Radiotherapy in Cancer Pain

Two-thirds of patients with metastatic cancer experience pain. Pain originating from skeletal metastases is the most common form of cancer pain. Radiotherapy is the single most effective oncological treatment of cancer pain. In the treatment of bone metastases, the pain-relieving efficacy of both external radiotherapy and systemic radionuclide therapy is well documented. Radiotherapy is also effective in treating pain caused by soft-tissue tumors, although only a limited number of studies have investigated its efficacy in relieving pain caused by soft-tissue tumors.

The mechanism behind the pain-relieving effect of radiotherapy is incompletely understood. There is no direct correlation between the effectiveness of radiotherapy and the radiosensitivity of the tumor or the dose administered. Tumor shrinkage and inhibition of the release of chemical pain mediators seem to be the main mechanisms by which radiotherapy acts. The rapid onset of pain relief—within days—is attributed to the decrease of various chemical pain mediators, whereas tumor shrinkage and recalcification of osteolytic bone lesions contribute to the long-lasting effect [5].

Local Field Radiotherapy in the Treatment of Bone Metastases

- Several large controlled studies obtained complete pain relief in 15–60% of patients and at least 50% pain relief in 50–80% of patients. The onset of pain relief varied from a few days to 4 weeks, and the duration of relief ranged between 3 and 6 months [2,8,10].
- In a Cochrane analysis, radiotherapy produced complete pain relief in 25% of patients and at least 50% relief in 41% of patients at some time during the trials. The number-needed-to-treat (NNT) to achieve complete relief in one patient at 1 month was 4.2 (95% CI 3.7–4.7) [3].

Single-Fraction Therapy

- Single-fraction treatment (8 Gy) is as effective as a multifraction regimen with 20 Gy in 5 fractions or 30 Gy in 10 fractions [2,3,8,10].
- Re-treatment after single-fraction therapy is twice as common compared to multifraction therapy (20–25% vs. up to 10%, respectively) [2,8,10].
- There are no differences between single- and multifraction therapy in the time to initial improvement in pain, time to complete pain relief, or time to first increase in pain at any time up to 12 months from randomization, nor in the class of analgesics used.
- Single-fraction therapy (8 Gy) is as effective as multifraction therapy (20 Gy in 5 fractions) for neuropathic pain due to bone metastases. However, time to treatment failure seems to be shorter after single-fraction treatment (2.4 vs. 3.7 months, respectively) [6].
- There is no difference in quality of life or side effects between the different fractionation schedules. Acute grade II–IV toxicity seems to be more common among patients receiving fractionated radiotherapy (17% vs. 10%); late toxicity of palliative radiotherapy is rare (4%) [2].

Re-irradiation

- Re-irradiation is effective in two-thirds of patients. Intensive pain and previous single-fraction treatment predict re-treatment [9].

Radiotherapy in the Treatment of Pain Caused by Soft-Tissue Tumors

- The efficacy of radiotherapy in the alleviation of pain arising from soft-tissue tumors is less well documented.
- Radiotherapy alleviates local symptoms of inoperable lung cancer in two-thirds of patients. Complete symptom relief is seen in one-third of patients. Hemoptysis is alleviated in most patients, pain in two-thirds, and dyspnea and cough in approximately half of all patients treated. Symptom control lasts approximately 2–3 months.

- Single-fraction therapy alleviates symptoms as effectively as multiple fractions [4].

Wide-Field Radiotherapy and Systemic Radionuclide Therapy

Wide-field radiotherapy and radioisotopes are used to alleviate pain caused by widespread painful skeletal metastases. They may also be administered prophylactically to reduce the number of new symptomatic sites.

Wide-Field Radiotherapy

- Scattered painful skeletal lesions may be treated with single-fraction and fractionated wide-field or half-body irradiation to the upper, lower, or mid-body depending on the extent of metastases and symptoms.
- A single fraction of 6 Gy is given to the upper half-body field in order to avoid pulmonary toxicity and 8 Gy to the lower half-body field.
- Half-body irradiation relieves pain as effectively as local external radiotherapy. In patients with advanced disease, more than half stay free from pain the rest of their life.
- Half of those who respond obtain pain relief within 48 hours, and 80% experience relief within a week [7].
- The side effects include nausea, vomiting, diarrhea, fever, transient increase in bone pain, hematologic toxicity, and, rarely, pneumonitis. Patients are usually admitted to hospital for intravenous hydration and premedication. An interval of at least 4 weeks is recommended before administering the other half-body treatment or continuing chemotherapy to avoid severe hematologic toxicity.

Systemic Radionuclide Therapy

- Strontium-89 and samarium-153 are the most commonly used radioisotopes for alleviating pain caused by bone metastases. The effect is best documented in prostate cancer, where bone lesions are predominantly osteosclerotic.
- Radioisotope therapy is as effective as external radiotherapy in alleviation of pain [1].
- The average onset of pain relief is somewhat slower, taking 2 to 4 weeks.
- Radioisotope therapy is well tolerated. It can be administered on an outpatient basis. Transient hematologic toxicity should be taken into consideration.

References

1. Finlay IG, Mason MD, Shelley M. Radioisotopes for the palliation of metastatic bone cancer: a systematic review. Lancet Oncol 2005;6:392–400.
2. Hartsell WF, Scott CB, Bruner DW, Scarantino CW, Ivker RA, Roach M 3rd, Suh JH, Demas WF, Movsas B, Petersen IA, et al. Randomized trial of short- versus long-course radiotherapy for palliation of painful bone metastases. J Natl Cancer Inst 2005;97:798–804.
3. McQuay HJ, Collins SL, Carroll D, Moore RA. Radiotherapy for the palliation of painful bone metastases. Cochrane Database Syst Rev 2000;(2):CD001793.
4. Medical Research Council Lung Cancer Working Party. Inoperable non-small-cell lung cancer (NSCLC): a Medical Research Council randomised trial of palliative radiotherapy with two fractions or ten fractions. Br J Cancer 1991;63:265–70.
5. Mercadante S. Malignant bone pain: pathophysiology and treatment. Pain 1997;69:1–18.
6. Roos DE, Turner SL, O'Brien PC, Smith JG, Spry NA, Burmeister BH, Hoskin PJ, Ball DL; Trans-Tasman Radiation Oncology Group, TROG 96.05. 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;75:54–63.
7. Salazar OM, Rubin P, Hendrickson FR, Komaki R, Poulter C, Newall J, Asbell O, Mohiuddin M, van Ess J. Single-dose half-body irradiation for palliation of multiple bone metastases from solid tumors. Cancer 1986;58:29–36.
8. Steenland E, Leer JW, van Houwelingen H, Post WJ, van den Hout WB, Kievit J, de Haes H, Martijn H, Oei B, Vonk E, et al. The effect of a single fraction compared to multiple fractions on painful bone metastases: a global analysis of the Dutch Bone Metastasis Study. Radiother Oncol 1999;52:101–9.
9. van der Linden YM, Lok JJ, Steenland E Martijn H, van Houwelingen H, Marijnen CA, Leer JW, Dutch Bone Metastasis Study Group. Single fraction radiotherapy is efficacious: a further analysis of the Dutch Bone Metastasis Study controlling for the influence of re-treatment. Int J Radiat Oncol Biol Phys 2004;59:528–37.
10. Yarnold JR. 8 Gy single fraction radiotherapy for the treatment of metastatic skeletal pain: randomised comparison with a multifraction schedule over 12 months of patient follow-up. On behalf of the Bone Pain Trial Working Party. Radiother Oncol 1999;52:111–21.

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