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Research Article

Image-Guided Percutaneous Biopsy for the Diagnosis of Musculoskeletal Tumors: An Analysis of 698 Cases and a Literature Review

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ABSTRACT

Purpose: Incisional biopsy is still used to obtain material for a straightforward histological diagnosis in musculoskeletal lesions. The aim of our study was to evaluate 1) the percentage of diagnostic procedures, 2) diagnostic accuracy, and 3) the incidence of complications after imaging-guided percutaneous biopsy (PCB).

Case Series: This is a retrospective analysis of imaging-guided PCB performed between January 2016 and September 2019 by fluoroscopy in bone lesions or under ultrasound-guidance in soft tissue lesions. Specimens were classified as diagnostic or non-diagnostic according to the pathologist's report; diagnostic accuracy was determined by comparing histopathological results from biopsy and tumor resection. PCB was diagnostic in 94% and 97% of cases, with a diagnostic accuracy for detecting tumor disease in soft tissue and bone lesions of 98% and 100%, respectively. No complications were observed.

Discussion: The PCB is safe, minimally invasive, and cost-effective; thus, it should be the gold standard for the diagnosis of musculoskeletal lesions.

Introduction

Diagnosis for patients with musculoskeletal tumors is based on history, clinical, radiological, and histological examination. Most frequent mistakes in treatment are due to delay in diagnosis or misdiagnosis, affecting the patient's survival and the possibility of limb salvage [1, 2]. When clinical and radiologic features do not allow to distinguish with certainty about biological behaviour or in patients with a history of malignancy, histological diagnosis is fundamental [1-6]. It is even more critical in sites in which salvage surgery is demanding, such as pelvis or limb reconstructions, where it is essential to preserve as much tissue as possible to allow soft tissue coverage and function [7-10]. Consequently, it is mandatory to always perform a biopsy before treating musculoskeletal lesions, with very few exceptions.

The biopsy is the last step of staging, and it is a compromise between the need to have significant tissue and the need to avoid local or systemic contamination [3-6]. Different procedures such as incisional biopsy (IB), fine-needle aspiration (FNA), or percutaneous biopsy (PCB) were used with specific advantages and disadvantages [11-44]. IB has high diagnostic accuracy but also complications up to 17% [11-14, 21, 24]. FNA has limited application in musculoskeletal oncology because of the need for architectural evaluation: it should only be used for diagnosis of recurrence [12-18]. PCB has few complications (less than 7%), even if its diagnostic accuracy is lower than IB (range, 76-97%) [12-44]. PCB could be performed CT, ultrasound or fluoroscopy guidance, in order to target tumor area [14, 18, 20, 21, 26-28, 31, 34-36, 38, 40-44]. In the last years, new types of PCB guided were proposed like MRI-guided biopsy, PET/CT-guided biopsy, or radionuclide-guided biopsy; however, these techniques are costly and are not used routinely in clinical practice [45-47].

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The aim of this study was to review our experience with imaging-guided PCB for musculoskeletal lesions in order to define if this could be defined as the gold standard for diagnosis, evaluating 1) percentage of diagnostic procedures, 2) diagnostic accuracy and 3) incidence of complications.

Case Series

This is a retrospective series of imaging-guided PCB performed at our institution between January 2016 and September 2019. PCB was performed in all cases under imaging guidance: using 14-gauge (1, 62 mm) semi-automatic tru-cut needle guided by ultrasound in soft tissue lesions (322 cases), or with 8-gauge (3, 26 mm) core needle in bone lesions guided by fluoroscopy (376 cases). Sites are summarized in (Tables 1 & 2). For each patient, we reviewed data regarding sex, age, site, history and imaging, expected diagnosis, type of biopsy, complications, histopathology report of biopsy and final histopathology report in those subsequently treated.

Table 1: Anatomical distribution of ultrasound-PCB sites in 322 patients with soft tissue lesions.

Site	*Number*
Upper limb	**83**
Shoulder	16
Arm	19
Elbow	14
Forearm	15
Wrist	3
Hand	16
Lower limb	**205**
Hip	16
Thigh	85
Knee	37
Leg	28
Ankle	10
Foot	29
Axial skeleton	**34**
Trunk	33
Neck	1
Total biopsy sites	**322**

All PCBs were performed after accurate patient history, clinical and radiological evaluations according to 3 main principles. First, a biopsy was located along the surgical approach for future limb-salvage resection in order to be able to remove en-bloc the needle track (potentially contaminated by tumor cells) at the time of definitive resection. Second, the biopsy was performed avoiding contamination of compartments not involved by tumor to prevent cell dissemination that could determine the necessity of major tissue removal during further surgery. Third, areas of the lesion where biopsy was performed were chosen according to preoperative MRI or CT scan, selecting zones with contrast enhancement, avoiding necrotic tissue, including capsule or pseudo-capsule. A mean of 7 samples was performed (range, 6-10), and the material was transferred to our Pathological Institute (and to microbiological evaluation when osteomyelitis is suspected).

Table 2: Anatomical distribution of fluoroscopy-PCB sites in 376 patients with bone lesions.

Site	*Number*
Upper limb	**93**
Humerus	77
Ulna	8
Radius	5
Phalanges	3
Lower limb	**212**
Femur	139
Patella	1
Tibia	56
Fibula	6
Calcaneus	3
Metatarsals	3
Phalanges	4
Axial skeleton	**71**
Scapula	10
Clavicle	5
Acromion	1
Sternum	1
Ribs	1
Vertebrae	1
Pelvis	35
Acetabulum	17
Total biopsy sites	**376**

Pathologists specialized in orthopaedic oncology evaluated all specimens for the nature of the lesion and specific histological diagnosis. We classified specimens as "diagnostic" (sufficient material) or "non-diagnostic" (insufficient material), according to the histological diagnosis. Moreover, we compared histopathological results from the biopsy with the definitive one in patients subsequently treated surgically. In these cases, we also evaluated Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and Diagnostic Accuracy.

In soft tissue, PCB was diagnostic in 304 cases (304/322, 94.4%). In non-diagnostic cases, the biopsy was repeated as PCB in 14 cases and as IB in 4 cases (tumor close to vessels and nerves). In the 14 repeated PCB, diagnostic specimens were obtained in 11, while 3 required further IB. At least 315 PCBs were diagnostic (98%). Diagnoses of soft tissue lesions were reported in (Table 3). One-hundred-nineteen patients were subsequently surgically treated, and in 95% of cases (113/119), there was concordance between histological diagnoses. In 7 cases, final diagnosis differed from biopsy diagnosis: one well-differentiated liposarcoma (vs. soft tissue chondroma), two schwannomas (vs. fibromatosis and pigmented villonodular synovitis), one angiomyxoma (vs. fibromyxoma), one atypical lipomatous tumor (vs. myxofibrosarcoma), one angiolipoma (vs. non-tumor disease) and one infundibular cyst (vs. pigmented villonodular synovitis). PCB in soft tissue has proven to have the ability to distinguish for the nature of the lesions (tumor vs. non-tumor disease) with a Sensitivity of 99%, Specificity of 94%, Diagnostic Accuracy of 98%, PPV of 99% and NPV of 94%. Diagnostic Accuracy for diagnosing benign tumors was 96%, with a Sensitivity of 97%, Specificity of 96%, PPV of 97%, and NPV of 96%. Diagnostic Accuracy

for diagnosing malignant tumors was 99%, with a Sensitivity of 97%, Specificity of 100%, PPV of 100%, and NPV of 98%.

Table 3: Final diagnosis of 322 ultrasound-PCB in soft tissue lesions.

Lesion	*Number*
Benign lesion	**211**
Lipoma	68
Hemangioma	31
Pigmented Villo-Nodular Synovitis	20
Fibromatosis	18
Schwannoma	14
Cyst	11
Synovial Chondromatosis	7
Elastofibroma	5
Others (e.g. Fibromyxoma, Neurofibroma, Fibrolipoma)	37
Malignant lesion	**50**
Undifferentiated Pleomorphic Sarcoma	8
Extraskeletal Chondrosarcoma	6
Liposarcoma	6
Metastatic tumor	6
Lymphoma	5
Myxofibrosarcoma	4
Atypical Lipomatous Tumor	2
Rhabdomyosarcoma	2
Myxoid liposarcoma	2
Synovial Sarcoma	2
Others (e.g. Melanoma, Extraskeletal Osteosarcoma, Extraskeletal Ewing's Sarcoma)	7
Non-tumor (e.g. Infection, Granuloma, Pseudotumor)	**43**
Undiagnostic	**18**
PCB repeated in 14 cases	
Benign lesion	**6**
Hemangioma	3
Lipoma	1
Pigmented Villo-Nodular Synovitis	1
Fibromatosis	1
Malignant lesion	**2**
Undifferentiated pleomorphic sarcoma	1
Lymphoma	1
Non-tumor (e.g. Granuloma)	**3**
Undiagnostic	**3**

In bone lesions, PCB was diagnostic in 366 (366/376, 97.3%). In non-diagnostic cases, the biopsy was repeated as PCB in 7 cases and as IB in 3 cases. In the 7 repeated PCBs, diagnostic samples were obtained in 6. At least 372 PCB were diagnostic (99%). Diagnoses of bone lesions were reported in (Table 4). One-hundred-seventy-three patients were subsequently surgically treated, and in 98% of cases (170/173), there was concordance between histological diagnoses. In 3 cases, the final diagnosis differed from biopsy diagnosis: one lymphoma (vs. osteosarcoma), one chondrosarcoma grade 2 (vs. chondroma), and one plasmacytoma (vs. diffuse large B cell lymphoma). PCB in bone lesions has proven to have the ability to distinguish for the nature of the lesions (tumor vs. non-tumor disease) with a Sensitivity of 100%, Specificity of 100%, Diagnostic Accuracy of 100%, PPV of 100% and NPV of 100%. Diagnostic Accuracy for diagnosing benign tumors was 99%, with a Sensitivity of 100%, Specificity of 99%, PPV of 98.5%, and NPV of 100%. Diagnostic Accuracy for diagnosing malignant tumors was 99%, with a Sensitivity of 99%, Specificity of 100%, PPV of 100%, and NPV of 99%. Complications, such as hematoma or wound infection, were not observed after PCB.

Table 4: Final diagnosis of 376 fluoroscopy-PCB in bone lesions.

Lesion	*Number*
Benign lesion	**136**
Chondroma	48
Giant Cell Tumor	17
Aneurysmal Bone Cyst	21
Fibrous dysplasia	14
Chondroblastoma	5
Others (e.g. Histiocytic fibroma, Intraosseous lipoma, Periosteal chondroma)	31
Malignant lesion	**152**
Osteosarcoma	29
Chondrosarcoma	20
Metastatic Tumor	68
Lymphoma/ Myeloma	30
Others (e.g. Leiomyosarcoma, Biphasic synovial sarcoma)	5
Non-tumor (e.g. Bone necrosis, Granuloma, Bone marrow reconversion, Metabolic diseases)	**78**
Undiagnostic	**10**
PCB repeated in 7 cases	
Benign lesion	**2**
Fibrous dysplasia	1
Hemangioma	1
Malignant lesion	**1**
Ewing's sarcoma	1
Non-tumor (e.g. Bone necrosis)	**3**
Undiagnostic	**1**

Discussion

Obtaining a specific histological diagnosis is mandatory before the treatment of musculoskeletal lesions [1-6]. Different types of biopsy could be used with related advantages and disadvantages [3-6, 12-44]. PCB is reported to be a safe procedure burdened by few minor complications only; however, its diagnostic accuracy is lower than with IB due to the limited material obtainable, especially in soft tissue lesions usually presenting necrotic tissue, that makes anatomopathological diagnosis more complicated (Table 5) [12-44]. For this reason, incisional biopsy is still used in some Specialized Centers.

The aim of our study was to review our experience with PCB for the diagnosis of musculoskeletal lesions in order to evaluate if this type of biopsy could be defined as the gold standard. All PCBs were imaging-guided to provide significant/adequate samples containing vital tumor cells targeting the correct tumor area based on preoperative studies (CT or MRI with contrast).

Table 5: Summary of the published studies reporting on PCB for diagnosis of musculoskeletal tumors: systematic review.

Study	***Pt (n)***	***Bone (n) or Soft tissue (n)***	***Imaging-guidance***	***Gauge of needle***	***Passes (n)***	***Diagnostic results after CNB (%)***	***Diagnostic accuracy after surgical treatment***	***Complications***
Zornoza, 1982 [35]	42	Soft tissue	CT or US	18 or 14	>2	83% (35/42)	-	None
Skrzynsky, 1996 [14]	62	Bone (17) Soft tissue (45)	None	-	3-6	84% (52/62)	DA 100% in Bone DA 78% in Soft tissue	Track infection (1)
Schweitzer, 1996 [17]	138	Bone	FS	12 or 18	2-3	98% (135/138)	-	-
Heslin, 1997 [19]	60	Soft tissue	None	-	-	93% (56/60)	Cc in diagnosis malignancy (56/56) Cc in diagnosing grade (40/56)	-
Dupuy, 1998 [31]	176	Bone Soft tissue	CT	14	-	-	Cc 93% (164/176)	Hematoma (1) Vasovagal symptom (1)
Yao, 1999 [33]	141	Bone (56) Soft tissue (85)	CT (122) FS (13) US (4) None (2)	12-14 14-18	3-8	Bone 75% (42/56) Soft tissue: 82% (70/85)	Cc 73% (41/56) in Bone Cc 75% (64/85) in Soft tissue	None
Welker, 2000 [32]	161	Bone (83) Soft tissue (78)	None (90) CT (55) FS (28)	14-17 / 8-11 14-15	3-5	88% (142/161)	DA nature of the lesion 92% DA grade 89% DA specific diagnosis 73%	Hematoma (1) Drainage (1)
Konermann, 2000 [38]	65	Bone Soft tissue	US	14	3-5	94% (61/65)	-	None
Torriani, 2002 [36]	65	Bone (27) Soft tissue (38)	US	14	>5	96% (63/65)	Cc 97% (47/48)	None
Jelinek, 2002 [22]	110	Bone	CT (85) FS (25)	7-14 / 12-16 14-18	3-10	88% (97/110)	Cc 98% (89/91) in diagnosis malignancy Cc 91% (83/91) in diagnosing grade	Hematoma (1)
Issakov, 2003 [40]	215	Bone (135) Soft tissue (80)	CT	11-14 14-18	3-10	Bone 87% (118/135) Soft tissue 94% (75/80)	-	Hematoma (3)
Ray-Coquard, 2003 [30]	110	Soft tissue	CT or US	14	4	94% (103/110)	Cc 88% (91/103)	Bleeding (1) Hematoma (6)
Yang, 2004 [15]	50	Bone Soft tissue	-	-	6	98% (49/50)	DA nature of the lesion 94% (47/50) DA specific diagnosis 86% (43/50) DA histologic grading 87% (27/31) DA histologic typing 92% (46/50)	None
Mitsuyoshi, 2006 [18]	163	Bone (91) Soft tissue (72)	None (119) CT (44)	16 -	>2	Bone 88% (80/91) Soft tissue 88% (63/72) No guidance: 85% CT-guided: 93%	Cc 88% (126/143)	Hematoma (1)
Battaglia, 2007 [44]	164	Soft tissue	US	14-18 or 13-14	3-4	D 90% (148/164)	-	-
Sung, 2009 [41]	309	Bone (167)	US (151)	-	-	Bone 92%	In 185 surgically treated	-

		Soft tissue (142)	CT (89) FS (69)			Soft tissue 89%	DA 89% in Bone DA 79% in Soft tissue	
Kasraeian, 2010 [12]	57	Soft tissue	None	14	3-5	86% (49/57)	Cc 81%	None
Adams, 2010 [27]	233	Bone (16) Soft tissue (217)	None	-	1-10	94% (219/233)	Cc 97% in diagnosing malignancy Cc 81% in diagnosis and grade	None
Strauss, 2010 [37]	530	Soft tissue	None	-	>4	93% (493/530)	In 371 surgically treated DA 98% in diagnosing sarcomas DA 86% in diagnosing grade DA 88% in diagnosing benign subtype DA 88% in diagnosing malignant subtype	Hematoma (1) Bleeding (1)
Yang, 2010 [29]	508	Bone (272) Soft tissue (236)	CT (339) US (169)	16 or 20	1-6	Bone 87% (237/272) Soft tissue 96% (226/236)	-	-
Rimondi, 2011 [28]	2027	Bone	CT	8/15	>2	77% (1567/2027)	-	Transient paresis (18) Haematoma (4)
Peer, 2011 [42]	223	Soft tissue	US	14-18	3-10	95% (211/223)	In 113 surgically treated DA 100% in diagnosing malignancy	-
Pohlig, 2012 [13]	46	Bone (33) Soft tissue (13)	CT or US	14	3-5	Bone 100% (33/33) Soft tissue 92% (12/13)	DA 100% in Bone DA 85% in Soft tissue	None
Seng, 2013 [43]	134	Bone Soft tissue	CT	-	3-5	95% (127/134)	Cc 88% (118/134) DA 94% (31/33) in Bone DA 96% (71/74) in Soft tissue	Wound bruising
Nouh, 2014 [34]	49	Bone	CT	16-18 or 12-15	6	88% (43/49)	Cc 1005 (29/29)	None
Trieu, 2016 [26]	1131	Bone (380) Soft tissue (751)	CT	14 or 18	-	Bone 88% (334/380) Soft tissue 94% (703/751)	DA 81% in Bone DA 83% in Soft tissue	0.8%
Walker, 2018 [39]	105	Soft tissue	None	-	-	-	In 69 surgically treated Cc 87% DA 94% nature of the lesion	Hematoma (2) Bleeding (1)
Current study	722	Bone (400) Soft tissue (322)	FS (376) US (322) CT (24)	8 in Bone 14 in Soft tissue	6-10	Bone 97% (366/376) Soft tissue 94% (304/322)	Cc 170/173 (98%) in Bone Cc 113/119 (95%) in Soft tissue	None

Pt: Patients; -: Not Reported; PCB: percutaneous biopsy; US: Ultrasound; CT: Computed Tomography; FS: Fluoroscopy; D: Diagnostic; Cc: Concordance between histology of biopsy and of surgery; DA: Diagnostic Accuracy.

This study had some limitations. First, this is a retrospective nonrandomized series, in which we perform PCB for bone as well as soft tissue lesions. However, PCB was performed with a tru-cut needle guided by ultrasound in all soft tissue lesions and with a core needle guided by fluoroscopy in all bone lesions. Second, PCB was performed to detect tumor as well as to exclude it. Consequently, not all patients underwent surgery, according to the treatment required by histological diagnosis, limiting our series and statistical power of analysis. However, non-surgically treated patients were periodically followed in the out-patient clinic, and no cases of misdiagnosis were observed. Third, diagnoses were heterogeneous, precluding evaluation of diagnostic accuracy related to histotypes. However, these kinds of tumors are rare, and we do not preclude further study with more specific analysis.

Imaging-guided PCB can allow diagnosis in most musculoskeletal lesions. Bony PCBs are usually fluoroscopy-guided and performed with a trocar of 11 Gauge, with a percentage of diagnostic results ranging between 75% to 98% [14, 17, 18, 22, 27, 31-33, 41]. Instead, PCBs for soft tissue lesions are generally ultrasound-guided and performed with a 14-gauge tru-cut needle, with a diagnostic result reported in literature ranging from 83% to 96% [12, 13, 19, 20, 29, 32, 33, 35-44]. The incidence of non-diagnostic PCB is higher in soft tissue than in bone lesions, probably due to the high presence of necrotic areas that could make histological interpretation more difficult [34, 43, 44]. In our series, adequate material for diagnosis was obtained more frequently in bone (97%, 366/376), than in soft tissue (94%, 304/322). Repeating another PCB led to diagnosis in 99% and 98% of cases, respectively in bone and soft tissue lesions: non-diagnostic results could be defined as sampling error, due to necrotic, fibrous, or haemorrhagic tissue. In order to reduce non-diagnostic procedures, multiple samples from different areas of the tumor should be done using larger needles [44].

Our results seem to be better than those reported in the literature obtaining only 2.7% and 5.6% of non-diagnostic samples, respectively in bone (we used 8 Gauge trocar) and soft tissue (we performed at least 6 samples). Moreover, targeting with CT the proper area of the lesion to obtain vital tumor cells could be useful. Mitsuyoshi *et al.* [18] compared CT guided and fluoroscopy-guided PCB in 163 patients and report a decrease of non-diagnostic results with CT compared with fluoroscopy (7% vs. 14%), concluding that CT-guidance is more efficacious, thanks to high contrast resolution and spatial definition. However, since CT is more expensive and exposes to a high dose of radiation, its use should be limited.

Also, the diagnostic accuracy is usually higher for bone tumors than for soft-tissue masses, ranging from 80% to 100% and from 76% -100%, respectively [13-15, 18, 26-28, 35-38, 40-42]. The diagnosis of bone lesions can be aided by imaging tools, whereas soft-tissue lesions have more tumor necrosis and more different diagnoses [13]. In our series, diagnostic accuracy was determined by comparing histopathological results from PCB and subsequent tumor resection, in patients that subsequently were surgically treated. We identified an overall diagnostic accordance of 98% in bone lesions, and 95% in soft tissue tumors.

Complications are frequent (up to 17%) when IB is performed [6, 11, 13, 14, 18, 23]. Mankin *et al.*, were the first in 1982 to report the percentages of complications that occurred following an open biopsy in 329 patients [6]. In 17% of cases, there were hematomas, infections, surgical wound dehiscence, and dispersion of tumor cells in adjoining tissues. In 8.5% of patients, it was found that this procedure negatively affected the prognosis. Finally, it emerged that 4.5% of the patients underwent amputation following the open biopsy [6]. Conversely, complications after PCB are infrequent (less than 2%) for both bone and soft tissue lesions and are usually minor complications, such as biopsy tract infection, post-procedural bleeding, transient paresis [14, 15, 26-28, 35-39]. According to the literature, in our series, we did not encounter any complications related to PCB.

In conclusion, PCB is a safe, minimally invasive, and cost-effective technique for the diagnosis of bone and soft tissue lesions. Indications should be carefully evaluated by an experienced orthopaedic oncologist concerning the suspected entity, size, and location of the lesion to avoid incorrect or deficient results. Targeting the proper area of the lesion to obtain vital tumor cells is mandatory; it is based on pre-biopsy careful imaging evaluation (especially MRI) and imaging-guidance during the procedure. Obtaining multiple samples from different areas of the tumor is essential to have more representative specimens. IB should be reserved for "difficult" cases or after previous non-diagnostic PCBs.

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