosis, calcification	SE
6	Adipose tissue, mononuclear cells	Open bx—metastatic myxoid liposarcoma	Metastatic myxoid liposarcoma	SE
7	Large cell lymphoma, B-cell	Open bx—Ewing sarcoma	Large cell atypical Ewing sarcoma	IE
8	Epithelioid sarcoma	None	Nodular fasciitis	IE
9	Epithelioid sarcoma	Open bx—dermatofibrosarcoma protuberans	Nodular fasciitis, pyogenic granuloma	IE
10	Pleomorphic, spindle cell sarcoma, high grade	None	Low grade myxoid spindle cell sarcoma	IE
11	Malignant melanoma	NCB—hemosiderin, Touton giant cell-rich mesenchymal tumor	PHAT	IE
12	Pleomorphic, spindle cell sarcoma, high grade	Open bx—consistent with hematoma capsule, resolving clot, reactive granulation tissue	None	IE
13	Few malignant cells	NCB—benign fibroadipose tissue; open bx—fibrin clot, granulation tissue	None; final diagnosis—Charcot arthropathy	IE
14	Suspicious for synovial sarcoma	Open bx—epithelioid hemangioendothelioma	None	IE; SE
15	WDL	None	Lipoma, degenerating skeletal muscle, chronic inflammation	IE

bx = biopsy; NCB = needle core biopsy; WDL = well-differentiated liposarcoma; PHAT = pleomorphic hyalinizing angiectatic tumor of soft parts; IE = interpretation error; SE = sampling error.

patients had subsequent tissue diagnosis after the initial malignant FNA through open incisional biopsy or definitive resection. The remaining patients (28), 18 of whom were diagnosed with recurrent or metastatic sarcoma or lymphoma, were referred to oncology or hospice without additional histopathologic confirmation.

Retrospective analysis of the false positive and false negative cases revealed seven sampling errors and nine interpretation errors (Table 6).

Discussion

The majority of patients seen at the relatively few musculoskeletal oncology centers across America travel far from home to receive specialized care [31]. Although open incisional biopsy remains the diagnostic gold standard by

providing ample tissue specimen, visual confirmation of accurate sampling, and full histologic architecture, it has substantial drawbacks [39]. Unlike a surgical procedure which incurs the risk of anesthetic complications, wound healing problems, infection, and tumor seeding, FNA is relatively painless, has rare complications, provides expedient patient triage, and is more cost effective [2, 15, 20, 21, 27, 30, 36, 37]. Compared with NCB, FNA is less expensive and less invasive, can sample a lesion more extensively, and provides quicker results [39]. The aim of this study was to determine the ability of FNAC to detect, grade, and subtype malignancy in patients presenting with palpable soft tissue masses. The rate of nondiagnostic FNAs and the effectiveness of FNAC to direct treatment options without secondary biopsy also were evaluated. In cases in which the nature of the lesion was diagnosed incorrectly by FNAC, the type of error, sampling or interpretive, was recorded.

There are several weaknesses in this study. First, because excising every benign lesion is impractical and unnecessary in many instances, not all benign FNAs had histopathologic confirmation. Nevertheless, clinical followup or telephone contact with patients or outside physicians verified that no symptoms concerning for a malignancy arose in subsequent years. Second, the determination of interpretation versus sampling error for discrepant cases was performed retrospectively by the same cytopathologist who rendered the initial FNAC diagnosis. Although this raises the possibility of bias and repeat interpretive error, the larger histopathologic specimen provided by definitive resection or open biopsy allowed for easy objective retrospective comparison.

The sensitivity, specificity, and PPV and NPV of FNAC in this study were comparable to published rates (Table 7). Although predictive values are affected primarily by false positive and negative cases, sensitivity and specificity are decreased by indeterminate FNACs as well. Close interdisciplinary collaboration and constant vigilance by the surgeon can help prevent adverse patient outcomes attributable to incorrect FNAC. It was suggested that for cytopathologists of all levels of experience, knowledge of the patients' clinical background increased the proportion of correct diagnoses and accuracy of classification [17].

The rate of nondiagnostic FNA samples in this study compared favorably with rates in previous studies (Table 7). The relatively small sample size produced by FNA combined with the subtle spectrum from benign to low-grade to high-grade lesions can undermine the confidence of many pathologists to render a definitive diagnosis. Without an experienced on-site cytopathologist to interpret the FNAC and determine whether an additional specimen is necessary, many of the advantages afforded by FNAC are lost [21]. It can be difficult to collect adequate cells from masses with abundant acellular matrix [7, 24]. In the indeterminate group, there were six spindle cell lesions, six myxoid-containing tumors, and one well-differentiated liposarcoma. Determining the nature of masses in these categories with FNAC can be difficult and incisional biopsy may be necessary [14, 20, 25, 37, 39]. Pathologists should not be reluctant to request more tissue or to establish minimal criteria for specimen adequacy based on number of unobscured cells per slide [10, 25].

The ability to grade and subtype malignant soft tissue lesions compared favorably with those provided in a limited number of published reports (Table 7). One disadvantage of FNAC compared with NCB and incisional biopsy is the loss of tissue architecture making cytopathologic analysis difficult and specific subtyping less accurate. Ancillary techniques such as immunohistochemistry, cytogenetics, flow cytometry, and electron microscopy are useful if the smear is nondiagnostic [28].

One-fourth of all patients required a secondary biopsy before a definitive management plan was rendered. A previous study analyzed the combination of NCB and FNAC and found 63% were useful to guide treatment and 26.5% required open biopsy [22]. The clinical usefulness of FNAC for evaluation and management of soft tissue masses is based on whether the technique reliably supplies adequate information for initial triage and selection of appropriate therapy. When FNA reveals benign cellular material, the clinician must have confidence in conjunction with clinicoradiographic information to pursue conservative measures or local resection without additional pathologic evaluation. When a malignancy is encountered, the cytopathologist must be able to differentiate high- from low-grade lesions. At most institutions, specific histologic subtyping is not required for treatment to proceed [13, 29]. In certain cases such as high-grade pleomorphic sarcoma, additional specification is unnecessary until another tissue sample is available [35]. Anatomic location, proximity to neurovascular structures, size, and grade determine treatment options. Low-grade malignancies usually can undergo wide excision without neoadjuvant therapy. High-grade malignancies may require chemotherapy or radiation before surgical resection.

Analysis of the discrepant cases revealed seven sampling errors and nine interpretation errors. The ADASP warned the heterogeneity of many soft tissue tumors renders them susceptible to sampling error and misdiagnosis [10]. Contamination from surrounding tissues can occur if cells are aspirated from overlying structures. If the lesion contains cystic, hemorrhagic, or necrotic areas, misrepresentative samples may be aspirated. Specimens from surrounding tissue containing reactive lipocytes, fibroblasts, myofibroblasts, and other cells often have the cytomorphic appearance of liposarcoma or pleomorphic sarcoma. Pseudosarcomatous proliferations such as nodular fasciitis and pseudomalignant myositis ossificans can have worrisome features and mimic high-grade lesions [26]. Two of the discrepant cases involved relatively rare entities, a large cell Ewing sarcoma, and a pleomorphic hyalinizing angiectatic tumor of soft parts. Recognition of rare tumors and unprecedented new entities can be difficult owing to the lack of published criteria for cytologic diagnosis [7, 32].

FNAC is highly effective in diagnosing malignancy for patients presenting with a palpable soft tissue mass. Nondiagnostic samples and cytologic-histopathologic discrepancies seldom occur with experienced cytopathologists, but close multidisciplinary collaboration can determine when a secondary biopsy is necessary. In most cases, management decisions can be made on the basis of the FNAC and a thorough assessment of the clinicoradiographic presentation.

Table 7. Literature review of FNAC for soft tissue masses

Study	Cases (number)	Sensitivity	Specificity	PPV	NPV	Grading accuracy of malignant lesions	Subtyping accuracy of malignant lesions	Indeterminate FNA	Comments
Dey et al. [6]	82	91.5%	92.5%	96.0%	86.2%	NA	46.8%	0%	
Domanski et al. [8]	130	98.7%	96.2%	97.5%	98.0%	90%	77%	0%	FNA/NCB used together
Trovik et al. [34]	95	93.6%	91.7%	100%	95.7%	NA	NA	5.3%	Recurrent lesions only
Yang and Damron [39]	50	87.1%	79.0%	100%	93.8%	81%	78%	14%	Bone and soft tissue lesions
Barth et al. [2]	35	85.7%	36.4%	100%	100%	NA	50%	25.7%	
Akerman et al. [1]	365	84.6%	90.6%	85.7%	97.0%	NA	NA	5.5%	
Oland et al. [23]	196	97.6%	96.1%	100%	94.1%	NA	NA	3.1%	
Bennert and Abdul-Karim [4]	117	71.2%	55.4%	100%	100%	NA	NA	37.6%	
Nagira et al. [20]*	301	89.5%	88.4%	94%	96.4%	NA	50%	7.3%	
Palmer et al. [25]	84	NA	NA	NA	NA	90%	14%	NA	Soft tissue sarcomas only
Wakely and Kneisl [35]*	82	91.3%	86.1%	100%	97%	NA	83%	9.8%	
Jones et al. [13]	77	NA	NA	NA	NA	52–58%	42.7–50%	NA	Bone/soft tissue sarcomas only
Kilpatrick et al. [15]	96	95.8%	NA	100%	NA	NA	63%	3.1%	Soft tissue sarcomas only
Miralles et al. [19]	117	100%	96.5%	96.8%	100%	NA	NA	NA	
Layfield et al. [16]	114	95.1%	69.3%	95.1%	98.1%	NA	NA	16.2%	
Current study	432	89.2%	89.8%	96.1%	98.1%	77.2%	95.2%	8.1%	

* Values for sensitivity and specificity recalculated to include indeterminate FNAC cases were lower than originally reported values which excluded nondiagnostic FNAs.

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