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Review Article

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Radiotherapy in the Management of Bone Metastases: An Updated Review of Current Evidence

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Abstract

Bone metastases are a frequent and clinically consequential manifestation of advanced malignancy, contributing significantly to pain, skeletal-related events like fractures and impaired quality of life. With improvements in systemic therapies, patients are living longer with metastatic disease, making optimal management of bone metastasis a major determinant of morbidity and quality of life. Radiotherapy remains a central component of treatment, evolving from purely palliative intent to a modality capable of durable local control in selected patients.

This narrative review synthesizes evidence from randomized trials, observational studies, translational research and contemporary international guidelines. It addresses the classification, prognosis and multimodality treatment of bone metastases, with particular emphasis on radiotherapy.

Bone metastases arise via a complex tumor–bone microenvironment interactions and present as osteolytic, osteoblastic or mixed lesions. Management requires a multidisciplinary approach integrating systemic therapy, bone-modifying agents, interventional procedures or radiotherapy. Conventional external beam radiotherapy (EBRT) provides reliable pain palliation, while stereotactic body radiotherapy (SBRT) offers superior local control, reduced re-irradiation with potential disease-modifying effects in oligometastatic and selected high-risk patients.

Radiotherapy remains indispensable in the management of bone metastases. Contemporary evidence supports individualized treatment selection based on prognosis, disease burden keeping in mind the anatomical considerations, with increasing adoption of stereotactic techniques in appropriately selected patients.

Introduction

Bone metastases is a category of cancer metastasis are seen with advanced cancer and represent a major source of pain, functional impairment and skeletal-related events (SREs). Historically regarded as an end-stage manifestation warranting symptomatic palliation alone, bone metastases are now increasingly encountered earlier and managed over prolonged disease courses due to advances in therapy. As emphasized by Clézardin and colleagues1, metastatic bone disease although incurable, but is frequently compatible with survival measured in years, particularly in breast and prostate cancer.

Radiotherapy has long formed the backbone of local management for bone metastases. Technological advances and improved understanding of disease biology have expanded its role beyond simple analgesia toward durable local control and selective disease modification. This review provides a comprehensive overview of bone metastases, including definitions, biological mechanisms, classification, prognosis and management strategies, with a

particular focus on the contemporary radiotherapeutic approaches.

2. Definition and Epidemiology of Bone Metastases

Bone metastases or osseous metastatic disease is defined as the invasion and growth of malignant cells within the bone and bone marrow microenvironment originating from a distant primary tumor.[1-3] Autopsy and clinical series demonstrate high rates of skeletal involvement in breast and prostate cancers (approximately 70%), followed by lung, renal, bladder and thyroid malignancies. Tsukamoto et al. noted that improved cancer survival has led to a steady rise in the prevalence of metastatic bone disease worldwide.[2]

Clinically, bone metastases are associated with pain, pathological fractures, spinal cord compression and hypercalcemia, contributing substantially to morbidity and healthcare utilization. Dong et al. demonstrated that baseline bone metastases independently predict inferior progression-free and overall survival in metastatic non-small cell lung cancer treated with immune checkpoint inhibitors, underscoring their prognostic relevance.[3]

3. Biological Basis of Bone Metastasis

The contemporary understanding of bone metastasis extends beyond Paget's classical "seed and soil" hypothesis, recognizing bone as a biologically active organ with specialized vascular, immune and stromal niches that regulate metastatic colonization and progression.[4,5] Mechanistic work summarized by Satcher[5] and Clézardin et al.[1] describe bone metastasis as a multistep process involving tumor cell dissemination, homing to bone marrow niches, cellular dormancy and eventual reactivation.

Tumor cells may colonize pre-metastatic niches through interactions with the bone matrix even before the primary tumor becomes clinically apparent.[6] Hematogenous spread is facilitated by the Batson vertebral venous plexus, a valveless vascular network linking the breast, lung, prostate, kidney and thyroid to the axial skeleton, accounting for the predilection for metastases in the pelvis, vertebrae, ribs and metaphyses of long bones.[6,7]

Post colonization, disseminated tumor cells can persist in a dormant, radiologically occult state for prolonged periods. Once activated, tumor–bone interactions drive a vicious cycle wherein tumor derived factors like prostaglandin E, TGF-α, TGF-β, TNF and interleukins promote osteoclast activation, uncoupled osteoclast–osteoblast regulation, osteoclast-mediated osteolysis, extensive lytic disease and malignancy-associated hypercalcemia. Importantly, bone metastases may also serve as reservoirs for secondary dissemination into distant organs, underscoring their systemic biological significance.[5-7]

4. Classification and Types of Bone Metastases

Bone metastases are commonly classified according to radiographic and biological characteristics.[6-8]

4.1 Osteolytic Metastases

Osteolytic lesions result from predominant osteoclast activation and bone destruction and are typical of non-small cell lung cancer, Non-Hodgkin lymphoma, renal cell carcinoma multiple myeloma and Langerhans cell histiocytosis. These lesions carry a high risk of pathological fracture and spinal instability. Liakouli et al. demonstrated radiographic remineralization following radiotherapy, particularly with multifractionated regimens, in osteolytic disease.[8]

4.2 Osteoblastic Metastases

Osteoblastic metastases are characterized by abnormal new bone formation and are classically associated with prostate cancer, carcinoid, small cell lung cancer, Hodgkin lymphoma and medulloblastoma. Despite their sclerotic appearance, these lesions are mechanically weak and clinically significant.

4.3 Mixed Lesions and Disease Burden

Many tumors produce mixed lytic–blastic lesions, like the breast cancer, squamous cell skin cancer, hepatocellular carcinoma, testicular and ovarian cancer.

5. Symptoms and Signs

Osseous metastatic disease cause significant morbidity. They commonly presenting with progressive bone pain characterized by a dull ache, unpredictable episodes of breakthrough pain. Pian is often worse at night and only partially relieved by activity.[9] Lesions in weight-bearing bones become symptomatic earlier than those in flat bones.[9]

Ongoing skeletal involvement may lead to pathological fractures, spinal instability, spinal cord or cauda equina compression, cranial nerve palsies, reduced mobility, anemia due to marrow suppression and hypercalcemia of malignancy. These major complications are collectively termed skeletal-related events (SREs).[7,9]

6. Disease Burden and Prognostic Factors

Beyond morphology, metastatic burden (oligometastatic or polymetastatic disease) has important prognostic and therapeutic implications. Evidence from the STAMPEDE analysis by Ali et al. demonstrated that aggressive local therapy confers a survival benefit in prostate cancer patients with low metastatic burden.[10] In this context, survival estimation becomes integral to radiotherapy decision-making, as expected prognosis directly influences treatment intent, dose–fractionation and technique.

Steinvoort-Draat et al.[11] identified performance status, primary tumor type, extent of metastatic involvement, opioid requirement and the availability of post-radiotherapy systemic therapy as key predictors of survival in patients receiving palliative radiotherapy for bone metastases. Together, these factors provide a pragmatic framework for aligning radiation therapy with anticipated benefit and overall goals of care.

7. Multidisciplinary Management of Bone Metastases

Management of bone metastases is inherently multidisciplinary. Contemporary evidence from clinical, population-based and translational studies emphasizes the complementary roles of systemic therapy, bone-modifying agents, surgery, interventional techniques alongside radiotherapy.

7.1 Systemic Anticancer Therapy

Systemic therapy remains the principal determinant of overall survival in patients with bone metastases. As highlighted by Venetis et al.,[12] the biological heterogeneity of bone metastases, particularly in breast cancer means that the outcomes are strongly

influenced by tumor subtype and responsiveness to endocrine, chemotherapy, targeted agents or immunotherapy. In metastatic non-small cell lung cancer, presence of bone metastases is associated with inferior outcomes despite immune checkpoint inhibition, underscoring that role of systemic disease control of paramount importance.[3]

Population-based evidence from Ren et al.,[13] analysing patients with bone metastases of unknown primary origin, further supports this paradigm. In the cohort of over 1,200 patients, both chemotherapy and radiotherapy were independently associated with improved overall and cancer-specific survival, indicating that in biologically aggressive or diagnostically challenging disease, combined-modality treatment confers benefit.

7.2 Bone-Modifying Agents

Bone-modifying agents, including bisphosphonates and denosumab, play a critical role in reducing skeletal-related events and improving quality of life. As reviewed by Clézardin et al.[1] and Venetis et al.,[12] these agents disrupt the osteoclast-mediated vicious cycle central to bone metastasis progression. Makita et al.[14] identified absence of bone-modifying agents as an adverse predictor of local control following radiotherapy in lung cancer, highlighting their synergistic role in local disease management. Although survival benefits with these agents are inconsistent, their integration with systemic therapy and radiotherapy is standard in patients with adequate life expectancy and renal function.

7.3 Surgical Management

Surgical intervention is primarily indicated for mechanical instability, impending or established pathological fractures and neurological compromise, with contemporary guidelines emphasizing functional and neurological benefit rather than oncologic control alone.[16,17] Postoperative radiotherapy is routinely employed to improve local control and reduce recurrence around fixation hardware, particularly in spinal and long-bone metastases.

Minimally invasive interventions like vertebroplasty, kyphoplasty, radiofrequency ablation and embolization serve as valuable adjuncts in selected patients. They offer rapid pain relief, structural stabilization and local tumor control, especially in those who are poor surgical candidates or require urgent palliation.[18] These techniques are most effective when integrated with radiotherapy rather than used in isolation.

8. Radiotherapy for Bone Metastases

Within this multimodal framework while systemic anticancer therapy remains the principal determinant of overall survival, bone-modifying agents reduce skeletal-related events and improve quality of life, radiotherapy remains the most versatile and widely applicable local treatment. It provides durable symptom relief, local control and a potential biological advantage when delivered early as part of integrated care in selected high-risk patients.

8.1 Mechanism of Action

Radiotherapy acts in bone metastases primarily through direct tumor cytoreduction and disruption of the tumor–bone microenvironment. Ionizing radiation induces lethal DNA damage in tumor cells, leading to reduced tumor burden and rapid alleviation of pain through decreased periosteal tension, neural compression and inflammatory mediator release.[15-17]

Beyond cytotoxicity, radiotherapy interferes with the self-perpetuating "vicious cycle" of bone metastasis.[1] By reducing tumor cell signaling and osteoclast activity, radiotherapy attenuates this feedback loop, contributing to disease stabilization and radiographic remineralization, main in osteolytic metastases.[1]

Emerging data suggest that radiotherapy may also modulate the metastatic niche and immune microenvironment within bone.[5,18] Direct experimental evidence is provided by Zhang et al., had demonstrated effects were associated with reduced neutrophil infiltration and increased cytotoxic T-cell populations.[18] Although clinical validation of these mechanisms remains sparse, these findings support a broader role of radiotherapy beyond palliation. It provides a rationale for exploring optimal timing, fractionation and integration with systemic therapies.

8.2 Evidence From Randomized and Observational Studies

Makita et al.[19] reported six and twelve month local control rates of 87.7% and 86.8%, respectively, in lung cancer related osteolytic bone metastases treated with palliative radiotherapy. Improved outcomes were associated with moderate dose escalation (BED 10-Biologically Effective Dose >39 Gy) in selected patients. Harada et al.,[16] in their prospective multi-institutional observational study of 224 patients, demonstrated pain relief in 52% at two months, low rates of severe toxicity (4%), and a six month overall survival of 70%, reflecting real-world practice.

Imano et al.[17] demonstrated an 88% pain response rate following a single fraction 8-Gy radiotherapy, reinforcing the robustness of hypofractionated schedules for palliation. Ren et al.,[13] analyzed over 1,200 patients with bone metastases of unknown primary origin, reported a one year overall survival of 14.5%. Radiotherapy was independently associated with improved survival, underscoring its relevance even in aggressive disease subsets. Translational evidence from Zhang et al.[18] showed that early fractionated radiotherapy in a murine breast cancer bone metastasis model suppressed local tumor growth, reduced secondary lung metastases and prolonged survival through favourable immune modulation.

8.3 Conventional External Beam Radiotherapy

Conventional EBRT remains the standard for palliation of painful bone metastases. Randomized trials demonstrate equivalent pain relief between single-fraction (8 Gy single) and multifraction regimens (20 Gy in 5 fractions or 30 Gy in 10 fractions). Contemporary guidelines, including the 2025 SFRO update summarized by Martz et al., recommend single-fraction radiotherapy for uncomplicated painful metastases, particularly in patients with limited life expectancy. Multifraction regimens remain appropriate postoperatively, in spinal cord compression or when long-term local control is desired.[19]

8.4 Stereotactic Body Radiotherapy

SBRT represents a major evolution in bone metastasis management. By delivering high biologically effective doses with steep dose gradients, SBRT achieves superior local control and reduced re-irradiation rates. Randomized data comparing stereotactic and conventional techniques are limited. The phase III NRG Oncology/RTOG 0631 trial by Ryu et al.[20] compared single-fraction stereotactic radiosurgery (16–18 Gy) with conventional radiotherapy (8 Gy including adjacent levels) in patients with one to three vertebral metastases. Pain response at three months favored conventional radiotherapy (60.5% vs 41.3%), with no

significant differences in toxicity, vertebral compression fracture rates or spinal cord complications. These results confirm that SRS does not improve short-term pain control but do not negate its role in selected patients where durable local control is prioritized. As survival improves, re-irradiation is increasingly encountered. Current guidelines position SBRT as the preferred approach for oligometastatic disease, re-irradiation and selected painful lesions.[18-20] Emerging evidence supports prophylactic radiotherapy for selected high-risk asymptomatic lesions to prevent SREs, representing a shift toward preventive strategies.[19]

Table 1. Radiotherapy techniques and fractionation schedules for bone metastases

Clinical scenario	Preferred approach	Typical dose–fractionation	Key considerations
Uncomplicated painful metastasis	cEBRT	8 Gy ×1; 20 Gy/5#; 30 Gy/10#	Single fraction favored for limited prognosis
Postoperative stabilization	cEBRT	20–30 Gy in 5–10#	Reduces recurrence around hardware
Spinal cord compression	cEBRT ± surgery	30 Gy/10#	Guided by neurologic status and prognosis
Oligometastatic disease	SBRT	BED10 ≥100 Gy (e.g., 24 Gy/2#)	Requires precise planning and immobilization
Re-irradiation	SBRT or IMRT	Individualized	Attention to cumulative spinal cord dose
High-risk asymptomatic lesion	SBRT or hypofractionated EBRT	Variable	Emerging preventive indication

Table 1. Adapted and synthesized from contemporary international guidelines and published evidence, including Martz et al. (SFRO 2025),[19] Shibata et al.,[15] Ryu et al.,[20] Makita et al.,[14] Harada et al.[16] and Imano et al.[17]

9. Clinical Implications and Future Directions

Osseous metastases represent a biologically heterogeneous spectrum rather than a uniform terminal event. Patient selection is based on prognosis, disease burden and expected survival is central to optimize radiotherapy benefit. Single-fraction cEBRT remains appropriate for patients with limited life expectancy, SBRT and multifraction regimens provide durable local control in selected patients with longer survival.

Future work should focus on standardized endpoints beyond pain relief. Integration of radiotherapy with systemic and immunotherapeutic agents and identification of biomarkers to guide personalized treatment is warranted in current senarious. Translational insights into tumor–bone and immune interactions may further redefine the timing and intent of radiotherapy.

Conclusion

Bone metastases represent a complex and clinically significant manifestation of systemic cancer. As systemic therapies continue to improve survival, radiotherapy remains central to the management, evolving from purely palliative treatment to a nuanced, stratified approach incorporating SBRT, re-irradiation and preventive strategies in selected patients. The role of radiotherapy in maintaining quality of life and achieving durable local control will continue to expand.

Author Contributions:

- Tanshi Daljit performed the literature search, conceptualized the manuscript, and prepared the initial draft.
- Saarthak Miglani contributed to manuscript conceptualization, literature search, and editing.
- Arun Kumar Rathi, Neha Sharma, and Renuka reviewed the manuscript.
- Sapna Yadav contributed to manuscript editing.

All authors reviewed and approved the final version of the manuscript.

Conflict of Interest:

The authors declare that they have no conflict of interest.

Ethical Statement:

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Clézardin P, Coleman R, Puppo M, Ottewell P, Bonnelye E, Paycha F, et al. Bone metastasis: mechanisms, therapies, and biomarkers. *Physiol Rev*. 2021;101(3):797-855. doi:10.1152/physrev.00012.2019.
2. Tsukamoto S, Kido A, Tanaka Y, Facchini G, Peta G, Rossi G, et al. Current overview of treatment for metastatic bone disease. *Curr Oncol*. 2021;28(5):3347-3372. doi:10.3390/curroncol28050290.
3. Dong H, Lan A, Gao J, An Y, Chu L, Yang X, et al. Prognostic significance of bone metastasis and clinical value of bone radiotherapy in metastatic non-small cell lung cancer receiving PD-1/PD-L1 inhibitors: results from a multicenter, prospective, observational study. *Transl Lung Cancer Res*. 2024;13(10):2603-2616. DOI: 10.21037/tlcr-24-441.
4. Fornetti J, Welm AL, Stewart SA. Understanding the Bone in Cancer Metastasis. *J Bone Miner Res*. 2018;33(12):2099-2113. doi:10.1002/jbmr.3618.
5. Satcher RL, Zhang XH. Evolving cancer-niche interactions and therapeutic targets during bone metastasis. *Nat Rev Cancer*. 2022;22(2):85-101. doi:10.1038/s41568-021-00406-5.
6. Hiraga T. Bone metastasis: Interaction between cancer cells and bone microenvironment. *J Oral Biosci*. 2019;61(2):95-98. doi:10.1016/j.job.2019.02.002.
7. Miller MD, Thompson SR. *Miller's Review of Orthopaedics E-Book*. Elsevier Health Sciences; 2019. ISBN: 978-0-323-60980-7. Available from: https://books.google.co.in/books?id=J5mzDwAAQBAJ.
8. Liakouli Z, Zygogianni A, Georgakopoulos I, Mystakidou K, Kouvaris J, Antypas C, et al. Osteolytic Bone Metastasis: Different Radiotherapy Fractionation Schedules Compared Clinically and Radiographically. *Curr Oncol*. 2024;31(6):3064-3072. doi:10.3390/curroncol31060233.
9. Macedo F, Ladeira K, Pinho F, Saraiva N, Bonito N, Pinto L, Goncalves F. Bone Metastases: An Overview. *Oncol Rev*. 2017;11(1):321. doi:10.4081/oncol.2017.321.
10. Ali A, Hoyle A, Haran ÁM, Brawley CD, Cook A, Amos C, et al. Association of Bone Metastatic Burden With Survival Benefit From Prostate Radiotherapy in Patients With Newly

Diagnosed Metastatic Prostate Cancer: A Secondary Analysis of a Randomized Clinical Trial. *JAMA Oncol*. 2021;7(4):555-563. doi:10.1001/jamaoncol.2020.7857.
11. Steinvoort-Draat IN, Otto-Vollaard L, Quint S, Tims JL, de Pree IMN, Nuyttens JJ. Palliative radiotherapy: New prognostic factors for patients with bone metastasis. *Cancer Radiother*. 2024;28(3):236-241. doi:10.1016/j.canrad.2023.09.003.
12. Venetis K, Piciotti R, Sajjadi E, Invernizzi M, Morganti S, Criscitiello C, et al. Breast Cancer with Bone Metastasis: Molecular Insights and Clinical Management. *Cells*. 2021;10(6):1377. doi:10.3390/cells10061377.
13. Ren Y, Qian S, Xu G, Cai Z, Zhang N, Wang Z. Predicting survival of patients with bone metastasis of unknown origin. *Front Endocrinol (Lausanne)*. 2023;14:1193318. doi:10.3389/fendo.2023.1193318.
14. Makita K, Hamamoto Y, Kanzaki H, Nagasaki K, Kozuki T. Local control of bone metastasis treated with palliative radiotherapy in patients with lung cancer: An observational retrospective cohort study. *Oncol Lett*. 2023;26(1):303. doi:10.3892/ol.2023.13889.
15. Shibata H, Kato S, Sekine I, Abe K, Araki N, Iguchi H, et al. Diagnosis and treatment of bone metastasis: comprehensive guideline of the Japanese Society of Medical Oncology, Japanese Orthopedic Association, Japanese Urological Association, and Japanese Society for Radiation Oncology. *ESMO Open*. 2016;1(2):e000037. doi:10.1136/esmoopen-2016-000037.
16. Harada H, Shikama N, Notsu A, Shirato H, Yamada K, Uezono H, et al. Multi-institutional prospective observational study of radiotherapy for metastatic bone tumor. *J Radiat Res*. 2024;65(5):701-711. doi:10.1093/jrr/rrae060.
17. Imano N, Kosugi T, Konishi K, Saito T. Pain response in single-fraction 8-Gy radiotherapy for painful non-bone-metastasis tumors: a single-center retrospective study. *J Radiat Res*. 2024;65(3):408-412. doi:10.1093/jrr/rrae025.
18. Zhang Y, Gao Z, Qi Z, Xu J, Xue J, Xiong L, et al. Fractionated radiotherapy initiated at the early stage of bone metastasis is effective to prolong survival in mouse model. *Cancer Biol Ther*. 2025;26(1):2455756. doi:10.1080/15384047.2025.2455756.
19. Martz N, Faivre JC, Beldjoudi G, Arnaud A, Chamois J, Supiot S, et al. Radiotherapy of bone metastases: 2025 update. *Cancer Radiother*. 2025;29(7-8):104769. doi:10.1016/j.canrad.2025.104769.
20. Ryu S, Deshmukh S, Timmerman RD, Movsas B, Gerszten P, Yin FF, et al. Stereotactic Radiosurgery vs Conventional Radiotherapy for Localized Vertebral Metastases of the Spine: Phase 3 Results of NRG Oncology/RTOG 0631 Randomized Clinical Trial. *JAMA Oncol*. 2023;9(6):800-807. doi:10.1001/jamaoncol.2023.0356.

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