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COMPREHENSIVE CARE FOR THE CHILD OR ADOLESCENT DIAGNOSED WITH A CHILDHOOD MALIGNANCY REQUIRING PALLIATIVE RADIATION THERAPY: A REVIEW

Description: Because of the low incidence of pediatric malignancies, no consensus has been reached on the best practices for the delivery of pediatric palliative radiation therapy. As a result, current practice is extrapolated from adult literature and single institutional series. In addition to the technologies for palliation of pediatric patients are essential components of communication for meeting medical and psychosocial needs of the families and patients; these needs are not always addressed. A multidisciplinary approach with appropriate care and communication addressing patient questions and needs provides meaning and improved quality of life during this phase of treatment.

Learning Objectives:

After completing this activity, participants will be able to:

1. Understand pediatric palliative radiation therapy treatment for the more common sites and disease-specific scenarios.
2. Adopt important considerations when caring for and treating children and families diagnosed with advanced malignancies that require palliative radiation therapy.

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Comprehensive Care For The Child Or Adolescent Diagnosed With A Childhood Malignancy Requiring Palliative Radiation Therapy: A Review

Tamara Vern-Gross, DO, FAAP

In the United States, an estimated 10 270 children ages birth to 14 years will be diagnosed with cancer in 2017, and 1190 children will die of cancer, the second leading cause of death for children following accidents.¹ Five-year survival has improved for all childhood cancers from 63% in the mid-1970s to 83% today.² The incidences of major childhood malignancies are shown in **Figure 1A-B**. Of these children, approximately 30% to

50%^{3,4} will require radiation therapy (RT) sometime during their disease course. And of children receiving RT, approximately 11% to 18%⁵⁻⁸ will require palliative radiation therapy (RT) to prevent or alleviate symptoms in the setting of incurable disease to optimize their quality of life (QOL).

In contrast to adults diagnosed with a malignancy, the need for palliative RT is exceptionally low; most likely underestimated. Reporting differs among institutions, highlighting the variability in the definition of “palliative intent,” especially within the pediatric population (**Table 1**). Radiation therapy has been initiated in the setting of “preventive palliation,” where progression of uncontrolled disease could negatively impact QOL. For instance, children diagnosed with diffuse infiltrating pontine glioma (DIPG) are treated to definitive doses with the goal of achieving symptomatic relief and optimizing disease control, with cure unlikely.

Adult randomized controlled trials have demonstrated the efficacy of palliative RT in the setting of progressive primary or metastatic disease.⁹⁻¹¹

Because of challenges in obtaining abundant quality-controlled data, there is no consensus in the standard of care for palliative RT for pediatric and adolescent patient malignancies. Current pediatric practice is extrapolated from adult palliative literature, but controversy persists about whether current adult regimens are appropriate.

Palliative Radiation Therapy: Differences Between Pediatric and Adult Patients

Pediatric malignancies have distinctive presenting symptoms, and diverse prognostic implications, treatment options, and subsequent responses. Compared with adults, children and adolescents are more likely to present with oncologic emergencies such as spinal cord compression (SCC) and superior vena cava syndrome (SVCS) earlier in the disease process at the time of diagnosis.^{12,13} For example, in a child, SCC or a mediastinal mass is frequently a sign of a new primary malignancy. It has been documented that sarcomas account for approximately 43% to 65% of SCC cases in children.^{13,14} Adults develop

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2. Vern-Gross TZ, Lam CG, Graff Z, et al. Patterns of end-of-life care in children with advanced solid tumor malignancies enrolled on a palliative care service. J Pain and Symptom Manage. 2015;50(3):305-312.

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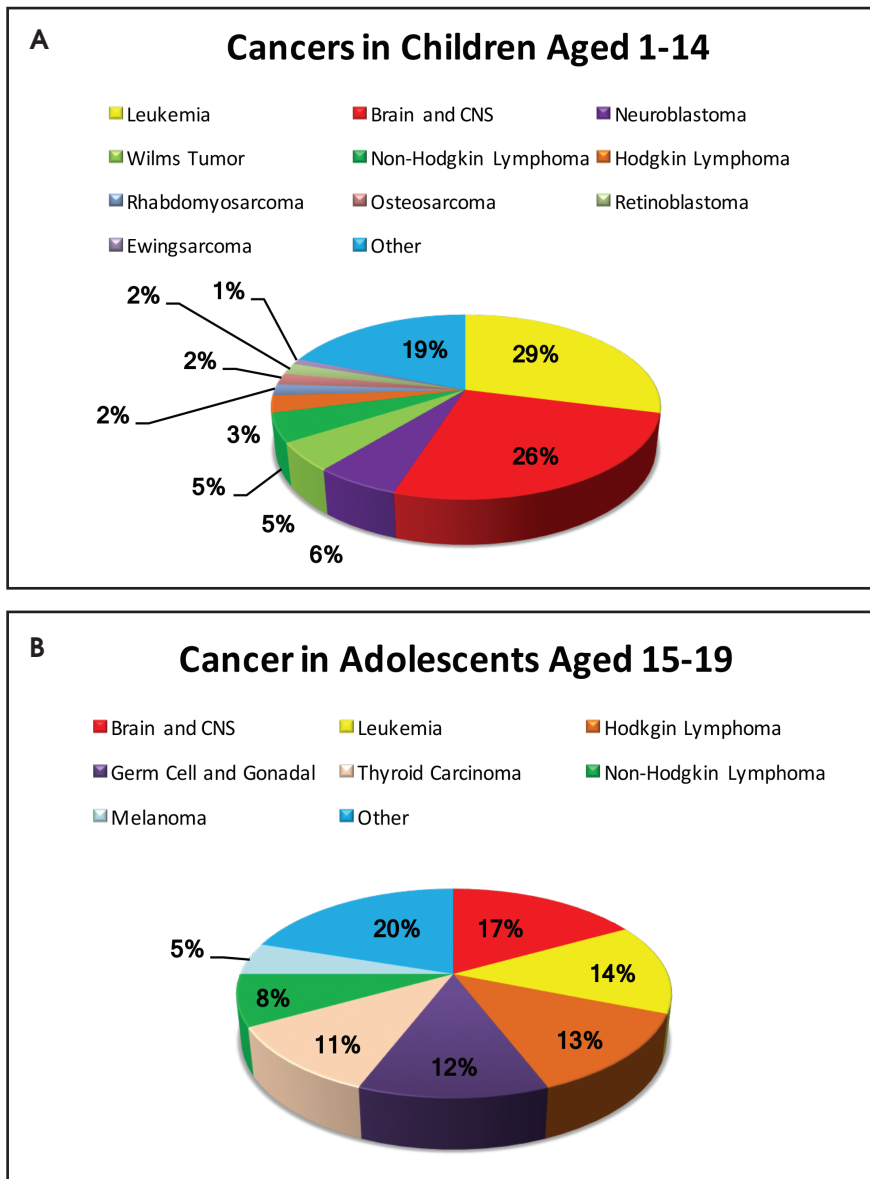


FIGURE 1. (A and B) The incidence of major childhood malignancies.¹

SCC more commonly as metastatic lesions from primary lung, prostate, and breast cancer.^{15,16} In the setting of SCC and paraplegia, children tend to have a more “forgiving” central nervous system (CNS) and are more likely to recover and regain ambulation with initiation of treatment compared with adults.¹⁷⁻²¹

Palliative RT is often not the first-line therapy in children and adolescents at the time of diagnosis, especially in those presenting with symptomatic spinal or mediastinal disease, as these tumors tend to be

more chemo-sensitive compared to adult malignancies. Unlike with adults, the utilization of RT is focused more on relieving life-threatening problems, rather than palliation of unwanted symptoms.

Comprehensive Management for Children Diagnosed with Advanced Malignancies

Children with high-risk cancer and their families endure significant physical symptoms, psychosocial issues, and spiritual challenges, which impact QOL

detrimentally.²²⁻²⁵ Because the “hope for cure” often remains a priority, children may undergo aggressive cancer-directed therapy, overlooking the comforts and supports necessary throughout a child’s illness.²⁶ comprehensive pediatric oncology teams collaborate with the child/family to execute high-quality care and support from initial diagnosis, throughout palliation of symptoms, and beyond the child’s death.

A personalized and often creative approach is required to optimize care in managing these patients, incorporating the interdisciplinary team so patient/family needs and goals of care are appropriately met.²⁷⁻²⁹ Pediatric palliative care (PPC) is a specialty that has gained accolades by providing an evolving backbone of support for children/families with life-threatening or life-limiting illness. It embodies total care through management of pain, complex symptoms, psychosocial and spiritual needs, coordination of care, medical decisions, and interaction with an interdisciplinary team.^{26,30-34} These specialists work closely with the patient/family to enhance function, and improve QOL.^{30,35,37} The World Health Organization (WHO) promotes pediatric palliative care (PPC) as an approach dedicated to “active total care of the child’s body, mind, and spirit, and support for the family” (Table 2).

Clinical Indications for Pediatric Palliative Radiation Therapy

Palliative RT is more valuable in the setting of recurrence or metastatic disease progression, after multiple unsuccessful systemic therapies, than at initial diagnosis. The indications for palliative RT are similar for both pediatric and adult patients, depending on location, involvement of surrounding structures, overall prognosis, and ultimately patient/family goals of care (Table 3). Because treatment is guided to minimize acute and late toxicities, systemic therapy continues to be the optimal first-line therapy, especially in

Table 1. Definition of Patients Eligible for Pediatric Palliative Radiation Therapy

Series	Definition
Rahn et al 2015	Patients treated with palliative radiation therapy are those thought to have incurable disease at the time of treatment.
Rao AD et al 2016	Treatment intent with palliative radiation therapy is defined as having the goal to improve symptoms or to prevent impending symptoms, such as in the case of intracranial or spine involvement.
Mak et al 2017	Children diagnosed with incurable advanced cancer. Patients enrolled on protocols that called for irradiation of metastases present at diagnosis are not included within this definition, as treatment intent was not palliative.
Varma S et al 2017	Radiation therapy is considered palliative in children with advanced cancer who are ineligible for or whose disease had persisted/progressed through standard-of-care first-line therapy, in whom the goal of RT is amelioration or prevention of a specific symptom. In most cases, patients have undergone multiple unsuccessful lines of systemic, cure-directed therapy.

Adapted from references 5–7, and 147

Table 2. The WHO Definition of Palliative Care

- Provides relief from pain and other distressing symptoms
- Affirms life and regards dying as a normal process
- Intends neither to hasten or postpone death
- Integrates the psychological and spiritual aspects of patient care
- Offers a support system to help patients live as actively as possible until death
- Offers a support system to help the family cope during the patient's illness and in their own bereavement
- Uses a team approach to address the needs of patients and their families, including bereavement counseling
- Enhances quality of life, and may also positively influence the course of illness
- Is applicable early in the course of illness, in conjunction with other therapies that are intended

Adapted from World Health Organization 2018

Table 3. Indications for Palliative Radiation Therapy

- Bone and soft tissue metastases secondary to impending or pathologic fracture, soft tissue/nerve root compression or infiltration
- Neurologic dysfunction, including cranial nerve palsies, secondary to brain or leptomeningeal disease
- Spinal cord compression
- Airway obstruction resulting in dyspnea
- Obstructions of gastrointestinal, and genitourinary tracts
- Bleeding secondary to involvement of genitourinary, gastrointestinal, or pulmonary sites
- Superior vena cava syndrome or superior mediastinal syndrome
- Hepatic metastases causing pain from capsular stretch
- Esophageal or gastric outlet obstruction

Adapted from Vern-Gross 2013

children with chemo-sensitive spinal cord tumors (eg, neuroblastoma, Ewing sarcoma, and lymphoma) in the absence of neurologic deficits.³⁸⁻⁴³ When palliative RT is initiated, treatment focuses on reducing acute toxicities (eg, radiation dermatitis, esophagitis) and anesthesia requirements by decreasing RT dose and treatment days. Despite attempts to accurately prognosticate, children may outlive initial survival predictions, underscoring the importance of always considering the implications of long-term toxicities.⁴⁴ Although most radiotherapeutic techniques are extrapolated from the adult literature, several pediatric series have reported effective outcomes of palliative RT for various pediatric indications (Table 4).

Importance of biopsy prior to emergency treatment

On a new patient presentation, it is critical to obtain a tissue diagnosis to identify the primary disease and to rule out a benign or malignant process, which may require a specific treatment course. Patients may not require palliative RT, but rather a multidisciplinary approach that guides definitive treatment. If a tissue diagnosis cannot be established secondary to anesthesia risk, absence of marrow involvement,

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Table 4. Patterns of Pediatric Palliative Radiation Therapy

Series	No. of Patients	Tumors Treated	Most Common Symptom at Presentation	Radiation Dose	Treatment Outcomes	Survival Outcomes
Bertsch et al ⁸ 1998	N = 104 115 sites	CNS-PNET gliomas (20%) Neuroblastoma (20%) Other (sarcoma, lymphoma, Wilim's, NHL, leukemia, nasopharynx, retinoblastoma, craniopharyngioma, germinoma)	Group I: SCC Group II: respiratory compromise Group III: infra-diaphragmatic distress Group IV: intracranial signs Group V: pain	Solid tumors: 1.5-4 Gy, fx to a total dose of 3-55.8 Gy Leukemia/lymphoma 1.4-4 Gy fx to a total dose of 2.2-22.5 Gy	Overall response rate: 80% stabilization or improvement Group I: 85% response rate with (55%) improvement or stabilization (30%) Group III: 66% response rate; Group IV: 63% response rate; 19% stabilization; Group V: 93% overall response	N/A
Koontz et al ⁵⁶ 2006	N = 21 63 sites	Ewing sarcoma	Group I: soft tissue Lung (N = 8) Brain (N = 5) Group II: bone Spine (N = 11) Pelvis/hip (N = 10) Lower extremity (N = 7)	Median RT dose 30 Gy (4.5 Gy-68.5 Gy)	Overall response rate: (84%) Median overall treatment response: 81 days (range, 0-1760 days) Group I: soft tissue CR (44%), PR (21%), NR (11%) Group II: bone CR (11%), PR (8%), NR (5%)	Median survival 1 year (range, 17 days to 6.8 years)
Rahn et al ⁷ 2015	N = 45 76 sites	Ewing sarcoma (20%) Osteosarcoma (16%) Rhabdomyosarcoma (13%) Neuroblastoma (13%) Brain/CNS (11%) Leukemia/lymphoma (7%) Other (20%)	Bone pain (49%) Neurologic (28%) Respiratory compromise (13%) Painful liver metastases (5%) Bleeding or painful abdomen (5%)	Bone tumors or abdominal masses: 2.5 Gy x 14 fx (35 Gy) 3 Gy x 10 fx (30 Gy) 4 Gy x 5 fx (20 Gy), 1 Gy x 8 fx (8 Gy) Leukemia: 1.5-2 Gy x 10 fx (15-20 Gy) Non-bulky lung metastases: 10 Gy x 5 fx (50 Gy), 12 Gy x 4 fx (48 Gy) Brain metastases 16-20 Gy x 1 fraction Usually treat with SRS	Overall response rate (72%) Bone pain (80%) Neurologic symptoms (58%) Dyspnea or chest pain (55%) Liver pain or ascites (100%) Bleeding (50%) No grade > 3 RTOG toxicities 7% did not complete treatment course	Median survival was 6.5 months 23% alive at last visit
Reo et al ⁶ 2016	N = 365* 427 sites	Neuroblastoma (20%) Leukemia/Lymphoma (15%) Rhabdomyosarcoma (14%) Brain/CNS (14%) Ewing sarcoma (8%) Osteosarcoma (12%) Other non-CNS (8%)	Pain (57%) Intracranial (16%) Spinal cord compression (10%) Respiratory compromise (9%) Abdominal distension (3%) Postop-spine (2%), Bleeding (1%) Bowel obstruction (1%), Other (1%)	N/A	Treatment was delivered to metastatic disease in 54%	N/A
Varma et al ⁵ 2017	N = 50 83 sites	Neuroblastoma (23%) Rhabdomyosarcoma (18%) Ewing Sarcoma (10%) Leukemia/Lymphoma (9.6%) Osteosarcoma (4.8%) Brain/CNS (3.6%), Other (26.4%)	Progression of oligometastatic disease (58%), Pain (13%) Neurologic (21%) Respiratory Compromise (10%) Other (10%)	Median RT Dose 20 Gy (1.5-59.74 Gy) Median # of fractions 6 fx (1-32)	Overall response rate (77%) asymptomatic for pain at 12 months (>80%) neurologic symptoms success (71%) asymptomatic (100%) dyspnea (62%), other (50%)	Median survival was 124 days (1 day-141 days) 74% had hospice care at last follow-up 10% did not complete treatment course
Mak et al ¹⁴⁷ 2017	N = 46 76 sites	Neuroblastoma (20%) Rhabdomyosarcoma (7%) Ewing sarcoma (11%) Leukemia/lymphoma (9%) Osteosarcoma (7%) Brain/CNS (37%) Other (11%)	Progression of oligometastatic disease (39%), Pain (25%) Neurologic (43%), Spinal cord compression (1%), Leptomeningeal disease (8%), Facial mass (5%), Liver or biliary obstruction (3%), Other (1%)	Median RT dose 30 Gy (2.5 Gy-54) Median dose/fraction 2.5 Gy (1.5-4.0 Gy) Median # of fractions 12 (1-30)	During RT: 91% improved or stable 0-3 months: 73% improved or stable 3-6 months: 58% improved or stable 6-12 months: 43% improved or stable 8% did not complete treatment course	Median survival was 4.2 months 19% had hospice care at last follow-up

*Six international institutions are involved in the research consortium. Values represent the average from all institutions. Key: CNS = central nervous system, PNET = primitive neuroectodermal tumor, SCC = spinal cord compression, Gy = Gray, fx = fraction, N/A = not applicable, RT = radiation therapy, CR = complete response, PR = partial response, NR = no response, SRS = stereotactic radiosurgery, RTOG = Radiation Therapy Oncology Group, NHL = non-Hodgkin lymphoma

or lack of peripheral lymphadenopathy, systemic chemotherapy should be considered as initial therapy to stabilize the mediastinal mass and prevent further respiratory compromise.⁴⁵ While initiation of chemotherapy often is concordant with the primary malignancy, administering radiation prior to obtaining a biopsy may compromise accurate identification of the primary disease.^{45,46}

Superior Vena Cava Syndrome and Superior Mediastinal Syndrome

Children and adolescents diagnosed with mediastinal tumors are at risk for developing SVCS and superior mediastinal syndrome (SMS) (12%), as a result of major vessel or airway compromise.⁴⁶⁻⁴⁹ Acute lymphoblastic leukemia and non-Hodgkin lymphoma (NHL) are the most common causes of SVCS in children, whereas lung cancer is the chief cause in adults.⁵⁰ With a primary diagnosis of leukemia or lymphoma, which are curable and sensitive to chemotherapy, palliative RT for SVCS or SMS is often not the first line of treatment. Palliative RT is indicated for dyspnea secondary to a malignant process in the chest or mediastinum resulting in SVCS or SMS, usually in the setting of known recurrent or relapsed disease that is otherwise resistant to systemic chemotherapy.¹² RT is delivered in either standard fractionation or hypofractionation using a 3-dimensional conformal radiation therapy (3DCRT) technique. Because treatments are often based on adult literature, maintaining perspective and acknowledging the differences between child and adult is essential, especially when attempting to achieve disease control. Minimizing treatment times, reducing fractions, and using anesthesia are important considerations to decrease treatment-related toxicity.

Bone and Soft-tissue Metastases

Bone and soft-tissue metastases are one of the more common indications for palliative RT in pediatrics to reduce

discomfort secondary to infiltrative lesions, tumor obstruction, and surrounding structures stretch.^{51,52} Most pediatric radiation oncologists extrapolate from adult landmark studies such as the Dutch Bone Metastasis Study, the Bone Pain Trial Working Party Study, and most recently the American Society for Radiation Oncology (ASTRO) guidelines.^{9,53-55} Although the benefits of palliative RT have been observed, a standardized fractionation scheme has not been established because of the variable tumor histologies and treatment responses.^{5,44,55-58} One study reported characteristics of unsuccessfully completed palliative RT courses on clinical outcomes and patterns of care in children diagnosed with advanced cancer.⁵ There was no difference in success rates of RT courses prescribed in ≤ 10 fractions (84%) compared with >10 fractions (94%), $P = 0.43$; the most unsuccessful median total dose delivered was 800 cGy. For children who are earlier in their disease trajectory, a short course of palliative RT can provide symptomatic relief without significant burden on the child or family. In the setting of widely disseminated or rapidly progressive disease, where life expectancy is unpredictable, the potential benefit of palliative RT may be quickly lost. Single fraction treatments of 800 cGy x 1 fraction to address an intractable focal symptom should still be considered in select situations. When anesthesia is required to deliver therapy, single-fraction courses are especially favorable to optimize comfort and to ensure appropriate immobilization during treatment. In terms of radiation treatment, fractionation schemes of 1-5 fractions are preferred to optimize QOL, especially in the setting of anesthesia requirements. Dose responses of ≥ 15 Gy and ≥ 20 Gy have been more effective in treating soft-tissue and bone metastases, respectively.^{44,58}

Traditionally, bone and soft-tissue metastases have been treated using 3D

conformal RT. More advanced technologies have been incorporated into the management of metastatic lesions, including intensity-modulated radiation therapy (IMRT), stereotactic body radiation therapy (SBRT), stereotactic radiosurgery (SRS), radioisotopes, and radiofrequency ablation (RFA).⁵⁹⁻⁶³ SBRT has been used for metastatic tumors in the palliative, curative settings and re-irradiation settings. A median dose of 40 Gy in 5 fractions (range: 16 to 50 Gy in 1 to 10 fractions) provided successful outcomes for disease control and relief of painful metastatic and recurrent osteosarcoma lesions.⁶¹

University of San Diego demonstrated lower response rates in the treatment of bone metastases based on histology.⁷ Median dose for bone metastases treatment was 3 Gy with a median fraction of 10. Osteosarcoma had a lower response rate compared to other histologies (58% vs 87%, respectively; $P = .048$). As a result, larger palliative doses have been incorporated into practice of 6 Gy for 6 fractions.⁵⁶

The most recent metastatic pediatric Ewing sarcoma protocol is finally evaluating SBRT for the definitive management of metastatic bone lesions.⁶⁴ Treatment doses range from 3000 to 4000 cGy in 5 fractions at 600 to 800 cGy per daily fraction. Selection of these various modalities will depend on patient prognosis, physician preference, availability, tumor location, prior treatments and response.

Spinal Cord Compression

Also rare are children diagnosed with malignancies who are at risk of developing symptomatic SCC, presenting toward the end of life (EOL) or at initial diagnosis.^{65,66} Ewing sarcoma, primitive neuroectodermal tumors (PNET), soft-tissue sarcoma, and neuroblastoma are some of the most common causes of SCC in children and adolescents.⁶⁷ Presenting signs and symptoms include, but are not limited to, back and radicular

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pain, motor and sensory deficits, sphincter dysfunction, and gait abnormalities.

Whether in an initial or recurrent setting, surgical intervention to prevent and/or restore neurologic deficits, initiation of systemic chemotherapy, and RT should be evaluated to optimize care management.⁶⁸ Even in the setting of neurologic compromise, surgery is often reserved for children and adolescents with a poor response to chemotherapy or RT.⁶⁹ Series have demonstrated that children presenting with disease that compromises motor function continue to be at risk for significant neurologic impairment, despite initial intervention.^{43,70} Palliative RT in cases of relapsed or refractory disease has been used alone and as an adjunct to surgery to alleviate symptoms, and restore and maintain function.^{65-67,71-73}

Brain Metastases

The incidence of brain metastases in children and adolescence is significantly lower compared to adults, described at rates of approximately 1.5% to 2.5% in children diagnosed with solid tumors.⁷⁴⁻⁷⁸ Tumors reported with the greatest metastatic potential include neuroblastoma, soft-tissue sarcoma, osteosarcoma, Ewing sarcoma, Wilm's tumor, germ cell tumor, retinoblastoma, and melanoma.^{77,79,80} Depending on age, systemic disease burden, tumor histology, and prognosis, a standard treatment course of 30 to 36 Gy in 1.5 to 2.5 Gy fractions is appropriate. In the setting of previously irradiated tissue, SRS may be reasonable to consider to relieve symptom burden, optimize tumor control, and minimize risk of tissue toxicity.^{77,81,82}

Symptoms and Distress in Pediatric Cancer

Children and adolescents are at risk of considerable distress as a result of tumor involvement, procedures, and treatment toxicities. Several pediatric series have demonstrated that symptoms and suffer-

ing at EOL are poorly controlled.^{27,29,83} Self-reporting measures have described pain, fatigue, loss of appetite, psychological distress, and nausea as the most common symptoms.^{84,85,87}

Symptom management at EOL is an ongoing treatment obstacle for many clinicians. Pain is one of the most commonly studied symptoms, but most challenging to manage.⁸⁴⁻⁸⁷ An EOL study indicated that parents of dying children identified that 89% of the children suffered from at least one symptom, with pain, fatigue, and dyspnea as the most common; relief was only achieved in 27%.²⁹ Another study reported that 94% suffered from ≥ 3 symptoms, whereas 76% had ≥ 5 or more symptoms at EOL.⁸⁸ The most frequent complaint included pain (100%), nausea/vomiting (63%), constipation (57%), and anxiety (56%).⁸⁸ Incorporating age-appropriate communication, assessment tools, integrative therapies, and modifying factors into child or adolescent care can help alleviate the level of discomfort and improve responses to pain.^{23,89-92}

To accurately assess pain level, intensity, and treatment response, age-appropriate assessment tools and baseline parental assessments are valuable when caring for these patients. Unlike older children and adolescents who may express emotion, pain, and treatment-related discomfort, younger counterparts may demonstrate pain through withdrawal and decreased activity.⁸⁹

An assessment of distress, which can be complex, may require a comprehensive evaluation. Several scales assess symptoms: PQ-Memorial Symptom Assessment Scale (PQ-MSAS),^{23,84,85} and Pediatric Quality of Life Inventory 4.0 Generic Core Scales (PedsQL 4.0).⁹²

Early Integration of Comprehensive Pediatric Palliative Care Team

To provide a supportive network for the evolving needs of the patient/family, early initiation of palliative care is recommended at diagnosis for children

and adolescents with advanced malignancies. PPC focuses on the integration of expectations of life extension and disease-directed therapy, while honoring goals of comfort and QOL. Early integration of palliative care, advanced end-of-life conversations, and systematic symptom management have demonstrated improved outcomes and enhanced QOL.^{30,37}

The American Academy of Pediatrics (AAP) has provided guidelines recommending early consultation of PPC to ensure that distressing symptoms are prevented and treated, and complicated decisions at initial diagnosis are facilitated when the goals of care focus on cure.^{34,93} Many patients receiving palliative RT are seeking disease-directed therapy or are enrolled in experimental therapy. A recent study from St. Jude reported that 79.4% of patients who received palliative care underwent experimental therapy, with 40.5% enrolled on a phase I trial.²⁵ One-third of the patients (35.5%) received cancer-directed therapy during their last month of life. Delayed palliative care (PC) (< 30 days before death) led to higher odds of death in the intensive care unit compared to a home/hospice setting for patients who received earlier PC intervention ($P < .0001$).

In addition to initiation of earlier PPC involvement, one study described the clinical outcomes of 50 children who completed 83 courses of RT and their relationship with the palliative and hospice services.⁹ Of all treatment, 15 palliative RT courses were delivered to patients within the last 30 days of life, 7 of which were completed within the last 7 days of life. Treatment delivered within the last month of life had a lower success rate at palliation compared to courses delivered prior to 30 days, 28% vs 89%, respectively ($P < .0001$). Location of death for 7 patients who received palliative RT within the last 7 days of life were all within a hospital setting (inpatient floor or ICU) except for 1 patient for whom medical records

Table 5. Identifying Patient and Family Goals of Care

- Tell me about your child (as a person). What was he or she like before this illness?
- How has this diagnosis changed your child and the dynamics of the family?
- What is your understanding of your child's illness? What does the illness mean to you and your family?
- In light of your understanding, what is most important regarding your child's care?
- What are your hopes for your child? What are your fears regarding your child? What are your greatest concerns?
- Where do you find support and strength?

Adapted from Waldeman & Wolfe 2013³⁷

were not available. Of the patients who received palliative RT, 28% already had PC involvement, whereas 60% were referred to the institutional PC team during their clinical course. Patients receiving palliative RT received supportive services: PC alone, hospice alone, both PC and hospice, or neither, at 14%, 18%, 46%, and 12%, respectively.⁹ The median time to hospice referral was 96 days following the last palliative RT treatment (range: 0 to 924 days). With the support of the PPC, advanced care planning can assist with early delivery of home services and ensure that death takes place in the preferred location of the child/family.^{88,94}

Communication

Effective communication facilitates appropriate patient, parent and team knowledge, trust, and a common goal.⁹⁵⁻⁹⁸ Identifying the patient/family goals of care^{99,100} prior to initiating palliative RT will assist communication and future medical decision-making processes, identify necessary supports, and optimize QOL (Table 5). Specific to radiation oncology, it is critical to identify the patient/family understanding of the illness, how much they would like to know, the associated risks/benefits, and treatment limitations, and respond to their emotions, physical presence during conversations, and high-quality care.^{96,101-103} Specific to

radiation treatment planning, it is essential to address patient needs based on age, sedation requirements, and management of uncontrolled symptoms to ensure treatment accuracy and safety. Child-life therapy, social work, and interpreter services are valuable resources to facilitate information sharing and improve their experience.¹⁰⁴

Prognostication

When faced with a life-threatening illness, most parents prefer to be well-informed about their child's diagnosis, treatment-related complications, survival outcomes, and the potential impact on function and QOL.¹⁰⁵⁻¹¹⁰ If the children are diagnosed with advanced malignancies, parents often prefer cancer-directed therapy (eg, surgery, chemotherapy, biologic agents, RT) rather than more palliative therapies with an emphasis on comfort measures of prolonging life and/or relief of symptoms.^{99,110,111} Parents' understanding and perception of their child's disease depends on the effectiveness of communication from the primary care team.^{26,114-117} Explicit or clear sources of information regarding a parent's child, conversations with the oncologist at the time of diagnosis, or daily conversations with the oncologist and nurses, were informative approximately 73% to 85% of the time.¹¹⁶ Implicit, or inherent sources of information, including "how

parents feel their child is doing," or "how the oncologist appears to feel the child is doing," were informative. Parents who valued implicit information had lower prognostic accuracy, particularly when focusing on a "general sense of how my child's oncologist seems to feel my child is doing."¹¹⁸ Parental preference, developmental stage variabilities, the family provider, and patient should be included in conversations about their disease and decision-making.^{26,117,118} Children and adolescents are aware of their disease and prognosis as early as age 3 years; it is critical for clinicians to encourage open and honest conversations.^{118,119}

Advanced Care Planning and EOL

Early introduction of PPC by the team facilitates discussions around advanced care planning EOL hospice conversations and enrollment, improved symptom control, introduction of do-not-resuscitate orders, and preparations during the child's last month of life.^{88,120}

It is important to appreciate the perspective of the child, siblings, and parents regarding the emotional experience and medical-decision making, and address supports following the child's death to reduce complicated bereavement risk.¹²¹⁻¹²⁴ Children harbor a strong intuition and sensitivity to the experience of loneliness, anxiety, and imminent death.²⁸ Despite their young age, children ages 10 to 20 years who are diagnosed with advanced malignancies are competent to participate in medical-decision making, engage in EOL discussions, and understand the consequences and impact of their decisions on how their death may influence loved ones.¹²⁵

Bereavement

The death of a child can be shattering and transformative, influencing the psychosocial and physical health of family and caregivers involved.¹²⁶⁻¹²⁹ Bereaved

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parents are at long-term risk of developing physical and psychosocial co-morbidities.¹³⁰⁻¹³⁷ Mortality rates have been reported the highest among bereaved parents within the first 3 years following a child's death; however, some studies report no difference in morbidity or mortality rates between bereaved and nonbereaved parents.^{138,139} Studies have confirmed increased chronic illnesses during the first 6 months following a child's death.^{129,140} To assist with emotional and psychological adjustment prior to the child's death and to assure appropriate support throughout the deteriorating disease state, bereavement support should be initiated well before the dying phase.^{27,141,142} As a radiation oncologist, acknowledgement of the evolving palliative and bereavement supports needed for the patient, siblings, and family is essential.¹⁴²

Barriers to Pediatric Palliative Care

The low incidence of pediatric malignancies and death, differences in pediatric developmental stages, insufficient exposure of current medical school and residency programs to palliative education and competencies, lack of insurance provider reimbursement, and the limitations of prospective data on the incidence and management of symptoms are some of the major barriers to delivering high-quality comprehensive PC in children with advanced malignancies.¹⁴³ Despite attempts to provide effective comprehensive EOL care, various barriers remain, including unrealistic expectations from the family (47.5%), prognostic denial from the family (35.7%), familial conflict (30.3%), the patient's unrealistic expectations (10.1%), and prognostic denial from the patient (7.6%).¹⁴⁴ The growth and execution of dedicated PC may be curtailed due to the child/family requirements for additional emotional and psychosocial support; limited resources, scarcity of trained staff, and institutional budget constraints.¹⁴⁵ Clinical

triggers for PC consultations may help facilitate earlier involvement.³¹

Barriers to Palliative Radiation Therapy

Several barriers have been identified resulting in the underutilization of pediatric palliative RT, predominately secondary to misconceptions or concerns for treatment-related toxicities. In a Canadian survey, formally trained palliative medicine physicians were more likely to refer children for palliative RT compared to responders without a palliative background (94 % vs 73 %, $p < .01$).¹⁴⁶ Numerous barriers include, but are not limited to, patient/family reluctance, potential benefit ignorance, potential treatment-related side effect misconceptions, short life expectancy, cancer center proximity, transportation limitations, concern for lack of improvement, and impact on QOL.¹⁴⁶

A collaborative multi-institutional survey reported on the practice patterns of palliative RT in 365 pediatric patients in an international pediatric research consortium.⁶ Treatment toxicity (83%) was the most common physician-reported barrier to initiation of RT, and treatment resources, insurance authorization/cost, anesthesia availability, and parental concerns were less of a deterrent.⁶ A recent publication noted that the 2 most common indications for palliative RT were oligometastatic disease in asymptomatic patients (39%) and pain (25%).¹⁴⁷ A similar study reported only low-grade self-limiting acute toxicity outcomes of 45 children treated with palliative RT: Nausea (3.6%), dermatitis (6.0%), and fatigue (3.6%); no grade 3 or late toxicities were described.⁷

Education and innovative oncology curriculums emphasize increasing clinical exposure and didactic lectures to improve communication skills and develop a stronger knowledge base of palliative competencies. Greater clinical education and addressing parental and provider concerns may increase the appropriate

consideration and implementation of palliative RT.^{135,146,148,149}

Future Directions

Most palliative RT treatments are delivered using 3D-CRT, varying 41% to 63%.^{6,7,147} Incorporating more advanced radiotherapeutic techniques including IMRT, SBRT, SRS, and proton beam therapy (PBT), can deliver highly conformal treatment to achieve the desired tumor response dose and spare normal tissue, while achieving symptomatic relief.^{60,61,64} Current controversy centers on cost of these modalities if a child is not expected to live long enough to benefit from the therapy received; however, if a potential for decreased toxicity and local failure exists, a more conformal dose-escalated approach would be favorable, especially in the re-irradiation setting.^{147,150,151}

Research

Future research direction is necessary to better define guidelines for palliative RT delivery for pediatric patients. Although there are standard guidelines for palliative RT in adults, it is well known that response rates vary depending on tumor histologies.⁵ Similarly, pediatric tumors vary in histology and response specifically to RT, as described in several series.^{6,7,9,44,152,153} Leukemia, neuroblastoma, and Ewing sarcoma are more likely to achieve a complete response with RT compared to CNS malignancies. There is a need to standardize doses by reducing the required treatment doses to maintain optimal local control and symptomatic relief, decrease treatment time and lower toxicity. A meta-analysis of the collective literature or a collaborative effort for a multi-institutional prospective study is warranted to evaluate optimal dose and fractionation schema specific to disease sites, symptomatic response, treatment-related toxicities, survival outcomes, and QOL measures to summarize the evidence and identify

a consensus of comprehensive care and treatment guidelines.

Conclusion

Prospective research is necessary to establish palliative RT guidelines for management of pediatric malignancies to honor preferences and maintain best practices. With more technologic advances, multidisciplinary team plan of care and communication will become extremely important in providing the correct medical, emotional and psychosocial decisions and supports for the patient and family unit.

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