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CLINICAL PRACTICE GUIDELINES

Pediatric Blood & Cancer

Practice patterns and recommendations for pediatric image-guided radiotherapy: A Children's Oncology Group report

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Abbreviations: 2D, two-dimensional; AAPM, American Association of Physicists in Medicine; ACR, American College of Radiology; ALL, acute lymphocytic leukemia; AP/PA, anteroposterior/posteroanterior; ASRT, American Society for Radiologic Technologists; ASTRO, American Society for Radiation Oncology; BEIR, Biological Effects of Ionizing Radiation; CBCT, cone-beam computed tomography; CNS, central nervous system; COG, Children's Oncology Group; CRT, conformal radiation therapy; CT, computed tomography; CTDI, computed tomography dose index; CTV, clinical target volume; DOF, degrees of freedom; HDR, high dose rate; IGRT, image-guided radiation therapy; IMRT, intensity-modulated radiation therapy; IROC, Imaging and Radiation Oncology Core; kV, kilovoltage; kVi, kilovoltage planar imaging; kVp, kilovoltage peak; mAs, milliampere second; MOSFET, metal-oxide semiconductor field-effect transistor; MRI, magnetic resonance imaging; MV, megavoltage; MVCT, megavoltage computed tomography; MVi, megavoltage planar imaging; NRSTS, non-rhabdomyosarcoma soft-tissue sarcoma; OSLD, optically stimulated luminescence detector; PT, proton therapy; SBRT, stereotactic body radiotherapy; SRS, stereotactic radiosurgery; TLD, thermoluminescent dosimeter; VMAT, volumetric modulated arc therapy; XVI, X-ray volume imaging

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Abstract

This report by the Radiation Oncology Discipline of Children's Oncology Group (COG) describes the practice patterns of pediatric image-guided radiotherapy (IGRT) based on a member survey and provides practice recommendations accordingly. The survey comprised of 11 vignettes asking clinicians about their recommended treatment modalities, IGRT preferences, and frequency of in-room verification. Technical questions asked physicists about imaging protocols, dose reduction, setup correction, and adaptive therapy. In this report, the COG Radiation Oncology Discipline provides an IGRT modality/frequency decision tree and the expert guidelines for the practice of ionizing image guidance in pediatric radiotherapy patients.

KEYWORDS
COG, IGRT, pediatric patients, practice patterns, radiation oncology

1 | INTRODUCTION

The delivery of advanced radiotherapeutic techniques is directed by tumor localization and patient alignment confirmation. Intensity-modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), and proton therapy (PT), all with daily image guidance, provide highly conformal treatments with the prospect of treatment margin reduction.[1-3] Setup errors may result in under-treatment of target volumes and increased doses to critical organs, thereby compromising disease outcomes and increasing the risk of complications in normal tissue.[4-6] To mitigate these uncertainties, image-guided radiation therapy (IGRT) verification methods have been implemented.

As in adults, IGRT is commonly used to treat multiple malignancies in pediatric patients, facilitating target volume localization and normal structure avoidance.[7-12] Image guidance with both planar/volumetric imaging and internal/surface markers is used to increase treatment accuracy.[8] The use of bony landmarks and fiducials may be necessary to confirm the alignment within two radiographic planes.[7,13] Three-dimensional (3D) volumetric image guidance with cone-beam computed tomography (CBCT) or computed tomography (CT)-on-rails can provide position reproducibility for body and internal anatomy to within a millimeter if 6-degrees-of-freedom (6DOF) treatment couch positioning is implemented. Also, with improved soft-tissue visualization, interval changes in tissues can be observed, expediting treatment replanning.[7,13,14]

Although it is imperative to optimize IGRT techniques to improve pediatric disease outcomes, it is also important to minimize the cumulative radiation exposure to normal tissues from IGRT, thus reducing late effects.[15-17] Volumetric and frequent imaging prolongs the treatment time, which is unsatisfactory for older, unsedated children, who may find it difficult to maintain their position, or for children who require extended imaging volumes for craniospinal, whole-abdomen, or whole-lung irradiation. Prolonging the anesthesia times for younger children also entails risks that should be minimized. The additional costs and secondary cancer risk due to the added radiation exposure have been reported for CBCT and portal imaging.[14,18] The Image Gently Alliance for pediatric patients,[19] endorsed by the American College of Radiology (ACR), the American Society for Radiologic Technologists (ASRT), and the American Association of Physicists in Medicine (AAPM), recommends using lower radiation doses when imaging children.

The Children's Oncology Group (COG) has reported on the portal imaging practice patterns of member institutions and provided recommendations to minimize unnecessary radiation exposure without compromising verification accuracy.[10] A consensus on IGRT among pediatric providers remains complex because the evolving technology has resulted in practice preferences, imaging frequency, and verification protocols varying greatly among institutions. The adult IGRT protocols are suboptimal for imaging the distinct pediatric malignancies with their diverse prognostic implications, disease-specific treatments, and risk of unique late toxicities. The COG Radiation Oncology Discipline designed two surveys to understand clinical and technical practice patterns of pediatric IGRT among member radiation oncologists and affiliated medical physicists. This report summarizes the survey results and provides expert recommendations on IGRT practice in children.

2 | MATERIALS AND METHODS

2.1 | Survey participants

A total of 347members of the COG Radiation Oncology Discipline at national and international institutions were invited to participate in the survey of practice patterns of IGRT in patients aged 21 years or younger (entire questionnaire in Supporting File I). Participants were eligible if they had a valid email address, were working at the institution, and did not have a suspended membership.

2.2 | Survey protocol

The survey was conducted between October 27, 2017, and December 17, 2017, by using the COG Survey Monkey website. After the survey responses were received, the COG Radiation Oncology Discipline created a task force to summarize current data on radiation exposure during IGRT and develop pediatric IGRT guidelines for modern use. These guidelines were then reviewed by the 10 disease-site committees and the COG before a consensus recommendation was reached.

2.3 | Clinical survey questions for radiation oncologists

The physicians completed a 39-item clinically oriented survey that included a series of demographic questions and clinical scenarios. Because of the diverse tumor histologies, disease sites, and management strategies, we created 11 disease-specific vignettes (Supporting File II) with both closed- and open-ended options to elicit the participants' description of clinical practice most effectively. For each vignette, physicians were asked to identify their preferred treatment technique (photons-parallel opposed, 3D conformal radiation therapy [CRT], IMRT/VMAT, TomoTherapy , PT, or other), preferred method of image guidance (none, megavoltage planar imaging [MVi], kilovoltage planar imaging [kVi], kilovoltage [kV] stereotactic imaging, megavoltage [MV] CBCT, kV CBCT, in-room CT, or other, and frequency of in-room verification (daily, weekly, first week, daily 2D and weekly 3D imaging, frequently in the beginning and weekly thereafter, or other). kVi, MVi, and kV stereotactic imaging represent 2D planar imaging modalities, which help verify patient position predominately based on bony anatomy and static treatment volumes. kV and MV CBCT, in-room CT, and MV CT are 3D volumetric imaging modalities, offering better visualization of soft tissues and body surface.

2.4 | Technical survey questions for medical physicists

The physicists received a 23-item technical survey. The technical questions concerned institutional capabilities for treating pediatric malignancies (IMRT, brachytherapy, high-dose-rate [HDR] brachytherapy, stereotactic radiosurgery [SRS], stereotactic body radiotherapy [SBRT], and 4D simulation), the pediatric-specific IGRT image-acquisition protocol, and technical practice patterns. Additional specific questions encompassed PT practice, setup corrections, measures to facilitate dose reduction, and the use of adaptive therapy. IGRT credentialing has been a requirement for several COG sarcoma trials. Based on data obtained from the Imaging and Radiation Oncology Core (IROC Houston and Rhode Island), among 212 COG centers, 68 sites are credentialed for IGRT using bony landmarks and 115 COG sites that are credentialed for IGRT in soft tissue. For PT, 31 proton centers are approved to enroll patients on National Cancer Institute–funded clinical trials. All 31 centers have 2D image guidance capability, and 16 centers can perform 3D image guidance.

2.5 | Perspectives on IGRT

Based on Likert rating scales, physicians and physicists were asked to provide their perspectives on the importance of various IGRT-related topics. Concepts included, but were not limited to, the risk of secondary malignancies, setup margins, workflow efficiency, imaging dose reduction strategies, and immobilization techniques. Each respondent rated their agreement with the various IGRT priorities on a scale from 1 to 5, with 5 representing the greatest agreement and 1 representing the least agreement (Table 3).

3 | RESULTS

3.1 | Participant demographics and institutional capabilities

Details are presented in Tables 1 and 2. Of the 347 individuals to whom surveys were sent, 105 physicians and 63 physicists responded, resulting in 168 evaluable responses (a 48% response rate). Most institutions (47%) treated more than 30 children annually. Conventional linac photons (95%) and electrons (92%) were the most commonly available treatment modalities for managing pediatric malignancies. Only 20% of physicians reported having direct access to PT.

3.2 | Preferences and perspectives regarding pediatric IGRT

Both physicians and physicists were queried about areas for future practice improvement. Specific to IGRT, most physicians (54%) and physicists (71%) strongly agreed that image guidance improved treatment outcomes. On the possibility of radiation exposure from image guidance posing a nonnegligible risk of secondary cancer, 37% physicians and 39% physicists either agreed or strongly agreed. A similar percentage of respondents expressed a neutral position. There was strong agreement among both physicians (55%) and physicists (54%) on the importance of identifying setup margins with IGRT. The priorities determined by respondents to additional topics relating to future practice improvement are presented in Table 3.

3.3 | Clinical scenario–based questions for radiation oncologists

A collective summary of the responses throughout all disease sites regarding the recommended treatment technique, image guidance, and in-room verification is presented in Figure 1A-C. As the survey did not ask what individuals would do *if* they had all imaging or treatment

TABLE 1 Demographics and institutional capabilities reported by physicians in the Children's Oncology Group pediatric IGRT survey

Survey item	Responses (%)
Number of physician responses	N = 105
Institution location	
The United States	86 (81)
Canada	9 (9)
Australia	9 (9)
Middle East	1 (1)
Number of pediatric patients treated per year	
< 11	11 (15)
11-20	23 (22)
21-30	19 (18)
> 30	47 (45)
What modalities are available to treat pediatric patients?	
Conventional linac photons	100 (95)
Conventional linac electrons	97(92)
Stereotactic radiosurgery	93 (89)
Stereotactic body radiotherapy	88 (84)
Brachytherapy	71 (68)
CyberKnife	23 (22)
TomoTherapy	21 (20)
Protons	21 (20)
Combined MR-cobalt or MR-linac	2 (2)
Carbon ions	0 (0)
Do you incorporate fiducials into your practice?	
Yes, regularly	11 (11)
Occasionally, if surgical implants such as hardware or clips are not already in place	54 (52)
No	39 (37)

TABLE 2 Institutional capabilities reported by physicists in the Children's Oncology Group pediatric IGRT survey

Survey item	Responses (%)
Number of medical physicist responses	***N* = 63**
Which institutional modalities are available to treat pediatric patients?	
Intensity-modulated radiation therapy	62 (98)
Stereotactic body radiotherapy	61 (97)
Four-dimensional simulation	60 (95)
Stereotactic radiosurgery for central nervous system tumors	58 (92)
HDR brachytherapy[a]	55 (92)
Image registration methods for body tumors	
We combine multiple methods.	25 (40)
We rely on bony anatomy.	22 (35)
We rely on soft tissues.	11 (15)
We rely on fiducial markers.	5 (8)
Do physicians discuss with physicists pros and cons of IGRT technique and frequency for specific patients?	
Yes	56 (89)
No	7 (11)
Current institutional practice if your institution offers proton therapy[b]	
We rely on 2D IGRT and other techniques and will not/cannot incorporate 3D volumetric imaging.	1 (2)
We rely on 2D IGRT and other techniques but plan to incorporate 3D volumetric imaging in future.	0 (0)
We currently utilize 3D volumetric image guidance for selected pediatric proton therapy patients.	4 (6)
We currently utilize 3D volumetric image guidance for all pediatric proton therapy patients.	1 (2)
Our institution currently does not have proton capabilities.	57 (90)

Abbreviations: HDR, high dose rate; IGRT, image-guided radiation therapy.
[a]Only 60 responses.
[b]As of April 8, 2020, the record of proton facility questionnaire at IROC Houston indicates all 31 proton centers which were approved to enroll patients in NCI-funded cooperative group trials have 2D image guidance capability whereas only 16 of them have 3D on-board imaging.

modalities, the stated preference may be biased by the availability of IGRT technologies and also insurance approval.

3.4 | Ependymoma

As shown in Figure 1, the most commonly reported IGRT method for ependymoma was IMRT/VMAT (52%) or PT (35%, treat locally or referral) guided by daily (69%) in-room verification using kVi (28%) or CBCT (26%) or a combination thereof (23%).

3.5 | Craniopharyngioma

For craniopharyngioma treatment, many respondents supported the use of IMRT/VMAT (51%) or PT (38%) guided with daily (61%) kV CBCT (25%) or combined kV CBCT/kVi (32%).Regarding tumor changes during radiotherapy, 86% respondents agreed with the importance of reassessment. Magnetic resonance imaging (MRI) was performed weekly by 15% of the respondents, every other week by 3%, first week only by 2%, and midway through course by 1%.

TABLE 3 Prioritization and understanding of IGRT-related topics by medical doctors (MDs) and medical physicists (MPs)

Agreement	(1 = strongly disagree; 5 = strongly agree) 1	2	3	4	5	Total responses	Average
	Responses *N* (%)						
1. Image guidance improves treatment outcomes.							
MPs	2 (3)	0 (0)	4 (7)	12 (19)	45 (71)	63	4.6
MDs	1 (1)	3 (3)	17 (16)	27 (26)	57 (54)	105	4.3
2. Radiation exposure from image guidance poses a nonnegligible risk of secondary cancer and, therefore, should be lowered.							
MPs	3 (5)	12 (19)	23 (37)	16 (25)	9 (14)	63	3.3
MDs	9 (9)	17 (16)	40 (38)	28 (27)	11 (10)	105	3.1
3. It is a high priority to improve image quality (DRR, portal images, CT, CBCT) and/or soft-tissue contrast.							
MPs	1 (2)	1 (2)	11 (17)	22 (35)	28 (44)	63	4.2
MDs	0 (0)	6 (6)	17 (16)	40 (38)	42 (40)	105	4.1
4. It is a high priority to determine appropriate setup margins with IGRT.							
MPs	0 (0)	3 (5)	2 (3)	24 (38)	34 (54)	63	4.4
MDs	1 (1)	2 (2)	8 (8)	36 (35)	57 (54)	104	4.4
5. Better tools or workflow is needed to reduce the time spent on image review and approval.							
MPs	2 (3)	8 (13)	16 (25)	16 (25)	21 (34)	63	3.7
MDs	5 (5)	14 (13)	22 (21)	39 (37)	25 (24)	105	3.6
6. It is important to develop nonionizing image guidance techniques.							
MPs	3 (5)	6 (9)	18 (29)	21 (33)	15 (24)	63	3.6
MDs	2 (2)	6 (6)	30 (29)	34 (32)	33 (31)	105	3.9
7. It is necessary to estimate age- and organ-specific doses from radiological image guidance procedures and implement imaging dose reduction strategies.							
MPs	1 (2)	11 (17)	18 (29)	23 (36)	10 (16)	63	3.5
MDs	0 (0)	6 (6)	27 (26)	37 (36)	33 (32)	103	3.9
8. It is important to establish practice guidelines such as optimal imaging frequency, recommended age-specific planar X-ray techniques, and CBCT scan protocols.							
MPs	1 (2)	1 (2)	10 (16)	24 (38)	27 (42)	63	4.2
MDs	3 (3)	4 (4)	15 (14)	45 (43)	37 (36)	104	4.1
9. It is important with IGRT to improve immobilization and reproducibility.							
MPs	1 (2)	0 (0)	1 (2)	14 (22)	47 (74)	63	4.7
MDs	3 (3)	2 (2)	9 (9)	31 (29)	60 (57)	105	4.4
10. It is important to facilitate adaptive replanning, e.g., to improve the CT number accuracy of CBCT for dose escalation and efficient replanning workflow.							
MPs	3 (5)	1 (1)	12 (19)	30 (48)	17 (27)	63	3.9
MDs	0 (0)	8 (8)	28 (27)	34 (32)	35 (33)	105	3.9
11. There are no pressing needs for pediatric IGRT. Efforts should focus on other tasks.							
MPs	26 (41)	22 (35)	7 (11)	6 (10)	2 (3)	63	2.0
MDs	45 (43)	33 (32)	16 (15)	9 (9)	1 (1)	104	1.9

Abbreviations: CBCT, cone-beam computed tomography; CT, computed tomography; DRR, digital reconstructed radiograph.

3.6 | Germinoma

The most commonly reported focal treatment strategy for central nervous system (CNS) germinoma was IMRT/VMAT (59%) or PT (29%) with daily (68%) kV CBCT (30%), kVi (25%), or combined kV CBCT/kVi (23%).

3.7 | Medulloblastoma

The most frequently reported technique for managing pediatric medulloblastoma with craniospinal irradiation was PT (52%) or, less commonly, IMRT/VMAT (20%) guided with daily (74%) kVi (33%) or combined kV CBCT/kVi (24%).

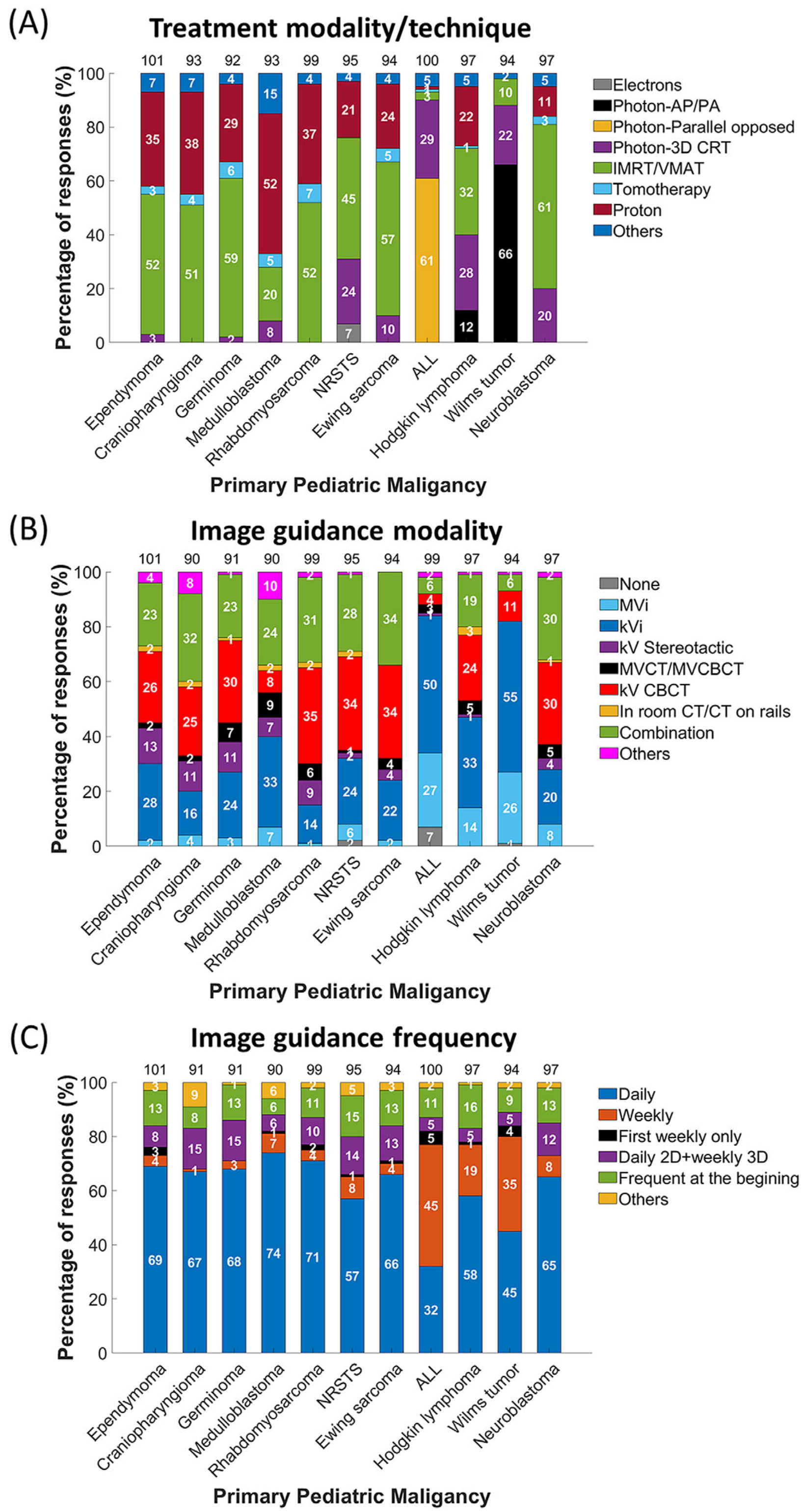

FIGURE 1 Clinical scenario–based survey outcomes for (A) treatment modality/technique, (B) image guidance modality, and (C) image guidance frequency. The number on top of each column represents the number of responses
Abbreviations: ALL, acute lymphocytic leukemia; AP/PA, anteroposterior/posteroanterior; CBCT, cone-beam computed tomography; CRT, conformal radiotherapy; CT, computed tomography; IMRT/VMAT, intensity-modulated radiotherapy/volumetric modulated arc therapy; kVi, kilovoltage imaging; MVi, megavoltage imaging; NTSTS, non-rhabdomyosarcoma soft-tissue sarcoma; 3D, three-dimensional

3.8 | Rhabdomyosarcoma

IMRT/VMAT (52%) and PT (37%) were the most reported management modalities for the rhabdomyosarcoma vignette, with 71% of respondents suggesting daily imaging using kV CBCT (35%) or combination (31%).

3.9 | Non-rhabdomyosarcoma soft-tissue sarcoma

The favored approaches to managing non-rhabdomyosarcoma soft-tissue sarcoma (NRSTS) were IMRT/VMAT (45%), 3D CRT (24%), and PT (21%) guided by daily (57%) kV CBCT (34%), combined CBCT/kVi (28%), and kVi (24%).

3.10 | Ewing sarcoma

For treating Ewing sarcoma, many providers recommended IMRT/VMAT (57%) or PT (24%) guided with daily (66%) kV CBCT (34%), combined CBCT/kVi (34%), or kVi (22%).

3.11 | Acute lymphoblastic leukemia

For patients with CNS-3 leukemia receiving whole-brain radiotherapy, most respondents reported the use of photon therapy with parallel-opposed fields (61%) or 3DCRT (29%) guided with daily (45%) or weekly (32%) kVi (50%) or MVi (27%). No image guidance (i.e., using skin/mask markings) was reported by 7%.

3.12 | Hodgkin lymphoma

Clinician preferences for the Hodgkin lymphoma case included IMRT/VMAT (32%), 3DCRT (28%), and PT (22%) guided by daily (58%) kVi (33%), CBCT (24%), or combined CBCT/kVi (19%).

3.13 | Wilms tumor

Preferred methods for treating flank or whole abdomen in Wilms tumor patients involved anteroposterior/posteroanterior photons (66%) guided by daily (45%) or weekly (35%) kVi (55%).

3.14 | Neuroblastoma

The favored management for high-risk neuroblastoma included IMRT/VMAT (61%) guided by daily (65%) kV CBCT (30%) or combined kV CBCT/kVi (30%).

3.15 | Technical survey for medical physicists

3.15.1 | Institutional capabilities and image registration

The participating physicists reported institutional capabilities specifically for treating pediatric malignancies. As detailed in Table 2, 98% respondents reported IMRT capability. For image registration for body tumors, 35% relied on bony anatomy and 40% combined multiple methods or were case, disease site, modality, or physician dependent.

3.15.2 | Setup corrections

For intracranial tumors in a non-SRS setting, 53% of responding physicists reported correcting patient setup regardless of how small the calculated shifts were, whereas others used tolerances of 1 mm (19%), 2 mm (16%), 3 mm (2%), or > 3 mm (3%). Reimaging to confirm patient setup after correction was completed only for shifts that exceeded a certain amount by 34% of respondents: 19% did not reimage at all, 18% reimaged only after SRS/SBRT or suspected patient movement, 15% always reimaged, and 15% had other responses. The use of 6DOF couches and both translational and rotational setup corrections with pediatric patients varied greatly between institutions. The percentage of physicists with 6DOF couches that they used for none, 0-50%, 50%-75%, and 75%-100% of their pediatric patients was 34%, 32%, 12%, and 23%, respectively.

3.16 | Pediatric-specific IGRT image-acquisition protocols and dose reduction

Most (85%) agreed that using IGRT changed their setup margin or the clinical target volume (CTV) robustness parameter setting. Regarding modifications of the manufacturer's default adult IGRT protocols for pediatric patients, most physicists (54%) elected to reduce the kilovoltage peak (kVp)/milliampere second (mAs) setting. However, those who did not reduce the setting stated that there was a lack of guidelines (39%), did not consider there was a need to reduce the setting (3%), or were not allowed to modify vendor protocols (3%). Most physicists (60%) recommended incorporating site-specific pediatric imaging protocols into routine practice. Most institutions neither routinely documented the imaging dose (89%) nor subtracted the image guidance dose from the prescribed dose (95%), with 64% considering the imaging dose to be insignificant when compared with the treatment dose, with no evidence that it posed a high risk to patients. Of those physicists who did not subtract the imaging dose from the prescribed dose or document the dose, 62% answered that it was not possible to incorporate the dose accurately, whereas 25% felt that it was possible and 13% responded "N/A" (i.e., accounting for the imaging dose was not necessary). As listed in Table 4, the most common method to measure image guidance doses was using an ion chamber with a CT dose index phantom (67%). The most common institutional efforts to reduce image guidance dose were lowering the mAs/kVp or using low-dose protocols from vendors (65%) and using kV imaging in preference to MV techniques (63%) (Table 4).

3.17 | Adaptive planning

Most physicists reported a routine practice of adaptive planning during the treatment course to address tumor or anatomic changes (64%). For nine physicists in institutions offering PT, six respondents (67%) routinely performed adaptive PT, whereas three (33%) did not. Of the 62 of 63 physicists who responded to this question, 79% represented institutions that used setup verification images from image guidance procedures to trigger or make decisions regarding adaptive planning.

TABLE 4 Institutional measures to calculate/estimate and reduce the image guidance dose to pediatric patients

Survey item	Responses (%)
Methods/tools to calculate or measure image guidance dose	
Ion chamber with CTDI phantom	38 (67)
Ion chamber/TLD/MOSFET/OSLD with anthropomorphic phantom	6 (10)
TLD/MOSFET on patient	4 (7)
Treatment planning modeling of imaging beam	0 (0)
Monte Carlo simulation	0 (0)
Not calculated or measured	9 (16)
Methods to reduce image guidance dose	
Lower mAs/kVp or use low-dose protocols from vendors	41 (65)
Use of kV instead of MV	40 (63)
Use of collimation to reduce scan range	30 (48)
Imaging less frequently	24 (38)
Utilize age- and size-specific protocols	19 (30)
Upgrade image guidance software and hardware	13 (21)
Supplement with nonionizing techniques	9 (14)
Add filtration or shielding	1 (2)
None	5 (8)

Abbreviations: CTDI, computed tomography dose index; kVp, kilovoltage peak; mAs, milliampere second; MOSFET, metal-oxide semiconductor field-effect transistor; MV, megavoltage; OSLD, optically stimulated luminescence detector; TLD, thermoluminescent dosimeter.

4 | DISCUSSION

4.1 | Key observations

It is well recognized that image-guided techniques increase accuracy of patient positioning, which enables normal tissue sparing by reducing the safety margin around tumor. As a result, this increases the confidence and utilization of treatment technologies that produce sharp dose gradients, including IMRT/VMAT and PT. The COG survey results indicate that pediatric radiation oncologists have embraced frequent image guidance by incorporating it into their clinical practice. However, treatment techniques and image guidance modality varied greatly among clinicians. Pediatric-specific IGRT image-acquisition protocols and dose reduction methods remain underdeveloped. Physicists cited the lack of guidance as the main reason why adult IGRT protocols continue to be applied to children.

4.2 | Frequency of image guidance

The survey found that daily imaging guided by kVi, CBCT, or combined kVi/CBCT in-room verification was the predominant strategy for patient-specific diseases for approximately 70% of respondents except for whole-brain and whole-abdomen radiotherapy. Alternatively, parallel-opposed photon beams for leukemia and anterior/posteriorphoton beams for Wilms tumor were favored. Both daily and weekly imaging guided by MVi or kVi were more commonly preferred for these two diseases.

The survey shows that 70% of physicians conducted daily imaging with either planar (e.g., kVi) or volumetric (e.g., CBCT) imaging for children with brain tumors or rhabdomyosarcomas to ensure appropriate setup. The prevalence was slightly lower (57%-66%) for NRSTS, Ewing sarcoma, neuroblastoma, and Hodgkin lymphoma. The International Pediatric Research Consortium reported the use of daily image guidance in approximately 60% of institutions for children with CNS, abdomen/pelvis, or head and neck cancers.[7] Seventy-four percent of participants in the International Paediatric Radiation Oncology Society survey stated that the same imaging frequency was used for both adults and children with CNS tumors.[12] The national survey of American Society for Radiation Oncology (ASTRO) members reported daily image guidance rates of 62%-96%.[20] However, daily image guidance for brain tumors in adults was much lower at 18%. Differences in the imaging techniques reported in other series may be secondary to the patient population, treatment modalities, and available resources.

4.3 | 2D versus 3D image guidance

The COG survey showed that up to 38% and 42% of the clinicians would use solely 3D image guidance for focal radiotherapy at brain and body sites, respectively. In contrast, the 2016 ASTRO survey[20] found that 60% and 66%-77% of respondents used 3D IGRT for adult brain and body tumor sites, respectively. Differences between adult and pediatric practices might reflect the concerns regarding the imaging dose and increased anesthesia/treatment time.[7] Although bony landmarks visible on kVi are generally believed to serve as reliable surrogates for localizing intracranial targets, CBCT enables planning marginreduction.[7,13,21] For craniopharyngioma with both solid and cystic components, MRI can detect the dynamic cystic change during the radiotherapy course. Periodic,[22] biweekly,[23] or weekly[24] MRI to assess the necessity of adaptive therapy has been recommended in craniopharyngioma treatment.

4.4 | Organ doses from IGRT procedures in pediatric patients

The IGRT literature describes the use of a wide range of doses depending on the imaging modality, beam quality, imaging technique, and patient size. Organ dose estimates for CBCT have been tabulated by Alaei and Spezi,[25] and similar tables for other imaging modalities were included in the AAPM TG-75 and TG-180 reports.[18,26] However, data are scarce on organ doses resulting from IGRT procedures in pediatric patients.[27] Table 5 provides sample organ doses for pediatric patients imaged with various CBCT protocols using Elekta kV X-ray volume

TABLE 5 Examples of pediatric organ doses calculated from Elekta kV XVI CBCT scans[28,29,a]

Age group (years)	Organ dose per scan (mGy)												
Low-dose/head and neck protocol—S20 Cassette, 100 kVp, 0.1 mAs/frame, 205 degrees rotation, 366 frames													
	Bladder	**Rectum**	**Bowel**	**R kidney**	**L kidney**	**Liver**	**Stomach**	**Spleen**	**Heart**	**R lung**	**L lung**	**Esophagus**	**Gonads**
2-5	1.1	0.8	1.2	0.7	1.1	0.9	1.3	1.3	1.2	0.9	1.1	0.9	0.9
6-10	1.0	0.7	0.9	0.6	0.8	0.8	1.1	1.1	1.1	0.8	1.1	[b]	1.0
11-15	0.7	0.5	[b]	0.5	0.9	0.7	1.1	1.1	1.0	0.7	0.9	0.8	[b]
	Brain	**Brainstem**	**Chiasm**	**R optic nerve**	**L Optic Nerve**	**R cochlea**	**L cochlea**	**R eye**	**L eye**	**R lens**	**L lens**	**Pituitary**	**Thyroid**
2-5	0.9	0.9	1.05	1.1	1.3	0.8	1.3	1.25	1.6	1.35	1.7	1.1	1.2
6-10	1.0	1.0	1.1	1.0	1.3	0.8	1.3	1.2	1.6	1.6	1.6	1.0	1.0
11-15	[b]	[b]	[b]	[b]	[b]	[b]	[b]	[b]	[b]	[b]	[b]	[b]	[b]

Age group (years)	Organ dose per scan (mGy)													
Medium dose/thorax protocol—L20 Cassette, 120 kVp, 0.25 mAs/frame, 360 degrees rotation, 660 frames														
	Bladder	**Rectum**	**Bowel**	**R kidney**	**L kidney**	**Liver**	**Stomach**	**Spleen**	**Heart**	**R lung**	**L lung**	**Esophagus**	**Thyroid**	**Gonads**
2-5	5.5	4.6	5.2	5.2	4.9	5.0	5.0	5.1	5.5	4.8	4.7	5.1	5.8	4.9
6-10	5.1	4.5	4.3	4.1	4.4	4.7	4.3	4.6	4.8	4.6	4.4	[b]	5.3	4.4
11-15	3.3	3.4	[b]	4.2	4.1	4.1	4.6	4.3	4.5	4.0	4.0	5.0	4.3	
High dose/pelvis protocol—M20 Cassette, 120 kVp, 1.0 mAs/frame, 360 degrees rotation, 660 frames														
	Bladder	**Rectum**	**Bowel**	**R kidney**	**L kidney**	**Liver**	**Stomach**	**Spleen**	**Heart**	**R lung**	**L lung**	**Esophagus**	**Thyroid**	**Gonads**
2-5	29.8	25.9	31.9	30.1	30.5	29.9	29.2	32.9	31.2	29.3	29.4	25.9	34.2	27.2
6-10	26.8	24.5	24.7	23.4	24.2	25.9	25.3	24.6	27.8	26.1	25.7	33.1	33.4	23.6
11-15	17.4	16.8	[b]	22.6	22.0	22.1	25.3	23.9	23.3	23.0	21.6	24.8	20.4	

Conditions: CBCT scans were performed with the isocenter placed approximately at the patient midline. All organs listed were fully within the imaged volume. Effects of the treatment couch were ignored. Doses reported are average organ doses computed using a treatment planning system. The dose to bone was underestimated by this method; hence, bony structure doses were not included. Number of patients analyzed for calculating average values: 7 in the age 2-5 group, 5 in the 6-10 group, and 4 in the 11-15 group.

Abbreviations: CBCT, cone-beam computed tomography; L, left; R, right.

[a]Organ doses were calculated based on the methods described in these publications.

[b]No data available.

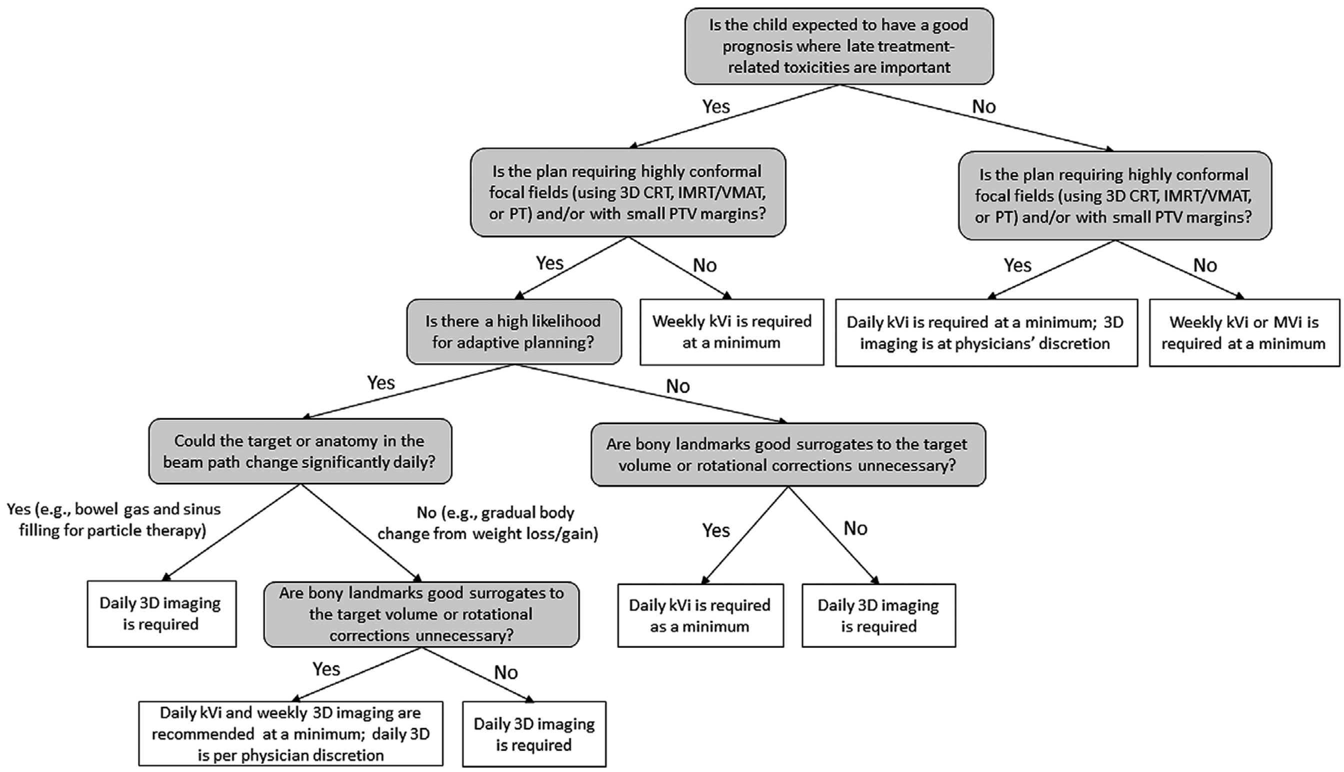

FIGURE 2 Recommended image guidance decision tree for pediatric IGRT
Abbreviations: CRT, conformal radiotherapy; IMRT/VMAT, intensity-modulated radiotherapy/volumetric modulated arc therapy; kVi, kilovoltage imaging; MVi, megavoltage imaging; PT, proton therapy; PTV, planning target volume; 3D, three-dimensional

imaging (XVI). The organ doses were calculated using a treatment planning system with an imaging beam model.[28,29]

Often presumed insignificant, portal imaging can also contribute an excessive radiation dose to pediatric patients, especially with double-exposure techniques, ranging up to 0.75 to 2.5 Gy over a treatment course for MV port films.[30,31] More recently, Deng et al.[32] provided Monte Carlo–calculated organ doses from kVi/CBCT and concluded that critical structures in pediatric patients receive imaging doses two to three times greater than those in adults. For a given kV CBCT protocol, organ doses increase with decreasing patient size and body mass index, making it important to consider size-specific protocols.[29,33] As a result, using adult imaging protocols for pediatric imaging will ultimately increase the radiation dose burden for children.[32,34,35]

4.5 | Risks of secondary malignancies from IGRT procedures

Accurately predicting the adverse effects and risk of death in individuals exposed to radiation doses of less than 100 mSv remains challenging. The Biological Effects of Ionizing Radiation (BEIR) VII Committee reported on the risks from medical imaging radiation, acknowledging the limitations and uncertainties of risk estimates.[36] Zhou and colleagues recently reported the cumulative imaging doses from IGRT and the associated secondary cancer risk of 4832 cancer patients.[37] Based on BEIR VII models, the associated average lifetime attributable risks of cancer incidence per 100 000 persons were estimated to be 78, 271, and 510 for brain cancer, lung cancer, and leukemia patients, respectively. However, we advise caution when calculating the secondary cancer risk from low-dose exposures in patients with cancer receiving radiotherapy by using models derived from atomic-bomb survivors. The study by Little determined that, in many organs, the risk per Gy was substantially lower for therapeutic irradiation than for non-therapeutic exposures.[38] In any case, it is prudent to limit the imaging dose to what is minimally needed to provide the information required.

Despitethe risks associated with image guidance, its potential advantages must be acknowledged.[9,39] The significantly reduced setup margin will decrease the dose not only to adjacent healthy tissues near the target that are exposed to higher doses of radiation but also to those tissues distal from the target that are exposed to lower doses, thereby diminishing the risk of secondary cancers. As a result of the use of smaller margins and better positioning with IGRT, higher therapeutic doses are more frequently delivered with modern advanced radiotherapy techniques such as SRS, SBRT, and VMAT. The benefits of being able to make informed decisions about margins, adapt the target volume during treatment, and ensure accurate treatment delivery outweigh the risk of secondary cancer that results from diagnostic imaging or other low-dose exposures.

TABLE 6 Choose wisely recommendations for pediatric IGRT practice

The following recommendations for wise selection of pediatric IGRT are based on the community practice revealed by the COG survey results, existing evidence, and COG member consensus.

Image guidance modality

- Guiding 2D treatments with 2D kV imaging is generally sufficient without 3D imaging and normally gives a lower imaging dose. These treatments may include whole-brain irradiation for acute lymphocytic/lymphoblastic leukemia, nodal irradiation fields for lymphoma, or flank/whole-abdomen radiotherapy for Wilms tumor.
- 3D imaging is recommended when bony landmarks are not reliable surrogates for tumor positions, when margins are small, or when rotational corrections are needed without the guidance of implanted fiducials.Consider 3D imaging to reduce margins before prioritizing 2D imaging to reduce imaging dose.
- Do not use MV imaging for more than verifying the field shape on the first fraction unless the low-dose setting is adopted. Consider an alternative method of using the light field projection on field shape diagram in advance.
- Be cautious about electron therapy and light field verification without image guidance for superficial tumors such as chest wall sarcoma. The majority of pediatric radiation oncologists favor conformal treatment with image guidance.

Imaging frequency

- Do not rely solely on weekly imaging at the start of 3D CRT, including CSI beam placement. Such practice is uncommon. Consider reducing imaging frequency to weekly only after daily imaging has confirmed stable anatomy.
- Do not reduce the imaging frequency solely in an effort to reduce the imaging dose. The benefits of accurate tumor targeting with reduced margins may outweigh the risk from the imaging dose.
- Minimize repeated imaging in a session to adjust the patient position. Improve patient setup procedures and immobilization devices to minimize multiple exposures.

Imaging dose reduction

- When both MV and kV imaging are available on the same treatment delivery system, choose kV to reduce imaging dose to patients.
- Use field-limiting devices (e.g., blades, collimators, cassettes) to block radiation-sensitive organs (e.g., lens, thyroid, gonads) if target verification is not compromised.
- When volumetric image guidance is preferred in situations where only bony anatomy is used for registration (e.g., for rotational correction), utilize institutional 3D low-dose image-acquisition techniques. Superior guidance can still be provided without exposing patients to a significantly higher dose than that with 2D X-rays.
- Do not directly apply imaging guidance techniques designed for adults to young children without modifications. If it is not possible to modify technique parameters such as mAs, consider using the vendor's low-dose techniques.
- Consider using non-ionizing position verification methods (e.g., surface imaging or MRI guidance) to replace or supplement ionizing radiation methods whenever possible.

Abbreviations: CNS, central nervous system; COG, Children's Oncology Group; CRT, conformal radiotherapy; CBCT, cone-beam computed tomography; CSI, craniospinal irradiation; IGRT, image-guided radiotherapy; kV, kilovoltage; mAs, milliampere second; MRI, magnetic resonance imaging; MV, megavoltage; RO, radiation oncologist; RT, radiotherapy; 2D, two-dimensional; 3D, three-dimensional.

4.6 | Strategies for reducing the image guidance dose

Methods to reduce the imaging dose to patients include using separate techniques for smaller patients; reducing the imaging field size by either closing the blades or using cassettes instead of open fields; using an appropriate kVp for the imaged site; using kVin preference to MV; reducing the total mAs; using a decreased angular range or projection number for CBCT acquisition; and avoiding repeated imaging with an improved setup device/procedure. These strategies can be employed if they do not compromise image interpretation. For example, administering an adult head-and-neck rather than abdomen/pelvis imaging protocol to image a pediatric abdomen/pelvis could decrease the imaging dose by a factor of 18.[40] When only bony anatomy visualization is needed for CBCT, reducing the kV from 100 to 80 and the mAs by a factor of 3 will reduce the dose by a factor of approximately 8 from that with the standard linac imaging protocol, yet the resulting images will be no less accurate in 3D matching with the planning CT images.[41] Iterative CBCT reconstruction is now commercially available, providing the opportunity to further reduce the imaging dose without sacrificing image quality.[42]

Surface imaging does not employ ionizing radiation. This method may help reduce the need for repeated imaging by guiding the initial setup for IGRT and monitoring patient motion during treatment.MR-linac or MR-cobalt systems are recent inventions that localize and track tumors without relying on ionizing radiation.[43] Although our surveyed respondents reported very limited use of surface imaging and MR guidance for positioning, we encourage publications on the accuracy and practical implementation of this technology for pediatric patients.

4.7 | Weaknesses and limitations of the survey

One main limitation of this study is that not all members responded to the survey. Because the data were anonymized, interpretations of the data were limited by an inability to relate the responses to large versus small centers and the available resources. It was also not possible to determine why nonrespondents did not reply, and this could lead to biased estimates of IGRT application. Furthermore, a bias may exist for those individuals more likely to respond to the survey, depending on their prior experience with IGRT or their current institutional capabilities and limitations guided by insurance authorization. As the survey did not ask what individuals would do if they had all imaging modalities, the stated preference for imaging modality (2D or 3D) and treatment modality (IMRT or PT) may be biased by the availability of IGRT technologies and also insurance approval. Finally, the use of internal, national, and international guidelines and the demands of trials can also bias practice and this was not fully explored.

4.8 | Recommendations

Based on the survey results and expert consensus, the COG Radiation Oncology Discipline recommends using the IGRT modality/frequency decision tree (Figure 2) and the Choose Wisely recommendations (Table 6) for using ionizing image guidance in pediatric radiotherapy patients. These recommendations are meant to optimize the benefits of IGRT to accurately treat the tumor while minimizing the long-term risks of normal tissue radiation exposure from image guidance modalities.

5 | CONCLUSIONS

The COG survey shows that daily image guidance was used approximately 60%-70% of the time for most disease sites. Although disease specific, kVi was most commonly used for simple treatments, CBCT was more frequently used for complex treatments. We present recommendations to optimize the benefits of IGRT while minimizing the long-term risks of normal tissue radiation exposure. Further research is required to establish the risks from imaging doses, to provide guidance on pediatric imaging techniques, to develop nonionizing image guidance approaches, to reduce setup margins, to optimize positioning of pediatric patients, and to conduct cost-benefit analyses.

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CONFLICTS OF INTEREST

The authors declared no conflict of interest related to this study.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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