Top 10 Tips Palliative Care Clinicians Should Know About Radiation Oncology

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Abstract

As palliative care (PC) moves upstream in the course of advanced illness, it is critical that PC providers have a broad understanding of curative and palliative treatments for serious diseases. Possessing a working knowledge of radiation therapy (RT), one of the three pillars of cancer care, is crucial to PC providers given RT's role in both the curative and palliative settings. This article provides PC providers with a primer on the vocabulary of RT; the team of people involved in the planning of RT; and common indications, benefits, and side effects of treatment.

Keywords: pain management; palliative radiation; radiation oncology; radiation therapy; supportive oncology; symptom management

Introduction

RADIATION THERAPY (RT) is an integral component of multidisciplinary supportive oncology care.¹ As a treatment modality, it has the unique advantage of being highly effective and durable without requiring invasive procedures or long recovery periods. Because RT directly targets and kills cancer cells, the symptom relief experienced from a single treatment course is usually sustained for months to years.

The use of radiation for palliation or prevention of tumor-related symptoms is quite common. In fact, ~40% of patients referred to a radiation clinic are treated with palliative intent.² Symptomatic bone, brain, and spine metastases are the most common reasons for referral for palliative radiation. When utilized in the appropriate setting, palliative radiation therapy can substantially improve functional mobility and quality of life for the majority of individuals.^{3,4}

At present, the main barriers to receiving palliative radiation are related to under-referral. Patients are not referred to a radiation oncologist for a variety of reasons. Some of these include incomplete knowledge about the utility of radiation as a potential pain management option in patients, especially for those patients who might have already received some radiotherapy in the past. Other reasons include worries about interrupting systemic therapy or concerns about the toxicity profile of a treatment course. Thus, for any referring provider, it is helpful to have a solid appreciation of the advantages and potential drawbacks of radiotherapy to better understand how palliative radiation might fit into a patient's cancer treatment. This article seeks to share some of the most important concepts that radiation oncologists and palliative care (PC) colleagues use when caring for advanced cancer patients.

We present here a list of 10 tips PC clinicians will find helpful to know about palliative radiation therapy. These

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were chosen and vetted by a combination of PC clinicians and radiation oncologists specializing in palliative radiation therapy. Although the information is intended for an audience of PC practitioners, it is applicable to providers of all specialties who are managing patients with advanced malignancies. We hope the tips discussed herein will address many issues commonly encountered by PC specialists caring for patients who might be receiving radiation or for whom palliative radiation might be warranted.

Tip 1: Radiation treatment is given in fractions, or small daily doses, and is described in a radiation “prescription.”

A radiation prescription includes information about the anatomic site, technique, radiation energy, dose, and how the dose is divided or fractionated. At the end of a treatment course, the radiation oncologists will document the course in a radiation treatment summary, which lists the anatomic site(s) treated, planning technique employed, actual doses delivered, and dates of treatment. Treatment summaries also give information about how well the radiation course was tolerated, including any adverse effects encountered and whether the radiation course was interrupted or stopped for any reason. Treatment summaries may also be part of a cancer survivorship care plan.⁵

Radiation dose is the amount of radiation energy absorbed by a patient. It is measured in Gray and commonly abbreviated Gy (1 Gray = 100 centigray = 100 rads). Typical curative doses are 50–80 Gy, whereas palliative radiation treatments can effectively alleviate symptoms with a smaller dose (~7–35 Gy). Fractionation describes when the total dose of radiation is divided into several small doses delivered for a period of several days. Total radiation dose is typically fractionated to safely deliver a large total dose to the tumor while limiting the adverse effects to the nearby normal tissues by giving them time to recover between fractions. Standard fraction sizes are 1.8–3.0 Gy daily, whereas a dose given in larger amounts (e.g., 4 Gy daily) is termed hypofractionated, meaning that the total radiation dose may be given completely within a smaller number of fractions while still achieving a therapeutic outcome. Palliative radiation therapy is sometimes hypofractionated to limit the number of treatment days.

Tip 2: From the initial consultation to delivery of the first dose, palliative radiation therapy typically requires input from several individuals and computer systems, usually for several days to weeks. During emergencies, radiation can be initiated on the same day as a consult.

Once a consult has occurred, the typical process for preparing a radiation therapy plan includes (1) a planning scan, (2) contouring, (3) definition or computation of the radiation beams, and (4) quality assurance. Given these complex tasks, a typical curative radiation plan can take up to two weeks between consultation and the start of therapy. For the most complex treatments, radiation planning may take even longer and require more extensive quality checks.

A planning scan is usually a nondiagnostic computerized tomography performed in the radiation oncology suite, with the patient properly positioned to gain access to the anatomic site and ensure reproducible positioning on a daily basis with individualized molds. This scan may be used in conjunction with others (e.g., magnetic resonance imaging) to provide

complete anatomic information for the radiation oncologist. The radiation oncologist then contours the tumor target areas and pertinent nontumor areas using specialized computer software. For simple plans, the radiation oncologist chooses the appropriate beam arrangement. A dosimetrist then calculates the amount of time the radiation beams need to be activated (termed “beam-on time”) to deliver the prescribed dose. For complex treatment plans, the radiation oncologist and dosimetrist work together to determine criteria for an appropriate plan and a computer algorithm computes the plan, often in an iterative manner. The completed plan is evaluated by a medical physicist who checks the plan for appropriateness and determines whether adjustments are needed. Once a plan has been finalized, a medical physicist performs quality assurance to ensure that the plan is safe for delivery. Owing to the many people and systems involved and differences in radiation machines, radiation treatments that have already been planned or started at one center cannot typically be transferred to another center.

In certain instances, palliative radiation therapy may be able to begin more rapidly. Emergent radiation may be given the same day as consultation when the planning technique needed is simple (e.g., only one or two radiation beams are needed), although it will still usually take several hours for treatment planning, checks, and delivery, as multiple computer systems and individuals are still needed to complete and check the plan. Simpler techniques generally require less treatment planning and calculation time.

Tip 3: The most common indications for palliative radiation therapy are symptomatic bone, vertebral, and brain metastases.

Radiation is extremely effective in controlling pain from osseous metastases.⁶ Outcomes are generally similar whether single fraction or multiple fraction radiation is used, although some studies indicate that single fraction may lead to higher rates of retreatment.⁷ Approximately one-third of patients may experience complete pain response (no longer requiring analgesics), whereas about 60% will experience a partial pain response (measured by a decrease in analgesic use). Most patients experience an improvement in function after treatment.⁸ Symptom relief usually begins about four to six weeks after the final radiation treatment session. Patients may be retreated at the same site if necessary. Treatment-associated rates of potential pathologic fracture are low (1%–8%). Generally other adverse effects are minimal but may include fatigue or mild skin redness. If the spine or pelvis is treated, the scattered dose may result in transient gastrointestinal (GI) disturbances such as nausea or diarrhea.

Radiation is also a highly effective noninvasive strategy for managing symptomatic brain metastases. The expected outcomes for brain metastasis treatment vary widely and are based on the number, size and location of lesions, and the treatment technique employed. In the case of brain metastases with surrounding edema, initiating steroids (usually dexamethasone) about one to two days before radiation therapy provides the greatest immediate relief of symptoms. Stereotactic radiation (SRS) (also known as Gamma Knife®, CyberKnife®, stereotactic radiosurgery, etc.), a single large dose fraction of radiation, may be indicated for patients with fewer lesions or lesions that are smaller (3 cm or less) or have been resected. SRS generally demonstrates excellent tumor

control, with >75% of patients having a positive response, with minimal adverse effects.⁹ However, this technique does not prevent the development of further metastases in nontreated areas of the brain. Whole brain radiation therapy may decrease development of additional lesions by 50%, but usually requires 5–10 days of treatment and comes with additional adverse effects of two to four months of fatigue, nausea, appetite loss, hair loss, and subacute cognitive decline.¹⁰

Tip 4: Malignant spinal cord or nerve root compression, brain metastases with edema, and superior vena cava syndrome are radiation oncology emergencies that should be treated as soon as possible to maintain or regain recently compromised function.

Although radiation oncologists try to minimize delays when beginning palliative radiation, there are several clinical scenarios for which radiation therapy must begin urgently. Situations wherein emergent radiation therapy may be warranted include malignant spinal cord or nerve root compression, symptomatic brain metastases, and superior vena cava syndrome.

Malignant spinal cord or nerve root compression can cause a host of symptoms including pain, weakness, sensory loss, and/or loss of bowel or bladder function. These symptoms can have a significant and sometimes irreversible impact on a patient's functional status and quality of life if not addressed quickly. For patients with good performance status and limited disease, surgery followed by radiation is considered the standard of care. However, for patients who are not surgical candidates due to limited performance status, short prognosis, or widespread cancer, radiation should be started emergently. The goal of emergent radiation therapy is to stop the progression of tumor and ideally reverse the presenting neurologic symptoms. The likelihood of regaining or maintaining ambulatory status sharply declines 24–48 hours after development of neurologic symptoms (e.g., weakness and numbness) and/or loss of ambulatory ability. The use of moderate steroids before the start of radiation treatment, usually dexamethasone 4 mg two to four times a day, is recommended to decrease swelling and improve outcomes slightly.

For patients who present with symptomatic brain metastases, urgent workup and intervention are often warranted. Surgical resection followed by postoperative radiation is the standard of care for patients with a good performance status and a limited number of brain metastases.^{9,11} For patients who are not appropriate for neurosurgical intervention, radiation can be initiated rapidly with the goal of shrinking the lesions and reducing compression on critical structures (e.g., brainstem and optic structures).

Malignant superior vena cava syndrome occurs when the superior vena cava is compressed by tumor, leading to symptoms such as cyanosis, facial edema, upper extremity edema, laryngeal edema, or cerebral edema. Although rare, laryngeal and cerebral edema can be life threatening. Although itself fairly uncommon (about 15,000 cases per year), the most common malignant causes of superior vena cava syndrome are lung cancer and lymphoma. Treatment options include steroids, radiation, chemotherapy, and endovascular stenting. The ideal treatment depends on both patient- and tumor-specific factors. Radiation has been shown to be quite effective, with the initial improvement generally seen around 72 hours after the start of radiation and complete relief of symptoms in 63%–78% of those with lung cancer; however,

its use ideally requires a tissue diagnosis before treatment. Radiation is typically given in small daily fractions of 1.8–2.0 Gy for several weeks, and the total dose of radiation should be based on a multidisciplinary plan that incorporates systemic therapy.¹²

Tip 5: For patients with painful, uncomplicated bone metastases, a single radiation fraction of 8 Gy is as effective as longer treatment courses.

Radiation oncologists determine the dose and fractionation of treatment by balancing the probability and timeline for the treatment to be effective with the patient's life expectancy and likelihood of adverse effects. Shorter radiotherapy courses have benefits of time, money, and convenience. Patients may have limited energy, or they may have discomfort when lying on the treatment table. If patients live far from the facility, they may have insurmountable transportation issues or even need to remain hospitalized during a longer radiation course. Patients completing radiation courses can resume their systemic treatments more rapidly. If patients are waiting to complete radiation before hospice enrollment, a shorter course can make a valuable difference in their available support.

Radiation courses of more than one fraction are generally recommended for patients with complicated bone metastases defined by the presence of spinal cord compression, tumor extending beyond the bone, or an increased risk of fracture in a weight-bearing area. In some cases, a radiation oncologist may recommend a longer duration of therapy in patients with prognoses more than six months.

Symptom relief from radiation is typically apparent by four to six weeks after completion of the course, regardless of its duration. It is important to note that some studies of palliative radiation for uncomplicated, painful bone metastases have shown that patients are more likely to require retreatment if they receive a single 8 Gy treatment than if they have a longer course, although pain relief (extent and time course) is similar.^{13,14} Patients with a life expectancy of more than six months may also be at risk of developing significant late adverse effects, particularly after hypofractionation.

Tip 6: The side effects most commonly encountered during palliative radiation fall into two categories: acute and late toxicities.

Both acute and late side effects can develop as a result of radiation therapy. Acute side effects are those that develop during the radiation course or up to three months after the course has completed. Late side effects develop more than three months after radiation therapy. Late side effects are less commonly encountered in the setting of palliative radiation, both because the total radiation dose delivered is generally less and because prognosis may also be shorter.

Both general side effects and site-specific effects centered around the area of the body receiving radiation may occur. The acute general side effect most commonly encountered is fatigue. Area-specific side effects (Table 1) can occur because the region of treatment may be in proximity to sensitive organs or structures. For example, when giving radiation to the thoracic spine, the esophagus will often receive radiation, which can lead to the acute side effect of odynophagia or esophagitis. Development of a days-long pain flare can occur during and/or immediately after treatment of symptomatic bone metastases. It is related to the transient swelling

TABLE 1. COMMON RADIATION THERAPY SIDE EFFECTS BY AFFECTED ORGAN

<i>Organ</i>	<i>Acute toxicity</i>	<i>Late toxicity</i>
Skin	Dermatitis, hyperpigmentation, hair loss	Permanent hair loss, telangiectasia
Bone marrow	Decreased blood counts	
Brain	Nausea, fatigue	Memory/cognitive changes
Eyes	Watery eyes, dry eye	Cataracts, dry eye
Mucosal surfaces	Mucositis leading to pain	Ulceration
Esophagus	Esophagitis leading to dysphagia and/or odynophagia	Stricture, ulceration, fistula
Lungs	Pneumonitis ^a	Scarring, worsening lung function
Stomach	Nausea, acid reflux	Ulceration, fistula
Bowel	Loose stools, diarrhea, nausea	Stricture, ulceration, fistula
Bladder	Urgency, frequency, dysuria	Ulceration, fistula, scarring
Rectum	Urgency, frequency, tenesmus	Ulceration, fistula, scarring

^aTypically one to six months after radiation.

occurring in and around the treated bone and is easily mitigated by a short course of steroids.¹⁵

The likelihood and time course of development of acute side effects varies significantly between individuals and occurs more commonly toward the end of radiation treatment. Most acute side effects should resolve within four to six weeks after radiation therapy has ended. Pneumonitis, which typically develops between one and six months after radiation therapy, has a uniquely delayed time course.

Effective supportive treatments (Table 2) exist for many of the mentioned toxicities. Some side effects can also be prevented with prophylactic medications. For instance, pain flares can be prevented with the use of prophylactic dexamethasone, and nausea and vomiting can be mitigated or prevented by prophylactic ondansetron.¹⁶

Tip 7: Prophylactic radiation to treat nonpainful lytic lesions at weight-bearing sites probably does not prevent fractures.

Prophylactic radiation for nonpainful lytic bone lesions at weight-bearing sites is not routinely performed. If a patient has a good performance status and prognosis more than three months, surgical intervention is typically the first-line therapy since metal rods and orthotopic implants can improve the strength of

weight-bearing sites. Surgical stabilization should then be followed with postoperative radiation to limit tumor regrowth. There are no randomized controlled trials on the role of prophylactic radiation; however, a single-institution prospective trial found that of 102 patients with femoral metastasis, 14 developed a pathologic fracture within 36 weeks after radiation therapy.¹⁷ Both axial cortical involvement >3 cm and circumferential cortical involvement >50% were predictive of developing femur fractures. Given these limited data, if either of these two radiologic features is present, surgical evaluation is warranted. A weighted scoring system for long bones was proposed by Mirels in 1989 for quantification of pathologic fracture risk based on location (upper extremity, lower extremity, or peritrochanteric), pain level, type of lesion, and size of lesion. A higher summed Mirels' score suggests that prophylactic internal fixation may be warranted before RT.¹⁸ For nonsurgical candidates, nonpainful long bone metastasis can result in fractures due to torsional forces and may warrant radiation therapy.

Tip 8: Tumor-related bleeding or obstruction and leptomeningeal carcinomatosis may benefit from palliative radiation.

Bleeding in advanced cancer patients may be related to local tumor effects, tumor angiogenesis, or systemic effects

TABLE 2. COMMON TREATMENTS USED FOR SIDE EFFECTS OF RADIATION THERAPY

<i>Symptom</i>	<i>Prophylaxis</i>	<i>Treatment</i>
Fatigue	Exercise; increased level of activity	Stimulants (e.g., methylphenidate)
Pain flare	Steroids	Pain medications; anti-inflammatory medications; corticosteroids
Dermatitis		Steroid cream; Aquaphor ± lidocaine
Mucositis/esophagitis		Sucralfate; Magic mouthwash (Maalox, Benadryl, lidocaine); opioid pain medications
Nausea	Ondansetron; lorazepam; steroids	Ondansetron; lorazepam; prochlorperazine
Pneumonitis		Prednisone
Acid reflux		Proton pump inhibitors; H2 blockers
Loose stools/diarrhea		Loperamide; Lomotil (diphenoxylate/atropine)
Bladder irritation		NSAIDs
Rectal irritation		Sucralfate enemas

NSAIDs, non-steroidal anti-inflammatory drugs.

of the malignancy. Episodes of bleeding can be categorized in three ways: acute catastrophic bleeding, episodic major bleeding, and low-volume oozing. Visible bleeding may manifest as bruising, petechiae, epistaxis, hemoptysis, hematemesis, hematochezia, hematuria, vaginal bleeding, and melena. RT can be used to reduce or control hemoptysis, hematuria, vaginal bleeding, and bleeding from the GI tract (e.g., melena, hematemesis, and hematochezia). Radiation therapy can provide hemostasis within one or two days of the first dose. Overall goals of care, life expectancy, and quality of life considerations should continue to guide therapeutic interventions. Patients must be hemodynamically stable to safely be transported to and from radiotherapy departments for treatment.^{19–22}

Growing tumor masses can also result in symptomatic blockages that obstruct the airways or intestines and cause dyspnea, dysphagia, constipation, and pain among other troublesome symptoms. Radiation therapy can effectively relieve the mass effect by shrinking tumor away from the lumens in the bronchial tree or GI tract, although long-term disease control is rarely achieved.^{23,24}

In the setting of bleeding or obstruction at most any location, hypofractionated palliative schedules may be useful. For instance, long-established hypofractionated regimens have been used in bleeding or obstructing pelvic malignancies with 10 Gy delivered to the whole pelvis in one fraction and repeated monthly for up to three fractions.²⁵ Among patients with gynecological primaries, symptom responses were noted ranging from 45% palliation of bleeding with a single fraction to 100% with three fractions in the patients.²⁶ Among patients with advanced bladder cancer, a three-fraction treatment (21 Gy for three fractions) achieved palliation of symptoms with similar efficacy as compared with longer treatment schedules.²⁷ In the head and neck region, the “quad shot” regimen (3.7 Gy given twice a day for two consecutive days and repeated monthly up to three times) has resulted in effective palliation of symptoms up to 53% of individuals with advanced head and neck malignancies.²⁸

Leptomeningeal carcinomatosis due to solid tumors carries a grave prognosis. Local radiation therapy to a particularly symptomatic area may be indicated, but widespread craniospinal irradiation is associated with significant toxicities and is rarely indicated.²⁹

Tip 9: If symptoms persist and the surrounding tissues have not reached their cumulative dose lifetime limits, palliative radiation treatment can be repeated to the same region.

Up to 55% of patients will have recurrent pain at the site of prior radiation for bone metastasis or recurrent tumor in a previously irradiated site. Whenever palliative radiation is considered, the benefit and time course of palliative effect must be weighed against the risks of retreatment and the length of remaining life. For most indications, the palliative effect is seen a few days to a few weeks after delivery, although it can begin as quickly as 24–48 hours for indications such as bleeding. Concerns about normal tissue toxicity must be balanced against the likelihood of an adverse effect during a patient's remaining life. Certain regimens can be repeated in most cases; for example, 8 Gy can be given twice to any site in the body without reported adverse events.^{30,31} With other regimens, cumulative dose, interval between radiation

courses, and remaining life expectancy must be considered. Among the most important variables is the cumulative dose to the spinal cord. Advanced technologies may be extremely helpful in the treatment of patients who have previously received full dose to the spinal cord for prior definitive courses of radiation.

Tip 10: Complex technologies are rarely indicated in palliative radiation oncology, outside of stereotactic radiation for brain, spine, or previously irradiated areas.

Rarely are complex technologies such as proton therapy, stereotactic radiosurgery, or intensity-modulated radiation therapy needed in the palliative radiotherapy setting. Commonly encountered exceptions include patients with a limited number of brain metastases, those with spinal cord compression or epidural disease who have previously received radiation treatment to the spinal cord, or those who have previously received radiation treatment to an area that reached the lifetime limits of what the regional tissues can safely tolerate. In these settings, stereotactic brain or spine radiosurgery may be appropriate.²⁶ In general, palliative radiation therapy should be as convenient as possible, use no more resources than necessary, and be no longer than necessary to achieve the desired palliative effect.³²

Conclusion

Radiation therapy is a highly effective, noninvasive intervention that aims to halt progression or even eradicate tumor in cancer patients. When used appropriately in the palliative setting, RT can lead to substantial improvements in the function and quality of life for patients suffering from symptoms of advanced cancer. As the fields of PC and radiation oncology continue to grow in their partnership with each other, it is important that PC clinicians understand when palliative radiation therapy can both help our patients and also appropriately recognize its limitations and burdens. Developing a working understanding of the expected time course for RT's onset of efficacy and treatment and typical resolution of toxicities is critical to provide high-quality symptom management for cancer patients.

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