A Baseline Survey on the Treatment Workflow and Pediatric IGRT Practice Among European Members of the Project-Based Consortium and the Pediatric Radiation Oncology Society (PROS).

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Abstract

Background Image-guided radiotherapy (IGRT) enables high precision tumor treatment with potential for sparing healthy tissues. The value of pediatric IGRT is widely acknowledged, but there is no consensus on 'best practice'. We aimed to assess clinical pediatric IGRT practice among European members of the Pediatric Radiation Oncology Society (PROS) and members of our project-based consortium.

Methods A survey addressing radiotherapy preparation, planning and delivery in seven treatment sites was sent to European PROS members and/or our IGRT project-based consortium (70 institutes). Responses were collected from June-September 2018.

Results Of the 42 responding institutes (response rate 60%), 33 indicated to treat children. 28/33 are photon-only institutes, 3/33 are dedicated proton ('proton-only') institutes and 2/33 use both. Immobilization includes facial masks (in 100% of brain, craniospinal axis (CSA) and head-and-neck (H&N) treatments), and vacuum cushions (all sites, except brain and H&N). Intensity-modulated radiotherapy and volumetric-modulated arc therapy are most frequently applied ranging from 71%-81% in respectively CSA (20/28), and extremities (21/26), followed by 3D conformal radiotherapy ranging from 36%-69% in respectively H&N (10/28), and extremities (18/26). Isotropic planning target volume (PTV) margins varied widely in brain and abdomen (range, 1-10mm). The use of in-room kilovolt cone-beam computed tomography ranges from 57%-86% in respectively CSA (16/28), and thorax (24/28). Daily online imaging is used by the majority of institutes, ranging from 85%-90% in respectively extremities (22/26) and pelvis (27/30). Offline imaging protocols are used by 14%-21% in respectively H&N (4/28) and thorax (6/28).

Conclusions Our survey shows comparable practice in pre-treatment imaging, planning and treatment techniques, and IGRT application among the participating European institutes. However, wide ranges in PTV margin sizes exist, supporting the need to define international 'best practice' guidelines for pediatric IGRT, and to aim for consensus on optimal margin definitions in view of available IGRT facilities and workflows among institutes.

Background

Long-term childhood cancer survival has significantly increased over recent decades, mainly due to multimodality treatment strategies combining surgery, chemotherapy and radiotherapy (1, 2). The quality of radiotherapy delivery has improved with the introduction of image-guided radiotherapy (IGRT), enabling high precision tumor treatment with potential for sparing healthy tissues. IGRT generally refers to in-room imaging and guidance during radiotherapy to improve geometrical precise target localization during treatment (3–5). Accurate tumor irradiation potentially leads to a reduction of safety margin sizes, and may allow for tumor dose escalation resulting in better local control without increasing the risk of long term side effects (4). Margin reduction is especially important when treating children as the risk of radiation-associated toxicity and late effects in this group are of great concern (6–8).

IGRT practices among adult cancer patients have been reported in multiple studies (9–13), showing a tendency towards an increased IGRT use over time. A British survey in 2008 showed that routine IGRT use was low (8%), and that 25% of surveyed institutes intended to implement IGRT within a year(9). A follow-up survey showed that IGRT implementation was increased, however with broad variability in its application due to a lack of funds or trained staff (10). A survey among ASTRO (American Society for Radiation Oncology) members indicated a high prevalence of IGRT practice and daily cone-beam computed tomography (CBCT) imaging, but with wide variabilities in IGRT frequency and verification methodologies (11). Studies from Australia and New Zealand reported IGRT as being commonly available, yet with considerable variations in clinical application (12, 13).

IGRT practice for pediatric cancer patients has been less thoroughly investigated. Two studies on pediatric IGRT show similar results as reported in adult studies (14, 15). IGRT for children is widely used, but with great variations concerning how, when and for which treatment sites (14). In a more recently published survey, IGRT protocols and practice for adults and children were compared (15). The use of treatment protocols varied widely, and only about one-third of the responding institutes used tailored IGRT protocols for children.

Both adult and pediatric surveys on IGRT practices indicated a lack of specific consensus-based IGRT guidelines. Practice guidelines published in 2010 merely focused on the clinical implementation of IGRT (5). Recently, the European Society for Paediatric Oncology (SIOPE) published consensus-based guidelines for children receiving radiotherapy to the vertebrae and the craniospinal axis; the guidelines included recommendations for patient immobilization, imaging, and target delineation, but not specifically for IGRT practices (16, 17). The Pediatric Radiation Oncology Society (PROS) stressed the importance of further investigations of the current status of pediatric IGRT (18). In this first –baseline– survey we aim to assess the current status of pediatric IGRT practice in Europe uniquely following the entire clinical workflow from pre-treatment imaging to treatment planning and radiation delivery.

Methods

A survey consisting of multiple-choice and open-ended questions was created in Castor (19) (Supplementary Material). The survey comprised questions on demographics, the availability of external beam radiotherapy (EBRT) facilities and IGRT availability. Subsequently we asked in-depth questions for seven treatment sites: brain, craniospinal axis (CSA), head and neck (H&N), thorax, abdomen, pelvis and extremities. Per treatment site, we distinguished four items: 1) the estimated number of annually treated children; and, because IGRT is not a solitary step in the radiotherapy workflow: 2) radiation treatment preparation; 3) radiation treatment planning and delivery; and 4) IGRT practice. The second item, radiation treatment preparation, included questions on patient positioning, immobilization devices, and additional (diagnostic) pre-treatment imaging (e.g. 3D or 4D-CT, PET-CT, MRI) to fuse with the planning CT in order to define the Gross Target Volume (GTV) and Clinical Target Volume (CTV). The third item enquired about modalities for treatment simulation, the most common treatment planning and delivery techniques, the use of fiducials and clinical target volume to planning target volume (CTV-to-PTV) margin application. In the last item, we elaborated on the use of IGRT devices, online/offline imaging use and frequency.

Participants were identified amongst European PROS members and the international consortium involved in our overarching pediatric IGRT project (KWF project no. 10113). In June 2018, the survey was sent to 77 radiation-oncologists, 17 medical physicists, six radiation therapists (RTTs) and one nurse representing 70 institutes in 21 European countries. After the initial invitation, participants were reminded every two weeks until the date of closure three months later. We encouraged participants to consult their colleagues when filling out the survey. Implicitly, physicists could involve physicians and vice versa, however, participants working in the same institute were notified to complete and return one survey.

Data analysis

We quantified response-rates for all multiple-choice questions and presented responses by percentage. Open-ended questions were analyzed descriptively. We processed data using IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, N.Y., USA) (20), and created figures in Microsoft Excel (2016), distinguishing between the answers from photon institutes and proton-only institutes. Differences between these groups were not analyzed statistically due to the low number of proton-only centers. We performed sensitivity analyses to investigate the influence of extreme values on isotropic CTV-to-PTV margins, and to rule out the possible bias due to the rather large number of participating Dutch centers.

Results

Of the 70 invited institutes, 42 participated (response rate 60%), of which 33 denoted to treat children. We thus included the answers of 33 institutes from 18 countries, and restricted our analyses to these institutes only. An overview of participants is presented in Supplementary Table 1.

Participating institutes

Altogether, the 33 included institutes treated 1714 children annually. Figure 1 reflects the typical incidence of pediatric cancers (21) and the proportion of children treated with radiotherapy (22), showing brain as the most frequently treated site, and extremities as the least treated site (Table 1). EBRT was available as photon therapy in 28 institutes, 25 used MeV electron therapy as well. Two institutes indicated to have both photon and proton therapy (PT), one of which additionally used electrons, and three institutes exclusively used protons (i.e. ‘proton-only’ institutes). Furthermore, several photon institutes refer patients to proton centers (abroad), depending on treatment site. Two institutes reported an MR-linac facility.

Table 1
Clinical practice for all treatment sites.

Institutes:	**Brain** **N = 31**		**CSA** **N = 28**		**H&N** **N = 28**		**Thorax** **N = 28**		**Abdomen** **N = 29**		**Pelvis** **N = 30**		**Extremities N = 26**	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Patient positioning	29	(94)	23	(82)	26	(93)	24	(86)	26	(90)	27	(90)	24	(92)
Supine	2	(6)	5	(18)	2	(7)	4	(14)	3	(10)	3	(10)	2	(8)
Prone	31	(100)	28	(100)	28	(100)	25	(89)	27	(93)	30	(100)	25	(96)
Pre-treatment imaging*	9	(29)	6	(21)	22	(79)	21	(75)	21	(72)	23	(77)	14	(54)
3D-CT	30	(97)	27	(96)	25	(89)	22	(79)	23	(79)	26	(87)	22	(85)
3D-PET-CT	-	-	-	-	-	-	12	(43)	9	(31)	-	-	-	-
3D-MRI	-	-	-	-	-	-	3	(11)	1	(3)	-	-	-	-
4D-CT	-	-	-	-	-	-	0	(0)	1	(3)	-	-	-	-
4D-PET-CT														
4D-MRI														
Imaging for treatment field simulation†	0	(0)	2	(7)	0	(0)	0	(0)	0	(0)	0	(0)	1	(4)
Conventional (2D)	31	(100)	27	(96)	28	(100)	23	(82)	28	(97)	30	(100)	26	(100)
3D-CT (free-breathing)	-	-	-	-	-	-	5	(18)	2	(7)	-	-	-	-
3D-CT (breath-hold)	-	-	-	-	-	-	14	(50	6	(21)	-	-	-	-
4D-CT	2	(6)	3	(11)	0	(0)	2	(7)	2	(7)	2	(7)	3	(12)
Planning/treatment technique	17	(55)	11	(39)	10	(36)	18	(64)	17	(59)	15	(50)	18	(69)
Conventional 2D RT	27	(87)	20	(71)	23	(82)	23	(82)	25	(86)	25	(83)	21	(81)
3D conformal RT	4	(13)	2	(7)	3	(11)	2	(7)	2	(7)	3	(10)	2	(8)
IMRT/VMAT	5	(16)	4	(14)	6	(21)	3	(11)	3	(10)	6	(20)	2	(8)
3D conformal PT														
IMPT														
In-room IGRT devices	9	(29)	9	(32)	6	(21)	4	(14)	5	(17)	6	(20)	8	(31)
	15	(48)	13	(46)	12	(43)	13	(46)	11	(38)	14	(47)		
	8	(26)	0	(0)	1	(4)	0	(0)	2	(7)	2	(7)		
MV-planar imaging (2D); MV film or EPID	23	(74)	16	(57)	22	(78)	24	(86)	24	(83)	24	(80)	13	(50)
kV-planar imaging (2D)	4	(13)	4	(14)	5	(18)	2	(7)	4	(14)	4	(13)	0	(0)
Stereotactic targeting (2D, 1 kV and 1 MV image)	1	(3)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	19	(73)
kV-CBCT (3D)													4	(15)
MV-CBCT (3D)													0	(0)
MR-guidance														
IGRT protocols	27	(87)	24	(86)	24	(86)	24	(86)	26	(90)	27	(90)	22	(85)
Daily online	5	(16)	5	(18)	4	(14)	6	(21)	5	(17)	5	(17)	5	(19)
Offline	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
NAL	5	(16)	5	(18)	4	(14)	6	(21)	5	(17)	5	(17)	5	(19)
eNAL	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)
SAL														

Institutes:	Brain N = 31	CSA N = 28	H&N N = 28	Thorax N = 28	Abdomen N = 29	Pelvis N = 30	Extremities N = 26

Institutes frequently indicated to use more than one of the listed techniques by selecting more options.

Abbreviations: CSA = craniospinal axis; H&N = head and neck; 3D-CT = 3D computed tomography; 3D-PET-CT = 3D positron emission tomography - computed tomography; MRI = magnetic resonance imaging; IMRT = intensity modulated radiotherapy; VMAT = volumetric modulated arc therapy; IMPT = intensity modulated proton therapy; IGRT = image-guided radiotherapy; EPID = electronic portal imaging device; CBCT = cone-beam computed tomography; MR = magnetic resonance; NAL = no-action level; eNAL = extended no-action level; SAL = shrinking action level; - = not applicable.

* Pre-treatment imaging to fuse with the planning CT in order to define the Gross Target Volume (GTV) and Clinical Target Volume (CTV).

† Imaging for treatment field simulation and treatment planning.

In-room imaging modalities in the 30 institutes using photons included MV-planar (N = 23), kV-planar (N = 20), and kV-CBCT (N = 28). Furthermore, stereotactic imaging (2D-kV/MV) was available in ten institutes, MV-CBCT in five institutes and MR-guidance in two institutes. All three proton-only institutes used kV-planar imaging.

Radiation treatment preparation

Patients were generally treated in supine position for all sites (Table 1). Two-out-of-three proton-only centers treated CSA in prone position. For brain, CSA and H&N immobilization, all institutes used (thermoplastic) facial masks or head casts (Fig. 2; Supplementary Table 2). Unexpectedly, some participants indicated to use a head cast for abdominal radiation, and for treatment of extremities. (Partial) body casts were mainly used when treating thoracic sites (15/28 photon institutes). Vacuum cushions were used by the majority of institutes for all treatment sites, except for brain and H&N. A knee support was used over all treatment sites, most often for abdominal radiotherapy. Furthermore, institutes mentioned the use of cushions (for brain, CSA, and H&N), wing boards (for thorax and abdomen) and customized limb casts (for extremities). Combinations of several immobilization devices varied per institute over all treatment sites.

Additional pre-treatment (diagnostic) imaging to be fused with the planning CT to define the GTV and CTV showed great similarity for certain treatment sites but also variation for other sites in all institutes (Table 1). For brain and CSA, 3D-CT and 3D-MRI were frequently combined, whereas 3D-PET-CT was scarcely used. For H&N and pelvis, all institutes used 3D-CT, often combined with PET-CT and MRI. 4D-CT was used by 12 of 28 institutes treating the thorax, including two proton-only centers, and in 9 of 29 institutes treating the abdomen, including one proton-only center. To prepare the treatment of extremities, 25 of 26 institutes used 3D-CT, and one standardly used 3D-PET-CT; sometimes combined with MRI.

Radiation treatment planning and delivery

Modalities for treatment simulation included 3D-CT for all institutes treating brain, H&N and pelvis (Table 1). Conventional 2D-simulation was used by only two institutes for CSA treatment, and by one institute for treatment of extremities. Breath-hold (BH) 3D-CT was used in 5/28 institutes treating thorax and 2/29 treating abdomen. 4D-CT was used in 14/28 institutes treating thorax and 6/29 treating abdomen. Patients potentially eligible for BH were individually assessed to check their compliance with instructions. The institutes acquiring 4D-CTs for thoracic treatment planning used the following techniques (some indicated using more than one) to account for respiratory motion: defining an internal target volume (ITV; n = 12), mid-position technique (n = 2), mid-ventilation technique (n = 2), gating (n = 1), and tracking (n = 2). For abdominal treatment planning, five institutes defined an ITV, and one used mid-ventilation position based on 4D-CT.

Fiducials were implanted by three institutes; one photon institute for abdominal stereotactic treatments, another photon institute used surgical clips for renal tumors, and one proton-only institute used suprapubic catheters as a surrogate for target position.

The most frequently used treatment techniques were intensity modulated radiotherapy (IMRT) and volumetric arc therapy (VMAT), followed by 3D-CRT (Table 1). Institutes frequently indicated to use more than one of the listed techniques by selecting more options.[18]

Margins

The CTV-to-PTV margin sizes reported here are based on photon institutes that used 3D-CRT or IMRT/VMAT. Most photon institutes used isotropic PTV margins (Table 2, Supplementary Fig. 1A). Median CTV-to-PTV margins were 5 mm for all sites, except for brain tumors for which 3 mm was the most reported margin. The wide range of isotropic margins in brain results from answers of one respondent reporting a 1 mm margin, and another reporting a 10 mm margin. Likewise, two respondents reported 10 mm margins for brain as part of CSA, and one respondent reported to use 1 mm margins for abdominal tumors. Repeated analysis neglecting these extremer values showed that 3–5 mm margins were most commonly used (Supplementary Fig. 1B) and might be considered as standard margin sizes to be used. The applied isotropic margin sizes per treatment site did not correlate with the number of annually treated children (Supplementary Fig. 2).

Table 2

Isotropic CTV-to-PTV margins sizes.

Margins (mm)	Brain N = 21	CSA (brain) N = 17	CSA (spine) N = 11	H&N N = 20	Thorax N = 14	Abdomen N = 18	Pelvis N = 18	Extremities N = 17
1	1	0	0	0	0	1	0	0
2	1	0	0	0	0	0	0	0
3	13	4	1	5	0	1	1	2
4	0	2	0	4	0	0	0	0
5	5	9	6	11	8	11	9	7
7	0	0	1	0	2	1	3	2
8	0	0	0	0	1	0	1	1
10	1	2	3	0	3	4	4	5
Median (mm)	**3**	**5**	**5**	**5**	**5**	**5**	**5**	**5**

Isotropic margins were reported by participants treating Brain, 21/31; CSA (brain), 17/28; CSA (spine), 11/28; H&N, 20/28; Thorax, 14/28; Abdomen, 18/29; Pelvis, 18/30; Extremities, 17/26.

Non-isotropic margin sizes generally depended on the use and type of immobilization devices, target volumes and/or patient-specific characteristics (e.g. age, weight), as indicated in free-text fields. Six institutes treating thoracic tumors indicated that the CTV-to-PTV margins were individually assessed per patient, possibly including motion or compensation techniques in the decision-making. For abdominal targets, one institute used 10–20 mm non-isotropic margins, depending on tumor location and diagnosis. Non-isotropic margins for pelvic tumors ranged from 5–10 mm and depended on the proximity of OARs, and patients' ages. For tumors located in the extremities, two institutes indicated to use variable (not specified) margins based on the immobilization device used.

The three proton-only centers used isotropic 3 mm PTV margins for brain tumors (two occasionally used non-isotropic margins depending on beam configuration). For the spine (as part of CSA), one proton-only center used 5 mm margins, whereas the other two used individualized non-isotropic margins. In H&N treatment, two proton-only institutes used 4 and 5 mm isotropic margins; the third used 3 mm isotropic margins. One of the two proton-only centers treating thorax targets used isotropic 5 mm margins, the other reported that margin sizes depended on the defined ITV and beam configuration. In both institutes the same strategy as used in the thorax was used for abdominal tumors. For pelvic tumors 5 mm isotropic margins were used. The one proton-only institute treating extremities used isotropic 5 mm margins.

IGRT

IGRT devices mainly included kV-CBCT and kV-planar imaging for photon therapy (Table 1). One institute indicated to use MR-guidance for brain tumors, another indicated to use 4D-CBCT for thoracic tumors. All proton-only centers used kV-planar imaging for all sites.

A daily online imaging protocol was used by the majority (85–90%) of institutes across different treatment sites (Table 1). All institutes using offline protocols, applied an extended no-action level eNAL protocol, in which typically systematic setup errors are corrected based on images from the first 3–4 fractions followed by weekly images and setup corrections, if indicated by the predefined action level (23).

Discussion

In this first –baseline– survey we assessed the current clinical IGRT practice among 33 European institutes treating children. With this survey, currently the most extensive one on pediatric IGRT, we followed the entire workflow including treatment preparation, planning and radiation delivery. Modern EBRT techniques and IGRT modalities were widely available and accepted, marking a trend that has been described in previous surveys (2007–2017; Table 3) (9–14). Sophisticated high-precision techniques using smaller margins require high-standard (daily online) image guidance (13, 24). For example, IMRT/VMAT techniques lead to a steep dose gradient, where IGRT becomes extremely important to prevent the risk of partially missing the target. Site-specific questions revealed some variations in treatment preparation, planning and delivery techniques, including IGRT devices (Table 1). The widest variation was found in isotropic CTV-to-PTV margin sizes, especially for brain as a consequence of two respondents reporting a 1 mm and a 10 mm margin, respectively, and for abdominal tumors due to a single respondent reporting a 1 mm margin. The large variations in margin sizes for brain and spine as part of CSA could be explained by the relatively low percentage of 3D-CBCT use in CSA treatment (57%). Margins sizes were not found to be correlated with the number of annually treated children.

Table 3. Overview of surveys on IGRT/IGPT.

Study	Jefferies 2009[9]	Mayles 2010[10]	Alcorn 2014[14]*	Nabavizadeh 2015[11]	Padayachee 2017[13]	Batumalai 2017[12]	Wall 2018[15]*	Bolsi 20
Survey sent:	**2007**	**2009**	**Not specified**	**2014**	**2015**	**2015**	**2015**	**2016**
Geographical	UK	UK	Worldwide	USA	New Zealand	Australia	International†	Europe
Responded/invited	48/58	50/58	7/9	601/5979	7/9	33/46	43/119	19/19
Response rate (%)	83	86	88	10	88	72	36	100
Treatment preparation								
Patient positioning	-	-	-	-	-	-	-	+
Immobilization devices	-	-	+	-	-	-	-	+
Pre-treatment imaging	+	-	-	-	-	+	-	-
Treatment planning								
Imaging for field simulation	+	-	-	-	-	+	-	+
Treatment technique	-	+	-	-	+	+	-	+
PTV margins	-	-	+	+	-	-	-	
Treatment delivery								
Use of IGRT devices	+	+	+	+	+	+	-	+
Imaging frequency (on/offline)	-	-	+	+	+	+	+	+
Aim	· Evaluate current image acquisition in RT. · Evaluate assessment of target volume definition. · Review types of radiation technology being used. · Evaluate IGRT implementation next 2 years.	· Evaluate increase of IMRT and shortfall of patient treatments compared to Jefferies et al.[9] . Availability of IGRT.	· Evaluate range of pediatric IGRT practices.	· Define US IGRT utilization and impact on workflow. · Evaluate relation IGRT use and applied PTV margin.	· Assess current in-room IGRT practice. · Assess IGRT quality using White Paper recommendations. · Understand barriers to implementation/ improvement in New Zealand.	· Evaluate current use of imaging for planning/ delivery of EBRT.	· Evaluate IGRT in adults vs. pediatric patients.	· As differen between centres terms of IGPT us for treat preparat planning and deli . Identific of develop needed improve IGPT. . Identific of resea activitie
Main outcomes	· Lack of IMRT and IGRT implementation due to multi-fold barriers. · Lack of formal training in tumour and normal tissue outlining in	· Inverse-planned IMRT falls short of what clinicians feel should be offered. · IMRT implementation developed as	· High IGRT prevalence, but treatment site-specific variability in IGRT use and technique	· High prevalence of IGRT and daily CBCT. · Wide variability in site-specific imaging frequency and	· IGRT widely used, with wide variation in application between institutes. · IGRT complies highly to ASTRO White Paper recommendations.	· IGRT widely used, and the installation of new imaging modalities is expected to increase.	· Most institutes apply site-specific protocols, not considering patient size and age.	· Confirm variety i clinical I practice and procedu

	several staff groups.	was found by Jefferies et al.[9] · High IGRT uptake in centers that have the necessary equipment.	between institutes. Practices varied less in proton centers. · No consensus on optimal PTV margin per treatment site.	verification methodologies. · No statistically significant association between IGRT frequency and PTV margin selection. · Poor resident involvement in IGRT practices.	· Multi-fold barriers restricting IGRT implementation.

Abbreviations: CBCT = cone-beam computed tomography; EBRT = external beam radiotherapy; IGRT = image-guided radiotherapy; IMRT = intensity modulat PTV = planning target volume; + = applicable topic; - = not applicable;

* Survey focusses on children.

† International; region not specified.

‡ 33/42 institutes denoted to treat children and were included in the analysis.

§ Weighted average response rate pediatric surveys Alcorn and Wall: 39%.

Prone positioning for photon irradiation was rare, possibly because prone positioning could be subjected to larger setup and residual uncertainties than supine positioning (25). Also, prone positioning may be considered to potentially induce patient discomfort, and might not be appreciated for anesthesia. On the other hand, treating under anesthesia in prone position is safe and feasible (26). Besides, in proton therapy, prone positioning could be favorable because of healthy tissue sparing, or due to beam configuration limitations, e.g. in CSA treatment, to avoid radiation through the treatment couch. Contrarily, when the couch and immobilization devices are properly modeled by the treatment planning system, treating with beams traversing some devices was proved feasible, which counters this limitation (27).

As immobilization is of great importance, especially for complex targets in in pediatric patients, we would have expected knee/foot supports to be used even more frequently than reported. However, knee/foot supports are not always used as on the one hand pediatric specific supports are lacking and in-house made or adjusted devices are used, whilst on the other hand small children do not need them when immobilized in a vacuum cushion. Similar to Alcorn et al (14), we found an extensive use of vacuum cushions (> 62%) for thoracic, abdominal and pelvic treatments. Our survey did not disclose anesthesia practices, whereas anesthesia or sedation is often required in the very young to ensure complete immobility during radiotherapy (28).

Additional pre-treatment imaging for GTV-to-CTV definition was used more extensively among our participants than reported earlier by Jefferies et al (9). Batumalai et al reported the use of PET-CT to prepare for CSA treatment in adults, whereas our survey showed that PET-CT was hardly used in children. For H&N, thoracic and abdominal/pelvic sub-sites the use of PET-CT was comparable or higher than in our sample (12); differences might be due to the typically different cancer types in children and adults. Imaging for planning purposes included 3D-CT in all institutes. Besides 3D-CT, two institutes also used conventional 2D-simulations. This could be explained by them being in a transition period, having acquired newer techniques only recently. This is consistent with Jefferies et al, who predicted that conventional 2D-simulation would decline in favor of 3D-CT (9). All participants in our survey had access to CT simulators, and frequently used additional MRI and PET-CT, in alignment with Batumalai et al (12). We also notice the use of breath-hold techniques during 3D-CT acquisitions for thoracic and abdominal treatment simulations. Implementation of breath-hold protocols depends on the patients' ability to comply with instructions (29, 30), but is promising, and dosimetric benefit has already been shown even in a vulnerable adult patient group (31). Most centers using 4D-CT scans for treatment simulation define an ITV. This approach needs less quality assurance compared to other techniques (e.g. gating/tracking). Only two institutes used gating/tracking techniques, suggesting that more development is needed to confidently apply these methods in children, but we did not enquire about specific details.

Regarding photon therapy, we found that IMRT/VMAT were widely applied. This corresponds to the results of surveys focusing on adults (12, 13), and indicates development of the field since 2010, when Mayles et al reported a low IMRT use (10). Interestingly, we found that a number of institutes still used 3D-CRT, even with IMRT/VMAT available. An explanation could be the concerns about the large low dose volume in IMRT/VMAT with a potentially increased risk of secondary cancer induction (32). Alternatively, even when the hardware is available, the planning software is not always fit to deal with extensive volumes or the implementation is time consuming. Few institutes indicated to use simulator-based 2D techniques, but we did not specifically enquire in which situations. Similarly, information on specific proton treatment techniques such as passive scattering or pencil beam scanning was not collected. Technical developments have led to a transition from passive scattering proton therapy to active pencil-beam scanning (33). Scanning techniques potentially realize an even better conformal target volume coverage, and facilitate intensity-modulated proton therapy (IMPT) minimizing dose to healthy tissues (33, 34). As IGRT in photon therapy, image-guided particle therapy (IGPT) is a crucial step in the treatment workflow (35). The EPTN (European Particle Therapy Network) survey confirmed a variety in IGPT practice in European particle therapy centers, and identified the priority of research to improve daily image guidance (35).

In accordance with previous surveys on IGRT use in both pediatric and adult patients (9, 11–14), 3D-CBCT was the most frequently used device for in-room IGRT. Padayachee et al found that kV-planar and CBCT imaging were, averaged over all sites, used in similar frequency (13). The low prevalence of abdominal and thoracic MV and kV-planar imaging is encouraging as position verification based on bony anatomy might not always be sufficient. CBCT scanning is superior in visualizing soft tissue compared to 2D-imaging, but the extra imaging dose of (daily) CBCT has to be considered. To account for this, IGRT protocols to minimize imaging dose and volume are being introduced for pediatric IGRT. This comes at the expense of image quality but not of registration accuracy (24). On the other hand, high quality IGRT to improve geometrical accuracy may yield a significant shrinkage of the target margins. This should outweigh the concern of imaging dose in children and needs to be further investigated. Besides, MV imaging dose is often integrated in the treatment plan. Nevertheless, the wide use of IGRT for children across different European institutes as shown in the present survey reflects the significance of geometrical accuracy.

The use of daily online position verification by our participants is higher compared to Alcorn's results in 2014 (~ 35 to ~ 60%) (14), and compared to adult surveys, where daily online imaging is frequently, but not continuously used (11–13). Also eNAL protocols are used widely in adults (11–13), similar to our sample. We did not specifically inquire on the decision when to use daily online, or offline protocols, or both. Theoretically, this decision strongly depends on treatment planning technique and the margin applied. For example, an offline protocol will be sufficient for whole brain irradiation, whereas partial brain irradiation will require an online protocol.

Margins applied by our participants are similar to those reported by Alcorn et al in all treatment sites except thorax (mean 6.6 mm in our study vs. 10.8 mm in Alcorn (14)). Nabavizadeh et al found similar lung tumor margins in adults, distinguishing between treatment planned on 4D-CT (median 5 mm; IQR 5–7 mm) and 3DCT (median 10 mm; IQR 7–13 mm) (11). Comparing the brain and H&N sites of our study and Nabavizadeh et al, margins were also similar (both median 5 mm, IQR 3–5 mm). Margin sizes should be in line with IGRT facilities and all steps in the chain of the (department-specific) radiotherapy workflow (5, 16). Complementary to the standardization and optimization of the organization of patient care, education and clinical research (36), knowledge of geometrical uncertainties including organ motion (37–44) is necessary to develop 'best practice' guidelines, distinguishing between hospital and patient specific factors.

The sample size might form a limitation. Eligible participants included European PROS members and our IGRT project-based consortium, totaling 70 institutes. The 60% response rate is comparable to that of other IGRT surveys, and it appeared that almost 33 of the 42 (80%) responding institutes actually treat children. Additional analyses to investigate the possible risk of bias due to the relatively high number of participating Dutch institutes (n = 7) did not change the results. Therefore, we consider our results a reasonable representation of pediatric radiotherapy in Europe, although non-IGRT-users or IGRT-users working with less sophisticated equipment might have been less likely to respond, resulting in a potential overestimation of the availability of modern techniques. Our survey specifically focused on pediatric IGRT and since pediatric tumors and their treatment substantially differ from that from adults, we have not compared pediatric and adult IGRT practices within participating institutes. The survey did not include specific questions how long each institute has practiced their reported use of IGRT methods. While our standardized electronic form assured complete responses since empty fields were not allowed, some uncertainties were still involved in the study design and response analysis. Firstly, numerical fields are vulnerable for typing errors, potentially leading to under/overestimations. Secondly, the possibility to select more than one answer on multiple-choice questions could have led to erroneous answers, which hampered investigation of associations between e.g. treatment techniques, IGRT modalities, online-offline protocols and margin size definitions. Thirdly, open fields for additional free-text responses were non-obligatory and only part of the participants elaborated on their answers, which may have led to misinterpretations (e.g. referral to proton centers). Finally, completing the survey was estimated to take 45 minutes. Although participants could save their answers to continue later, lengthy surveys might lead to inaccuracies in questions that were enquired later on, or were forgotten altogether. We will consider these issues when conducting the follow-up survey, aiming to involve the participants into a new consensus driven practice. Subsequent steps, preferably in collaboration with experts (e.g. PROS, SIOPE) include the development of guidelines, and the definition of optimal margin sizes considering available IGRT facilities and workflows among institutes.

Conclusions

Our survey shows comparable practice in pre-treatment imaging, planning and treatment techniques, and IGRT application among the participating European institutes. However, wide ranges in PTV margin sizes exist, supporting the need to define international 'best practice' guidelines for pediatric IGRT, and to aim for consensus on optimal margin definitions in view of available IGRT facilities and workflows among institutes.

List Of Abbreviations

ASTRO: American Society for Radiation Oncology; BH: breath-holding; CBCT: cone beam computed tomography; CSA: cranio-spinal axis; CTV: clinical target volume; EBRT: external beam radiotherapy; eNAL: extended no-action level; EPTN: European Particle Therapy Network; GTV: gross target volume; H&N: head-and-neck; IMPT: intensity-modulated proton therapy; IGRT: image guided radiotherapy; IMRT: intensity modulated radiotherapy; ITV: internal target volume; kV: kilo volt; MeV: mega electron volt; MV: mega volt; MR(I): magnetic resonance (imaging); OAR: organ at risk; PET-CT: positron emission tomography - computed tomography; PROS: Pediatric Radiation Oncology Society; PT: proton therapy; PTV: planning target volume; SIOPE: European Society for Paediatric Oncology; RTT: radiation therapist; VMAT: volumetric arc therapy.

Declarations

Ethics approval and consent to participate

Based on the Dutch regulations regarding survey studies and the national guideline of the Central Committee on Research Involving Human Subjects (https://www.ccmo.nl/onderzoekers/soorten-onderzoek/overig-onderzoek/vragenlijstonderzoek), consent and IRB approval were not needed and ethical approval was not required (AMC-IRB; W20_275#).

Consent for publication

Not applicable.

Availability of data and materials

Data are available from the corresponding author on reasonable request.

Competing interests

Dr. Beldjoudi reports his collaboration with Elekta; the department of radiation oncology of Centre Léon Berard acts as training center for stereotactic radiation therapy treatments.

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Authors' contributions

All authors read and approved the final manuscript. CW, AB, BB, RdJ and IvD substantially contributed to the design of the survey. All authors provided data by completing and returning the survey. CW, AB, and IvD analyzed and interpreted the data and drafted the manuscript. All authors reviewed the manuscript.

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Figures

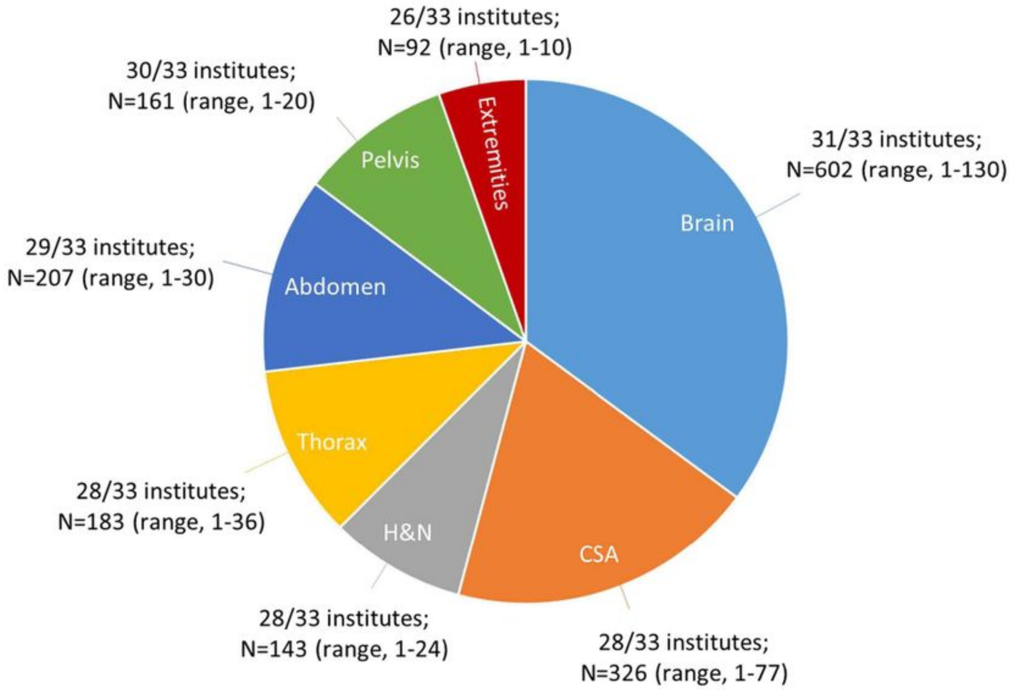

Figure 1

Estimated number (N) of patients per treatment site annually treated in the participating institutes.

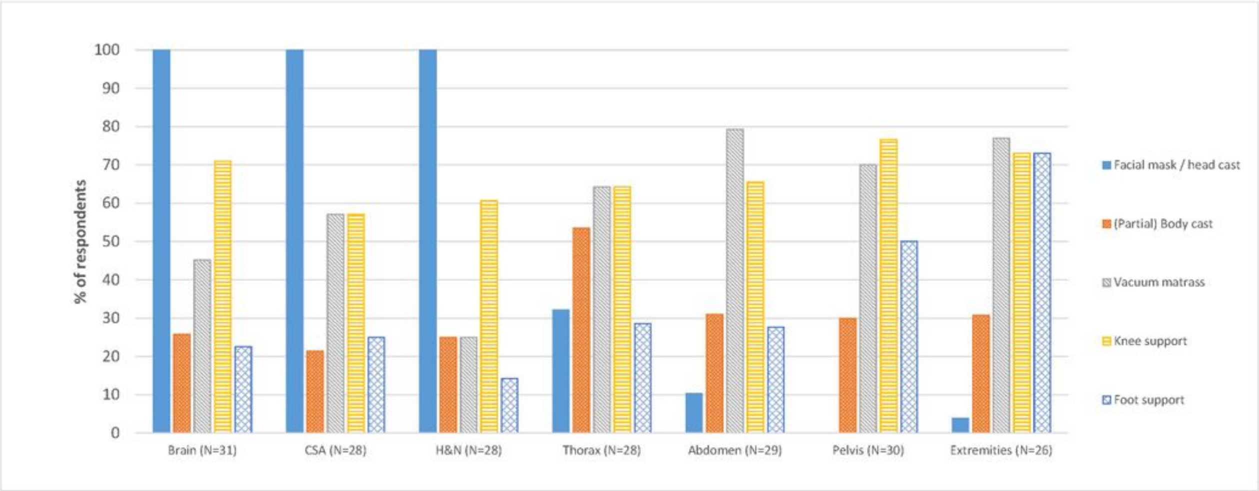

Figure 2

Use of immobilization devices per treatment site. Abbreviations: N, number of institutes; CSA, craniospinal axis; H&N, head and neck.

Supplementary Files

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