TITLE: Palliative Radiation for an Uncomplicated and Painful Bone Metastasis: Clinical Effectiveness and Guidelines

DATE: 27 March 2015

RESEARCH QUESTIONS

1. What is the clinical effectiveness of palliative radiation for an uncomplicated painful bone metastasis?

2. What are the evidence-based guidelines for palliative radiation for an uncomplicated painful bone metastasis?

KEY FINDINGS

Five systematic reviews and three evidence-based guidelines were identified regarding the clinical effectiveness of palliative radiation for an uncomplicated painful bone metastasis.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2015, Issue 3), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2010 and March 20, 2015. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.
SELECTION CRITERIA

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Patients with uncomplicated painful bone metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Palliative radiation</td>
</tr>
<tr>
<td>Comparator</td>
<td>No radiation; Radiation treatment strategies compared with each other</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Clinical effectiveness (benefits [survival, mortality], harms [quality of life, treatment harms, complications of testing, other harms]); Guidelines</td>
</tr>
<tr>
<td>Study Designs</td>
<td>Health technology assessments, systematic reviews, meta-analyses, evidence-based guidelines</td>
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</table>

RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by evidence-based guidelines.

Five systematic reviews and three evidence-based guidelines were identified regarding the clinical effectiveness of palliative radiation for an uncomplicated painful bone metastasis. No relevant health technology assessments were identified.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

Five systematic reviews\(^1\)\(^-\)\(^5\) and three evidence-based guidelines\(^6\)\(^-\)\(^8\) were identified regarding the clinical effectiveness of palliative radiation for an uncomplicated painful bone metastasis.

An analysis of a systematic review and other study results\(^1\) that examined radiation response rates in patients with painful uncomplicated bone metastases reported high response rates (71% to 87% depending on the study population) to initial treatment and retreatment. This analysis also found little difference in response rates with single or multiple fractions of radiation treatment, as well as with initial treatment and re-treatment. The authors recommended that patients receive a single 8 Gy fraction of radiation for both initial treatment and retreatment of uncomplicated painful bone metastases.

A systematic review\(^2\) of the efficacy of retreatment of painful bone metastases with radiation reported complete, partial and overall response rates of 20%, 50% and 68%, respectively, and found that the efficacy of reirradiation was similar to that of initial radiation treatment. The authors noted that there was little evidence regarding adverse events.

An update of a systematic review and meta-analysis\(^3\) of randomised trials of palliative radiotherapy that compared single fractions versus multiple fractions reported similar overall and complete response rates for this comparison. Patients in the multiple fraction group had more
favorable retreatment response rates than patients who received a single fraction, and there were no significant differences in acute toxicities in the two groups.

A systematic review with meta-analysis\textsuperscript{4} of the effectiveness of reirradiation for painful bone metastases reported a pain response rate of 58%, but noted that there was significant heterogeneity between studies.

A systematic review of various breast cancer interventions\textsuperscript{5} found that, based on observational studies, chronic and localized bone pain can be treated successfully in the majority of women with radiotherapy and concomitant analgesia. Based on data from two randomized controlled trials, this review reported no difference between single fraction and multiple fraction courses of radiation. Reported adverse effects of radiotherapy included nausea and vomiting, and higher dose fractions were associated with increased toxicity.

Three evidence-based guidelines\textsuperscript{6-8} were identified regarding the use of palliative radiation for an uncomplicated painful bone metastasis. Detailed recommendations are provided in Table 2.

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| EAU (2013)\textsuperscript{9} | “3.3.3 Radiotherapy for metastatic bone pain
3.3.3.1 Clinical background
Radiotherapy alleviates metastatic bone pain in approximately 70% of patients, with complete pain relief at the treated site in up to 40% of patients. The onset of pain relief varies from a few days to 4 weeks. The median duration of pain relief reported by most studies is 3-6 months.
3.3.3.2 Radiotherapy scheme
Single-fraction radiotherapy is as effective as multifraction radiotherapy in relieving metastatic bone pain. However, the rates of retreatment and pathological fractures are significantly higher after single fraction radiotherapy. Single-fraction radiotherapy remains the treatment of choice for alleviating bone pain because of its greater convenience for patients, faster patient turnover for the radiotherapy unit and lower costs. The recommended dose is 8 Gy. Pain relief can be achieved with lower doses. These lower doses should be borne in mind if a third retreatment is necessary, or if there is concern about radiation tolerance. In cases of oligometastases (< 5), a case can be made for aggressive therapy, such as radiosurgery or highdose radiotherapy, to improve survival.” Page 13 |
| Simoff et al. (2013)\textsuperscript{7} | “6.7.1. In patients with lung cancer who have pain due to bone metastases, external radiation therapy is recommended for pain relief (Grade 1A). Remark: A single fraction of 8 Gy is equally effective for immediate relief of pain and more cost-effective than higher fractionated doses of external radiation therapy.” Page e457S |

Palliative Radiation for an Uncomplicated and Painful Bone Metastasis
Table 2: Summary of Guidelines and Recommendations

<table>
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<th>Author (year)</th>
<th>Recommendations</th>
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<tr>
<td>AHS(2010)</td>
<td>“Uncomplicated bone metastases. A single 8Gy treatment is recommended as the standard therapy for uncomplicated bone metastases. Numerous randomized controlled trials published over the past two decades have consistently demonstrated the equivalence of single and multiple fraction schedules for the palliation of pain due to uncomplicated bone metastases. Meta-analyses of these trials have repeatedly shown no significant differences with regards to rates of pathological fractures, spinal cord compression, QoL, acute toxicity, time to first improvement in pain, time to complete pain relief, time to pain progression, or opioid use. There is insufficient evidence to recommend a specific dose fractionation schedule for treatment indications other than pain relief, such as long-term disease control for patients with a solitary bone metastasis.”</td>
</tr>
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REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses

   PubMed: PM25023043

   PubMed: PM24094630

   PubMed: PM22130630

   PubMed: PM22300568

   PubMed: PM21418674

Guidelines and Recommendations

   See: 3.3.3 Radiotherapy for metastatic bone pain, page 13

   See: Palliation of bone metastasis, page e457S
See: Uncomplicated bone metastases, page 8

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APPENDIX – FURTHER INFORMATION:

Guidelines – Unclear Methodology

See: 6.11.8.2. Painful bone metastasis, page 96

See: Palliative radiotherapy, page iii127

See: Radiotherapy, page vii146

See: Results, pages 969-970

PubMed: PM21494406
See: Radiotherapy, page 403

Review Articles

PubMed: PM25493222

PubMed: PM25473313
