

# Non-surgical management of musculoskeletal malignancy

Lesley Speed

## Abstract

The majority of patients with a musculoskeletal malignancy will have bone metastases from a distant primary tumour. This could be apparent at diagnosis or later in the course of the disease. Some primary tumour types are more likely than others to develop bone secondaries. This common clinical problem requires a multidisciplinary approach in order to reduce patient suffering and maintain quality of life. Almost all patients with metastatic bone disease will have incurable cancer and this needs to be acknowledged when considering treatment options. Conversely primary musculoskeletal cancers are relatively rare conditions and thus need to be managed by specialist centres. Multimodality, multiprofessional treatment is required which may last for many months and can be associated with considerable toxicity. Patients with localized disease can be cured but prognosis has to be guarded due to high rates of local recurrence and metastases for both primary bone and soft tissue sarcomas.

**Keywords** bisphosphonates; bone metastases; chemotherapy; Ewing's sarcoma; osteosarcoma; radiotherapy; soft tissue sarcoma

## Introduction

Musculoskeletal malignancy can be divided into two main categories.

- 1) Primary malignancy including primary bone tumours (such as sarcomas, solitary plasmacytoma and primary bone lymphoma), and primary soft tissue sarcomas (STS).
- 2) Secondary malignancy (i.e. bone metastases).

The incidence of metastatic bone disease is far higher than that of both primary bone malignancy and STS.<sup>1</sup> Whereas the treatment of these two groups is vastly different, all patients need a multidisciplinary approach to management. All patients with a musculoskeletal malignancy, can require the input of specialist nurses, medical and clinical oncologists, orthopaedic, spinal and plastic surgeons, radiologists, pathologists, palliative care teams, occupational and physiotherapists and other members of the wider multi-disciplinary team.

This article is an overview of the non-surgical, oncological management of bone metastases, primary bone tumours and extremity STS. A thorough discussion of all these topics is beyond the scope of this article.

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## Metastatic bone disease

Bone is the third most common site of metastatic disease after liver and lung for malignancies in general. The incidence of bone metastases varies depending on the site of the primary cancer. It occurs in approximately 70% of patients with prostate and breast cancer and 30–40% of patients with lung, kidney and thyroid cancer.<sup>2</sup> Patients may have bone metastases at diagnosis or they may become apparent during the disease course.

Bone metastases can cause significant morbidity which adversely impacts on the patient's quality of life and survival. Skeletal-related events (SRE) help to objectively measure the impact of bone metastases and are often chosen as end points in clinical studies. SRE include pain, pathological fracture, hypercalcaemia, spinal cord compression, the need for palliative radiotherapy or surgical intervention.<sup>2</sup>

Prognosis in patients with bone metastases from breast and prostate cancer can be several years, however survival for lung cancer patients is generally measured in months. The aim of all palliative treatment for bone metastases should be pain relief, preservation of function and skeletal integrity.

Simple measures should be adopted first. Adequate analgesia is essential to allow the patient to maintain functional ability and also to help them tolerate other treatment modalities. The World Health Organization (WHO) analgesic ladder should be used to help guide pain management. Physiotherapy is also important – does the patient need a walking aid, are they able to weight bear?

Chemotherapy, hormone treatment and biological agents are systemic modalities that can in some cancers help improve survival as well as improve symptoms and quality of life by controlling the underlying disease. Analgesia, bisphosphonates, radiotherapy, radiological interventions and surgery are treatment modalities to help improve symptoms and quality of life but do not generally impact on survival time. Treatment is different for each cancer subtype and will also vary for each individual patient depending on performance status, previous treatments and patient choice.

## Palliative radiotherapy for bone metastases

There are two main methods of employing radiation therapy to treat bone metastases: local external beam radiotherapy, and radiopharmaceuticals.

**Local external beam radiotherapy:** local external beam radiotherapy is a reliable and effective modality for treating bone metastases. It is an outpatient treatment and is generally well tolerated. The definition of response to radiotherapy varies, however there are consistent reports of partial response rates (improvement in pain) of approximately 70–80% and complete responses in 30–40%. This can significantly improve a patient's quality of life.

Many different radiotherapy fractionation schedules have been reported. In the UK, a single 8 Gy fraction is recommended. There is an abundance of level 1a evidence including three meta-analyses<sup>3–5</sup> that conclude that shorter fractionation schedules are as effective as longer schedules in controlling pain. Single fraction treatment is far easier on a frail patient where quality of life is paramount. The need for retreatment however is slightly higher in the shorter schedules and the greater the dose per

fraction, the higher the risk of significant late toxicity, the relevance of this depends on individual prognosis. If a single fraction is prescribed, the standard dose is 8 Gy, however there is evidence of efficacy for single doses as low as 4 Gy. There is a tendency for oncologists to prescribe longer fractionation schedules for those patients in whom the prognosis indicates survival for several years. This reduces the need for retreatment and limits late toxicity. An example of this would be a patient with breast cancer and bone metastases as the only site of metastases. However, there is little evidence to support this practice and for the majority of such patients, a single 8 Gy fraction is entirely appropriate.

It usually takes at least 1 week before any relief in pain and the response may subsequently increase until a plateau is reached at 4–6 weeks. Radiotherapy to bone metastases is well tolerated especially in long bones where there is little normal tissue to be damaged. If large volumes of the pelvis or thoracolumbar spine are treated, acute small bowel toxicity may cause nausea and diarrhoea, and one needs to look out for myelosuppression due the large amount of bone marrow in the treatment field. 'Pain flare' – a temporary increase in pain shortly after radiotherapy is reported from 2% to 44% and this is observed both with single and multi-fraction regimes.<sup>6</sup>

Large metastatic lesions involving the cortex, particularly in weight-bearing bones should be considered for prophylactic fixation as they pose a significant risk for pathological fracture (Figure 1). Mirels' score can be used as a guide in this situation. Post-operative radiotherapy is then recommended. In patients with a poor life expectancy and deteriorating condition surgery may be inappropriate and palliative radiotherapy alone may help to reduce pain and aid healing even once fracture has occurred (Figure 2).

Patients may present with a pathological fracture as their first manifestation of malignancy and it is always important to send bone reamings for histological diagnosis. Even when a patient is known to have a malignancy occasionally a second malignancy is identified and this may alter future treatment decisions.

**Stereotactic radiotherapy:** stereotactic radiotherapy (SBRT) involves the delivery of high doses of radiotherapy to precise targets whilst minimizing dose to adjacent normal structures. It is delivered in one or a small number of fractions. It can be useful for treating spinal metastases due to the sensitivity of normal surrounding tissues to radiation and the concern regarding late toxicity as a result of this. Those tumours that are traditionally radio-resistant such as melanoma or renal carcinomas may also benefit from this technique and those patients who require re-irradiation.<sup>7</sup> SBRT is now becoming more widely available with several centres in the UK now approved to deliver this technique for metastatic disease particularly oligometastases.

**Hemi-body irradiation (HBI):** bone metastases are frequently multiple and patients may complain of pain that is not easily localized. Attempts to 'chase' the source of pain may lead to multiple visits to the radiotherapy department with unsatisfactory results. HBI can be an alternative option for such patients and has also been shown to delay the appearance of new painful bone metastases in the treatment field.<sup>8</sup> When treating large volumes with radiotherapy, acute toxicity can be a major

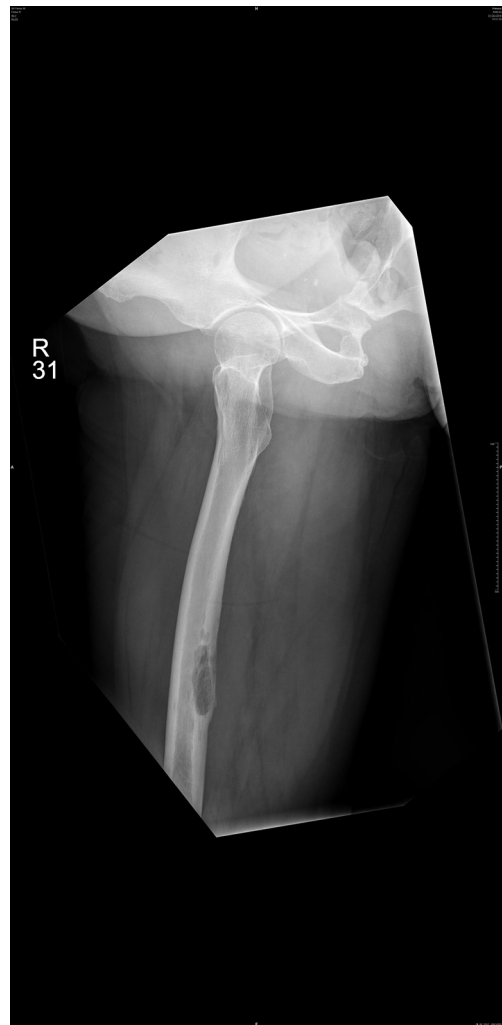


Figure 1 Lateral view of femur showing bone metastasis.

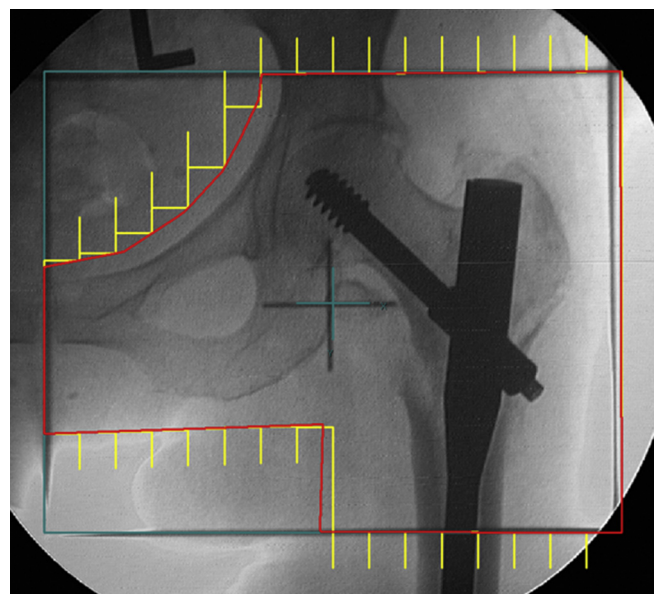


Figure 2 Radiotherapy field to encompass pathological fracture of femur (post-operative).

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