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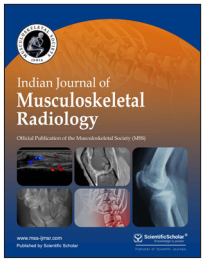

Original Article

Soft-tissue sarcoma biopsy: A safe and well-tolerated technique with a high diagnostic yield – A 5-year review of more than 800 cases

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ABSTRACT

Objectives: The objectives of this study were to assess the diagnostic yield, accuracy, and complication rate of the US-guided core-needle biopsy technique for suspected soft-tissue sarcomas (STSs) and review this against other published practices.

Material and Methods: A 5-year retrospective study was performed of consecutive US-guided percutaneous biopsy for suspected STSs, with 815 planned procedures in 799 patients (average age 57.8 years, [range 15–95] with 54.7% male). Diagnostic yield was recorded as positive for a sample that allowed differentiation of benign and malignant lesions. Diagnostic accuracy was defined as the correlation between biopsy and surgical specimen when excision was performed. Immediate and late complications were documented. The patient procedural experience was recorded by a departmental questionnaire.

Results: Diagnostic yield was positive in 751/778 (96.5%) with no immediate, short- or long-term complications. Of 815 planned biopsies, 778 core biopsies were obtained. Of the 37 biopsy cases, where the tissue was not obtained, nine were not performed due to patient factors and a further 28 could not be obtained for other technical reasons (e.g., the lesion being too hard to penetrate or too painful to the core). 27/778 (3.5%) of biopsies were non-diagnostic (96.5%) and of these 27, nine patients were followed up clinically, 13 biopsies were repeated, and five cases were surgically excised without further biopsy attempts.

Conclusion: The described soft-tissue mass US-guided percutaneous core-needle biopsy technique demonstrates a high diagnostic yield and accuracy with a low complication rate. The diagnostic yield appears comparable to data published by other institutions with more invasive techniques.

Keywords: sarcoma, US-guided biopsy, sarcoma biopsy, soft-tissue sarcoma, sarcoma histology

INTRODUCTION

Soft-tissue sarcomas (STSs) are a heterogenous group of malignant tumors with varying radiological and histopathological features that can make an accurate diagnosis and lesion grading challenging. STS is rare with the average GP seeing only one of these lesions in their career.[1] Approximately 3000 of these tumors are diagnosed annually in the United Kingdom.[2] Due to their rarity and significant implications for patient survival, suspected STSs are referred to specialist centers within the UK for review by a multidisciplinary team.

It is recognized that a definitive diagnosis of a suspected STS on imaging is challenging and may only be possible in less than a third of cases (24%), with imaging not always reliably distinguishing between benign and malignant soft-tissue tumors.[3] Patients with clinically and/or radiologically suspicious masses typically proceed to biopsy. Ultrasound-guided percutaneous core-needle biopsy (US-CNB), therefore, plays a significant role in allowing histological analysis to guide further management which can alleviate the need for open biopsy.[4,5] Imaging allows assessment of the biopsy approach to target the most appropriate and viable area(s) for tissue sampling while minimizing tissue disruption and optimizing patient safety and comfort. Despite clear consensus on the use of US-CNB, variations in practice exist within the United Kingdom and internationally with no agreed standard biopsy technique, sample number, or needle gauge size.[6] In addition, no specific guidance outlines the minimum expected diagnostic accuracy with a Royal College of Radiologists figure of "80–90%" yield for percutaneous biopsy procedures in general based on Society of Interventional Radiology data from 2004.[7] It is currently unclear whether this is optimal in the context of malignant STS, where an accurate histological diagnosis is complicated by marked subtype variety and increasing dependency on additional molecular analysis.

The primary objective of this 5-year retrospective review was to assess the diagnostic yield and accuracy of our standardized US-CNB technique and assess how this compares to other documented evidence in the literature. Our institution attempts to maintain a high-diagnostic yield while ensuring a positive patient experience with a low complication rate.

MATERIALS AND METHODS

Institutional guidance deemed ethics committee/IRB approval was not required for this retrospective review of clinical service.

A retrospective review was performed of continuous US-CNB cases for suspected appendicular and truncal STS referred from the regional sarcoma service over 5 years between January 2016 and December 2020. Retroperitoneal and intrathoracic STS were excluded from the study. All cases were obtained from the Computerised Radiology Information System (CRIS) between January 1, 2016, and December 31, 2020, using the US biopsy code "UBIOP." A total of 815 planned US-CNB procedures were identified in 799 patients (This included repeated biopsies and one patient with a biopsy of two separate lesions).

US-CNB technique

US-CNB was performed by one of five experienced consultant musculoskeletal radiologists (with 5–21 years of experience), a post-CCT musculoskeletal radiology fellow or senior trainee under supervision. The optimal intralesional location for biopsy was planned before the procedure using prior MRI and/or US in addition to further US evaluation during the procedure in real time.

Patients underwent verbal informed consent and were screened for anticoagulant medication; however, the clotting profile was not routinely checked. All biopsies were performed under local anesthesia using lidocaine 1%. A sterilized covered high frequency linear transducer (ML6-15 matrix array transducer, Logiq E9, General Electric, Boston, USA) was used to guide a 16-gauge trucut biopsy needle (Original Temno® 16G 6 cm [T166] biopsy needle, Merit Medical, Utah, USA) into the lesion. For more superficial and/or smaller lesions, a smaller 18-gauge biopsy needle (Original Temno® 18G 6 cm [T186] biopsy needle) was used for technical optimization and patient comfort (e.g., symptomatic neural lesion).

Where possible, three macroscopically good-quality solid cores of tissue were obtained but in cases of patient agitation or discomfort, if two good-quality cores were obtained that the procedure was terminated at that point. Rarely, more than three cores were obtained if the initial cores appear macroscopically non-diagnostic (e.g., highly necrotic or fluid-filled lesions).

Following the procedure, after achieving hemostasis patients were discharged following a 10-min period of observation.

Diagnostic yield and accuracy

Diagnostic yield was defined when the histopathologist had enough biopsy tissue that allowed provisional differentiation of benign versus malignant tumors.

Diagnostic accuracy was defined as the ability of the histopathologist to differentiate the histological subtype of malignant or benign tumor and allow assessment of tumor grade in cases of malignancy and this could be compared to the surgically excised sample taken as the gold standard.

Following US-CNB the CRIS, PACS and Electronic Health Records (EHRs) systems were used to assess whether the sample was adequate for histological analysis and diagnosis. If malignant, the tumor subtype and grade were documented [Figure 1]. Other data metrics, such as the patient's age, sex, the level of experience of the performing radiologist, a gauge of biopsy needle, the number of cores obtained, and lesion location were also recorded.

Where a discrepancy arose between the US-CNB and surgical specimens in both benign and malignant cases, consideration was made for "true" discrepancies that would lead to a change in subsequent management [Figure 2]. True discrepancies were defined using four different metrics: (1).

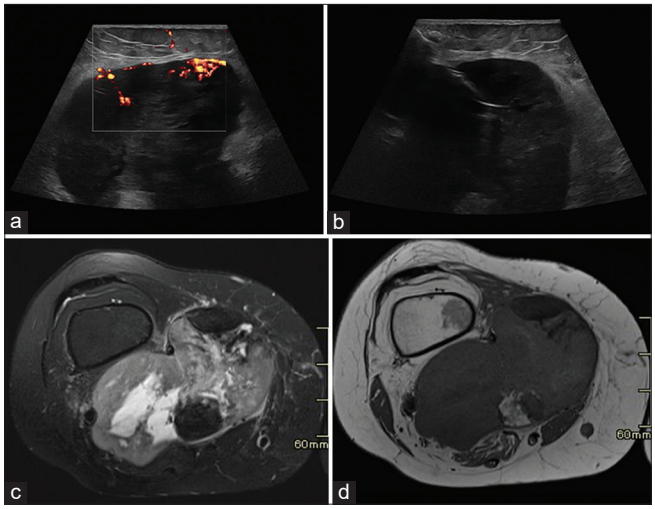

Figure 1: Grade 3 liposarcoma. Core biopsy and surgical specimens were concordant. Ultrasound (a) shows a solid hypoechoic and hypervascular mass. (b) Ultrasound-guided biopsy with a 16-gauge needle in position within the lesion (3) cores obtained). Axial STIR (c) and T1-weighted (d) MRI show the mass involving multiple compartments of the thigh.

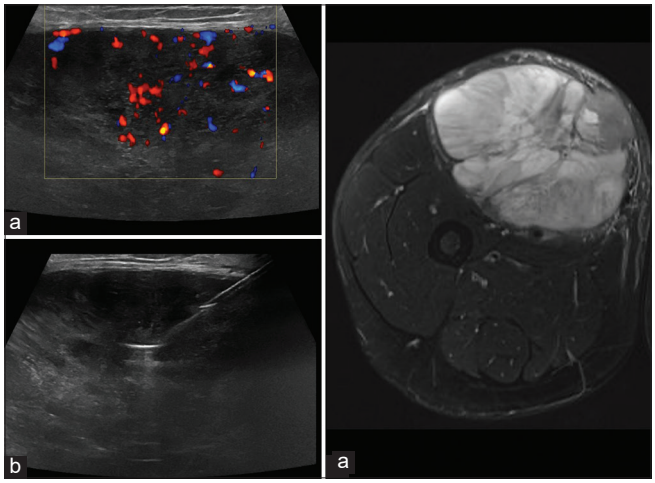

Figure 2: True discrepant lesion with a diagnosis of Grade 1 spindle cell sarcoma on core biopsy and Grade 3 fibromyxosarcoma following surgical excision. (a) Ultrasound demonstrates a hypervascular and heterogeneously hypoechoic mass in the right thigh. (b) Ultrasound image depicting 16-gauge core biopsy needle within the lesion (3 cores obtained). Axial STIR MRI (c) shows an aggressive mass centered on the sartorious muscle displacing the femoral neurovascular bundle.

Benign lesion on US-CNB that was subsequently proven malignant on surgical resection, (2). malignant lesion on US-CNB that was subsequently proven benign on surgical resection, (3). low-grade (Grade 1) malignancy on US-CNB that was subsequently proven high-grade (Grade 2/3) on surgical resection, and (4). the discrepancy between the histological subtype of malignancy between US-CNB and surgical specimens.

Procedural complications and patient procedure feedback

Immediate complications were defined as prolonged bleeding (>10 min), hematoma formation, or a significant increase in pain following the procedure. All patients were reviewed in the sarcoma clinic 3–5 weeks post-procedure by a consultant oncological surgeon and specialist oncological nurse. Late complications included any documented evidence of infection, hematoma, or if the patient stated any other problems since the procedure. Immediate complications were assessed through a review of the radiological report and late complications through the clinical outpatient EHR record.

Immediate quantitative and qualitative patient experience data were collected through a post procedural questionnaire during the 5 years. This comprised the following questions: (1) Were you aware of what the procedure would involve? (2) Was the procedure explained in a way that you fully understood? (3) Were you happy with the treatment by staff during the procedure? (4) Were you fully aware of what happens after the procedure? (5) Was the procedure more or less painful than you expected?

RESULTS

In the total cohort of 799 patients, the average age was 57.8 years (range 15–95 years). Four hundred and thirty-seven patients were male (54.7%) with 362 female patients (45.3%).

Diagnostic yield and accuracy

US-CNB yield was diagnostic in 751/778 (96.5%) of the biopsy cases. Of the 27 non-diagnostic samples, four were necrotic, four contained normal skeletal muscle/tissue, ten had insufficient tissue, two samples contained non-specific inflammatory tissue/fat, one sample contained keratin only, one contained fibrous tissue only, and five cases were not specified.

Of these 27 cases, 13 patients underwent repeat radiologically guided biopsy, five had excision biopsy, one patient died before repeat, and eight patients were managed conservatively through the sarcoma MDT with lesion monitoring [Figure 3]. Overall, 15% of non-diagnostic samples were necrotic which is assessed for in the pre-procedural scan, but in some instances of highly necrotic lesions, it may still be challenging to obtain tissue. Of the 13 repeated biopsies, seven were malignant and six were benign lesions. Of the malignancies, sub-types were as follows; liposarcoma, spindle cell sarcoma, fibrosarcoma, and alveolar sarcoma. Of the six

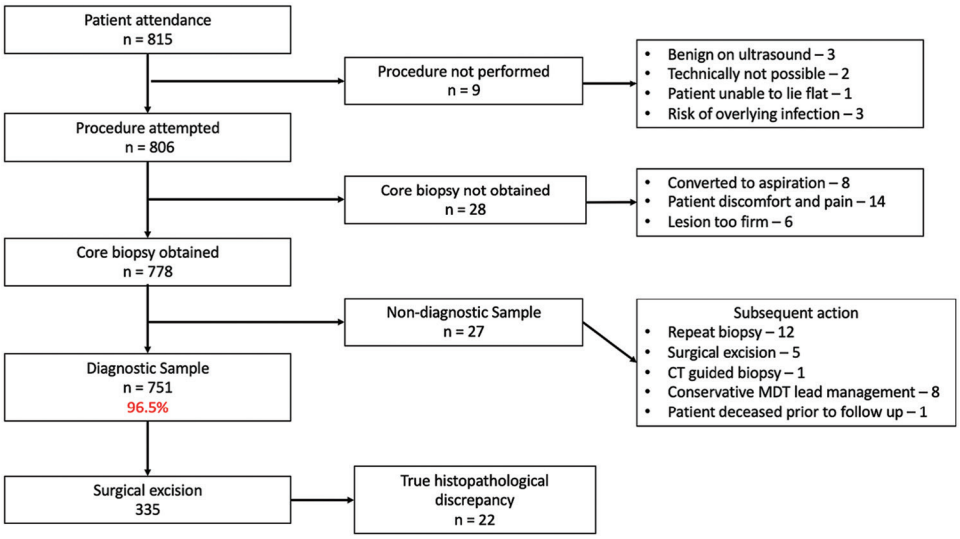

Figure 3: Flowchart showing the study population for the 5-year period between January 2016 and December 2020.

benign cases, five were lipomas with one case of fibromatosis. Of the five cases, where a non-diagnostic biopsy was followed by excision, two were benign lipomatous lesions, one case of fat necrosis, and two were malignant cases (liposarcoma and malignant ossified fibromyxoid tumor).

Of the 751 diagnostic samples, 335 lesions (43%) were subsequently excised surgically. US-CNB diagnostic accuracy was 313/335 (93.4%) resected lesions which were concordant. Twenty-two (6.6%) discordant lesions met the criteria for the true discrepancy which equates to an overall true discrepancy rate of 2.8% of the 778 biopsies performed. These discrepancies are summarized in [Table 1].

Secondary data outcomes are presented in [Table 2]. A 16-gauge biopsy needle was used in 636 biopsies (81.7%) and an 18-gauge needle was used in 78 (10.3%) cases. In 7% of cases, the gauge was not documented. A further 1% of cases had a mixture of 16/18G cores or sampling with smaller 20 or 22G needles [Table 2]. Seven hundred and eight of 778 cases (91%) had either two or three cores obtained (334 patients [42.9%] had two cores and 374 patients [48.1%] had three cores) with 32 patients (4.1%) requiring four and 23 patients (3%) only tolerating a single core. In 12 cases, the number of cores was not clearly documented.

Procedural complications and patient procedure feedback

No significant intra- or post-procedural complication was documented over the 5 years reviewed. Patient feedback was positive and consistent over the 5 years. Data show that patients were aware of what the procedure would involve with annual feedback ranging from 92% to –98% in agreement. About 100% of patients felt that the procedures were explained in a way that they fully understood and 100% were happy with their treatment by staff during their procedure. About 98–100% of patients were aware of the process following their procedure. About 4% of patients who biopsied found the procedure more painful than expected. It is worth noting that of the 28 biopsies that were unable to be taken 14 of these were due to pain with eight out of 14 of these confirmed as Schwannomas at excision biopsy. A further unexcised lesion in a patient with known neurofibromatosis type 1 was clinically suspected to be neural in origin.

DISCUSSION

STSs require an accurate and timely diagnosis to guide appropriate management pathways including neoadjuvant chemotherapy or radiotherapy. Accurate tissue sampling is an important step in the characterization of soft-tissue tumors to determine treatment and prognosis. In our institution, US-CNB is preferred to CT-guided or excision biopsy as it does not require radiation exposure, provides real-time images of the biopsy needle, and is faster and less invasive than a surgical excision biopsy. Our US-CNB technique using 14-16 gauge needles with 3 or fewer samples taken shows a high diagnostic yield and accuracy. Historically, an incisional biopsy was proven to have a slightly higher histological yield with one 1996 paper quoting 94% diagnostic compared to 83% for US-CNB.[8] Subsequently, the adequacy of US-CNB was shown to be analogous when compared to surgical excision when Heslin *et al.* reviewed 164 cases of primary STS in 1997, showing that US-CNB was adequate for diagnosis with a yield of 93% and an accuracy for malignancy of 95% when compared with the final surgical specimen.[9] It is worth

Table 1: True discrepancies between core-needle biopsy and the surgical specimen.

Core-needle biopsy benign versus surgical specimen proven malignant (*n*=8)	
Core-needle biopsy	**Excision biopsy**
Soft-tissue tumor of uncertain nature	Grade 2 spindle cell sarcoma
Benign lipoma	Grade 1 liposarcoma
Spindle cell tumor of uncertain nature	Grade 3 pleomorphic sarcoma
Borderline malignant fibroblastic tumor	Pleomorphic liposarcoma
Malignant myxoid tumor	Grade 3 pleomorphic liposarcoma
Myxoid neoplasm	Acral myxoinflammatory myofibroblastic sarcoma
Schwannoma	Grade 3 malignant nerve sheath tumor
Spindle cell tumor	Grade 2 myxofibrosarcoma
Core-needle biopsy malignant and surgical specimen benign (*n*=4)	
Core-needle biopsy	**Excision biopsy**
Low-grade fibromyxoid sarcoma	Desmoplastic fibroblastoma
Spindle cell sarcoma	Desmoid fibromatosis
Low-grade spindle cell malignancy	Benign ancient Schwannoma
Recurrent well-differentiated grade 1 liposarcoma	Lipoma
Core-needle biopsy low-grade (Grade 1) tumor but surgical specimen high-grade tumor (Grade 2 or 3) (*n*=8)	
Core-needle biopsy	**Excision biopsy**
Grade 1 spindle cell sarcoma	Grade 3 fibromyxosarcoma
Grade 1 spindle cell sarcoma	Grade 3 leiomyosarcoma
Well-differentiated liposarcoma	Well-differentiated liposarcoma with area of de-differentiation.
Fibrous low-grade tumor	Grade 3 spindle cell sarcoma
Low-grade sclerosing liposarcoma	De-differentiated liposarcoma
Grade 1 liposarcoma	Dedifferentiated liposarcoma
Borderline tumor	Grade 2 spindle cell sarcoma
Grade 1 spindle cell sarcoma	Grade 3 myxofibrosarcoma
Malignant core-needle biopsy and surgical specimen with a discordant sarcoma diagnosis (*n*=2)	
Core-needle biopsy	**Excision biopsy**
Lymphoma	Myxofibrosarcoma
Grade 2 myxoid sarcoma	Malignant nerve sheath tumor

noting that these papers and many others do not discuss yield or accuracy concerning benign masses.

Recent data from a 2020 review of the STS biopsy technique with subsequent histological results compared the radiological and surgical grading of proven malignant lesions.[10] The authors suggested the use of 14-gauge needles with an average of 5 cores obtained. Again, benign masses were excluded. In this paper, histological discrepancies still occurred despite this relatively larger volume of tissue sampling with four out of 118 (3.3%) cases deemed to be "true" discrepancies. Although there were 17 cases of tumor grade mismatch overall (15%), only four of these were from low grade (grade 1) to high grade (grade 2/3). In 2011, Peer *et al*. reported a diagnostic yield of 94.6% in 223 lesions biopsied consisting of both benign and malignant masses. About 94.5% of biopsies were performed using a 14-gauge trucut needle with the remainder using a 16-gauge. When taking three to five cores, the diagnostic yield was 94.3%, and with 5–10 cores this was 94.7% with no statistically significant difference. They found a yield of 100% with more than 10 cores; however, this was only performed in eight biopsies. Overall the authors found no significant difference between the needle gauge, number of cores, or other technical factors concerning the overall diagnostic yield or accuracy.[11] Further, work by Kim and Chung in 2015 undertook a retrospective review of 500 US-CNB's of both benign and malignant lesions and described a diagnostic yield of 437/500 (87%) for lesions >2 cm. In the paper, this figure only contained "category 1" lesions, in which an accurate diagnosis was able to be made that correlated with surgical resection. There were 41 further "category 2" lesions that, although not necessarily concordant with definitive histological subtype, were predictive of benign versus malignant disease. This, in combination with category 1, gives a subsequent "true" diagnostic yield of 95.6% which is analogous when compared with our own institutional definition of diagnostic yield (96.5%). The biopsies were

Table 2: Summary data of needle gauge used, number of cores obtained, and documentation of needle position within the lesion on PACS.

Diagnostic ultrasound biopsy result		
Benign or malignant	**Number (*n*=751)**	**Percentage**
Benign	448	59.7
Malignant	303	40.3
Needle biopsy gauge		
Gauge of needle	**Number (*n*=778)**	**Percentage**
16G	636	81.7
16G and 18G	3	0.4
18G	80	10.3
20G	2	0.3
22G	3	0.4
Not specified	54	6.9
Image documentation of needle position		
Image saved to PACS	**Number (*n*=778)**	**Percentage**
Yes	718	92.3
No	60	7.7
Number of cores obtained		
Number of cores	**Number (*n*=778)**	**Percentage**
1 core	23	3.0
2 core	334	42.9
3 core	374	48.1
4 core	32	4.1
5 core	2	0.3
6 core	1	0.1
Not specified	12	1.5

performed using a variety of needle gauges (14–20-gauge); an 18-gauge needle was used in just over half of cases (253/500 or 50.6%) with the remaining needle size breakdown not specified. The number of cores obtained ranged from 1 to 12 with an average of 4.7 cores.[12]

Further, data on CNB gauge were undertaken by Lin *et al*. The authors used 16–20 gauge trucut needles and sampled between two to four cores demonstrating a 100% sample yield for histological assessment.[13] Our data confirm a high diagnostic yield of 96.5% for our US-CNB technique while predominantly using a 16- or 18-gauge needle and typically obtaining 3 or fewer cores. In 2016, Colletti *et al*. reviewed that 215 consecutive biopsies performed with an 18- or 20-gauge trucut biopsy needle and assessed both benign and malignant diagnoses in their analysis. One hundred and sixty-one cases (74.9%) were surgically resected (130 were malignant, 8 suspicious, and 23 benign). The overall diagnostic concordance rate of 96.9% only included those lesions that were subsequently surgically resected.[14]

Few studies assess the analysis of the patient's perception of the procedure or complications. Our described technique using a 16-gauge needle and a 2.5 core average should result in a more efficient process with less patient morbidity and discomfort. Although our complication rate was low and patient satisfaction high, there are little data to directly compare with procedures using larger gauge biopsy needle and the number of sample cores. Our technique may be modified on a case-by-case basis, for example, an increased size biopsy needle or a number of cores has been suggested if certain diagnoses are clinically or radiologically suspected before biopsy and require more tissue for specialist tests (e.g., lymphoma).[15] Conversely, lesions within a critical area (e.g., highly vascular or innervated) may require smaller cores to reduce the risk of complication.[15]

In our institution, we do not routinely mark the biopsy tract for surgical excision, although we do pragmatically try to contaminate as few compartments as possible when obtaining tissue. It remains a contentious topic with STS biopsy whether tumor seeding of the biopsy tract is a real risk. While this is a recognized issue for bone tumors, it has yet to be confirmed to be an issue in soft-tissue primary tumors. Barrientos-Ruiz *et al*. suggested that biopsy tract contamination could occur but only described a single case of tract contamination occurring through a percutaneous approach which was confirmed to be bone chondrosarcoma with no documentation of STS tract recurrence in their review of 221 cases.[16] Siddiqi *et al*. reviewed this contentious area in 2017 and did not find any significant difference in risk of subsequent recurrence in 73 patients who did undergo tract excision and 43 patients who did not. There were two recurrences in the tract resection group and three in the group without tract resection which was not statistically significant.[17] More recently in 2019, Seeger reviewed tract and intercompartmental seeding and did not find any evidence to suggest an increased risk of STS recurrence.[18] Most evidence suggests that the risk of seeding with US-CNB of STS is incredibly rare with no documented cases in our institution. It remains prudent, however, that perform careful planning of the biopsy path to reduce the risk of intercompartmental contamination.

There are limitations to our study, most notably that this was a retrospective review and potentially limited by the quality of documentation including complications. We have relied on its accuracy which overall appears contemporaneous and consistent throughout the data collection. As mentioned, this retrospective review does not allow formal evaluation for potential differences in accuracy, complications, and patient perception between different techniques. Not all benign lesions on US-CNB were resected; however, on follow-up, no patients were re-presented with malignant masses. We have assumed discrepancies between US-CNB and surgical resection as the gold standard; however, histopathology can also require subjective analysis outside of complex cytogenetic and molecular testing. For example, difficult histological

cases can be influenced by clinical and radiological features especially in borderline versus malignant lesions and lower versus higher grade lesions that do not necessarily equate to a fault with the initial radiological sampling.

CONCLUSION

Our described US-CNB technique with 2–3 good quality cores using a 16-gauge biopsy needle shows a high histopathological yield and accuracy. The benefits of shortened procedural time, low complication rate and reduced tissue damage due to obtaining fewer smaller cores whilst maintaining high diagnostic accuracy should be considered by radiologists working in specialist STS services.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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