Palliative Radiotherapy for Prostate Cancer: Encouraging Single-Fraction Radiotherapy

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As new data and new treatment options emerge, palliative radiotherapy algorithms will need to undergo continuous modifications and updates to ensure that patients receive optimal symptom relief.

Palliative radiotherapy is an effective treatment for the management of symptoms from advanced and metastatic prostate cancer, particularly for relief of pain from bone metastases. In their review, Drs. Boyer, Salama, and Lee concisely examine the data for external beam radiation therapy for uncomplicated bone metastases and cord compression in men with prostate cancer metastatic to bone.[1] The authors are to be commended for such a comprehensive review, which includes a detailed analysis of recent advances in radiopharmaceuticals, including radium-223, and discusses the potential role of stereotactic radiotherapy for patients with oligometastatic prostate cancer.

Beyond the scope of the review, however, is the fact that the optimal management of bone metastases from prostate cancer requires an interdisciplinary approach, with input from surgeons (orthopedic and spine surgeons, as well as urologists), medical oncologists, pain management specialists, and palliative care clinicians. It is only with an integrated approach that patients can receive optimal care. As a standard of care, palliative radiotherapy for bone metastases predates recent advances in systemic therapy, including androgen deprivation, osteoclast inhibitors, chemotherapy, vaccines, surgical interventions, and pain management techniques. Today more than ever, palliative radiation must be integrated with these therapies. Trials of osteoclast inhibitors have demonstrated that they increase the time to “skeletal-related events,” defined as development of cord compression, pathologic fracture, need for surgery to bone, or need for radiotherapy to bone.[2] When a previous standard of care (palliative radiation for bony metastases) has become an endpoint to be avoided, patterns of referral and practice are changing.

Drs. Boyer, Salama, and Lee review the equivalence of single- and multi-fraction radiotherapy, as documented in multiple systematic reviews and the American Society for Radiation Oncology (ASTRO) evidence-based guidelines. The only statistically significant difference between various multi-fraction regimens and a single fraction of 8 Gy in the updated systematic review of 2012 was a higher rate of retreatment among patients receiving single-fraction radiotherapy.[3] After a detailed discussion of the benefits and drawbacks of single- vs multi-fraction radiotherapy, Boyer and colleagues conclude their discussion of dose-fractionation for uncomplicated bone metastases by quoting the ASTRO “Choosing Wisely” campaign’s approach to management of bone metastases: “Don’t routinely use extended fractionation schemes (> 10 fractions) for palliation of bone metastases.”[4]

The ASTRO statement goes on to encourage use of single-fraction radiotherapy only for patients with a “limited prognosis,” allowing for broad interpretation of when single-fraction vs multi-fraction radiotherapy might be useful. In contrast, the American Academy of Hospice and Palliative Medicine (AAHPM), partnering with radiation oncologists in caring for patients with bone metastases, has created a different “Choosing Wisely” campaign statement regarding radiotherapy and bone metastases: “Don’t recommend more than a single fraction of palliative radiation for an uncomplicated painful bone metastasis.”[5]

While ASTRO recommends treating with no more than 10 fractions, AAHPM recommends suggesting no more than a single fraction for uncomplicated bone metastases. When implementing either the ASTRO or AAHPM recommendations, one significant challenge is that “limited prognosis” and “limited life expectancy” in the AAHPM statement are left to the interpreter. Would 1 year be a limited enough prognosis to consider single-fraction radiotherapy? Would 6 months? Three months? Patterns of practice studies have shown that estimated prognosis weighs heavily in a radiation oncologist’s selection of dose-fractionation schemes for patients with bone metastases.[6,7] However, multiple studies have demonstrated that we are not good at predicting...
life expectancy, even in patients with advanced cancer.[8] This question has been studied in the context of patients referred for palliative radiotherapy. Even for experienced clinicians evaluating patients for palliative radiotherapy, estimates of prognosis are overly optimistic.[9] Two seminal studies on palliative radiotherapy for bone metastases independently evaluated clinicians’ predictions of survival. In the Radiation Therapy Oncology Group 9714 study, radiation oncologists’ survival estimates were, on average, 3 months more optimistic than actual survival.[10] In the Dutch Bone Metastasis Study, the authors specifically attempted to study the utility of single-fraction radiotherapy in patients with better prognoses. Eight participating centers randomized 92 patients thought to have a good prognosis to a single fraction of 8 Gy vs 6 fractions of 4 Gy. Patients were considered to have a good prognosis if they had breast cancer without visceral metastases and 1 year complete remission on first-line chemotherapy, or if they had prostate cancer with Karnofsky performance status > 60% and had not yet started androgen deprivation therapy. Surprisingly, only 53% of these patients lived > 52 weeks, and 25% of patients who did not meet criteria for “good prognosis” lived > 52 weeks.[11] Of note, the authors found equivalent and high response rates among patients who received single- vs multi-fraction radiotherapy (87% vs 85%) and who lived at least 1 year. While various prognostic scores have been developed for patients with bone metastases, there are still challenges in determining individual life expectancy. Moreover, given the equivalence of single- and multi-fraction radiotherapy, even among patients who survive > 1 year, the default for patients with uncomplicated bone metastases should be single-fraction radiotherapy.

The question remains: Are there ever times when multi-fraction radiotherapy should be utilized in the management of bone metastases? Absolutely. Bone metastases that do not fit the definition of uncomplicated metastasis (ie, metastatic epidural spinal cord compression, pathologic fracture) should receive therapy that can address both pain relief and the importance of local tumor control. Moreover, studies have shown that bone metastases causing neuropathic pain and bone metastases with a soft tissue component may benefit from longer courses and higher doses of palliative radiotherapy.[12] Ongoing studies evaluating the role of stereotactic body radiation therapy for select patients with oligometastatic disease may demonstrate improved pain control over conventional single-fraction radiotherapy. Palliative radiotherapy needs to be provided to patients to complement the multidisciplinary management of bone metastases. The AAHPM has weighed in on their view of single-fraction radiotherapy, but it remains unclear whether medical oncologists and other partners in managing bone metastases would be more or less likely to refer patients for palliative radiotherapy if those patients were more likely to receive a single fraction. As new data and new treatment options emerge, palliative radiotherapy algorithms will need to undergo continuous modifications and updates to ensure that patients receive optimal symptom relief.

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References:


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