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Clinical Radiology
The Royal College of Radiologists

Recommendations for cross-sectional imaging in cancer management, Second edition

Musculoskeletal tumours

Faculty of Clinical Radiology

Contents

Primary bone tumours

Clinical background

Primary bone tumours are rare, but represent a widely diverse group of neoplasms. Virtually any connective tissue elements found in bone can undergo malignant change. The common malignant bone tumours in young people are osteosarcoma and Ewing's sarcoma/primitive neuroectodermal tumour (PNET). In older patients, chondrosarcoma, secondary osteosarcoma (associated with Paget's disease, radiotherapy and dedifferentiated chondrosarcoma) and spindle cell sarcoma of bone are more common. There is also a wide variety of bone lesions which are non-malignant, such as chondroma, osteoid osteoma, non-ossifying fibroma, simple and aneurysmal bone cyst and Langerhans' cell histiocytosis. Plain film radiography is the most useful investigation for differential diagnosis. Any bone can be involved, but the distribution within the skeleton is an important factor in differential diagnosis. Biopsy is necessary to make a firm diagnosis of bone malignancy.

Who should be imaged?

All patients should be imaged at presentation to assess the extent of disease within the bone and soft tissues. This should be performed before biopsy when a strong clinical suspicion of a primary bone tumour exists. Failing this, local staging may be performed following biopsy. All patients with a suspected high-grade primary bone sarcoma should have unenhanced thoracic CT at presentation.

Staging objectives

- To detect extent of bone marrow involvement, including involvement of the growth plate and skip lesions within the same bone.
- To detect the presence and extent of extra-osseous soft tissue mass. These may extend into joint spaces and involve adjacent neurovascular bundles.
- To plan the optimal site and route for biopsy.
- To establish feasibility of surgical resection and design of endoprosthesis if indicated.
- To identify regional lymph node involvement, although this is very rare.
- To assess for haematogenous metastatic spread, most frequently to the lung, but occasionally to other bones.

Staging

For primary diagnosis, plain radiographs should be used. For staging of local disease, MRI is the technique of choice, although contrast-enhanced CT can be employed when MRI is contraindicated. A local surface coil should be used if the tumour is not too large. Placement of skin surface markers may be useful.

MRI

Protocol for imaging of primary bone tumours

Sequence	Plane	Slice thickness/gap	Field of view	Reason
T1W spin echo (SE)	Sagittal/coronal	4–5 mm	To cover lesion	To show full extent of local disease. Skip lesions should be investigated with a whole bone T1W SE coronal or sagittal sequence, including joints at both ends in long bones
Fat suppressed T2W/ short tau inversion recovery (STIR)	Sagittal/coronal	4–5 mm	To cover lesion	To show full extent of local disease and identify extent of tumour related marrow oedema
Proton density-weighted (PDW) fast-spin echo (FSE) and fat suppressed PDW FSE	Axial	4–5 mm	To cover lesion	To assess size of mass, compartmental involvement in limbs, proximity to neurovascular bundles and joint extension

** Note: Caution should be used when interpreting STIR sequence, as it may overestimate extent of disease. Reactive oedema in bone and soft tissue can return abnormal signal on STIR sequence and T1W imaging should be used to confirm disease extent. Use of contrast enhancement is not mandatory, but many radiologists prefer to use enhanced sequences with fat suppression to demonstrate extent of soft tissue masses. This does not, however, improve the staging of extra-osseous disease.*

CT

CT is recommended in all patients with suspected high-grade primary bone sarcoma at diagnosis for assessment of pulmonary metastatic disease. If thoracic CT is normal at presentation, CXR may be used in follow-up. Follow-up for osteosarcoma entails more frequent use of chest CT, in particular, to follow previously demonstrated metastases, after thoracotomy or when new lesions are seen on CXR. For evaluation of regional nodal disease, ultrasound is the preferred technique in children.

Whole-body 99m Tc-MDP isotope bone scintigraphy is the initial investigation for assessment of skeletal metastases in the setting of high-grade primary bone sarcoma. Whole-body MRI is, however, a viable alternative.

Values of $CTDI_{vol}$ should normally be below the relevant national reference dose for the region of scan and patient group (see Appendix and section on Radiation protection for the patient in CT in Section 2).

PET-CT

^{18}FDG PET-CT has a variable efficacy in sarcomas, depending on the tumour type and grade. The appearances range from very low-grade ^{18}FDG uptake through to intense uptake. ^{18}FDG PET-CT can be a useful modality for staging the extent of overall disease, particularly in primary tumours showing intense ^{18}FDG uptake, when surgery is being considered. It is not, however, a routine investigation.

Follow-up

Neoadjuvant chemotherapy is routinely used for most high-grade bone sarcomas (osteosarcoma and Ewing's/PNET). Follow-up MRI using a technique similar to that employed at initial staging is carried out preoperatively. Soft tissue masses are usually reduced in bulk by

chemotherapy, and pathological evidence of necrosis in greater than 90% of the tumour implies a good prognosis. MRI can predict to some extent the expected degree of necrosis but is not entirely reliable. Marrow signal frequently remains abnormal, but prediction of histology from the residual abnormality is not possible. Granulocyte colony stimulating factor (G-CSF) is sometimes administered to prevent neutropenic sepsis, and regenerating islands of bone marrow may cause new areas of apparent abnormal MRI signal in the affected bone and elsewhere which should be interpreted with caution. Bone metastases are very unlikely to develop during neoadjuvant chemotherapy.

^{18}FDG PET-CT is helpful in determining response to neoadjuvant chemotherapy, when this response may determine the extent of surgery contemplated. This evaluation relies on a baseline investigation having been carried out. The response to neoadjuvant chemotherapy may also correlate with histological response to therapy and hence final prognosis.

Following surgery and adjuvant chemotherapy, routine imaging follow-up consists of radiography of the operated limb and chest X-ray (CXR). If there is suspicion of local recurrence, this can be investigated with MRI plus/minus US. Development of suspicious nodules on CXR requires further chest CT.

Tips

- When staging primary bone tumours with MRI, skip lesions within the same bone should be actively sought. These occur in approximately 10–13% of appendicular osteosarcoma.
- The STIR sequence may overestimate the extent of disease within the marrow in primary bone neoplasms.

Metastatic bone tumours

Clinical background

Bone metastases can be seen with any extracranial primary cancer. They are most frequently seen in patients with breast and prostate cancer, but lung, kidney, thyroid and gastrointestinal primaries frequently metastasise to bone. The initial investigation is usually isotope bone scan with confirmation by radiography, but MRI is slightly more sensitive in detecting metastatic bone disease. Isotope studies have the advantage of imaging the entire skeleton, but if patients have symptoms suggestive of metastatic bone disease, even with a normal bone scan and radiography, bone disease can still be documented by MRI.

Treatment of metastatic bone disease depends on the pathology of the primary tumour, and the number and distribution of lesions within the skeleton. Radiotherapy, chemotherapy and surgery may all be used in management of secondary bone deposits.

The majority of bone metastases develop in the same distribution as red marrow, with the spine in the lumbar region being most frequently affected. Pelvis, upper femora, upper humeri and skull vault are also commonly affected, but the more peripheral bones are unusual sites for bone metastases.

Who should be imaged?

Patients with suspected metastatic disease to bone should be selected for imaging on clinical grounds, taking into account the nature of the primary tumour and the length and severity of symptoms such as pain. These factors give an index of suspicion which helps to select patients for further investigation and, in turn, a high index of suspicion will lead to more intensive imaging investigation.

Imaging objectives

- To detect metastatic disease, define the number of metastases and extent within the same or other bones, and to demonstrate extent of soft tissue involvement.
- To detect actual or imminent epidural spinal cord compression by spinal lesions.
- To detect extent of bone disease at sites of high risk for fracture such as the femoral neck.
- To distinguish between metastatic and osteoporotic causes of vertebral collapse.

Imaging

MRI

This depends on the site of suspected abnormality. T1W SE sequences oriented to the bone or bones to be imaged will detect the majority of bone metastases. Metastatic tumour is of identical signal intensity to muscle and contrasts well with fat in the marrow cavity. In the spine, islands of residual red marrow can lead to diagnostic difficulty, but normal marrow distribution will be the same in each of the vertebral bodies. If there is doubt on the T1W sequence, the STIR sequence is helpful in highlighting pathology particularly in the dorsal elements. On T2W sequences, a tumour can be close to the signal of normal fatty marrow, and gadolinium enhancement on T1-weighted sequences reduces tumour to marrow contrast. Occasionally, gradient echo T2*W sequences, contrast medium enhancement and diffusion-weighted imaging can be used to differentiate malignant from osteoporotic vertebral collapse. Whole-body MRI using STIR and T1-weighted sequences may also be helpful in determining the extent of bone metastatic disease.

CT

Reformatted MDCT spinal and pelvic images should be reviewed in the coronal and sagittal planes in patients with suspected bone metastases and in those with widespread soft tissue disease with primary tumours with a predilection to spread to bone (such as breast).

Using MDCT, slice thickness will depend on scanner capability. In general, sections are acquired at 1.25–2.5 mm and reformatted at 5 mm for viewing.

Values of $CTDI_{vol}$ should normally be below the relevant national reference dose for the region of

scan and patient group (see Appendix and section on Radiation protection for the patient in CT in Section 2).

PET-CT

^{18}FDG PET-CT is a particularly useful modality for the detection of metastatic bone disease being more specific than bone scintigraphy (uptake on PET represents uptake of tracer by active tumour cells whereas MDP bone scintigraphy demonstrates an osteoblastic response). ^{18}FDG PET-CT has the advantage of being able to demonstrate lytic bone metastases (which may not be demonstrated on bone scintigraphy). ^{18}FDG PET-CT, however, can be less sensitive in detecting sclerotic osteoblastic metastatic disease, although this can be improved by the use of ^{18}F-Fluoride PET-CT. A particularly promising area for ^{18}FDG PET-CT is in the evaluation of treatment response of metastatic bone disease.

Tip

- When bone metastases are suspected, bone scintigraphy is slightly less sensitive for detection of marrow disease than MRI particularly in the spine, but isotope studies are more sensitive in detecting metastatic disease in ribs, small and flat bones. Bone scintigraphy covers the whole skeleton; whole-body MRI may, however, be considered.

Soft tissue sarcomas

Clinical background

These rare tumours represent a heterogeneous group of neoplasms with a wide spectrum of histological and clinical features. Most primary sarcomas are treated by surgery, but some such as rhabdomyosarcoma are treated with neoadjuvant chemotherapy followed by surgery if technically feasible. Sarcomas which cannot be completely resected may be treated with adjuvant radiotherapy. For primary diagnosis, plain film radiography may be useful to demonstrate fat or mineralisation within a lesion and any associated skeletal abnormality. MRI is the investigation of choice for demonstration of extent of soft tissue tumours owing to its improved contrast resolution. Contrast medium-enhanced CT may be substituted when MRI is not available or is contraindicated.

Who should be imaged?

All patients with suspected soft tissue sarcoma should have imaging staging of the primary tumour prior to biopsy. Once the diagnosis is established by needle biopsy, all patients should have thoracic CT to stage for lung metastases. In certain tumour types, such as rhabdomyosarcoma of the lower limb or pelvis, abdomino-pelvic CT should be undertaken for nodal staging. Abdomino-pelvic CT is also obtained for lower limb myxoid liposarcomas.

Whole-body 99m Tc-MDP isotope bone scintigraphy is rarely obtained except to stage Ewing's sarcoma/PNET of soft tissues as per staging of a primary bone lesion.

Staging objectives

- To identify the site and extent of soft tissue tumour.
- To plan biopsy.
- To define spread within muscle compartments and feasibility of resection.
- To identify regional lymph node metastases, which are very rare.

Staging

MRI

Surface coils or local coils should be used, where possible, if the tumour is not too large. Skin markers over palpable lesions are useful. STIR, PDW FSE and fat suppressed PDW FSE, and T2W SE sequences yield the best contrast resolution, with tumour shown as high signal intensity when compared to adjacent muscle. T1W sequences are useful in the limbs to demonstrate any penetration into adjacent bone marrow.

Sequence	Plane	Slice thickness	Field of view
T1W SE	Sagittal/coronal	4–5 mm	To cover lesion
STIR	Sagittal/coronal	4–5 mm	To cover lesion
*PDW FSE and fat suppressed PDW FSE OR *T1W SE and high-resolution T2W SE	Axial	4–5 mm	To cover lesion
	Axial	4–5 mm	To cover lesion

*Footnote: STIR sequence is useful to highlight pathology but may overestimate size of lesion. *The axial PDs are the same as for bone sarcomas; more conventional SEs including high-resolution T2W without fat saturation are favoured by some radiologists for assessment of fat planes/neurovascular involvement. Routine use of contrast does not improve local staging. Field of view (FOV) should include the nearest joint.*

Whole-body MRI using STIR and T1-weighted sequences may also be helpful in determining the extent of any clinically suspected metastatic disease in soft tissue and/or bone or to locate the site of an unknown primary soft tissue sarcoma that presents with metastatic lung disease.

CT

CT of thorax should be carried out at the time of diagnosis to detect pulmonary metastases. CXR should be performed at intervals in follow-up, depending on tumour biology.

Using MDCT, slice thickness will depend on scanner capability. In general, sections are acquired at 1.25–2.5 mm and reformatted at 5 mm for viewing.

Values of CTDIvol should normally be below the relevant national reference dose for the region of scan and patient group (see Appendix and section on Radiation protection for the patient in CT in Section 2).

PET-CT

Soft tissue sarcomas demonstrate a variable appearance with ^{18}FDG PET-CT, ranging from very low- grade through to intense uptake depending on the histological type and grade. In tumours which demonstrate intense ^{18}FDG uptake, the technique can be particularly useful for defining the overall extent of disease prior to surgery. Pulmonary nodules less than 7–10 mm in diameter may not be resolved on the PET component of current PET-CT scanners.

Follow-up

Following surgical resection, MRI is a valuable technique for identifying recurrence. A baseline follow-up six months after surgery is useful, particularly if tumour was close to, or involving, resection margins and for histologically high-grade tumours (Trojani grade 2 or 3). Skin markers placed at the extents of the surgical scar are helpful. The MR imaging protocol is similar to primary staging using fast SE sequences without fat saturation. Radiotherapy change and postoperative seromas have classical appearances. Dynamic-enhanced studies may be of value for differentiating between mass-like scar and soft tissue recurrence. Any recurrent soft tissue mass should undergo biopsy.

^{18}FDG PET-CT in follow-up and response to therapy may be helpful when a baseline study has demonstrated that the primary sarcoma has shown uptake of ^{18}FDG. Careful timing in relation to surgery, chemotherapy and radiotherapy should be considered.

Tip

- Thoracic CT should be undertaken in patients with soft tissue sarcomas to identify pulmonary metastases.

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Further reading

The Royal College of Radiologists. *iRefer: Making the best use of clinical radiology*, 7th edn. London: The Royal College of Radiologists, 2012. (www.irefer.org.uk)

The Royal College of Physicians and The Royal College of Radiologists. *Evidence-based indications for the use of PET-CT in the United Kingdom 2013*. London: Royal College of Physicians, 2013.

Authors:

Dr Julia Fairbairn, Nottingham University Hospital, Nottingham

Dr Ruth Green, Royal National Orthopaedic Hospital, Middlesex

Dr Asif Saifuddin, Royal National Orthopaedic Hospital, Middlesex

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The Royal College of Radiologists
63 Lincoln's Inn Fields, London WC2A 3JW
Tel: +44 (0)20 7405 1282
Email: enquiries@rcr.ac.uk **www.rcr.ac.uk**

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