Journal of Orthopaedic Science 27 (2022) 448–455

Contents lists available at ScienceDirect

Journal of Orthopaedic Science

journal homepage: http://www.elsevier.com/locate/jos

Original Article

Image-guided core needle biopsy for musculoskeletal lesions

Shunichi Toki [a, e, *], Miyuki Sone [b], Akihiko Yoshida [c, d], Toshihiko Nishisho [e], Tabu Gokita [f], Eisuke Kobayashi [a, d], Fumihiko Nakatani [a, d], Hirokazu Chuman [a], Shunsuke Sugawara [b], Yasuaki Arai [b], Akira Kawai [a, d]

[a] *Department of Musculoskeletal Oncology, National Cancer Center Hospital, 5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan*
[b] *Department of Diagnostic Radiology, National Cancer Center Hospital, Tokyo, Japan*
[c] *Department of Diagnostic Pathology, National Cancer Center Hospital, Tokyo, Japan*
[d] *Rare Cancer Center, National Cancer Center Hospital, Tokyo, Japan*
[e] *Department of Orthopedics, Institute of Biomedical Sciences, Tokushima University Graduate School, Tokushima, Japan*
[f] *Department of Orthopedic Oncology, Saitama Cancer Center, Saitama, Japan*

A R T I C L E I N F O

Article history:
Received 23 June 2020
Received in revised form
3 December 2020
Accepted 4 December 2020
Available online 30 January 2021

A B S T R A C T

Background: Image-guided percutaneous core needle biopsy (CNB) has been an important diagnostic procedure for musculoskeletal lesions. Here we surveyed the variety of diagnostic strategies available and assessed the clinical usefulness and limitations of image-guided CNB carried out by a multidisciplinary team comprising specialists in various fields.

Methods: We conducted a retrospective study of 284 image-guided CNBs among 1899 consecutive biopsy procedures carried out at our institution for musculoskeletal tumorous conditions, focusing on their effectiveness including diagnostic accuracy and utility for classification of specimens according to malignant potential and histological subtype as well as their correlation with biopsy routes.

Results: Among the 284 studied biopsies, 252 (88.7%) were considered clinically "effective". The sensitivity for detection of malignancy was 94.0% (110/117) and the specificity was 95.3% (41/43). The diagnostic accuracy for detection of malignancy was 94.4% (151/160) and that for histological subtype was 92.3% (48/52). The clinical effectiveness of the procedure was correlated with the complexity of the biopsy route ($P = 0.015$); the trans-pedicular, trans-retroperitoneal and trans-sciatic foramen approaches tended to yield ineffective results. Repeat biopsy did not have a significant impact on the effectiveness of image-guided CNB ($P = 0.536$).

Conclusions: The diagnostic accuracy rates of image-guided CNB performed at multidisciplinary sarcoma units were usable even for patients who have variety of diagnostic biopsy procedures. It is important to establish and implement diagnostic strategies based on an understanding that complicated routes, especially for spine and pelvic lesions, may be associated with ineffectiveness and/or complications.

1. Introduction

Accurate biopsy of musculoskeletal tumors is important for correct pathological diagnosis and adequate treatment. Several types of biopsy procedure are available, including fine-needle aspiration biopsy, core needle biopsy (CNB), incisional biopsy and excisional biopsy [1]. Historically, incisional biopsy has been widely employed [2]. Although incisional biopsy can yield sufficient material for pathological examination, it is associated with issues such as cost, patient discomfort, and relatively high complication and implantation rates [1,3–5].

Image-guided CNB for musculoskeletal lesions has been employed over the last 20 years [6–15]. Didolkar et al. demonstrated that even non-diagnostic CNB which is reported to be 5%–31% may be effective for avoiding unnecessary surgery in certain clinical settings [16]. In line with the worldwide spread of image-guided CNB, there has been an increase in its use for tumors hitherto regarded as ineligible for such procedures, such as those that

* Corresponding author. Department of Orthopedics, Institute of Biomedical Sciences, Tokushima University Graduate School, 3-18-15 Kuramoto-cho, Tokushima, 770-8503, Japan. Fax: +81 88 633 0178.
E-mail address: toki830926@gmail.com (S. Toki).

https://doi.org/10.1016/j.jos.2020.12.017
0949-2658/

are deep-seated or adjacent to vital organs. However, no previous attempt has been made to exhaustively evaluate the various strategies available for diagnosis of bone and soft-tissue tumors in clinical practice, or methods for increasing the usefulness of image-guided CNB, including the diagnostic accuracy rate. Specifically, hardly any reports have addressed the direct relationship between the choice of route for needle biopsy and outcome. Although the basic principles of transcutaneous biopsy have been widely publicized [17], most reports that have discussed how and from where target lesions should be approached by needle biopsy merely state that the shortest route should be taken, and that the decision in each case should be made on the basis of discussion, considering the subsequent definitive surgery [6–10,12,13,16].

In the present study, we retrospectively surveyed the clinical variety of diagnostic processes adopted for a wide range of subjects. We reviewed all biopsies carried out at the authors' institution and assessed the clinical usefulness and limitations of image-guided CNB carried out by a multidisciplinary team (MDT) comprising specialists in various fields.

2. Materials and methods

We retrieved data on 1899 consecutive biopsy procedures for musculoskeletal lesions from the medical records and archives at our institution for the period between 2006 and 2016 after this research had been approved by the institutional review board of the authors' affiliated institution. Fig. 1 shows the temporal changes in the types of biopsy procedures performed during this period, including CNB with/without image guidance, incisional biopsy and excisional biopsy. Images defined in the present research were fluoroscopy, computed tomography (CT) and real-time ultrasound. For this study, we analyzed the data for 284 image-guided CNBs. The evaluated items were patient age and sex, the type, localization, size and occurrence of the targeted lesion, date, radiological modality used, reason, route selection, prior biopsy and any complication of the image-guided biopsy executed, pathological information including turn-around time, auxiliary diagnostic tool(s) and definitive diagnosis, and clinical diagnosis.

2.1. Strategy and practical execution of image-guided CNB

The reasons for the use of image guidance were categorized as follows: 1) The lesion was not palpable. 2) The lesion was adjacent to critical organs. 3) The lesion was adjacent to a neurovascular unit. 4) The lesion was heterogeneous, necessitating sampling from a specific portion of the tumor. The approach adopted for CNB was decided through discussion among the MDT, comprising expert radiologists, musculoskeletal oncologists and pathologists, regarding the subsequent definitive surgery, avoidance of complications, and any specific portion of the lesions that should be targeted.

During the biopsies, the musculoskeletal oncologists in charge also attended the interventional radiology theater room and confirm the executed routes. Image-guided percutaneous CNB was performed by board-certified interventional radiology specialists using a 14-gauge core needle for skeletal lesions and an 18-gauge automated or semi-automated cutting needle for soft tissue lesions. A coaxial system was used to facilitate multiple tissue sampling from one needle penetration and reduce the risk of dissemination and bleeding by embolization of the needle tract. The number of specimens taken was determined according to the size of the cores actually obtained and diagnostic requirements. At least two cores were usually obtained. Then, together with request forms, the CNB specimens are delivered to expert pathologists and detailed discussion is immediately held whenever needed. Four-micrometer-thick sections from paraffin blocks of all biopsy materials were routinely deparaffinized and stained with hematoxylin and eosin. For selected cases, immunohistochemistry and fluorescence *in situ* hybridization (FISH)

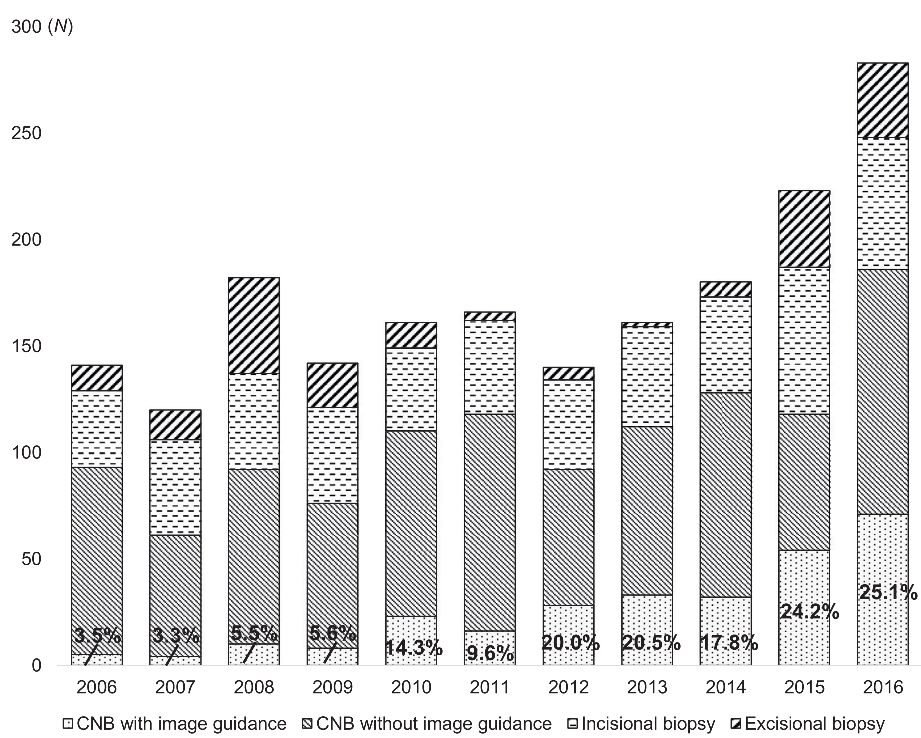

Fig. 1. Changes in the number and distribution of biopsy procedures for musculoskeletal lesions at our institution from 2006 to 2016. CNB, core needle biopsy.

were performed. Histological diagnosis was made by expert pathologists.

2.2. Biopsy route selection

We especially categorized the biopsy route into mainly two groups: direct routes that involved the shortest path unassociated with any obstruction to avoid during biopsy, and complicated routes. Additionally, the latter were divided into a transpedicular approach to the pedicle itself or vertebra (Fig. 2A), paravertebral approach to the retroperitoneal or posterior mediastinal areas (Fig. 2B), intercostal route targeting the inside of the thoracic cage (Fig. 2C), trans-retroperitoneal approach to the pelvis and pelvic space (Fig. 2D), trans-sciatic foramen approach to the small pelvic space (Fig. 2E), infraclavicular approach to lesions more deeply seated than the clavicle (Fig. 2F), and miscellaneous others.

2.3. Definition of the assessment terms for biopsy

In the microscopic evaluation, specimens consisting of normal tissue alone or lacking any part of the representative targeted lesion were considered to represent “sampling error”. Specimens that included some tissue of the targeted lesion were designated “classifiable” or “unclassifiable” on the basis of whether malignant potential could be determined by pathologists. Among “classifiable” biopsy materials, those that did not match the final diagnosis regarding malignancy were considered to represent “discrepancy”. All “classifiable” biopsies excluding “discrepancy” and “re-biopsy”, which necessitated clinically additional CNB or incisional biopsy for diagnosis, were categorized as an “effective” subset (Fig. 3).

2.4. Diagnostic confirmation

The diagnostic accuracy of image-guided CNB was analyzed. The reference standard of the classification in terms of the malignant potential of the specimen was the final pathological diagnosis based on surgical specimens or the final clinical diagnosis based on the clinical course and outcome. Clinical judgment of a benign lesion was defined as non-progression of the disease for a minimum follow-up period of 2 years. Among cases of true neoplasia with a definitive pathological diagnosis, the accuracy of the histological subtype was also calculated.

2.5. Statistical analyses

Associations between effectiveness and background variables, and clinical parameters related to image-guided CNB, were subjected to univariate analysis. We used the Mann–Whitney *U* test, chi-squared test and Fisher's exact test. Differences at $P < 0.05$ were

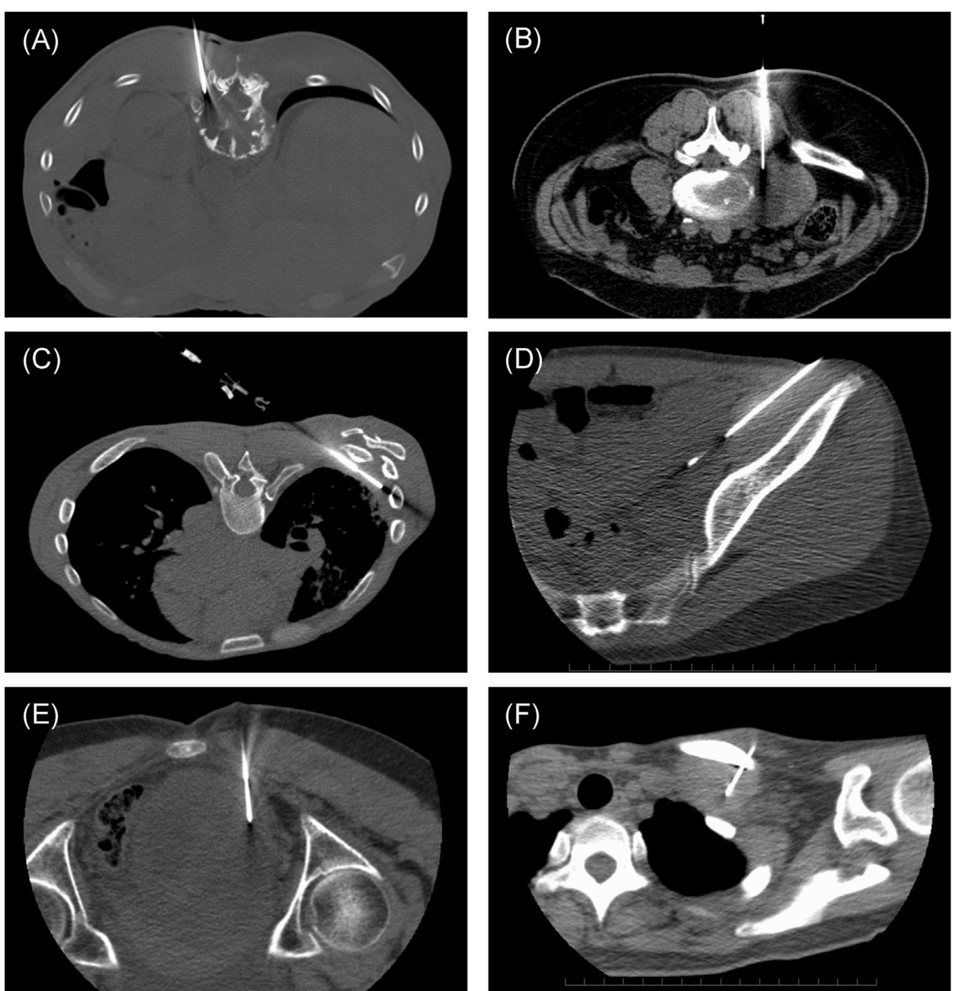

Fig. 2. Typical axial views of computed tomography indicating complicated biopsy routes categorized into mainly 6 types in the present study.

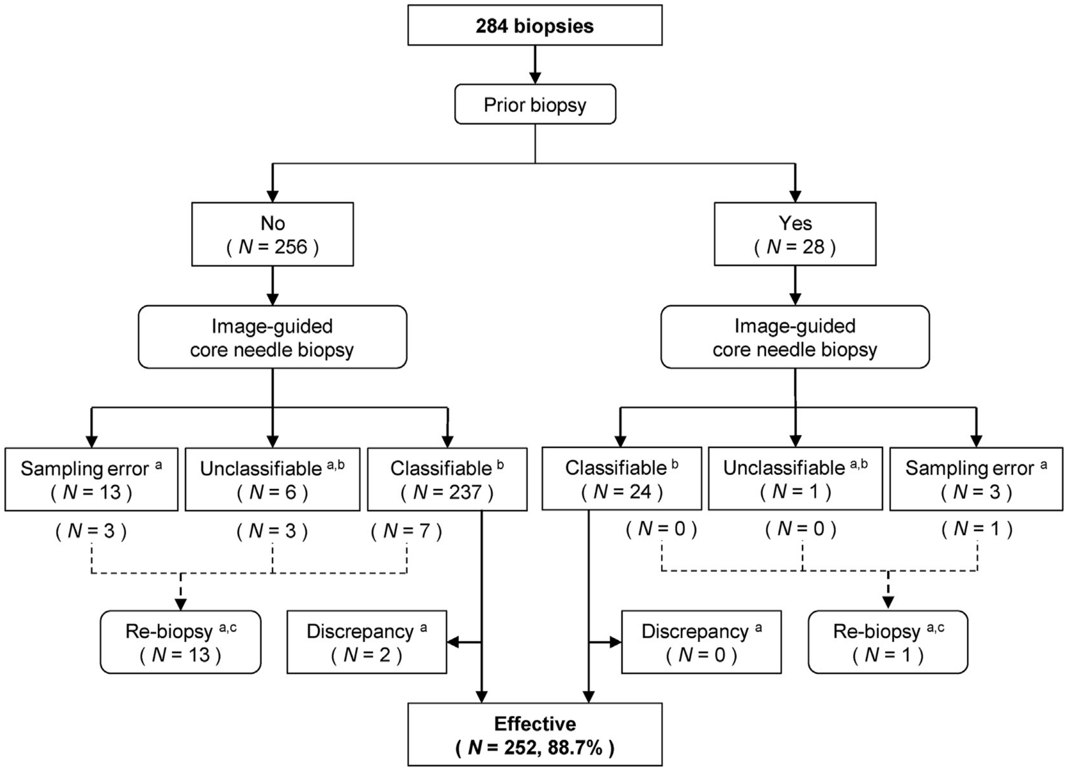

Fig. 3. Flow diagram showing the backgrounds and characteristics of the overall biopsies included in this study. [a] Considered as "ineffective". [b] In terms of classification as benign/intermediate or malignant. [c] Additional needle biopsy or incisional biopsy.

considered to be significant. Analyses were carried out using the SPSS software program (version 20; SPSS Statistics, Armonk, NY, USA).

3. Results

The clinical characteristics revealed by the image-guided CNBs overall are summarized in Table 1. There were 125 (44.0%) bone lesions and 159 (56.0%) soft tissue lesions, which were located in the trunk in 242 cases (85.2%) and the extremity in 42 (14.8%). Lesion size ranged from 0.9 cm to 30 cm with an average of 7.7 cm. Prior biopsy before the current image-guided CNB had been done in 28 cases (9.9%). Fluoroscopy, computed tomography (CT), and real-time ultrasound were used to assist CNB in 84 (29.6%), 207 (72.9%), and 92 (32.4%) cases, respectively, and multiple image guidance modalities were applied for 98 of the biopsy procedures (34.5%). One hundred and eighty-nine (66.5%) biopsy procedures were performed for reason 1, 186 (65.5%) for reason 2, 100 (35.2%) for reason 3, and 132 (46.5%) for reason 4. The rate of complications in the present series was 3.9%. Among these complications, 6 (55%) were associated with complicated biopsy routes and 5 with direct routes. The target lesions included 4 localized in the thorax/chest wall, 3 in the retroperitoneal space, 2 in the vertebrae, and one each in the pelvic space and neck. The diagnosis of image-guided CNB was confirmed regarding the malignant potential by pathological examination of the subsequent surgical specimens in 85 (29.9%), final clinical diagnosis in 75 (26.4%) and none in 124 (43.7%).

3.1. Effectiveness of overall image-guided CNBs

Table 2 details the overall assessment of our CNB specimens. Sixteen biopsy procedures (5.6%) were inadmissible due to sampling error, and 7 (2.5%) yielded specimens that were unclassifiable (Fig. 3). Among the 261 (91.9%) classifiable biopsies, 60 (23.0%) were diagnosed as benign lesions, 27 (10.3%) were intermediate tumors and 174 (66.7%) were malignant tumors; there were 2 cases of "discrepancy" (Fig. 3). Re-biopsy after image-guided CNB was carried out in 14 (4.9%) cases. Among them, re-biopsy was performed for 7 of the classifiable biopsies: 5 because they had not yielded a definitive diagnosis of the histological subtype, and 2 because the diagnosis of histological subtype had been uncertain. Eventually, 252 biopsies (88.7%) were classified as "effective" (Fig. 3). Among 237 true neoplastic lesions due to CNBs, 186 (78.5%) were diagnosable to histological subtype. The utility of the diagnostic workup for malignancy and histological subtype is summarized in Table 3. The 160 cases meeting the reference standard included 117 cases of malignancy and 43 others. The sensitivity for detection of malignancy was 94.0% (110/117) and the specificity was 95.3% (41/43). The overall diagnostic accuracy for malignancy versus others was 94.4% (151/160) (Supplementary Material 1) and that for histological subtype was 92.3% (48/52).

3.2. Distribution and effectiveness of the various biopsy routes

Table 4 shows the variety of biopsy routes that were selected. While 192 biopsies (67.6%) were performed via direct routes, 92 (32.4%) involved complicated routes that were significantly less effective ($P = 0.015$): the trans-pedicular approach in 22 cases (7.7%), the paravertebral approach in 18 (6.3%), the intercostal route in 17 (6.0%), the trans-retroperitoneal approach in 14 (4.9%), the trans-sciatic foramen approach in 12 (4.2%), the infraclavicular approach in 3 (1.1%), and miscellaneous routes in 6 (2.1%). Although the categories of complicated route did not impact significantly on the effectiveness of the biopsy as a whole ($P = 0.056$), use of the trans-pedicular, trans-retroperitoneal and trans-sciatic foramen

Table 1
Descriptive backgrounds of overall image-guided core needle biopsies in the current study.

	Average (range) or *N* (%)
Age, yrs	53 (6–91)
Sex	
Male/Female	147/137 (51.8/48.2)
Type of target lesion	
Bone/Soft tissue	125/159 (44.0/56.0)
Deep/Superficial	151/8 (95.0/5.0)
Localization of target lesion	
Trunk/Extremity	242/42 (85.2/14.8)
Size, cm	7.7 (0.9–30)
Occurrence of lesion	
Initial/Recurrent	259/25 (91.2/8.8)
Prior biopsy[a]	
0/1/2	256/26/2 (90.1/9.2/0.7)
Modality of imaging including multi-application	
Fluoroscopy/Computed tomography/ Real-time ultrasound	84/207/92 (29.6/72.9/32.4)
Reason for the use of image guidance	
1: Not palpable mass over the skin	189 (66.5)
2: Lesion or biopsy route adjoins critical organ	186 (65.5)
3: Lesion or biopsy route adjoins neurovascular unit	100 (35.2)
4: Heterologous lesion	132 (46.5)
Turn-around time for the pathological diagnosis, days	8.8 (2–48)
Use of diagnostic tool in pathology and laboratory	
Immunohistochemistry	200 (70.4)
Fluorescence *in situ* hybridization	17 (6.0)
Complication	11 (3.9)
Bleeding, subcutaneous hematoma	6
Nerve injury	2
Pneumothorax	2
Vagovagal reflex	1
Diagnostic confirmation of biopsy in terms of the malignant potential	
Pathology of surgical specimen	85 (29.9)
Final clinical diagnosis	75 (26.4)
None	124 (43.7)

[a] The number of prior biopsy before the current image-guided core needle biopsy in our institution.

approaches tended to yield ineffective results. The characteristics of all biopsies using the trans-pedicular approach in which most specimens have resulted in ineffectiveness are summarized in Table 5. Among the ineffective subset (N = 6), in 4 cases (66.7%) the lesions were located in the thoracic spine, and in 2 cases (33.3%) internal lesion heterogeneity was observed. Also, the lesions tended to be smaller in the ineffective subset than in the effective subset.

3.3. Analysis of candidate factors related to effectiveness of image-guided CNB

Univariate analysis of factors in relation to effective clinical application detected only biopsy route selection (Table 6). Since no other significant factors emerged, no multivariate analysis model was applicable.

Table 2
Assessment of specimen acquired by image-guided core needle biopsy.

	N (%)
Classifiable	261 (91.9)
Benign lesion	60 (23.0)
Intermediate tumor	27 (10.3)
Malignant tumor	174 (66.7)
Unclassifiable	7 (2.5)
Sampling error	16 (5.6)
True neoplastic lesion[a]	237
Diagnosable to histological subtype	186 (78.5)

[a] Expect for non-neoplastic lesion i.e. infection, pseudotumor and tumor-like lesion.

Table 3
Analysis of the utility of image-guided core needle biopsy for diagnosis.

	N	%
Detection of malignancy[a]		
Sensitivity	110/117	94.0
Specificity	41/43	95.3
Positive predictive value	110/112	98.2
Negative predictive value	41/48	85.4
Diagnostic accuracy	151/160	94.4
Histological subtype[b]		
Diagnostic accuracy	48/52	92.3

[a] It was compared with definitive diagnosis by subsequent surgical specimen or final clinical diagnosis, and "Intermediate" tumors defined in WHO classification were not includes "malignancy" subsets.
[b] It was compared with definitive diagnosis by subsequent surgical specimen alone.

4. Discussion

In this study, conducted at a specialist cancer hospital with a sarcoma MDT including radiologists and pathologists with expertise in bone and soft-tissue tumors, image-guided CNB carried out in combination with molecular diagnostic techniques such as immunostaining and FISH was shown to be highly useful, with diagnostic accuracy rates of 94.4% for malignancy versus benignancy, and 92.3% for classification by histological subtype. According to previous reports on the use of CNB, the diagnostic accuracy rates for benignancy versus malignancy and for histological subtype were 90–97% and 77–84%, respectively, without image guidance [18–20], and 89–96% and 76–97% with image guidance [6,9–15]. Therefore, the diagnostic accuracy rates in this study were acceptable, similar to those identified in previous reports. As the current concept of molecular pathological disease can now be applied to discriminate some conditions from others, and a wide range of sarcoma treatments is available, including molecular-targeted therapeutic agents that have recently been approved, such prompt treatment offers a significant practical advantage.

Mesenchymal tumors are a pathologically heterogeneous set of rare tumors that can develop anywhere in the body, sometimes making accurate diagnosis difficult; in fact the divergence in diagnosis between specialists and non-specialists has been reported to range between 27% and 46% [21,22]. Through third-party assessment we independently designed and investigated using 14 cases extracted from our series, the variety of diagnostic strategies and CNB methods likely to be selected for the tumors in clinical practice (Supplementary Material 2). The potential diagnostic failure rate of image-guided CNB is still 5–31% of cases [16]; indeed, there is clearly room for improvement in this respect. CNB is preferable to incisional biopsy for various reasons, as it has low invasiveness, does not require general anesthesia, can be performed in only a short time, has a low risk of complications and tumor cell dissemination, and has low cost [5,18,23]. Therefore, from the viewpoint of clinical techniques, it is important to determine whether or not the usefulness of image-guided CNB, including its diagnostic accuracy rate, can be increased. Our study was conducted to address this issue, and revealed that selection of the biopsy route is a statistically significant factor enabling intervention.

The present study represents the first attempt to assess the relationship between biopsy route and the usefulness of image-guided CNB for bone and soft-tissue lesions (Tables 4 and 6). We demonstrated that a direct route is a significantly correlated with usefulness. As shown even in our third-party assessment, no

Table 4
Distribution of the biopsy route selection.

N (%)	Overall	Effective	Ineffective	P-value
	284	252	32	
Direct route	192 (67.6)	177 (70.2)	15 (46.9)	0.015
Complicated route	92 (32.4)	75 (29.8)	17 (53.1)	
Trans-pedicular approach	22 (7.7)	16 (6.3)	6 (18.8)	0.056
Paravertebral approach	18 (6.3)	18 (7.1)	0	
Intercostal route	17 (6.0)	15 (6.0)	2 (6.3)	
Trans-retroperitoneal approach	14 (4.9)	9 (3.6)	5 (15.6)	
Trans-sciatic foramen approach	12 (4.2)	8 (3.2)	4 (12.5)	
Infraclavicular approach	3 (1.1)	3 (1.2)	0	
Miscellaneous	6 (2.1)	6 (2.4)	0	

Table 5
Characteristics of all biopsies using trans-pedicular approach.

Assessment of biopsy	Characteristics of case and targeted lesion						Image-guided core needle biopsy							
	No.	Age (yrs)	Sex	Localization	Size (mm)	Occurrence	Prior biopsy	Rt/Lt[b]	Modality of imaging	Reason[a]				Benign/Intermediate/ Malignant
										1	2	3	4	
Effective (*N* = 16)		53.4			40.5									
	6	32	M	L, VB	45	Initial	0	Rt	CT, Fluoroscopy	+		+		Intermediate
	7	68	F	L, pedicle	40	Initial	0	Rt	CT, Fluoroscopy	+		+		Malignant
	21	72	F	L, VB	40	Initial	0	Lt	CT, Fluoroscopy	+	+	+		Benign
	31	71	M	C, VB	35	Initial	0	Rt	CT, Fluoroscopy	+	+	+		Malignant
	38	36	F	L, VB	45	Initial	0	Rt	CT, Fluoroscopy	+	+	+		Intermediate
	52	10	M	L, VB	32	Initial	0	Rt	CT, Fluoroscopy	+	+	+		Intermediate
	83	63	F	L, VB	N/A	Initial	0	Lt	CT, Fluoroscopy	+	+	+		Benign
	94	73	M	L, VB	N/A	Initial	0	Lt	CT, Fluoroscopy	+	+	+		Benign
	103	46	F	L, VB	N/A	Initial	0	Lt	CT, Fluoroscopy	+	+	+		Benign
	104	40	M	T, VB	55	Initial	0	Rt	CT, Fluoroscopy	+	+	+		Benign
	130	58	F	T, VB	27	Initial	0	Rt	CT, Fluoroscopy	+	+	+		Benign
	143	64	M	T, VB	60	Initial	0	Rt	CT, Fluoroscopy	+	+	+	+	Malignant
	147	50	M	T, VB	55	Initial	0	Lt	CT, Fluoroscopy	+	+	+		Intermediate
	154	46	M	L, pedicle	20	Initial	0	Lt	CT, Fluoroscopy	+	+			Benign
	215	82	M	L, VB	44	Initial	0	Lt	CT, Fluoroscopy	+	+	+		Malignant
	276	43	F	L, VB	28	Initial	0	Lt	CT, Fluoroscopy	+	+	+	+	Benign
Ineffective (*N* = 6)		47.8			29.1									
Sampling error	3	55	F	L, VB	42	Initial	1	Lt	CT, Fluoroscopy	+		+		
Sampling error	5	75	F	T, VB	28	Initial	0	Lt	CT, Fluoroscopy	+	+	+	+	
Sampling error	100	9	M	T, VB	25	Initial	0	Rt	CT, Fluoroscopy	+	+	+		
Sampling error	108	42	M	T, VB	10	Initial	0	Rt	CT, Fluoroscopy	+	+	+		
Sampling error	150	41	F	T, VB	22	Initial	1	Lt	CT, Fluoroscopy	+	+	+	+	
Re-biopsy	170	65	F	L, VB	48	Initial	0	Lt	CT, Fluoroscopy	+	+	+		Benign

No., registry number of biopsy; M, male; F, female; C, cervical spine; T, thoracic spine; L, lumbar spine; VB, vertebral body; N/A, not available; Rt, right; Lt, left; CT, computed tomography.

[a] Reason for the use of image guidance; 1, The lesion is not palpable; 2, The lesion is adjacent to critical organs; 3, The lesion is adjacent to a neurovascular unit; 4, The lesion is heterogeneous, necessitating sampling from a specific portion of the tumor.

[b] Puncture side, right or left.

specific biopsy route be assigned for any given lesion site (Supplementary Material 2). Therefore, it is necessary to discuss individual cases within the MDT to identify the biopsy routes most likely to result in success. Although no statistically significant differences were demonstrated for the complicated-route category as a whole (P = 0.056), the transpedicular (6 of 22; 27.3%), trans-retroperitoneal (5 of 14; 35.7%), and trans-sciatic foramen approaches (4 of 12; 33.3%) tended to yield unsatisfactory and/or inaccurate results. Especially, smaller heterogeneous lesions in the thoracic spine are more challenging for effective biopsy (Table 5). Rimondi et al. have reported that, even for vertebral lesions within the cervical to the lumbar regions, needle biopsy is not restricted to a single route, which means there the transpedicular and posterolateral approaches are available [24]. They also concluded that if the histological diagnosis after the percutaneous biopsy is still doubtful, or the result is not consistent with the suspected clinical and/or radiological imaging diagnosis, the CNB should be repeated [24]. Hadjipavlou et al. reported that false negative results obtained with transpedicular vertebral biopsies were due to technical errors when dealing with lytic and sclerotic lesions, and that it was possible to avoid such pitfalls by adopting a parallel approach using biopsy forceps [25]. Accordingly, in our opinion, image-guided CNB should be given priority as a diagnostic strategy even for challenging spinal lesions. On the other hand, for lesions in the pelvic area amenable to the trans-retroperitoneal and trans-sciatic foramen approaches, it was been suggested that recurrent lesions, a location adjacent to critical organs and heterogeneity might be factors associated with potential ineffectiveness (Supplementary Material 3). Even for such lesions, the first-choice route should, in principle, be the shortest and not surrounded by structures that must be avoided, if reasonably practicable and effective with respect to the final surgery. Furthermore, this allows the option of applying real-time magnetic resonance imaging [14] and/or contrast ultrasonography [12].

Among the ineffective biopsies in the direct-route group, sampling error accounted for 6 (3.1%), unclassifiable for 3 (1.6%),

Table 6
Univariate analysis of candidate factors related to effectiveness of image-guided core needle biopsy.

Variable	Effective	Ineffective	P-value[a]
Period			
2006–2013	113	15	0.852
2014–2016	139	17	
Type of target lesion			
Bone	108	17	0.500
Soft tissue Deep	138	14	
Superficial	6	1	
Localization			
Trunk	213	29	0.440
Extremity	39	3	
Size			
Less than 7.0 cm	136	18	0.849
Over 7.0 cm	111	13	
Modality			
Single	167	19	0.437
Multiple	85	13	
Reason for the use of image guidance			
Single	58	4	0.255
Multiple	194	28	
Prior biopsy			
Yes	24	4	0.536
No	228	28	
Biopsy route selection			
Direct route	177	15	0.015
Complicated route	75	17	
Definitive pathological diagnosis			
Classifiable	66	14	0.052
Unclassifiable	2	3	

[a] Fisher's exact test except for “Type of target lesion” by qhi-squared test.

re-biopsy for 9 (4.7%), and discrepancy for 2 (1.0%), whereas among those in the complicated-route group, sampling error accounted for 10 (10.9%), unclassifiable for 3 (3.3%), and re-biopsy for 5 (5.4%); there were no cases of discrepancy. Inconsistent diagnoses in the direct-route group were due to modifications to the chemotherapeutic regimen, and did not cause clinical problems. On the other hand, sampling errors and unclassifiable cases tended to occur readily in the complicated-route group, perhaps reflecting the difficulty of collecting typical tissues making up part of the interior of heterogeneous target tumors.

Other recent studies have suggested that the complication rate of needle biopsy ranges from 0% to 6% [1]. The complication rate in this study was 3.9%, and thus similar to those reported previously. Among them, a complicated biopsy route was chosen for 6 subjects (55%), possibly as the target lesions were located in the thorax and/or thoracic wall in 4 of them, the retroperitoneum in 3, and the vertebrae in 2. All of these complications were temporary and non-serious, and recovery was achieved with conservative treatment, necessitating no change in subsequent treatment.

The present study had a number of limitations. It was a retrospective investigation and certain biopsy parameters and reference standards were lacking for some patients. The overall number of image-guided CNBs was insufficient for multivariate analysis of the factors related to effectiveness because of the small number of samples designated ineffective. While, in general, a certain proportion of carcinomas arise in the bone, retroperitoneal space, and subclavicular region in clinical settings, data were available for only a small number of such carcinomas among the archived cases used in the present study. Another potential study limitation was that we included not only sarcomas but also carcinomas located in any part of the body among the patients who underwent image-guided CNB in our department of musculoskeletal oncology, in the setting of a high-volume center. The definition of a reference standard, especially for clinical judgment, was incomplete and should have been based on definitive pathological diagnosis. The fact that this series of subjects included both those with initial biopsy and those with re-biopsies was a partial limitation. However, the authors' data (Supplementary Material 4) show that re-biopsy was correlated with only tumor size ($P = 0.004$), and not with the reasons for using image guidance or with selection of the biopsy route. Also, as shown in Table 6, re-biopsy was not an important determinant of the effectiveness of image-guided CNB. It was therefore judged that analysis with both initial biopsies and re-biopsies did not constitute a problem with the study.

In conclusion, image-guided CNB carried out at a comprehensive institution, and verified as current data obtained in real clinical situations, was shown to be clinically useful. When the shortest transcutaneous puncture route includes no anatomical structures that need to be avoided, and the direct route is judged to be rational by consensus within the MDT, the execution of direct-route biopsy is recommended for achieving a positive outcome. It is important to establish and put into practice diagnostic strategies based on the understanding that a complicated biopsy route can be a factor impacting on effectiveness and/or complications.

Funding information

This work was supported by the National Cancer Center Research and Development Fund (31-A-14 to A.K.).

Declaration of competing interest

Dr. Arai reported receiving the lecture fee from Canon Medical System. No other disclosures were reported.

Acknowledgement

The authors thank Drs. Takeshi Hirose, Tomoaki Mori, Makoto Endo, Shintaro Iwata and Yoshikazu Tanzawa for support.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jos.2020.12.017.

References

[1] Tuttle R, Kane 3rd JM. Biopsy techniques for soft tissue and bowel sarcomas. J Surg Oncol 2015 Apr;111(5):504–12.
[2] den Heeten GJ, Oldhoff J, Oosterhuis JW, Schraffordt Koops H. Biopsy of bone tumours. J Surg Oncol 1985 Apr;28(4):247–51.
[3] Mankin HJ, Lange TA, Spanier SS. The hazards of biopsy in patients with malignant primary bone and soft-tissue tumors. J Bone Joint Surg Am 1982 Oct;64(8):1121–7.
[4] Mankin HJ, Mankin CJ, Simon MA. The hazards of the biopsy, revisited. Members of the Musculoskeletal Tumor Society. J Bone Joint Surg Am 1996 May;78(5):656–63.
[5] Barrientos-Ruiz I, Ortiz-Cruz EJ, Serrano-Montilla J, Bernabeu-Taboada D, Pozo-Kreilinger JJ. Are biopsy tracts a concern for seeding and local recurrence in sarcomas? Clin Orthop Relat Res 2017 Feb;475(2):511–8.
[6] Yang J, Frassica FJ, Fayad L, Clark DP, Weber KL. Analysis of nondiagnostic results after image-guided needle biopsies of musculoskeletal lesions. Clin Orthop Relat Res 2010 Nov;468(11):3103–11.
[7] 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 Jul 1;94(1):21–7.
[8] Pohlig F, Kirchhoff C, Lenze U, Schauwecker J, Burgkart R, Rechl H, von Eisenhart-Rothe R. Percutaneous core needle biopsy versus open biopsy in diagnostics of bone and soft tissue sarcoma: a retrospective study. Eur J Med Res 2012 Nov 1;17(1):29.
[9] Trieu J, Schlicht SM, Choong PF. Diagnosing musculoskeletal tumours: how accurate is CT-guided core needle biopsy? Eur J Surg Oncol 2016 Jul;42(7):1049–56.
[10] Kiatisevi P, Thanakit V, Sukunthanak B, Boonthatip M, Bumrungchart S, Witoonchart K. Computed tomography-guided core needle biopsy versus incisional biopsy in diagnosing musculoskeletal lesions. J Orthop Surg (Hong Kong) 2013 Aug;21(2):204–8.

[11] Altuntas AO, Slavin J, Smith PJ, Schlict SM, Powell GJ, Ngan S, Toner G, Choong PF. Accuracy of computed tomography guided core needle biopsy of musculoskeletal tumours. ANZ J Surg 2005 Apr;75(4):187–91.
[12] De Marchi A, Brach del Prever EM, Linari A, Pozza S, Verga L, Albertini U, Forni M, Gino GC, Comandone A, Brach del Prever AM, Piana R, Faletti C. Accuracy of core-needle biopsy after contrast-enhanced ultrasound in soft-tissue tumours. Eur Radiol 2010 Nov;20(11):2740–8.
[13] Torriani M, Etchebehere M, Amstalden E. Sonographically guided core needle biopsy of bone and soft tissue tumors. J Ultrasound Med 2002 Mar;21(3):275–81.
[14] 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 Oct;89(10):2179–87.
[15] Sung KS, Seo SW, Shon MS. The diagnostic value of needle biopsy for musculoskeletal lesions. Int Orthop 2009 Dec;33(6):1701–6.
[16] Didolkar MM, Anderson ME, Hochman MG, Rissmiller JG, Goldsmith JD, Gebhardt MG, Wu JS. Image guided core needle biopsy of musculoskeletal lesions: are nondiagnostic results clinically useful? Clin Orthop Relat Res 2013 Nov;471(11):3601–9.
[17] Anderson MW, Temple HT, Dussault RG, Kaplan PA. Compartmental anatomy: relevance to staging and biopsy of musculoskeletal tumors. AJR Am J Roentgenol 1999 Dec;173(6):1663–71.
[18] 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 May;78(5):644–9.
[19] Adams SC, Potter BK, Pitcher DJ, Temple HT. Office-based core needle biopsy of bone and soft tissue malignancies: an accurate alternative to open biopsy with infrequent complications. Clin Orthop Relat Res 2010 Oct;468(10):2774–80.
[20] 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 Aug 25;105(4):229–39.
[21] Thway K, Fisher C. Histopathological diagnostic discrepancies in soft tissue tumours referred to a specialist centre. Sarcoma 2009;2009:741975. Epub 2009 May 27.
[22] Lurkin A, Ducimetiere F, Vince DR, Decouvelaere AV, Cellier D, Gilly FN, Salameire D, Biron P, de Laroche G, Blay JY, Ray-Coquard I. Epidemiological evaluation of concordance between initial diagnosis and central pathology review in a comprehensive and prospective series of sarcoma patients in the Rhone-Alpes region. BMC Cancer 2010 Apr 19;10:150.
[23] Ceraulo A, Ouziel A, Lavergne E, Perrier L, Decouvelaere AV, Chotel F, Thiesse P, Marec-Berard P. Percutaneous guided biopsy for diagnosing suspected primary malignant bone tumors in pediatric patients: a safe, accurate, and cost-saving procedure. Pediatr Radiol 2017 Feb;47(2):235–44.
[24] Rimondi E, Staals EL, Errani C, Bianchi G, Casadei R, Alberghini M, Malaguti MC, Rossi G, Durante S, Mercuri M. Percutaneous CT-guided biopsy of the spine: results of 430 biopsies. Eur Spine J 2008 Jul;17(7):975–81.
[25] Hadjipavlou AG, Kontakis GM, Gaitanis JN, Katonis PG, Lander P, Crow WN. Effectiveness and pitfalls of percutaneous transpedicle biopsy of the spine. Clin Orthop Relat Res 2003 Jun;(411):54–60.