

The Role of Intra-operative Pathological Evaluation in the Management of Musculoskeletal Tumours

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Abstract A tissue biopsy is usually a critical aspect in guiding appropriate initial management in patients with musculoskeletal tumours. We have previously outlined the role of intra-operative frozen section in both the determination of adequacy of a biopsy and for its diagnostic utility. In this article, the options and techniques for intra-operative pathological evaluation, namely frozen section, fine needle aspiration cytology and touch imprint cytology are reviewed. Frozen section examination may be applicable in the following Sections, including (1) at core biopsy, (2) at surgical margins, (3) at confirming diagnosis prior to definitive treatment or to evaluate tumour spread, and (4) at establishing a diagnosis of a metastasis prior to intramedullary nailing. There are also situations in which frozen section is inappropriate. Pitfalls associated with frozen sections are also highlighted. There are also cost implications, which we have quantified, of performing frozen sections.

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In our experience that the use of intra-operative pathological evaluation reduces the non-diagnostic rate of bone and soft tissue sarcoma biopsies, eliminates the need for re-biopsy hence alleviating stress, and is a useful addition to the armamentarium in evaluating musculoskeletal tumours.

2.1

Introduction: Indications for Intra-operative Pathological Evaluation in Musculoskeletal Surgical Oncology

The optimal management of musculoskeletal tumours requires a multidisciplinary team approach that includes input from surgical, medical and radiation oncologists, radiologists and pathologists. Because it usually establishes a definite pathological diagnosis, a tissue biopsy is a critical aspect in guiding appropriate initial patient management. However, it is very important that the biopsy is carefully planned. This usually requires assessment with appropriate radiological imaging [18, 23] which is necessary to assess the anatomical extent of the

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tumour prior to biopsy. There are a number of principles that apply to performing a tissue biopsy of sarcomas. In order to avoid compromising subsequent treatment, the biopsy should be in a site that can be included en bloc within the definitive tumour resection and ideally should be performed following consultation with the surgeon who will be performing the definitive surgical procedure. The previous author has already outlined the potential consequences of poorly performed biopsies. These include pathological misdiagnosis (as a consequence of non-representative sampling), functional impairment, amputation and death. The types of biopsy that may be performed include core biopsy, fine needle biopsy (FNB), and incisional or excisional biopsies. For a number of years in our clinical practice at the Royal Prince Alfred Hospital (RPAH), Sydney, Australia, we have been performing biopsies (usually core biopsies) under general anaesthetic, with intra-operative frozen section to confirm that representative and diagnostic tissue has been obtained [2]. There are a number of reasons for using this biopsy protocol in our clinical practice. First, it has been shown that the technique is highly accurate, with a zero non-diagnostic biopsy rate [2], and the infrastructure is in place to support it. Second, many of the patients who are referred to our unit for management reside in excess of 1,000 km away and it is therefore particularly important that a diagnosis be established with a single biopsy procedure because it is not practicable for them to return at a later date for a second biopsy if the initial biopsy is inadequate or non-diagnostic. While our initial diagnostic protocol may not be suitable for every patient in all units, it can be utilised for some or all patients depending on local logistical arrangements of the multidisciplinary sarcoma service and individual patient circumstances.

Apart from determining whether an adequate tissue biopsy has been obtained, intraoperative pathological examination in soft tissue sarcoma surgical oncology may occasionally be indicated

for other reasons. Determination of whether or not tumour is present at the margins of excision specimens can be determined pathologically (including by frozen section examination) and this may influence the extent of tissue removed during the surgical procedure. Intraoperative pathological evaluation may also be used for confirmation of the diagnosis of some benign tumours such as aneurysmal bone cyst, giant cell tumour of bone and chondroblastoma. Many such cases with typical clinical and radiological features can be treated definitively with curettage, which can be performed relatively easily and safely as a single operative procedure.

2.2

Pathological Options for Intra-operative Evaluation

2.2.1

Frozen Section

Microscopic examination of frozen tissue sections is the most commonly used technique for intraoperative pathological evaluation. The procedure is performed as follows. Representative fresh, unfixed tissue is selected for examination. The quantity and type of tissue frozen will vary depending on the indication and the amount and appearance of the tissue obtained. The pieces of tissue are placed on a “chuck” (which is about 50% of the size of a standard paraffin block) in a mounting medium such as OCT (optimal cutting temperature; Fig. 2.1A). The tissue is then rapidly frozen in liquid nitrogen (Fig. 2.1B). The chuck is placed in a cryostat and progressively trimmed with a microtome blade until “full face” sections (i.e. sections including all areas of the tissue) are obtained (Fig. 2.1C). Frozen tissue sections that are 5 µm thick are cut and placed onto glass slides. The slides are stained with haematoxylin and eosin (H&E) using the progressive method. The latter can be performed

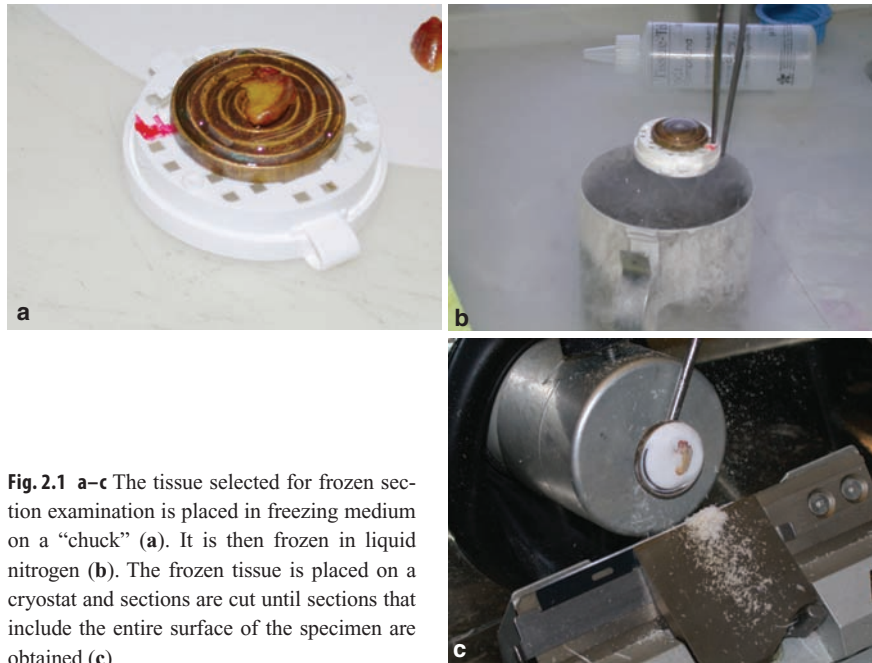


Fig. 2.1 a–c The tissue selected for frozen section examination is placed in freezing medium on a “chuck” (a). It is then frozen in liquid nitrogen (b). The frozen tissue is placed on a cryostat and sections are cut until sections that include the entire surface of the specimen are obtained (c)

considerably more quickly than the regressive method of H&E staining used for permanent sections but generally results in inferior staining quality. Usually two sections from each frozen section block are examined microscopically. It usually takes about 10–15 min to dissect, freeze, cut, stain and evaluate frozen sections.

In the case of multiple core biopsies from a suspected soft tissue sarcoma where the primary purpose of frozen section assessment is to determine whether diagnostic tissue has been obtained, only a portion of the procured tissue sample should be frozen. Ideally the selection of the tissue submitted for frozen section examination should involve input from both the surgeon and the pathologist. Depending on the frozen section appearances, portions of the unfrozen fresh tissue should remain available for any appropriate ancillary investigations such as flow cytometry (in the case of suspected haemopoietic malignancies), cytogenetics (which is particularly useful in soft tissue sarcomas that harbour specific

balanced chromosomal translocations), electron microscopy and immunohistochemistry (which may be suboptimal when performed on tissue that has previously been frozen).

At the Royal Prince Alfred Hospital, Sydney, Australia, patients with suspected sarcomas admitted for a core needle biopsy (CNB) attend our day case unit. Under general anaesthetic the CNB is performed, through a stab incision, using a 14G Trucut (Allegiance Healthcare, McGaw Park, IL) needle. Multiple specimens are taken. For purely intra-osseous lesions, the medullary cavity is opened with a 3.5-mm drill prior to CNBs being taken. The specimen is taken fresh to the pathology laboratory by the surgeon along with the imaging. Typically two representative cores selected by the pathologist in conjunction with the surgeon are chosen for frozen section examination. The frozen sections are then evaluated by a musculoskeletal pathologist (in the presence of the surgeon) and the features correlated with the clinical and radiological findings.

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2.2.2 Fine Needle Aspiration Cytology

Fine needle aspiration cytology (FNAC) is a rapid, minimally invasive and cost-effective technique employed in the diagnostic workup of mass lesions occurring in a wide variety of organs. FNAC is reported to have high sensitivity and specificity in the diagnosis of musculoskeletal sarcomas when performed by experienced cytopathologists and is commonly used as the primary diagnostic modality in Scandinavian countries [5, 25]. It can be performed and interpreted in a short period of time (about 10 min) and hence is a technique suitable for intraoperative pathological evaluation. FNAC requires minimal specialised equipment. In some instances, particularly hypocellular lesions or tumours associated with a prominent fibrous stroma or reticulin network, it may be impossible to obtain sufficient material for definitive diagnosis. Furthermore, limited sampling may also make it problematic to perform and interpret appropriate ancillary investigations such as immunochemistry (usually performed on a cell block preparation), cytogenetics or electron microscopy. Because the preparation of a cell block takes a number of hours, it is not possible to determine with certainty at the time of the FNAC procedure whether satisfactory material has been obtained. For these reasons, FNAC is not the preferred method for intraoperative pathological evaluation, except perhaps in some specialised centres staffed by individuals with excellent skills and appropriate experience with this technique who have awareness of its limitations and potential pitfalls.

FNAC may be performed using the needle-only technique or the aspiration technique on palpable or impalpable lesions, the latter under radiological guidance. Palpable lesions are localised and stabilised with the fingers of the non-dominant hand. A hollow bore needle (generally 25 gauges) is inserted directly into the mass and the needle is moved swiftly back and forth within the mass for approximately 10 s.

As a result, the tip of the needle dislodges cells within the mass, which, along with a small amount of fluid (blood and interstitial fluid) travel up the needle by capillary action. When a small amount of material (blood and cells) is visible in the hub of the needle, the needle is withdrawn from the mass and the bulk of the procured material is ejected onto glass slides by pushing air from a syringe through the needle. The material is spread evenly across the slide using another glass slide. In some cases, where insufficient material is obtained using the 'needle-only' technique, a syringe may be attached to the needle, and while the needle is being moved within the lesion, suction is applied to the syringe in an attempt to aspirate the cellular components of the lesion. The former technique is preferred for several reasons. First, it affords better control of the needle. Second, it allows for a better 'feel' of where the needle tip is located, and experienced operators can judge from the 'feel' whether the needle is well within the mass. Third, unlike the 'aspiration' technique, it is less likely to result in excessive blood dilution of the sample or in the formation of blood clots, within which the cellular material is often entrapped (and is therefore very difficult to interpret under the microscope). Non-palpable lesions are generally localised by a radiologist using imaging modalities such as ultrasound or computed tomography (CT). The radiologist inserts the needle into the mass under radiological guidance and follows a similar procedure to that described above.

The slides may be air-dried and stained immediately with a rapid Romanowsky stain such as Diff Quik (Lab AIDS Pty, Narrabeen, NSW, Australia) or fixed in alcohol and later stained with the Papanicolaou method (Fig. 2.2). While the bulk of the procured material in the needle is expelled onto slides as described above, the small amount of residual material in the needle is washed into Hank's balanced salt solution for later preparation of cell blocks using the serum/prothrombin method or cyto-centrifuge preparations. Immunochemical stains

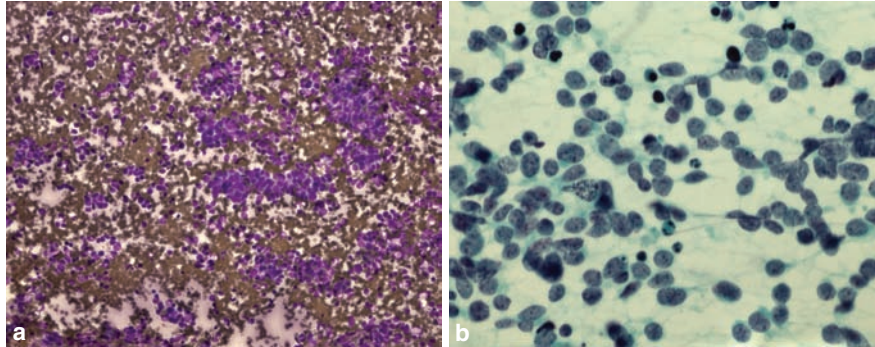


Fig. 2.2 a, b Cytology slides from a fine needle biopsy specimen stained with a Romanowsky stain (a) and by the Papanicolaou method (b)



Fig. 2.3 At the time of the fine needle biopsy procedure the material can be stained with the Romanowsky method and interpreted in real time. The staining

method involves placing the slide sequentially in a series of solutions

may be applied to the cell block and cytocentrifuge preparations later. The air-dried, rapid Romanowsky-stained slides are examined by the cytopathologist at the time of the procedure (Fig. 2.3). Depending on the amount, type and morphological features of the cellular material obtained, additional passes are performed if necessary to obtain material for further smears or ancillary tests such as immunochemistry. An immediate provisional result, based on

the interpretation of the air-dried, rapid Romanowsky-stained slides, may be communicated to the clinician. The puncture tract can be tattooed immediately after performing the biopsy to enable removal of the tract at definitive surgery. Once again consultation with the sarcoma surgeon is advisable to ascertain the surgical approach for the definitive resection.

When used as a combined approach, Domanski reported an accuracy of 97.7% (127 of 130 cases);

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however, there were diagnostic discrepancies between FNAC and CNB in another 10 cases (usually one or another specimen being insufficient or inconclusive) [5]. When used as an isolated biopsy procedure, FNAC performs well for metastatic disease, myeloma and lymphoma [25]. With an experienced cytopathologist, Wedin et al. were able with FNAC to determine the site and type of malignancy in two-thirds of patients with skeletal metastases [25]. Dupuy et al. compared CT-guided FNAC and CT-guided CNB in the same connective tissue oncology unit and the accuracy was 80% for FNAC compared with 97% for CNB [6]. Jelinek et al. used FNAC to confirm adequacy of specimen quality [11].

2.2.3

Touch Imprint Cytology

Imprint cytology is a technique in which slides are placed directly onto fresh tissue and some of the tissue is transferred onto slides (Fig. 2.4). The latter are usually stained by a Romanowsky method (as described above for FNAC) and examined microscopically, and the appearances are similar to those seen cytologically in FNAC

specimens. The technique allows for rapid assessment of the presence of viable tissue, and can often distinguish between benign and malignant tissue. Because it requires fresh tissue, it is often used in conjunction with frozen section evaluation of fresh tissue. It can be particularly helpful in diagnosing haemopoietic tumours, including lymphomas and leukaemias, or in difficult-to-interpret frozen sections in which imprint cytology may provide supportive evidence of a particular diagnosis.

2.3

Uses of Frozen Section in Musculoskeletal Tumours

Simon and Biermann in their Instructional Course Lecture [22] stated that “wherever possible, the surgeon should obtain a specimen for frozen section at biopsy”, in order to determine whether enough viable and representative tissue has been obtained. It is our experience that frozen section rarely takes more than 15 min to perform. By notifying the pathologist in advance of the list, and then give them a further warning

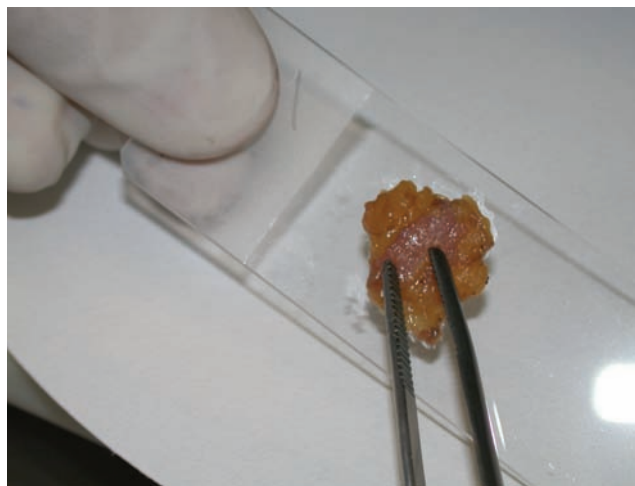


Fig. 2.4 Performing a touch imprint preparation

at the start of the case, delays are less likely to occur. The mean length of operating time, including frozen section, in our series was 34 min (range 25 to 45) [2]. Over a much larger series involving 700 hospitals in seven countries, 90% of frozen sections were turned around in 20 min in one study [17].

2.3.1

Operative Core Biopsy of Presumed Sarcoma

There are two aspects to the use of frozen section for presumed sarcoma. It is our opinion that confirmation that the sample is adequate for diagnosis is the primary reason for using frozen section. Achieving the final diagnosis at the time of frozen section should be seen as a bonus.

Our protocol at RPAH, Sydney for management of presumed sarcomas has been described previously (Fig. 2.5) [2]. A biopsy is performed in accordance with standard sarcoma practice and then a frozen section performed whilst the patient remains anaesthetised. It is our practice to ensure that sufficient cores of tissue (at least four) are taken to allow both frozen section examination to be performed and keeping some unfrozen tissue available for permanent paraffin sections and any necessary ancillary investigations such as immunochemistry or electron microscopy. If the frozen section either establishes the diagnosis or clearly demonstrates that electron representative tissue has been obtained, on which a definitive diagnosis can be made, then the protocol is complete and the patient is recovered from their general anaesthetic. If there is no representative tissue then either a repeat CNB or an open biopsy is performed and a further frozen section analysis undertaken to determine whether representative tissue has been obtained. The procedure is repeated until adequate tissue is obtained to enable a diagnosis to be made. The presence of extensive necrosis or cyst formation may make it difficult to obtain a

diagnostic specimen and are common reasons for multiple biopsies [15].

We reviewed 104 patients who were put through this protocol over a two-year period at RPAH, Sydney. These were compared with 24 patients who had CT-guided biopsies of musculo-skeletal. The latter were principally performed because the tumours were located at sites inaccessible to surgical biopsy. There were 71 malignant bone lesions, 20 malignant soft tissue lesions and 37 benign lesions (24 bone, 13 soft-tissue). Using the biopsy and frozen section protocol there were no non-diagnostic biopsies.

In our series the chance of needing to convert to an open biopsy was 23% for soft-tissue lesions and 4% for bone lesions. In 96% of malignant lesions the diagnosis was established on CNB, but this figure was lower 73% in ultimately benign lesions. This may represent the fact that it is easier for a pathologist to establish that something is malignant than to be certain that it is not.

There was one minor diagnostic error in the group attributable to misinterpretation at frozen section. This case involved a 62-year-old female who had a thigh mass with non-specific clinical and radiological features. A core biopsy was non-diagnostic. A decision was made to proceed to open biopsy rather than repeat the CNB. Frozen section analysis of the open biopsy revealed atypical lymphoid tissue possibly Hodgkin lymphoma. The definitive tissue diagnosis was B cell non-Hodgkin lymphoma. Surgical management of this patient was not affected.

Whilst a biopsy, if performed with poor technique, can have immediate complications, if performed well, they are unlikely. We had no infections, haematomas or unplanned return to theatres in any of the patients in our series.

Whilst we have emphasised the role of frozen section in biopsy, subsequent review of clinical, pathological and radiological data is performed at the weekly multidisciplinary Bone and Soft Tissue Tumour Meeting at our institution and a final

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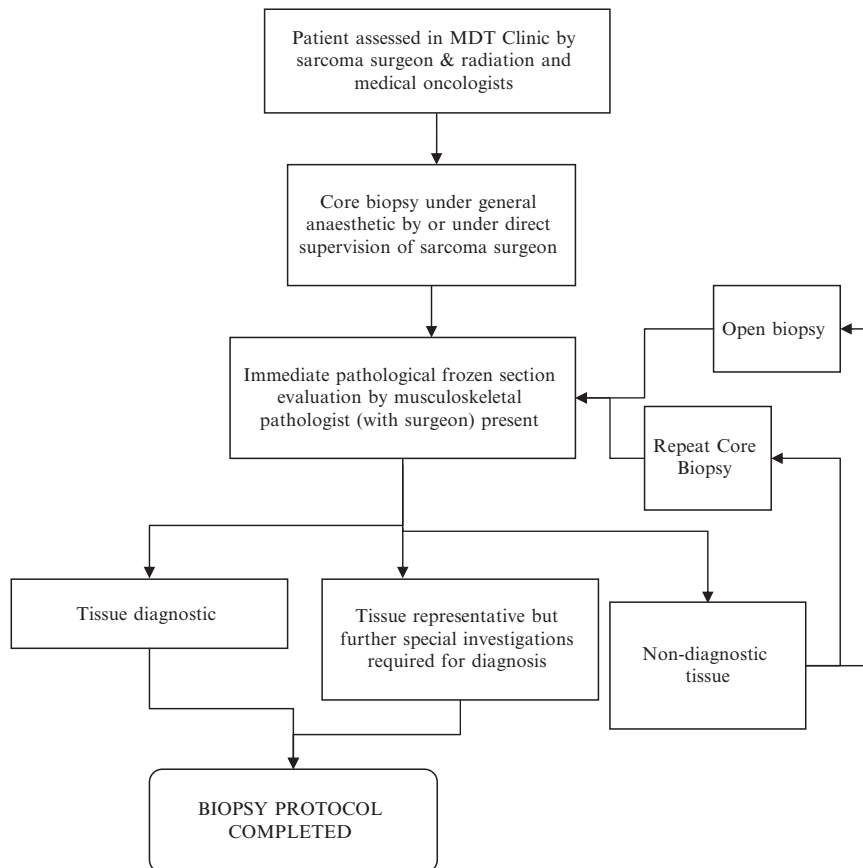


Fig. 2.5 Surgeon-led operative core biopsy with frozen section evaluation protocol of the NSW Sarcoma Service. (Reproduced with permission and copyright of the British Editorial Society of Bone and Joint Surgery [2])

diagnosis is only established upon review of all of the data [2].

We are not the only authors to report on the use of frozen section analysis in musculoskeletal tumours. Dupuy and colleagues at Massachusetts General Hospital have utilised frozen section on CNB samples taken under CT guidance. The accuracy of those where frozen section was utilised was 94% compared with 88% where it was not [6].

If there are any doubts on frozen section diagnosis, definitive surgery should be delayed pending full pathological analysis [22].

The majority of this article has been concerned with diagnosis of bone and soft tissue sarcomas, however there are other circumstances in our practice where we utilise intra-operative frozen section.

2.3.2

Surgical Margin Biopsy/Imprint

When resecting a primary bone sarcoma where there is residual long bone, the medullary contents may be curetted as a margin biopsy. A frozen

section can be performed on the specimen to determine whether or not tumour is present. If there is malignant or even questionable tissue at that margin, then re-resection of that margin and re-biopsy of the new margin and repeat the frozen section is indicated. Once the all clear has been given for the margins, one can proceed with the reconstruction [15].

2.3.3

Confirmation of Diagnosis Prior to Definitive Treatment

Frozen section evaluation may be used in the definitive management of some benign lesions. Aneurysmal bone cyst, giant cell tumour of bone and chondroblastoma (Fig. 2.6) all have characteristic radiological appearances. Definitive management is usually curettage for all three of these pathologies. In cases with typical clinical and radiological in features, frozen section examination can be used to confirm the diagnosis allowing the definitive management to be safely performed.

Frozen section evaluation may also be useful in patients with metastases. In patients with known primary tumours and a solitary lesion, then it is wise to confirm the diagnosis with a biopsy and exclude the possibility of a primary bone tumour. In the event of a pathological fracture this can be undertaken immediately prior to intra-medullary nailing.

Intraoperative pathological examination can also be used to avoid a “whoops procedure” such as the shelling out of a lump only to find that it is a sarcoma a few days later when the results of routine pathological analysis become available [3, 16]. A frozen section performed on a CNB or open biopsy will most likely reveal malignancy if present.

Heslin et al reported results of frozen section biopsies as part of their series of biopsies in soft tissue sarcoma [8]. They defined a frozen section biopsy as “a tumour resection without prior biopsy and a frozen section diagnosis given at time of operation”. They had two false-negatives (both reported as benign adipose tumours that were subsequently revealed as liposarcomas) and two false-positives (a desmoid tumour that was

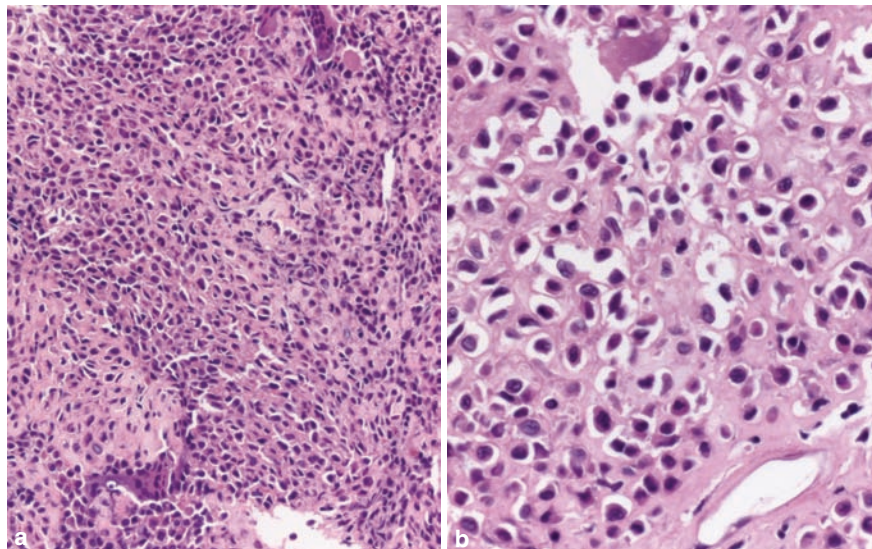


Fig. 2.6 a, b Histological features of a chondroblastoma

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in fact an atypical lipoma and a skin tumour that was finally classified as hidradenoma). Distinguishing atypical lipomatous tumour (low-grade liposarcoma) from lipomas can be notoriously difficult and the former may include large areas indistinguishable from the latter on microscopic examination. For these reasons, we recommend marginal excision (without frozen section evaluation) for all low grade fatty tumours and establishing the diagnosis by routine pathology.

There are other circumstances where one should be wary of using frozen section for confirmation of diagnosis. While, for example in high grade chondrosarcoma and giant cell tumour, only a small amount of tumour may be necessary to establish the diagnosis, in low-grade chondroid tumours it is often difficult or impossible to determine the diagnosis on frozen section [15].

2.3.4

Evaluation of Tumour Spread

Whilst performing musculoskeletal tumour surgery, one sometimes encounters a questionable or suspicious area separate from the main tumour. Frozen section can help determine the nature of such a focus. For example, frozen section may establish that the focus is a satellite deposit of tumour or that the area is an enlarged lymph node, and furthermore frozen section can determine if it is involved by an inflammatory or malignant process. Alternatively FNAC of a suspicious lymph node could be performed before surgery (if it is detected preoperatively) or during the operative procedure. The results of such investigations can aid surgical decision making intra-operatively.

2.3.5

Intramedullary Nailing of Presumed Metastasis

In patients with known primary tumours and radiological evidence of disseminated skeletal metastases it is probably not necessary to perform a

biopsy. However, if the skeletal metastasis is isolated or there is a pathological fracture then utilising frozen section is probably appropriate. In the instance of an isolated skeletal metastasis, in our institution the biopsy would usually be as a separate diagnostic procedure along the lines of our sarcoma biopsy protocol [2]. In the second, as outlined earlier, we would perform a biopsy and if it proves metastatic malignancy, immediately proceed to intramedullary nailing.

2.3.6

Frozen Section for Everyone?

There are situations where frozen section evaluation is inappropriate. The main one is in the diagnosis of low grade fatty tumours. The discrimination between benign lipoma and atypical lipomatous tumour (formerly known as low-grade liposarcoma) is notoriously difficult. We would treat both by marginal excision (without biopsy or frozen section), enabling the pathologist to receive the whole specimen and so make a final diagnosis upon pathological examination of entire specimen.

The other situation that does not avail itself to frozen section is the pure bone lesion. Well mineralised tissue cannot be cut for frozen section, however, almost all malignant tumours of bone have soft areas suitable for frozen section analysis [21].

2.3.7

Beware the Pitfalls of Frozen Section

We have outlined the pros and cons of frozen section throughout this article. It is important to clarify the pitfalls, so that one can avoid them. The first is inadequate tissue, both for frozen and permanent section analysis. It is beholden on the surgeon to provide the pathologist with sufficient representative tissue and the pathologist indicate when the biopsy contains insufficient tissue or is non-diagnostic so that the surgeon can return to the operating theatre to collect a further biopsy if

it is appropriate. The second and third pitfall relate to the tissue provided. If the tissue is not representative of the entire lesion then the diagnosis ventured may be wrong. This highlights the importance of tying together clinical, radiological and pathological data. Tissues that are heavily calcified are difficult to section and therefore difficult to provide an intra-operative diagnosis upon. Another pitfall is artefact. These can be surgical caused by technique (crushing of the specimen, for example by removing the CNB from the biopsy needle with forceps) or pathological caused by poor freezing technique. Because frozen sections are almost always of inferior quality to permanent paraffin embedded sections (Fig. 2.7), misinterpretation of frozen sections is another potential hazard.

2.4
Cost-Effectiveness

There is obviously a cost implication to performing frozen sections on biopsies. Based on our biopsy strategy we estimated costs to be approximately €1,119 (AU \$1,804) per case. In his further opinion, Grimer proposed a compromise strategy, upon which we also have included costings [7]. Whilst we maintain that our strategy is the gold standard, we do accept that it may not be reproducible in some healthcare situations.

The compromise suggested is as follows (Table 2.1):

We estimated costs based on the Australian Medicare rebate system and have converted to

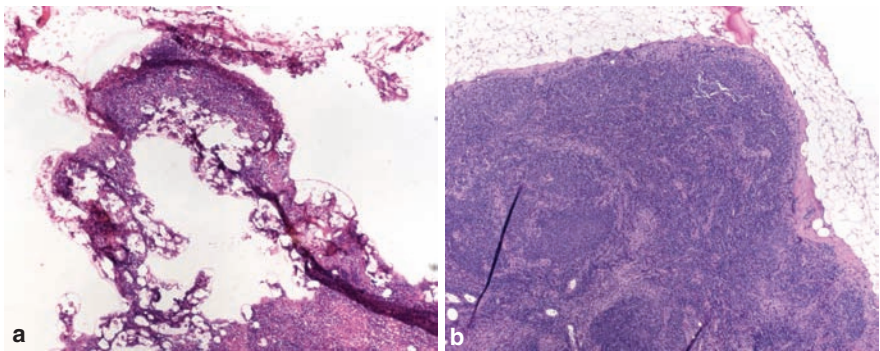


Fig. 2.7 a, b Frozen sections (a) are generally of inferior quality to those of paraffin sections (b)

Table 2.1 Different biopsy strategies for various musculoskeletal tumour scenarios, based on Grimer [7]

	Outpatient (LA)	Frozen Section	Image Guidance	GA
Accessible soft-tissue lesion	✓			
In-accessible soft tissue lesion		✓	✓	✓
”Worrying” bone tumours	✓		✓	
”Worrying” deep tumours/children		✓	✓	✓

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Euros based on a mean exchange rate for the latter half of 2005 of AU \$1:€0.62. Theatre and scan time have been estimated at 1 h per procedure. Full details of the remainder of the estimates are documented in our original article [2]. We have also estimated costs for the other scenarios mentioned earlier (Table 2.2).

Core needle biopsy with frozen section is more expensive than outpatient biopsy as one would expect. CT-guided biopsy is approximately three-quarters of the cost of our protocol biopsy. If one considers there is up to a 20% re-biopsy rate, which makes the true cost of each CT-guided biopsy €1,035. Outpatient CNB remains a valuable and cost-effective technique.

Furthermore, when we utilise intra-operative frozen section for confirmation of a benign diagnosis, rather than doing a separate biopsy procedure, if one allows an extra €800 for the additional theatre time, surgical and anaesthetic charges, there are significant cost savings over two separate procedures.

2.5 Discussion

Simon and Biermann have stated that biopsy “frequently demands relatively few technical skills” but that the “decisions related to the performance of the biopsy requires considerable thought and expertise” [22].

A poorly performed biopsy may result in inappropriate treatment and have a negative impact on patient survival [4]. CNB has been shown to be accurate in diagnosing musculoskeletal tumours, with reported accuracies of 93%–99% in soft-tissue sarcomas [8, 9] and between 97% and 98% in bone tumours [20, 24] when performed in some specialist centres. However, low rates of accuracy, even in specialist centres, have also been reported. For image-guided CNB there are reports of error rates (incorrect diagnosis) of between 6% and 12% [13, 14].

Table 2.2 Approximate cost (€) for core needle biopsies performed with and without image guidance or frozen section

Service	CNB with frozen section (protocol)	Outpatient CNB	Image-guided (CT) CNB	Image-guided CNB with F/S and GA
MDT assessment	320	320	320	320
Pre-op assessment	112	0	0	112
Anaesthesia	117	20	62	117
Surgeon/radiologist	99	0	62	62
Operating theatre cost	146	0	0	0
Scanner cost	0	0	211	211
Consumables	37	37	62	62
In-patient bed	131	0	0	131
Pathology cost				
Frozen section	63	0	0	63
Definitive section	94	94	94	94
Total	1,119	471	811	1,172

CNB, core needle biopsy; F/S, frozen section; GA, general anaesthetic

When the biopsy has been performed in the referring centre, incorrect diagnosis can be a problem as can adverse consequences of the biopsy. In a series reported from our unit, errors related to the biopsy significantly altered definitive treatment in 38% of cases where the biopsy had been performed in the referring centre [19]. Of the patients in this series, 15% required an amputation where limb-salvage would have been appropriate had the biopsy been performed in a satisfactory manner. When directly comparing referring and treating centres the complication rate of biopsy was 29.1% in referring centres and 4.1% in treating centres [14]. In the same article, from referring centre biopsies there was a diagnostic error rate of 27.4% and a non-representative rate of 5.7%. It was necessary to alter treatment in 36.3% and amputate in 4.3% [14]. These two series add to the evidence on why biopsies should be performed in specialist centres.

Non-representative biopsies are another problem in musculoskeletal tumour surgery. There is no question that the time spent waiting for a biopsy result is difficult for the patient. In a number of studies, image-guided biopsies have been demonstrated to fail to determine the diagnosis between 5% and 20% of the time [1, 6, 10, 11, 12, 20].

By incorporating frozen section into our biopsy protocol at the Royal Prince Alfred Hospital in Sydney, Australia, it has been possible to eradicate the problem of the non-diagnostic protocol. This is in part necessary because of the geographical distribution of our patients. It is unreasonable to expect patients to travel in excess of 1,000 km for a biopsy and to return that same distance for a repeat biopsy when the initial biopsy is non-diagnostic. Simon suggested back in 1982 that “wherever possible a specimen for frozen section should be obtained at all biopsies” [21] and reiterated the message a decade later [22].

There may be infrastructure reasons why frozen sections are inappropriate in some units and the cost may appear prohibitive, but at the

very least, any patient undergoing a biopsy under general anaesthetic should have a frozen section performed.

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