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SYMPOSIUM: HIGHLIGHTS OF THE ISOLS/MSTS 2009 MEETING

A Comparison of Fine-needle Aspiration, Core Biopsy, and Surgical Biopsy in the Diagnosis of Extremity Soft Tissue Masses

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Abstract

Background Biopsy tissue can be obtained through a fine needle, a wider coring needle, or through an open surgical incision. Though much literature exists regarding the diagnostic yield of these techniques individually, none compare accuracy of diagnosis in the same mass.

Questions/purposes We asked how the diagnostic accuracy of fine-needle aspiration, core biopsy, and open surgical biopsy compare in regard to identifying malignancy, establishing the exact diagnosis, and guiding the appropriate treatment of soft tissue masses.

Patients and Methods We prospectively studied 57 patients with palpable extremity soft tissue masses, performing fine-needle aspiration, followed by core biopsy, followed by surgical biopsy of the same mass.

Results Open surgical biopsy was 100% accurate on all accounts. With regard to determining malignancy, fine-needle aspiration and core biopsy had 79.17% and 79.2% sensitivity, 72.7% and 81.8% specificity, 67.9% and 76% positive predictive value, 82.8% and 84.4% negative predictive value, and an overall accuracy of 75.4% and 80.7%, respectively. In regard to determining exact diagnosis, fine-needle aspiration had a 33.3% accuracy and core biopsy had a 45.6% accuracy. With regard to eventual treatment, fine-needle aspiration was 38.6% accurate and core biopsy was 49.1% accurate.

Conclusions In soft tissue mass diagnosis, core biopsy is more accurate than fine-needle aspiration on all accounts, and open biopsy is more accurate than both in determining malignancy, establishing the exact diagnosis, and the guiding appropriate treatment.

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

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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.

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Introduction

Biopsy is often necessary to diagnose a mass that is indeterminate based on history, physical, laboratory, and imaging studies alone. The goal of biopsy is to obtain diagnostic tissue while minimizing morbidity, limiting potential tumor spread, and avoiding interference with future treatments. Techniques that have evolved to accomplish these goals include open surgical biopsy, core biopsy, and fine-needle aspiration (FNA). Open (incisional)

biopsy has long been the gold standard for soft tissue mass diagnosis, with a diagnostic accuracy of 94% to 99% [1, 48]; however, it is expensive ($4321.25 to $7234.00) and carries a complication rate of up to 16%, including hematoma, tumor spread, and wound problems that may interfere with adjuvant treatments [1, 48, 53]. Therefore, less invasive methods have emerged.

Defined as the sampling of tissue through a 20-gauge or smaller needle, FNA has the advantages of speed, convenience, decreased cost (average $1060 per case), minimal morbidity, and a theoretically lower risk of local contamination [1, 10, 20, 52]. Downsides include the limited sample, inaccessibility of some masses, and variable accuracy, especially in the diagnosis of sarcoma. In regard to FNA of general soft tissue masses, the literature reports a wide range of sensitivities (86%–100%), specificities (36%–100%), and diagnostic accuracies (21.9%–98%) [3, 5, 8, 10, 16–18, 20, 32–35, 37, 39, 44, 45, 49, 54]. In these studies, however, nondiagnostic samples have generally been excluded, artificially improving results.

Because of the limited tissue retrieved with FNA, core biopsy has evolved as an alternative, using a 10- to 14-gauge coring needle to obtain cylindrical tissue blocks. A block of tissue allows the pathologist to examine tumor architecture and cellular interrelation, improving the diagnosis of histologic subtype and grade compared to FNA [13, 19, 56]. Other advantages of core biopsy, as with FNA, include speed, convenience, decreased cost (average $1106 per case), minimal morbidity, minimal contamination, and a 0.1% to 1.1% complication rate; disadvantages are also similar to FNA and include limited sampling and inaccessibility of some masses (secondary to size, depth, density, or location) [8, 24, 25, 40, 50, 53, 56]. Improved from FNA, core biopsy's soft tissue mass sensitivity ranges from 81.8% to 100%, specificity from 91% to 100%, and diagnostic accuracy from 72.7% to 100% [6–9, 12, 19, 23–26, 31, 36, 40, 42, 43, 50, 53, 57–59]. However, as with FNA, these studies often excluded nondiagnostic samples, improving apparent accuracies. In the only previously published Level I study evaluating soft tissue mass biopsy techniques, Yang and Damron [57] elegantly compared FNA and core biopsy to each other in the diagnosis of the same soft tissue mass and found core biopsy to be more accurate than FNA on all accounts, with FNA 64% accurate and core 83% accurate in establishing the specific diagnosis.

No previous study has prospectively evaluated FNA, core biopsy, and open surgical biopsy in the diagnosis of the same soft tissue mass. Therefore, to determine and compare the diagnostic accuracies of these biopsy techniques, we asked the following questions: How do FNA, core biopsy, and open biopsy compare to the final clinical diagnosis (and to each other) in regard to (1) identifying malignancy, (2) establishing the exact diagnosis (grade and subtype), and (3) guiding appropriate treatment?

Patients and Methods

From January 2007 to January 2009, we invited all 106 patients evaluated by the Orthopedic Oncology Service with a palpable primary soft tissue mass not previously diagnosed to participate in this prospective study. Indications for biopsy were inability to confidently characterize the nature of the soft tissue mass with history, physical, laboratory, and imaging studies alone and patient desire for diagnosis. Before initiation of the study, a power analysis was performed. The choice of sample size was made on the basis of the primary outcome of ability to determine malignancy in the tissue sample. We excluded 32 patients who were unwilling to participate in the study and 17 patients with poorly or relatively inaccessible masses adjacent to vital structures. Fifty-seven of the 106 patients met these criteria. Assuming a beta error of 0.05 and a power of 0.80, it was anticipated 45 specimens would be required in each group of FNA, core biopsy, and open biopsy to demonstrate a 10% difference in the accuracy between the groups. Complications were defined as those that caused patient morbidity, required clinical intervention, or interfered with future treatment. Patients were followed for at least 6 months, and no patients were lost. Two masses were in the neck, seven in the back, 18 in the upper extremity, and 30 in the lower extremity (Table 1). The Institutional Review Board and Cancer Research Committee approved this study protocol and all patients were also individually registered with our institution's Cancer Center Research Participant Registry.

After consent was obtained, each patient was taken to the operating room and placed under general anesthesia. According to a standardized protocol, FNA was performed on the tumor mass in line with the planned surgical incision by a cytopathologist or surgeon trained in FNA technique. After the skin was prepared with an alcohol pad, FNA was performed using a 1.5-inch 23-gauge needle attached to a 20-mL syringe in a standard syringe holder according to standardized guidelines [22]. Three to five passes of the lesion were performed to provide sampling from circumferential areas of the tumor without breaching the far wall. The aspirates were divided into two sets: one air-dried and the other fixed in 95% ethanol. Both sets were stained with hematoxylin and eosin (H&E). Tissue fragments were retrieved from needle rinse and embedded in paraffin for cell blocks and H&E-stained sections. The cell blocks were also used for molecular biology and tumor marker analysis (keratin, vimentin, smooth muscle actin, myoglobin, Factor VIII, CD34, S100, HMB45, CD117, desmin). All FNA

Table 1. Demographic and pathologic information for the 57 patients, with the FNA, core biopsy, open biopsy, and final diagnoses

Patient	Age (years)	Gender	Location	Final diagnosis	FNA diagnosis	Core biopsy diagnosis	Open biopsy diagnosis	Malignancy			Diagnosis			Treatment/ management		
1	37	Male	Right buttock	Lipoma	Mature adipose tissue	Favor lipoma, recommend rsxn for dx	Lipoma	B	B	B	Y	Y	Y	Y	Y	Y
2	63	Male	Left scapula	Melanoma	Metastatic malignant melanoma w/extensive necrosis	Malignant melanoma	Malignant melanoma	M	M	M	Y	Y	Y	Y	Y	Y
3	83	Male	Left flank	Dedifferentiated leiomyosarcoma	Rhabdomyosarcoma, high grade	Fat tumor, recommend excision to r/o liposarcoma	Dedifferentiated leiomyosarcoma	M	M	M	O	O	O	O	Y	O
4	36	Male	Left leg	MFH	High-grade sarcoma	Sarcoma, NOS	MFH	M	M	M	O	Y	O	O	Y	O
5	60	Male	Right axilla	Lipoma	Mature adipose tissue	Lipoma	Lipoma	B	B	B	Y	Y	Y	Y	Y	Y
6	20	Female	Left thigh	Hemangioma	Mature adipose tissue, marked acute inflammation, and amorphous debris, NTI	Spindle cell neoplasm	Hemangioma, spindle cell	B	ND	B	O	O	O	O	O	O
7	75	Female	Left knee	Tumoral calcinosis	Neoplastic process with numerous giant cells, NTI	Favor reactive process	Tumoral calcinosis	B	ND	B	ND	O	ND	O	O	ND
8	27	Male	Left thigh	Benign inflammatory process	Mature adipose tissue, NTI	Muscle, no tumor identified	Mixed inflammation	B	B	B	O	O	O	O	O	O
9	61	Male	Right thigh	Scar tissue only, no tumor	Proteinaceous material, NTI	Dense fibrous tissue	No tumor identified	B	B	B	O	O	O	Y	Y	Y
10	53	Male	Left foot	Lipoma	Mature adipose tissue, NTI	Lipoma	Lipoma	B	B	B	Y	Y	Y	Y	Y	Y
11	77	Female	Left foot	Tumoral calcinosis	Collections of crystalline material and blood, NTI	Favor calcinosis	Tumoral calcinosis	B	B	B	O	O	Y	Y	Y	Y
12	57	Female	Left thigh	Schwannoma	Mature adipose tissue, skeletal muscle, and minute fragment of cellular spindle cell stroma, ND	Spindle cell tumor, r/o schwannoma	Cellular schwannoma	B	B	B	ND	ND	O	ND	ND	O
13	65	Female	Left ankle	Abscess	Vascular lesion with delicate capillaries and marked acute inflammation, favor granulation tissue/reactive process	Acute and chronic inflammation	Abscess	B	B	B	Y	Y	Y	Y	Y	Y
14	59	Male	Left elbow	Desmoid fibromatosis	Blood only, ND	Spindle cell tumor, benign	Desmoid fibromatosis	ND	B	B	ND	ND	Y	ND	ND	Y
15	84	Male	Left arm	High-grade myxofibrosarcoma	Malignant pleomorphic myxoid sarcoma, high grade	Myxoid sarcoma, high grade	Myxofibrosarcoma, high grade	M	M	M	Y	Y	Y	Y	Y	Y
16	51	Male	Left thigh	Myxoid liposarcoma	Myxoid spindle cell tumor, ddx includes lipoma versus liposarcoma	Liposarcoma	Myxoid liposarcoma	ND	M	M	O	O	Y	O	O	Y
17	46	Female	Right arm	Squamous cell carcinoma	Malignant cells present, favor squamous cell carcinoma	Squamous cell carcinoma vs adnexal skin tumor	Squamous cell carcinoma	M	ND	M	O	Y	O	O	Y	O

Table 1. continued

Patient	Age (years)	Gender	Location	Final diagnosis	FNA diagnosis	Core biopsy diagnosis	Open biopsy diagnosis	Malignancy			Diagnosis			Treatment/ management		
18	54	Female	Left thigh	Atypical lipoma	Mature adipose tissue	Muscle and dense fibrous tissue	Atypical intramuscular lipoma	B	B	B	O	Y	O	O	Y	O
19	53	Female	Back	Desmoid fibromatosis	Mature adipose tissue and blood, NTI	Lipoma	Desmoid tumor	B	B	B	Y	O	O	Y	O	O
20	29	Male	Right elbow	Clear cell sarcoma	Sarcoma, NOS, high grade	Malignant melanoma	Clear cell sarcoma	M	M	M	O	O	Y	O	O	Y
21	71	Male	Right shoulder	MFH	ND	Skin with elastosis	MFH	ND	B	M	ND	ND	O	ND	ND	O
22	86	Female	Right knee	MFH	Pleomorphic myxoid sarcoma, low grade	Sarcoma, high grade	MFH	M	M	M	O	O	Y	O	O	Y
23	57	Female	Right shoulder	Lipoma	Mature adipose tissue, NTI	Lipoma	Lipoma	B	B	B	Y	Y	Y	Y	Y	Y
24	60	Female	Left buttock	MFH	Pleomorphic malignant sarcoma, high grade	Sarcoma, high grade	MFH	M	M	M	Y	Y	Y	Y	Y	Y
25	71	Male	Right thigh	Merkel cell carcinoma	Small cell neuroendocrine carcinoma: Merkel cell tumor versus metastatic neuroendocrine carcinoma.	Merkel cell carcinoma	Merkel cell carcinoma	M	M	M	Y	Y	Y	Y	Y	Y
26	65	Male	Left buttock	Myxoid chondrosarcoma	High-grade myxoid sarcoma (S100 +) chondrosarcoma versus MPNST	Sarcoma	Myxoid chondrosarcoma	M	M	M	O	O	O	O	Y	O
27	80	Female	Left thigh	Schwannoma	Poorly preserved paucicellular specimen showing few groups of malignant cells and fat	Fibrosis and injury vessels	Schwannoma	M	B	B	O	O	O	O	O	O
28	63	Male	Right arm	Lipoma	Mature adipose/blood c/w lipoma	Muscle and fibrous tissue	Lipoma	B	B	B	Y	Y	Y	Y	Y	Y
29	46	Male	Right forearm	Schwannoma	Spindle cell tumor, favor malignant, no grade	Schwannoma	Cellular schwannoma	M	B	B	O	O	Y	O	O	Y
30	30	Female	Left foot	Chondroma	Benign cartilage/blood, r/o chondroma	Mature cartilage	Chondroma	B	B	B	O	O	O	O	O	O
31	58	Female	Left back	Desmoid fibromatosis	Blood/mature adipose tissue: NTI	Spindle cell tumor, minute	Desmoid fibromatosis	B	B	B	O	O	O	O	O	O
32	61	Female	Left thigh	MFH	ND	Sarcoma, high grade	MFH	ND	M	M	ND	ND	Y	ND	ND	Y
33	72	Male	Left hip	Well-differentiated liposarcoma	Dense, watery proteinaceous material and blood, NTI	Necrotic material	Well-differentiated liposarcoma	B	ND	M	ND	O	ND	ND	O	ND
34	64	Male	Right back	Intramuscular myxoma	Sarcoma, NOS, low grade	Myxoma	Myxoma	M	B	B	O	O	Y	O	O	Y
35	61		Back	MFH	Sarcoma, NOS (cell block only, no tumor in smears), low grade	Lipoma	MFH	M	B	M	O	O	O	O	O	O

Table 1. continued

Patient	Age (years)	Gender	Location	Final diagnosis	FNA diagnosis	Core biopsy diagnosis	Open biopsy diagnosis	Malignancy			Diagnosis			Treatment/ management		
36	25	Male	Right buttock	PVNS	Malignant cells present, favor sarcoma, no grade	PVNS	PVNS	M	B	B	O	O	Y	O	O	Y
37	30	Male	Right arm	Clear cell sarcoma	Malignant small round blue cell tumor, favor sarcoma, no grade	Sarcoma, high grade	Clear cell sarcoma	M	M	M	O	O	O	O	O	O
38	69	Female	Right thigh	MFH	Numerous foamy macrophages c/w cystic process, NTI	Malignant melanoma	MFH	B	M	M	O	O	O	O	O	O
39	78	Female	Posterior neck	Myxofibrosarcoma	Rhabdomyosarcoma, high grade	Spindle cell sarcoma	Myxofibrosarcoma	M	M	M	O	O	O	O	O	O
40	74	Female	Right shoulder	Lipoma	Mature adipose tissue	Lipoma	Lipoma	B	B	B	Y	Y	Y	Y	Y	Y
41	48	Male	Left knee	PVNS	Predominantly muscle and fat, rare poorly preserved atypical cell suspicious for malignancy, favor sarcoma	Small round blue cell tumor, recommend excision for definitive diagnosis	PVNS	M	M	B	O	O	O	O	O	O
42	50	Female	Right neck	Leiomyosarcoma	Leiomyosarcoma, high grade	Spindle cell sarcoma	Leiomyosarcoma, high grade	M	M	M	O	Y	O	O	Y	O
43	47	Male	Left foot	Ganglion cyst	Proteinaceous material/blood: NTI	Minute superficial skin	Ganglion cyst	B	B	B	O	O	O	O	O	O
44	65	Male	Back	Melanoma	Malignant cells present, r/o melanoma, no grade	Malignant melanoma	Malignant melanoma	M	M	M	O	O	Y	O	O	Y
45	61	Female	Right arm	MFH	Sarcoma, high grade	Spindle cell sarcoma	MFH	M	M	M	O	Y	O	O	Y	O
46	64	Male	Back	Elastofibroma	Mature adipose tissue/blood: NTI	Elastofibroma	Elastofibroma	B	B	B	O	O	Y	O	O	Y
47	47	Female	Right forearm	Hemangioma	ND	Nondiagnostic	Hemangioma	ND	ND	B	ND	ND	ND	ND	ND	ND
48	88	Male	Left knee	Coccidiomycosis	Mature adipose tissue/blood: NTI	Muscle and fat	Coccidiomycosis	B	B	B	O	O	O	O	O	O
49	65	Male	Left thigh	Lipoma	Mature adipose tissue/blood: NTI	Lipoma	Lipoma	B	B	B	Y	Y	Y	Y	Y	Y
50	78	Male	Left elbow	Melanoma	Malignant tumor with extensive necrosis	Malignant melanoma	Melanoma	M	M	M	O	O	Y	O	O	Y
51	43	Female	Left leg	Hemangioma	Mature adipose tissue c/w lipoma	Nonspecific fibrosis	Intramuscular hemangioma	B	B	B	O	O	O	O	O	O
52	40	Male	Left shoulder	Lipoma	Mature adipose tissue c/w lipoma	Lipoma	Lipoma	B	B	B	Y	Y	Y	Y	Y	Y
53	35	Female	Right foot	Plantar fibromatosis	Nondiagnostic	Fibrosis, r/o fibromatosis	Plantar fibromatosis	ND	B	B	ND	ND	Y	ND	ND	Y
54	52	Male	Right knee	Extraskeletal osteosarcoma	Malignant spindle cell lesion	Sarcoma	Extraskeletal osteosarcoma	M	M	M	O	O	O	O	O	O
55	39	Male	Right thigh	Pilomatrixoma	Acute inflammation and some features of inclusion cyst	Keratinaceous debris c/w pilomatrixoma	Pilomatrixoma	B	B	B	O	O	Y	O	O	Y
56	52	Male	Left arm	Angiolipoma	Mature adipose tissue c/w lipoma	Lipoma	Angiolipoma	B	B	B	Y	O	O	Y	Y	Y

Table 1. continued

Patient	Age (years)	Gender	Location	Final diagnosis	FNA diagnosis	Core biopsy diagnosis	Open biopsy diagnosis	Malignancy		Diagnosis		Treatment/ management	
								M	M	M	Y	Y	Y
57	57	Male	Right arm	Plasmacytoma	Malignant plasma cell tumor c/w multiple myeloma, recommend clinical correlation	Plasmacytoma	Plasmacytoma	24	21	24	16	19	28	18	24	Y
							M/Y	27	31	33	33	32	26	32	27	24
							B/O	6	5	0	8	6	3	7	6	3
							ND									

FNA = fine-needle aspiration; MFH = malignant fibrous histiocytoma; PVNS = pigmented villonodular synovitis; NTI = no tumor identified; ND = nondiagnostic; ddx = differential diagnosis; NOS = not otherwise specified; MPNST = malignant peripheral nerve sheath tumor; c/w = consistent with; r/o = rule out; rsxn = resection; dx = diagnosis; B = benign; M = malignant; Y = match; O = nonmatch.

biopsies were reviewed by a senior cytopathologist trained in oncology who was given a complete clinical history. The FNA smears were assigned to one of the following categories: malignant, benign, or nondiagnostic. Smears were deemed nondiagnostic when the cells obtained were insufficient for any type of diagnosis. Sarcomas were graded as low grade, high grade, or not gradable. Grading criteria included the presence of mitoses, cellularity, differentiation, nuclear pleomorphism, and necrosis [2, 15, 41]. When possible, a specific histologic diagnosis was reported.

Directly after completion of FNA, core biopsy was performed on the tumor mass in line with the planned incision by the orthopaedic oncology team. The core biopsies were performed using a Tru-Cut® soft tissue biopsy needle (Cardinal Health, Dublin, OH), through the FNA insertion site, taking multiple samples (three to five passes) throughout the tumor circumferentially with care to obtain adequate tissue for evaluation, but not to breach the far wall of the tumor. The biopsies were not sent for frozen section analysis, were fixed immediately in 10% buffered formalin, and were stained routinely with H&E. Histochemical stains (alkaline phosphatase and Prussian blue) were applied. Special stains, such as van Gieson, McManus, and reticulin (Gordon-Sweet), were applied when appropriate. For those specimens suggestive of sarcoma, immunohistochemical stains were selected from a panel of antibodies: cytokeratins (AE1/AE3, CAM1.2, MNF116, CK5, CK7, CK20), epithelial membrane antigen, S100, HMB45, melanin A, desmin, actin (muscle-specific actin), α-smooth muscle actin, h-caldesmon, vimentin, CD30, CD15, CD45, CD45-RO, CD20, CD3, CD10, CD5, CD23, bcl-2, MIB-1, CD34, CD31, Factor VIII, kappa- and lambda-light chains, and osteonectin. Two senior musculoskeletal pathologists specializing in orthopaedic oncology independently, and blindly with regard to other specimens taken from the same patient, reviewed the core biopsy specimens. The biopsy specimens were classified as diagnostic or nondiagnostic based on the adequacy of the tissue obtained for histologic analysis to yield any basic diagnosis. The specimens were evaluated for the nature of the lesion (benign or malignant), specific histologic diagnosis, and grade. Sarcomas were graded according to the American Joint Committee on Cancer grading criteria as either low grade (Grades 1 and 2) or high grade (Grades 3 and 4) [22].

After FNA and core biopsy procedures were performed, open biopsies were performed by a trained orthopaedic oncologist in accordance with sarcoma principles. An incision was made through the FNA and core puncture site and in line with the planned resection, and specimens were sampled from the tumor periphery until frozen section revealed adequate sampling. The nonfrozen tissue was

immediately placed in 10% buffered formalin. The tissue handling, fixation, and staining and pathologic analysis were identical to those of the core biopsy specimens. The results of the FNA, core, and open biopsy were compared to both the complete resection final pathology reports and the final clinical diagnosis given to the patient.

Outcome variables of determining malignancy, determining exact diagnosis, and guiding eventual treatment for FNA, core biopsy, and open biopsy were measured against the final clinical diagnosis determined by analysis of the completely resected specimen in combination with the final clinical impression. Malignancy and exact diagnosis (subtype and grade) were determined by a cytopathologist (in the case of FNA) and by a musculoskeletal pathologist (in the case of core and open biopsy) as previously described. Concordance with indicated treatment was determined by comparing the indicated treatment determined by a trained orthopaedic oncologist with the given diagnosis resulting from the FNA, core, and open biopsy final pathologic results.

All information collected in this study was recorded and analyzed using SPSS® software (SPSS Inc, Chicago, IL). Sensitivities, specificities, positive predictive values (PPVs), negative predictive values (NPVs), and concordances were determined. These values were then compared with the t test for proportions, set to a 95% confidence interval.

Results

Adequate tissue sample to determine any kind of diagnosis was obtained in 50 of the 57 (87.7%) FNAs, in 49 of 57 (86.0%) core biopsies, and in 57 of 57 (100%) open biopsy specimens. These diagnostic sample proportions were similar in both benign (29 of 33 [87.9%] for FNA and 28 of 33 [84.9%] for core) and malignant (21 of 24 [87.5%] for each) cases. Open surgical biopsy determined malignancy (or a benign diagnosis) correctly 100% of the time when compared to the complete resection and final clinical diagnosis results, with FNA only 75.4% ($p < 0.0002$) accurate and core biopsy only 80.7% ($p < 0.0015$) accurate in this regard. Open biopsy had better results than both percutaneous techniques in terms of sensitivity, specificity, PPV, NPV, and concordance with the final diagnosis (Table 2).

As with determining malignancy, open biopsy was able to determine the correct grade and subtype in 100% of cases, with no discrepancies after full resection and final clinical diagnosis. FNA and core biopsy were concordant with the final exact diagnosis in 33.3% and 45.6% of cases, respectively, which were both less ($p < 0.0001$) concordant than open surgical biopsy (Table 3).

Correct treatment would have been initiated in 38.6% and 49.1% of cases on the basis of FNA specimens and core specimens, respectively, while all patients who underwent open biopsy would have had correct treatment initiated based on the biopsy results. Compared to open biopsy, FNA and core biopsy were both less ($p < 0.0001$) accurate in this regard (Table 3).

Five of the 23 FNA samples that reported malignancy turned out to be pigmented villonodular synovitis (two), schwannoma (two), and myxoma (one) on final pathology (Table 1). Of the five pigmented villodular synovitis and schwannoma cases, four were reported as malignant and one as nondiagnostic on FNA, while on core biopsy, one was reported as malignant and two as nondiagnostic. None of the open surgical biopsy results were changed after complete resection or final clinical impression.

There was one complication of the 57 cases (1.8%) in which a patient developed a wound dehiscence 10 days after the procedure on the posterior neck, which was successfully treated nonoperatively with dressing changes and oral antibiotics, with no effects on the patient's ultimate treatment and outcome. There were no postbiopsy hematoma complications causing morbidity, requiring intervention, or compromising treatment or outcome.

Discussion

Open biopsy has long been considered the gold standard for diagnosis of an extremity soft tissue mass [1, 11, 14, 38, 51]; however, proponents of percutaneous techniques suggest FNA or core biopsy is just as effective and should replace open biopsy as the method of choice [28–30, 40, 56]. No study has prospectively compared the accuracy of these three biopsy techniques in a standardized fashion. Therefore, we asked how accurate FNA, core biopsy, and open surgical biopsy are and how they compare to each other with regard to determining malignancy, establishing the exact diagnosis, and guiding the appropriate treatment.

We note some limitations to our study. First, we studied only palpable and safe soft tissue masses, which excludes deeper masses and those in close proximity to neurovascular structures, which may be more challenging to sample. Second, the need for patient consent could potentially make the cohort less representative, since a patient with an aggressive tumor may be less likely to engage in "experimental" surgery. Third, the diagnostic standard by which all three diagnostic techniques were judged was based on the complete surgical resection and the final clinical impression of the orthopaedic oncologist; although this measure is the best we have, this diagnosis could still be wrong and skew our comparative results. Lipomas are

Table 2. Accuracy of biopsy techniques in regard to determining malignancy when compared to the final diagnosis

Variable	FNA	Core biopsy	Open biopsy
Sensitivity	79.2% ($p = 0.0009$)	79.2% ($p = 0.0009$)	100%
Specificity	72.7% ($p = 0.0001$)	81.8% ($p = 0.0023$)	100%
PPV	67.9% ($p < 0.0001$)	76.0% ($p = 0.0003$)	100%
NPV	82.7% ($p = 0.0033$)	84.4% ($p = 0.0058$)	100%
Concordance with final	75.4% ($p = 0.0002$)	80.7% ($p = 0.0015$)	100%

P values indicate the differences when compared to open biopsy; FNA = fine-needle aspiration; PPV = positive predictive value; NPV = negative predictive value.

Table 3. Summary of FNA, core biopsy, and open biopsy concordances with the final diagnosis

Variable	FNA	Core biopsy	Open biopsy
Determining malignancy	75.4% ($p = 0.0002$)	80.7% ($p = 0.0015$)	100%
Determining exact diagnosis	33.3% ($p < 0.0001$)	45.6% ($p < 0.0001$)	100%
Guiding appropriate treatment	38.6% ($p < 0.0001$)	49.1% ($p < 0.0001$)	100%

P values indicate the differences when compared to open biopsy; FNA = fine-needle aspiration.

Table 4. Comparison of our study with published literature regarding FNA of extremity soft tissue masses

Study	Malignancy	Grade	Subtype	Specific diagnosis	Sensitivity*	Specificity*
Fleshman et al. [20] (2007)†		91%			94%	
Yang and Damron [57] (2004)	88%	78%	74%	64%		
Maitra et al. [37] (2000)	88%				89%	87%
Wakely and Sneisl [54] (2000)			70%		100%	97%
Kilpatrick et al. [29] (2001)	86%		54%			
Palmer et al. [45] (2001)†	92%	90%	14%			
Costa et al. [16] (1996)	88%		21%			
Kasraeian et al. [current study]	75.4%			33.3%	79.2%	72.7%

* Refers to accuracy, sensitivity, or specificity of differentiating malignant from benign lesions; †excluded inadequate samples; FNA = fine-needle aspiration.

diagnostic based on MRI alone and are notoriously difficult to diagnose through percutaneous techniques or on frozen sections; our study included eight lipomas, and their inclusion may skew results and detract from data regarding masses that cannot be diagnosed using available noninvasive techniques. Finally, the accuracy of percutaneous biopsies depends on the operator technique of biopsy and pathologic analysis; much attention was placed toward proper biopsy technique in all cases and having the pathology read by a well-informed and specialized cytopathologist (in the case of FNA) and musculoskeletal pathologist (in the case of core and open biopsies).

Adequate tissue sample to determine any kind of diagnosis was obtained in all of our open biopsy specimens but in only 87.7% of the FNAs and 86.0% of the core biopsies; furthermore, open biopsy was more sensitive, specific, predictive, and accurate in regard to determining malignancy than the percutaneous techniques. Literature supports the disconcerting fact that a percutaneous biopsy result negative for malignancy is not confirmatory [55], and our FNA and core biopsy NPVs also support this claim (Table 2). As sarcomas enlarge, they typically outgrow their blood supply, leading to areas of central necrosis, and inadvertent sampling of these areas may lead to nondiagnostic specimens [11, 14, 38, 51]. In addition, mesenchymal tumors or sarcomas are difficult to diagnose (even basically) on cellular morphology alone without visualizing the stromal structure [19, 21, 56], especially in regard to spindle cell tumors [46]. The improved diagnostic sampling in the open biopsy group is likely due to the sending of frozen sections until histologic evidence of diagnostic sampling was achieved, a procedure not followed with the percutaneous techniques. We compared our findings with those of the most applicable published studies regarding FNA (Table 4) and core biopsy (Table 5) of extremity soft tissue masses, although it should be noted

Table 5. Comparison of our study with published literature regarding core biopsy of extremity soft tissue masses

Study	Malignancy	Grade	Subtype	Specific diagnosis	Sensitivity*	Specificity*
Serpell and Pitcher [50] (2008)	84%				94%	100%
Mitsuyoshi et al. [40] (2006)	94%†		78%†		100%	90%
Yang and Damron [57] (2004)	93%	83%	90%	83%		
Hoeber et al. [25] (2001)	98.7%	85%	80%		99.4%	98.7%
Welker et al. [56] (2000)†	92%	89%	73%		82%	100%
Heslin et al. [24] (1997)†	95%	88%	75%		95%	100%
Skrzynski et al. [53] (1996)		78%†	84%			
Barth et al. [8] (1992)	100%	100%			100%	
Kasraeian et al. [current study]	80.7%			45.6%	79.2%	81.8%

* Refers to accuracy, sensitivity, or specificity of differentiating malignant from benign lesions; †excluded inadequate samples.

previous studies often excluded nondiagnostic samples in their accuracy calculations.

The exact diagnosis (matching grade and subtype) was obtained in 100% of open biopsies and in only 33.3% and 45.6% of FNA and core biopsies, respectively. Decreased accuracy of FNA (Table 4) and core biopsy (Table 5) in regard to determining the grade and subtype was also found in other studies, even with most of the studies excluding nondiagnostic samples. Identifying the correct grade and exact histologic subtype is critical in the case of malignancies [2]. Proponents of percutaneous techniques suggest taking multiple samples from multiple different locations within the tumor to obtain a representative sample [25] or combining both FNA and core biopsy to improve the accuracy in subtype diagnosis [19]. However, multiple passes from varying locations have the potential to increase contamination and thereby theoretically increase the risk for local recurrence or theoretically cause distant spread by introducing tumor cells directly into the vasculature [11, 14, 38, 51].

Previous studies have looked at accuracy of biopsy techniques in terms of determination of malignancy, grade, and subtype, but none have looked at the effect on eventual treatment. Since guiding the management plan is the ultimate benefit of any test, we added this outcome measure. Again, open biopsy guided the appropriate treatment 100% of the time; however, based on FNA and core biopsy specimens alone, correct treatment would have been initiated only 38.6% and 49.1% of the time, respectively.

Proponents of percutaneous techniques cite less morbidity and fewer complications [2]. Prior studies of open biopsy have reported complications ranging between 0% and 17% [11, 14, 38, 51]. Most studies on FNA either do not specifically state complications or have a very low complication rate (0%–1%) [2–5, 10, 15–18, 20, 27–30, 32–35, 37, 39, 44, 45, 49, 54, 55], with most complications related to local tenderness and bleeding. Core biopsy has a reported complication rate ranging between 0% and 7.4%, most commonly hematoma, bleeding, and infection [9, 47, 56]. In our series, there was only one complication of 57 cases (1.8%), which was a wound dehiscence treated nonoperatively without any effect on the patient's further treatment.

In summary, core biopsy had greater sensitivity, specificity, predictive value, and accuracy than FNA in regard to determining malignancy; however, both were inferior to open surgical biopsy, with FNA only 75.4% accurate and core biopsy only 80.7% accurate in this regard; therefore, a negative FNA or core biopsy result does not ensure absence of malignancy. Core biopsy had greater accuracy than FNA in regard to establishing the exact diagnosis and guiding the appropriate treatment; however, these accuracy values for both FNA and core were very low (< 50%) and both were inferior to open biopsy. Therefore, we recommend open biopsy of indeterminate soft tissue masses as a more reliable, accurate, and confirmatory means of determining malignancy, establishing the exact diagnosis, and guiding their appropriate treatment.

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References

1. Aboulafia AJ. Biopsy. In: Schwartz HS, ed. *Orthopaedic Knowledge Update: Musculoskeletal Tumors 2*. Rosemont, IL: AAOS; 2008:3–11.
2. Akerman M. Fine-needle aspiration cytology of soft tissue sarcoma: benefits and limitations. *Sarcoma.* 1998;2:155–161.
3. Akerman M, Killander D, Rydholm A, Rooser B. Aspiration of musculoskeletal tumors for cytodiagnosis and DNA analysis. *Acta Orthop Scand.* 1987;58:523–528.
4. Akerman M, Rydholm A, Persson BM. Aspiration cytology of soft-tissue tumors: the 10-year experience at an orthopedic oncology center. *Acta Orthop Scand.* 1985;56:407–412.
5. Amin MS, Lugman M, Jamal S, Mamoon M, Anwar M. Fine needle aspiration biopsy of soft tissue tumours. *J Coll Physicians Surg Pak.* 2003;13:625–628.

6. Ashford RU, McCarthy SW, Scolyer RA, Bonar SF, Karim RZ, Stalley PD. Surgical biopsy with intra-operative frozen section: an accurate and cost-effective method for diagnosis of musculoskeletal sarcomas. *J Bone Joint Surg Br.* 2006;88:1207–1211.
7. Ball AB, Fisher C, Pittam M, Watkins RM, Westbury G. Diagnosis of soft tissue tumours by Tru-Cut biopsy. *Br J Surg.* 1990;77:756–758.
8. Barth RJ Jr, Merino MJ, Solomon D, Yang JC, Baker AR. A prospective study of the value of core needle biopsy and fine needle aspiration in the diagnosis of soft tissue masses. *Surgery.* 1992;112:536–543.
9. Bennert KW, Abdul-Karim FW. Fine needle aspiration cytology vs. needle core biopsy of soft tissue tumors: a comparison. *Acta Cytol.* 1994;38:381–384.
10. Bezabih M. Cytological diagnosis of soft tissue tumours. *Cytopathology.* 2001;12:177–183.
11. Bickels J, Jelinek JS, Shmookler MB, Neff RS, Malawer MM. Biopsy of musculoskeletal tumors: current concepts. *Clin Orthop Relat Res.* 1999;368:212–219.
12. Carrino JA, Khurana B, Ready JE, Silverman SG, Winalski CS. Magnetic resonance imaging-guided percutaneous biopsy of musculoskeletal lesions. *J Bone Joint Surg Am.* 2007;89:2179–2187.
13. Carter RJ, Qin LX, Maki RG, Brennan MF, Ladanyi M, Singer S. A synovial sarcoma-specific preoperative nomogram supports a survival benefit to ifosfamide-based chemotherapy and improves risk stratification for patients. *Clin Cancer Res.* 2008;14:8191–8197.
14. Cormier JN, Pollock RE. Soft tissue sarcomas. *CA Cancer J Clin.* 2004;54:94–109.
15. Costa J, Wesley RA, Glatstein E, Rosenberg SA. The grading of soft tissue sarcomas: results of a clinicopathologic correlation in a series of 163 cases. *Cancer.* 1984;53:530–541.
16. Costa MJ, Campman SC, Davis RL, Howell LP. Fine-needle aspiration cytology of sarcoma: retrospective review of diagnostic utility and specificity. *Diagn Cytopathol.* 1996;15:23–32.
17. Dalen BPM, Meis-Kindblom JM, Sumathi VP, Ryd W, Kindblom L. Fine-needle aspiration cytology and core needle biopsy in the preoperative diagnosis of desmoid tumors. *Acta Orthop.* 2006;77:926–931.
18. Dey P, Mallik MK, Gupta SK, Vasishta RK. Role of fine needle aspiration cytology in the diagnosis of soft tissue tumours and tumour-like lesions. *Cytopathology.* 2004;15:32–37.
19. Domanski HA, Akerman M, Carlen B, Engellau J, Gustafson P, Jonsson K, Mertens F, Rydholm A. Core-needle biopsy performed by the cytopathologist: a technique to complement fine-needle aspiration of soft tissue and bone lesions. *Cancer.* 2005;105:229–239.
20. Fleshman R, Mayerson J, Wakely PE. Fine-needle aspiration biopsy of high-grade sarcoma. *Cancer.* 2007;111:491–498.
21. Fletcher CD, Kempson RL, Weiss SW. Recommendations for the reporting of soft tissue sarcomas. Association of Directors of Anatomic and Surgical Pathology. *Mod Pathol.* 1998;11:1257–1261.
22. Greene FL, Page DL, Fleming FD, Fritz AG, Balch CM, Haller DG, Morrow M, eds. *American Joint Committee on Cancer: Cancer Staging Manual.* 6th ed. New York, NY: Springer; 2002:221–226.
23. Hau A, Kim I, Kattapuram S, Hornicek FJ, Rosenberg AE, Gebhardt MC, Mankin HJ. Accuracy of CT-guided biopsies in 359 patients with musculoskeletal lesions. *Skeletal Radiol.* 2002;31:349–353.
24. Heslin MJ, Lewis JJ, Woodruff JM, Brennan MF. Core needle biopsy for diagnosis of extremity soft tissue sarcoma. *Ann Surg Oncol.* 1997:4;425–431.
25. Hoeber I, Spillane AJ, Fisher C, Thomas JM. Accuracy of biopsy techniques for limb and limb girdle soft tissue tumors. *Ann Surg Oncol.* 2001;8:80–87.
26. Issakov J, Flusser G, Kollender Y, Merimsky O, Lifschitz-Mercer B, Meller I. Computed tomography-guided core needle biopsy for bone and soft tissue tumors. *Isr Med Assoc J.* 2003;5:28–30.
27. Jones C, Liu K, Hirschowitz S, Klipfel N, Layfield LJ. Concordance of histopathologic and cytologic grading in musculoskeletal sarcomas: can grades obtained from analysis of fine-needle aspirates serve as the basis for therapeutic decisions? *Cancer.* 2002;96:83–91.
28. Kilpatrick SE, Cappellari JO, Bos GD, Gold SH, Ward WG. Is fine-needle aspiration biopsy a practical alternative to open biopsy for primary diagnosis of sarcoma? Experience with 140 patients. *Am J Clin Pathol.* 2001;115:59–68.
29. Kilpatrick SE, Ward WG, Bos GD, Chauvenet AR, Gold SH. The role of fine needle aspiration biopsy in the diagnosis and management of osteosarcoma. *Pediatr Pathol Mol Med.* 2001;20:163–187.
30. Kilpatrick SE, Ward WG, Cappellari JO, Bos GD. Fine-needle aspiration biopsy of soft tissue sarcomas: a cytomorphologic analysis with emphasis on histologic subtyping, grading, and therapeutic significance. *Am J Clin Pathol.* 1999;112:179–188.
31. Kissin MW, Fisher C, Carter RL, Horton LW, Westbury G. Value of Tru-cut biopsy in the diagnosis of soft tissue tumours. *Br J Surg.* 1986;73:742–744.
32. Klijanienko J, Caillaud JM, Lagace R, Vielh P. Comparative fine-needle aspiration and pathologic study of malignant fibrous histiocytoma: cytodiagnostic features of 95 tumors in 71 patients. *Diagn Cytopathol.* 2003;29:320–326.
33. Klijanienko J, Caillaud JM, Lagace R, Vielh P. Fine-needle aspiration biopsy of leiomyosarcoma: a correlative cytohistopathological study of 98 tumors in 68 patients. *Diagn Cytopathol.* 2003;28:119–125.
34. Kumar S, Chowdhury N. Accuracy, limitations and pitfalls in the diagnosis of soft tissue tumors by fine needle aspiration cytology. *Ind J Pathol Microbiol.* 2007;50:42–45.
35. Layfield LJ, Anders KH, Glasgow BJ, Mirra JM. Fine-needle aspiration of primary soft-tissue lesions. *Arch Pathol Lab Med.* 1986;110:420–424.
36. Logan PM, Connell DG, O'Connell JX, Munk PL, Janzen DL. Image-guided percutaneous biopsy of musculoskeletal tumors: an algorithm for selection of specific biopsy techniques. *AJR Am J Roentgenol.* 1996;166:137–141.
37. Maitra A, Ashfaq R, Saboorian MH, Lindberg G, Gokaslan ST. The role of fine-needle aspiration biopsy in the primary diagnosis of mesenchymal lesions: a community hospital-based experience. *Cancer.* 2000;90:178–185.
38. Mankin HJ, Mankin CJ, Simon MA. The hazards of the biopsy, revisited. *J Bone Joint Surg Am.* 1996;78:656–663.
39. Miralles TG, Gosalbez F, Menenedez P, Astudillo A, Torre C, Buesa J. Fine needle aspiration cytology of soft-tissue lesions. *Acta Cytol.* 1986;30:671–678.
40. Mitsuyoshi G, Naito N, Kawai A, Kunisada T, Yoshida A, Yanai H, Dendo S, Yoshino T, Kanazawa S, Ozaki T. Accurate diagnosis of musculoskeletal lesions by core needle biopsy. *J Surg Oncol.* 2006;94:21–27.
41. National Committee on Clinical Laboratory Standards. *Fine Needle Aspiration Biopsy (FNAB) Techniques; Approved Guidelines.* NCCLS Document GP20-A. 1996;16:1–20.
42. Oetgen ME, Grosser DM, Friedlaender GE, Lindskog DM. Core needle biopsies of musculoskeletal tumors: potential pitfalls. *Orthopaedics.* 2008;31:pii: orthosupersite.com/view.asp?rID = 32927.
43. Ogilvie CM, Torbert JT, Finstein JL, Fox EJ, Lackman RD. Clinical utility of percutaneous biopsies of musculoskeletal tumors. *Clin Orthop Relat Res.* 2006;450:95–100.
44. Oland J, Rosen A, Reif R, Sayfan J, Orda R. Cytodiagnosis of soft tissue tumors. *J Surg Oncol.* 1988;37:168–170.

45. Palmer HE, Mukunyadzi P, Culbreth W, Thomas JR. Subgrouping and grading of soft-tissue sarcomas by fine-needle aspiration cytology: a histiopathology correlation study. *Diagn Cytopathol.* 2001;24:307–316.
46. Powers C, Berardo M, Frable W. Fine needle aspiration biopsy: pitfalls in the diagnosis of spindle-cell lesions. *Diagn Cytopathol.* 1994;10:232–242.
47. Ray-Coquard I, Ranchere-Vince D, Thiesse P, Ghesquieres H, Biron P, Sunyach MP, Rivoire M, Lancry L, Meeus P, Sebban C, Blay JY. Evaluation of core needle biopsy as a substitute to open biopsy in the diagnosis of soft-tissue masses. *Eur J Cancer.* 2003;39:2021–2025.
48. Rougraff BT, Aboulafia A, Biermann JS, Healey J. Biopsy of soft tissue masses: evidence-based medicine for the Musculoskeletal Tumor Society. *Clin Orthop Relat Res*. 2009;467:2783–2791.
49. Sapi Z, Antal I, Papai Z, Szendroi M, Mayer A, Jakab K, Pajor L, Bodo M. Diagnosis of soft tissue tumors by fine-needle aspiration with combined cytopathology and ancillary techniques. *Diagn Cytopathol.* 2002;26:232–242.
50. Serpell JW, Pitcher ME. Preoperative core biopsy of soft tissue tumors facilitates their surgical management. *Anz J Surg.* 2008; 68:345–349.
51. Simon MA. Biopsy of musculoskeletal tumors. *J Bone Joint Surg Am.* 1982;64:1253–1257.
52. Singh HK, Kilpatrick SE, Silverman JF. Fine needle aspiration biopsy of soft tissue sarcomas: utility and diagnostic challenges. *Adv Anat Path.* 2004;11:24–37.
53. Skrzynski MC, Biermann JS, Montag A, Simon MA. Diagnostic accuracy and charge-savings of outpatient core needle biopsy compared with open biopsy of musculoskeletal tumors. *J Bone Joint Surg Am.* 1996:78:644–649.
54. Wakely PE Jr, Sneisl JS. Soft tissue aspiration cytopathology: diagnostic accuracy and limitations. *Cancer.* 2000;90:292–298.
55. Ward WG, Savage P, Boles CA, Kilpatrick SE. Fine-needle aspiration biopsy of sarcomas and related tumors. *Cancer Control.* 2001;8:232–238.
56. Welker JA, Henshaw RM, Jelinek J, Shmookler BM, Malawar MM. The percutaneous needle biopsy is safe and recommended in the diagnosis of musculoskeletal masses. *Cancer.* 2000;89: 2677–2686.
57. Yang YJ, Damron TA. Comparison of needle core biopsy and fine-needle aspiration for diagnostic accuracy in musculoskeletal lesions. *Arch Pathol Lab Med.* 2004;128:759–764.
58. Yao L, Nelson SD, Seeger LL, Eckardt JJ, Eilber FR. Primary musculoskeletal neoplasms: effectiveness of core-needle biopsy. *Radiology.* 1999;212:682–686.
59. Zornosa J, Bernardino ME, Ordonez NG, Thomas JL, Cohen MA. Percutaneous needle biopsy of soft-tissue tumors guided by ultrasound and computed tomography. *Skeletal Radiol.* 1982;9:33–36.