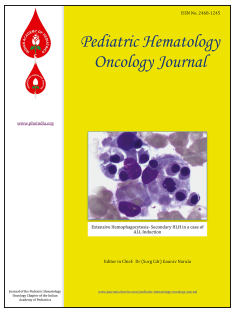

Diagnostic yield and accuracy of image-guided percutaneous core needle biopsy of paediatric solid tumours: An experience from Italy

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Title Page

Diagnostic yield and accuracy of image-guided percutaneous core needle biopsy of paediatric solid tumours: an experience from Italy

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L. Serati, Department of Paediatrics, IRCCS Foundation National Cancer Institute, Milan, Italy

C. Morosi, Department of Radiology, IRCCS Foundation National Cancer Institute, Milan, Italy

F. Barretta, Unit of Clinical Epidemiology and Trial Organization, IRCCS Foundation National Cancer Institute, Milan, Italy

P. Collini Department of Pathology, IRCCS Foundation National Cancer Institute, Milan, Italy

G. Calareso, Department of Radiology, IRCCS Foundation National Cancer Institute, Milan, Italy

S. Chiaravalli, Department of Paediatrics, IRCCS Foundation National Cancer Institute, Milan, Italy

F. Spreafico, Department of Paediatrics, IRCCS Foundation National Cancer Institute, Milan, Italy

R. Luksch, Department of Paediatrics, IRCCS Foundation National Cancer Institute, Milan, Italy

A. Ferrari, Department of Paediatrics, IRCCS Foundation National Cancer Institute, Milan, Italy

M. Massimino, Department of Paediatrics, IRCCS Foundation National Cancer Institute, Milan, Italy

A. Marchianò, Department of Radiology, IRCCS Foundation National Cancer Institute, Milan, Italy

Address of the institution: IRCCS Foundation National Cancer Institute, Giacomo Venezian, 1, 20133, Milan, Italy

Corresponding author: Lisa Serati, (+39)0223902060, lisa.serati@unimi.it, IRCCS Foundation National Cancer Institute, Giacomo Venezian, 1, 20133, Milan, Italy

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Abbreviations: CI = confident interval, CTCAE = Common Terminology Criteria for Adverse Events, FNAB = fine needle aspiration biopsy, ICCC-3 = International Classification of Childhood Cancer Volume 3, IQR = interquartile range, OR = odds ratio, PCNB = percutaneous core needle biopsy, SIR = Society of International Radiology.

Diagnostic yield and accuracy of image-guided percutaneous core needle biopsy of paediatric solid tumours: an experience from Italy

Abstract

Background Percutaneous core needle biopsy (PCNB) has become an accepted method to collect tumour tissue samples given its safety, minimal invasiveness, high accuracy and cost-effectiveness.

Procedure It is a single centre, retrospective evaluation of 213 ultrasound (US) or computed tomography (CT) guided PCNBs of paediatric solid tumours performed from 2005 to 2017. Safety, diagnostic yield, accuracy, and efficacy assessments of the PCNB procedure were performed. Univariate logistic models were applied to assess the relation of the diagnostic yield with patient, procedure and lesion features.

Results The image-guide was US in 91.08% of biopsies; the needle gauge was ≥ 16 G in 69.01% of the biopsies. The anatomical site of lesion was deep in 113 biopsies (53.05%). The nature of the lesion was the only factor associated with diagnostic yield (OR: 4.04; 95% CI 1.23 – 13.28; p: 0.022), with benign lesion as an unfavourable factor. Complication incidence was 1.41%. Overall, the diagnostic yield of PCNB was 93.90% (95% CI: 89.79%-96.71), the diagnostic accuracy was 96.86% (95% CI: 93.29%-98.84%) and the diagnostic efficacy was 93.33% (95% CI: 86.75% - 97.28%). Sensitivity was 97.94% (95% CI: 92.75%-99.75%) and specificity 100% (95% CI: 66.37%-100%).

Conclusion PCNB can be recommended as the first-choice method for solid tumours diagnosis in paediatric, adolescent and young adult patients because of its high diagnostic success, safety and accessibility.

1. Introduction

In absolute terms, tumours are rare events in children, adolescents and young adults, concerning 1% of all the cancer diagnoses in the world; however, they represent the main cause of disease-related deaths in this population (1,2). In such patients, tumours show a characteristic biological and clinical behaviour: rapid and very invasive growth is typically observed, often causing severe symptoms (3). The minimization of the time lag between the onset of the first symptoms and the pathological diagnosis allows to start promptly the proper treatment, reducing the psychological stress of the patient and of his/her family. This could also improve the subsequent prognosis, together with reducing morbidity and mortality and increasing the percentage of early stage-diagnosed tumours (3,4). Tissue sampling is necessary to obtain a pathological diagnosis whenever there is a clinical-radiological suspicion of a tumour; moreover, the histopathological diagnosis of the disease is a prerequisite for treatment planning, prognostic classification of the patient and the definition of further surgical approaches. Percutaneous core needle biopsy (PCNB) has been demonstrated to be a safe, accurate and inexpensive technique, which allows limiting invasiveness while avoiding surgical morbidity and delays in treatments onset. In Italy, PCNB is not frequently used in the paediatric context. However, we believe that it should be taken into account as a valuable method to collect tumour tissue samples in the paediatric population, although the presence of some risks should be noted, in particular related to deep thoracic-abdominal masses (5–9). More specifically, there exist a theoretical risk of not collecting enough tissue for an accurate diagnosis, while accidentally pricking other vital organs or causing haemorrhages/infections; there is also the possibility of tumour seeding and radiation exposure when CT is used as a guidance method (9). Surgical biopsy should instead be preferred for lesions located in anatomic sites that are difficult to reach by a percutaneous approach, with a severe risk of injuring adjacent organs.

The aim of our study was to assess if PCNB techniques can be used as a first-choice method for diagnosing both superficial and deep solid lesions in paediatric, adolescent and young adult patients. As hypotheses we assumed that biopsy is a safe procedure, characterized by high

diagnostic success and short timing in terms of both execution of the procedure and commencement of management of the patient. Furthermore, some factors related to the patient, procedure and lesion features have been evaluated to identify their association with the diagnostic yield.

2. Materials and methods

2.1 Study Method

The study was approved by the institutional review board. Written informed consent was acquired before each PCNB procedure.

All data of the first US/CT guided PCNB performed on children, adolescents and young adults (≤ 20 years old) with suspicious neoplastic processes (primary solid tumour or disease recurrence) at IRCCS Foundation National Cancer Institute, Milan, Italy, from January 1st, 2005 to December 31st, 2017, were included. Older patients were included when a recurrent disease was suspected.

2.2 Biopsy procedure

The indication to the PCNB was discussed by a multidisciplinary group. Pre-procedural images were reviewed by the interventional radiology to select the more suitable image guidance, patient's position, access route, needle type and trajectory.

The setting of the intervention was inpatient hospitalisation, day hospitalisation or outpatient surgery. When a thoracic or abdominal biopsy was scheduled, the patient was admitted in the hospital. The eventual need for sedation was evaluated for each biopsy procedure. Younger and non-cooperative children usually underwent PCNB in general anaesthesia whereas the others in analgosedation or local anaesthesia. If the PCNB required a prone position or was very difficult, patients were subject to Oral-Tracheal Intubation and general anaesthesia.

Biopsies were performed by highly qualified interventional radiologists (with more than 10 years of experience in paediatric biopsies), specialised in the execution of paediatric percutaneous

biopsies or by junior radiologists (less than 5 years of experience), under the supervision of the senior. US was the preferred image guidance method if it achieved a complete visualization of the mass, of its solid parts and all of the relevant anatomical details. CT was instead used when the masses were not well visualized with the use of US. For PCNB procedure, a coaxial technique with Tru-Cut needles was used. For abdominal lesions (e.g. neuroblastoma, Wilms' tumour), a retroperitoneal approach should be preferred, when possible. An intravenous contrast media was administered when lesions presented necrotic components or peri-lesion vascular structures were to be avoided during sampling. The choice of the needle gauge depended on anatomical site, lesion size, perilesional or intralesional vessels and vital structures near the lesion. At least three samples were collected (or more when the suspected lesion was a lymphoma, to provide enough material for immunohistochemical investigations).

Children were observed for 4-5 hours following the procedure. For patients undergoing lung biopsy, chest radiography was required 2-3 hours after the procedure completion to verify the absence of pneumothorax.

The biopsy procedure was rarely attended by the pathologist, except situations presenting an elevated risk of inadequate biopsy, such as for lesions with a large necrotic component visualized in pre-biopsy imaging. The samples were analysed by the pathologist of our institute. In the case of uncertainties in samples' interpretation, the opinion of a second pathologist was requested to avoid the repetition of the procedure.

2.3 Statistical analysis

Safety was assessed as the incidence of complications occurred. Complications were classified by outcome (10) and severity (11).

According to the Society of Interventional Radiology (SIR) guidelines, the biopsy was defined diagnostic if it provided enough material to establish a pathological diagnosis or guide the subsequent management (10,12). The diagnostic yield was calculated as the fraction of

diagnostic biopsies among the total number of biopsies performed. Non-diagnostic results included the ones related to insufficient cellularity, necrosis, blood or tissue artefacts.

A biopsy was considered accurate if it was diagnostic or suggestive of the diagnosis (not requiring further analysis to establish a pathological diagnosis) and was followed by an appropriate medical or surgical management. Therefore, only patients whose biopsy was followed by surgical pathology findings or clinical follow-up were included in the diagnostic accuracy assessment. The diagnostic accuracy was defined as the ratio between the number of accurate biopsies and the total number of patients in whom this accuracy could be assessed (10,13,14).

For those patients who underwent a subsequent open biopsy or surgical resection, biopsy result was compared with the final diagnosis (malignancy vs benignity, including non-neoplastic diagnoses). The diagnostic efficacy of biopsy was defined as the number of concordant biopsies among all biopsies coupled with a final surgical diagnosis (15). The concordance was estimated by using Cohen's kappa coefficient. Sensitivity, specificity, positive predictive value and negative predictive value for biopsy were also estimated.

All the collected data were described as median and interquartile range (IQR) for numerical variables or absolute and relative frequencies for categorical ones. The differences in timing between two events in different groups were tested according to the Wilcoxon-Mann-Whitney test.

The correlation between the diagnostic yield and the *a priori* selected potential explanatory variables was assessed by using univariate logistic models. The potential explanatory variables assessed included: biopsy year (≤ 2010, >2010), age at biopsy (0-2, 3-6, 7-12, > 13), sex, indication (primary, recurrence), operator experience (senior, junior), imaging guidance (US, CT), depth of the lesion (for this study we assumed as "deep" all the lesions with intra-thoracic or intra-abdominal location, while soft part masses of the head-neck region, extremities and trunk wall were assumed as "superficial"), Tru-Cut needle (≥ 16, <16), anatomical site (head-

neck, chest, abdomen, lymph nodes, limbs), histology (malignant, non-malignant), and diagnostic group (ICCC-3) (16).

The univariable logistic regression models were performed using the Firth's penalized likelihood approach to address the data separation issue (17). Results were expressed as odds ratios (OR) along with their 95% confidence intervals (CI). In case of a very dispersed variable, the association was evaluated through the Fisher Exact test. All tests are two-sided and a p-value <0.05 was considered statistically significant. Statistical analyses were performed with SAS™ (SAS Institute, Cary, NC) and R software (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1 Study cohort

Table 1 reports the demographic, clinicopathologic and treatment features of patients. Of the 213 PCNBs evaluated, 103 were performed on boys (48.36%) and 110 on girls (51.64%). The median age of patients at the time of the biopsy was 10 years (median: 10; IQR: 4-14 years). One hundred eighty-four procedures (86.38%) led to primary diagnosis while 29 (13.62%) recurrent or disseminated disease. Most procedures (184/213; 86.38%) were performed by senior radiologist. Junior radiologists performed the procedure in the other 29 cases (13.62%). Ultrasound was the prevalent imaging guidance (194/213; 91.08%) whereas CT was indicated in only 19 procedures (8.92%). The gauge of PCNB was in most biopsies $\geq$ 16 G (147/213; 69.01%). In 57 procedures (26.76%) the gauge of the Tru-Cut needle was 18 or 20 G. Abdomen was the most commonly biopsied anatomical site (100/213; 46.95%). The remaining percutaneous biopsies were performed on extremities (36/213; 16.90%), chest (34/213; 15.96%), superficial lymph nodes (29/213; 13.62%, 21 of which cervical), and on the head-neck area (14/213; 6.57%). The site of suspected neoplastic mass was deep in 113 biopsies (53.05%) and superficial in 100 (46.95%).

The PCNB was performed in the outpatient unit in 20 (9.39%) cases, in Day Hospital in 43 (20.19%), and as inpatient surgeries in 150 (70.42%). In the latter, excluding those who performed a biopsy and started the treatment during the same hospital stay (67/150 patients, 44.67%), patients were hospitalised for a median of 2 days (IQR: 2-3 days). The median time lag between the first oncologist examination and the biopsy was 5 days (IQR: 2-11 days). Ninety-six procedures (45%) were performed within 3 days following the first clinical evaluation, 45 (21%) of which on the same or the following day. Time interval was reduced when there was an indication of primary diagnosis compared to recurrence ($P < 0.001$). The median time lag between the biopsy and the beginning of the treatment was 11 days (IQR: 4-21 days).

3.2 Diagnostic results

One hundred sixty lesions (75.12%) were malignant, 43 (20.19%) benign and 8 (3.76%) non-neoplastic. Out of 29 procedures with the suspicion of disease recurrence, 22 (75.86%) confirmed the recurrence (Table 2), 3 diagnosed a second tumour while the remaining 4 resulted non-neoplastic.

3.3 PCNB assessment

Two hundred samples out of 213 procedures were diagnostic, resulting in a diagnostic yield of 93.90% (95% CI: 89.79%-96.71). Among the 13 non-diagnostic biopsies, 3 were inadequate with a report of cellular debris, blood and necrosis. In the first case, a surgical biopsy was performed leading to the diagnosis of a benign lesion; in the second case the diagnosis of neuroblastoma was made with a bone marrow biopsy; in the latter case the treatment for neuroblastoma was set on a clinical-radiological basis and this diagnosis was confirmed after surgical removal. Six biopsies did not lead to a definitive diagnosis, but they drove the suspicion towards a benign pathology; all the lesions were confirmed as benign by incisional biopsy (two), excisional biopsy (three) and prolonged clinical-radiological monitoring that showed the stability of the lesion (one). One biopsy of a complex cystic kidney formation drove the suspicion to malignant form, then confirmed after surgical removal. The PCNB of 2 lymph nodes did not

allow the histopathological, immunohistochemical and molecular characterization of the lymphoproliferative disease; excisional biopsy was used to collect the necessary tissue. In the last case of non-diagnostic biopsy, characterized by poor cell differentiation, a final diagnosis was not completed due to the rapid progression of the disease and the patient's death.

The results of the assessment of the relationship between selected putative influencing factors and the diagnostic yield are reported in Table 3. The diagnostic yield was not associated to patient-related factors, year and indications to biopsy, technical factors (operator experience, imaging guidance, Tru-Cut needle), depth and anatomical site of lesions and diagnostic group. The only associated factor was the nature of lesion, with non-malignant lesions having lesser diagnostic yield (OR: 4.04; 95% CI 1.23 – 163.28; $P = 0.022$).

The diagnostic accuracy was 96.86% (185/191; 95% CI: 93.29%-98.84%). In 3 biopsies the sample was inadequate and did not provide any information for patient management. In one case a wide surgical excision was performed for suspected malignancy, but the result was a benign lesion. A biopsy sample suggested a non-Hodgkin's lymphoma, while excisional biopsy diagnosed a Hodgkin's lymphoma. Finally, a poorly differentiated malignant tumour diagnosis was treated with possible effective chemotherapy; a rapid disease progression occurred, followed by the patient’s death.

The diagnostic efficacy was 93.33% (98/105; 95% CI: 86.75% - 97.28%). Biopsies resulted in misdiagnoses of malignant tumours as benign or low malignant tumours in 7 lesions, 4 of which were of neuronal origin (ganglioneuroma instead of intermixed ganglioneuroblastoma). All the 7 lesions were excised and the pathological analysis of surgical samples highlighted the malignant component of the lesions. Concordance Kappa’s coefficients of the PCNB and the subsequent open biopsy or surgical resection for the diagnosis of malignancy was as high as 0.890 (95% CI: 0.739-1), depicting a very good agreement. Table 4 reports the PCNB procedure evaluation indices. The sensitivity of percutaneous biopsy was 97.94% (95/97; 95% CI: 92.75%-99.75%), correctly identifying 95 patients with malignancy. The specificity of the test, the positive

predictive value (PPV) and the negative predictive value (NPV) were 100% (66.37%-100%), 100% (96.19%-100%) and 81.82% (48.22%-97.72%), respectively.

3.4 Safety

There occurred 3 complications out of 213 procedures (1.41%). Only one of these (0.47%), observed in a patient subjected to US-guided PCNB of the liver with 18 G needle, was of a major type, with grade 3 severity according to the SIR guidelines and the Common Terminology Criteria for Adverse Events (CTCAE) (10,11). Such complication consisted of a haemorrhagic effusion in the pelvic, perihepatic and perisplenic areas, together with a small laceration in the liver parenchyma. The patient was transfused and the lesion in the arterial branch was embolized. The other two minor complications consisted of modest bleeding with spontaneous resolution occurred after a CT-guided PCNB with a 20 G needle of the lung and after a CT-guided PCNB with a 20 G needle at the abdominal level.

4. Discussion

This study was aimed at assessing the safety, accessibility, diagnostic success and the factors influencing the diagnostic yield of US/CT-guided PCNB of paediatric, adolescent and young adult solid tumours. Complication incidence was 1.41% (3/213). Overall, the diagnostic yield of PCNB was 93.90% (200/213), the diagnostic accuracy was 96.86% (185/191) and the diagnostic efficacy was 93.33% (98/105). Malignancy was the only factor associated with diagnostic yield (OR: 4.04; 95% CI 1.23 – 13.28; p: 0.022), with benign lesion as an unfavourable factor. Sensitivity was 97.94% (95% CI: 92.75%-99.75%) and specificity 100% (95% CI: 66.37%-100%). Ninety-six procedures of 213 (45%) were performed within 3 days from the first observation. Patients were hospitalised for a median of 2 days (IQR: 2-3 days).

Literature reveals that US is preferred over CT for image-guided biopsy in children because it is readily available, portable, fast, without radiation exposure and it provides a real-time needle visualization during sampling (10,18–20). Furthermore, the US guidance biopsy, instead of the

CT guided one, allows the execution of further procedures in the surgical room, such as central venous catheter placement, during the same session of biopsy, avoiding other eventual anaesthesia interventions (21). In literature, as in our study, it was reported that the operator experience was not statistically significant (18,22–24), probably because PCNB is now performed with a standardized technique, using automatic, accurate and reliable sampling tools (25). It would be anyway interesting to observe whether the evaluation of the pre-procedural images, the choice of the biopsy site and the needle gauge by an expert interventional radiologist are predictors of diagnostic yield. To collect enough tissue for morphological, immunohistochemical, cytogenetic and molecular analyses (7,26) our interventional radiologists chose the larger needle gauge in relation to the anatomical site and the tumour size and they took at least 3 samples from the lesion. In several studies, the number of samples ≥ 3 was a predictor of the diagnostic yield (22,27).

The overall complication rate was 1.41%, which is in line with other studies and lower than 2% as recommended by the SIR guidelines (12,19,21). In Sebire et al. there is a complication rate of 1.00%(13). Hassan et al. compare the use of percutaneous biopsy and surgical biopsy: there is no significant difference in the incidence of minor complications (P = 0.30), while major complications occur more frequently after open biopsy (28).

In recent studies, the analysis is not limited to the technical success of percutaneous biopsy but extends to evaluate its clinical utility (14,22). Some non-diagnostic results, although requiring further investigation to establish a correct diagnosis, can guide clinical decisions, in terms of medical-surgical treatment or monitoring (29,30). In our study, the diagnostic success of PCNB was high for both superficial and deep lesions and it was comparable with previous studies. Blondiaux et al. showed a diagnostic yield of 89.4% and an accuracy of 90.9% (14). In Zhao et al., diagnostic yield and accuracy were both 96.4% (31). Ilivitzki et al. indicated a sensitivity of 97.1% and a specificity of 100% (21). Wang et al. reported that PCNB had a diagnostic yield of 96.5% for the diagnosis of deep, abdominal and pelvic malignant tumours of paediatric patients

(19). In literature, as in our study, it was reported that malignancy of the lesion was a predictive factor of the diagnostic yield of PCNB (8,20,32). Probably, this should be attributed to the clinician's high suspicion of malignancy when a patient comes into observation at a reference centre and to the better diagnostic skill of the referent pathologist. Consequently, the lack of confidence of clinician and pathologist with a diagnosis different from cancer requires further investigation to confirm the non-malignancy. The concordance between the diagnostic result of the PCNB and the subsequent final surgical diagnosis has failed especially in neuroblastoma tumours. These diagnostic difficulties can be ascribed to the biological heterogeneity of neuroblastoma and the procedure of limited percutaneous biopsy, which allows collecting small samples, perhaps missing the undifferentiated component (31). As suggested in literature, the diagnostic yield could be increased by taking samples from multiple sites within a neuroblastoma tumour, especially in areas of inhomogeneity (33).

In literature, the PCNB was associated with short organization time, fewer days of hospitalization and lower costs than surgical biopsy. Ilivitzki et al. found that the mean time lag between the clinical indication and the procedure was 2 days and around 65% of the patients underwent a biopsy within a day from the indication (21). In our study, the median time lag between the first oncologist examination and the biopsy was 5 days; 45% of the procedures were performed within 3 days following the first clinical evaluation. The PCNB was easily accessible thanks to the close collaboration between the paediatric oncologist and the radiologists and to the greater availability of radiological operators, tools and rooms for the percutaneous biopsy compared to the surgical procedure. Ceraulo et al. suggested a mean length of stay of 2 days for percutaneous biopsy, in line with our data, and 6 days for open biopsy (15). In our study, the median time lag between the biopsy and the beginning of treatment was 11 days. A more efficient multidisciplinary approach, involving the pathologist from the beginning of the case discussion with clinicians might be helpful, in principle, to reduce such time.

This study has several limitations related to its retrospective nature. Data on lesion size were not collected due to the fact that the first radiological investigations were often performed externally, and the extent of the lesion was not measured with a standardized method. The distance of the lesion from the skin was categorical for the same reason. Although the results of our study can be considered positive and consistent with those present in literature, the retrospective and monocentric study design does not allow any rigorous causal inference.

In summary, US/CT-guided PCNBs have a high diagnostic yield, are effective, efficient and safe. Moreover, they allow to reach a timely diagnosis and promptly start proper treatment, in relation to the histological report. The PCNB could be recommended as a first-choice method to obtain a diagnosis in paediatric, adolescent and young adult patients. However, we also highlight the need for a multidisciplinary approach, with the collaboration between oncologists, interventional radiologists and pathologists. Thus, an appropriate pre-procedural clinical-radiological evaluation of the patients selected for PCNB together with the expertise of interventional radiologists and pathologists allows a high diagnostic success of PCNB both for deep and superficial masses.

Conflict of Interest statement

The authors declare that they have no conflict of interest.

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410 # Tables

Table 1. Demographic, clinicopathologic, and treatment characteristics of the cohort study.

	n (%)
Sex	
Male	103 (48.36)
Female	110 (51.64)
Age (years)	
Median (IQR)	10 (4 - 14)
0-2	39 (18.31)
3-6	38 (17.84)
7-12	61 (28.64)
>13	75 (35.21)
Biopsy year	
≤ 2010	90 (42.25)
> 2010	123 (57.75)
Indication	
Primary diagnosis	184 (86.38)
Recurrence	29 (13.62)
Clinical-radiological suspect	
Malignant	179 (84.04)
Benign	28 (13.15)
Unknown	6 (2.82)
Operator experience	
Senior	184 (86.38)
Junior	29 (13.62)
Imaging guidance	
US	194 (91.08)
CT	19 (8.92)
Tru-Cut needle (Gauge)	
≥ 16	147 (69.01)
< 16	57 (26.76)
Unknown	9 (4.23)
Anatomical site	
Chest	34 (15.96)
Head-neck	14 6.57)
Abdomen	100 (46.95)
Limb	36 (16.90)
Lymph nodes	29 (13.62)
Depth of lesion	
Deep	113 (53.05)
Superficial	100 (46.95)
Interventional set-up	
Inpatient hospitalisation	150 (70.42)
Day hospitalisation	43 (20.19)
Outpatient surgery	20 (9.39)
Hospitalisation time, biopsy only (days)*	
Median (IQR)	2 (2 - 3)
Treatment scheme, patients in charge to INT only**	
Surgery+chemotherapy	78 (41.05)
Chemotherapy only	65 (34.21)
Surgery only	33 (17.37)
Clinical-radiological monitoring	14 (7.37)

Abbreviation: IQR: interquartile range; US: ultrasound guide; CT: computed tomography

guide

*On 83 patients, 8 in the non-diagnostic group and 75 in the diagnostic group.

**On 190 patients.

Table 2. Diagnostic results

	n (%)	Reccurence/ dissemination confermation
Histology		
Malignant	160 (75.12)	21
Non malignant	51 (23.94)	1
Unknown	2 (0.94)	0
Diagnostic group		
Benign	43 (20.19)	1
Non neoplastic*	8 (3.76)	0
Malignant	160 (75.12)	21
I. Leukemias, myeloproliferative diseases, and myelodysplastic diseases	0 (0.00)	
II. Lymphomas and reticuloendothelial neoplasms	32 (15.02)	2
III. CNS and miscellaneous intracranial and intraspinal neoplasms	0 (0.00)	
IV. Neuroblastoma and other peripheral nervous cell tumors	48 (22.54)	4
V. Retinoblastoma	0 (0.00)	
VI. Renal tumors	14 (6.57)	0
VII. Hepatic tumors	5 (2.35)	0
VIII. Malignant bone tumors	9 (4.23)	2
IX. Soft tissue and other extraosseous sarcomas	41 (19.25)	11
X. Germ cell tumors, trophoblastic tumors, and neoplasms of gonads	1 (0.47)	0
XI. Other malignant epithelial neoplasms and malignant melanomas	6 (2.82)	2
XII. Other and unspecified malignant neoplasms	4 (1.88)	0
Unknown	2 (0.94)	0

*6 inflammation and 2 normal tissue.

Table 3. Univariate logistic models for diagnostic yield (odds ratio of diagnostic yield).

	OR (95% CI)	P-value
Biopsy year		0.161
> 2011 vs ≤ 2010	2.22 (0.73; 6.76)	
Age (years)		0.932
0-2 vs > 13	1.17 (0.25; 5.59)	
3-6 vs > 13	0.79 (0.19; 3.26)	
7-12 vs > 13	1.30 (0.32; 5.26)	
Sex		0.881
Male vs Female	1.09 (0.37; 3.24)	
Indication		0.299
Primary diagnosis vs Recurrence	0.22 (0.01; 3.90)	
Operator experience		0.234
Senior vs Junior	2.19 (0.60; 8.01)	
Imaging guidance		0.854
US vs CT	1.18 (0.20; 7.17)	
Tru-Cut needle (Gauge)*		0.346
< 16 vs ≥ 16	0.58 (0.19; 1.79)	
Depth of lesion		0.612
Deep vs Superficial	1.33 (0.45; 3.95)	
Anatomical site		0.672
Head-neck vs Chest	0.40 (0.04; 4.48)	
Abdomen vs Chest	0.78 (0.12; 5.05)	
Limb vs Chest	0.32 (0.05; 2.25)	
Lymph nodes vs Chest	0.49 (0.06; 4.10)	
Histology*		0.022
Malignant vs Non malignant	4.04 (1.23; 13.28)	
Diagnostic group*		0.390**

Abbreviation: OR: odds ratio; CI: confidence interval; US: ultrasound guide; CT: computed tomography guide

*Unknown data were excluded

**Fisher's Exact test

Table 4. Percutaneous core needle biopsy procedure evaluation indices.

Classification functions	***Estimate***	***[95% CI] ****	***Diagnostic performance indices***	***Estimate***	***[95% CI] ****
Sensivity	95/97 (97.94)	[92.75 - 99.75]	Diagnostic yield	200/213 (93.90)	[89.79 - 96.71]
Specificity	9/9 (100)	[66.37 – 100]	Diagnostic accuracy	185/191 (96.86)	[93.29 - 98.84]
PPV	95/95 (100)	[96.19 – 100]	Diagnostic efficacy	98/105 (93.33)	[86.75 - 97.28]
NPV	9/11 (81.82)	[48.22 - 97.72]	Diagnostic concordance	0.890	[0.739 – 1]
			Safety		
Global	1.41%		Major complication (Grade >2)	0.47%	

Abbreviation: CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value
*Exact confidence interval.

Tables

Table 1. Demographic, clinicopathologic, and treatment characteristics of the cohort study.

	n (%)
Sex	
Male	103 (48.36)
Female	110 (51.64)
Age (years)	
Median (IQR)	10 (4 - 14)
0-2	39 (18.31)
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