Defining the radiation oncologist’s role in palliative care and radiotherapy

Tai Chung Lam¹, Yolanda Tseng²

¹Department of Clinical Oncology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, China; ²Department of Radiation Oncology, University of Washington, Washington, DC, USA

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Correspondence to: Tai Chung Lam. Department of Clinical Oncology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, China. Email: lamtc03@hku.hk.

Abstract: Radiation oncologists play an important role in the palliative care of advanced cancer patients. The article discusses the various clinical indications of palliative radiation therapy, which include the control of bone pain, acute treatment of cord compression, the control of thoracic and gastrointestinal symptoms. The importance of survival estimates for individualization of radiation therapy regime is elaborated. Besides prescription of radiation treatment, radiation oncologists should also function as primary palliative care providers by assessing and initial management of symptoms and other sources of distress, making prompt referrals to specialists for complex symptom management and contributing to the multidisciplinary palliative care team. Additionally, communication skills, including prognostic disclosure and goals of care discussions, should also be a core competency of radiation oncologists.

Keywords: Palliative care; radiation oncologist; prognosis; symptom management; communications

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Independent of disease site, location of practice, and type of practice, nearly all radiation oncologists take care of advanced cancer patients. Approximately 40% of advanced cancer patients receive palliative radiotherapy (1), and 40% of radiotherapy is delivered with palliative intent (2). Most radiation oncology clinics do not have formalized or dedicated palliative radiotherapy programs, which may have the infrastructure and resources to deliver timely multi-disciplinary palliative and supportive care. However, given the ubiquity and complexity of advanced cancer patients with symptomatic disease, all radiation oncologists should be comfortable providing general palliative care for these patients—a belief that was vocalized by respondents in a recent survey of American Society for Radiation Oncology (ASTRO) members (3).

The radiation oncologist’s role in the palliative care team

Patients with advanced cancer have complex and multi-faceted needs, including those related to physical symptoms and to emotional, social or spiritual distress. With progressive disease, a patient’s needs may evolve; questions surrounding prognosis and end of life (EOL) care may surface. Given the different skill sets required to provide effective, holistic care for advanced cancer patients, a team-based approach is employed for pain/symptom management, social/spiritual issues, prognosis discussion, and goals of care. A palliative care team is a “comprehensive group of specialized clinicians from a variety of disciplines who share a common goal to improve the quality of life for patients and families facing serious illness” (4). Palliative
care teams providing care to patients and families, though variable by institution, generally are comprised of palliative care physicians, who receive specialized training in advanced communication skills and treatment of complex symptom management; nurses; social workers; pharmacists; chaplains; and the patient’s medical, radiation, and surgical oncologists. Palliative care teams may be distinguished as generalists, which include oncology clinicians and nurses that provide primary palliative care, versus specialists, which include clinicians that have received specialized training in provision of palliative care. Among a survey of ASTRO members, 79% respondents reported having a palliative medicine service at their institution (3). This number will likely increase over time, as palliative care becomes integrated as part of the global service of every hospital or clinic treating cancer patients (5).

By virtue of a radiation oncologist’s training and day-to-day multi-disciplinary approach to treating curative-intent, cancer patients, radiation oncologists already have the know-how and are familiar with the benefits of multi-disciplinary interaction. Radiation oncologists provide effective palliation of multiple symptoms from advanced cancer (see clinical indications for palliative radiotherapy). As patients may have several radiation oncology visits over a short time, radiation oncologists also have the unique opportunity to provide basic supportive care (e.g., nausea, pain, constipation) and screen patients, who may require more complex symptom management and/or psychosocial support. Many patients considered for palliative radiotherapy have concomitant symptoms. For example, approximately 10–15% of palliative radiotherapy patients have concurrent depression/anxiety (6,7). This strategy of screening and referring to appropriate team members has been associated with improved patient symptoms including fatigue, depression, anxiety, drowsiness, and well-being among patients seen in a palliative radiotherapy clinic (8). In this model, the patient’s primary oncology providers—radiation oncologists, medical oncologists, and oncology nurses included—provide general palliative care and refer patients to a palliative care specialist if/when more complex needs arise.

Radiation oncologists can also educate members of the palliative care team regarding indications for and misconceptions of palliative radiotherapy. This important interaction may improve patient care, in particular with referral of patients that palliative medicine specialists or oncologists did not otherwise consider radiotherapy for and/or referral of patients at an earlier time point.

**Estimating life expectancy for patients and treatment recommendations**

For advanced cancer patients, referral for palliative radiotherapy may herald progressive disease. In these moments, patients may reflect on the trajectory of their cancer treatment and inquire about prognosis. As providers who see patients at these critical moments, radiation oncologists must be comfortable with estimating life expectancy to effectively counsel patients and to determine a patient’s likelihood of benefiting from palliative radiotherapy. Furthermore, in patients that are deemed to be palliative radiotherapy candidates, radiation oncologists must choose a dose/fractionation scheme that balances the patient’s life expectancy with long-term efficacy and side effects (9,10). In fact, among an international survey of radiation oncologists, patient life expectancy was the factor most frequently influencing dose/fractionation prescription (11).

Despite this, physicians are generally poor at prognosticating (12) and tend to be optimistic in survival estimates, especially for patients with limited life expectancy (13,14). This is significant as overestimates of patient life expectancy may contribute to patients receiving a proportionally long radiation treatment course to their remaining life span (15,16).

Realizing that prognostication is complex, several groups over the last decade have developed prognostic models for palliative radiotherapy patients (Table 1). These models provide quantitative estimates of how various prognostic factors impact patient life expectancy. Prognostic models developed for advanced cancer patients receiving palliative care (24) are as accurate or more accurate than physician estimates. The available prognostic models for advanced cancer patients being evaluated for palliative radiotherapy vary in regard to the time frame of the training cohort [e.g., 1999 for Chow number of risk factors (NRF) model (17); 2008–2011 for TEACHH model (18); and 2012–2013 for NEAT model (19) and the setting in which patients were evaluated (e.g., in academic versus community clinics)]. While subtle, they are important to consider when evaluating whether a prognostic model may be generalizable to a patient of interest.

Regardless, for each model a training cohort was evaluated to identify a set of prognostic variables that were significantly associated with patient survival. Most models use a point system in which each significant adverse prognostic factor is assigned a value or counted. The sum of points or number of risk factors determines which group...
## Table 1 Summary of available prognostic models for advanced cancer patients evaluated for palliative radiotherapy

<table>
<thead>
<tr>
<th>Studies</th>
<th>Chow NRF (17)</th>
<th>TEACHH (18)</th>
<th>NEAT (19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validation cohort(s)</td>
<td>Temporal validation of RRRP patients in 2000 (18,20);</td>
<td>External validation for patients referred for palliative RT (19);</td>
<td>Temporal validation of 119 patients seen 2013–2015 (21)</td>
</tr>
<tr>
<td></td>
<td>External validation for palliative RT: patients referred in 2002 for palliative RT at Princess Margaret Hospital (17), patients with bone metastases treated on RTOG 9714 (12), DFCI/BWH 2008–2011 (18);</td>
<td>External validation for palliative spine RT patients (22)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>External validation for palliative care patients: patients referred to MSKCC palliative care clinic from 2008–2010 (23);</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>External validation for palliative spine RT patients (22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Prognostic variables</strong></td>
<td>NRF:</td>
<td>NRF:</td>
<td>Points in parentheses based on number of applicable factors:</td>
</tr>
<tr>
<td></td>
<td>Non-breast cancer;</td>
<td>Type of cancer: non-breast or prostate cancer;</td>
<td>Number of active tumors &gt;5 (1);</td>
</tr>
<tr>
<td></td>
<td>Site of metastases other than bone only;</td>
<td>ECOG PS &gt;1;</td>
<td>ECOG PS of 2 (1) or 3–4 (2);</td>
</tr>
<tr>
<td></td>
<td>KPS ≤60</td>
<td>Age &gt;60 years;</td>
<td>Albumin 2.4–3.3 g/dL (0.5) or &lt;2.4 (1);</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;2 palliative chemotherapy courses;</td>
<td>Primary tumor site: non-breast, kidney, or prostate (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hepatic metastasis;</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hospitalization within last 3 months</td>
<td></td>
</tr>
<tr>
<td><strong>Estimates</strong></td>
<td>Group 1 (NRF =0–1): median 60 weeks (95% CI, 37–70);</td>
<td>Group A (NRF =0–1): median 19.9 months (95% CI 13.9–31.1);</td>
<td>Very low risk [0–1]: median 37.5 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Group B (NRF =2–4): median 5.0 months (95% CI, 4.3–5.6);</td>
<td>Low risk (1.5–2): median 14.8 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Group C (NRF =5–6): median 1.7 months (95% CI, 1.2–2.1)</td>
<td>Intermediate risk (2.5–3.5): median 4.0 months</td>
</tr>
<tr>
<td></td>
<td>v Group 3 (NRF =3): median 9 weeks (95% CI, 6–11)</td>
<td></td>
<td>High risk [4–5]: median 1.2 months</td>
</tr>
<tr>
<td><strong>Training set C-statistic</strong></td>
<td>0.65</td>
<td>0.59</td>
<td>0.76</td>
</tr>
</tbody>
</table>

NRF, number of risk factors; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; KPS, Karnofsky Performance Scale.
a patient falls into, with each group having an estimated survival. While it is beyond the scope of this review to discuss development of a prognostic model, it is important to note that each model was validated to confirm that the model can predict for survival in other cohorts separated by time (temporal validation) or location (external validation). The three summarized models—Chow NRF, TEACHH, and NEAT models—have relatively high C-statistics varying from 0.59 to 0.76, reflecting goodness of the model; a C-statistic of 0.5 suggests that the model is no better than a flip of a coin with predicting an outcome, while 1 suggests that the model perfectly predicts those who will have a certain outcome and those who will not.

The Chow NRF model has been the most extensively validated and is the simplest, having just 3 factors to consider. Notably, in all three models, performance status is a significant predictor for survival. Indeed, performance status has been found to be most strongly correlated with survival (12) and highlights the importance of clinical evaluation of these patients. Newer therapies such as immunotherapy are emerging, which may alter cancer progression and mortality. While all three prognostic models were developed prior to wide spread use of immunotherapy, it is helpful to note that the Chow NRF model, which was developed among patients seen in 1999, still performs quite well among more contemporary cohorts (19,21,22), who inevitably are being exposed to newer systemic agents.

**Prognostic disclosure and communication**

Recent guidelines from American Society of Clinical Oncology (ASCO) advocate that “clinicians should reassess a patient’s goals, priorities, and desire for information whenever a significant change in patient’s care is being considered” (25). Triggers for prognostic disclosure and goals of care discussions will occur throughout a patient’s illness, including at diagnosis, relapse or progression, change in treatment approach, and/or at the patient’s and family’s request. At each of these junctures, the physician should ascertain the patient’s interest in disclosure and the how much information is desired, if so.

Many patients are referred for consideration of palliative radiotherapy in the setting of relapsed or progressive disease and at times when treatment approaches (e.g., systemic therapy) are being changed. Radiation oncologists therefore shoulder the responsibility for prognostic disclosure and assessing a patient’s goals to appropriately tailor radiation treatment recommendations, but also to address questions from advanced cancer patients, who may be encountering uncertainties with their disease course.

**Goals of communication**

Gaps in physician-patient communication may contribute to patients’ misunderstandings of the goals and limitations of their care. Among 1,193 newly diagnosed patients with stage IV lung or colorectal cancer, 69% of lung cancer and 81% of colorectal cancer patients had inaccurate understandings of whether palliative chemotherapy would cure their cancer (26). Similar findings were seen in a subset of this cohort, who were surveyed about their expectations on palliative radiotherapy. Among 384 irradiated patients with wet stage IIIB or IV lung cancer, 78% believed that radiotherapy was very or somewhat likely to help them live longer and 43% felt that radiotherapy was very or somewhat likely to cure their cancer. Not surprisingly, 92% of patients with inaccurate beliefs on the curative potential of radiotherapy also had inaccurate beliefs about chemotherapy (27). The frequency of prognostic disclosure by the treating physician was not captured in these studies, but interestingly, one of the independent predictors of patients with inaccurate beliefs of chemotherapy was a patient’s very favorable rating of their physician’s communication (26). These findings suggest that there is room for physicians to improve their patients’ understanding of palliative treatment, but this may potentially come at the cost of patient satisfaction.

Physician prognostic disclosure and communication also provides patients a realistic framework of their life expectancy, upon which patients can provide informed consent or dissent for treatment, frame their goals of care, and enhance communication with their family. Like physicians, patients may base treatment preferences on perceived life expectancy. Recall of prognostic disclosure has been associated with more accurate patient-derived life expectancy estimates. Longer (less accurate) patient-derived life-expectancy estimates are associated with preference for life-extending care and lower likelihood of a do-not-resuscitate order (28). These findings suggest that more accurate awareness of life expectancy permits patients to tailor their EOL care accordingly. Indeed, patients who recognize that their cancer is terminal are more likely to prefer symptom-directed care over life-extending care and to ultimately receive EOL care that is consistent with their baseline preferences (29). Notably, a small subset (~20%) of patients that understand their imminent mortality from
cancer may still choose to receive life-extending care (30). Prognostic disclosure and accurate understanding of prognosis is also important for patients and caregivers to better support each other through enhanced patient-family communication (30) and to prepare caregivers emotionally and logistically for the possibility of the patient’s death (31).

**Misconceptions of prognostic disclosure and/or EOL discussions**

Physicians are often hesitant to disclose prognosis, given concerns of potentially damaging a patient’s hope or provoking emotional distress, fear of being blamed, fear of confronting their own emotions, and/or instilling a sense of abandonment. Physicians’ fears are not completely unfounded: patients perceive physicians that deliver more optimistic messages as having more compassion (32). However, multiple studies with patients spanning different countries (30,33), stages of disease (early versus advanced) (34), and age (35) have documented that most patients desire prognostic disclosure (28). Among over 2,000 patients across 34 UK hospitals, 87% of patients preferred to have as much information as possible, both good and bad (33).

A similar proportion of adolescent and young adults (AYA) with cancer (83%) considered prognostic information to be extremely or very important, although patients with a lower likelihood of cure (<50%) were less likely to consider prognostic information important (35).

While oncologists are adequately aware of their patient’s desire for information on side effects from treatment and likelihood of tumor response, identifying the amount of prognostic information to disclose is more challenging (36). Although cancer patients desire prognostic disclosure, patients may prefer that the oncologist first confirm whether they would like this information (34). Indeed, among AYA cancer patients, 10% considered knowing about the likelihood of cure to be extremely or very upsetting (35).

Based on this, it may be helpful to first give a patient a preview of the type of information available, ask whether the information is desired, and then follow the patient’s request.

Contrary to commonly-held beliefs, disclosing prognosis to cancer patients is not associated with increased anxiety (28,35,37,38), depression (39), worry (39), or decreased hope (28,38,40) among cancer patients. In fact, in a study evaluating surrogate decision makers’ attitudes toward balancing hope and honesty with prognostic disclosure, 93% felt that avoiding discussions about prognosis was an unacceptable way to maintain hope (31). Moreover, prognostic disclosure does not appear to be associated with decreased patient-derived ratings of patient-physician relationship (28).

**Potential benefits of communication**

As previously alluded to, clear, honest communication may provide the patient critical information to inform his treatment decisions, goals of care, and planning. Within pediatric oncology, data also suggests that in addition to content, the process of communication may in of itself engender hope, peace of mind, and trust. Among 353 parents of children with newly diagnosed cancer, high-quality physician communication, as rated by the parent, was associated with greater rated trust of the oncologist, peace of mind, and decreased anxiety (38). Even in the setting of poor prognoses, receipt of high-quality information was associated with greater peace of mind and communication-related hope among parents of children in which a chance of cure was <75% (38). It is notable that among this cohort, accurate understanding of prognosis was not significantly associated with parental report of high-quality information or high-quality communication from the oncologist. Therefore, while any bad news can be difficult, patients and family members still find hope in the process of communication. Last, facilitating prognostic disclosures and EOL discussions have been associated with earlier hospice referrals and less aggressive medical care near death. The latter is notable as aggressive medical care at the EOL is associated with worse patient quality of life and worse bereavement adjustment among caregivers (39).

**Patient preferences of communication**

Like other scenarios of delivering bad news (41), most patients prefer physicians to obtain permission prior to disclosing information (34). Most patients prefer physicians to be realistic, provide opportunities to ask questions, and approach the patient as an individual when discussing prognosis (34,42). In a study of inpatients’ preferences on EOL communication with physicians, two major themes surfaced. Patients want their physician to “know me” and acknowledge the influence of family roles and life history on a patient’s values and priorities. In addition, patients desire “conditional candor” from physicians, a process of assessing the patient’s readiness, being invited to the conversation, and delivering information with sensitivity (43).
Hope is a broad concept, which can hold different meanings for each individual. In a written survey of 126 patients with metastatic cancer, patients were asked their definition of hope through provision of four exemplars and the option of free text. The most commonly endorsed exemplar (although only by 19% of the cohort) was “that you can still enjoy a good quality of life even if life expectancy is uncertain.” The majority of patients (62%) wrote their own definition with or without also picking a given exemplar (34). In this same survey, patients were queried on physician behaviors that were hope-giving. Most frequently rated behaviors included physicians offering the most up to date treatment, appearing to know all there is to know about the patient’s cancer, reassuring the patient that the pain will be controlled, and reviewing all treatment options (34). Similar themes have also emerged in interview-based studies of advanced cancer patients and their caregivers. Patients felt that by emphasizing what can be done (e.g., controlling physical symptoms, emotional support), exploring realistic goals, and discussing day-to-day living, physicians can still foster coping and nurture hope even when discussing prognosis and EOL issues (44). Strategies to foster hope when discussing prognosis and EOL issues are summarized in Table 2. In this issue, Dharmarajan et al. also reviews communication skills in palliative radiation oncology.

### Clinical indications for palliative radiotherapy

Uncontrolled, progressive tumor growth in advanced cancer patients may be associated with pain, neurologic impairment, bleeding, ulcerative mass, obstruction of luminal organs, or other functional impairments. The efficacy and safety of radiation therapy for palliating these symptoms is well established in multiple settings, including those with loco-regionally advanced, inoperable, metastatic, or previously irradiated recurrent tumors (45). Optimizing the therapeutic ratio of palliative RT in this heterogeneous patient population requires detailed assessment of symptomatology, tumor characteristics, and accurate prognostication by the radiation oncologist.

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**Table 2** Principles and proposed strategies for prognostic disclosure, communication, and to foster hope when discussing prognosis and EOL issues (42)

<table>
<thead>
<tr>
<th>Principles and proposed strategies for prognostic disclosure and communication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potential significant changes in a patient’s care should trigger a clinician to assess a patient’s desire for information, including prognostic disclosure</td>
</tr>
<tr>
<td>Providing patients with a realistic framework of their life expectancy allows patients to provide informed consent or dissent for treatment, frame their goals of care including end of life care, and enhances communication with their family</td>
</tr>
<tr>
<td>Most patients desire prognostic disclosure, but identifying the amount of prognostic information to disclose can be challenging; provide the patient with a preview of the type of information available and ask whether the information is desired</td>
</tr>
<tr>
<td>Prognostic disclosure is not associated with increased anxiety, depression, worry, or decreased hope among cancer patients</td>
</tr>
<tr>
<td>The process of communication can provide hope to patients and family members</td>
</tr>
<tr>
<td>Most patients prefer physicians to be realistic, provide opportunities to ask questions, and approach the patient as an individual when discussing prognosis</td>
</tr>
<tr>
<td>Proposed strategies to foster hope</td>
</tr>
<tr>
<td>After determining individual preferences for information, be honest and open in prognostic discussions without being blunt or giving too much detailed or factual information</td>
</tr>
<tr>
<td>Offer reassurances that the patient/caregiver will be supported throughout the illness trajectory, emphasizing available support</td>
</tr>
<tr>
<td>Emphasize what can be done (particularly when disease-specific treatments are no longer working)</td>
</tr>
<tr>
<td>Reassure that many treatments are available for controlling pain and other symptoms, where applicable</td>
</tr>
<tr>
<td>Identify areas where control can be fostered (e.g., advance care planning)</td>
</tr>
<tr>
<td>Recognize the spectrum or many forms of hope that are possible even in the face of a terminal illness</td>
</tr>
</tbody>
</table>

EOL, end of life.
Painful bone metastases

Bone is the third most common site of cancer metastases after lung and liver (46). Bone metastases may be associated with various local complications, varying from pain at the site of metastases, pathological bone fracture, to compression of the spinal cord or nerve roots (47). Based on a meta-analysis of 25 randomized trials, palliative RT is highly efficacious for pain control, with 60–80% achieving improvement of pain within 3–4 weeks (48).

Single-fraction radiation therapy provides excellent pain control for uncomplicated bone metastases (48). In general, uncomplicated bone metastases refer to lesions without an associated large soft tissue mass, have low risk of imminent fracture (i.e., no planned surgical fixation), no evidence of spinal cord or cauda equina compression, and not previously irradiated (49). Rates of efficacy and durability of pain control with single-fraction radiation are equivalent to more protracted radiotherapy courses (i.e., ≥ 5 fractions) (50-52). While rates of retreatment may be higher with single- versus multi-fraction RT (52,53), it is unclear whether this is secondary to physician comfort with retreating after a lower initial RT dose versus lower rates of durability. In addition to cost and resource utilization, single fraction treatment allows patients to undergo the planning procedure and RT delivery on the same day. For many patients, especially those with poor performance status, this maximizes both convenience and delivery of an effective treatment (54-56).

Palliative RT for bone metastases is well tolerated (48). Specific side effects depend on the irradiated anatomical site, size of radiation field, and radiation dose. Transient fatigue, pain flare, mild nausea and mild local skin erythema are commonly reported. Inclusion of the upper gastrointestinal tract may be associated with transient odynophagia and nausea, while diarrhea may be noted with bowel irradiation. These are usually self-limiting (57,58). Frequency and severity of side effects are lower with single fraction versus multi-fraction palliative RT (59).

However, in certain scenarios multi-fraction RT may be preferred to single fraction RT, including bone metastases causing neuropathic pain (51) or associated with an extra-osseous soft tissue mass (60). Studies suggest longer durability of pain control with a multi-fraction regimen. Patients irradiated after surgical fixation of bone metastases have not routinely been included in prior randomized trials comparing single- to multi-fraction RT; a longer RT course has historically been performed (47).

Palliative RT can be given in repeated courses to different sites of the body. Re-irradiation of a bone metastasis for recurrent pain after prior palliative RT may also be feasible, depending on the location, prior palliative RT dose, and time between RT treatments (61). Randomized data by Chow et al. suggest that a single-fraction RT for retreatment of painful bone metastasis results in similar efficacy and safety compared with multi-fractions RT (55). Retreatment can be given 1 month after the initial treatment if the response was not optimal (55).

Spinal metastases

Spinal vertebrae are the most frequently affected sites for bone metastases. In addition to minimizing pain, adequate control of spine metastases may help preserve the mechanical integrity of spinal column and prevent malignant spinal cord compression (MSCC) (62). While skeletal related events of asymptomatic spinal metastases may be reduced by bone modifying agents [e.g., bisphosphonate or denosumab (63) or radio-nucleotide treatment (64), symptomatic spinal metastases should be assessed by radiation oncologists for consideration of radiation therapy].

External beam palliative RT is the standard therapy for symptomatic spinal metastasis (62). Surgery is also an important option for selected patients with expected survival over 3 months (65). In patients with limited survival of 6 months or less, hypofractionated multi-fraction palliative RT prevented severe complications including vertebral compressive fractures, cord compression or neurological deterioration in more than 90% of irradiated patients (66). Multi-fraction RT is also associated with higher remineralization rates of irradiated vertebrae, compared with single-fraction RT (67). Improved mechanical strength of the spinal column could potentially prevent future complications.

Mechanically unstable spinal metastases are associated with higher risk of failure after RT (68) and compared to “uncomplicated” spinal metastases, nearly a 3-fold increased risk of adverse spinal events such as cord compression, pathologic fracture, or need for salvage surgery (66). Classification of spine instability is facilitated by the “Spinal Instability Neoplastic Score” (SINS; Table 3) (70). The SINS is a composite score (range 0–18) of 6 sub-scores: spine location, nature of bone pain, morphology of the bone lesion, spinal alignment, extent of vertebral body fracture, and involvement of posterolateral spinal elements. SINS has good content validity and excellent inter-observer agreements.
and intra-observer reliability among surgeons and radiation oncologists (71), hence can be used as a common language among surgeons and radiation oncologists. SINS should be routinely assessed for each patient referred for consideration of spinal RT. This can help identify patients who will likely respond poorly to RT alone and may benefit from referral to a spine surgeon for consideration of spine stabilization (72) or an interventional procedure like kyphoplasty (73).

Retreatment of a progressing, previously irradiated spinal metastasis can be challenging given that the spinal cord is radiosensitive (74,75) and at risk of radiation myelopathy and irreversible paralysis. Cohort studies, as well as a randomized controlled study, have shown that reirradiation with conventional RT techniques is safe if the cumulative biological equivalent dose (BED with alpha/beta =2) is in the range of 100–135 Gy, time between radiotherapy treatments is >6 months, and the BED dose of each course is ≤98 Gy (55,61,76). However, to respect the cumulative tolerance of the spinal cord, the RT dose used for re-irradiation is often lower than what was used in the first RT course, which may lead to unsatisfactory clinical outcome and disease control after reirradiation (76).

Stereotactic body radiation therapy (SBRT), a highly conformal radiation technique that employs high dose per fraction with near-rigid patient immobilization, has been increasingly used for spine metastases (77). Because of the 1–1.5 mm accuracy achieved through patient immobilization, image-guided RT, and steep dose fall off, SBRT is an attractive alternative to conventional RT (78). SBRT can achieve high, ablative radiation doses for spinal tumor control and at the same time, geographically spare the spinal cord from the damage of re-irradiation (62). While radiation myelopathy has been reported after SBRT re-irradiation (79), findings from Sahgal and colleagues suggest that >5 months interval between conventional palliative RT and SBRT re-irradiation, limiting the maximum point dose to the thecal sac to nBED 20–25 Gy (2/2) appears to be safe as long as the cumulative point max to the thecal sac is ≤70 Gy (2/2) and that the SBRT thecal sac point max dose does not comprise more than 50% of the total cumulative dose (79).

Early experience with spinal SBRT has demonstrated impressive local control results and favorable side effects profile (80). One-year local control rates of 90% or higher are achievable in multiple series across different histologies (81). As such, there is interest to use spine SBRT for initial RT treatment. An ongoing multi-center randomized controlled trial (82) is comparing spinal SBRT against single fraction palliative spinal RT in upfront setting. Recent data from a phase II randomized trial comparing SBRT (24 Gy/1 fraction) with conventional palliative RT (30 Gy/10 fractions) demonstrated quicker and improved pain response with SBRT (83). These and ongoing work are important to define the clinical efficacy, toxicity, and cost-effectiveness of spine SBRT. We caution against unselected use of SBRT for all spinal metastases, especially amongst

**Table 3** Spinal instability neoplastic scale (SINS) (69)

<table>
<thead>
<tr>
<th>SINS component</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>Junctional (occiput-C2, C7-T2, T11-L1, L5-S1)</td>
<td>3</td>
</tr>
<tr>
<td>Mobile (C3-C6, L2-L4)</td>
<td>2</td>
</tr>
<tr>
<td>Semirigid (T3-T10)</td>
<td>1</td>
</tr>
<tr>
<td>Rigid (S2-S5)</td>
<td>0</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
</tr>
<tr>
<td>Yes*</td>
<td>3</td>
</tr>
<tr>
<td>Occasional pain but not mechanical</td>
<td>1</td>
</tr>
<tr>
<td>Pain-free lesion</td>
<td>0</td>
</tr>
<tr>
<td>Bone lesion</td>
<td></td>
</tr>
<tr>
<td>Lytic</td>
<td>2</td>
</tr>
<tr>
<td>Mixed (lytic/blastic)</td>
<td>1</td>
</tr>
<tr>
<td>Plastic</td>
<td>0</td>
</tr>
<tr>
<td>Radiographic spinal alignment</td>
<td></td>
</tr>
<tr>
<td>Subluxation/translation present</td>
<td>4</td>
</tr>
<tr>
<td>De novo deformity (kyphosis/scoliosis)</td>
<td>2</td>
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*, pain improvement with recumbency and/or pain with movement/loading of spine; †, facet, pedicle, or costovertebral joint fracture or replacement with tumor.
patient with limited life expectancy, since conventional palliative RT is supported by high-level evidence, high efficacy, and lower cost (84).

Cord compression

Assessment of a patient with MSCC can be summarized with the mnemonics “NOMS” (85). Neurological (N) examination is essential to correlate findings with the spinal magnetic resonance imaging (MRI). Degree of cord compression can be classified by the Bilsky score (86). Bilsky grade II to III cord compression on MRI warrants consideration of urgent surgical decompression (87). The baseline lower limb function assessment by Frankel score (88) can aid subsequent review of treatment outcome.

Oncological “O” assessment of tumor radio-sensitivity may help identify those patients (e.g., those with radio-resistant tumors) that may benefit from a more aggressive surgical approach. Mechanical “M” stability should be as assessed by the SINS (Table 3). Last, systemic “S” assessment of a patient's co-morbidities and life expectancy may help identify who may benefit from more aggressive local treatment. Discussion of treatment options should ideally occur in a multi-disciplinary setting (89) with a spine surgeon, primary oncologist, radiation oncologist and palliative care physician.

For patients with radioresistant tumors, neurologic compromise, unstable spinal mechanics, and a reasonably long life-expectancy, an aggressive approach with surgical decompression, stabilization, and radiation therapy should be considered (65). The landmark study by Patchell et al. (90) demonstrated superior lower limb function, preservation of continence and overall survival when surgery was performed prior to radiation therapy (RT).

In contrast, for patients presenting with >48 hours of paralysis, limited life expectancy (≤3 months), multiple levels of spine involvement, conservative treatment with RT alone is appropriate (91). In a randomized comparison of single- versus multi-fraction RT for MSCC in patients with limited life expectancies (SOCRAD III), rates of overall survival were similar, in addition to ambulatory status at 8 weeks (92).

In the acute cord compression setting, SBRT for radiosurgical decompression (62) is still considered investigational, since a physical distance of 2–5 mm between the tumor and cord is necessary to achieve adequate epidural tumor coverage (93). Separation surgery, which clears the epidural component of the tumor, can help achieve this distance (94). SBRT can then safely ablate the residual tumor in vertebral body and paraspinal areas. This type of post-operative spinal SBRT is technically challenging due to metallic implant artifacts that may obscure organ localization and compromise dosimetry (93). Close collaboration between spinal surgeons, radiologists, radiation oncologists and medical physicists is necessary. Figure 1 was an illustrative patient who benefited from this multidisciplinary approach.

Brain metastases

Brain metastases affect around 40% of advanced cancer patients (95). This is a very heterogeneous group of patients with widely different survival estimates (96–98). On one end of the spectrum, these include patients with poor performance status, uncontrolled extracranial disease, high volume brain metastases not amenable for surgical or radiosurgical treatment (OS ≤3 months). The other end of the spectrum may instead include breast cancer patients with a single, small volume brain metastasis and minimal extracranial disease burden (OS >2 years). Treatment should therefore be personalized based on patient performance status, disease histology, and prognostication.

Whole brain radiation therapy (WBRT) is the conventional therapy for brain metastases (99). It provides transient control for brain metastases and helps to decrease the development of new metastases after focal therapies. However, no clinical trial has demonstrated a survival benefit with WBRT. Associated side effects including alopecia, scalp dermatitis, and neurocognitive function impairment may lead to significant deterioration in quality of life, especially in the first 3 months post-WBRT (100,101). Recently, the QUARTZ trial (102), a non-inferiority trial that randomized patients with brain metastases from lung cancer to WBRT versus supportive care, demonstrated that WBRT was associated with a benefit, but of only a mean quality-adjusted life years (QALY) of 4.7 days. While supportive care was not shown to be non-inferior to that of WBRT, many believe that a mean QALY of 4.7 days is clinically not meaningful.

Focal therapies, including radiosurgery and surgery, are associated with higher local tumor control rates compared with WBRT (103) and are considered for patients with expected survival longer than 3 months (104). Brain metastases larger than 3 cm may benefit from surgery over radiosurgery given higher rates of local control and more rapid relief of edema (103). Focal treatment alone (i.e.,
without WBRT) requires routine surveillance MRI scans to monitor for new distant brain metastases that may require salvage treatment. Risk of new distant intracranial disease is approximately 50% or higher at 6 months (105,106).

Recent advances in RT techniques have increased the therapeutic ratio of cranial RT. Multiple randomized controlled trials confirm the role of post-operative surgical cavity radiosurgery, which spares patients from the neurotoxicity of WBRT (106-108). Hypofractionated stereotactic radiotherapy (SRT) for large volume brain metastases is also efficacious based on prospective cohort studies (109,110).

Given that relatively low doses to the hippocampus are associated with neuro-cognitive decline (111), hippocampal sparing WBRT (112) has been studied using advanced RT planning techniques such as intensity modulated radiotherapy. Preliminary results on neurocognitive preservation showed superior outcome compares with a historical cohort (113).

Beside advanced RT techniques, the use of memantine, an oral NMDA receptor antagonist, had been shown to moderately delay time to cognitive decline and reduce the rate of decline in memory, executive function, and...
processing speed in patients receiving WBRT (114). It is a well-tolerated drug with minimal toxicity but a prolonged course of treatment of 24-week is needed.

**Thoracic malignancies**

RT has been used to relieve symptoms caused by tumor's compressive effect on thoracic structures (115), including major airway invasion (trachea and/or bronchus) causing dyspnea, cough, and hemoptysis. Tumors compressing the superior vena cava may cause neck, face and upper limb edema and shortness of breath. Large tumor or bulky mediastinal lymph nodes may cause esophageal obstruction. Tumor direct invasion in brachial plexopathy by apical tumor may cause severe pain and limb weakness.

Fourteen randomized clinical trials evaluating palliative RT for lung cancer have been performed and were summarized in meta-analysis (116). Various dose fractionation regimens had been tested, including short (10 Gy in 1 fraction, 17 Gy in 2 weekly fractions or 20 Gy in 5 daily fractions) and long RT courses (30–45 Gy in 10–15 daily fractions). In general, a high proportion of patients achieve satisfactory symptomatic relief, especially for cough and hemoptysis. Short course RT are highly effective for symptom relief with relatively mild side effects (117). This is an attractive option for patients with poor performance status and limited survival expectancy. Those with better performance status may benefit from longer course RT (118) given association of potentially improved overall survival, albeit at the cost of higher toxicity, mainly esophagitis (46).

**Gastrointestinal malignancies**

Obstructive and bleeding symptoms of locally advanced gastrointestinal tract cancer can be very distressing to patients and caregivers. As these patients usually have limited overall survival, a brief RT course is preferred. Single fraction treatment, 1-week treatment (20 Gy in 5Fr) to 2-week treatment (30 Gy in 10Fr) have all been commonly employed in clinical practice (119).

For cancer of esophagus, dysphagia may be addressed through stenting of the obstructed site (120), although the tumor may grow through or around the stent lumen in more than one-third of patients. Hypofractionated palliative RT (27 Gy in 6 fractions in 3 weeks) to the esophagus can be used to relieve dysphagia in nearly 80% of patients (121). Median duration of relief was 24 weeks (122).

Bleeding and gastric outlet obstruction from gastric cancer may be palliated with a brief course of RT (1 to 5 fractions) in patients with poor performance status. Time to relief is rapid (123). Delivery of higher dose using 3D conformal or intensity-modulated radiation therapy (IMRT) techniques may be considered in patients with satisfactory performance status and is associated with improvement in bleeding, obstructive symptoms, and/or pain in more than 70% of cases (124).

Locally advanced or recurrent rectal cancer may present with bleeding, pain on defecation, sacral plexus neuropathic pain, mucous discharge, infections or fistula formation. Palliative RT to pelvis, either with conventional fractionation (45 Gy in 25 fractions) or hypofractionated RT (30 Gy in 6 fractions) both can give satisfactory symptom pain relief in ~70–90% of patients, decrease bleeding in more than 70% of patients, and control tumor growth in about 50% (125,126). However, the duration of the disease control after external beam RT is short (~3–9 months). Dose escalation with high dose rate intra-luminal brachytherapy may be a promising way to improve duration of tumor control (127).

**Primary palliative care assessment by radiation oncologists**

As pain control is a frequent indication for palliative RT referral, radiation oncologists should be familiar with diagnosing and managing pain. Patient-reported questionnaires have been proposed for daily clinical use. The Edmonton Symptom Assessment System (ESAS) (128) is one of the most popular and well validated scoring systems. It assesses 9 symptoms—pain, fatigue, nausea, depression, anxiety, drowsiness, appetite, well-being, and shortness of breath—on a scale of 0 to 10. Changes in physical, emotional, and total symptom distress scores have been validated with clinically significant symptom improvement or deterioration (129). ESAS can be conveniently integrated routinely into radiation oncology clinic session (130). Persistent high scores warrant early review and referral to palliative care specialist for further evaluation.

As pain relief should be achievable in 60–80% of patients after RT (48), assessment of a patient’s opioid regimen should be performed before, during and after palliative RT. Universal screening for patients on opioid is recommended. Patients who are younger; male; and had a mental health or substance abuse disorder, a history of alcohol abuse, or a history of tobacco use are at greater risk for aberrant opioid use (131). Two simple screening tools for substance

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Dependence include the CAGE-AID questionnaire (132), which has been adapted to include drug use, and the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R) (133).

Patients that test positive on CAGE-AID or SOAPP-R should have their pain levels regularly monitored. Aberrant behavior, such as complaints of pain inconsistent with disease status or repeated reports of lost opioid medications, should be red flags. Referral of these patients to a specialist palliative care physician may be warranted to address pain safely.

Depression may also be readily screened in the radiation oncology clinic. Up to 10–15% of patients undergoing RT report depression and/or anxiety (6,7). The Patient Health Questionnaire (PHQ-9) (134) is a validated instrument for screening patients who may benefit from referral to the psycho-oncology service. PHQ-9 is a 9-item scale with a possible score of 0–27. Scores >9 should prompt screening for symptoms of depression and consideration of a psycho-oncology specialist referral. Patient should be re-evaluated for progress during follow-up at the radiation oncology clinic with the aim of symptom remission within 3 months.

Last, spirituality assessment is recognized as one of the domains of high-quality palliative care (135). Spirituality is an integral dimension of human beings and has been recognized as a critical factor in the well-being of patients. Unresolved spiritual distress can lead to poor quality of life and poor health outcome (136). While detailed assessment and provision of spiritual care should be referred to chaplains, basic spiritual distress screening can be done with relatively simple assessment tools such as “FIGA” (137,138), a validated tool, or “Hope” (139) and “Spirit” (140). Radiation oncologist should be able to address spiritual issues of the patient, diagnose and facilitate early treatment of spiritual distress and integrate patients’ spiritual resources of strength into the treatment plan.

Conclusions

Radiation oncologists play an important role in the holistic care of advanced cancer patients. Through collaboration with multidisciplinary care team, radiation oncologist can contribute substantially in the overall care plan, including communication, prognostication, and provision of radiotherapy to palliate local effect of tumor progression. Radiation oncologists are also primary palliative care providers, monitoring and managing symptoms, and screening for distress (Table 4). By attending to all dimensions of a patient’s suffering, radiation oncologists can provide compassionate care to improve the quality of life of patients and their caregivers.

| Table 4 Summary |
| Role of the radiation oncologist in palliative cancer care |
| Prognostication and communication |
| Control symptoms from cancer progression |
| Bone metastases: pain control |
| Spinal metastases/spinal cord compression: pain control and function preservation |
| Brain metastases: symptom control, function preservation |
| Thoracic tumors: pain, cough, bleeding control, relieve obstruction |
| Gastro-intestinal symptom control: pain, bleeding control, relieve obstruction |
| Gynaecological and urological symptom control: pain and bleeding control |
| Malignant ulcers: pain and bleeding control |
| As a primary palliative care provider |
| Opioid use assessment, review and safety monitoring |
| Physical, psychological and spiritual symptoms monitoring |
| Referral to palliative care specialists or palliative care team if symptom burden is persistent |
| Participate in palliative care multidisciplinary team |
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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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