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1. Explain how estimation of a patient’s likely survival influences the use of palliative radiotherapy and choice of fractionation regimens.
2. Describe common indications and contraindications to the use of palliative radiotherapy.

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When delivered with palliative intent, radiotherapy can help to alleviate a multitude of symptoms related to advanced cancer. In general, time to symptom relief is measured in weeks to months after the completion of radiotherapy. Over the past several years, an increasing number of studies have explored rates of radiotherapy use in the final months of life and have found variable rates of radiotherapy use. The optimal rate is unclear, but would incorporate anticipated efficacy in patients whose survival allows it and minimize overuse among patients with expected short survival. Clinician prediction has been shown to overestimate the length of survival in repeated studies. Prognostic indices can provide assistance with estimations of survival length and may help to guide treatment decisions regarding palliative radiotherapy in patients with potentially short survival times. This review explores the recent studies of radiotherapy near the end of life, examines general prognostic models for patients with advanced cancer, describes specific clinical circumstances when radiotherapy may and may not be beneficial, and addresses open questions for future research to help clarify when palliative radiotherapy may be effective near the end of life.

Palliative Radiotherapy at the End of Life: A Critical Review

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Introduction

In 2013, the Institute of Medicine released Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis, detailing the many complex issues patients and providers face in the changing health care environment.1 Key among the recommendations of the committee were engaging patients and providers in ongoing and open discussions regarding prognosis; the benefits and harms of treatments; navigating changing cost and payment structures; and supporting patient preferences through the continuum of care, including end-of-life care. In the setting of advanced cancer, the committee noted the significant variability in aggressiveness of end-of-life care around the United States,2,3 and the Institute of Medicine committee recommended providing patients with information and care consistent with their needs, values, and preferences, including timely referral to hospice. However, care near the end of life varies widely by hospital and geographic area.2 In addition, patient misconceptions of the goals of therapy persist, with up to 70% of patients with metastatic colorectal cancer and up to 80% of patients with metastatic non-small cell lung cancer not understanding that chemotherapy was “not at all likely” to cure their cancer.4 Similar misconceptions persist in other areas of cancer treatment, with up to 64% of patients receiving palliative radiotherapy for metastatic non-small cell lung cancer misconstruing the intent of therapy.5 Based on studies of early palliative care for patients with metastatic cancer, improvement in patient understanding of the intent of therapy appears to have an impact on the aggressiveness of cancer care toward the end of life, including receipt of chemotherapy in the last 60 days of life and rates of hospice use.6 It is in this context that the current review of palliative radiotherapy near the end of life is presented.

For more than a century, palliative radiotherapy has been a cost-effective, time-efficient treatment to help patients manage the symptoms of advanced and metastatic cancer.7 In the most general terms, palliative radiotherapy may be effective in controlling pain, neurologic symptoms, and obstructive symptoms and providing local control of tumors in any organ system in the body. Palliative radiotherapy may be considered in any patient in whom local tumor is causing symptoms (Table 1).

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Radiation Oncology (ASTRO) evidence-based guidelines has also recently endorsed palliative radiotherapy dose fractionation schemes that follow the American Society for Radiation Oncology (ASTRO) evidence-based guidelines (30 gray [Gy] in 10 fractions, 24 Gy in 6 fractions, 20 Gy in 5 fractions, or 8 Gy in a single fraction) as a quality indicator in palliative radiation oncology.\textsuperscript{16} However, although palliative radiotherapy use within the last 14 or 30 days of life may impact these other quality measures, it has not, on its own, been defined as a specific quality measure. As such, an “optimal” rate of palliative radiotherapy use near the end of life (either within 14 or 30 days of death) is unknown. Rates that are very low might indicate underuse of palliative radiotherapy, meaning that some patients who might have benefitted from radiation are not being treated, whereas rates that are very high might indicate overuse and an excessive burden of radiotherapy without significant clinical benefit. Nonetheless, several recent studies have begun to explore radiotherapy use at the end of life.

Multiple population-based and descriptive studies have explored rates of palliative radiotherapy use at end of life in various contexts (Table 3).\textsuperscript{10,12,13,16–22} These studies provide a starting baseline of characteristics of patients receiving radiotherapy near the end of life. Although the number of patients receiving radiotherapy in the final 14 days, 30 days, or 45 days of life varies based on multiple factors, many of these patients will not live long enough to achieve clinical benefit from palliative radiotherapy. Moreover, as each type of study indicates, many patients with short survival after radiotherapy receive extended dose fractionation schemes within the final 30 days of life, potentially increasing side effects compared with shorter dose fractionation schemes and possibly delaying hospice referral or other end-of-life care and planning. Accurate prognostication would allow patients who might live long enough to benefit from radiotherapy to have...

### Table 1. Symptoms of Cancer That May Be Successfully Addressed by Palliative Radiotherapy

| Primary sites of disease                                                                 | Secondary sites of disease (metastases)                                                                 |
|------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| • Brain: headaches, seizures, neurologic dysfunction                                      | • Brain: headaches, seizures, neurologic dysfunction                                                  |
| • Head and neck: pain, bleeding, dysphagia, shortness of breath                           | • Bone: pain, spinal compression, postsurgical fixation status                                         |
| • Lung: pain, cough, hemoptysis, postobstructive pneumonia, superior vena cava syndrome  | • Skin and subcutaneous tissues                                                                      |
| • Esophagus: dysphagia, odynophagia, bleeding, obstruction                                | • Orbit: pain, double vision, blindness                                                               |
| • Gynecologic: pain, bleeding, urinary outlet obstruction, hydronephrosis                | • Spleen: pain, early satiety, portal hypertension                                                    |
| • Genitourinary: pain, hematuria, urinary outlet obstruction                               |                                                                                                         |
| • Rectum: pain, bleeding, tenesmus, rectal obstruction                                    |                                                                                                         |

However, time to optimal symptom control, even after short courses of radiotherapy, is usually measured in weeks to months after radiation treatments are delivered, as clearly demonstrated in the case of pain relief from bone metastases.\textsuperscript{8,9} In spite of this delay in efficacy, recent reports have found that many patients receive courses of radiotherapy in the final weeks or months of life.\textsuperscript{10–13} When survival is short, palliative radiotherapy may have minimal, if any, clinical benefit for patients, may delay referral to hospice, and may impede optimal end-of-life planning and care delivery (Table 2). In 2010, Lutz et al explored the concept of when palliative radiotherapy has value and when it does not.\textsuperscript{14} This review updates their findings, with a focus on the recent literature, the use of prognostic models to guide decision-making in palliative radiotherapy referrals, and treatment decisions in specific instances in which palliative radiotherapy may be beneficial.

### Table 2. Circumstances in Which Palliative Radiotherapy May Not Be Indicated

| Factors related to the patient                                                                                           | Factors related to the treatment                                                                                  |
|-------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| • Death is imminent                                                                                                     | • Potential side effect risks outweigh potential benefit                                                          |
| • Multiple progressive symptoms                                                                                         | • Retreatment exceeds normal tissue tolerance                                                                     |
| • Inability to provide informed consent                                                                                  | • Required course would be too lengthy                                                                            |
| • Transportation is impossible                                                                                           | • Unnecessary expense treatment                                                                                   |
| Factors related to the health care system                                                                               | Factors related to the treatment                                                                                  |
| • Radiotherapy facility is unavailable                                                                                    | • Potential side effect risks outweigh potential benefit                                                          |
| • Lack of specialized radiotherapy technology                                                                             | • Retreatment exceeds normal tissue tolerance                                                                     |
| • Insufficient communication between radiation oncologist and palliative care                                            | • Required course would be too lengthy                                                                            |

Patterns of Palliative Radiotherapy Use at End of Life

The National Quality Forum (NQF) lists chemotherapy use within the last 14 days of life, intensive care unit (ICU) admissions during the last 30 days of life, more than one emergency room visit within the final days of life, and hospice admission for fewer than 3 days or not at all as indicators of lower-quality care, conclusions that are endorsed by the American Society of Clinical Oncology.\textsuperscript{15} The NQF has also recently endorsed palliative radiotherapy dose fractionation schemes that follow the American Society for Radiation Oncology (ASTRO) evidence-based guidelines.
referral and treatment and would also allow patients who might not benefit from treatment to receive end-of-life care without radiotherapy. Thus, the accurate prediction of survival is of utmost importance in the determination of when palliative radiotherapy may be beneficial and when it may cause undue side effects or burden to the patient with advanced or metastatic cancer.

### General Prognostic Models for Survival in Advanced Cancer

The benefits of accurate prognostication for patients with advanced and metastatic cancer are numerous; patients may want to know their likely survival time, and such information may help patients, families, and clinical teams with treatment decision-making. Studies have demonstrated that patients who are overly optimistic in their understanding of their illness are more likely to receive aggressive care near the end of life. Estimates of prognosis may incorporate many factors, including clinician prediction of survival, performance status (PS), symptoms, and laboratory values. Of necessity, prognosis estimates are based on statistical models that incorporate a median as well as ranges of survival for a sample of patients with a given set of characteristics. An optimal prognostic model would account for best-case and worst-case scenarios in multiple clinical contexts and over a range of cancer types and a range of life expectancies to allow clinicians and patients and their families to use the information in treatment decision-making and preparations for end of life. However, such a prognostic

### Table 3. Results of Population-Based and Descriptive Studies of the Use of Palliative Radiotherapy in the Final Days of Life

| STUDY             | STUDY TYPE           | NO. OF PATIENTS | STUDY SPECIFICS AND FINDINGS                                                                 |
|-------------------|----------------------|-----------------|-----------------------------------------------------------------------------------------------|
| Guadagnolo 2013   | US Medicare Database | 202,299         | Patients had cancers of the lung, breast, prostate, pancreas, colon, or rectum                 |
|                   |                      |                 | 7.6% received radiotherapy in the final 30 d of life                                           |
|                   |                      |                 | 10.8% of those treated in the final mo. of life received >10 fractions                         |
|                   |                      |                 | Shorter courses correlated with radiotherapy at a hospital-based center and hospice enrollment |
| Murphy 2013       | US Medicare Database | 51,610          | Patients had stage IV cancers of the lung, breast, prostate, colon, or rectum                 |
|                   |                      |                 | 41% of patients received palliative radiotherapy                                             |
|                   |                      |                 | Lower rates of use were observed in patients with colorectal cancer and greater number of comorbidities |
|                   |                      |                 | Patients with lung cancer were the most likely to receive palliative radiotherapy in the final 2 wk of life |
| Yeung 2014       | US Medicare Database | 64,960          | Patients with cancers of the lung, breast, prostate, colon and rectum                         |
|                   |                      |                 | 13% received radiotherapy within 30 d of hospice enrollment                                    |
|                   |                      |                 | Median length of radiotherapy treatment was 14 d, whereas median length of hospice stay was 13 d |
|                   |                      |                 | Longer radiotherapy courses did not correlate with longer hospice stays                       |
| Lavergne 2011    | Nova Scotia Population-based study | 13,494 | Of all patients who died due to cancer, 22% received palliative radiotherapy                  |
|                   |                      |                 | Factors associated with decreased use of palliative radiotherapy included older age, greater comorbid disease, female sex, distance to radiotherapy facility, residence in a nursing home, and shorter life expectancy |
| Kapadia 2012     | Eight US centers     | 1098            | Patients with stage IIIb or IV non-small cell lung cancer                                     |
|                   |                      |                 | 66% received palliative radiotherapy                                                          |
|                   |                      |                 | 10% received radiotherapy in the last 14 d of life                                              |
|                   |                      |                 | An additional 28% received radiotherapy within the last 30 d of life                           |
|                   |                      |                 | 47% did not complete the therapy course prescribed                                              |
| Gripp 2007, Gripp 2010 | Prospective single-institutional review | 216 | Evaluation of patients sent for palliative radiotherapy                                      |
|                   |                      |                 | Physicians were poor predictors of survival                                                    |
|                   |                      |                 | 15% received radiotherapy in the final 30 d of life                                             |
|                   |                      |                 | Of those who died within 30 d of completion of radiotherapy, only 25.8% had symptom improvement and 60% spent more than one-half of their final days in treatment |
| Toole 2012       | Retrospective single-institution review | 63   | Review of all patients who died within 30 d of completion of palliative radiotherapy, treatment intent not withstanding |
|                   |                      |                 | 52% did not complete their planned radiotherapy                                               |
|                   |                      |                 | 69% died within 10 d of treatment completion                                                    |
| Berger 2014      | Retrospective single-institution review | 52   | Review of palliative radiotherapy patients who died shortly after completion of treatment     |
|                   |                      |                 | 78% did not complete their intended course                                                     |
|                   |                      |                 | Median time from treatment completion to death was 4 d                                        |
|                   |                      |                 | None of the patients were prescribed single-fraction therapy                                  |
model does not exist (and is likely not to exist) because models for patients with a likely longer life expectancy often account for tumor histology and stage whereas histology and stage do not necessarily impact prognostication in patients with a shorter life expectancy. Communicating prognosis is a complicated task that requires an assessment of patient expectations and information desired and an explanation of the statistical data used (median survival), as well as typical, best-case, and worst-case scenarios. It is beyond the scope of this review to detail the extensive work done on prognostication in patients in advanced cancer, although several studies relevant to the survival prognostication of patients receiving radiotherapy have been completed and provide a good backdrop for evaluation of the topic.

The simplest prognostic model for survival in patients with advanced cancer would be clinician prediction of survival. However, multiple prospective studies and systematic reviews have confirmed that clinicians are frequently inaccurate in survival estimates and tend to be overly optimistic of survival time, even in patients with short expected survival. These findings of clinician inaccuracy in the prediction of survival have been corroborated among patients referred to palliative radiotherapy programs (Table 4). Various prognostic models have been developed to help predict survival among patients with advanced cancer and a short life expectancy. Krishnan et al recently reviewed general prognostic models for prediction of survival in patients referred for palliative radiotherapy consultation (Table 5). The “number of risk factors” model developed and validated by Chow et al was first developed by analyzing 16 factors potentially predictive of survival among 395 patients referred for palliative radiotherapy in 1999. Six factors were found to have an impact on survival on Cox modeling: primary cancer site, metastasis characteristics, or physician survival prediction in the prognostic model. The majority of these models for short survival were developed among patients in medical oncology or palliative care clinics, palliative care inpatient units, or hospice programs. As such, their validity among patients referred for palliative radiotherapy is unknown.

### Prognostic Models for Patients With Advanced Cancer Referred for Palliative Radiotherapy

Two prognostic models for survival among patients referred for palliative radiotherapy have been developed in addition to numerous cancer-specific or metastasis-specific models of prognostication (Table 5). The “number of risk factors” model developed and validated by Chow et al was first developed by analyzing 16 factors potentially predictive of survival among 395 patients referred for palliative radiotherapy in 1999. Six factors were found to have an impact on survival on Cox modeling: primary cancer site, metastasis site, Karnofsky performance status (KPS), fatigue, appetite, and dyspnea (all measured with the Edmonton Symptom Assessment Scale [ESAS]). The validation data used 2 methodologies to validate the initial model among 445 patients included in the prospective database. The authors validated the data using both a “partial score” method in which they assigned a weight to each factor based on the training set data to construct a survival prediction score and a “number of risk factors” method in which the adverse risk factors from the initial data set were nonbreast cancer primary site, metastases to other...
than bone only, KPS of 50 or less, fatigue score of 4 to 10 on ESAS, appetite score of 8 to 10 on ESAS, and a shortness of breath score of 1 to 10 on ESAS. For each validation method, the probability of survival at 3, 6, and 12 months was estimated. It was found that 0 to 3, 4, or 5 to 6 risk factors discriminated survival equally to the partial score method with 3-month, 6-month, and 12-month survival probabilities of 80%, 64%, and 41%, respectively, for patients with 0 to 3 risk factors; 51%, 25%, and 10%, respectively, for patients with 4 risk factors; and 29%, 13%, and 3%, respectively, for patients with 5 or 6 risk factors. This model provides a general framework for evaluating likely survival among patients referred for palliative radiotherapy in an outpatient clinic. The authors caution that the model has been validated at the population level and again stress the need for individualized counseling regarding the meaning of the model for individual patients.

Krishnan et al recently proposed a second model for the prediction of survival among patients referred for palliative radiotherapy: the TEACHH (Type of cancer, ECOG PS, Age, prior Chemotherapy, prior Hospitalizations, Hepatic metastases) model. In this model, 862 records of patients treated with palliative radiotherapy between 2008 and 2011 were reviewed retrospectively to generate a model capable of predicting short (less than 3 months) and long (greater than 1 year) life expectancy. The median survival for all patients was found to be 5.6 months. Factors found to be significant predictors of survival included type of cancer (lung and other vs breast and prostate), PS (Eastern Cooperative Oncology Group PS of 2-4 vs 0-1), age (>60 years vs ≤60 years), prior palliative chemotherapy (>2 courses vs 0 or 1 course), prior hospitalizations within 3 months of radiotherapy (0 vs 1 or more), and liver metastases (present vs absent). Using a number of risk factors model, the authors were able to define 3 distinct groups with different median survivals: patients with 0 or 1 risk factor had a median survival of 19.9 months, patients with 2 to 4 risk factors had a median survival of 5.0 months, and patients with 5 or more risk factors had a median survival of 1.7 months. Although this model has not yet been validated externally, it holds promise for extending the work of Chow et al in helping to discriminate those patients referred for palliative radiotherapy into groups with a short life expectancy (who may be less likely to benefit from palliative radiotherapy) and those with a likely longer life expectancy. Other models for survival estimation for specific clinical scenarios (such as brain metastases or metastatic spinal cord compression) will be explored in more detail under each clinical scenario below.

### Specific Clinical Scenarios for Radiotherapy Use at End of Life

#### Radiotherapy Management of Bone Metastases

Multiple randomized controlled trials and several systematic reviews over the past 30 years have demonstrated the efficacy of radiotherapy in palliating pain from uncomplicated bone metastases. Overall, approximately 25% of patients can expect to have complete pain relief whereas a total of 60% of patients can expect some response to radiotherapy. According to the ASTRO guidelines for the management of bone metastases, a single fraction of 8 Gy is

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### TABLE 5. Factors Included in 2 Prognostic Models for Patients Referred for Palliative Radiotherapy

| MODEL | NO. OF PATIENTS | CRITERIA FOR DETERMINING PROGNOSIS | SURVIVAL ESTIMATES |
|-------|----------------|----------------------------------|--------------------|
| Chow 2005* | 840 total 395 (initial model) 445 (validation) | • Nonbreast cancer primary site  • Metastases to other than bone only  • KPS of ≤50  • Fatigue score 4 to 10 on ESAS  • Appetite score 8 to 10 on ESAS  • Shortness of breath score 1 to 10 on ESAS | Score 0-3: 80%: 3 mo 64%: 6 mo 41%: 12 mo  |
| Krishnan 2013* | 862 (retrospectively studied) | • Type of cancer (lung and other vs breast and prostate)  • ECOG performance status (2-4 vs 0-1)  • Age (>60 y vs ≤60 y)  • Chemotherapy (>2 courses vs 0-1 course)  • Hospitalizations within 3 mo of radiotherapy (0 vs ≥1)  • Hepatic metastasis (present vs absent) | Score 0-1: median survival, 19.9 mo  Score 2-4: median survival, 5 mo  Score 5-6: median survival, 1.7 mo |

ECOG indicates Eastern Cooperative Oncology Group; ESAS, Edmonton Symptom Assessment Scale; KPS, Karnofsky performance status; NRF, number of risk factors; TEACHH, Type of cancer, ECOG PS, Age, prior Chemotherapy, prior Hospitalizations, Hepatic metastases. *For each model, the calculation is completed by adding the total number of risk factors present to determine likely prognosis. The Chow model has been validated whereas the Krishnan model has not yet been validated.
TABLE 6. Studies That Confirm That Palliative Radiotherapy Is Effective for the Management of Bone Pain in Patients With a Short Life Expectancy

| STUDY            | STUDY TYPE                          | NO. OF PATIENTS | STUDY SPECIFICS AND FINDINGS                                                                 |
|------------------|-------------------------------------|----------------|---------------------------------------------------------------------------------------------|
| Dennis 201124    | Retrospective single-institution review | 232            | • Patients who died within 3 mo of treatment  
• Pain response 70% at one mo, 63% at 2 mo  
• Lack of follow-up due to decline in patient performance status and limited data accrual |
| Meeuse 201026    | Dutch Bone Metastases Study Group trial | 274            | • Patients who died within 12 wk of treatment  
• Pain response of 45% overall  
• Median time to pain response of 2 wk  
• Lack of follow-up due to decline in patient performance status and limited data accrual |

equivalent to longer courses of radiotherapy, including 5 or 6 fractions of 4 Gy and 10 fractions of 3 Gy.41 These dose fractionation schemes are recommended as quality indicators of palliative radiotherapy by the NQF.16 Acute and late side effects of radiotherapy for bone metastases are generally similar with single-fraction versus multifraction regimens, with some studies showing decreased acute side effects in patients receiving single-fraction radiotherapy. Time to pain relief also appears similar, with an optimal time to measure pain relief of 2 months after the completion of palliative radiotherapy.9 In patients with survival of greater than one year, single-fraction treatment provides noninferior pain relief and freedom from pathologic fracture and long-term side effects when compared with fractionated courses, although retreatment rates may be up to 2.6 times more likely with single-fraction therapy.40,42 Furthermore, successful single-fraction treatment may well provide secondary relief in the form of diminished cost and side effects caused by narcotic pain analgesics. Caregivers and loved ones surely appreciate the option to choose an efficient and effective means by which to alleviate disease symptoms and the toxicity of pain medicine by means of one shared decision. Moreover, there is now randomized evidence demonstrating the efficacy of repeat irradiation in patients initially treated with a single fraction of 8 Gy or 5 fractions of 4 Gy, with up to 50% of patients having symptom improvement after reirradiation.43

Despite these data regarding the equivalence of long-course and short-course radiotherapy, multifraction regimens are still commonly used in the United States and around the world with the adoption of single-fraction radiotherapy based primarily on training and geographic location.44-46 A recent population-based study by Bekelman et al examining palliative radiotherapy for patients with prostate cancer with bone metastases in the Surveillance, Epidemiology, and End Results-Medicare database showed that an only 3.3% of 3050 patients received single-fraction radiotherapy for bone metastases, whereas 50.3% received 11 or more fractions.47 Although differences in survival are not expected among patients who receive different dose fractionation regimens for bone metastases, this analysis revealed a median survival of 5.0 months for patients receiving single-fraction radiation and 11.9 months for patients receiving more than single-fraction radiation, suggesting that radiation oncologists tend to use multifraction radiotherapy for patients with longer anticipated survival. Nevertheless, given its equal efficacy and greater convenience even for patients with longer survival, many individuals and groups advocate for the use of single-fraction radiotherapy for patients with uncomplicated bone metastases regardless of prognosis.48,49 The influence of reimbursement based on the length and complexity of treatment course on physician behavior is not fully understood, yet this model persists in the United States and may be one of the causes for the reluctance to offer single-fraction treatment for appropriate patients. Although exact estimates of cost depend upon several variables, a single fraction may cost less than one-half that of a fractionated course, and potentially several times less than stereotactically delivered treatments.

Studies have confirmed the efficacy of palliative radiotherapy for painful bone metastases, even among patients with limited life expectancy (Table 6).26 Therefore, survival prediction should impact radiotherapy for bone metastases only if anticipated survival is less than 4 weeks because patients with such short anticipated survival are unlikely to benefit from radiotherapy (Table 7). Using the proposal from Gripp et al, the percentage of remaining life spent receiving palliative radiotherapy may be a useful metric to evaluate the utility of radiotherapy in patients with short anticipated survival.21 If some patients are able to receive benefit, even with very short survival, it may be reasonable to offer single-fraction radiotherapy with the goal of minimizing inconvenience and side effects while still potentially providing benefit from palliative radiotherapy. This is an open and unexplored question. In the interim, the Dutch Bone Metastasis Study criteria of a KPS less than 40 alone may be a sufficient predictor of survival to guide radiotherapy decision-making in patients with advanced cancer.42 Validation of the TEACHH model may also help to clarify the usefulness of palliative radiotherapy for bone metastases at the end of life.37
TABLE 7. Suggestions for a Prognosis-Driven Approach to Palliative Radiotherapy for Patients With Painful Bone Metastases

| PROGNOSIS/CLINICAL CIRCUMSTANCE | TREATMENT OPTIONS |
|----------------------------------|-------------------|
| Prognosis <1 mo | • Supportive care alone  
|                    | • Short-course radiotherapy  
|                    | (ie, single 8-Gy fraction) |
| Prognosis >1 mo | • Supportive care alone  
|                    | • Short-course radiotherapy  
|                    | (ie, single 8-Gy fraction)  
|                    | • Higher-dose radiotherapy  
|                    | (20-30 Gy in 5-6 fractions for large lytic lesions, soft tissue mass, or neuropathic pain) |
| Prognosis >1 mo, with risk for pathologic fracture (appropriate for surgery) | • Surgical stabilization with postoperative radiotherapy to 30 Gy in 10 fractions |

Potential adjuvant treatments include:
- Pain medication including nonsteroidal antiinflammatory medicines, steroids, narcotic analgesics, antidepressants, antiseizure medicine for neuropathic pain
- Radiotherapeutics for widespread painful and osteoblastic bone metastases
- Bisphosphonates to promote osteoblast activity and to diminish the risk of formation of additional bone metastases
- Nerve root injection

Gy indicates gray.

Radiotherapy Management of Malignant Epidural Spinal Cord Compression

Malignant epidural spinal cord compression (MESCC) is a special case of bone metastasis in which tumor metastasis compresses the thecal sac. The first sign of MESCC is generally back pain, but symptoms can progress to include radicular pain, loss of sensation, paralysis, and loss of function of the bladder and bowels. Diagnosis is generally made with magnetic resonance imaging and management involves an interdisciplinary team including spine surgeons, radiation oncologists, medical oncologists, and palliative care clinicians. Based on a population analysis of 15,367 patients in the Nationwide Inpatient Sample, the annual incidence of MESCC requiring hospitalization among patients dying of cancer is 3.4% per year and varies by primary tumor site. Over the time period 1998 to 2006, inpatient radiotherapy decreased while inpatient surgery increased, likely reflecting the results of the randomized controlled trial by Patchell et al of radiation alone versus surgery followed by radiotherapy for patients with MESCC. This trial compared surgery followed by radiotherapy with radiotherapy alone among patients with histologically confirmed cancer with an expected survival of greater than 3 months, at least one neurological sign including pain, paraplegia for less than 48 hours if present, and a single area of MESCC demonstrated improved ambulatory status and survival in patients treated with surgery followed by radiotherapy compared with those treated with radiotherapy alone. Of note, Patchell et al and others have found that improvements in the control of neurologic symptoms and ambulatory status from MESCC leads to improvements in survival. Tokuhashi et al have developed scoring systems for survival for the preoperative evaluation of metastatic spine tumors. The scoring system assigns a score based on PS, number of extraspinal bone metastases, number of vertebral bone metastases, metastases to visceral organs, primary cancer site, and nerve palsy. Patients with low scores are likely to survive less than 6 months and conservative measures (including radiotherapy) are recommended. Surgery is not commonly recommended for this group because the time spent healing and undergoing physical rehabilitation after the procedure might extend over much of the patient’s expected lifespan. Hernanz et al found that, although the scoring system of Tokuhashi et al was accurate for patients in the short-prognosis group, it did not accurately predict survival between 6 and 12 months, but conservative measures including radiotherapy are recommended for patients with a short life expectancy. Rades et al conducted a matched pair analysis and found similar rates of ambulatory status, local control, and survival among patients treated with surgery plus radiotherapy versus those treated with radiotherapy alone. Multiple studies have focused on prognostic factors and appropriate radiotherapy dose fractionation for patients diagnosed with MESCC (Tables 8 and 9). An overview of these studies reveals that radiotherapy plays an important role in the management of MESCC, allowing for improvements in pain control, motor function, and durable responses, thus limiting the likelihood of recurrent MESCC. Radiotherapy is estimated to restore ambulation in approximately 60% of patients with MESCC, although that estimate is variable and depends on several factors such as tumor histology, absence of mechanical compression by fractured bone, and interval since the onset of symptoms. Surgery also plays an important role in patients with good prognosis, one area of cord compression, and spinal instability. However, although the role of radiotherapy versus best supportive care in patients with poor prognosis and MESCC is still being explored, the available data can provide a suggested decision tree for treatment options by clinical circumstance (Table 10). If validated, use of the prognostic score developed by Rades et al for patients with anticipated short survival would provide a valuable tool to assist with decision-making regarding radiotherapy use near the end of life in patients with MESCC. The concept of the percentage of remaining life spent receiving palliative radiotherapy may be the basis of a quality indicator, potentially allowing patients to benefit from palliative radiation for MESCC without significant burden.
Whole-Brain Radiotherapy in Patients With Brain Metastases

Similar to the management of malignant epidural spinal cord compression, the management of brain metastases involves a multidisciplinary approach including radiation oncologists, neurosurgeons, medical oncologists, and palliative care providers. The ASTRO guidelines for the management of brain metastases describe several algorithms, including the use of neurosurgical resection, stereotactic radiosurgery (SRS), whole-brain radiotherapy, and best supportive care based on the number and size of brain metastases, resectability, and anticipated prognosis based on a number of prognostic models. Resection seems most reasonable for patients with good PS and favorable prognosis whose disease is confined to a single lesion measuring less than 3 to 4 cm in diameter and that is anatomically located in a site that can safely be approached surgically. Patients with adequate PS and a single lesion measuring

### TABLE 8. A Summary of Studies That Evaluated Prognostic Factors and for Patients Treated With Radiotherapy for MESCC

| STUDY       | STUDY TYPE                      | NO. OF PATIENTS | STUDY SPECIFICS AND FINDINGS                                                                                                                                 |
|-------------|--------------------------------|----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Rades 2008  | Multivariate survival analysis  | 1852           | • Patients were scored by tumor histology, presence of bone metastases, presence of visceral metastases, interval from diagnosis to MESCC, ambulatory status, and time since onset of any motor deficits    |
|             |                                |                | • Scoring successfully separated patients into 3 groups with 6-mo survival rates of 4%, 11%, and 48%, respectively, and median survival > 6 mo                              |
| Rades 2010  | Survival validation analysis    | 476            | • Confirmatory study of patients scored by tumor and patient factors                                                                                       |
|             |                                |                | • Prognostic estimates were simplified to 3 groups with 6-mo survival rates of 16%, 48%, and 81%, respectively                                              |

MESCC indicates malignant epidural spinal cord compression.

### TABLE 9. Studies of Radiotherapy Fractionation for Patients With MESCC

| STUDY       | STUDY TYPE                      | NO. OF PATIENTS | STUDY SPECIFICS AND FINDINGS                                                                                                                                 |
|-------------|--------------------------------|----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Rades 2005  | Retrospective review            | 1304           | • Multiple fractionation regimens were assessed, including 8 Gy in one fraction, 20 Gy in 5 fractions, 30 Gy in 10 fractions, 37.5 Gy in 15 fractions, and 40 Gy in 20 fractions    |
|             |                                |                | • No difference in functional outcomes between schema was noted                                                                                               |
| Maranzano   | Prospective randomized trial    | 300            | • Patients were randomized to split-course treatment of 5 Gy times 3 doses plus 3 Gy times 3 doses vs short-course 8 Gy times 2 doses                                |
|             |                                |                | • The 2 arms showed no difference in initial response rates or durability of response                                                                         |
| Maranzano   | Prospective randomized trial    | 327            | • Patients were randomized to 8 Gy times 2 doses or a single 8-Gy fraction                                                                                   |
|             |                                |                | • The 2 arms showed no difference in initial response rates or durability of response                                                                         |
| Rades 2011  | Prospective observational study | 265            | • Treatment was chosen to be shorter (1 times 8 Gy or 5 times 4 Gy) vs longer-course (10 times 3 Gy, 15 times 2.5 Gy, or 20 times 2 Gy) radiotherapy based on patient prognosis |
|             |                                |                | • One-year survival was 23% in the shorter-course group and 30% in the longer-course group                                                                   |
|             |                                |                | • Long-course radiotherapy was associated with improved local control/no recurrence of MESCC at 81% at one y vs 61% at one y for patients treated with short-course radiotherapy |
| Rades 2013  | Retrospective review            | 2029           | • Prognostic factors were evaluated to define the group of patients who should be treated with shorter-course therapy                                          |
|             |                                |                | • A prognostic score was discovered that yielded a 99.8% specificity and 96% positive predictive value                                                          |

Gy indicates gray; MESCC, malignant epidural spinal cord compression.
less than 3 to 4 cm in size that is not amenable to safe complete resection should be considered for SRS. For those with multiple brain metastases, SRS can also be considered for patients with a favorable prognosis and a limited number of appropriately sized lesions. Whole-brain radiotherapy may be offered to patients after surgical resection or SRS in an attempt to address occult metastases, although the risk of cognitive difficulties increases with this approach. Whole-brain external beam radiotherapy alone remains the standard of care for patients who do not have disease that qualifies for treatment with resection or SRS, although patients with extremely poor prognoses may be best treated with supportive care alone. Of note, multiple studies have confirmed the equivalence of various dose fractionation schemes for whole-brain radiotherapy, including 5 fractions of 4 Gy, 10 fractions of 3 Gy, 15 fractions of 2.5 Gy, and 20 fractions of 2 Gy without statistically significant differences in overall survival or symptom control noted among the regimens. Improvement in neurologic symptoms should be expected in approximately two-thirds of patients who undergo palliative external beam radiotherapy. Various studies have evaluated the available prognostic instruments while seeking the optimal treatment of this patient group (Table 11). Thus, the management of brain metastases has evolved significantly over the past 30 years, but challenges remain in the treatment of patients with brain metastases and poor prognosis. Although whole-brain radiotherapy may offer some clinical benefit, the extent of this benefit remains poorly defined, particularly in patients with short survival. Continued work on prognostic models that predict short survival (1 month or less) will allow better decision-making and care for patients with brain metastases near the end of life (Table 12).

TABLE 10. Suggestions for a Prognosis-Driven Approach to Palliative Radiotherapy for Patients With MESCC

| PROGNOSIS/CLINICAL CIRCUMSTANCE | TREATMENT OPTIONS |
|----------------------------------|-------------------|
| Prognosis <3 mo                   | • Supportive care alone |
|                                   | • Short-course radiotherapy (ie, single 8-Gy fraction or 16 Gy in 2 fractions given one wk apart) |
| Prognosis >3 mo (not appropriate for surgery) | • Supportive care alone |
|                                   | • Short-course radiotherapy (20 Gy in 5 fractions, 30 Gy in 10 fractions, or 35 Gy in 14 fractions) |
| Prognosis >3 mo (appropriate for surgery) | • Surgical decompression with postoperative radiotherapy to 30 Gy in 10 fractions |

Potential adjuvant treatments include:
- Chemotherapy or targeted immunotherapy for symptomatic locoregional disease for which further surgery or radiotherapy cannot be safely delivered or for symptomatic visceral metastases
- Hormonal therapy for breast or prostate cancer, if not previously delivered
- Radiopharmaceuticals for multifocal, symptomatic bone metastases
- Medication or nerve root injection for intractable pain

Gy indicates gray; MESCC, malignant epidural spinal cord compression.

TABLE 11. Evaluation of Prognosis and Prognostic Instruments for Patients With Brain Metastases

| STUDY            | STUDY TYPE                  | STUDY SPECIFICS AND FINDINGS                                                                 |
|------------------|-----------------------------|-----------------------------------------------------------------------------------------------|
| Rodrigues 201366 | Comparison of existing prognostic instruments | • Nine existing prognostic instruments were compared  
• Factors used to predict outcome were similar but not identical across these tools  
• Major misclassification rates varied from 2% to 39%, with 6 of the 9 instruments having misclassification rates >25%  
• The 2 instruments with the lowest misclassification rates have not yet been validated |
| Nieder 201377    | Retrospective analysis      | • A total of 124 patients with poor prognosis who received best supportive care, whole-brain radiotherapy, or stereotactic radiosurgery  
• Factors favoring best supportive care rather than radiotherapy included age ≥75 y, KPS ≤50, and uncontrolled primary tumor with extracranial metastases to at least 2 organs |
| Craighead 201278 | Population-based study, Alberta, Canada | • A total of 568 poor-prognosis patients treated with whole-brain radiotherapy  
• Overall survival was 3 mo, with factors predicting poor prognosis including low KPS, advanced age, and a larger number of brain lesions |
| Langley 201379   | Ongoing prospective randomized trial | • Randomization of poor-prognosis patients with non-small cell lung cancer metastasized to brain between best supportive care plus whole-brain radiotherapy vs best supportive care alone  
• Interim report suggests no improvement in overall survival or quality of life for patients treated with whole-brain radiotherapy |
| Nieder 201380    | Retrospective analysis      | • Patients with brain metastases, poor prognosis, and diagnoses other than non-small cell lung cancer  
• The addition of whole-brain radiotherapy did not add to median survival other than perhaps a slight amount in those with small cell lung cancer metastases |

KPS indicates Karnofsky performance score.
TABLE 12. Suggestions for a Prognosis-Driven Approach to Palliative Radiotherapy for Patients With Brain Metastases

| PROGNOSIS/CLINICAL CIRCUMSTANCE | TREATMENT OPTIONS |
|---------------------------------|-------------------|
| Prognosis <1 mo                  | • Supportive care alone  |
|                                 | • Short-course radiotherapy (ie, 20 Gy in 5 fractions) |
| Prognosis >1 mo (multiple metastases) | • Supportive care alone  |
|                                 | • If all lesions are <4 cm in size: Whole-brain radiotherapy alone  |
|                                 | • Whole-brain radiotherapy plus radiosurgery  |
|                                 | • Radiosurgery alone  |
|                                 | • If any lesion > 4 cm in size: Whole-brain radiotherapy alone  |
| Prognosis >1 mo (solitary metastasis) | • If completely resectable, then surgery plus whole-brain radiotherapy, radiosurgery, or both  |
|                                 | • If not completely resectable but <4 cm, then radiosurgery alone or with whole-brain radiotherapy  |
|                                 | • If not completely resectable and >4 cm, then whole-brain radiotherapy alone  |

Potential adjuvant treatments include:
• Steroids for symptoms of edema, antiseizure medications as indicated
• Chemotherapy or targeted immunotherapy for systemic disease, if warranted by performance status
• Hormonal therapy for breast or prostate cancer, if not previously delivered

Gy indicates gray.

TABLE 13. Studies That Assess the Usefulness of Radiotherapy in Patients With Locally Advanced Lung Cancer

| STUDY                        | STUDY TYPE                  | STUDY SPECIFICS AND FINDINGS                                                                 |
|------------------------------|-----------------------------|-----------------------------------------------------------------------------------------------|
| Fairchild 200882             | Meta-analysis of prospective randomized trials | • Evaluated 13 radiotherapy regimens used in randomized trials  |
|                              |                             | • There was no significant difference in symptom control with short courses of radiotherapy (ranging from a single fraction of 8 Gy to 10 Gy, 17 Gy in 2 fractions one wk apart up to 35 Gy in 10 fractions over 2 wk) to longer courses of radiotherapy with higher doses (ranging from 17 Gy in 2 fractions one wk apart to 60 Gy in 30 fractions over 6 wk)  |
|                              |                             | • There appeared to be a survival advantage for patients with good prognosis treated with higher doses of radiotherapy  |
|                              |                             | • A biological equivalent dose of 35 Gy in 10 fractions had a higher survival rate with 26.5% vs 21.7% of patients treated with high-dose vs low-dose radiotherapy alive at one y and 8.1% vs 6.7% alive at 2 y  |
|                              |                             | • Rates of pneumonitis and myelopathy were very low, but slightly higher in the high-dose arms  |
| Chen 201383                  | Prospective observational study | • Evaluated patterns of radiotherapy care for patients with non-small cell lung cancer at multiple institutional sites  |
|                              |                             | • Of those patients treated to the chest, 65% received >30 Gy whereas 33% received >50 Gy  |
|                              |                             | • Patients treated in integrated networks (the Veterans Affairs Administration of Health Maintenance Organizations) received fewer fractions whereas those who received chemoradiotherapy received more fractions  |

Gy indicates gray.

health professionals saw 100 consecutive patients with brain metastases between January 2011 and May 2012. A total of 75 patients ultimately received radiotherapy, whereas 25 were treated without radiotherapy, either due to patient preference or rapid clinical deterioration.81 The authors found that with the joint clinic with palliative care and radiation oncology, the number of patients who received whole-brain radiotherapy within 30 and 14 days of death decreased from 19% to 9% and 6% to 1%, respectively, based on historical rates at the same institution. Such multidisciplinary assessments could help patients, families, and clinicians with complex decision-making regarding whole-brain radiotherapy versus supportive care near the end of life.

Palliative Thoracic Radiotherapy
Palliative thoracic radiotherapy for patients with very locally advanced or metastatic lung cancer or lung metastases can be highly effective in the palliation of symptoms related to advanced cancer in the lung, including cough, hemoptysis, dyspnea from airway obstruction, symptoms of superior vena cava syndrome, and chest pain. After radiotherapy, intrathoracic symptom relief is excellent and includes palliative rates of 40% to 97% for dyspnea, 77% to 92% for hemoptysis, 60% to 91% for cough, and 70% to 78% for pain. In contrast to the data for bone and brain metastases, there appears to be a survival advantage for patients with a good prognosis who are treated with higher doses of radiotherapy. Two influential studies have examined the use of palliative radiotherapy in this setting (Table 13).82,83 These data have been summarized in the ASTRO evidence-based guidelines for palliative radiotherapy for lung cancer.84 The guidelines suggest shorter courses of radiotherapy for patients with poor PS and describe no role for upfront concurrent chemoradiotherapy or endobronchial brachytherapy for the palliation of advanced/metastatic lung cancer. At the current time, the primary factors that influence radiotherapy dose fractionation schemes for thoracic radiotherapy should continue to be PS and comorbidities while prognostic models continue to be evaluated (Table 14).

Other Symptoms Palliated by Radiotherapy
There are myriad other symptoms that may be palliated by radiotherapy, including dysphagia from esophageal cancer; bleeding, pain, and obstruction from head and neck cancer; pelvic pain and bleeding from advanced gynecologic, gastrointestinal, and genitourinary malignancies; and neurologic...
symptoms including pathologic brachial plexopathy or blindness from orbital metastases. The theoretical benefits and burdens associated with these clinical scenarios have remained unchanged since the first description by Lutz et al in 2010, but comparatively little work has been done to evaluate prognostic models and optimal palliative outcomes for these patients compared with those referred for the palliation of bone metastases, MESCC, and brain metastases. In this context, the palliation of lung cancer can be used as a model for considering the role of short-course versus long-course versus best supportive care in patients referred for palliative radiotherapy. There are ongoing opportunities to further define optimal palliative radiotherapy regimens in each of these clinical scenarios along with prognostic indices that may help to guide the optimal use of palliative radiotherapy. Algorithms for the use of palliative radiotherapy in specific clinical scenarios have recently been outlined, including estimation of likely survival and weighing the risks of the side effects of longer versus shorter dose fractionation schemes versus improved local control and palliative benefit from the same longer dose fractionation schemes and the use of advanced technologies including intensity-modulated radiation therapy and image-guided radiation therapy.

General principles also hold for times when palliative radiotherapy may not be worthwhile. Palliative radiotherapy is not likely to be worthwhile when death is imminent, when radiotherapy would palliate a single symptom among many, when neither the patient nor proxy are able to consent, when radiotherapy would exceed normal tissue tolerance to radiotherapy, when treatment would be excessively lengthy or expensive, or when radiotherapy facilities are not available in a given clinical scenario. Models continue to grow, encouraging increased collaboration between palliative care clinicians and radiation oncologists, and therefore it is hoped that a lack of coordination of care between radiotherapy and palliative care/hospice physicians will become a smaller issue moving forward.

### Palliative Radiotherapy Use and Hospice

Hospice is a philosophy of care and a medical benefit in the United States that involves a team approach to care for patients with life-limiting illness. The focus of care is on providing care that fits with patient needs, including symptom management and emotional and spiritual care for the patient and family. There is no inherent conflict between palliative radiotherapy and hospice care because radiotherapy can be highly effective in palliating the symptoms of advanced cancer. Nevertheless, palliative radiotherapy is infrequently used in patients enrolled in hospice. Lutz et al used a survey to explore potential barriers to palliative radiotherapy use in hospice care with a survey of hospice providers’ understanding and use of palliative radiotherapy. The authors found that most hospice professionals believe radiotherapy is an effective treatment for symptom management in patients with advanced/metastatic cancer. However, less than 3% of the 480 hospice programs surveyed actually offered palliative radiotherapy. Impediments to closer collaboration between hospice clinicians and radiation oncologists include cost, transportation difficulties, short life expectancy, and a lack of collaboration/education among palliative care clinicians and radiation oncologists, including a lack of willingness on the part of radiation oncologists to offer single-fraction radiotherapy. The previously described population-based study of Medicare patients receiving hospice care who received palliative radiotherapy within 30 days before death demonstrated long radiotherapy courses before hospice, potentially delaying hospice referral and end-of-life planning with a very small number of patients excluded from that analysis because they received radiotherapy while on hospice.

Schuster et al conducted an updated survey of hospice professionals with a smaller sample size (16 licensed hospices) and found differences in knowledge regarding the equivalence of single-fraction and multifraction palliative radiotherapy among hospice physicians, hospice nurses, and hospice administrators. Among this group, less than 1% of patients were referred to a radiation oncologist, based on concerns about cost and transportation burden.

### TABLE 14. Suggestions for a Prognosis-Driven Approach to Palliative Radiotherapy for Patients With Locally Advanced Non-Small Cell Lung Cancer

| PROGNOSIS/CLINICAL CIRCUMSTANCE | TREATMENT OPTIONS |
|---------------------------------|------------------|
| Prognosis <1 mo                 | • Supportive care alone  
|                                 | • Short-course radiotherapy (ie, single 8-Gy fraction or 17 Gy in 2 fractions given one wk apart) |
| Prognosis >1 mo                 | • Supportive care alone  
|                                 | • Short-course radiotherapy (ie, single 8-Gy fraction or 17 Gy in 2 fractions given one wk apart)  
|                                 | • Higher-dose radiotherapy (≥30 Gy in 10 fractions) with the goal of moderately increased survival at the cost of more acute side effects |
| Locally recurrent disease       | • Supportive care alone  
|                                 | • Retreatment with external beam therapy, taking into account increased acute and long-term side effect risks due to cumulative dosing  
|                                 | • Brachytherapy for intraluminal obstruction by tumor |
| Potential adjuvant treatments   | • Endobronchial stenting for obstructing lesions  
|                                 | • Chemotherapy given in sequential rather than concurrent time frame  
|                                 | • Narcotic analgesics to minimize the sense of air hunger or shortness of breath |

Gy indicates gray.
A study by Jarosek et al examined Medicare’s Healthcare Cost Report Information System to determine rates of palliative radiotherapy use among Medicare-certified freestanding hospices during the year 2002 to explore barriers to radiotherapy use in hospice. Overall, 23.8% of freestanding hospice programs offered radiotherapy, with hospice size (larger), profit status (nonprofit), and length of Medicare certification being associated with the availability of radiotherapy services. The authors concluded that reimbursement practices are at least in part responsible for the low rates of palliative radiotherapy use among hospice patients. Given the potential for collaboration between hospice and radiation oncology professionals, Schuster et al have created a dedicated hospice palliative radiotherapy program to allow for affordable and efficient radiotherapy for patients on hospice. Such innovative models will be necessary to continue to bridge the worlds of hospice and palliative radiotherapy to allow for the optimal care of patients, even those on hospice, who might benefit from radiotherapy.

Palliative Radiotherapy Use in the ICU
Radiotherapy can potentially be beneficial for patients in the ICU, but outcomes of radiotherapy for patients receiving maximal support in the ICU have not been well described in the literature. By definition, a patient requiring ICU-level care has a poor PS and potentially poor prognosis, but does that mean that patients in the ICU never benefit from radiotherapy (palliative or definitive)? Most likely not. A recent retrospective analysis of intubated patients in the ICU with malignant airway obstruction who were treated with palliative radiotherapy found that 26 patients over 10 years were treated with radiotherapy. Seven patients were able to be extubated (27%), with 6 of those 7 patients ultimately discharged to home. Nevertheless, the median overall survival was 0.36 months with a range up to 113 months, demonstrating the wide range of survival in patients treated with radiotherapy in the ICU. However, to our knowledge, this study is unique in its examination of intubated patients requiring ICU-level care. In patients who would almost certainly die without radiotherapeutic intervention, does the calculus need to be different in analyzing radiotherapy near the end of life? Is a higher percentage of patients receiving radiotherapy near the end of life acceptable if the potential benefit of radiotherapy could include long-term survival? Many questions remain to be answered about the role and initiation of radiotherapy in intubated patients in the ICU.

Conclusions
Palliative radiotherapy can be highly beneficial to patients with advanced or metastatic cancer causing significant symptoms. Radiotherapy can be used to help with pain relief in the management of bone metastases, neurologic symptoms in patients with MESCC, and brain metastases and other symptoms that cause focal symptoms from local tumor progression. However, the role of radiotherapy in patients toward the end of life continues to be clarified. Prognostic models can help to predict survival, but challenges continue to exist in understanding the clinical benefits versus burdens for patients with anticipated short survival. Patients with bone metastases can potentially have pain relief, sometimes within a few weeks of the completion of radiotherapy. Similarly, patients with MESCC may have significant clinical benefit from radiotherapy, but the benefit remains unclear in patients toward the end of life. The optimal management of patients with brain metastases and poor prognosis is being actively studied among patients with metastatic non-small cell lung cancer in the QUARTZ trial in the United Kingdom. Further studies should continue to explore the question of when radiotherapy is worthwhile and when it is futile.

Larger questions persist regarding whether radiotherapy administered in the last 14 days, 30 days, or even 60 days of life might be useful as a quality indicator. Other measures of aggressiveness of care at end of life including chemotherapy, visits to the emergency department, hospitalizations, and ICU stays have been described as quality measures by the American Society of Clinical Oncology and the NQF, but palliative radiotherapy at end of life has not. If radiotherapy at end of life is considered as a quality indicator, what should the measurement be? Receipt of radiotherapy in the final 14 or 30 days of life could potentially measure aggressiveness of care, but does not account for differences in risk/benefit calculi between single-fraction radiotherapy and multifraction radiotherapy regimens. As such, if radiotherapy at the end of life is to be incorporated as a quality indicator, we would recommend using the percentage of remaining life spent receiving radiotherapy as the indicator with a cutoff of 10% of remaining days receiving radiotherapy as a potential indicator that merits further exploration. Regardless of whether radiotherapy at the end of life is determined to be a quality indicator in evaluating palliative radiotherapy, a number of other questions remain to be explored:

1. What prognostic models are most likely to be clinically useful to help classify which patients are likely to have prolonged survival and which patients are likely to have short survival?
2. How can these prognostic models be incorporated into practice to allow clinicians to use evidence-based medicine in recommending palliative radiotherapy treatments?
3. If palliative radiotherapy is being underused, how can increased collaboration among radiation oncologists,
5. What is the role of highly conformal radiotherapy (intensity-modulated radiation therapy) or stereotactic radiotherapy or SRS in patients with poor prognosis?

These and other questions must continue to guide research and clinical care in patients receiving palliative radiotherapy to allow for the continued optimization of care for patients with advanced disease.

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