

Research Article

# Effectiveness of Palliative Radiotherapy in Pain Relief and Reduction of Analgesic Dependence among Patients with Painful Bone Metastases: A Prospective Observational Study

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## ABSTRACT

**Background:** Bone metastases are a common complication of advanced malignancies and are frequently associated with severe pain, reduced mobility, impaired quality of life, and increased analgesic dependence. Palliative radiotherapy is an established modality for symptomatic relief in these patients.

**Aim:** To evaluate the effectiveness of palliative radiotherapy in achieving pain relief, reducing analgesic dependence, and improving quality of life among patients with painful bone metastases.

**Materials and Methods:** This prospective observational study was conducted in the Department of Radiation Oncology of a tertiary care center over a period of two years. A total of 68 patients aged 30-80 years with painful bone metastases from various primary malignancies were included. Pain intensity was assessed using the Visual Analogue Scale (VAS), while analgesic dependence and quality-of-life parameters were evaluated during follow-up. Patients received either single-fraction or multiple-fraction external beam radiotherapy. Follow-up assessments were performed at 10 days, 2 weeks, 4 weeks, 2 months, 6 months, 1 year, and 2 years after treatment.

**Results:** In patients with painful bone secondaries, breast carcinoma was the most common primary malignancy, followed by lung and prostate carcinoma. Significant pain relief was observed as early as 10 days following radiotherapy, with maximal response noted between 2 and 4 weeks. Complete pain relief was achieved in 35.3% patients, while 48.5% showed partial relief. Reduction in analgesic dependence was observed in 85.3% of patients. Overall quality of life improved in 76.5% patients. Refractory pain requiring further intervention was noted in 16.2% cases. Comparable efficacy was observed between single- and multiple-fraction radiotherapy schedules.

**Conclusion:** Palliative radiotherapy provides effective pain control, reduces opioid dependence, and improves quality of life in patients with painful bone metastases, with both single and multiple fractionation schedules demonstrating similar clinical outcomes.

**Keywords:** Bone Metastases, Palliative Radiotherapy, Pain Relief, Analgesic Dependence, Opioid Reduction, Quality Of Life, Visual Analogue Scale.

## INTRODUCTION

Bone metastases represent one of the most common complications of advanced malignancies and are a major cause of cancer-related morbidity worldwide. The skeletal system is the third most frequent site of metastatic spread after the lungs and liver. Bone involvement is particularly common in malignancies such as carcinoma breast, prostate, lung, thyroid, and multiple myeloma<sup>[1]</sup>. The vertebral column, pelvis, ribs,

and long bones are among the most frequently affected sites due to their rich vascular supply and active bone marrow content. Skeletal metastases can result in severe pain, pathological fractures, spinal cord compression, hypercalcemia, impaired mobility, and significant deterioration in quality of life. Among these manifestations, pain remains the most distressing symptom and substantially contributes to physical disability, psychological stress, and increased healthcare utilization<sup>[2]</sup>.

The incidence of bone metastases has increased over recent decades due to improved survival among cancer patients and advancements in diagnostic imaging. Approximately 60–70% of patients with advanced breast or prostate carcinoma and 30–40% of patients with lung carcinoma develop skeletal metastases during the course of their illness<sup>[3]</sup>. Pain associated with bone metastases is often multifactorial, resulting from periosteal irritation, inflammatory mediator release, nerve compression, and structural instability. Management of metastatic bone pain therefore requires a multidisciplinary approach involving systemic therapy, analgesics, surgery, bisphosphonates, and radiotherapy.

Palliative radiotherapy is considered one of the most effective and widely accepted modalities for pain control in patients with bone metastases. External beam radiotherapy provides pain relief by reducing tumor burden, decreasing inflammatory response, and promoting recalcification of osteolytic lesions. Previous studies have demonstrated that nearly 60–80% of patients experience significant pain relief following palliative radiotherapy, while complete pain resolution occurs in approximately one-third of patients<sup>[4]</sup>. Rapid onset of pain improvement is commonly observed within 1–2 weeks, with peak response occurring by 4–6 weeks after treatment. Furthermore, radiotherapy has been shown to reduce analgesic and opioid dependence, improve mobility, and enhance overall quality of life<sup>[5]</sup>. Several randomized trials and systematic reviews have compared single-fraction and multiple-fraction radiotherapy schedules for painful bone metastases. The Radiation Therapy Oncology Group and Dutch Bone Metastasis Study demonstrated comparable pain response rates between single-fraction regimens such as 8 Gy in one fraction and multifraction schedules such as 20 Gy in 5 fractions or 30 Gy in 10 fractions<sup>[6]</sup>. Single-fraction treatment offers advantages including convenience, reduced hospital visits, lower treatment cost, and improved patient compliance, particularly in individuals with poor performance status. However, retreatment rates may be slightly higher with single-fraction schedules.

Despite substantial evidence supporting palliative radiotherapy, variability exists in treatment response, duration of pain control,

opioid requirement, and long-term quality-of-life outcomes across different patient populations. In developing countries, limited data are available regarding real-world clinical outcomes and analgesic dependence following palliative radiotherapy for bone metastases<sup>[7]</sup>. Therefore, the present study was undertaken to evaluate pain relief, reduction in analgesic dependence, improvement in quality of life, and treatment response patterns among patients receiving palliative radiotherapy for painful bone metastases in a tertiary care setting.

## AIM AND OBJECTIVES

### Aim

To evaluate the effectiveness of palliative radiotherapy in achieving pain relief, reducing analgesic dependence, and improving quality of life among patients with painful bone metastases.

### Objectives

1. To assess the degree and timing of pain relief following palliative radiotherapy.
2. To evaluate reduction in analgesic (opioid) dependence following radiotherapy.
3. To assess improvement in quality of life and treatment response patterns, and compare outcomes between single- and multiple-fraction radiotherapy schedules.

## MATERIALS AND METHODS

### Study Design and Setting

This prospective observational study was conducted in the Department of Radiation Oncology of a tertiary care teaching hospital over a period of two years (August 2021 – September 2023). The study evaluated the effectiveness of palliative radiotherapy in achieving pain relief, reducing analgesic dependence, and improving quality of life among patients with painful bone metastases secondary to advanced malignancies.

### Study Population

The study included adult patients aged between 30 and 80 years with radiologically or histopathologically confirmed primary malignancy and clinically significant painful bone metastases requiring palliative radiotherapy. Both male and female patients were included. The common primary malignancies encountered included carcinoma breast, lung carcinoma, carcinoma prostate, multiple myeloma, carcinoma cervix/endometrium, and hepatocellular carcinoma.

### Inclusion Criteria

- Patients aged 30–80 years.
- Histopathologically confirmed primary malignancy.
- Radiological evidence of bone metastases.
- Presence of painful skeletal metastases requiring palliative radiotherapy.
- Eastern Cooperative Oncology Group (ECOG) performance status permitting radiotherapy.

### Exclusion Criteria

- Prior radiotherapy to the same metastatic site.
- Patients with spinal cord compression requiring urgent surgical intervention.
- Patients with severe cognitive impairment or psychiatric illness affecting pain assessment.
- Patients unable to comply with follow-up evaluation.

### Sample Size Calculation

The sample size was calculated using the formula for estimating a single population proportion:

$$n = \frac{Z^2 P(1 - P)}{d^2}$$

Where:

- $n$  = required sample size
- $Z$  = standard normal deviate at 95% confidence interval = 1.96
- $P$  = expected proportion of pain response following palliative radiotherapy
- $d$  = allowable absolute error

A prospective cohort study conducted by van der Velden et al<sup>[8]</sup>, reported an overall pain response rate of approximately 61% following palliative radiotherapy for bone metastases. Therefore, the expected proportion ( $P$ ) was taken as 0.61.

Assuming:

- $P = 0.61$
- $Z = 1.96$
- Allowable error ( $d$ ) = 12% = 0.12

Substituting into the formula:

$$\begin{aligned} n &= \frac{(1.96)^2 \times 0.61 \times (1 - 0.61)}{(0.12)^2} \\ n &= \frac{3.84 \times 0.61 \times 0.39}{0.0144} \\ n &= \frac{0.914}{0.0144} \\ n &= 63.5 \end{aligned}$$

The calculated minimum sample size was approximately 64 patients. Considering possible attrition and loss to follow-up due to mortality during the 2-year follow-up period, an additional 5–10% was included. Hence, the final sample size was rounded to approximately 68 patients.

### Sampling Technique

Consecutive sampling was employed, and all eligible patients presenting during the study period were included until the required sample size was achieved.

### Baseline Assessment

At enrollment, detailed clinical evaluation was performed and the following information was recorded:

- Age and gender
- Primary malignancy
- Site and number of bone metastases
- Duration and severity of pain
- ECOG performance status
- Current analgesic/opioid usage
- Previous oncological treatment history
- Radiological findings

Relevant investigations including radiographs, CT scan, MRI, PET-CT, or bone scan findings were reviewed whenever available.

### Pain Assessment

Pain intensity was assessed using the Visual Analogue Scale (VAS), scored from 0 to 10.

$0 \leq \text{VAS Pain Score} \leq 10$

Where:

- 0 indicated no pain
- 10 indicated worst imaginable pain

Pain assessment was performed before radiotherapy and during each follow-up visit.

### Assessment of Analgesic Requirement

Analgesic usage was documented before treatment and during follow-up. Opioid and non-opioid analgesic requirements were categorized according to the World Health Organization analgesic ladder. Reduction in frequency or dosage of analgesic use following radiotherapy was considered improvement in analgesic dependence.

### Quality of Life Assessment

Quality of life was assessed clinically based on:

- Improvement in mobility
- Sleep quality
- Ability to perform daily activities

- Reduction in pain-related functional limitation
- Overall patient-reported well-being

### Radiotherapy Protocol

All patients received external beam palliative radiotherapy to the symptomatic metastatic site using standard departmental protocols. Treatment planning was individualized based on site of metastasis, performance status, prognosis, and treating physician discretion. Patients received either:

- Single-fraction radiotherapy (e.g., 8 Gy in a single fraction)
- or
- Multiple-fraction radiotherapy schedules such as:
  - 20 Gy in 5 fractions
  - 30 Gy in 10 fractions

Appropriate immobilization and simulation techniques were employed before treatment planning.

### Follow-Up and Response Assessment

Patients were followed up at:

- 10 days
- 2 weeks
- 4 weeks
- 2 months
- 6 months
- 1 year
- 2 years after completion of radiotherapy

Pain relief was categorized as:

### Complete Response

Complete disappearance of pain without increase in analgesic requirement.

### Partial Response

Reduction in pain intensity by at least 2 points on the VAS scale and/or reduction in analgesic usage.

### Refractory Disease

Persistent or worsening pain requiring additional interventions such as:

- Escalation of opioid therapy
- Nerve block procedures
- Surgical intervention
- Re-irradiation

Patients who failed to show response within 2 months following radiotherapy were considered less likely to derive subsequent benefit and were evaluated for alternative pain management strategies.

Patients lost to follow-up due to death during the study period were also documented and included in survival and follow-up analysis.

### Outcome Measures

### Primary Outcome

- Degree and timing of pain relief following palliative radiotherapy.

### Secondary Outcomes

- Reduction in analgesic/opioid dependence.
- Improvement in quality of life.
- Comparison between single- and multiple-fraction radiotherapy schedules.
- Identification of refractory cases requiring additional intervention.

### Statistical Analysis

Data were entered in Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) software version 25.0. Categorical variables were expressed as frequency and percentage, while continuous variables were expressed as mean  $\pm$  standard deviation.

The following statistical tests were applied:

- Chi-square test for categorical variables
- Paired t-test or Wilcoxon signed-rank test for comparison of pre- and post-treatment pain scores
- Kaplan–Meier survival analysis for long-term follow-up outcomes where applicable

A p-value of less than 0.05 was considered statistically significant.

### Ethical Considerations

Institutional Ethics Committee approval was obtained prior to commencement of the study. Written informed consent was obtained from all participants before enrollment. Confidentiality of patient information was maintained throughout the study in accordance with ethical guidelines and the Declaration of Helsinki (revised in 2024).

### RESULTS

A total of 68 patients with painful bone metastases who received palliative radiotherapy were included in the study. Majority of the patients belonged to the age group of 51–70 years, with females constituting a slight predominance due to the higher proportion of breast carcinoma cases. Breast carcinoma was the most common primary malignancy, followed by lung and prostate carcinoma. Significant pain relief was observed as early as 10 days following radiotherapy, with maximal response noted between 2 and 4 weeks. Most patients demonstrated reduction in analgesic dependence and improvement in quality of life during follow-up.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population (n = 68)

| Variable                     | Frequency (n) | Percentage (%) |
|------------------------------|---------------|----------------|
| <b>Age Group (Years)</b>     |               |                |
| 30–40                        | 8             | 11.8           |
| 41–50                        | 14            | 20.6           |
| 51–60                        | 22            | 32.4           |
| 61–70                        | 18            | 26.5           |
| 71–80                        | 6             | 8.8            |
| <b>Gender</b>                |               |                |
| Male                         | 31            | 45.6           |
| Female                       | 37            | 54.4           |
| <b>Primary Malignancy</b>    |               |                |
| Breast carcinoma             | 22            | 32.4           |
| Lung carcinoma               | 16            | 23.5           |
| Prostate carcinoma           | 11            | 16.2           |
| Multiple myeloma             | 8             | 11.8           |
| Cervix/Endometrial carcinoma | 7             | 10.3           |
| Hepatocellular carcinoma     | 4             | 5.9            |

Table 2. Radiotherapy Fractionation Schedules Among Study Participants (n = 68)

| Fractionation Schedule | Frequency (n) | Percentage (%) |
|------------------------|---------------|----------------|
| Single fraction RT     | 29            | 42.6           |
| Multiple fraction RT   | 39            | 57.4           |

#### Multiple Fraction Schedules

| Schedule           | Frequency (n) | Percentage (%) |
|--------------------|---------------|----------------|
| 20 Gy/5 fractions  | 24            | 35.3           |
| 30 Gy/10 fractions | 15            | 22.1           |

Table 3. Pain Response Following Palliative Radiotherapy during Follow-Up (n = 68)

| Follow-Up Period | Mean VAS Score $\pm$ SD | Patients with Pain Relief n (%) |
|------------------|-------------------------|---------------------------------|
| Pre-radiotherapy | 8.4 $\pm$ 1.1           | —                               |
| 10 days          | 6.3 $\pm$ 1.5           | 29 (42.6)                       |
| 2 weeks          | 4.8 $\pm$ 1.6           | 46 (67.6)                       |
| 4 weeks          | 3.2 $\pm$ 1.4           | 55 (80.9)                       |
| 2 months         | 2.9 $\pm$ 1.3           | 57 (83.8)                       |
| 6 months         | 3.4 $\pm$ 1.5           | 48 (70.6)*                      |

\*Reduced number due to disease progression and mortality during follow-up

Table 4. Treatment Response and Analgesic Dependence after Palliative Radiotherapy (n = 68)

| Variable                                 | Frequency (n) | Percentage (%) |
|------------------------------------------|---------------|----------------|
| <b>Treatment Response</b>                |               |                |
| Complete pain relief                     | 24            | 35.3           |
| Partial pain relief                      | 33            | 48.5           |
| Refractory disease                       | 11            | 16.2           |
| <b>Reduction in Analgesic Dependence</b> |               |                |
| Significant reduction                    | 41            | 60.3           |
| Mild reduction                           | 17            | 25.0           |
| No reduction                             | 10            | 14.7           |

Table 5. Quality of Life Improvement and Follow-Up Outcomes (n = 68)

| Outcome Variable        | Frequency (n) | Percentage (%) |
|-------------------------|---------------|----------------|
| Improved mobility       | 49            | 72.1           |
| Improved sleep quality  | 44            | 64.7           |
| Improved daily activity | 46            | 67.6           |

|                                               |    |      |
|-----------------------------------------------|----|------|
| Overall improvement in quality of life        | 52 | 76.5 |
| Required additional pain intervention         | 11 | 16.2 |
| Lost to follow-up due to death within 2 years | 21 | 30.9 |

## DISCUSSION

Bone metastases are a major source of morbidity among patients with advanced malignancies, significantly affecting pain perception, physical functioning, and quality of life. Palliative radiotherapy remains one of the most effective modalities for symptomatic management of metastatic bone pain. The present study evaluated pain relief, reduction in analgesic dependence, improvement in quality of life, and treatment response following palliative radiotherapy among 68 patients with painful bone metastases. In the present study, the majority of patients belonged to the age group of 51–70 years, with a slight female predominance. Breast carcinoma was the most common primary malignancy, followed by lung and prostate carcinoma. These findings are comparable with the observations reported by Coleman et al., who noted that breast and prostate cancers account for the largest proportion of skeletal metastases because of their prolonged survival and high propensity for osseous spread<sup>[9]</sup>. Similar demographic distributions were also reported in studies by Chow et al. and Lutz et al.<sup>[4,10]</sup>.

Pain relief following palliative radiotherapy was observed as early as 10 days after treatment, with maximal response occurring between 2 and 4 weeks. In the present study, 83.8% of patients experienced either complete or partial pain relief. These findings are consistent with the systematic review by Chow et al., which demonstrated overall pain response rates of 60–80% following external beam radiotherapy for painful bone metastases<sup>[10]</sup>. Hartsell et al., in the Radiation Therapy Oncology Group trial, also reported significant pain improvement in approximately 66% of treated patients irrespective of fractionation schedule<sup>[5]</sup>. The early onset of pain relief observed in the present study may be attributed to reduction in tumor-associated inflammatory mediators and decreased periosteal irritation following irradiation. Complete pain relief was achieved in 35.3% of patients in the current study, while 48.5% experienced partial relief. Comparable complete response rates ranging from 25% to 40% have been documented in previous randomized studies. Steenland et al. reported complete pain response in nearly one-third of patients receiving palliative radiotherapy for

skeletal metastases<sup>[6]</sup>. Similar findings were also described by van der Linden YM et al.<sup>[11]</sup>. The proportion of refractory cases in the present study was 16.2%, which may reflect aggressive disease biology, extensive skeletal involvement, or poor baseline performance status.

A substantial reduction in analgesic dependence was observed in the present study, with nearly 85% of patients demonstrating decreased opioid requirement following treatment. This finding is in agreement with the ASTRO evidence-based guidelines, which state that palliative radiotherapy not only alleviates pain but also reduces opioid consumption and associated adverse effects<sup>[4]</sup>. Reduction in analgesic dependence contributes significantly to improved patient comfort, functional status, and treatment compliance. Improvement in quality of life was noted in 76.5% of patients, particularly in terms of mobility, sleep quality, and daily activities. Similar improvements have been reported by Wu et al., who demonstrated better functional outcomes and enhanced patient-reported well-being following radiotherapy for bone metastases<sup>[12]</sup>. Relief of pain enables patients to perform routine activities more effectively and reduces psychological distress associated with chronic cancer pain.

The present study also demonstrated comparable clinical efficacy between single-fraction and multiple-fraction radiotherapy schedules. These findings are concordant with the Dutch Bone Metastasis Study and the RTOG trial, both of which concluded that single-fraction radiotherapy provides pain relief equivalent to multifraction regimens<sup>[5,6]</sup>. Single-fraction schedules may therefore be advantageous in patients with limited life expectancy because of improved convenience, shorter treatment duration, and reduced healthcare burden. Overall, the findings of the present study support the role of palliative radiotherapy as an effective, safe, and practical modality for pain management in patients with bone metastases. Early intervention with radiotherapy can significantly reduce pain severity, minimize opioid dependence, and improve overall quality of life in advanced cancer patients.

### Limitations

The study was conducted in a single tertiary care center with a relatively small sample size, which may limit generalizability of the findings. Heterogeneity in primary malignancies and metastatic sites could have influenced treatment response. Quality-of-life assessment was primarily based on clinical evaluation rather than standardized validated questionnaires. In addition, loss to follow-up due to disease progression and mortality during the 2-year follow-up period may have affected long-term outcome assessment.

### CONCLUSION

Palliative radiotherapy is an effective and well-tolerated treatment modality for patients with painful bone metastases. The present study demonstrated significant pain relief, reduction in analgesic/opioid dependence, and improvement in quality of life following radiotherapy. Pain relief was observed as early as 10 days after treatment, with maximal response occurring within 2–4 weeks. Both single-fraction and multiple-fraction radiotherapy schedules showed comparable efficacy in symptom control. Early use of palliative radiotherapy can therefore play an important role in improving functional status and overall patient comfort in advanced malignancy.

### Declarations

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### Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Author Contributions

K.L. Jayakumar: Methodology, Resources, Supervision, Validation, Critical revision of manuscript. Rasi.S : Conceptualization, Data curation, Formal analysis, Investigation, Writing – original draft preparation, Writing – review & editing. All authors read and approved the final manuscript.

### Availability of Data and Materials

The datasets generated and/or analysed during the current study are not publicly available due to institutional data protection policies but are available from the

corresponding author on reasonable request, subject to approval by the Institutional Ethics Committee.

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