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Palliative Radiotherapy for Oncologic Emergencies in the setting of COVID-19: Approaches to Balancing Risks and Benefits

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Abstract:	

Palliative Radiotherapy for Oncologic Emergencies in the setting of COVID-19: Approaches to Balancing Risks and Benefits

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Introduction

Radiotherapy (RT) is critical for the treatment of oncologic emergencies, including neurologic injury from cord compression or brain metastases, airway compromise and bleeding (1–4). Palliative RT for patients with limited functional status is crucial for providing effective care and limiting morbidity from disease progression. The current COVID-19 pandemic has heightened our awareness of resource constraints, prompting institutions to create guidelines to delay treatments whenever possible and prioritize cases that are clinically urgent (5–8).

Recent data from China and Italy have demonstrated that cancer patients have a higher risk of contracting the virus, as well as a higher case-fatality rate (9–12). It is therefore imperative to be judicious in the use of RT and to consider shorter courses of palliative RT for oncologic emergencies. Existing recommendations, such as those from the Choosing Wisely campaign, support the use of short-course RT as a component of value-based care (13). However, utilization in the United States has been limited, and therefore less equipped to optimally manage patients considered for palliative radiation (8,14,15). Here, we aim to provide a more detailed departmental approach to triaging and shortening radiation therapy for oncologic emergencies at a major comprehensive cancer center in New York City, an epicenter of COVID-19 in the United States.

Methods

Radiation oncologists with expertise in the management of metastatic disease and inpatient oncologic emergencies at a high-volume comprehensive cancer center in the initial epicenter of the current COVID-19 outbreak emergently convened to discuss best practices at this time. We reviewed high-impact evidence, prior systematic reviews, and national guidelines

to compile recommended practices for the treatment of common oncologic emergencies. While this was not a comprehensive systematic review of the literature, we discussed our individual institutional best practices in the unique circumstances of this global pandemic. Specific attention was given to balancing the risk of infection with SARS-CoV-2 and the potential morbidity of delaying treatment.

Suggested Considerations

Clinical Evaluation

In response to departmental guidance to limit clinical exposure and maximize single-use personal protective equipment, the majority of patient assessments, including history of present illness, performance status, current symptoms and imaging are evaluated virtually via telemedicine. Prior studies have shown the feasibility and efficacy of assessing symptoms and performance status through electronic and telemedicine platforms (16–18). When in-person physical examination is crucial to treatment decision-making, including neurologic evaluation and pain assessments, patient encounters are limited to a single radiation oncologist or an advanced practice provider.

We recommend discussion of the patient's overall prognosis and goals of care with the patient, the primary medical oncologist, and supportive care specialists prior to determining a radiation plan, with validated prognostic models at provider preference (19–21). For patients with an estimated life expectancy of days to weeks, best supportive care with medical therapies alone is encouraged.

For subsequent on-treatment visits and follow-ups, our institution has implemented telemedicine visits as default to reduce the risk of exposure. For patients needing urgent

supportive care while receiving RT, a nursing visit and/or physician visit can be arranged with the designated rotating radiation oncology healthcare providers of the day. When face-to-face evaluation is clinically indicated, we recommend that all patients, caregivers and providers adhere to institutional policies and CDC recommendations on social-distancing, handwashing, assessment of personal risk factors and using appropriate personal protective equipment (PPE) to mitigate risk of exposure of patients and staff (22).

Patient Triage

In the setting of the COVID-19 pandemic, our department developed and implemented a three-tiered system to identify clinically urgent cases, in which delaying treatment would result in compromised outcomes or serious morbidity. For patients with metastatic cancer requiring palliative RT, patients with oncologic emergencies are assigned with the Tier 1 designation (Table 1). This includes patients with cord compression, symptomatic brain metastases requiring whole brain radiotherapy, life-threatening tumor bleeding and malignant airway obstruction (Table 2). Tier 2 includes patients with symptomatic disease exclusionary of oncologic emergencies which RT is the standard of care, and patients with asymptomatic disease which RT is recommended to prevent imminent functional deficits. Tier 3 includes patients with symptomatic or asymptomatic disease which RT is one of the effective treatment options.

Need for urgent RT is guided by a simple triage flowsheet which includes active symptoms that can be addressed with RT, prognosis, goals of care, and Tier 1 designation (Fig 1). The following management recommendations below pertain to patients with oncologic emergencies, which are departmentally categorized with Tier 1 designation.

Management of Oncologic Emergencies

Brain Metastases

The management of brain metastases has been an evolving clinical paradigm for which patient prognosis, histology, age, competing risks and neurologic symptoms must be considered. Patients with favorable prognosis and appropriate for stereotactic radiosurgery (SRS), we continue to provide SRS for patients an treat all or the dominant lesion(s) that is most likely to cause morbidity, in order to delay or potentially avoid whole brain radiation. However, for patients with urgent indications, such as progressive neurologic symptom from multiple brain metastases or leptomeningeal disease, whole brain radiation is often indicated. For these patients, particularly those who are hospitalized, ten-fraction treatment increases the risks for patients and staff exposure to SARS-COV-2. Thus, while several dose options are available, though we favor 20 Gy in 5 fractions, which has been safely used in multiple studies (23,24). Standard fractionation (30 Gy in 10 fractions) with memantine could be considered for patients in whom longer term survival is expected, in order limit neurocognitive complications (25). In patients with limited prognosis, the QUARTZ study demonstrated similar rates of overall survival and quality of life with steroids and best supportive care alone as compared to whole brain radiation therapy (26), and therefore observation is likely preferred to limit unnecessary exposure to SARS-COV-2.

Spinal Cord Compression

The management of patients with spinal cord compression requires multidisciplinary discussion especially with neurosurgery, and evaluation of several factors including degree of spinal cord compression and presence or absence of spinal instability. We utilized the NOMS

paradigm to facilitate selection of optimal treatment (27). If radiation is indicated, over 30 studies have shown equivalent functional outcomes of single-fraction radiation treatment instead of multifraction radiation treatment (4,28), with recent meta-analysis of three randomized clinical trials demonstrating preserved motor response with no clinical difference between single-fraction radiation treatment (8 Gy x 1 fraction) and multifraction treatment at a two month timepoint (29–33). While there is conflicting evidence regarding the role of single-fraction radiotherapy for spinal cord compression, particularly given that the SCORAD III study did not meet its prespecified non-inferiority endpoints even though the absolute difference of ambulatory status at 8 weeks was small (69.3% in the single-fraction group vs. 72.7% in the multifraction group). However, 8 Gy x 1 provides acceptable rates of palliation and allows for safe retreatment with either conventionally fractionated or SBRT approaches if warranted. In the setting of COVID-19 pandemic, the risk for nosocomial infection from patient daily exposure and prolonged hospitalizations, and the potential exposure to staff and other patients must be balanced against the potential benefit of multifractionated treatment.

Tumor Bleeding

Uncontrolled tumor bleeding is a life-threatening condition that can be effectively relieved with palliative radiation. RTOG 8502 used 10 Gy x 1 to palliate advanced pelvic malignancies, but due to frequent late gastrointestinal toxicities (grade 3-4 late toxicities in 49% of patients), it was closed prematurely and replaced with 3.7 Gy x 4 fractions twice daily, repeated at three week intervals for a total of 3 courses (34). This “Quad Shot” regimen has also been effective in head and neck malignancies (35). Due to potential increased risk of nosocomial SARS-COV2 exposure, our center has recommended limiting treatment of COVID-confirmed or suspicious cases to a single treatment machine at the end of the day to facilitate disinfection and

risk reduction procedures. As such, it may be logistically preferable to avoid twice-daily treatments and instead, favor 4 Gy x 5 as an alternative.

SVC Syndrome/ Airway Obstruction

Superior vena cava (SVC) syndrome can present with clinically severe airway, neurologic or hemodynamic compromise. Radiation can be effective in relieving hemoptysis but has limited utility for relieving dyspnea and cough. Sundstrom et. al reported excellent outcomes with 8.5 Gy x 2 fractions given a week apart for patients with central airway emergencies, although our institutional practice favors 4 Gy x 5 daily fractions (36,37). While 8.5 Gy x 2 one week apart may offer logistical advantages, particularly for inpatients who may be discharged after the first fraction, we felt that this must be balanced with concerns for spinal cord toxicity, especially in patients with prior radiation treatments and those who may need future treatments.

For patients with airway obstruction from a lung or mediastinal tumor, there is no data at this time on the effect of RT exposure to lung in patients with SARS-COV-2 infection. Given the danger of acute respiratory distress syndrome, the possible need for mechanical ventilation and the potential of structural and obstructive lung disease, a multidisciplinary discussion is recommended for patients requiring RT palliation for malignant airway obstruction.

Painful Bone Metastases

While not an oncologic emergency, patients with painful bone metastases frequently required radiation oncology consultation for symptom management. Per NCCN guidelines for Supportive Care, many medical strategies can also be considered for the management of bone metastases (38). If patients have an impending fracture, we recommend a multidisciplinary discussion with

orthopedic surgery and/or interventional radiology to decide on mechanical stabilization and potential role for radiation therapy. The risk of prolonged hospitalization from pathologic fracture may expose the patient to potential hospital acquired infections including SARS-COV-2, and thus planned surgical intervention should be considered for patients with impending fracture. Otherwise, radiation should be considered if it is anticipated that localized pain from a metastasis would result in potential admission for pain crisis. If radiation is indicated, several studies and the Choosing Wisely campaign support 8 Gy x 1 fraction treatment for uncomplicated bone metastases (13,39,40). Additionally, for patients with less urgent symptoms who are able to wait for complex treatment planning, single-fraction stereotactic body radiotherapy (SBRT) may also be an appropriate way to provide faster and more durable palliation still in a single treatment session, based on randomized evidence (41).

Conclusion

Palliative radiation therapy plays a critical role in the prevention of serious morbidity for patients with metastatic cancer in the setting of oncologic emergencies, even in the midst of the current COVID-19 pandemic. For patients with metastatic cancer, prognosis must first be clearly estimated and communicated with the patient, followed by a goals of care conversation. Data from China suggests that 40% of patients with active cancer diagnoses required either intubation or died, although the authors report that they are only presenting a small sample size, and acknowledge the presence of other comorbidities such as age, and smoking history (9). Patients who have prognostic awareness are less likely to choose and therefore receive aggressive oncologic treatments in the last month of life (43). As such, these patients may opt for medical supportive care. For patients suitable and requiring palliative RT, abbreviated courses of

treatment is of particular importance to reduce the risk of viral exposure to all patients and staff, without compromising functional outcomes. Furthermore, as staffing and clinical treatment capacity remains at risk for fluctuation, abbreviated RT courses better allow for treatment completion without delay. Fortunately, there is high-level evidence supporting these courses for oncologic emergencies to maximize patient benefit and resource allocation. As such, hypofractionated regimens for palliative radiation are preferred to reduce risk and maximize benefit for both individuals and the population during the COVID-19 pandemic.

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Table 1. Assignment of radiation tiers based on treatment indication	
Tier 1 (highest priority)	Patients with oncologic emergencies (neurologic symptoms, tumor bleeding, airway compromise, etc.) requiring palliative RT.
Tier 2	Patients with symptomatic disease exclusionary of oncologic emergencies which RT is the standard of care. Patients with asymptomatic disease which RT is recommended to prevent imminent functional deficit.
Tier 3 (lowest priority)	Patients with symptomatic or asymptomatic disease which RT is one of the effective treatment options.

Table 2. Hypofractionated Palliative Regimens		
<u>Indication</u>	**<u>Treatment</u>**	**<u>References</u>**
Brain Mets, for whom whole brain is indicated	4Gy x 5 daily fractions Steroids alone	**Rades, 2008 (24):** 20Gy/5fx well tolerated. **QUARTZ (26):** Steroids alone for patients with poor performance status.
Cord Compression	8Gy x 1 daily fraction	**Maranzano, SCORAD III, ICORG 05-03** (30–32,44)**:** Similar impact on OS and post-RT motor functions. Retreatment is safe.
Tumor bleeding	3.7 Gy x 4 twice daily fractions 4Gy x 5 daily fractions	**RTOG 8502, RTOG 7905** (34,35,45)**:** "Quad Shot" is safe and effective. **Avoid BID fractionation for COVID+ patients.*
SVC syndrome *Airway Obstruction*	8.5 Gy x 2 weekly fractions 4Gy x 5 daily fractions	**Sundstrom**(36,37): Equivalent symptom relief and no diff in survival compared to standard fractionation. *Exercise caution with COVID+ patients*
Bone metastases	8Gy x 1 daily fraction	**RTOG 9714** (13,38–40)**:** 8Gyx1 similar efficacy in pain relief with less acute toxicity; Retreatment is safe.

Figures

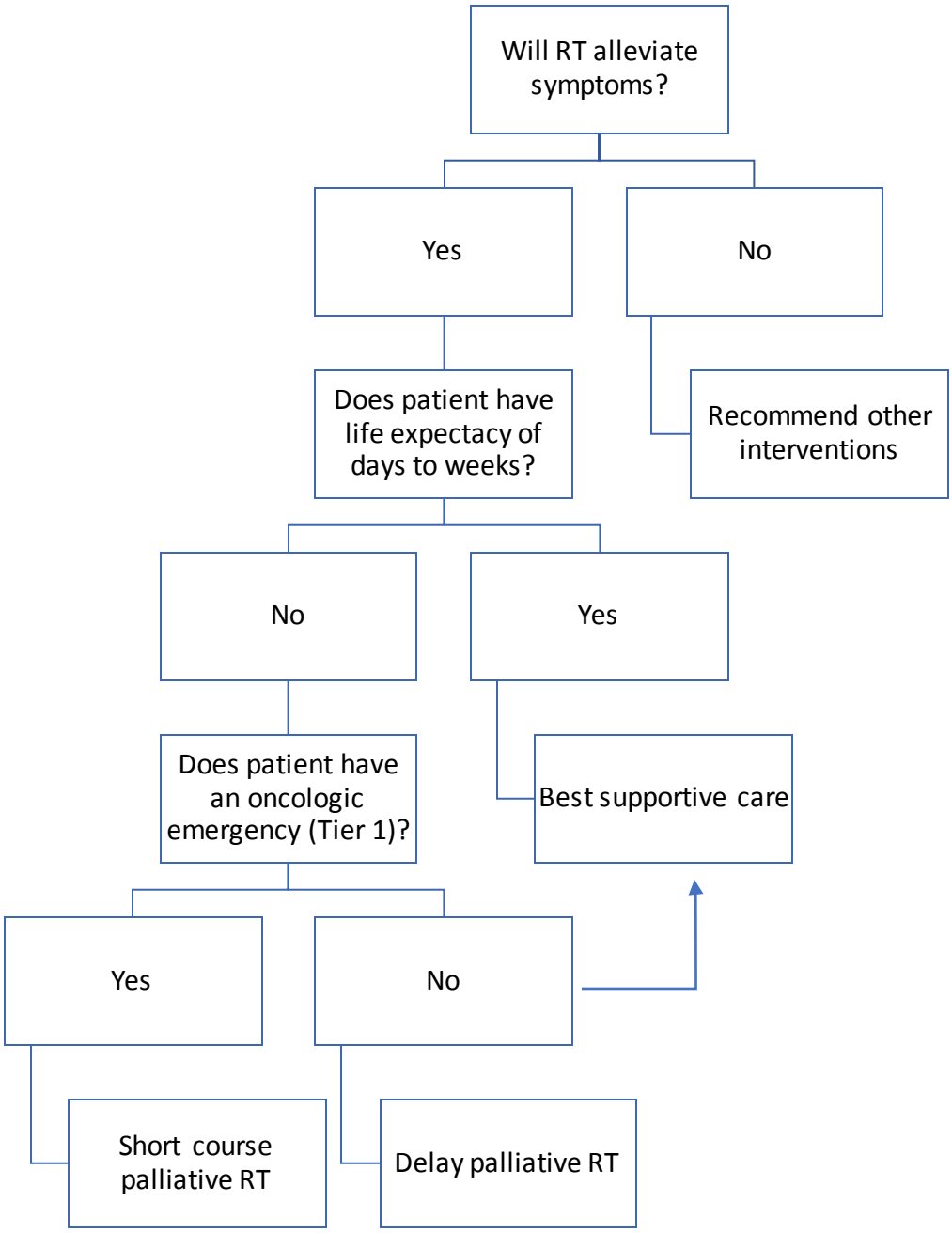

Figure 1. Triaging a patient with an oncologic emergency

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