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Evaluation of core needle biopsy as a substitute to open biopsy in the diagnosis of soft-tissue masses

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Abstract

Open biopsy is recommended for a soft-tissue sarcoma (s-t-S) diagnosis. Core needle biopsy (CNB) was recently associated with minimal morbidity, cost and time-consumption, but also potential inaccuracy. Its diagnostic utility was investigated retrospectively in 110 patients with soft-tissue masses (s-t-M) undergoing CNB between September 1994 and September 2000. Sensitivity (Se), specificity (Sp), positive (PPV) and negative (NPV) predictive values were determined for malignancy (benign/malign), soft-tissue tumour (yes/no), and sarcoma diagnosis (yes/no), comparing CNB and the best standard test available; concordance was evaluated. 103/110 CNB were suitable for analysis. Final diagnosis was 23 benign tumours (19%), 65 s-t-S (59%), 9 lymphomas (8%), 6 fibromatoses (desmoid) (5%) and 7 carcinomas (6%). CNB Sp and PPV were 100%, Se was 95, 99 and 92%, and NPV 85, 95 and 88% for diagnosing malignancy, soft-tissue tumour and sarcoma. CNB Se and NPV were 100% for malignancy, connective tumour and sarcoma in lymphomas, high-grade sarcomas and desmoid tumours. In low grade sarcomas, Se was 94 and 85%, and NPV 84 and 77% for malignancy and sarcoma. Histological grade on CNB seems uneasy, except for grade-III tumours. CNB is accurate, not misleading for s-t-M diagnosis, avoids open biopsy complications, and allows one-surgery or neo-adjuvant chemotherapy planning when combined with appropriate imaging.

Keywords: Core needle biopsy; Sarcoma; Medical practice; Soft-tissue mass

1. Introduction

A diagnosis using the tissue of musculoskeletal masses is necessary before initiating a treatment plan. Open incisional biopsy has traditionally been used to ensure that adequate tissue is available for the pathological evaluation. Classic teaching has advocated the use of an open biopsy to diagnose and grade soft-tissue sarcomas [1,2]. However, open incisional biopsies have a complication rate of 16%; these complications affect the treatment plan in 8% of all patients undergoing biopsy [3]. Reported advantages of core needle biopsy (CNB) include a decreased morbidity, cost and time consumption [4]. From a patient-care perspective, using a less invasive biopsy method would be preferable and CNB should become increasingly popular.

It has long been thought that CNB of musculoskeletal neoplasms does not provide adequate tissue for a definitive diagnosis. A care survey by the American College of Surgeons including 3457 patients with sarcoma treated from 1983 to 1984 showed that only 9% underwent a needle biopsy [5]. In 2000, Welker and colleagues reported an informal survey of the 1999 American Academy of Orthopaedic Surgeons annual meeting indicating that only 40% of respondents had used needle biopsy over the previous 15 years; it continues to indicate an under-utilisation of this technique [6]. In contrast, many articles show consistently good results with CNB [7,8]. The main issue, namely the adequacy of the sample, was the object of several studies [9,10].

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Sufficient, viable tissue, both representative of the lesion and available for histopathological and immunohistochemical evaluation, is required. As molecular markers become a factor in determining prognosis, meticulous attention to the adequacy of CNB, tissue preservation and evaluation will be paramount. Histopathological interpretation varies from centre to centre and may be a major variable in the decision-making process. In soft-tissue tumours, as in other relatively rare lesions, it is essential that the histopathology is reviewed by an experienced group [11]. In the current era of surgical and medical audit and increasing sub-specialisation, the purpose of the present study was to identify and discuss the use of CNB for the diagnosis of soft-tissue masses, over a 6-year period at a referral centre for the management of soft-tissue masses. We therefore wanted to investigate the advantages, disadvantages and the diagnostic utility of this biopsy method.

2. Patients and methods

Diagnosis from CNB and primary surgery, or recurrences were compared for all CNB performed in the centre over the period of study.

2.1. Criteria for interventional radiology

A complete radiological work-up (magnetic resonance imaging (MRI) and ultrasound) was necessary to locate the lesion precisely and determine the optimal route with the surgeon so that the needle route could be excised as part of the tumour excision. Patients were informed of the procedure and its potential complications. Normal coagulation parameters were required. After the patient was aseptically prepped and draped, a local anaesthesia was performed from the skin to the lesion with a 22-gauge fine needle (Yale® spinal Becton Dickinson & Co, Grenoble, France) using 10 cc of lidocaine (Xylocaine 1% adrenaline®; AstraZeneca, Rueil Malmaison, France). A 2 mm incision allowed the radiologist to introduce a 14-gauge semi-automatic Tru-cut biopsy gun (Galini Mantova, Italy) in front of the lesion [12,13]. Ultrasound or Computed Tomography (CT) scan guidance allowed sample cysts or necrotic tumours to be avoided, as well as minimising the damage to vessels or vital organs. Biopsies were performed free-hand so that the needle route was continuously controlled. An average of four needle passes was routinely performed in order to obtain sufficient material for analysis. The needle passes fanned out from a single percutaneous access to different portions of the tumour. Samples were immediately dispatched into Roswell Park Memorial Institute (RPMI) 1640 solution and Bouin liquid, then passed on to the pathologist. The site of the puncture was ink-tattooed, a Cold Pack® (3M Health Care, Borken, Germany) was placed on the biopsy site and the patient was watched for signs of haemorrhage over 1 h in the outpatient clinic.

2.2. Criteria for histological examination

Biopsy cores were partly fixed in neutral buffered formalin or Bouin liquid, and then partly frozen after microscopic analysis of touch imprints when molecular histology analysis was necessary for diagnosis. All specimens were subsequently reviewed by the same musculoskeletal pathologist who was requested to:

1. Categorise biopsies as malignant, benign or inadequate for diagnosis.
2. Make a specific diagnosis when possible.
3. Provide a histological grade for malignant tumours.
4. Provide immunohistochemical and molecular analysis studies on Tru-cut samples and surgical specimens when appropriate.

2.3. Criteria for patient selection

All patients with soft-tissue masses undergoing CNB between September 1994 and September 2000 were selected and analysed. Extraction of data was performed by one of the authors.

2.3.1. Sensitivity, specificity, positive and negative predictive values

Sensitivity (Se), specificity (Sp), positive (PPV) and negative (NPV) predictive values were determined for malignant criteria (benign or malignant), for soft-tissue tumour (yes or no) and for sarcoma (yes or no), comparing CNB and the best standard diagnostic test: histological examination after CNB surgical procedure, previous histological responses before CNB in cases of relapse, molecular analysis when appropriate (example: Ewing sarcoma).

2.3.2. Concordance score

For all patients, a concordance score (total accuracy) was delineated as 0 for total concordance between the two tests (CNB and the best standard), 1 for partial concordance (malignant soft tumour, but not the histological classification of tumour), and 2 for discordance.

2.4. Statistical analysis

Descriptive analyses were performed using the procedures of the Statistical Package for the Social Sciences (SPSS)®) 10.0 software (Chicago: SPSS, Inc. 2000). Univariate analyses of factors predictive of sensitivity and accuracy were performed using Pearson χ^2 tests or Fisher's exact tests when appropriate.

3. Results

One hundred and ten CMB procedures were performed on 110 musculoskeletal masses in the 6-year period of study. Of these, seven were judged unsatisfactory for diagnosis: 3 patients without material for diagnosis (haemangioma, lipoma and one soft-tissue sarcoma), 3 patients with only a non-specific fibrosis (neurofibroma, haematoma and one renal sarcoma) and 1 patient with only a fat cell sample for a cavernous haemangioma at the time of surgery.

The most common location was the proximal lower extremities (55%), whereas 39% of the masses concerned the trunk, 4% the head and neck and 2% the sacrum or a vertebral location with soft tissue extent. The median size of the samples was 9 mm (range 1–30 mm).

Patients' characteristics were as follows: median age: 54 years (range 11–87 years); Gender: 52 males (50%) versus 51 females (50%); Clinical stage at CNB: 72 (70%) localised versus 31 (30%) metastatic. All patients had a presumptive diagnosis of soft-tissue masses, final diagnosis including 85 malignant tumours (83%) and 18 (17%) benign mesenchymal tumours (Table 1). Of all patients, 31 (30%) with a previous tumour diagnosis underwent biopsy for a probable recurrence.

From a direct comparison of the biopsy specimen and the best standard examination, we calculated the positive and negative predictive values, sensitivity and specificity of the CNB for malignant criteria, soft-tissue tumour, and diagnosis of sarcoma (Table 2). Considering the malignant criteria, only four of 23 samples judged as non-malignant tumours by CNB were malignant low grade soft-tissue tumours (17%); these four false-negative cases were one malignant peripheral nerve sheath tumour, one paraosteal low grade sarcoma and two soft-tissue tumours with uncertain malignancy (two sarcomas not otherwise specified (NOS)). Considering soft-tissue tumour criteria (yes versus no), only one sample was mistakenly judged as non-conjunctive tissue (previous case of osteosarcoma). Concerning the diagnosis of sarcoma, five of the 43 samples classified as malignant NOS tumours were sarcomas (12%); these five false-negative cases were the malignant peripheral nerve sheath tumour and the paraosteal low-grade sarcoma previously described above two low-grade liposarcomas and one malignant fibrous histiocytoma. In a second part of our study, we tried to determine the subgroup of patients for whom sensitivity, specificity, negative and positive predictive values reached 100%. Concerning all patients with lymphoma, high-grade sarcoma and fibromatosis, no false-positive or -negative cases were described for the diagnosis of malignant criteria, soft-tissue tumour criteria and definition of sarcoma. By contrast, the sensitivity was less than 95% and the negative predictive value less than 85% for low-grade sarcoma.

We also calculated the concordance score for all tumours, as described in the Patients and methods section. Total concordance (overall accuracy) was found in 91/103 (88%) tumours, partial concordance in 7/103 (7%) and discordance in 5/103 (5%). The 5 cases of discordance were one achromatic melanoma (CNB: malignant undifferentiated NOS tumour), one liposarcoma (CNB: lipoma), one myxoïd sarcoma (CNB: myxoïd connective NOS tumour), one malignant schwannoma (CNB: schwannoma), one juxtacortical osteosarcoma (CNB: fibrous lesion).

There were no complications from the CNB among patients with soft-tissue masses of the limbs. One patient (1%) with an Ewing's sarcoma of the shoulder presented local bleeding not requiring blood transfusion and no subsequent problem for histological diagnosis and treatment plan. Another 6 patients (6%) presented

Table 1
Definitive diagnosis of 103 soft-tissue masses

Malignant tumours (85)	*N* (%)	Non-malignant tumours (18)	*N* (%)
Liposarcoma	7 (8)	Lipoma	3 (17)
Malignant schwannoma	4 (5)	Haemangioma	2 (10)
Malignant fibrous histiocytoma	2 (2)	Schwannoma	2 (10)
Leiomyosarcoma	9 (11)	Fasciitis	2 (10)
Synovial sarcoma	2 (2)	Sclerotic lesion	2 (11)
Triton tumour	4 (5)	osteomyelitis	2 (10)
Fibrosarcoma	9 (11)	Anevrysmal bone cyst	1 (5)
Chondrosarcoma—extraskeletal	3 (4)	Connective benign tumour NOS	4 (22)
Osteosarcoma—Ewing's sarcoma	15 (19)		
Sarcoma NOS	8 (11)		
Desmoid tumour	6 (7)		
Non-Hodgkin's lymphoma	9 (11)		
Carcinoma	7 (8)		

N, number; NOS, not otherwise specified.

Table 2
Results of core needle biopsy (CNB) at the Centre Léon Bérard

	Malignant criteria (yes/no) (%)	Soft-tissue tumour (yes/no) (%)	Sarcoma (yes/no) (%)
Sensitivity	95	99	92
Specificity	100	100	100
Positive predictive value	100	100	100
Negative predictive value	85	95	88

only haematoma not requiring any medication or special treatment.

4. Discussion

Despite the presence of considerable data establishing its efficacy at identifying mesenchymal tumours, CNB continues to be under-utilised for the diagnosis of musculoskeletal masses. The sensitivity and specificity of CNB in our series are consistent with those previously reported [4,6,14–17]. In the present study, the overall accuracy of CNB for the diagnosis of malignancy was 96% and the specific diagnosis of sarcoma also had an accuracy of 95%. Our results compare favourably with the 76–99% rates reported in previous studies. Indubitably, these previous reports reported on studies conducted with large numbers of patients, particularly the study by Hoeber and colleagues that included no less than 570 cases. We might consider that increasing experience may result in increased accuracy. The very good results obtained in our study may be due to the inclusion of patients with a previous histological diagnosis, which facilitates further the histological interpretation. However, CNBs were realised and examined by an interventional radiologist and a musculoskeletal pathologist with considerable experience in the diagnosis of soft-tissue tumours, which indubitably contributed to the level of accuracy achieved [3,18]. On the basis of results obtained in this study and in previous reports, we believe that a reliable diagnosis of soft-tissue sarcoma can be made from the relatively small quantity of tissue that is obtained by CNB. CNB has a high degree of accuracy in the diagnosis of soft-tissue malignant tumours, and is not misleading. The 'gold standard', as defined by Mankin and colleagues, of an open biopsy for the diagnosis of sarcomas must be questioned. The literature clearly documents the pitfalls that can accompany an open biopsy [3,18,19]. It is often associated with a relatively high (up to 17%) rate of complications including seroma, infection, wound dehiscence and, most seriously, tumour fungation [18,20]. Furthermore, it has been claimed [18,21] that haematomas accompanying an open biopsy may predispose to local recurrence, although other retrospective studies have shown that preliminary biopsy followed by delayed definitive resection does not affect survival [2,22–24]. Core biopsy avoids the complications of an open biopsy and makes it possible to plan a single surgery or neo-adjuvant chemotherapy management, when used in combination with appropriate imaging studies. Our 1% complication rate was identical to that reported in the literature [6,15]. In addition, it should be noted that complications affected patients' treatment plan or overall outcome. Finally, when a CNB proves non-diagnostic, the procedure can easily be repeated or an open biopsy can be performed without any major morbidity to the patient.

CNB is especially useful for diagnosing recurrent neoplasms, lymphomas, desmoid tumours and high-grade sarcomas [4]. In our series, the overall diagnostic accuracy of CNB was 100% in 18 patients. However, this number is too small to allow definitive conclusions to be drawn. Careful attention must be paid to low-grade sarcomas, where an open biopsy must be discussed. In these tumours, surgical procedures were probably not able to determine the histological diagnosis of malignancy in the same way as CNB. Histological grading with CNB is also open to argument. Hoeber and colleagues described very good results using Tru-cut, that made it possible for them to identify both the tumour subtype and grade in approximately 80% of STS. Also, it seems difficult to determine grading by biopsy examination, notably on CNB, except for high-grade tumours. For this reason, the pathologist in our institution determined grading on biopsy only when high-grade tumours were suspected on sample. In the present series, information concerning grading on CNB was missing for 49 patients. 30 of the other 54 patients had high-grade tumours; of these, 25 were detected by CNB (data not shown).

Classically, the diagnostic accuracy of CNB is higher for bone tumours than for soft-tissue masses. In bone tumours, unlike soft-tissue masses, diagnostic radiographs are usually available so that the biopsy is only confirmatory. In addition, patients who have soft-tissue masses have much more variable diagnoses and often have much more tumour necrosis [4]. However, in the present series, bone tumours and soft-tissue tumours presented identical rates of misinterpretation (6%) with CNB.

These results may also be criticised on various points. The most important aspect of the study was the selection of the patients for outpatient CNB by an experienced interventional radiologist and a specialised musculoskeletal pathologist. We suspect that the average practitioner would have considerable difficulty matching the high rate of diagnostic accuracy reported here for patient selection, and the correct interpretation of imaging studies is critical. Another issue is that the tumours selected for outpatient CNB were the 'easy' ones. What about a small soft-tissue mass that is deep in the thigh, or a tumour in the body of a lumbar vertebra? Less than 2% of CNB considered in this study concerned vertebras. Seven of the 110 patients (6%) had non-diagnostic CNB because of central tumour necrosis, sampling error, or geographical misses. Most of these tumours finally proved benign, suggesting that CNB could be inaccurate in some types of benign lesions. However, other authors reported similar rates of non-diagnostic CNB [9,15].

The perceived disadvantage of this technique was diagnostic inaccuracy. Wound complications, tracking haematomas and inappropriate incision may be avoided by using CNB. However, with previously determined and detailed procedures in radiology and in pathology these could also be avoided with surgical biopsy. CNB may enable a one-stage surgery and preserve the patient's tumour so that it may be imaged and subjected to multidisciplinary assessment, resulting in appropriate surgical treatment. Finally, patients with suspected sarcoma should be evaluated by a skilled multidisciplinary team because their diagnosis is necessarily based on a consideration of clinical, radiographical and histological findings. We recommend the use of CNB in the initial diagnostic evaluation of all patients suspected of having a sarcoma.

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