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Image-guided Percutaneous Core Needle Biopsy of Musculoskeletal Tumors in Children

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Summary: The use of image-guided percutaneous core needle biopsy (PCNB) to obtain tissue diagnosis of musculoskeletal lesions has become the standard of care in adult patients with a success rate of over 80%. Previous reports indicate a similar success rate in diagnosing pediatric solid tumors. In this large study, we analyzed >10 years of data in which PCNB was used for tissue diagnosis of musculoskeletal lesions in children; we evaluated the histopathologic accuracy, anesthetic requirements, and complications of these procedures. In 122 children, tissue diagnosis was successfully obtained in 82% of cases, and there were 0 complications associated with the procedure. There was a significantly higher PCNB diagnostic success rate in malignant lesions (93%). These data suggest that the use of PCNB is a safe and effective means of diagnosing musculoskeletal lesions in children.

Key Words: pediatric cancer, solid tumor, diagnostics, biopsy, sarcoma

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Rapid, safe, and accurate diagnosis of solid tumors in children is of the utmost importance. In children, open or excisional biopsy has been the procedure of choice to obtain tissue for histologic, histochemical, and molecular diagnosis for musculoskeletal lesions. In contrast, percutaneous core needle biopsy (PCNB) has long been the mainstay of diagnosis of suspicious solid lesions in the adult population. In the adult population, PCNB is sufficient to yield an accurate diagnosis in 60% to 93% of cases, with most case series reporting an 80% to 90% success rate.[1–17] PCNB has several advantages over excisional or open biopsy. The procedure is associated with less pain, is cost-effective,[12,14–16,18,19] poses less risk of interruption of body compartments intraoperatively,[10,20] and is capable of yielding sufficient material for histologic and molecular studies.[21–23] The minimally invasive nature of this procedure allows the use of neoadjuvant chemotherapy or radiation shortly after the procedure when warranted, whereas the required healing process after open biopsy may delay the institution of systemic chemotherapy.[7,24–26] Finally, image guidance allows for targeting of specific areas within heterogenous tumor.

We have conducted a 10-year retrospective study of children undergoing PCNB for the diagnosis of suspicious musculoskeletal lesions at our institution. The purpose of the study was to assess the accuracy and safety of image-guided PCNB in the pediatric population. We hypothesized: (1) PCNB in children would yield a diagnostic accuracy equivalent to that reported in adults and (2) PCNB would be associated with few complications. Our data indeed demonstrate a diagnostic success rate in keeping with that in the adult and pediatrics literature. The overall success rate was 83%, with 93% of malignant lesions successfully identified by PCNB.[3,7,21–23,27–35] There were no complications after the procedure and no reports of needle biopsy tract recurrences. These observations support the use of PCNB in children for the diagnosis of musculoskeletal lesions.

MATERIALS AND METHODS

A retrospective review of children aged less than or equal to 18 years old who received image-guided PCNBs for bone and soft tissue lesions over a 10-year period (2001 to 2011) at UCLA was performed. Cases were analyzed for age, location of biopsy, imaging modality, ability to obtain a diagnostic specimen, cases leading to open biopsy, ability to perform cytogenetic and molecular analysis, anesthesia requirements, complications, and needle tract recurrences. Success rate and accuracy were determined as previously described in literature.[36] This study was reviewed and approved by the UCLA IRB, Study #10-000076.

For soft tissue masses and bone lesions with interrupted or destroyed cortex, a coaxial system consisting of an 11-G outer cannula and a 14-G biopsy gun was used (Quick-Core Biopsy Needle Set; Cook Medical). Medullary lesions with intact cortex were accessed with a bone coaxial set, often with use of a mallet to penetrate the cortex (KyphX, Kyphon; or Bonopty, AprioMed). Multiple samples were obtained, with the number primarily depending on the appearance of the core. An average of 6 cores, if possible, were obtained for each lesion, with approximately 4 placed in formalin for primary histology, immunochemistry, and fluorescence in situ hybridization, and 2 in saline for tissue culture or electron microscopy if necessary. In 10 patients where the diagnosis was malignant, patients were enrolled with informed consent to an appropriate Children's Oncology Group (COG) Tumor Biology study. Twenty to 40 unstained slides were prepared from these core samples for COG, and none were deemed as insufficient tissue for analysis.

Pathologic specimens were examined by one of 2 experienced musculoskeletal pathologists. Most soft tissue

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TABLE 1. Patient Characteristics

Mean patient age (y)	13.2 ± 4.2
Male:female (%)	57:43
Lesion location (%)	
Bone	66.6
Soft tissue	33.3
Upper extremities	23.2
Lower extremities	58.9
Trunk/axial skeleton	17.8
Image-guidance used (%)	
Computed tomography guidance	91
Ultrasound guidance	9
Anesthesia administered (%)	
Local anesthesia	74
Moderate sedation	13
General anesthesia	14

and all bone lesions were biopsied under computed tomography (CT) guidance. Ultrasound guidance was used for superficial masses or small soft tissue masses.

RESULTS

A total of 122 children aged 3 months to 18 years (mean age ± SD = 13.2 ± 4.2 y) underwent 128 biopsy procedures by image-guided PCNB for bone (n = 84) and soft tissue (n = 38) lesions (Table 1). These were all performed under CT (n = 117) or ultrasound (n = 11) using coaxial needle biopsy systems yielding 14 g cores. Of the lesions biopsied, 61 (48%) were malignant and 67 (52%) were benign (Table 2). Six children underwent 2 separate PCNB procedures; 5 of these children were being assessed for local recurrence of a solid tumor 6 to 27 months after initial diagnosis. Recurrent disease was demonstrated by PCNB to be present in 4 patients of these patients, and the fifth did not have recurrence. The sixth patient underwent 2 separate PCNB procedures to diagnose osteosarcoma of the femur with later metastasis to a vertebral body. PCNB yielded the correct diagnosis in all instances of suspected relapse or metastasis, avoiding the need for open biopsy.

TABLE 2. Frequency of Diagnoses

Benign Lesions (n = 67)		Malignant Lesions (n = 61)	
Acute or subacute osteomyelitis	8	Osteosarcoma	26
Giant cell tumor	6	Ewing sarcoma	16
Hemangioma	6	Langerhans cell histiocytosis	5
Normal tissue, nondiagnostic	6	Rhabdomyosarcoma	5
Osteoid osteoma	6	Synovial sarcoma	4
Aneurysmal bone cyst	5	Alveolar soft part sarcoma	1
Benign cystic lesions	4	High-grade undifferentiated soft tissue sarcoma	1
Chondroblastoma	3	Metastatic meningioma	1
Chronic osteomyelitis	3	Non-Hodgkin lymphoma	1
Abscess	2	Rhabdoid tumor	1
Fibroma	2		
Fibrous dysplasia	2		
Neurolemmoma	2		
Osteochondroma	2		
Chondromatosis	1		
Chronic synovitis, with granuloma	1		
Desmoid fibromatosis	1		
Fracture	1		
Heterotopic ossification	1		
Muscle rupture	1		
Neurofibroma	1		
Osteoblastoma	1		
Solitary fibrous tumor	1		
Tuberculosis granuloma	1		

TABLE 3. Biopsy Characteristics

	Cases (n)	Cases (%)
Successful Diagnostic PCNB		
Malignant lesions	57 of 61	93.4
Nonmalignant lesions	48 of 67	71.6
Total	105 of 128	82.0
Cases requiring open biopsy		
Malignant lesions	4 of 59	6.8
Nonmalignant lesions	11 of 69	15.9
Total	15 of 128	11.7
Successful diagnostic open biopsy		
Malignant lesions	4 of 4	100
Nonmalignant lesions	11 of 11	100
Total	15 of 15	100
Core biopsy samples sufficient for FISH analysis	66 of 77	85.7

FISH indicates fluorescence in situ hybridization; PCNB, percutaneous core needle biopsy.

Overall, there was an 82% diagnostic success rate with PCNB, and a higher success rate in children with malignancies versus benign lesions (93.4% vs. 71.6%, respectively) (Table 3). The success rate of diagnosing malignancies by PCNB was significantly higher than that of benign lesions ($P = 0.002$, Fisher exact test). Of the 22 children in whom PCNB was not definitively diagnostic, 15 went on to open biopsy. Open biopsy revealed a malignant lesion in 4 of these children. The other 11 children undergoing open biopsy were determined to have benign lesions. The remaining 7 children who did not undergo open biopsy after a nondiagnostic PCNB were observed carefully on the basis of their clinical presentation and course. None of these patients developed evidence of malignancy on close follow-up.

The most frequent malignant diagnosis was osteosarcoma (n = 26), followed by Ewing sarcoma (n = 14), rhabdomyosarcoma (n = 5), and Langerhans cell histiocytosis (n = 5). All 4 (6.8%) of the malignant cases that PCNB initially failed to diagnose had subsequent successful diagnostic open biopsies. In our study, there were no malignant cases in which PCNB failed and open biopsy was not performed or was not diagnostic. The most frequent diagnosis of benign lesions was osteomyelitis (a total of 11 acute, subacute, or chronic diagnoses), followed by biopsies consistent with a benign cystic lesion (a total of 9 aneurysmal or unicameral bone cysts).

Local anesthesia alone was used successfully in the majority of patients (74%), and only 1 patient did not tolerate this approach. Younger children more frequently underwent moderate sedation (13%) or general anesthesia (15%), based on clinical judgment. There were no complications (infections, bleeding, fracture, or hospitalization) from any image-guided PCNBs and no needle-tract

recurrences in our 10-year experience. Fluorescence in situ hybridization analysis was requested to assist in diagnosis in 77 cases, and the full desired analysis could be carried out on 85.7% of the core samples obtained. Cells failed to proliferate in the remaining cases. Ten patients in this study were enrolled into appropriate COG tumor biology studies; depending on the protocol, 20 to 40 unstained slides of the core tissue were submitted to central pathology at COG for processing and analysis. To our knowledge, these samples were adequate for study use.

DISCUSSION

In this 10-year retrospective study, we wished to assess the accuracy and safety of image-guided PCNB in the pediatric population. We hypothesized that PCNB in children would yield a diagnostic accuracy equivalent to that reported in adults and would be associated with few or no complications. Children presenting with solid lesions in a wide variety of locations were diagnosed successfully 83% of the time by image-guided PCNB; PCNB was even more accurate when the lesion was malignant (93%, $P = 0.002$). Our data are consistent with previously published data in both children and adults, with overall diagnostic success rates ranging from 69% to 96% for solid lesions.[35] In line with our experience, previous reports also describe a lower diagnostic accuracy using PCNB in lesions that ultimately prove to be benign.

This may contribute to a higher reported rate of unsuccessful PCNBs in children compared with adults, in whom solid malignancies are more frequent.[2,6–10] In contrast, literature exists that supports obtaining 3 to 10 core biopsies for analysis; this is frequently not feasible in the pediatric population, given that these lesions and the size of the patient are simply smaller.[7,37] This may also lead to some sampling error in heterogenous lesions, such as small blue round cell tumors.[23] For our study, the number of core biopsies obtained was not routinely recorded, and no formal analysis may be performed, although attempt was generally made to obtain 4 core specimens. All children with malignancies and nondiagnostic PCNBs were diagnosed by subsequent open biopsy, and PCNB was able to provide material sufficient for definitive diagnosis for all recurrent disease cases.

PCNB was performed using only local anesthesia in the majority of cases, and in 10 years, only 1 teenaged patient could not tolerate the PCNB procedure with local anesthesia alone. Of note, our patient population was mainly comprised of adolescents, which coincides with both the most rapid time, aside from infancy, of connective tissue growth and development and the highest incidence of connective tissue malignancies. This population would be expected to be more cooperative with the use of local anesthesia. In this study, no patient below the age of 6 underwent local anesthesia for the PCNB procedure. There were 0 complications with the PCNB procedure itself, including hospitalization, bleeding, infection, fracture, or seeding of the needle tract with tumor. Each of these adverse events has been reported in adults, with varying frequencies.[12,16,18–19,38,39] At our institution, CT-guided biopsy is used more frequently than ultrasound-guided biopsy, in part because the majority of lesions in our study arose from bone. Interestingly, when used, ultrasound-guided biopsy yielded successful PCNB diagnosis in 100% of attempts in our study. Shin et al[3] recommend the use of ultrasound-guided biopsy whenever feasible, with the caveat that not all bone lesions are visible on ultrasound. In contrast, Hryhorczuk et al[35] suggest that CT guidance be used for any bony lesion with an intact cortex in order to avoid unnecessary needle-tract injury. Our institutional preference is to use ultrasound whenever possible, as this avoids radiation exposure together with a high rate of achieving a definitive diagnosis.

Current literature recommendations for biopsy of musculoskeletal lesions suggest performing these procedures along a strict anatomic compartment with avoidance of "vital" anatomic compartments. For example, in the lower extremity this includes structures such as the knee joint capsule, greater trochanteric bursa, rectus femoris and vastus intermedius muscles, tibial tubercle, peroneus brevis, and peroneus longus distal tendons. For bony lesions, specific needle paths are recommended to be concordant with the surgical excision to assure that the entire biopsy tract can be excised during surgery.[40] In our patient population, attention to anatomic compartments was not consistently observed during image-guided PCNB. Rather, the focus was on minimizing patient pain, traversing the shortest skin to lesion distance, avoiding neurovascular structures and overall obtaining a diagnostic biopsy specimen.

One theoretical risk of PCNB is the potential to seed the needle tract with tumor cells, thus iatrogenically introducing tumor to additional tissue components, especially in cases where there is violation of anatomic compartments. This has been documented to rarely occur in adult patients in several lesions that do not occur commonly in children.[38–39] However, recent literature from our institution shows no association between PCNB technique and tumor seeding along the biopsy tract in musculoskeletal tumors of the lower extremity, even when anatomic compartments have been breached.[41] Furthermore, combining the data from other studies in the pediatric population that have been published to date with our data, the outcomes of some 600 PCNBs have been studied in children; there has not been a single reported needle-tract recurrence in the literature.[27–35] The absence of this phenomenon to date in children with musculoskeletal lesions should allay fears of this potential complication.

Another concern with using PCNB as the primary modality of obtaining diagnostic tissue is the inability to obtain specimens for central tumor banking and biology studies. Clearly, our further understanding of the molecular pathogenesis of disease and future molecular targets is highly important. We did enroll 10 patients on COG tumor biology studies with malignant diagnoses. In these patients, the tumor core biopsy specimens were resectioned and sent to COG. None of these cases were deemed insufficient for analysis. We do recognize that fresh/snap frozen tissue is optimal and because of this now, whenever possible we consent the patient before biopsy when a malignancy is suspected to obtain fresh tissue for further clinical research studies at UCLA.

As mentioned, the use of PCNB not only has practical benefits that include less pain at the biopsy site and the ability to perform the procedure on an outpatient basis, but may also facilitate earlier institution of neoadjuvant chemotherapy.[7] At various institutions, practices differ as to when chemotherapy should be started after open surgical procedures; there is concern for poor wound healing in the context of myelosuppression. The adverse effects of chemotherapy on wound healing have been documented in animal studies,

lending a basis for this concern.[42–44] However, human studies have not demonstrated a clear relationship between wound complications and early chemotherapy. Indeed, a large study of patients receiving neoadjuvant chemotherapy before surgery for soft tissue sarcomas did not demonstrate increased risk of wound complications, although the median latency between the 2 interventions was 45 days in this study.[45] Similar wound complication rates were reported for patients undergoing surgery for gynecologic malignancy as for patients undergoing surgery plus chemotherapy.[46] Finally, another recent study of >1300 patients showed chemotherapy given within 30 days of surgery had no effect on wound healing.[47] These findings may reflect advances in supportive care and evolution of neoadjuvant therapeutics. Nonetheless, our institutional practice is to allow a 2-week minimum healing period after open procedures before starting chemotherapy in order to permit sufficient wound healing. In contrast, we generally start chemotherapy the day after PCNB, sufficing the samples are diagnostic, and find no complications with wound healing in children.

In conclusion, we recommend PCNB as the primary modality to aid in the diagnosis of suspicious musculoskeletal lesions in children. Our data agree well with previously reported data; the rate of successful diagnosis is approximately 80% across studies, with an accuracy rate above 90% in lesions that prove to be malignant. The procedure is less invasive, poses fewer risks, and facilitates the earlier institution of definitive radiotherapy and/or chemotherapy.

Future directions for image-guided biopsies include the possible use of positron emission tomography (PET)/CT-guided biopsies, which may offer the advantage of demonstrating areas of maximum intralesional metabolic activity.[48] This could further aid in determining the optimal biopsy site, especially in the case of a heterogenous lesion. There have been a number of reports in which PET/CT image-guided biopsy proved useful in the diagnosis of lesions that did not enhance satisfactorily on CT scan or of lesions such as metastatic disease that are not reliably detected by magnetic resonance imaging or CT.[49,50] As with any technique, a number of potential impediments to the use of PET/CT-guided biopsies exist. Low-grade sarcomas, non-Hodgkin lymphomas, and well-differentiated adenocarcinomas of the lung can demonstrate low PET avidity, making this technique less useful in both initial diagnosis and assessment for progression.[51] In contrast, non-neoplastic processes such as sarcoidosis, a variety of fungal and acid-fast organism infections and even normal granulation tissue can demonstrate high PET avidity.[52] Thus, the use of PET/CT-guided biopsies should be carefully considered by the clinician, given the potential for both false-positive and false-negative examinations.

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