The role of radiotherapy in the palliation of painful symptomatic bone metastases is well established. Recently, it has been reported that single-fraction radiotherapy is as effective as multifraction radiotherapy (1,2), which is the most widely used regimen. We read the interest the article by Hartsell et al. (3), which compared the ability of a single 8-Gy fraction of radiation therapy with that of 30 Gy delivered in 10 treatment fractions to palliate pain from bone metastases. We conducted a similar trial in our hospital from July 15, 1999, to December 31, 2001, in which we enrolled a total of 160 patients and randomly assigned them to receive either a single fraction of 8 Gy of radiation therapy or 30 Gy in 10 fractions. The pain intensity was measured on a patient-assessed ordinal pain scale of 0–10. A partial response was defined as a pain reduction of two points or more on this scale, without the increased use of analgesic drugs. A complete response was defined as a pain score of zero at the treated area without increased use of analgesic drugs. Patient follow-up was at 3, 12, 24, 36, and 48 weeks after the onset of treatment.

The two groups did not differ with respect to age, sex, primary tumor type, localization of metastases, or analgesic drug consumption. There were no differences in survival rates between the two arms. The overall response rates were 75.5% in the 8-Gy arm and 86.6% in the 30-Gy arm (difference = 11.1%, 95% confidence interval [CI] = −2.4% to 24.2%). Complete response rates were 15.4% in the 8-Gy arm and 13.4% in the 30-Gy arm (difference = 2.0%, 95% CI = −14.1% to 10.2%). None of these differences were statistically significant.

Our acute toxicity outcomes were similar to those reported by Hartsell et al. Toxicity was higher in our 30-Gy arm (18.2%) than in our 8-Gy arm (12.7%), but these differences were not statistically significant (difference = 5.5%, 95% CI = −7.0% to 17.9%). In addition, as in Hartsell et al., the retreatment rate in our trial was statistically significantly higher in the 8-Gy arm than in the 30-Gy arm (28.2% versus 2.4%) (difference = 25.8%, 95% CI = −37.5% to −14.0%) (Table 1).

Hartsell et al. reported that one of the main limitations of their study was the trial included only patients with metastases from breast or prostate cancer. We enrolled all the patients with a life expectancy of longer than 1 month, regardless of the location of their metastases or their primary cancer. We did not find statistically significant differences between treatment arms, except for patients with lung cancer metastases. In these patients, the response was statistically significantly higher in the 30-Gy arm than in the 8-Gy arm for the crude response rates (90.9% versus 57.9%) (difference = 33%, 95% CI = 2.9% to 63.2%), but these differences disappeared in the actuarial rate of response.

We concluded that the regimen of a single fraction of 8 Gy was as safe and effective as a multifraction regimen for the palliation of painful bone metastases. The 8-Gy single fraction was the treatment of choice for most of the patients, except for patients with lung cancer metastases, for whom additional studies are required.

### Table 1. Overall rates of partial and complete response, toxicity, and retreatment

<table>
<thead>
<tr>
<th>Rate</th>
<th>Schedule</th>
<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30 Gy</td>
<td>8 Gy</td>
<td></td>
</tr>
<tr>
<td>Partial response, %</td>
<td>86.6</td>
<td>75.5</td>
<td>.076</td>
</tr>
<tr>
<td>Complete response, %</td>
<td>13.4</td>
<td>15.4</td>
<td>.723</td>
</tr>
<tr>
<td>Toxicity, %</td>
<td>18.2</td>
<td>12.7</td>
<td>.120</td>
</tr>
<tr>
<td>Retreatment, %</td>
<td>2.4</td>
<td>28.2</td>
<td>.001</td>
</tr>
</tbody>
</table>

### References


### Notes

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Hartsell et al. (1) reported that twice as many patients in the 8-Gy arm had received retreatment as in the 30-Gy arm. Higher rates of retreatment in single-fraction arms have been reported before by Nielsen et al. (2) and Steenland et al. (3). Hartsell et al. proposed that the retreatment rate difference between treatment arms may be the result of physician bias. However, this difference (18% versus 9%) may not be explained simply by physician bias alone—a conclusion also reached by Kachnic and Berk (4) in an accompanying editorial. Although van der Linden et al. (5) reported no relation between response to initial treatment and occurrence of retreatment and reached the same conclusion about the role of physician bias, many other factors in addition to bias, some of which were analyzed before (5), such as primary site, involvement and treatment of bone metastases, presence or absence of fracture, pain severity, duration of symptoms, and other treatments received, may affect the decision to retreat. Consequently, a group of patients who do not benefit from a single 8-Gy fraction may need retreatment. It may be helpful to analyze patients treated with a single...
8-Gy fraction to define the characteristics of patients who needed retreatment. If any characteristics are statistically significantly associated with retreatment, then the group of patients who need retreatment when treated with a single fraction may be defined and treated with conventional fractionation.

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REFERENCES


NOTES

Editor’s note: Dr. Kachnic declined our invitation to respond.
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RESPONSE

We appreciate the information from Foro et al. concerning their study showing the efficacy of short-course radiotherapy in the palliation of painful bone metastases. This is additional corroboration in the growing body of literature confirming the equivalence of one or a few treatments compared with 10 or more treatments for palliation of pain.

The higher incidence of retreatment after a short course of therapy is indeed a concern and should be the subject of further investigation to determine whether there is a specific subgroup that may benefit from longer-course, higher-dose radiotherapy. As suggested by Adli et al., there may be multiple factors related to the need for retreatment. We have begun to analyze our data to elucidate some of these factors, and we recently presented an analysis of the Radiation Therapy Oncology Group’s (RTOG) 97-14 Trial that evaluated the incidence of retreatment with regard to sex, marital status, and performance status (1). We found that both men and women who received 30 Gy in 10 fractions had a statistically significantly longer time to retreatment than those who received 8 Gy. Single men had no difference in retreatment rates between 8 and 30 Gy, whereas married men with a Karnofsky Performance Status of 70–80 Gy had a longer time to retreatment for the 30-Gy schedule than for the 8-Gy schedule. Both married and single women had a longer time to retreatment for the 30-Gy schedule than for the 8-Gy schedule. We are continuing to evaluate other factors that may help to differentiate those patients for whom the higher-dose, longer-course treatment is necessary. These data must be interpreted with caution, however. In most of the randomized bone metastasis studies (including RTOG 97-14), criteria for retreatment are typically not well defined and thus retreatment rates are not objective endpoints. Shakespeare et al. (2) have concluded that potential biases, including physician preference and patient selection, make retreatment rates an unreliable indicator of treatment efficacy.

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