ESSR CONSENSUS DOCUMENT FOR DETECTION, CHARACTERISATION AND REFERRAL OF BONE TUMOURS AND BONE TUMOUR MIMICKERS

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Abstract

Benign bone tumours are rare, but early, accurate diagnosis and reliable differentiation from malignant tumours and tumour mimickers with subsequent appropriate treatment or watchful waiting is crucial for the clinical outcome. This ESSR consensus document is intended to help radiologists in their decision-making and support discussion among clinicians who deal with patients with suspected or proven bone tumours, because bone tumours are uncommon clinical entities and often a source of diagnostic and therapeutic uncertainty. Evaluating these tumours starts with a patient history and physical examination. Imaging then begins with radiographs. Radiography is the principal imaging modality and often can reliably diagnose a benign bone tumour by providing information about localization, matrix, aggressiveness, size, and (potential) multiplicity. Then, additional imaging is not necessary. Potentially malignant entities recognized by radiography should be referred for magnetic resonance imaging (MRI), which also serves as a preoperative local staging modality, with specific technical requirements. Indeterminate tumours, or tumours in which therapy is dependent on histology results, should be biopsied. Biopsy can be performed to establish histlogic diagnosis by either closed or open means. For biopsy, we strongly recommend referral to a specialist regional sarcoma treatment centre, where a multidisciplinary tumour team, including a specialist pathologist, radiologist, and sarcoma surgeon are involved. In sarcoma, a CT scan of the chest is mandatory. Additional staging modalities are entity-specific. There are no evidence-based recommendations for routine follow-up in surgically treated sarcomas. However, we would recommend regular follow-up with intervals dependent on tumour grade, for 10 years after the initial diagnosis.

Notes: Approved by the ESSR MSK Tumour Subcommittee.

Rationale and Objective of the ESSR consensus document

The purpose of this article is to help general radiologists and clinicians working in healthcare settings, other than dedicated sarcoma treatment centres, to determine whether a bone tumour seen on imaging is aggressive or non-aggressive and to help further management and referral of these patients. This paper is a consensus document produced by the European society of musculoskeletal radiologists (ESSR) tumour working group. The phrase “bone tumour” is used throughout this article to refer to focal bone lesions identified on imaging which include bone neoplasms, tumour like conditions and also sequels of infection.

Incidence and prevalence of bone tumours in Europe

Primary malignant bone tumours are rare in all European countries. For instance, in the UK, in 2013, there were 582 new cases accounting for less than 1% of all new cancer cases [1]. This equates to about 10 new bone sarcomas per million populations. In Germany, the annual incidence of sarcomas
arising from the bone and joint cartilage in the years 1999 until 2012 ranged between 638 and 835 new patients [2]. In 2010, 400 incident cases of malignant tumours arising from the bone and joint cartilage affect men and 350 women in Germany, the mean age at diagnosis was 51 years for men and 57 years for women, 239 men and 197 women died, the relative 5-year survival rate in percentage for men and women in the period 2009-2010 was in total 62% [3]. The pattern of cancer diagnoses in children is completely different from that of adults. For example, children are mostly affected by embryonal tumours. While the largest diagnostic groups are leukaemias (33.8 %), bone tumours sum up to 4.4 % and soft-tissue sarcomas to 5.8 % [3]. In the Netherlands, the annual incidence of sarcomas arising from the bone and joint cartilage was 838 in 2013, 920 in 2014, and 973 in 2015 [4] and in Switzerland the number of malignant bone tumours was 210 for men and 164 for women between 2006 and 2010 [5]. Regarding Sweden, Finland and Denmark, the number of new malignant bone tumours between 2009 and 2013 is 136 for men and 106 for women, the proportion of bone cancer in relation to other cancers is 0.2% for men and 0.1% for women, the proportion of all cancer is 0.2% and the number of persons living with the diagnosis per 100.000 inhabitants is 16 for men and 13 for women [6]. Also in the United States, primary malignant bone tumours are rare with an incidence of 0.9/100.000 people compared with an estimated incidence of lung cancer equal to 56.2/100.000 people [7]. In short, the incidence in Germany, Scandinavian countries, United States and UK seems quite similar (about 10 per million). There has been no significant change in the incidence of bone sarcomas for the last few decades. For example, since the late 1970s bone sarcoma incidence rates have remained stable in Great Britain for males and females separately and for both sexes combined [1]. It is therefore uncommon for a general practising physician or a general radiologist to see many bone tumours in their working life. Benign bone tumours are, by far, more common than sarcomas. However, general clinicians and radiologists will encounter numerous patients with bone metastases and bone lesions due to haematological conditions. Therefore, while encountering an osseous tumour, skilled estimation of aggressiveness and knowledge about the further diagnostic algorithm is essential. The finding of a bone tumour was the main reason for seeking teleradiological advice at a referral centre for musculoskeletal diseases in Munich/Germany, with 57% of all 322 submitted cases. Among these cases 84% were diagnosed as being benign [8]. Thus, the purpose of this article is to help radiologists and clinicians to determine whether a bone tumour is benign or malignant and to help further imaging and referral of sarcomas and potential sarcomas.

**History and Clinical Features**

Patients with bone tumours may come to clinical attention for various different reasons [9]. Many of the benign bone tumours are usually asymptomatic. However, patients may present with bone pain or swelling. Benign tumours such as osteoid osteomas and chondroblastomas can cause significant pain which brings the patient to clinical attention. Pain from osteoid osteomas is typically worse at night time and is relieved with anti-inflammatory medication such as salicylates, diclofenac or ibuprofen. Pain could also be a mode of presentation when there is a pathological fracture in the affected bone. Sometimes patients come to attention following trauma to the area and associated pain. The trauma itself is probably incidental in these cases. A large proportion of patients however come to medical attention when a bone tumour is identified incidentally on imaging examination performed for other clinical reasons. For example, a CT scan performed as part of staging for a visceral malignancy may demonstrate an incidental bone tumour in the thoracic or lumbar spine. Similarly a radiograph performed as a preoperative examination prior to a hip replacement might
show an incidental bone tumour needing further analysis. For this reason, it is important for reporting radiologists to critically evaluate the bones on all imaging examinations performed for any reason.

Important considerations in history include recent trauma, rate of growth of the tumour, underlying oncological history, previous surgery. A standardized checklist, primarily filled out by the patient, and discussed with the radiologist, is considered advisable. Clinical examination should document pain related to the tumour, palpable swelling, skin alterations including warmth, tenderness to touch and single/multiple tumours. This information should be available for the radiologist and this information is similar to the recommendations for soft tissue tumours in adults by the European Society of Musculoskeletal Radiology (ESSR) [10].

Primary Imaging

The radiograph remains the most important tool for detection, analysis, interpretation of bone tumours and in arriving at a short differential diagnosis in most cases of bone tumours [11, 12]. Computed tomography (CT) may sometimes be needed in complex anatomical areas such as the spine, pelvis, shoulder girdle and ribs. Otherwise, advanced imaging modalities such as CT, magnetic resonance imaging (MRI), scintigraphy and positron emission tomography (PET) are useful for subsequent local and distant staging respectively, of the disease rather than the initial diagnosis. These additional imaging examinations aid in further assessment of the bone tumour and do not replace a radiograph. It is therefore entirely reasonable for a general clinician/radiologist to obtain a radiograph in two perpendicular planes (and a CT scan in the case of axial tumours) for initial assessment of a bone tumour. If a reasonable diagnosis of a benign tumour that does not need any further management can be made on the basis of this initial investigation, no further imaging is necessary. Some benign tumours such as giant cell tumour and chondroblastomas need specialist management and are best managed at the regional sarcoma treatment centre (RSTC) even though these tumours are not usually malignant. On the other hand, if on initial assessment, the nature of the tumour is indeterminate, referral to a RSTC is necessary. All suspected bone sarcomas should also be referred to the RSTC. The radiologists at the RSTC may prefer to perform advanced imaging locally to suit their protocols. In particular, a biopsy should only be performed by the multidisciplinary team at the RSTC. In addition, all initial local staging examinations should be performed prior to biopsy.

Role of imaging in bone tumours

Imaging plays a very important role in various stages of the diagnosis and management of bone tumours. The purpose of initial imaging in bone tumours includes detection and diagnosis with a view to arriving at a short differential diagnosis. Once a bone tumour is detected, further imaging may also be necessary for local and distant staging of the disease. Imaging may also be necessary to perform a guided biopsy in order to arrive at a conclusive histological diagnosis. When neo-adjuvant therapy such as chemotherapy and radiotherapy are used, imaging may also be necessary to assess response to therapy and restage the tumour. Once initial treatment has been performed, imaging is also needed for follow-up and detection of recurrence. Multiple imaging techniques including radiography, CT, MRI, and scintigraphy have different and complimentary roles in the management of bone tumours. Of note, a radiograph in two planes should be obtained if one is not already available before any interpretation of the tumour can take place. The temptation to make a bone
tumour diagnosis on MRI scan should be avoided, as mistakes can often arise in characterizing bone tumours on MRI.

**Terminology**

It is important to recognise that radiographs can distinguish between four different densities: Soft tissue, fat, air and calcium (bone, mineralisation and cement) [11]. Fat and air are unlikely to be encountered on radiographs of bone tumours even though fat can be seen as part of a number of bone tumours macroscopically and microscopically. Peri-osseous or peri-articular fat pads may be displaced secondarily due to soft tissue involvement. So, most bone tumours either demonstrate a soft tissue density or calcific (bony or mineralised) density on radiographs. The name tumour refers to a space occupying tumour, this may, or may not be a neoplasm.

It is the norm in imaging assessment of bone tumours to characterise them as either “aggressive” or “non-aggressive” rather than “malignant” and “benign”. Although most malignant tumours appear aggressive on radiographs and most benign tumours appear non-aggressive, this is not always the case. For example, it is not uncommon for a benign eosinophilic granuloma to look aggressive where as a malignant myeloma can appear non-aggressive.

Bone tumours may demonstrate internal calcified/mineralised density related to either a chondroid matrix or an ossified tumour matrix. Chondroid matrix typically appears as “rings and arcs” type of mineralisation and ossified matrix appears as a dense “cloudy” type of matrix. It is important to differentiate between the two types of matrix mineralisation as the differential diagnosis varies with each type of mineralisation. Occasionally it is difficult to differentiate and it is entirely reasonable to use the term “mineralisation” in these cases. Also, the reader should keep in mind that tumour mimics resulting from various causes such as anatomic and developmental variants, trauma, infection, or osteonecrosis should be considered and should be classified as bone tumour mimicker [13].

**Principles of assessment**

Whilst the assessment of a bone tumour on radiographs is based on certain rules described below, none of these rules are absolute. There are some exceptions to all the rules. It is important that at the end of radiographic assessment, the radiologist /clinician arrives at a short differential diagnosis of two or three possibilities. One can include most of the tumours in the differential diagnosis and never be wrong. However, if the differential diagnostic list is very long, it becomes useless to the referring clinician. If the differential diagnosis list is short and accurate 80% of the time, it is in our experience good enough for the referring clinician [12, 14]. However, even when the diagnosis is clear, a number of tumours still need biopsy to help with further management and therefore need referral to a sarcoma treatment centre. Again, all bone tumour assessment should be made on at least two radiographic projections of the affected bone performed at perpendicular direction to each other. If two such projections are impossible to obtain, CT may be useful.

**Clinical features—relevance to diagnosis**

Patients with bone tumours can present with symptoms including swelling, pain and limb dysfunction. In the spine, tumours can also present with neurological dysfunction. Some rare tumours such as mesenchymal phosphaturic tumours can also present with systemic features related to osteomalacia. There are reports of bone tumours presenting with para-neoplastic
syndromes, but this is very unusual. Clinical features are not particularly useful to differentiate benign from malignant tumours with certainty. Although malignant tumours are more likely to be painful, some benign tumours such as osteoid osteomas, osteoblastomas or chondroblastomas can also be very painful [15]. All bone tumours that affect cortical bone may carry a risk of pathological fracture although because of the rapidity and extent of bone destruction this is more common with malignant tumours. Nevertheless, fractures can occur with benign tumours and is well documented by their occurrence in simple bone cysts. The presence of symptoms should always be carefully considered, especially before a tumour is deemed to be a benign “do-not touch” lesion. A biopsy may still be indicated in these symptomatic patients, even if a specific benign diagnosis can be made of an innocuous tumour. At the very least, these patients need to be followed up until symptoms settle. It is useful to perform certain biochemical investigations on all patients with bone tumours including serum calcium/phosphate and alkaline phosphatase. This helps to identify tumours such as brown tumours resulting from hyperparathyroidism, which can be confused both on imaging and histology. Similarly, there are other tumours which can cause oncogenic osteomalacia.

Symptomatic patient, radiograph negative
The radiograph is not very sensitive to the early stages of a bone tumour. At least 50% of trabecular bone needs to be destroyed before the tumour becomes detectable on radiographs. All patients with symptoms related to an area of the skeleton, not fully explained by clinical examination and laboratory investigations need further imaging, even if the initial radiograph does not reveal a bone tumour. If a tumour is not visible on radiographs, it cannot be assumed that these patients do not have a bone tumour. Further imaging can be MRI, CT or scintigraphy and the choice depends on the clinical situation. However, MRI is probably suitable for most cases as it directly shows the tumour, is very sensitive for bone marrow replacement, can be used for local assessment of the tumour’s extension, and has a very high negative predictive value for bone tumours.

Age
Age is one of the most important considerations in bone tumour diagnosis. It is very uncommon to develop benign bone tumours after the age of 40. Any new bone tumour seen in patients over the age of 40 years should be considered malignant until proven otherwise. The exceptions to this would be tumours seen around joints such as subchondral cysts related to osteoarthritis. After the age of 40, the most common new bone tumours, especially when there is more than one tumour manifestation, are metastases and multiple myeloma. Primary bone tumours including sarcomas and lymphomas can also occur at this age but are less common. If a solitary bone tumour is identified in this age group, a primary sarcoma cannot be excluded and the patient needs referral to a RSTC. Under the age of 40, a bone tumour can be either benign or malignant. Most primary bone tumours (benign and malignant) are diagnosed in the adolescent and young adult (range, 13-21 years) age group.

Radiographic assessment—detection
It is important to realise that the bone tumour itself is not visible on radiographs in most instances unless the tumour is mineralised. The detection and diagnosis of the tumour is actually dependant on the effect of the tumour on the host bone (Fig. 1). As described earlier, whilst radiographs are reasonably specific for the differential diagnosis of bone tumours, they are not particularly sensitive
for purely medullary lesions in the early stages. For purely medullary tumours, there has to be a destruction of at least 50% of the trabecular bone architecture before a tumour becomes visible on radiograph. Small tumours are also easily missed on radiographs. Cortical and surface tumours become obvious earlier than medullary tumours on radiographs. MRI on the other hand, is more sensitive for marrow replacement and soft issue involvement. Furthermore, bone tumour diagnosis on radiography is also delayed when located in flat bones, axial skeleton and the ribs because the host bone changes are difficult to appreciate due to the superimposition of other structures in areas with a more complex anatomy [16]. As a general remark, another reason for misdiagnosis in bone tumours like other tumours elsewhere may be “search satisfaction” and not identifying the tumour usually at the periphery of the radiograph. This would then be an “observational” error.

**Radiographic assessment—analysis and interpretation**

**Aggressive vs. non-aggressive bone tumours:** Based on radiographs, bone tumours can be differentiated into aggressive and non-aggressive tumours accurately in the majority of instances. The main features that differentiate an aggressive from a non-aggressive bone tumour are [11]:

1. **Pattern of bone destruction**—geographic vs. non-geographic
2. **Zone of transition**
3. **Cortical destruction**
4. **Nature of periosteal reaction**
5. **Soft tissue and joint involvement**

All these features are based on the response of the host bone to the nature of the tumour. However, even malignant tumours in the early stages may not show aggressive radiographic features (Fig. 2). Follow-up radiography or further imaging needs to be performed in cases where the diagnosis is not clear. The patient should not be discharged from clinical care without a firm diagnosis.

**Pattern of bone destruction:** Non-aggressive tumours produce a geographic pattern of bone destruction, where the shape of the tumour is evident on the radiograph with good margins. The shapes of these non-aggressive tumours can, however, vary from simple shapes such as spheres and ovals to complex shapes. Aggressive tumours on the other hand, can produce non-geographic shapes, as the tumour often has one or more rapidly advancing edges. Aggressive tumours can produce “permeative” and “moth eaten” patterns of bone destruction, when the tumour is advancing partly through the marrow spaces with some intervening trabecular preservation (see figure above). This permeation can take place along haversian canals and may not be obvious on radiographs until late in the disease.

**Zone of transition:** The “zone of transition” refers to the margin of the tumour and the transition between normal bone and tumoural tissue as seen on radiographs. If we can draw a clear sharp line with a sharp pencil all around the tumour to demarcate the junction between “tumour” and native bone, this is defined as a “narrow” zone of transition. In non-aggressive tumours, due to the slow growth of the tumour, there is a narrow zone of transition between tumour and native bone. The narrow zone of transition, which is also the margin of the non-aggressive tumour, can be seen as a sclerotic line as in the case of tumours such as non-ossifying fibroma or chondromyxoid fibroma. On the other hand, aggressive tumours grow rapidly and do not allow for a sharp margin to form around the tumour and this is defined as “wide” zone of transition. Some locally aggressive tumours such as giant cell tumour can have a narrow zone of transition but this is usually non-sclerotic [17]. It is
important to realize that this zone of transition should only be assessed on radiographs or CT. MRI on the other hand, often demonstrates a narrow zone of transition between tumour and native bone and can be falsely interpreted as non-aggressive.

**Cortical destruction:** The presence of cortical destruction is a sign of aggressive bone tumour. This in effect means that the host bone did not have enough time to produce periosteal new bone (neocortex) around a tumour that is growing rapidly. Even though non-aggressive tumours also grow, they allow the host bone to mount a good response by forming enough periosteal new bone to envelope the tumour as they grow at a slower rate than aggressive tumours. The non-aggressive tumours may however cause significant cortical erosion/endoosteal scalloping.

**Nature of periosteal reaction:** The periosteal new bone formation is continuous (solid or lamellar) and smooth in the case of non-aggressive bone tumours as the periosteum has enough time to lay down a continuous layer of new bone. On the other hand aggressive tumours, due to their rapid growth generate a disorganised, discontinuous, complex periosteal response which may manifest as “sun-ray speculation” or “codman's triangle”. These descriptions are often associated with osteosarcoma diagnosis but it is important to realize that this periosteal response is not specific to osteosarcoma and can occur with any aggressive bone tumour or metastasis. However, benign and malignant bone tumours can exist without eliciting any cortical destruction or periosteal response especially in the case of early intramedullary tumours.

**Soft tissue and Joint involvement:** The presence of a soft tissue mass or joint destruction associated with a bone tumour is strongly in favour of an aggressive tumour. The tissue fat planes around bone surfaces and joints should therefore be carefully assessed in the presence of a bone tumour. Since the local staging is crucial for proper treatment planning, it is important to report on the affected compartments, infiltration or encasement of nerves and vessels and infiltration of the joint capsule.

It is important to consider the reason for classifying bone tumours into “aggressive/ non-aggressive” and not “benign/malignant” [12, 18]. Whilst most aggressive tumours are malignant and most non-aggressive tumours are benign, this is not always the case. Malignant tumours such as myeloma can often present as non-aggressive tumours on imaging and often innocuous tumours, such as eosinophilic granuloma can present as aggressive tumours. In addition, there are a number of intermediate but locally aggressive tumours such as giant cell tumours, chondroblastomas, etc. that can cause severe bone destruction. Nevertheless, the characterization of tumours as aggressive vs. non-aggressive is clinically useful as all “do not touch” tumours are in the non-aggressive category. Similarly “aggressive-looking” benign tumours such as eosinophilic granuloma cannot always be differentiated from Ewing’s sarcoma prior to a biopsy and therefore need referral to a RSTC. Of note, the differentiation of aggressive from non-aggressive bone tumour is the most important part of imaging assessment of a bone tumour. When a tumour is judged as aggressive, the patient should be referred to the appropriate RSTC for further assessment including a biopsy. As mentioned previously, all bone tumours in patients aged over 40 years should be considered to be aggressive until proven otherwise. Over the age of 40 years, metastases and multiple myeloma are more common than primary bone sarcomas. However, after further investigation such as a bone scan, PET-CT scan or whole-body MRI scan, the bone tumour is solitary, a primary bone sarcoma remains a possibility and the patient needs to be referred to the RSTC for further management including biopsy. Another important take home message, infection should be considered in the differential diagnosis of bone tumours. Depending on the type of infection, both aggressive and non-aggressive
tumours can occur. This is particularly the case in children and young adults with epiphyseal and metaphyseal tumours.

There are some other criteria in bone tumour assessment that should be addressed in the radiological report [19]:

1. Location of the bone tumour - epiphyseal/metaphyseal/diaphyseal or medullary (central, eccentric), cortical, surface.
3. Part of the body involved - for example hands and feet, tibia, posterior aspect of distal femur and posterior elements of spine (Fig 1).
4. Single or multiple tumours.

Osteolytic vs. sclerotic tumours

The majority of bone tumours are osteolytic in nature, although sclerotic and mixed tumours can also occur. The matrix itself is not a true indicator of whether a tumour is benign or malignant. However, it is important to note that a number of osteolytic benign tumours such as a simple bone cyst or a non-ossifying fibroma can heal spontaneously and during this process turn sclerotic (Fig 3). Similarly tumours may become sclerotic after treatment (Fig. 4). Reactive sclerosis can also occur around bone tumours such as Ewing's sarcoma and lymphoma and a bone lymphoma may present as a diffusely sclerotic tumour. The sclerotic (ivory vertebra) and mixed patterns are more common in Hodgkin disease [16].

Advanced imaging modalities following radiography – MRI and CT

After the initial assessment on radiographs, if the tumour is either aggressive or is potentially malignant, additional imaging of the local area is often needed (CT or MRI scan) [20]. Occasionally, these additional imaging examinations can give further information such as the intraleisonal matrix, lesional fat, blood products, associated soft tissue involvement or the presence of fluid-fluid levels in an aneurysmal bone cyst (Fig. 5). As a rule of thumb, MRI is particularly helpful in chondrogenic tumours and in cysts. MRI and CT can also be used to demonstrate the presence or absence of cortical destruction and periosteal reaction which will help in the differentiation of benign from malignant tumours when these features are difficult to determine on radiographs [21]. MRI is the best additional imaging modality, as it allows for accurate assessment of the extent of the disease and the effect of the tumour on the surrounding structures including the joint, neurovascular structures, and skin [14, 22]. MRI also gives details of the extent of the compartmental involvement to help complete excision (may it be radical, wide or marginal) of the tumour. Commonly used MRI protocols for bone tumours include a T1-weighted and STIR (short tau inversion recovery) sequence of the full length of bone along the long axis to assess the longitudinal extent of the tumour, to diagnose any skip lesions and to aid the resection level at surgery. Axial images through the bone should also be performed and typically include axial T1-weighted and fat-suppressed T2-weighted images to assess the involvement of surrounding structures including the neurovascular bundle. The adjacent joint should always be included in the scan. Some sarcoma treatment centres routinely use intravenous gadolinium chelates, whilst other centres only use gadolinium chelate enhancement in selected types of cases. Sarcoma treatment centres may however prefer to perform the MRI examination according to their own (often elaborate) protocols. It is useful to liaise with the local sarcoma treatment centre for advice before setting up MRI protocols. Technological advances of
MRI have enabled improvements in both delineation of anatomic detail, and in functional imaging techniques that interrogate tissues at the cellular level [23]. Recent developments in advanced MRI techniques are chemical-shift imaging, diffusion-weighted imaging (DWI), MR spectroscopy (MRS), and dynamic contrast-enhanced (DCE) MR imaging. Although, the potential of chemical-shift MRI to allow for discrimination of marrow infiltrating neoplasms from benign red marrow, of DWI to reveal tumour cellularity, MRS to noninvasively assess metabolic aberrations in a variety of sarcomas and DCE to assess treatment response in which traditional size-based assessment criteria may underestimate efficacy in clinical trials [22, 24], the mainstay of MRI remains in our opinion conventional MRI sequences including a pure T1 and T2 contrast and the delineation of the bone tumour using at least two perpendicular planes (better 3 planes). Also, the entire bone and the neighbouring joint should be imaged. The advanced MRI techniques are probably best performed at the RSTC.

When MRI is not available or contraindicated, CT can provide similar information as to the extent of the tumour and the degree of bone destruction. In addition, CT is useful for further characterisation of tumours with mineralised matrix and sclerotic tumours. CT is also useful in further characterisation of tumours in the cortex and periosteal locations. CT is often necessary in tumours in the ribs, posterior elements of the spine and other flat bones with higher cortex/medullary bone ratio. In the case of some bones like the ribs and phalanges, CT may perform better than MRI, because for instance of higher spatial resolution and less motion artefacts. CT also may perform better than MRI in the small bones of the feet due to the higher resolution. The degree of oedema on MRI is not in itself a measure of the malignant potential of a bone tumour. A number of benign bone tumours cause extensive surrounding bone and soft tissue oedema, for instance an osteoid osteoma [20]. When a tumour elicits a lot of surrounding reaction including sclerosis and oedema, the true extent of the tumour itself can be obscured by the reactive changes on MRI scan. For example, CT is far superior to MRI in demonstrating the nidus in osteoid osteomas and the true tumour extent in chondroblastomas and aggressive eosinophilic granuloma. CT is also useful to identify the origin of a tumour particularly when they are located in the periosteal and paraosteal locations and in assessing the relationship of the tumour to the medulla. Standard CT cannot however demonstrate soft tissue or bone marrow oedema which is a useful differentiating feature of certain tumours like osteoid osteomas, chondroblastomas and infection (of note new advents such as dual-Energy CT enable to display of bone marrow oedema [25]).

The role of PET/CT and PET/MRI in the initial diagnostic workup of bone tumours is still not established. There is an overlap in the maximum standard uptake value (SUVmax) between benign and malignant tumours. This is not surprising given that some benign bone tumours like osteoid osteomas, chondroblastomas, and aggressive eosinophilic granulomas are very active metabolically. A number of non-tumorous inflammatory lesions can also result in abnormally high SUV. Therefore, PET does not yet have a role in the initial differentiation of benign from malignant bone tumours but may aid in problem-solving in suspected local recurrence [26]. Similarly, other imaging investigations such as ultrasound and angiography have no role in the routine initial assessment of bone tumours. Once a radiograph and MRI/CT have been performed, further imaging should be performed at the RSTC as necessary. Staging imaging examinations in the case of malignant bone tumours are usually performed after obtaining histological diagnosis.
Non-aggressive tumours

A number of non-aggressive tumours do not need any further management and can be treated conservatively. These are referred to as “do not touch” tumours and include non-ossifying fibroma or fibrous cortical defect if less than 3 cm in diameter, simple bone cysts, small enchondromata, bone islands, eosinophilic granuloma etc. However, certain non-aggressive tumours may still need treatment such as infection, osteoid osteomas, chondromyxoid fibroma etc. Occasionally, following initial radiological assessment when a tumour is deemed non-aggressive, it may still be difficult to determine whether a tumour is a “do not touch” tumour or a tumour needing further diagnostic work-up and/or treatment. In these cases, it is preferable to obtain advice from the multidisciplinary team at the RSTC.

Indeterminate tumours and obvious malignancies

All these tumours should be considered to be primary bone malignancy (sarcoma/lymphoma) and referred to a RSTC for further assessment including biopsy. Depending on the local setting, indeterminate tumours could be referred to a RSTC with or without performing an MRI beforehand. This depends on the local collaboration setting, the communication between the RSTC and the referring physician and the general radiologists, as well as the quality of the MRI. Some RSTC have the policy that if all indeterminate tumours were referred to a tertiary centre without performing an MRI, this would often result in a delay in patient management. On the contrary, other RSTC think that performing an MRI examination in these patients locally would delay referral and management and thus they prefer that these patients were sent straight to complete the diagnostic work-up because in fact some of these patients do not need anything more than a radiograph after discussion.

Biopsy

A biopsy for a potential benign or malignant primary bone tumour should always be performed at the RSTC under the guidance of an appropriate multidisciplinary team which has expertise not only in the technical issues of the biopsy but also expertise in terms of histopathological and surgical assessment which can often be difficult in these rare tumours. The multidisciplinary team at the RSTC should include multiple clinicians specialising in sarcoma including radiologist, pathologist, oncological surgeon and oncologist among other people. The biopsy should always be performed after all initial imaging assessment has been completed including MRI and scintigraphy and in collaboration with the orthopaedic oncologist who performs the definitive surgery. In the extremities, attention to compartmental anatomy is paramount [27]. A bone biopsy for these tumours can involve fine needle aspiration, core needle biopsy, or incisional biopsy. Controversy regarding the diagnostic yield of these biopsy techniques continues. The current literature has not clarified the optimal biopsy technique for the diagnosis of bone and soft-tissue tumours. However, core needle biopsy is usually preferable to incisional biopsy because of the low risk of contamination and the low cost. In addition, the use of imaging guidance increases the diagnostic accuracy of musculoskeletal biopsies and reduces the risk of complications. If the result of a percutaneous biopsy is non-diagnostic, a small incisional biopsy should be performed [28]. CT-guided core needle biopsy is a safe, accurate, and highly effective procedure that obviates the need for open surgical biopsy in a significant number of cases. When combined with fusion imaging, CT guidance is an accurate method of targeting specific regions of interest. In a recent study on 380 bone tumours,
accuracy of 80.8% with diagnostic error of 7.1% and non-diagnostic rates of 12.1% has been reported [29]. It is recommended that biopsy samples are always sent for both histological and microbiological assessment as infection should always be considered in the differential diagnosis of all bone tumours.

**Conclusion**

All bone tumours should be initially assessed on radiographs to determine whether the tumour is aggressive or non-aggressive. Non-aggressive tumours, that fall under the “do not touch” category, can be managed at any healthcare setting. All tumours that are deemed aggressive and other tumours that are “non-aggressive” but need further management should be referred to the regional sarcoma treatment centre. Biopsy and surgery of these tumours should only be performed at the sarcoma treatment centre under the care of a dedicated sarcoma multidisciplinary team.

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Flow chart

Symptomatic Patient
Pain/Swelling

Incidental bone
lesion identified

Always obtain a radiograph
of the affected bone in two
perpendicular planes

< 40 years
Age

> 40 years

Aggressive until
proven otherwise

Radiographic Assessment
Aggressive Vs Non Aggressive
(cortical destruction, periosteal reaction,
zone of transition, pattern of bone destruction)

Non Aggressive lesion

Don't touch Lesion

Yes

Refer

No

Aggressive

Multiple
(consider metastases
/myeloma)

Single
(consider primary
bone sarcoma)

Refer to sarcoma
treatment centre