Background  Bone metastases are considered uncomplicated if they are not causing neurological compromise and have not resulted in and are not at imminent risk for pathological fracture. They are often accompanied by localized pain at the lesion site, which may be controlled at rest but is incident with activity and often difficult to control with analgesics alone. Clinicians may need to advocate for single-fraction radiation therapy courses for seriously ill patients with refractory pain from uncomplicated bone metastases. This Fast Fact provides guidance for the use of single-fraction radiation treatment for painful bone metastases. See Fast Facts #66 and 67 for information on standard courses of palliative radiation.

Efficacy and Toxicity  A single-fraction radiation treatment for uncomplicated bone metastases has the potential of offering quicker analgesia and lower patient burden in time, cost, and inconvenience than longer radiation schedules (1). Published data suggests that up to 60-80% of patients treated with single-fraction treatment achieve a partial or complete response in pain, meaning significantly lower patient-reported pain scores and decreased use of opioids (2). Pain relief can start within 24-48 hours of treatment but typically occurs within 2-3 weeks. Peak analgesia may not occur for up to 5-6 weeks (2). Patients with a life expectancy less than 1 month may not have sufficient time to warrant even single fraction radiation therapy for pain relief.

Pediatric Use  One study showed that single-treatment radiation courses were well tolerated and associated with rapid pain relief in 37% of pediatric patients (3). They may also reduce the risk of iatrogenic harm by limiting the need for sedation or general anesthesia.

Comparative Evidence  At least 25 randomized clinical trials and 4 meta-analyses have demonstrated equivalent analgesia with single-fraction versus multi-fraction radiation schemas without a difference in efficacy, pain recurrence, or toxicity (1,4). The duration of follow-up varies between studies with most being limited to 3-12 weeks after treatment completion. Multiple studies have showed that patients receiving a single treatment were more likely to require re-treatment (up to 20%) (4).

Pain Flare  Pain flare is a temporary increase in pain at the treated site and can occur following single-dose radiation treatment or any other radiation schedule. A pain flare develops in 30-40% of patients shortly after treatment and generally resolves within a few days (5). Patients should be given anticipatory guidance about pain flares to avoid misattributions of worsening cancer or a failure of radiation therapy. Anti-inflammatory based medications such as non-steroidal anti-inflammatories and corticosteroids are recognized analgesics for radiation induced pain flares (5,6). A randomized controlled trial of patients receiving single-fraction treatment showed that 8 mg of dexamethasone orally < 1 hour prior to the start of radiation therapy and 8 mg daily 1-4 days thereafter can help prevent radiation induced pain flares (5).

Re-Treatment  About 55% of patients who live > 1 year post-treatment develop pain again (typically 18 weeks or more after treatment completion) regardless of the radiation treatment course (7). If bone pain persists or returns, patients treated with any of the common radiation regimens can be considered for an additional single-fraction 8 Gy radiation retreatment to that site 4-6 weeks status post initial treatment (1,4). Patients usually experience moderate pain relief when re-treated (8).

Cost Analysis  One study found that single 8-Gy fraction treatment was less expensive than a 10-fraction course (mean cost $998 vs $2316), even when accounting for re-treatment risk and potential survival differences (10). Use of single-fraction radiation therapy can be a cost-effective choice for the palliation of bone metastases, even compared to chemotherapy or other treatments (9-12).

Use  Despite the evidence for single-fraction radiation therapy for uncomplicated bone metastases, it is not often used. A 2015 study of nearly 25,000 U.S patients who received radiation therapy for bone metastases from breast, prostate, and lung cancer showed <5% were treated with a single 8 Gy treatment (13). A Choosing Wisely campaign for the American Academy of Hospice and Palliative
Medicine recommends that clinicians advocate and pursue single fraction radiation therapy for seriously ill patients with an anticipated prognosis > 1 month and uncomplicated painful bone metastases (14). In Canada, the use of single-fraction radiation therapy is likely higher than in the US, but utilization varies substantially between physicians and centers, from 26-73% (15-16).

Summary
• Patients with incident pain from uncomplicated bone metastases may receive palliative benefit from single radiation treatment.
• About 1/3 of patients develop a temporary pain flare which may be alleviated by dexamethasone.
• Re-treatment for pain that is intractable or recurs is common.

References

Authors’ Affiliations: Mayo Clinic, Jacksonville, FL; Medical College of Wisconsin, Milwaukee, WI
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