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Imaging in Childhood Cancer: A Society for Pediatric Radiology and Children's Oncology Group Joint Task Force Report

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Abstract

Contemporary medical imaging is a cornerstone of care for children with cancer. As 5-year survival rates for children with cancer exceed 80%, imaging technologies have evolved in parallel to include a wide array of modalities. Here, we overview the risks and benefits associated with commonly used imaging modalities and survey the current landscape of medical imaging for children with cancer. We find evidence-based imaging guidelines to assist in protocol development and to guide decision-making for optimal patient care are often lacking. The substantial variation in protocol-based recommendations for imaging both during and following therapy may hinder optimal clinical research and clinical care for children with cancer.

Keywords

diagnostic imaging; ionizing radiation; imaging guidelines

INTRODUCTION

Contemporary medical imaging, a cornerstone of care for children with cancer, is integral for detecting disease, generating a differential diagnosis, supporting the surgical plan for biopsy or resection, disease staging, evaluating response to therapy, monitoring for recurrence, predicting outcome, and for diagnosing or managing both acute and late sequelae of treatment. As treatment of children with cancer has improved to produce cure rates exceeding 80%, imaging technologies available to clinicians and researchers have evolved to include a wide array of modalities. Yet the optimal approach to imaging children

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with cancer has neither been adequately studied nor fully defined, resulting in significant variation in techniques employed.

A joint task force of the Children's Oncology Group and the Society for Pediatric Radiology was charged with surveying the current landscape of medical imaging for children with cancer, including providing an overview of the risks and benefits associated with commonly used modalities. As part of this charge, select clinical trials being conducted by the Children's Oncology Group were evaluated to explore variation in imaging both during and following protocol-directed therapy.

Recommendations about modalities and frequency of imaging must encompass the natural history of the disease, prognostic information to be gained, the anti-cancer therapeutic modalities to be employed, and the age and developmental status of the child. Understanding the risks and benefits of imaging modalities, including the costs and psychological stress associated with cancer diagnostics, weighed against the value of information provided through imaging, will be important when defining evidenced-based imaging guidelines for diagnosis, treatment, and follow-up of children with cancer.

RADIATION EXPOSURE CONSIDERATIONS

Late adverse events associated with childhood cancer therapy are widely recognized. Particular attention has been directed towards the risk of second malignant neoplasms (SMNs) for which ionizing radiation associated with radiation therapy is an important contributor. Cumulative mortality is nearly 12% at 20 years and over 18% at 30 years from diagnosis of a childhood cancer, and SMNs are the most frequent cause of this late mortality [1]. Exposure to ionizing radiation is associated with an increased long-term risk of SMNs including leukemia, central nervous system tumors, malignant bone tumors, breast cancer, and thyroid carcinoma [2–5]. Children are more susceptible than adults to radiation-related cancers and it is reasonable to assume that there may be enhanced sensitivity for SMNs (Fig. 1) [5–7]. Age-related models of radiation carcinogenesis show that the risk for children younger than 5 years old may be more than fivefold greater than that of a 50-year-old [6,8]. Higher risk of SMNs tend to be associated with female sex, childhood cancer diagnosed at a younger age, Hodgkin lymphoma, soft-tissue sarcoma, and alkylating agent exposure and radiation therapy [3].

For children with cancer not requiring radiation therapy, medical imaging is the predominant source of exposure to ionizing radiation. The radiation doses associated with frequently employed imaging modalities are summarized in Figure 2, which notes the comparative effective dose across modalities [4,9]. Although there is concern that the cumulative effective dose of ionizing radiation from any source may be associated with increased risk for malignancy [5,9–13], estimating the actual risk is challenging, particularly because the incremental risk of diagnostic imaging is small compared to overall lifetime risk of malignancy. In a retrospective review, Pearce and colleagues reported that children who received two to three CT scans of the head had a threefold increased risk of developing brain cancer, while 5–10 scans raises the risk of leukemia threefold [14]. These observations are consistent with theoretical studies and the linear no-threshold hypothesis, where research

suggests that no dose should be considered completely inconsequential [4,7,12,13]. For example, lifetime cancer mortality risk attributable to ionizing radiation from one abdominal CT is estimated to be 0.14%, 0.1%, and 0.07% in a 1-, 5-, and 10-year-old, respectively [6,15–18] (the lifetime risk of dying from any malignancy is approximately 20% [19]). It is important to note that the summed risk of multiple doses of ionizing radiation is less than the risk of a single dose of radiation of the same cumulative magnitude [4].

The as low as reasonably achievable (ALARA) principle aims to minimize medical radiation exposure [20]. As opposed to workers in healthcare and the nuclear industry where radiation exposures can be regulated, patient exposures are not restricted, largely because the need for medical imaging is usually clinically driven [21]. Thus, the risk associated with cumulative exposure to ionizing radiation from medical imaging must be balanced with the risk of potential underutilization of medical imaging in a population of children at high risk for recurrence or complications of therapy.

IMAGING MODALITY AND TECHNIQUE CONSIDERATIONS

Primary cancer diagnosis, staging, response assessment, and surveillance require medical imaging modalities that vary by disease, treatment protocol, physician preference, radiologist skills, institution, ancillary staff, and modality availability. As such, there is limited standardization for imaging modality choice and subsequent technical considerations (e.g., MRI sequences, phase of contrast when imaged, method of administering contrast, slice thicknesses, technique parameters). There are also deficiencies and ambiguities in protocols that drive cancer treatment plans [11,22,23]. A primary problem for most childhood cancers is that, except for a few select examples [24–27], there are no evidence-based guidelines to guide frequency of imaging and choice of modality.

CT scans, nuclear medicine studies, and radiographs are associated with an exposure to ionizing radiation. As compared with MRI, CT is faster, more easily attained and considerably less expensive. Its use for children with solid tumors evolved in the 1970s and 1980s due to more sensitive detection of pulmonary metastases as compared with radiographs [28–31]. Physician familiarity with CT scans, ease of ordering and obtaining, rare need for sedation, high quality data, and rapidity of interpretation all contribute to its favored use.

In general, MRI is superior for evaluating soft tissue tumors of the trunk and extremities, and is preferred for imaging of the head and neck. MRI is increasingly utilized for assessment of tumors localized to the retroperitoneum, abdomen, and pelvis. MRI studies are more time intensive and therefore children frequently require sedation, with associated risks and costs, to complete the same series that could be done with CT without anesthesia. Technological advancements are shortening MRI scan times, and the lack of patient exposure to ionizing radiation makes it an important modality for use in pediatrics. There is a very small risk of nephrogenic systemic fibrosis for patients who receive MRI contrast in the setting of severe renal failure, but no other biologic hazards have been reported with the use of MRI [32]. Ultrasound, used less frequently for pediatric oncologic diagnosis in the

United States than in Europe, has no known hazards [33] and is considered a safe diagnostic imaging modality in oncology.

Nuclear medicine studies and functional imaging are also often incorporated into routine clinical use, often without evidence-based guidelines. For example, the metabolic activity revealed by PET scans, an important diagnostic and staging modality for certain malignancies including Hodgkin and non-Hodgkin lymphomas [34], have led to increased use in other cancers (e.g., sarcomas) [35]. As FDG-PET is incorporated into the imaging schema for various pediatric malignancies, establishment of guidelines for the number, interval, techniques, and frequency of scanning and significance of results will be important. Current consensus recommendations for administered FDG activities were formulated after a survey of major children's hospitals revealed wide discrepancy by as much as a factor of 10 in administered radiopharmaceutical activities [36–38], yet radiopharmaceutical doses contribute relatively little to overall radiation exposure from imaging.

The benefits provided by functional imaging assessment, as with all modalities and particularly those that emit radiation, need to be weighed against the small risk of increased ionizing radiation exposure. In patients for whom there is no need to maximize detection of small pulmonary nodules and in patients who cannot hold their breath, the contrast enhanced CT can be fully integrated into the PET-CT study. Data are needed to determine other scenarios when the PET-associated CT can obviate the need for a separate diagnostic contrast-enhanced CT, and when modified very low dose CT techniques can be used in conjunction with PET [39].

New technology permits variation in CT technique during a single study based on the need for diagnostic quality images of specific anatomic sites. Iterative reconstruction techniques, new dose guidelines and protocols, and other evolving approaches in CT (with or without PET) will reduce ionizing radiation exposures, particularly for many follow-up studies and hybrid imaging [40]. In addition, MRI-PET has recently been introduced and is an attractive alternative imaging modality without the radiation exposure of CT. Physiologic imaging with diffusion-weighted MRI (DW-MRI) uses no ionizing radiation and may find new uses as well.

For children with recurrent or relapsed solid tumors, medical imaging plays a key role in early phase clinical trials; it is the primary and least invasive means by which to evaluate response to therapy. A growing trend will be to identify and leverage emerging imaging modalities that will foster development of molecularly targeted agents for children with cancer [41].

CLINICAL APPLICATIONS

Staging and Response Assessment

Staging of cancer has evolved with advances in imaging technology. For example, in Wilms tumor, detection of pulmonary metastases by CT had been thought to be more predictive of disease progression and overall survival than radiographs [42–45], thus making CT an evidence-based component of staging for children with Wilms tumor. However, in one-third

of cases, lesions less than 1 cm do not represent metastatic disease, and a large comprehensive review demonstrated that increased sensitivity of chest CT versus chest X-ray for small pulmonary nodules at diagnosis did not alter overall survival [46]. Currently, stratification of these patients with stage IV disease is based on initial response to therapy, rendering upfront resection of nodules potentially unnecessary [47,48].

For patients with Hodgkin lymphoma, PET-CT is commonly employed in initial staging. Although techniques are available to minimize duplicate imaging with diagnostic CT, such techniques may be underutilized. Further, there is little evidence to support the use of a bone scan when performing FDG-PET imaging for these patients [49–51], and as such it is primarily used if FDG-PET is unavailable or if there is a question of osseous involvement.

For detecting non-pulmonary metastases in patients with sarcomas, FDG-PET may be more sensitive than conventional imaging modalities [52,53]. Yet despite the improved sensitivity of CT and PET for detecting metastases in patients with Ewing sarcoma, the fraction of patients with detectable metastases at diagnosis has remained fairly stable at 20–25% for the past 30 years [54], raising question as to the potential impact of these more sensitive imaging modalities on staging and outcome. For bone tumors, MRI of the primary site has emerged as the preferred staging and treatment planning imaging method because of the improved ability to evaluate soft tissues and extent of tumor invasion. With its excellent visualization of neurovascular bundles, MRI alone usually can fully support surgical planning of tumor resection.

The imaging modalities that guide diagnostic staging are usually the same as those used to assess response to treatment. To limit patient exposure to ionizing radiation, recent clinical trials limit CT monitoring to involved anatomic sites, other than for baseline and off-therapy evaluation. In contrast, patients with Hodgkin lymphoma often undergo sequential full-body PET-CTs (or historically gallium scintigraphy) even when full anatomic coverage may not be needed; literature is emerging on the role of limited whole-body PET-CT for follow-up imaging in patients with lymphoma [55].

Surveillance

With the exception of brain tumors, for which one in three recurrences are identified by surveillance scans, most recurrences are identified by symptomatology [56]. Early detection of relapse through aggressive radiologic surveillance may not improve survival in patients with Hodgkin lymphoma, solid tumors, or intracranial neoplasms [56–59]. Such imaging does not facilitate earlier recognition of recurrent soft tissue sarcoma in children and adolescents [60]. Importantly, there is a lack of specificity of sub-centimetric pulmonary lesions on imaging studies. More sensitive surveillance imaging with chest CT, as opposed to chest X-ray, promotes a greater likelihood of false positive results, which may be exacerbated in geographic regions that are endemic for histoplasmosis or other mycoses or mycobacteria [61]. In Ewing sarcoma, even though imaging modalities have changed over time, the frequency of surveillance has not, nor has the salvage rate significantly improved.

For patients with lymphoma, relapses are more frequently detected by physical examination than through medical imaging, and timing or method of detection does not appear to alter

the probability of survival [62,63]. Moreover, almost half of patients with lymphoma have surveillance studies performed when the recurrence risk is low or no clear indication is identified in the medical records [10]. Based on contemporary treatment, these patients undergo up to 15 CT scans—usually of the neck through pelvis—during therapy and as part of surveillance.

A concern with some clinical trials is that when adding a new imaging modality to surveillance, historical modalities may not be eliminated. More contemporary FDG-PET has been required along with a bone scan for metastatic evaluation in pediatric sarcoma, yet dedicated bone imaging does not add diagnostic value [64]. Similarly, though relatively minimal added radiation exposure, chest X-rays may continue to be used to monitor for pulmonary metastases when simultaneously performing a chest CT. Such compounding of imaging increases resource utilization, costs, and, depending upon the modality, patient exposure to ionizing radiation. Further, for patients requiring general anesthesia, multiple sedations may be required.

Supportive Care

Acute—Disease evaluation during therapy may involve searching for an underlying cause for persistent fever and neutropenia. For work-up of invasive fungal disease, CT scans of the sinuses, chest, abdomen, and pelvis are often employed, despite evidence that pelvic, abdominal, and sinus (especially if less than 2 years of age) scans appear unnecessary if not clinically suspected [65–67]. Abdominal fungal disease typically occurs only in the presence of fungal disease in the chest, suggesting that many evaluations seeking evidence of fungal infections could be more limited in scope [65]. The German oncology cooperative group DGHO recommends abdominal ultrasound and MRI in lieu of CT scans for evaluation of prolonged fever in the setting of neutropenia when pulmonary disease is not suspected [68]. PET-CT may be a promising approach for the evaluation of febrile neutropenia in adults and is being evaluated in children. Nevertheless, there is significant inter-institutional variation in timing and extent of imaging for fungal disease. An additional example is the approach to typhlitis, where ultrasound has been shown to provide adequate, and perhaps superior, diagnostic information as compared with traditionally used CT scans [69,70].

Chronic—Chronic toxicities during therapy are often evaluated with medical imaging. During therapy for ALL, children with suspected osteonecrosis may be imaged with radiographs, CT, bone scans, MRI, or a combination of modalities. No clear recommendations regarding optimal imaging modality and frequency are specified in most protocols, despite MRI being the most sensitive modality for detection of osteonecrosis. For neurotoxicity developing during treatment for ALL, several protocols recommend neuroimaging with either CT or MRI, but do not provide guidance on imaging method, timing, or technical parameters for scanning.

Psychological Considerations

Medical imaging can lead to false positive results that add cost, increase exposure to ionizing radiation and lead to potentially invasive diagnostic procedures. Additional appointments, sedations, and potentially further therapy place a burden on the patient,

family, and available resources. On the contrary, false negative results may delay treatment changes, add to costs, and compromise patient quality and length of life.

Cancer patients face a major challenge in the uncertainty of future relapse [71]. Patient and family anxiety around the time of surveillance screening should not be underestimated, as the fear of recurrence can be a significant psychological burden. As would be expected, the stress mounts prior to the follow-up appointment, peaks until the time results are presented, and then subsides. In adult patients with underlying anxiety, Thompson et al. [72] found that routine surveillance scans exacerbate symptoms and that a better doctor–patient relationship, defined through qualitative interviews, correlated with less anxiety. In contrast, minimizing imaging may inadvertently increase patient stress levels if they feel less reassured of no recurrence. Though not well-studied in pediatrics, the psychological aspect of surveillance scans should be considered along with risks and benefits when determining the optimal monitoring approach, particularly when there is equivocal benefit of such imaging.

RESEARCH APPLICATIONS

Staging

In clinical research protocols, there is variability in imaging modality employed and the frequency and extent of imaging. In a recently completed Children's Oncology Group osteosarcoma study, pulmonary metastases were to be considered as "certain" if three or more lesions were ≥ 5 mm in maximum diameter, or if a single lesion was ≥ 1 cm in diameter. In contrast, a Ewing sarcoma protocol recommends that for a single nodule >1 cm or for more than one nodule >5 mm, biopsy be considered. In protocols for children with non-rhabdomyosarcoma soft tissue sarcomas, biopsy or resection for nodules that are <1 cm in diameter are needed to confirm metastatic disease. Recognizing that the chemo- or radio-sensitivity of different sarcomas influences such recommendations, differences in approaches largely result from variation in expert opinion. As the sensitivity of imaging modalities continues to improve, very small pulmonary nodules have become an increasingly problematic management challenge for children with sarcomas and collaborative studies should continue to provide insight for evidence-based guideline development.

Response Assessment and Predicting Outcome

Beyond stratification, as in risk categorization in neuroblastoma at diagnosis, medical imaging can play a key role in predicting outcome. The change in FDG-PET avidity can be used in patients with Ewing sarcoma to assess response to therapy and findings suggest it to be independently predictive of progression-free survival [73]. Functional imaging may adequately identify bone marrow disease in patients with Hodgkin lymphoma and thus serve as a substitute for bone marrow examination by biopsy [49], and importantly as an excellent prediction tool for outcome [74].

Incorporation of functional imaging into clinical trials for novel pharmacologic agents may allow for early evaluation of efficacy, as such studies have the potential to demonstrate efficacy of pharmaceutical agents regardless of change in tumor size. Examples include FDG-PET imaging that has shown utility for early response assessment in adult patients

with non-small cell lung cancer receiving erlotinib [75], and in Hodgkin lymphoma trials worldwide, FDG-PET and PET-CT are increasingly being studied for response assessment and therapeutic stratification as their sensitivity and specificity is greater than that of CT alone (reviewed in Ref. [76,77]). Additionally, diffusion weighted and dynamic contrast enhanced MRI may permit efficacy evaluation of pharmacologic agents at a reduced radiation risk; it may predict response in patients with breast, prostate and rectal carcinomas, cerebral gliomas, and colorectal hepatic metastases [78]. It is also being explored in pediatric trials such as through measurement of changes in blood flow and permeability with the use of antiangiogenic agents [79]. Pediatric oncologists and radiologists should anticipate increasing use of functional imaging, especially in the setting of small molecule inhibitor therapy as part of adaptive treatment strategies. However, as with all early phase studies, it is not clear that assessment of activity leads to altered treatment decisions that improve overall survival, just as the role of PET-CT for therapeutic and prognostic stratification has not been fully elucidated in many malignancies.

The response evaluation criteria in solid tumors (RECIST) methodology was introduced in 2000 in an effort to standardize imaging interpretation and assess response for patients enrolled on clinical trials of investigational new drugs [80]. Prior to RECIST, early phase clinical trials generally used the product of the perpendicular diameters of tumors to record lesion size. RECIST attempted to address the high degree of inter-observer variability in quantitating tumor burden through summation of the perpendicular products of tumors by instead employing a single linear measurement. Accurate assessment of the change in tumor burden is critical for response assessment, a key factor in determining whether a new therapy moves into phase 3 clinical trials. Although the criteria have not been validated in pediatrics, a decrease in inter-observer variability appears to have emerged. Recent revisions to RECIST (version 1.1) represent efforts to address a number of shortcomings of the criteria, but even this approach has limitations [81,82]. Three-dimensional volume-based evaluation of tumor burden may provide greater sensitivity for evaluating tumor responsiveness, but it has not been widely studied.

Primary Outcome

The primary end-point for pediatric phase 3 trials is most often event-free survival. As such, the frequency and modality of surveillance imaging is inherent to protocol design. Figure 3 lists common pediatric cancer diagnoses and an estimated number of studies involving exposure to ionizing radiation, as based on high-risk patients enrolled on select Children's Oncology Group trials. The median cumulative effective dose from chest CTs during the course of therapy is also shown. Patients with high-risk neuroblastoma have off-therapy imaging evaluation with numerous CT scans and MIBG as often as every 3 months for the first year, and then every 6 months for an additional 2 years. Recurrent disease is usually detected based on the MIBG, yet salvage therapy after high-risk therapy is rarely curative. Ongoing studies are exploring the efficacy of early detection of relapse.

Through collaborative research over decades, the relapse rate, usual time to relapse, sites of relapse, and salvage rates for many tumor types is known. However, evidence-based literature to support the frequency of monitoring, usually determined by risk of treatment

failure, is limited [83–86]. Ongoing data collection regarding patient relapse will assist in the design of follow-up imaging protocols that balance diagnostic radiation exposure against the likelihood of identifying recurrent disease in the body region that is imaged.

RECOMMENDATIONS

There is a clear need for a systematic approach to better integrate contemporary imaging modalities into both clinical care and research for children with cancer. Experts in pediatric imaging, pediatric oncologists, pediatric surgeons, radiation oncologists, child psychologists, and medical economists will need to increasingly collaborate to provide a framework for recommendations and future research.

Radiation Exposure Risk and Imaging Modality Consideration

Children are particularly susceptible to the detrimental effects of ionizing radiation, with a primary concern being increased cancer risk. Even though most diagnostic CT and PET studies are associated with a very favorable risk–benefit ratio, there is a strong argument to be made that radiation exposure should be as low as reasonably achievable.

One way to reduce exposure to ionizing radiation is to consider MRI or ultrasound in place of CT scans and PET studies when feasible. This requires standardized approaches to cancer staging that look for commonality between diseases, as was done for bone tumors [35]. Here, it would appear that an increased understanding of the value added by differing imaging modalities could refine the number of studies required at the time of diagnosis. The Image Gently website (www.imagegently.org) has resources available including guidelines for the safe and efficient use of imaging that emits ionizing radiation with a goal of limiting patient exposures.

The Society for Pediatric Radiology, through the Alliance for Radiation Safety, also promotes safe imaging, as does the European Society of Pediatric Radiology. These entities strive to reduce the CT or PET-CT related dose in individual patients by incorporating low-dose guidelines into new protocols, including through the use of size- or weight-based tables or automated technology that adjusts dose to patient size (Table I). Further, focused response assessment may reasonably minimize exposure, such as with limited whole-body PET-CT after initial staging in FDG-avid malignancies. In the longer-term, clinical research should gather technical details about radiologic imaging studies so that inter-institution trends can be evaluated.

Clinical Applications

A key area for clinical investigation is with the approach to surveillance imaging, both during and following completion of therapy. Information could be gained from retrospective analyses examining the impact of early detection of disease recurrence, as is being undertaken for children with Hodgkin lymphoma [87]. Such data could impact the modalities of imaging employed by examining the value of detection of sub-centimeter metastatic disease for which chest CT scans are usually performed, versus larger disease that can be discerned by radiographs. Moreover, an assessment of the value of more versus less frequent imaging as an outcome could be made. Additional protocol aims focusing on such

key imaging objectives could potentially be incorporated into select pediatric phase 3 therapeutic trials.

Well-designed, prospective studies are needed for fully developing evidence-based guidelines for imaging children with cancer. Development of imaging algorithms would minimize uncertainty about optimal imaging approaches. The challenges will include the likelihood of multiple generations of new hardware and methods that emerge over the course of a clinical trial. Studies examining the psychological impact on patients and families surrounding imaging are also needed, with the goal of defining a reasonable balance between reassurance provided by normal imaging results and the negative impact of undergoing such studies on a frequent basis.

Research Applications

Layered upon these considerations are the prospects of increasing the use of functional imaging and utilizing novel imaging approaches in an era of molecularly targeted therapies. Further research is needed in assessing the use of newer imaging modalities in predicting outcome, including the use of three-dimensional volumetrics for assessing tumor response. Direct comparisons may be necessary such as with PET-CT versus contrast-enhanced CT, and the utility of PET-MRI, DW-MRI, and PET-CT must be further assessed for their diagnostic, prognostic and management potential. Adaptive treatment strategies, based on imaging criteria, have potential to improve patient outcome while also reducing the number of serial imaging studies.

The ability to potentially select a targeted therapy based upon imaging results may transform the approach to the child with newly diagnosed or relapsed cancer. Such future promise underscores the need to fully address today's challenges with medical imaging in pediatric oncology. The disciplines of medical imaging and pediatric oncology will become increasingly integrated, and thus the need for collaborative research in the field is more than evident. Approaches to addressing key issues outlined here have the potential to positively impact the lives of children with cancer, and should be an increasingly high priority for research support at funding agencies.

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Fig. 1.

Estimated attributable lifetime risk from a single small dose of radiation as a function of age at exposure [7]. Females have higher risk due to breast and thyroid cancers. Younger age at exposure imparts greater risk that is usually not expressed until late in life [5]. Grays (Gy) is the unit of measurement of the absorbed dose. (Reprinted with permission from the National Academies Press, Copyright 2006, National Academy of Sciences.)

Fig. 2.

Effective dose estimates of frequently used imaging modalities in relation to common exposures for a 10-year-old child [4,9]. Effective dose summates the absorbed organ doses in the exposed field and multiplies it by a weighting factor determined by the differential radiosensitivity of the organ, and is expressed in Sieverts (Sv). One Sievert equals 100 rem (roentgen equivalent man), and is roughly equivalent in biological effectiveness to one Gy (gray) of gamma radiation. It is important to note that these are estimates only and actual effective dose is dependent of patient body habitus, equipment settings and equipment manufacturer; doses can vary significantly within and across institutions and may vary amongst machines. Unless appropriate adjustments are made in exposure settings, pediatric patients receive higher effective doses of radiation than adult patients because their smaller size leads to less attenuation of the primary X-ray beam; these adjustments are now made in most pediatric and academic hospitals [89]. *If best practices are followed (see www.imagegently.org), the effective dose estimates may be lower than those noted (e.g., mean dose for a chest CT could be as low as 1.6 mSv based on a correction factor of 0.013 mSv/mGy/cm [90] applied to values derived from Ref. [91]).

Fig. 3.

Typical chest imaging involving ionizing radiation for select higher risk primary cancer diagnoses, based on Children's Oncology Group research protocols (AEWS02P1, ARMS0431, AHOD0831, and AREN0533), available via clinicaltrials.gov (identifier NCT00061893, NCT00354744, NCT01026220, and NCT00379340, respectively; **left panel**). Cumulative effective dose of ionizing radiation from chest CT scans from staging through to 5 years from diagnosis, estimated based on 4.1 mSv per study in a 10-year-old (**right panel**). Note that effective dose per study is likely less at pediatric imaging centers. In addition, when multiple examinations are performed, the risk per mSv is reduced by at least 50%. EWS, Ewing sarcoma; RMS, rhabdomyosarcoma; HD, Hodgkin lymphoma.

TABLE I

Strategies for Minimizing Exposure to Ionizing Radiation From Pediatric Imaging Studies (Adapted From Ref. [88])

Check if CT is the optimal imaging modality
Optimize equipment for pediatrics
Adjust exposure settings based on child size and organ(s) being imaged
Scan the smallest necessary area
Question if higher quality/resolution images are necessary
Follow ALARA principles
Review educational materials and quality assurance initiatives

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