



The tactics and technique of musculoskeletal biopsy

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- The treatment of musculoskeletal neoplasms and infection is usually based on an initial diagnostic biopsy.
- Prior to biopsy, a hypothesis should be formed about the most likely diagnosis and a differential diagnosis. These deliberations should consider whether the lesion is a primary benign or malignant tumour, a metastasis, a haematological problem or an infection.
- A tactical plan should be developed which evaluates the necessity, the risk, the approach and finally defines the technique of biopsy most likely to achieve a representative result in the clinical case.
- In developing this technical approach, the pitfalls should be anticipated, i.e. inadequate sampling, difficulty of pathological interpretation and contamination.
- The tactical approach should be developed in conjunction with a multi-disciplinary team together with appropriate pre-biopsy imaging.

Keywords: tumours; musculoskeletal; multi-disciplinary approach; imaging; biopsy techniques; complications

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Introduction

The basic concept of modern medicine is that treatment is based upon accurate diagnosis. In musculoskeletal problems and abnormalities, the diagnosis is frequently based upon pathological examination of a specimen taken from the lesion. This is termed a biopsy. The label of 'biopsy' refers to the process of removal of the piece of tissue itself, as well as the examination of that sample by an appropriate specialist.

It may be considered that biopsy itself is a simple technical procedure, but it can have the potential of adversely affecting the outcome of the case, particularly in malignant tumours. The importance of proper planning and

performance of appropriate biopsy in musculoskeletal lesions is well-known and a recent literature review by Traina et al¹ outlines the general approach to performing biopsies of bone and soft tissue, respectively. As there is no single standard approach for biopsy for very different conditions, personal opinions and judgement influence the decisions involved in a biopsy. Biopsies are inevitably based upon scientific discussion, particularly of pre-biopsy imaging and the personal experience and expertise of the multi-disciplinary team (MDT). A biopsy performed at a centre where there are experienced radiologists, pathologists, orthopaedic surgeons and oncologists will generally have greater accuracy and lower complication rates.² This is particularly important with the increasing use of limb-salvage surgery in primary treatment involving musculoskeletal malignancies.

Obviously, a successful biopsy must cause minimal harm to the patient and ensure that sufficient viable and representative tissue samples can be presented in an appropriate form to the pathologist. Harm can occur from taking a biopsy from a lesion that does not require biopsy as appropriate management, by damage to neurovascular structures or by inadvertent contamination of an uninvolved anatomical compartment. These mistakes are minimised by pre-operative tactical discussion in a MDT setting. Acquisition of tissue can be via open biopsy or needle biopsy. The latter includes both fine needle aspiration (FNA) and core needle biopsy. At present the most popular method is core needle biopsy.

It can be assumed that the purpose of the biopsy is to produce an accurate diagnosis. The topic of accuracy has been diagnosed by Layfield et al.³ Diagnostic accuracy is assessed as the number of correct cases as a percentage of the total performed. Therapeutic accuracy reports the number of correctly treated cases as a percentage of the total cases under study. The question that the surgeon needs to answer from the biopsy is the usual question of benign versus malignant, is the diagnosis absolutely specific, is a grading of tissue possible? Obviously the amount of tissue available plays a role and most studies show a

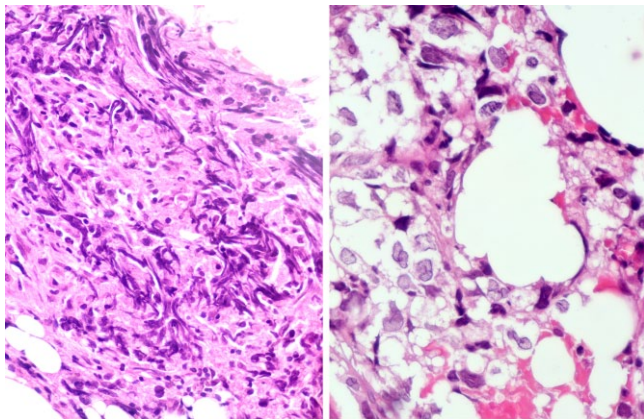


Fig. 1 Microphotographs of haematoxylin and eosin (H&E)-stained histological section of a core biopsy of a classical bone lymphoma: low power view (left side, 50× magnification) shows the characteristic shearing artefact with streaks of disrupted tumour cell nuclei, obliterating the nuclear detail and often preventing diagnosis in most segments of the biopsy tissue (left side). Focal preservation of the characteristic cellular and nuclear detail with clear cytoplasm and polylobated nuclei with somewhat coarser chromatin at high power magnification (right side, 400× magnification) leads to the correct diagnosis of diffuse large cell lymphoma.

slight superiority in diagnostic accuracy for core needle biopsy over FNA.⁴ However, even FNA has a reported diagnostic accuracy above 90%.⁵ A combination of the two methods has been reported as giving an overall diagnostic accuracy of 96%.⁶

In a recent study, the highest rate of non-diagnostic biopsies was for bone lymphoma (22%).⁷ Out of our own last 14 cases with bone lymphoma, the first biopsy was not conclusive in four out of 14. Because of high diagnostic suspicion, repeat biopsy was performed and a diagnosis was gained in three cases, and in one case a third biopsy was required. It is also recognised that bone lymphoma also presents difficulties for the pathologist. Figure 1 depicts the characteristic compression artefacts resulting in failure to diagnose bone lymphoma by a pathologist not familiar with this artefact. Faced with the artefact an experienced pathologist will carefully search for cells that do not show the artefact and eventually lead to the correct diagnosis. This case illustrates the need for close cooperation between clinician and pathologist and the role of an MDT.

The indication for biopsy

Most primary bone lesions present with focal bone pain and/or swelling and with a focal or multi-focal radiological abnormality. However, with increasing radiological sophistication, a number of variations of normal radiological artefacts or non-neoplastic lesions arise. Our experience is that

approximately 10% of MDT referrals are non-neoplastic. These may be congenital, traumatic, degenerative, infective or inflammatory in origin. Infected lesions are common, both acute⁸ and chronic, including chronic recurrent multi-focal osteomyelitis (CRMO),⁹ Brodie's abscess¹⁰ and tuberculosis^{11,12} which can all mimic a primary neoplasm. Perhaps the most common lesion-mimicking bone tumour or infection is a stress fracture.¹³

Similarly, many sarcomata, particularly Ewing's sarcoma, are well documented to mimic infection and wherever infection is thought a possibility, biopsy of the lesion should be sent for microbiological culture to assess sensitivity to antibiotics and for exclusion of the diagnosis of fungal infection or tuberculosis.^{14,15}

Tactical approach and MDT discussion

As stated above, the indication for biopsy is usually a radiological abnormality. However, the MDT need to take into account the patient's history and clinical findings prior to developing a working hypothesis. Many lesions, such as non-ossifying fibroma, fibrous dysplasia and osteoma, do not require a biopsy and biopsy of such lesions may even be misleading and distracting for the pathologist. As part of this hypothesis, the following questions should be discussed:

1. Does the lesion have its origin in the bone (primary bone tumour) or is it a metastasis?
2. Could the lesion be an expression of an underlying metabolic disease (Brown tumour caused by hyperparathyroidism) or could the process itself be causing a metabolic aberration?¹⁶
3. Could the process be an infection, especially in spinal lesions where tuberculosis can be more common?
4. Has the lesion a haematogenous origin, e.g. chloroma, lymphoma, plasmocytoma? In such cases, immune electrophoresis may be helpful prior to biopsy.

We consider that unselected screening blood tests are not usually very helpful but the simple metabolic studies, i.e. serum calcium, phosphorus, alkaline phosphatase, together with immune electrophoresis may add important information. Traditionally, plain radiographs are analysed according to the criteria of Lodwick,¹⁷ which can help to differentiate a destructive lesion, a bone-forming lesion, calcification within a chondrogenic process or a reaction to a neoplastic process or periosteal reaction. Although localisation of the lesion within a bone is also an important differential, it suggests that growth dynamics are best assessed by utilisation of PET-CT for systemic screening and assessment of local metabolic activity of a tumour. Whether PET-CT is performed before or after the

biopsy, depends on the type of lesion suspected. Most clinicians, however, would prefer that it was performed prior to biopsy if at all possible.

Pre-biopsy imaging

Once a decision has been made to perform a biopsy, planning should occur in an MDT setting. Although initial referral imaging may be adequate for deciding whether a biopsy is needed, imaging may have to be repeated where the whole lesion has not been covered or in the case of malignant disease the whole bone has not been imaged. For both bone and soft-tissue sarcomata, MRI is the technique of choice and this will give additional information on the type of biopsy to be considered in order to supply sufficient tissue for the pathologist, the approach and the appropriate part of the lesion to target. It will also define areas which need to be avoided, such as the neurovascular bundle and the team will also be able to decide which imaging technique to use for guidance of the biopsy itself. In cases where an additional lesion is discovered within the bone, which does not have the typical appearance of a skip metastasis, the second lesion may also require biopsy. MRI is also critical in defining whether there is local joint involvement.

The approach to be used by the biopsy must be discussed with the surgical team who will perform the actual appropriate resection of the tumour. This is because it is generally considered that needle track resection at the time of the definitive surgery is strongly advised.¹⁸ The small biopsy scar associated with core needle biopsy is usually visible for two to three months following performance, but if there is going to be significant delay, marking of the biopsy site with Indian ink should be considered.

Analgesia

The majority of bone and soft-tissue tumours in the appendicular skeleton can be biopsied under local anaesthetic without or without conscious sedation. Extensive local anaesthetic infiltration of the periosteum at the biopsy site is necessary to achieve adequate analgesia and this carries a theoretical risk of spread of the tumour. In children and in cases associated with pathological fracture, a local anaesthetic is unlikely to be tolerated. The biopsy of lesions in the posterior capsule of the knee, pelvic lesions and vertebral lesions may also be best performed on occasion from the use of general anaesthesia or sedation.

The types of biopsy and associated techniques

The biopsy should be as small as possible but as large as is needed to obtain material and make a diagnosis. Small

biopsies have the advantage of being less invasive, but the diagnostic yield is smaller. Large biopsies provide more material for more studies and allow preservation of material where required for research. Statistically they result in higher accuracy but carry a risk of more local complications.

Excisional biopsy

An excisional biopsy is the complete removal of the lesion. It is clear that this is permitted in potentially malignant processes only, if definitive treatment without the risk of contamination or marginality (penetration of the margins of the lesion) can be achieved. Furthermore, in cases which should receive chemotherapy, it may be important to have the tumour in place to observe the effects of the neo-adjuvant chemotherapy prior to resection.

Incisional biopsy

Incisional biopsy has long been considered to be to be the gold standard. Certainly, large samples of tumour tissue can be achieved and the accuracy is reported as up to 95%.²⁰ It carries with it the increased risks of haematoma which may delay treatment as well as an increased risk of local dissemination of tumour. It usually requires an inpatient setting and greater complications are reported.²¹

Core biopsies

Core biopsies provide a cylinder of tissue for histological examination by a pathologist. They provide more material than FNA and hence more pathological analysis can be performed. Presently, it is the most frequently used technique in the diagnostic work-up of soft-tissue and bone lesions. It usually uses systems of Gauge 8 to 18.

Where soft tissue is involved, the instruments are usually spring-loaded, e.g. Achieve[®] Automatic biopsy device by CareFusion (Fig. 2). It releases a cannula and stilette sequentially at high speed. It can be used within a guiding needle (co-axial system) to take several specimens with only one skin penetration. In addition, the co-axial system can be used for decontamination of the tract by radiofrequency.

For bone biopsy, our preferred instrument is the T-handle Jamshidi biopsy needle by CareFusion. An acquisition cradle increases the potential of removing a biopsy cylinder (Fig. 3). The needle can be partially withdrawn and re-directed within the lesion for more probes to be removed. Because occasionally very hard bone is encountered we have developed a power-driven cannulated special drill system with an external diameter of 8 mm and an internal diameter of 5 mm (Fig. 4). If no tissue can be removed either with the needle or the drill system, a fine rongeur (Figs 5 and 6) can be inserted through the 8 Gauge Jamshidi needle or an even larger standard rongeur



Fig. 2 The spring-loaded CareFusion® Core Biopsy device with the cannula for co-axial procedures.



Fig. 3 CareFusion® T-handle Jamshidi® bone biopsy set.

can be inserted through the opening created by the drill to allow material to be acquired. This is particularly useful in myxoid and cystic lesions. In suspected aneurysmal bone cysts, the use of contrast medium to confirm the venous drainage of the lesion can be considered and a sclerosant injection performed at the time of the core needle biopsy. The reported accuracy of core needle biopsy is in the range of 74%²² to 93%²³⁻²⁶ with complication rates in the range of 1%²⁶ to 2%.²⁷ No significant difference in accuracy of diagnosing soft-tissue or bone lesions has ever been demonstrated.²⁷ The paediatric literature and meta-analysis has a documented accuracy of 94% with complications of 1%.²⁸ However, it is worth noticing that the accuracy of this technique has been shown to decrease in the biopsy of spinal lesions (61%) and in cases of infection (50%).²² In a study of 151 consecutive core needle biopsies, factors affecting diagnostic yield included the type of lesion (87%), lytic bone lesion (57%), sclerotic bone lesions, lesion size (54%), less than 2 cm (86%), lesions greater than 5 cm, longer length



Fig. 4 The cannulated power drill system for larger core bone biopsies with rongeurs that can be inserted through the drill holes after removal, especially in cystic lesions.



Fig. 5 Fine rongeur, that can be inserted through the cannulated drill or even through the 8G Jamshidi needle shown in Fig. 2.

specimens and increasing numbers of specimens obtained. Again, no difference was identified between soft-tissue and bone lesions by imaging modality used or by needle size. The minimum of three specimens for bone lesions and four for soft-tissue lesions has been proposed.²⁹

Fine needle aspiration

In this technique, a fine hollow needle is inserted into the lesion and a syringe applied and aspirating material for pathological examination of the cells (cytology and/or cultures). Usually the needle is guided by ultrasound and several passes may be used to increase yield. This is usually performed under local anaesthetic. This technique is particularly useful in high-grade soft-tissue sarcoma where typing of individual cells or small tissue aggregates by conventional staining, immunohistochemistry or fluorescent in-situ hybridisation (FISH) will provide a diagnosis. It is the least invasive of the biopsy procedures and has the lowest risk of seeding of tumour along the needle tract.^{30,31} Studies have shown that in bone an excellent accuracy can be achieved from 97% to 100%^{32,33} and therefore it has been suggested as an effective initial investigation.³⁴ The main disadvantage, of course, is that it only offers cytological features of the lesion. Although this can be

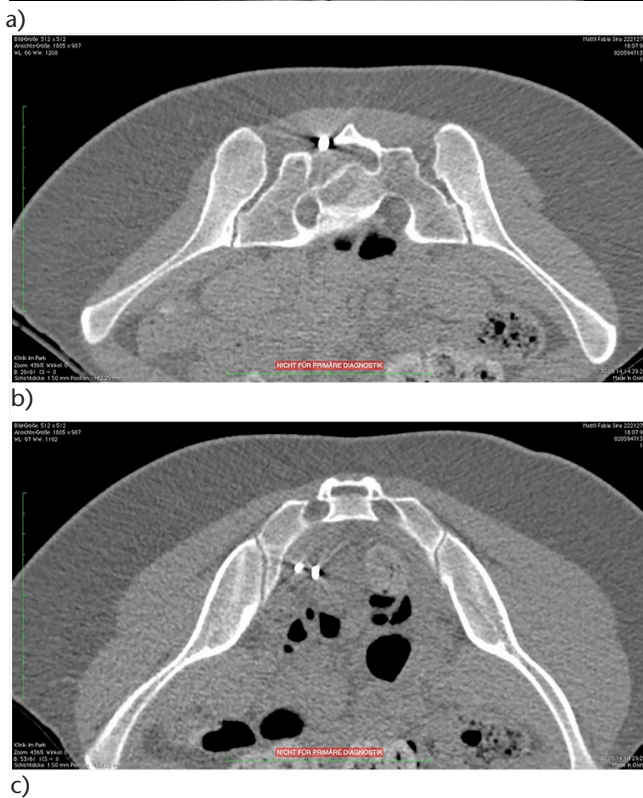
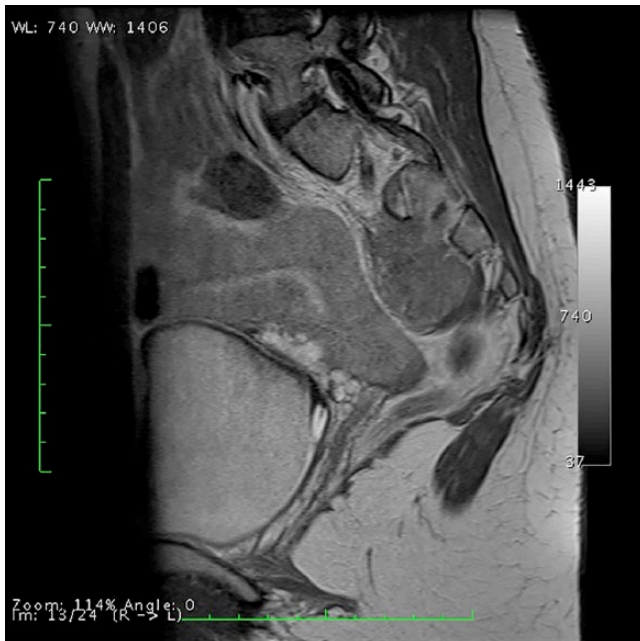


Fig. 6 a) Mass involving the sacrum. Dilated neurogenic bladder. Two non-diagnostic posterior core biopsies, one non-diagnostic open posterior biopsy. b) Nine months following the first non-diagnostic needle and open posterior attempts the diagnostic transforaminal (S2) CT-guided rongeur biopsy was performed by the author. Ewing sarcoma: top: posterior entry of the rongeur; bottom: rongeur within the pre-sacral lesion.

accurate in assessing metastatic bone lesions,³⁵ a more recent comparison with core needle biopsy shows that

the latter appears to be better in establishing the histological type and grade and achieving a specific diagnosis.^{20,25}

The type of imaging technique utilised during the biopsy can vary dependent upon a number of circumstances. Soft-tissue lesions or extra-osseous components of bone lesions in the appendicular skeleton can usually be assessed by ultrasound guidance. The additional use of colour Doppler can identify neovascularity within the tumour and such areas are more likely to be viable and should therefore be targeted. An adjacent neurovascular bundle can also be identified and avoided. Deep soft tissues around the pelvis or shoulder girdles or small lesions near neurovascular structures are perhaps more appropriately biopsied under CT guidance. CT is also perhaps best for intra-cortical lesions. Fluoroscopy is a very useful technique, particularly in the periphery and in lytic lesions. In studies comparing these three imaging modalities, accuracy has been shown to be very similar.³⁵

Complications

Tumour seeding and joint contamination

Although there are a number of individual studies which have reported seeding in a biopsy tract, the true incidence is unknown.³⁶ In a variety of malignant tumours, the incidence of needle tract seeding has been estimated at 0.003% and 0.009%.³⁷ As can be expected, given the rarity, several studies^{38,39} reported no risk of recurrence related to a biopsy tract, although tumour contamination in the biopsy tract, even in percutaneous techniques, has to be considered a real risk, re-inforcing the need for removal of the biopsy tract during tumour resection or already at biopsy (Fig. 7). This contamination of the biopsy tract and the need to remove it en bloc with the tumour resection was established in 1982.⁴⁰ An alternative way of sterilising the biopsy tract is by the radiofrequency technique described above (Fig. 7).

Cells showing characteristic Ewing's sarcoma translocations have been demonstrated in circulating blood during uncontaminated tumour removal, but no relationship to survival has been established.⁴¹ Whether such dissemination occurs during biopsy is unknown. In animal studies, after core needle biopsy an increased frequency of metastases from experimental carcinoma has been demonstrated.^{42,43} Undoubtedly, there must be some protective effect from chemotherapy against problems related to biopsy tract contamination. It can be assumed that this is likely in tumours which are successfully treated with chemotherapy and radiotherapy alone, such as lymphomas and some Ewing's sarcoma. During needle biopsy, particular care must be taken as to avoid joint contamination. This is a particular risk in the supra-patellar pouch of the knee joint.

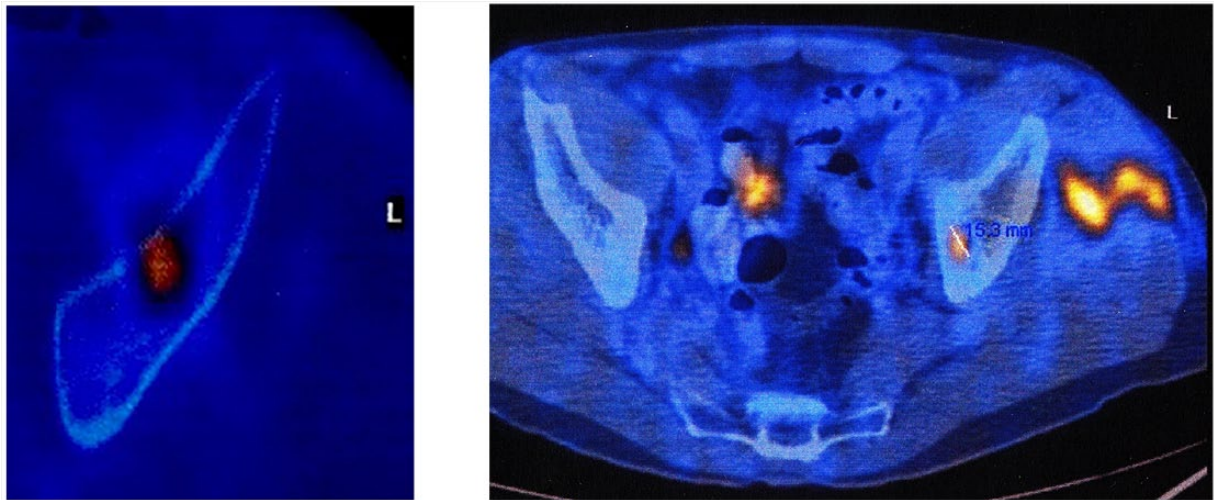


Fig. 7 Metastasis of cholangiocarcinoma (left). The metastasis was successfully inactivated by radiofrequency. The needle was removed after cooling. A new metastasis and biopsy proven contamination of the biopsy path is shown on the right.

Bleeding

Bleeding is a well-recognised risk of any biopsy technique and particular care should be taken with those tumours which have a particular vascular structure.⁴⁴ Bleeding into adjacent dead spaces can be difficult to control and the use of a pressure bandage should be considered.

Neural damage

It is well recognised that neural structures can be damaged by a cutting needle; however, pre-procedure planning and use of CT can usually avoid these problems. Instrument breakage that retains metal, smaller biopsy needles can break. Procedures should be performed at centres where orthopaedic surgeons can resect retained foreign bodies without difficulty.

Fracture

Great care has to be exhibited in lesions which are very lytic and on the verge of fracture. A biopsy can be the last straw in the integrity of the bone. Again, biopsy of such lesions in treating centres is ideal.

It can be seen that biopsy of bone and soft-tissue neoplasms is an essential component of the management of these difficult conditions. Although there have been algorithms presented for recommended biopsy approaches, we consider that the use of a MDT approach is essential to ensure that biopsy is, first, necessary, and, second, will ensure that it is successful. One should proceed with the least-invasive method following determination of the biopsy path and this can be based on an agreement between the treating surgeon, the radiologist, the pathologist and oncologist in the MDT setting. Pre-operative MRI to stage the lesion means that the highest-grade component of the lesion can be targeted by the biopsy clinician. The technical

procedure and the steps required can be planned and executed based on the appropriate imaging. Such an approach should result in the highest diagnostic yield for the patient and ensure the lowest possible rate of complications.

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