

## 18.

### Bone metastases

#### Localised bone pain in established metastatic disease

##### Background

Uncomplicated local bone pain responds well with response rates of 70–80% after localised external beam treatment. Since response may take 4–6 weeks to achieve, it is recommended that consideration be given to the patient's prognosis before treatment. A number of large randomised controlled trials have been undertaken to explore the optimal dose. Three reviews have been completed using the Cochrane methodology. On the basis of this information, the recommended fractionation is a single dose of 8 Gray (Gy) (Level 1a).<sup>1–4</sup>

Bone metastases may give rise to pain with neuropathic features rather than simple bone pain. One randomised controlled trial specifically addressed this question, comparing single-dose 8 Gy to multifraction treatment, for most patients 20 Gy in five fractions. No major advantage for the multifraction arm was identified, and the recommendation therefore is that these patients should also receive a single dose of 8 Gy.<sup>5</sup>

##### Recommendation

##### **For the initial therapy of pain from bone metastases:**

8 Gy single dose (Grade A)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.<sup>4</sup>

#### Bone metastases in oligometastatic disease

In the context of oligometastatic disease, stereotactic body radiotherapy (SBRT) can achieve local control rates of 80% and treatment has been shown to be well tolerated, with low rates of spinal cord myelopathy (see section 20).

##### Retreatment

Retreatment should be considered in patients still having clinically significant pain after 4–6 weeks despite optimal analgesic. After a single dose, around 25% of patients may need re-treatment at some point.<sup>6</sup> Limited evidence suggests that response rates are similar to those after primary treatment.<sup>7</sup> There are no data to guide optimal dose fractionation for retreatment; a randomised trial compared 8 Gy single dose with 20 Gy in five fractions (eight fractions over the spinal cord) and showed no significant difference (Level 1b).<sup>4,8</sup> Both may be considered acceptable treatments for re-irradiation.

##### Recommendations

##### **For the re-irradiation of bone metastases:**

8 Gy single dose (Grade B)

20 Gy in 5 daily fractions (or 8 fractions over the spinal cord) over 1 week (Grade B)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.<sup>4</sup>

## Scattered bone pain

For metastatic bone pain at several sites despite adequate analgesia, wide-field or hemibody external beam radiotherapy (EBRT) may be effective. Appropriate pre-medication, such as dexamethasone and a 5HT3 antagonist is advised to reduce radiation-induced nausea and vomiting. There are no randomised data to compare such treatment to isotope therapy, but case-control comparisons suggest that all are equally effective. However, EBRT is associated with more toxicity in terms of gastrointestinal and bone marrow side-effects.<sup>9</sup> A large international study tested two, four and five fraction regimens, but there is no evidence to suggest that any of these are superior to giving the treatment in a single-dose (Level 4).<sup>4,10</sup>

### Recommendation

#### **For patients with scattered bone pain:**

Upper hemibody 6 Gy single dose (Grade C)

Lower hemibody 8 Gy single dose (Grade C)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.<sup>4</sup>

## Pathological fracture

### Prophylaxis

Bone metastases with high risk of pathological fracture can be identified from their radiological appearances. Suggested parameters include: those with > 50% cortical destruction, >3 centimetre (cm) maximum diameter, axial cortical involvement >3 cm and multifocal lytic disease.<sup>11</sup> Surgical fixation should be considered.

If radiotherapy is to be used, there is no consensus on the best fractionation in this setting. Higher risk lesions were in general excluded from fractionation trials. Common practice would be for these patients to receive a fractionated regimen such as 20 Gy in five fractions or 8 Gy single dose (Level 5).<sup>4</sup>

### Recommendation

#### **To prevent pathological fracture:**

8 Gy single dose (Level 4) or

20 Gy in 5 fractions over 1 week (Level 4)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.<sup>4</sup>

### Established fracture

Bones such as ribs, vertebrae and pelvic and shoulder girdle bones are not amenable to surgical fixation and can be treated with local radiotherapy. There is no consensus on optimal fractionation.

#### Recommendation

##### **For inoperable pathological fractures:**

8 Gy single dose (Grade D) or  
20 Gy in 5 fractions over 1 week (Grade D)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.<sup>4</sup>

### Postoperative radiotherapy

After internal fixation of a fracture or prophylactic pinning of a high-risk lesion, postoperative radiotherapy is often recommended. There is limited literature to support its efficacy and no consensus on dose. Treatment should be considered for all patients with persisting bone pain after surgery. In cases where treatment is given with the aim of enabling bone healing and long-term rehabilitation, consideration should be given to performance status and predicted survival.

#### Recommendations

##### **Postoperative radiotherapy after fixation of bone metastases:**

8 Gy single dose (Grade D) or  
20 Gy in 5 fractions over 1 week (Grade D)

The types of evidence and the grading of recommendations used within this review are based on those proposed by the Oxford Centre for Evidence-based Medicine.<sup>4</sup>

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## References

1. McQuay H, Carroll D, Moore RA. Radiotherapy for painful bone metastases: a systematic review. *Clin Oncol* 1997; **9**(3): 150–154.
  2. Wu JS, Wong R, Johnston M *et al.* Meta-analysis of dose-fractionation radiotherapy trials for the palliation of painful bone metastases. *Int J Radiat Oncol Biol Phys* 2003; **55**(3): 594–605.
  3. Sze WM, Shelley MD, Held I, Wilt TJ, Mason MD. Palliation of metastatic bone pain: single fraction versus multifraction radiotherapy – a systematic review of randomised trials. *Clin Oncol (R Coll Radiol)* 2003; **15**(6): 345–352.
  4. [www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009](http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009) (last accessed 30/9/16)
  5. Roos DE, Turner SL, O'Brien PC *et al.* Randomized trial of 8 Gy in 1 versus 20 Gy in 5 fractions of radiotherapy for neuropathic pain due to bone metastases. *Radiother Oncol* 2005; **75**(1): 54–63.
  6. van der Linden YM, Lok YJ, Steenland E *et al.* Single fraction radiotherapy is efficacious: a further analysis of the Dutch Study controlling for the influence of retreatment. *Int J Radiat Oncol Biol Phys* 2004; **59**(2): 528–537.
  7. Mithal NP, Needham PR, Hoskin PJ. Retreatment with radiotherapy for painful bone metastases. *Int J of Rad Oncol Biol Phys* 1994; **29**(5): 1011–1014.
  8. Chow E, van der Linden YM, Roos D *et al.* Single versus multiple fractions of repeat radiations for painful bone metastases: a randomised, controlled, non-inferiority trial. *Lancet Oncol* 2014; **15**(2): 164–171.
  9. Dearnaley DP, Bayley RJ, A'Hern RP, Gadd J, zivanovic MM, Lewington VJ. Palliation of bone metastases in prostate cancer. Hemibody irradiation or strontium-89. *Clin Oncol (R Coll Radiol)* 1992; **4**(2): 101–107.
  10. Salazar OM, Sandhu T, da Motta NW *et al.* Fractionated half-body irradiation (HBI) for the rapid palliation of widespread, symptomatic, metastatic bone disease: a randomised Phase III trial of the International Atomic Energy Agency (IAEA). *Int J Radiat Oncol Biol Phys* 2001; **50**(3): 765–775.
  11. van der Linden YM, Kroon HM, Dijkstra SP *et al.* Simple radiographic parameter predicts fracturing in metastatic femoral bone lesions: results from a randomised trial. *Radiother Oncol* 2003; **69**(1): 21–31.
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