Editor's note:
"Palliative Radiotherapy Column" features in articles emphasising the critical role of radiotherapy in palliative care. Chairs to the columns are Dr. Edward L.W. Chow from Odette Cancer Centre, Sunnybrook Health Sciences Centre in Toronto and Dr. Stephen Lutz from Blanchard Valley Regional Cancer Center in Findlay, gathering a group of promising researchers in the field to make it an excellent column. The column includes original research manuscripts and timely review articles relating to palliative radiotherapy, and editorials and commentaries on recently published trials and studies as well.

Palliative Radiotherapy Column

Palliative radiotherapy: past, present and future—where do we go from here?

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Abstract: Radiotherapy is successful, time efficient, cost effective, and safe means to provide palliative relief for a variety of symptoms suffered by oncology patients. While the value of palliative radiotherapy has been understood for more than century, the radiation oncology specialty has only incompletely embraced its role in this setting. The optimization of palliative oncology requires accurate survival prognostication and a dedication to existing hypofractionated radiotherapy regimens that minimize toxicity and improve patient and caregiver convenience. The future of palliative radiotherapy demands more extensive treatment guidelines that explain the proper use of existing and novel technologies while remaining attentive to a growing population of cancer patients and a limited amount of resources with which to provide them care.

Keywords: Radiation oncology; palliative care; hypofractionation; quality measures

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Introduction

Radiotherapy has been used for palliating symptoms of cancer since soon after its discovery in the 1800's (1). While the radiation oncology specialty has incompletely embraced its usefulness in palliative oncology, this treatment modality has proven itself to be a cost-effective and time-efficient intervention that is associated with a low toxicity profile. Radiotherapy can relieve symptoms due to either primary or metastatic tumors, including common manifestations of cancer such as pain, obstruction, bleeding, and neurologic symptoms. While the complexity of palliative radiotherapy has increased with that advent of newer technologies and the need to collaborate with other involved specialties, the common sense goals of its delivery remain a good chance for symptom relief with a limited risk of side effects. Here we preview a series of upcoming papers in this and future issues of the *Annals of Palliative Medicine* that will highlight the benefits, controversies, and future promise of palliative radiotherapy for end-of-life

Table 1 Examples of prognosis-dependent treatment options for symptoms of primary cancer

Primary site	Treatment options		
	Poor prognosis	Average prognosis	Favorable prognosis
Central nervous system	Supportive care alone; temozolomide alone	30 Gy/10 fractions	59.4-60 Gy/30-33 fractions
Head and neck	Supportive care alone; 8 Gy/1 fraction; 14 Gy/4 fractions monthly to 42 Gy total	50 Gy/20 fractions	70 Gy/35 fractions
Breast	Supportive care alone; 8-10 Gy/1 fraction	20-30 Gy/4-5 fractions; 30 Gy/10 fractions	50 Gy/25 fractions
Lung	Supportive care alone; 8-10 Gy/1 fraction; 17 Gy/2 fractions given weekly	30 Gy/10 fractions; endobronchial brachytherapy for endoluminal obstruction	60 Gy/30 fractions
Esophagus	Supportive care alone; 8-10 Gy/1 fraction; 24 Gy/3 fractions	30 Gy/10 fractions	50 Gy/20 fractions; 50 Gy/25 fractions
Genitourinary	Supportive care alone; 8-10 Gy/1 fraction; 14.4 Gy/4 fractions monthly to 43.2 Gy total	30 Gy/10 fractions	50 Gy/20 fractions
Gynecologic	Supportive care alone; 8-10 Gy/1 fraction; 14.4 Gy/4 fractions monthly to 43.2 Gy total	30 Gy/10 fractions	50 Gy/20 fractions

oncology care.

Prognostic factors and life expectancy

Optimal palliative oncology care requires both an accurate estimation of life expectancy as well as a determination of whether palliative treatments are to be delivered concurrently with curative-intent therapy or with palliative intent, only. Several factors complicate the survival prognostication of cancer patients, including patient factors such as co-morbid illnesses, disease-related factors such as tumor stage and histology, and psychological factors such as the desire of caregivers to maintain a hopeful outlook. This third factor might explain why physicians often describe an unrealistically optimistic prognosis, commonly overestimating survival by a factor of three or more (2-6). Drawbacks of these inaccurately lengthy prognostications include unrealistic patient expectations and a tendency toward overly aggressive interventions (7-9). Prognostic models that assess multiple factors and predict survival in patients receiving palliative radiotherapy for advanced cancer have been developed and tested, giving hope that treatment decisions will come to more closely align with realistic survival estimates (10,11).

Hypofractionated palliative radiotherapy

Patient and caregiver convenience dictate that palliative radiotherapy treatment courses are given in as short a time period as will allow their effectiveness, especially in those patients where prognosis suggests a short lifespan. While curative treatment regimens have evolved to deliver daily fractions of 1.8 to 2.0 Gy for a total of 40 to 80 Gy, palliative radiotherapy can be effective with dose regimens of 8 to 30 Gy in 1 to 10 fractions. Beyond survival estimates, factors that influence palliative radiotherapy fractionation include: patient performance status, comorbidities, and transportation capabilities; tumor factors such as number, location, and behavior of local and metastatic lesions; and, radiotherapy toxicity risks, taking into account any previous radiotherapy to the same anatomic site as well as other potential combined toxicities caused by other modalities of treatment that have been given. Multiple studies have yielded information about hypofractionated regimens that provide palliative relief for a myriad of clinical circumstances (*Table 1*) (12).

Radiotherapy dose fractionation for bone metastases

The palliation of painful bone metastases with short courses of palliative radiotherapy remains one of the most striking examples of the value of this type of treatment to end-of-life cancer patients. Bone metastases are a very common manifestation of malignancy, and radiotherapy provides

partial pain relief in 60-80% and complete pain relief in 30-50% of patients within days to weeks after the initiation of therapy (13). The American Society for Radiation Oncology (ASTRO) Bone Metastases Guidelines concluded that pain relief is equivalent with fractionation regimens of 30 Gy in ten fractions, 24 Gy in six fractions, 20 Gy in five fractions, or a single 8 Gy fraction (14). Though retreatment rates may be higher in those who receive a single fraction, a second course of therapy can be expected to provide a reasonable rate of pain relief (15). Still, practice patterns within the US have not fully come to match the available data and guideline recommendations (16,17).

Radiotherapy management of complex spine lesions

Malignant epidural spinal cord compression (MESCC) is an important special circumstance of bone metastases because its effects may include neurologic compromise in addition to pain. Manifestations of this clinical condition may include loss of sensation, paralysis, and incontinence of bowel or bladder (18). Management of MESCC requires prompt diagnosis, initiation of corticosteroids to diminish edema, multidisciplinary evaluation of the potential benefits and risks of surgical decompression, and radiotherapy either as the main treatment type or as an adjuvant in the post-operative setting (19,20). The proper dose fractionation scheme for patients with MESCC remains an active topic of investigation (21-24).

Anticipation and management of palliative radiotherapy side effects

Every radiotherapy intervention can be associated with acute or late toxicity, with factors that influence those risks including volume of tissue irradiated, total radiation dose, dose per fraction, toxicities of other treatment modalities, and the radiosensitivity of normal adjacent tissues (25). As opposed to circumstances in which radiation is delivered with curative intent, palliative radiotherapy does not necessarily require complete tumor ablation or treatment of all known disease to provide symptom relief (26). In fact, lower total doses limit acute toxicity and allow for improved convenience through a shorter treatment course. In general, palliative radiotherapy doses are delivered with larger fraction sizes than are used for curative intent courses. These hypofractionated courses may provide the benefit of earlier symptoms response but at the cost of a greater risk of late side effects (27). Still, risks of late side effects can be minimized by limiting the total biologic equivalent dose of the palliative radiotherapy regimen delivered. Also, given that late side effects commonly occur months to years following completion of treatment, the sad truth is that the implications of this type risk may be irrelevant for palliative patients who may not live long enough to face late effects (25).

Palliative radiotherapy guidelines and quality measures

Documented disparities in palliative radiotherapy treatment approaches as well as resource limitations in the face of growing patient needs have combined to lead for calls to produce guidelines and quality measures. Whereas guidelines derive clinical treatment recommendations from available high-quality literature, quality measures are meant to both endorse standards and measure performance of individual caregivers and health care systems (28). Three of the first six ASTRO treatment guidelines dealt with palliative care scenarios, confirming the importance of the topic to the oncology community, at large (29).

The recognition of variable practice patterns in the radiotherapeutic treatment of bone metastases led to the completion of the ASTRO Bone Metastases Guidelines (14,30). The National Quality Forum accepted a submission based upon this guideline as its first quality measure for the evaluation of radiation oncology practices (31). Furthermore, the American Board of Internal Medicine initiative entitled Choosing Wisely chose as one of its first radiation oncology recommendations, “don’t routinely use extended fractionation schemes (>10 fractions) for palliation of bone metastases”. The successful progression of the initial bone metastases fractionation question into a treatment guideline, a quality measure, and a recommendation to all radiation oncologists and patients in the Choosing Wisely campaign suggests that further palliative radiotherapy initiatives will be well received.

Future directions

In addition to further palliative radiotherapy guidelines and quality measures, future initiatives will need to help the radiation oncology specialty to continue to balance the technological advances in treatment delivery with the special needs of dying patients. For instance, the promise for improved tumor control with diminished toxicity is great for newer treatment types such as stereotactic

radiosurgery for brain metastases and stereotactic body radiotherapy for clinical conditions such as primary lung cancer or metastases in the spine, liver, or lung. Still, the costs of this technology may further strain the resource limitations associated with the increased number of patients expected as 78 million "Baby Boomers" reach the age where their cancer incidence rises. Clearly, specialized treatments such as those offered by radiation oncologists will need to be better coordinated with overall palliative care goals of this patient group. One study, in particular, exemplified the usefulness of early palliative care intervention for patients with newly diagnosed, locally advanced non-small cell lung cancer. Those who were randomly assigned to early palliative care consultation in addition to stand care were shown to have improved quality of life, lower rates of depression, and longer survival (32).

Furthermore, just as academic radiation oncology departments have been subdivided into teams that care for patients with specific types of diagnoses, so too must they consider the formation of palliative radiotherapy services. Some centers have begun to pioneer this type of approach in an effort to optimize the coordinated delivery of end-of-life oncology care for patients consulted for palliative radiotherapy. Still other centers have tried to establish 'rapid response' clinical pathways that optimize throughput of palliative radiotherapy patients to allow them to undergo consultation, simulation, and treatment delivery in one visit (33).

Finally, in spite of the number of patients who receive palliative oncology care in the United States each year, as well as the severity of their symptoms, there are a paucity of research trials devoted to this topic. While the Radiation Therapy and Oncology Group (RTOG) has completed and published several trials regarding the most appropriate care of patients with bone and brain metastases, future research will require increased interdisciplinary input into trial designs, a greater number of validated quality of life instruments, and a more creative manner to collect follow up data in a setting where missing data points are common as a result of declining function or death of the patients.

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