



Review Article

Single Fraction versus Multi Fraction Radiotherapy Treatment Schedules for Management of Painful Bone Metastasis

Authors

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Introduction

Bone metastasis is very common in certain solid malignancies. The most common bones to be involved is vertebrae, lumbar vertebrae to be most commonly involved. The incidence of bone metastases varies significantly, depending on the primary site, with breast and prostate cancer accounting for up to 70% of patients with metastatic disease. Bone metastases may be found in up to 85% of patients suffering from breast, prostate, or lung cancer. Other primary sites with a propensity for bone metastases include thyroid, melanoma, and kidney. On the other hand, gastrointestinal sites of primary malignancy give rise to bone metastasis in only 3% to 15% of patients with metastatic disease. Some hematologic malignancies, including myeloma and lymphoma, can also cause significant pain and bone destruction. Patients with bone metastases from lung cancer have short median survival durations of 6 months. However, patients with bone metastases from breast or prostate primary sites may have significantly longer survival times.

Materials and Methods

The review article was compiled by searching PubMed and Medline databases. Electronic early-

release publications were also included. The search terms used included 'bone metastases', 'bone metastasis', 'metastatic spinal cord compression', 'malignant spinal cord compression', 'metastatic epidural spinal cord compression', 'malignant epidural spinal cord compression', 'pathological fracture'. When possible, primary sources were quoted.

Results

Randomized trials and metanalysis demonstrated that single fraction radiotherapy 8 Gy/# is as effective for pain relief as multi fraction regimens such as 20 Gy/5# or 30 Gy/10#. These results have been confirmed by three randomized trials. Kapoor et al took 250 consecutive patients of bone metastasis for the study. Sixty-two percent of the patients received a single fraction while the remaining received 10 fractions. In the 10-fraction group, overall response was present in 60% of the patients. Stable pain was present in 23% of the patients while 9% patients had progressive pain. In the single-fraction arm, overall response was seen in 58%, stable pain in 27% and progressive pain in 7% of the patients. Six percent of the patients were lost to follow-up.

Hamouda et al took 107 patients with painful localized bone metastases requiring palliative radiotherapy into a prospective randomized trial comparing 8 Gy single fraction (SF group) with 40 Gy in 20 fractions, five fractions/week (CF group). There were no significant differences in the frequency or duration of pain relief between the two study groups. The median duration of pain relief was 12 weeks in the single fraction group and 13.5 weeks in conventional fraction group.

Hartsell et al did prospective, phase III randomized study of palliative radiation therapy for patients with breast or prostate cancer who had one to three sites of painful bone metastases and moderate to severe pain. There were 455 patients in the 8-Gy arm and 443 in the 30-Gy arm. The overall response rate was 66%. Complete and partial response rates were 15% and 50%, respectively, in the 8-Gy arm compared with 18% and 48% in the 30-Gy arm ($P = .6$). At 3 months, 33% of all patients no longer required narcotic medications.

Foro et al took total of 160 patients to receive a single 8-Gy fraction or 30 Gy in 10 fractions. The overall response was 75% in the 8-Gy arm and 86% in the 30-Gy arm. Complete response and partial response rates were 15% and 60% in the 8-Gy arm, 13% and 73% in the 30-Gy arm. These differences were not statistically significant. The re-treatment rate was 28% vs 2% in the 8-Gy and 30-Gy arms, respectively, these were statistically significant.

STUDY (NO. OF PTS)	PAIN RELIEF IN SINGLE FRACTION RT	PAIN RELIEF IN MULTIPLE FRACTION RT
Kapoor et al (250)	58%	60%
Hamouda et al (107)	82%	44%
Hartsell et al (455)	48%	50%
Foro et al (160)	75%	86%

Meta Analysis

Wu et al compared two trials of single vs. single, eight trials of single vs. multiple, and six trials of multiple vs. multiple fractions. The complete and overall response rates from studies comparing

single-fraction RT (median 8 Gy, range 8–10 Gy) against multifraction RT (median 20 Gy in 5 fractions, range 20 Gy in 5 fractions to 30 Gy in 10 fractions) were homogeneous and allowed pooling of data. Of 3260 randomized patients in seven studies, 539 (33.4%) of 1613 and 523 (32.3%) of 1618 patients achieved a complete response after single and multifraction RT, respectively, giving a risk ratio of 1.03 (95% confidence interval 0.94–1.14; $p = 0.5$). The overall response rate was in favor of single-fraction RT (1011 [62.1%] of 1629) compared with multifraction (958 [58.7%] of 1631; risk ratio 1.05, 95% confidence interval 1.00–1.11, $p = 0.04$), reaching statistical significance. However, when the analysis was restricted to evaluated patients alone, the overall response rates were similar for single fraction and multifraction RT, at 1011 (72.7%) of 1391 and 958 (72.5%) of 1321, respectively (risk ratio 1.00; $p = 0.9$).

Chow et al compared 25 randomised controlled trials. For intention-to-treat patients, the overall response rate was similar in patients receiving single fractions (1696 of 2818; 60%) and multiple fractions (1711 of 2799; 61%). Complete response rates were 620 of 2641 (23%) in the single fraction arm and 634 of 2622 (24%) in the multiple fraction arm. No significant difference was seen in overall or complete response rates.

Conclusion

All the above studies and meta analysis suggest that in symptomatic pain relief for bone metastasis there is no difference between 8 Gy single fraction and conventional 30 Gy/10# or 20 Gy/5#. Overall response in pain relief would be same in both treatments. So in non-compliant patients, patients most likely lost to follow-up or patients with less overall survival single fractionation schedule can be considered as compared to multi fraction treatment.

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