

GSC Advanced Research and Reviews

eISSN: 2582-4597 CODEN (USA): GARRC2 Cross Ref DOI: 10.30574/gscarr Journal homepage: https://gsconlinepress.com/journals/gscarr/

(RESEARCH ARTICLE)



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Comparison of accuracy of fine needle aspiration biopsy with and without guidance on soft tissue tumor in a tertiary referral hospital in Indonesia

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GSC Advanced Research and Reviews, 2025, 22(01), 092-103

Publication history: Received on 02 October 2024; revised on 16 November 2024; accepted on 19 November 2024

Article DOI: https://doi.org/10.30574/gscarr.2025.22.1.0430

Abstract

Introduction: Diagnosing soft tissue tumors is challenging due to the complexity of soft tissue sarcomas, which are malignancies with heterogeneous histological and molecular subtypes, often resulting in delayed diagnoses. The gold standard for examining soft tissue tumors is histopathological examination, which, while definitive, is costly and invasive. Fine Needle Aspiration Biopsy (FNAB) is an alternative method that can be used as an initial screening tool to provide differential diagnoses of soft tissue tumors. FNAB is considered affordable and minimally invasive. Moreover, it can be performed under ultrasonographic (USG) guidance, offering several advantages, including real-time monitoring and visualization during the biopsy. This allows for precise positioning and adjustments to improve sample accuracy. This study aims to demonstrate the advantages of FNAB as a minimally invasive diagnostic tool, evaluate the effectiveness of USG-guided FNAB in assessing soft tissue tumors, and determine the comparative accuracy, sensitivity, specificity, negative predictive value, and positive predictive value of FNAB procedures, both with and without USG-guided.

Methods: The retrospective study with cross-sctional design carried out in Departement of Anatomics Pathology of a tertiary referral hospital in East Java, Indonesia from 2020 to 2022. The diagnostic test measured using a 2x2 table that presents data on the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of FNAB with or without USG-guided in diagnosing soft tissue tumors. The results will be compared with the final findings from histopathological or immunohistochemical examinations, which serve as the gold standard for diagnosing soft tissue tumors.

Results: FNAB with USG-guided show the higher accuracy than FNAB without USG-guided. The sensitivity was 83%, specificity of 100%, positive predictive value (PPV) of 100%, negative predictive value (NPV) of 75%, and accuracy of 88.88%.

Conclusion: FNAB can be used as an early diagnostic tool to assess the malignancy of soft tissue tumors. When performed with USG-guided, FNAB demonstrates higher accuracy compared to FNAB without USG-guided.

Keywords: Soft Tissue Tumor; Fine Needle Aspiration Biopsy; USG-Guided; Diagnostic Accuracy

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1. Introduction

Soft tissue tumors originate from mesenchymal tissues and differentiate into fat, skeletal muscle, smooth muscle, vascular tissue, fibrous tissue, and peripheral nerves [1]. Diagnosing soft tissue tumors is challenging because soft tissue sarcomas are complex malignancies with heterogeneous histological and molecular subtypes. Each sarcoma subtype has distinct clinical behavior, and there is considerable disease heterogeneity, making their management complex [2].

Although benign soft tissue tumors are more common than sarcomas, sarcomas account for 2% of all cancer-related deaths and are considered aggressive and resistant to chemotherapy. Soft tissue tumors are considered rare and may pose challenges related to diagnosis, assessment, and optimal therapeutic approaches [3,4,5]. Many patients present late to healthcare facilities, with tumors already at an advanced stage, increasing the risk of recurrence and metastasis even after appropriate treatment. Therefore, early diagnosis of soft tissue tumors is essential to prevent recurrence and mortality [6].

The gold standard for examining soft tissue tumors is histopathological examination via biopsy, conducted through an operative procedure considered invasive. It requires an operating room, anesthesia, and costly, with the risk of metastasis if excision is not done perfectly. Consequently, a less invasive examination method for obtaining tumor lesions is the Fine Needle Aspiration Biopsy (FNAB). FNAB is a screening technique that can be used to evaluate soft tissue masses. It can serve as an initial examination to differentiate between types of soft tissue tumors. FNAB is considered affordable, non-invasive, and patient-friendly due to its short procedure duration, high patient safety, faster evaluation, and easier recovery [7,8].

During FNAB sampling, it can be performed with or without imaging guidance. Both core biopsy and fine needle aspiration biopsy sampling techniques can be done with imaging guidance, including ultrasound (USG), computed tomography (CT), and magnetic resonance imaging (MRI). USG offers advantages in flexibility, speed, and minimal radiation exposure, and is the only real-time guidance modality. USG is widely used for guidance in FNAB specimen collection because it allows for direct monitoring. Another advantage is that the needle tip location can be visualized during the biopsy, allowing for positional adjustments to improve sample accuracy [9].

FNAB does have limitations, as it requires the experience of a pathologist to obtain a representative sample. If there is an error or delay, the sample may be non-representative [9]. This issue arises because soft tissue tumor lesions are highly variable, so FNAB alone cannot be used as a definitive diagnosis. There is significant variation in FNAB diagnostic accuracy, with a negative predictive value (NPV) below 50% in some cases [10,11,12,13]. Also the research about diagnostic accuracy in FNAB with or without USG-guided in this hospital has never been conducted before.

2. Methods

This is a retrospective study with cross-sectional design carried out in Departement of Anatomics Pathology at Dr. Saiful Anwar Regional Hospital, Malang as tertiary referral hospital in Indonesia from 2020 to 2022. The data form medical records of soft tissue tumor patients who underwent both FNAB with or without USG-guided and histopathological examinations with or without immunohistochemistry. The diagnostic test measured using a 2x2 table that presents data on the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of FNAB with or without guidance in diagnosing soft tissue tumors. The results will be compared with the final findings from histopathological or immunohistochemical examinations, which serve as the gold standard for diagnosing soft tissue tumors. This study has been approved by the Research Ethics Committee of our hospital with number 400/160/K.3/102.7/2024.

3. Results

A total of 124 cases of soft tissue tumors underwent FNAB examination. All data were combined and sorted according to inclusion and exclusion criteria. The inclusion criteria were as follows:

- All patients with soft tissue tumors who underwent FNAB examination followed by histopathology examination with or without immunohistochemistry examination,
- Soft tissue tumors include neoplasms and non-neoplasms,
- The diagnosis results with a clear malignant or non-malignant status and can be in the form of a differential diagnosis listed in the medical record and are considered to be in accordance with the histogenesis of the tumor,
- Examination or diagnosis was carried out at the Pathology Installation of Dr. Saiful Anwar Malang Hospital from January 1, 2020 to December 31, 2022.

There were 81 exclusion cases: 72 cases where only FNAB was performed, 4 cases not performed or diagnosed at RSUD Dr. Saiful Anwar or were not second opinions by musculoskeletal pathology consultants at RSUD Dr. Saiful Anwar, 3 cases with inconclusive FNAB results, and 2 cases where the biopsy site differed from the histopathology examination site.

For 43 inclusion cases, there were 25 case who undergoing FNAB, HPA (histopathology), and IHK (immunohistochemistry), and 18 cases undergoing only FNAB and histopathology, with 5 of these was conducted outside hospital but later reviewed by a musculoskeletal consultant as a second opinion. Based on sampling methods, 34 cases were done without USG-guided, and 9 cases were performed with USG-guided. In total, 43 cases underwent FNAB followed by histopathological examination, with or without immunohistochemistry.

In **Figure 1**, the distribution of soft tissue tumor cases examined at the Anatomical Pathology Department at RSUD Dr. Saiful Anwar from 2020 to 2022 shows an increase in the number of cases each year, with the highest number in 2022 with 29 cases (67.44%). In 2021 and 2020, there were 7 cases each, with a percentage of 16.28% for each year. The malignancy distribution also corresponds with the yearly case count. In 2020, there were 7 cases, with 5 malignant tumors and 2 benign tumors. In 2021, there were 7 cases in total, with 4 malignant tumors and 3 benign tumors, one of which was an intermediate tumor. In 2022, out of 29 cases, there were 16 malignant tumors and 13 benign tumors, with 3 classified as intermediate tumors.



Figure 1 Distribution of the Number of Soft Tissue Tumor Cases Undergoing FNAB and HPA with or without IHK

In Figure 2, the distribution of gender characteristics shows a higher number of females, with 24 individuals (55.8%), compared to 19 males (44.2%).



Figure 2 Percentage of gender of soft tissue tumor patients who underwent FNAB and HPA examination with or without IHK

In Table 1, Age characteristics vary from 13 to 84 years, with an average age of 39.67 years and a median of 22 years. Based on the age grouping of soft tissue tumor patients, the 21–30-year age group is the most common, representing 25.59% of cases, followed by the 11–20 and 61–70 age groups, each with a percentage of 16.28%.

Table 1 Distribution of the number of soft tissue tumor cases undergoing FNAB and HPA with or without IHK

Age Group	Frequency	Percentage
11 - 20	7	16.28%
21 - 30	11	25.59%
31 - 40	6	13.95%
41 - 50	6	13.95%
51 - 60	5	11.63%
61 - 70	7	16.28%
>71	1	2.32%
Total	43	100%

In Table 2, among the soft tissue tumor cases examined by FNAB and histopathology, with or without immunohistochemistry, the most common tumor location is the lower extremities, primarily the thigh, with 14 cases (32.56%). This is followed by the arm, with 9 cases (20.93%), and the knee and lower leg, each with 3 cases (6.98%).

Table 2 Tumor Locations in Patients with Soft Tissue Tumors Undergoing FNAB and HPA with or without IHK

Tumor Location	Frequency	Percentage
Thigh	14	32.56%
Knee	3	6.98%
Lower Leg	3	6.98%
Ankle	1	2.33%
Sacrum	1	2.33%
Vagina	1	2.33%
Arm	9	20.93%
Shoulder	2	4.65%
Hand	1	2.33%
Finger	1	2.33%
Neck	1	2.33%
Occipital	1	2.33%
Orbit	1	2.33%
Auricle	1	2.33%
Mediastinum	1	2.33%
Abdomen	1	2.33%
Intra-abdomen	1	2.33%
Total	43	100%

In this study, tumors are classified into non-malignant (benign and intermediate) and malignant tumors (Table 3). Among benign tumors, the most frequently seen is tenosynovial giant cell tumor (23.07%). Intermediate tumors, the type observed in this study sample was fibromatosis/desmoid tumor (locally aggressive) is the most common type (60%). The atypical lipomatous tumor, classified as intermediate in the 2020 WHO classification due to its predilection for the extremities, similarly in this study where the locations are in femur and arm. For malignant soft tissue tumors, there were 28 cases with identifiable tumor types. One case could only be determined by its malignancy based on histopathological examination. Among the malignant tumor types in this study, Non-Hodgkin Lymphoma (20%) was the most encountered malignant soft tissue tumor. The second most common was Ewing Sarcoma (12%).

Table 3 Types of Diagnosis of Soft Tissue Tumor Patients who undergo FNAB and HPA with or without IHK

Tumors	Frequency	Percentage
Benign Tumor		
Haemangioma	2	18.18%
Schwannoma	1	7.69%
Epithelioid Schwannoma	1	7.69%
Spindle Mesenchymal Tumor dd Nerve Sheath Tumor	1	7.69%
Tenosynovial Giant Cell Tumor (diffuse/localized) type	3	23.07%
Lipoma	1	7.69%
Osteolipoma	1	7.69%
Spindle mesenchymal tumor impressing adipocytes	1	7.69%
Cholesterol Granuloma	1	7.69%
Total	13	100%
Intermediet Tumor		
Fibromatosis / Desmoid Tumor (Locally Agressive)	3	60%
Atypical Lipomatous Tumor	2	30%
Total	5	100%
Malignant Tumor		
Dedifferentiated Liposarcoma	1	4%
Myxoid Liposarcoma	1	4%
Low - Grade Myofibroblastic Sarcoma	1	4%
Myxofibrosarcoma	2	8%
Leiomyosarcoma	2	8%
Rhabdomyosarcoma	1	4%
Mesenchymoma	1	4%
MPNST	2	8%
Synovial Sarcoma, biphasic	1	4%
Synovial Sarcoma, poorly differentiated	1	4%
Alveolar soft part sarcoma	2	8%
Round Cell Sarcoma, Malignant (NHL)	5	8%
Round Cell Sarcoma, Malignant, Ewing Sarcoma	3	8%
Anaplastic Large Cell Lymphoma	1	4%

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Extraskeletal Ewing Sarcoma	3	12%
High Grade Sarcoma	1	4%
Total	24	100%

The diagnostic test results between FNAB and the final histopathological results, with or without continuation of immunohistochemistry, the final results were divided into FNAB (all cases), with USG-guided, and without USG-guided. In FNAB (all cases), a total of 43 cases were analyzed, with 20 true positives, 18 true negatives, 0 false positives, and 5 false negatives. The calculated results were sensitivity of 80%, specificity of 100%, positive predictive value (PPV) of 100%, negative predictive value (NPV) of 78.26%, and accuracy of 88.37%.

In FNAB (with USG guiding) there were 9 cases, with 5 true positives, 0 false positives, 1 false negatives, and 3 true negatives. The results showed a sensitivity of 83%, specificity of 100%, PPV of 100%, NPV of 75%, and accuracy of 75%.

In the FNAB (without USG guiding), there were 34 cases, with 16 true positives, 0 false positives, 4 false negatives, and 14 true negatives. The calculated results showed a sensitivity of 80%, specificity of 100%, PPV of 100%, NPV of 77.77%, and accuracy of 88.24%.

	FNAB (all cases)	FNAB (With USG-guided)	FNAB (Without USG Guiding)
Sensitivity	80%	83%	80%
Specificity	100%	100%	100%
PPV	100%	100%	100%
NPV	78.26%	75%	77.77%
Accuracy	88.37%	88.88%	88.24%

Table 4 Results of sensitivity, specificity, PPV, NPV and accuracy of FNAB

Based on the results of histogenesis compatibility in the FNAB examination followed by HPA with or without IHK (Table 5), in benign non-cancerous tumors, which totaled 13 cases, 7 cases (53.85%) had samples with matching histogenesis types, and 6 cases (46.15%) had samples with mismatched histogenesis types. In intermediate tumors, all 5 cases (100%) had samples with mismatched histogenesis types. In malignant tumors, there were 24 cases, with 10 cases (41.67%) having matching histogenesis types and 14 cases (58.33%) having mismatched histogenesis types.

Table 5 Conformity of Histogenesis of FNAB with Histopathology Examination with or without Immunohistochemistry

Tumor Type	Histogenesis Conformity	Frequency	Percentage (per tumor type)
Benign	Appropriate Specific Type of Histogenesis	7	53.85%
	Specific Type of Inappropriate Histogenesis	6	46.15%
Intermediet	Appropriate Specific Type of Histogenesis	0	0%
	Specific Type of Inappropriate Histogenesis	5	100%
Malignant	Appropriate Specific Type of Histogenesis	10	41.67%
	Specific Type of Inappropriate Histogenesis	14	58.33%

4. Discussion

4.1. Description of the Distribution and Characteristics of Soft Tissue Tumors Patients who undergo FNAB and HPA with or without IHK

The distribution number of cases in 2022 was higher than in 2020 and 2021. This may be due to the Covid-19 pandemic, which occurred from 2020 to 2021, resulting in lower patient visits to hospitals during this period. Thus, it can be

concluded that the decrease in cases in 2020 and 2021, as observed in this study, was aligned with the impact of the Covid-19 pandemic [14].

Regarding the distribution of malignant (58.14%) and benign tumors (41.86%), malignant tumors were more frequently observed. This could be due to the clinical manifestations that more often pointed to malignancy, which were associated with improved diagnostic practices and referrals for early detection of malignant tumors. Additionally, warning signs or red flags, including increased tumor size, masses larger than 5 cm, deep masses, acute pain onset, recurrence of masses, firmer masses compared to surrounding tissues, and local infiltration, are predictors that a tumor may be malignant. Thus, tumors with the above signs can be classified as malignant [15]. Another factor contributing to the higher incidence of malignant tumors is their aggressive growth pattern, which can appear independently without a previous benign phase, leading to a higher frequency in certain populations [16]. The incidence of malignant tumors observed as the population ages, with more individuals at risk of developing malignant tumors [17]. Regarding size, masses larger than 5 cm are considered more correlated with malignancy, so larger lesions tend to be regarded as malignant [18]. Furthermore, many soft tissue tumors initially thought to be benign were later found to be malignant, changing the perception that malignant tumors might be more common than previously thought [19].

The number of female patients was higher than male patients, with 24 females (55.8%) and 19 males (44.2%). In global cancer statistics for 2022, the total incidence of soft tissue tumors was 13,190 cases, with 7,590 cases occurring in males and 5,600 cases in females [20]. Therefore, the percentage distribution of tumor types by gender in this study does not align with the total incidence of soft tissue tumors. However, it was found that benign tumors were more commonly seen in females, which is consistent with previous literature that states benign tumors are more common in females, with more variability in the results for malignant tumors [21]. This may also occur because the incidence of soft tissue tumors by gender is influenced by the histogenesis type of each tumor [22,4].

The highest number of cases was found in the age group of 21–30 years, with 11 cases (25.59%.) This was followed by the age groups of 11–20 years and 61–70 years, with 7 cases in each (6.28%). The next most common groups were the 41–50 years and 31–40 years groups, each with 6 cases (13.95%). The 51–60 years age group had 5 cases (11.90%), and the least common was the age group over 71 years, with only 1 case (2.32%). This differs from previous studies, where the peak age for soft tissue tumors was found to be between 40 and 60 years [15]. However, the distribution of soft tissue tumor types varies across age groups [22].

Based on the tumor location, the highest number of cases was found in the thigh, with 14 cases (32.56%). This was followed by the arm with 9 cases, representing 20.93%. Next, the knee and lower leg locations had 3 cases each (6.98%). This is consistent with WHO, which states that soft tissue tumors are most commonly found in the extremities, with the thigh being the most frequent site [4].

For benign tumors, 11 cases were found, with the most common tumor being Tenosynovial Giant Cell Tumor (TGCT) with 3 cases (23.07%). Previous literature has found that lipoma is the most common soft tissue tumor found in superficial areas, while TGCT is the most common benign soft tissue tumor found in deeper locations. This is consistent with the current study, where TGCT was the most frequently observed tumor, and there was 1 case each of lipoma and osteolipoma [16]. For intermediate tumors, the most common tumors is fibromatosis-desmoid tumors (locally aggressive) with 3 cases (60%). The incidence of this tumor represents 3% of all soft tissue tumors [23]. For malignant tumors, a total of 29 cases were identified, with the most common diagnosis being Non-Hodgkin Lymphoma (NHL) with 5 cases (20%). This is consistent with literature, which indicates that the most common malignant soft tissue tumors are primarily systemic soft tissue lesions, such as NHL [5].

4.2. Description of Diagnostic Accuracy Results for Soft Tissue Tumors Using FNAB and HPA with or without IHK

False negatives occurred in five cases within this study, as detailed below:

- **Case 1**: A 56-year-old woman with a tumor located in the thigh. FNAB concluded "spindle mesenchymal tumor with atypical cells," but the immunohistochemistry result revealed malignant peripheral nerve sheath tumor (MPNST).
- **Case 2**: A 45-year-old man with a tumor located in the thigh. FNAB concluded "spindle mesenchymal tumor (part of cystic hemorrhagic)," while the histopathology result diagnosed rhabdomyosarcoma.

- **Case 3**: A 51-year-old woman with a tumor in the abdomen. FNAB concluded "adipocytic tumor with atypical cells," whereas histopathology and immunohistochemistry confirmed myxoid liposarcoma.
- **Case 4**: A 65-year-old woman with a tumor in the arm. FNAB concluded "adipocyte cells with inflammation," but histopathology and immunohistochemistry revealed inflammatory leiomyosarcoma.
- **Case 5**: An 84-year-old woman whose FNAB result was "spindle mesenchymal tumor, likely benign." The histopathology result suggested atypical neurofibroma, and further immunohistochemistry confirmed a final diagnosis of low-grade myofibroblastic sarcoma (LGMS).

In **Case 1** and **Case 3**, where FNAB described atypical cells, the tumors were eventually diagnosed as MPNST and myxoid liposarcoma, respectively. For MPNST, diagnostic errors may occur due to the tumor's heterogeneous nature; if the biopsy samples a benign area, false negatives are likely [24]. Similarly, for myxoid liposarcoma, errors may arise due to inadequate sampling of the tumor's malignant areas. Additionally, misinterpretation of critical atypical features, such as necrosis and inflammation, might lead pathologists to mistakenly conclude the tumor is benign [25].

In **Case 2**, FNAB diagnosed a spindle mesenchymal tumor with cystic hemorrhagic changes, while HPA identified rhabdomyosarcoma, a type of malignant round cell tumor. FNAB's diagnosis of spindle cell tumor in this case, highlights the need for improved sampling techniques, as FNAB may not always capture the full spectrum of histological differentiation required for a definitive diagnosis, especially when hemorrhage obscures the specimen [26].

In **Case 4**, FNAB concluded "adipocyte cells with inflammation," while HPA and IHK revealed inflammatory leiomyosarcoma, a tumor originating from smooth muscle cells. The presence of inflammation may obscure the diagnosis and complicate the differentiation between benign and malignant tumors, as well as the tumor's morphology [26].

In **Case 5**, FNAB described the tumor as a "spindle mesenchymal tumor, likely benign." However, HPA raised suspicion of atypical neurofibroma, and further IHK confirmed LGMS. FNAB may sometimes fail to raise suspicion of malignancy because it does not capture the complete histological features [11]. Additionally, HPA and IHK findings between atypical neurofibroma and LGMS revealed similarities in spindle cell morphology, which could lead to interpretative errors [27][28]. Despite the final diagnosis in this case, it is essential to incorporate clinical and radiological data to ensure more accurate pathological conclusions.

The sensitivity results of FNAB (with and without USG-guided) indicate that FNAB (with and without USG-guided) has an 80% ability to correctly diagnose malignant soft tissue tumors as malignant. FNAB with USG-guided demonstrated an 83% accuracy in correctly diagnosing malignant soft tissue tumors as malignant, while FNAB without USG-guided showed an 80% accuracy in doing so. In terms of specificity, the FNAB (with and without USG-guided) results showed 100% specificity. This indicates that FNAB (with and without guidance) has a 100% ability to correctly diagnose nonmalignant soft tissue tumors, including intermediate and benign tumors, as non-malignant. The same specificity of 100% was observed for FNAB, both with and without USG-guided. The positive predictive value (PPV) represents the ability to confirm that individuals with a positive FNAB result indeed have the condition being tested. FNAB (with and without guidance) demonstrated a 100% ability to confirm that individuals with a positive FNAB result truly had the tested condition. This was consistent for FNAB with and without USG-guided, both yielding a PPV of 100%. The negative predictive value (NPV) represents the ability to confirm that individuals with a negative FNAB result do not have the condition being tested. FNAB (with and without guidance) showed a 78.26% ability to confirm that individuals with a negative FNAB result truly did not have the tested condition. FNAB with USG-guided had an NPV of 75%, indicating its ability to confirm the absence of the condition in individuals with a negative result. Meanwhile, FNAB without USGguided demonstrated a 77.77% ability to do so [29].

Regarding the accuracy of FNAB in this study, FNAB (with and without USG-guided) showed an 88.37% ability to predict the correct diagnosis for patients with soft tissue tumors. FNAB with USG-guided had an accuracy rate of 88.88%, while FNAB without USG-guided had an accuracy rate of 88.24%. This level of accuracy highlights the effectiveness of FNAB in diagnosing soft tissue tumors as an initial diagnostic tool, with an overall accuracy of 88.37%, 88.88% for FNAB with USG-guided, and 88.24% for FNAB without guidance [29]. FNAB with USG-guided showed the highest sensitivity, specificity, PPV, and accuracy compared to FNAB overall and without guidance. This finding is supported by several studies, which recommend the use of USG-guided in FNAB. USG-guided is not only cost-effective and easy to perform but also improves biopsy outcomes for soft tissue tumors and reduces errors in sample collection [29].

4.3. Description of Histogenesis Conformity Results for Soft Tissue Tumors Using FNAB and HPA with or without IHK

The histogenesis concordance results from the study of soft tissue tumors conducted in the Pathology Department of RSSA from 2020 to 2022 were classified based on the WHO 2020 classification of soft tissue tumors. The tumors were divided into three categories: benign, intermediate, and malignant. For benign tumors, a total of 13 cases were identified with specific histogenesis types, of which 7 cases matched the specific histogenesis type (58.85%), while 6 cases did not match (46.15%). In intermediate tumors, all 5 cases demonstrated non-concordant specific histogenesis (100%). Meanwhile, in malignant tumors, out of 24 cases with identified histogenesis, 10 cases had concordant specific histogenesis (41.67%), while 14 cases did not match (58.33%).

For benign soft tissue tumors with concordant histogenesis, the cases included schwannoma, epithelioid schwannoma, TGCT, spindle mesenchymal tumor suspected to be nerve sheath tumor, and lipoma. The non-concordant cases included mesenchymoma, two cases of hemangioma, cholesterol granuloma, osteolipoma, and fibroblastic myofibroblastic tumor with adipocyte focus. In the mesenchymoma case, errors may have occurred due to inflammation that caused interpretative challenges [30]. One hemangioma case was initially diagnosed as myositis ossificans, while another case was suspected to be "fibrous connective tissue dd benign vascular tumor." This discrepancy likely arises because hemangiomas consist of a mix of endothelial cells, pericytes, and smooth muscle cells, which may confuse cytological evaluation, especially if FNAB does not capture the tumor's full architecture [31]. For cholesterol granuloma, misdiagnosis may result from its complex composition, which includes foreign body giant cells and chronic inflammatory infiltrates that complicate FNAB diagnosis [32]. Similarly, in osteolipoma, initial diagnosis involved calcification with differential diagnoses of adipose, bony, and fibrous tissues. The overlap between adipose and bone tissues led to histogenesis discordance [33][34]. In one spindle mesenchymal tumor with adipocyte involvement (initially diagnosed as fibroblastic myofibroblastic tumor with adipocyte focus dd fibrolipomatous hamartoma), FNAB indicated "spindle mesenchymal tumor with myxoid matrix, potentially skeletal muscle tumor dd fibroblastic myofibroblastic tumor." This resulted in histogenesis discordance because the match was only morphological (spindle mesenchymal cell tumor), not histogenetically specific. However, the pathologist had already narrowed down the differential diagnosis.

For intermediate soft tissue tumors, all three desmoid tumor/fibromatosis cases showed non-concordant histogenesis. This is attributed to desmoid tumors' histological features, which resemble other fibrous lesions like fibrosarcomas. Inadequate FNAB sampling and overlapping histological characteristics make determining tumor histogenesis challenging [35][36]. In this study, FNAB diagnosed desmoid tumors as fibroosseous lesions, fibroblastic myofibroblastic tumors, and suppurative inflammation[37]. For two cases of atypical lipomatous tumors, significant overlap with benign lipomatous lesions, such as lipomas, was noted, as reported in this study.

Regarding malignant soft tissue tumors, 10 cases showed concordant histogenesis, including extraskeletal Ewing sarcoma, NHL, alveolar soft part sarcoma, MPNST, synovial sarcoma, and myxofibrosarcoma. Meanwhile, 14 cases demonstrated non-concordant specific histogenesis, including MPNST, rhabdomyosarcoma, poorly differentiated synovial sarcoma, anaplastic large cell lymphoma, myxoid liposarcoma, dedifferentiated liposarcoma, myxofibrosarcoma, leiomyosarcoma, LGMS, high-grade sarcoma, and NHL [38][39]. MPNST often presents with heterogeneous histological compositions, including pleomorphic cells, necrosis, and varying levels of cellularity. FNAB sampling may not represent the tumor's complete architecture, leading to interpretive challenges. MPNST morphology also overlaps with other sarcomas that similarly feature atypical spindle cells with myxoid backgrounds [40]. A similar issue arises with rhabdomyosarcoma, where the diagnosis of spindle mesenchymal tumors can resemble other sarcomas, complicating the diagnostic process. In poorly differentiated synovial sarcoma, the cytological features are highly heterogeneous, mixing pleomorphic spindle cells. This discordance arose because FNAB diagnosed the case as a small round cell tumor, differing in morphology. Leiomyosarcoma also overlapped with other spindle cell tumors, such as dermatofibrosarcoma protuberans [41]. Anaplastic large cell lymphoma exhibits significant cytological heterogeneity, complicating FNAB diagnosis. In this study, FNAB diagnosed the case as high-grade sarcoma [42]. For malignant small round cell tumors dd NHL, FNAB diagnosed the case as "malignant small round cell tumor dd metastatic carcinoma dd undifferentiated small round cell sarcoma, NHL." While both share a "small round cell tumor" morphology, their specific histogenesis differed, despite overlapping differential diagnoses. A similar error occurred in Ewing sarcoma cases, where FNAB identified "malignant small round cell tumor suspected of NHL lymphoblastic type dd Ewing sarcoma." This error may occur because both have the morphology of a small round cell tumor [43]. In myxoid liposarcoma, histogenesis discordance occurred because FNAB misdiagnosed the tumor's adipocyte cells as benign despite morphological clues toward adipocyte tumors. In dedifferentiated liposarcoma, while malignancy was suspected, histogenesis did not align. Myxofibrosarcoma, diagnosed as malignant lymphoma via FNAB, also showed discordance. Similarly, leiomyosarcoma was initially diagnosed as malignant spindle cell tumor. LGMS cytology

overlapped with other spindle cell tumors, and FNAB histogenesis remained non-concordant [44]. High-grade sarcomas often display significant cytological variability, including pleomorphic cells, atypical mitosis, and necrosis. Such variability complicates FNAB interpretation, as samples may not fully represent tumor characteristics. Their cytological features can resemble other malignancies, like undifferentiated pleomorphic sarcomas or metastatic tumors, further complicating diagnosis. In this study, FNAB identified high-grade sarcomas as malignant spindle cell tumors [44][41]. In malignant round cell tumor dd lymphoproliferative disorder suspected as NHL, the initial diagnosis was "malignant tumor with plasmacytoid cells dd plasma cell myeloma dd Non-Hodgkin Lymphoma of lymphoplasmacytic type." Despite malignancy being consistent, the similarity in plasma cell density caused diagnostic overlap [45].

Limitations of the Study

The limitations of this study include a lack of research samples. The limited number of samples from 2020 to 2021 posed a challenge because their distribution was significantly different compared to 2022. This discrepancy may have been caused by the COVID-19 pandemic, which reduced the public's participation in seeking medical care at hospitals. In terms of medical records, the limitations included a lack of integration for individual patients and the inclusion of all examinations they had undergone. This posed challenges for data collection by the researchers, as patient medical records had to be retrieved from multiple different sources. Additionally, factors such as patients discontinuing treatment, passing away, or failing to continue follow-up examinations could not be confirmed. This study evaluated the final pathological diagnosis of tumors with the involvement of radiological modalities. However, radiological conclusions were not included in this study.

5. Conclusion

Based on the results of this study, it can be concluded that FNAB with USG-guided has the highest sensitivity, specificity, positive predictive value (PPV), and accuracy compared to FNAB without USG-guided. Therefore, the use of FNAB with USG-guided can enhance the accuracy of diagnosing soft tissue tumors. These findings are beneficial for the wider community as they contribute to improving the diagnostic process for soft tissue tumors, enabling timely and precise treatment.

Compliance with ethical standards

Acknowledgments

The authors would like to express their gratitude to the Faculty of Medicine, Universitas Brawijaya, for providing the research grant that enabled the authors to conduct this study.

Disclosure of conflict of interest

The authors affirm that there are no conflicts of interest regarding the conduct, results, or publication of this study.

Statement of ethical approval

The data used in this study were obtained from medical records approved by the Ethics Committee of Dr. Saiful Anwar General Hospital.

Statement of informed consent

Informed consent was obtained from all patients prior to any procedures being conducted.

References

- [1] Kumar V, Abbas AK, Aster JC. Robbins Basic Pathology. 10th ed. Elsevier; 2018.
- [2] Gamboa AC, Gronchi A, Cardona K. Soft-tissue sarcoma in adults: An update on the current state of histiotypespecific management in an era of personalized medicine. CA Cancer J Clin. 2020;70(3):200–229.
- [3] Jarwani PB, Babaria SS, Joshi DS, Suri SK. Evaluation of soft tissue tumors with immunohistochemistry correlation. 2022.

- [4] Antonescu CR, Bridengane JA, Cunha IW, et al. WHO Classification of Tumours Soft tissue and bone tumours. 5th ed. International Agency for Research on Cancer (IARC); 2020.
- [5] Picci P, Donati DM, Gambarotti M, Righi A, Vanel D, Tos AP. Clinical, Radiological and Histological Correlations-The Rizzoli Case Archive Diagnosis of Musculoskeletal Tumors and Tumor-like Conditions. 2020.
- [6] Mahyudin F, Edward M, Basuki MH, Basrewan Y, Hernugrahanto KD, Wahyudiputra AG. Analysis of prognostic factors in soft tissue sarcoma: Cancer registry from a single tertiary hospital in Indonesia. A retrospective cohort study. Ann Med Surg (Lond). 2020; 57:257–63.
- [7] Choi JH, Ro JY. The Recent Advances in Molecular Diagnosis of Soft Tissue Tumors. Int J Mol Sci. 2023;24(6).
- [8] Cibas ES, Ducatman BS. Cytology: Diagnostic Principles and Clinical Correlates. 2014.
- [9] Orell S, Sterrett G. Fine Needle Aspiration Cytology. 5th ed. Elsevier; 2012.
- [10] Juniwan G, Hidayat L, Magetsari R. Evaluation of fine-needle aspiration biopsy as a supporting diagnostic tool in bone and soft tissue sarcoma patients at Sardjito General Hospital. Universitas Gadjah Mada; 2021.
- [11] Putri V, Stephanie M. Akurasi FNAB 2015-2019 RSCM FK UI. Maj Patol Indones. 2022;31(1):376-84.
- [12] Ariizumi T, Kawashima H, Yamagishi T, et al. Diagnostic accuracy of fine needle aspiration cytology and core needle biopsy in bone and soft tissue tumor: A comparative study of the image-guided and blindly performed procedure. Ann Diagn Pathol. 2022;59.
- [13] Sahu AK, Parkar MK. A retrospective study on utility of fine needle aspiration cytology (FNAC) in the diagnosis of soft tissue tumors and tumor-like lesions. Stud J Health Res Afr. 2023;4(3):8.
- [14] Sarasnita N, Raharjo UD, Rosyad YS. Dampak pandemi covid-19 terhadap pelayanan kesehatan rumah sakit di Indonesia. Jurnal Kesehatan. 2021;1(1):307–15.
- [15] Shakya S, Banneyake EL, Cholekho S, Singh J, Zhou X. Soft tissue sarcoma: clinical recognition and approach to the loneliest cancer. Explor Musculoskelet Dis. 2024;2(1):56–68.
- [16] Gassert FG, Specht K, Knebel C, Lenze U, Makowski MR, von Eisenhart-Rothe R, Gersing AS, Woertler K. Soft tissue masses: distribution of entities and rate of malignancy in small lesions. BMC Cancer. 2021; 21:1–10.
- [17] Achar S, Yamanaka J, Oberstar J. Soft tissue masses: evaluation and treatment. Am Fam Physician. 2022;105(6):602–12.
- [18] Araki Y, Yamamoto N, Maeda T, et al. Management of soft-tissue tumors with a size of 2–5 cm, including malignancy. Anticancer Res. 2022;42(3):1555–62.
- [19] Van Vliet M, Kliffen M, Krestin GP, et al. Soft tissue sarcomas at a glance: clinical, histological, and MR imaging features of malignant extremity soft tissue tumors. Eur Radiol. 2009; 19:1499–511.
- [20] Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72(1):7–33.
- [21] Teferi SM, Tadele AK, Ayele SA, Wodajo AA, Korga TI. Histopathologic patterns of soft tissue tumors in Hawassa University Comprehensive Specialized Hospital, Sidama Ethiopia: A 5-year retrospective study. Clin Oncol. 2022; 7:1951.
- [22] Lindberg MR. Diagnostic Pathology: Soft Tissue Tumors. Elsevier Health Sciences; 2023.
- [23] Ma J, Ma Z, Dong X, Yin H, Zhao Y. Abdominal wall desmoid tumors: a case report. Oncol Lett. 2013;5:1976–8.
- [24] Brahmi M, Thiesse P, Ranchere D, et al. Diagnostic accuracy of PET/CT-guided percutaneous biopsies for malignant peripheral nerve sheath tumors in neurofibromatosis type 1 patients. PLoS One. 2015;10(10):e0138386.
- [25] Bianchi G, Laranga R, Spinnato P, et al. Sensitivity, specificity, and predictive values of Tru-cut® biopsy in grading primary localized myxoid liposarcomas of the extremities. Cancers. 2023;15(5):1391.
- [26] Asim M, Mudassir G, Hashmi AA, Abid M, Sheikh AK, Naveed H, et al. Diagnostic accuracy of fine needle aspiration biopsy in pediatric small round cell tumors. BMC Res Notes. 2018;11(1):573. doi:10.1186/s13104-018-3678-x.
- [27] Park, H.J., Choi, Y.G., Chae, S.W. and Kim, W.S., 2023. Low-Grade Myofibroblastic Sarcoma on Back with Repeated Localized Recurrence and Regional Metastasis. *Annals of Dermatology*, *35*(Suppl 2), p.S219.
- [28] Suster, D., 2022. Spindle cell tumors of the mediastinum. *Annals of Diagnostic Pathology*, *60*, p.152018.

- [29] Shreffler J, Huecker MR. Diagnostic testing accuracy: sensitivity, specificity, predictive values and likelihood ratios. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023.
- [30] Ratzon, F., Feliciano, D.L., Katabi, N., Xu, B., Lin, O. and Wei, X.J., 2023. Salivary gland fine-needle aspiration biopsy: quality assurance results from a tertiary cancer center. *Journal of the American Society of Cytopathology*, *12*(3), pp.206-215
- [31] Chamli A, Aggarwal P, Jamil RT, et al. Hemangioma. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024.
- [32] Jin M, Wu Q, Miao B, et al. Multiple cholesterol granulomas of the breast: a case report and review of the literature. Medicine. 2023;102(8):e33084
- [33] Wong BLK, Hogan C. Osteolipoma of head and neck a review. Braz J Otorhinolaryngol. 2022;88 Suppl 4:S177– 87.
- [34] Ogun G. O. (2015). Fine needle Aspiration Biopsy (FNAB) in the initial evaluation and diagnosis of palpable soft tissue lesions and with histologic correlation. The Pan African medical journal, 20, 44. https://doi.org/10.11604/pamj.2015.20.44.4271
- [35] Master SR, Mangla A, Shah C. Desmoid Tumor. [Updated 2024 Mar 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459231/
- [36] Bektas M, Bell T, Khan S, Tumminello B, Fernandez MM, Heyes C, et al. Desmoid tumors: a comprehensive review. Adv Ther. 2023;40(9):3697-3722.
- [37] Lott-Limbach AA, Wakely Jr PE. Mediastinal sarcomas: experience using fine needle aspiration cytopathology. Mediastinum. 2020;4:13.
- [38] Rodriguez FJ, Folpe AL, Giannini C, Perry A. Pathology of peripheral nerve sheath tumors: diagnostic overview and update on selected diagnostic problems. Acta Neuropathol. 2012;123(3):295-319.
- [39] Prudner BC, Ball T, Rathore R, Hirbe AC. Diagnosis and management of malignant peripheral nerve sheath tumors: Current practice and future perspectives. Neuro-Oncol Adv. 2020;2(Suppl 1):i40-i49.
- [40] Kaseb H, Kuhn J, Gasalberti DP, et al. Rhabdomyosarcoma. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024.
- [41] Singh HK, Kilpatrick SE, Silverman JF. Fine needle aspiration biopsy of soft tissue sarcomas: utility and diagnostic challenges. Adv Anat Pathol. 2004;11(1):24-37.
- [42] Rapkiewicz A, Wen H, Sen F, Das K. Cytomorphologic examination of anaplastic large cell lymphoma by fineneedle aspiration cytology. Cancer Cytopathol. 2007;111(6):499-507.
- [43] Yoshida, A., 2023. Ewing and Ewing-like sarcomas: A morphological guide through genetically-defined entities. *Pathology International*, 73(1), pp.12-26.
- [44] Olson, M. T., & Ali, S. Z. (2012). Myxofibrosarcoma: cytomorphologic findings and differential diagnosis on fine needle aspiration. Acta cytologica, 56(1), 15–24. https://doi.org/10.1159/000333134
- [45] Chodijah N, Murti K, Rasyid RS. The relationship between plasma cell density and clinicopathological characteristics in diffuse large B-cell lymphoma. Sriwijaya J Med. 2021;4(2):92-9. doi:10.32539/SJM.v4i2.105.