



Original Article

Paediatric CBCT protocols for image-guided radiotherapy; outcome of a survey across SIOP Europe affiliated countries and literature review

Daniella Elisabet Østergaard^{a,b,1,*}, Abigail Bryce-Atkinson^{c,1}, Mikkel Skaarup^a, Bob Smulders^{a,d}, Lucy Siew Chen Davies^e, Gillian Whitfield^{f,g}, Geert O. Janssens^{h,i}, Lisa Lyngsie Hjalgrim^j, Ivan Vogelius Richter^{a,b}, Marcel van Herk^c, Marianne Aznar^{c,1}, Maja Vestmø Maraldo^{a,1}

^a Section of Radiotherapy, Department of Oncology, Centre for Cancer and Organ Diseases, Copenhagen University Hospital, Copenhagen, Denmark

^b Faculty of Health and Medical Sciences, Copenhagen University, Copenhagen, Denmark

^c Division of Cancer Sciences, School of Medical Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK

^d Danish Centre for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark

^e Department of Radiotherapy, The Christie NHS Foundation Trust, Manchester, UK

^f Manchester Academic Health Science Centre, The Christie NHS Foundation Trust, Manchester, UK

^g The Children's Brain Tumour Research Network, The University of Manchester, Royal Manchester Children's Hospital, Manchester, UK

^h Department of Radiation Oncology, University Medical Center Utrecht, Utrecht, the Netherlands

ⁱ Princess Máxima Center for Pediatric Oncology, Utrecht, the Netherlands

^j Department of Paediatrics and Adolescent Medicine, Copenhagen University Hospital, Copenhagen, Denmark



ARTICLE INFO

Keywords:

Radiotherapy
Image-guided radiotherapy
Paediatric cancer
cone-beam CT

As overall survival (OS) rates in children's cancer improve, the prevalence of long-term survivors in this patient group increases. The need for fine-tuning treatment to achieve best OS with minimal late effects has therefore become increasingly more critical [1–3]. Advancements in modern radiotherapy techniques such as the application of 3D volumetric image-guided radiotherapy (IGRT), adaptive radiotherapy (RT) and, in some cases, motion management techniques (e.g. breath-hold), are essential for enabling the accurate delivery of radiation to the target volume whilst sparing nearby organs at risk (OAR). These approaches are also applicable in paediatric radiotherapy, and are fundamental to improve patient outcomes [4–6]. 3D volumetric IGRT techniques, most often cone-beam CT (CBCT), is used to verify patient/tumour positioning and ensure adequate dose coverage of the tumour [4]. Technological advances have made daily image guidance feasible at a modest additional investment of machine and staff resources and IGRT is often considered standard of care. However, manufacturer default

acquisition protocols are designed with adults in mind. This is a concern, since children attenuate the imaging x-rays less and are more dose-sensitive and hence more susceptible to second primary tumours caused by lower doses, e.g. the imaging dose or low-dose baths from treatment plans [7–11]. Despite this, guidelines for optimising paediatric IGRT with dose as low as reasonably achievable (ALARA) are currently lacking [12–16].

Concerns over adding excess imaging dose for paediatric patients may lead to reluctance to use daily treatment verification protocols such as CBCT, and to some extent, even daily 2D kilovoltage (2D kV) imaging [17]. Paediatric patients of different ages vary greatly in body-size. Dose calculation studies in adults have shown imaging dose to be inversely related to body-size, with lower Body Mass Index patients receiving a higher dose from imaging [18]. Dose calculation studies have been important in recommendations for dose restriction from imaging to children to avoid severe late effects from imaging [17,19]. However,

* Corresponding author at: Department of Oncology, Copenhagen University Hospital, Blegdamsvej 9, 2100 Copenhagen, Denmark.

E-mail address: daniella.elisabet@gmail.com (D.E. Østergaard).

¹ Both authors contributed equally to the work.

dose calculation studies in children have been based on adult IGRT protocols applied to children, and not protocols specifically optimised for paediatric patients [19–21]. Newer studies have proven low-dose 3D protocols for children are possible without losing the benefits of IGRT. These studies suggest that the CBCT dose for IGRT can be decreased by at least a factor of 10 in children and adolescents and potentially decreased to similar exposure of 2D kV imaging, while maintaining positioning accuracy [7,22–24]. Practice patterns for paediatric IGRT have been studied before and have shown increasing focus on paediatric-specific protocols for IGRT as well as growing use of daily 3D imaging [25,12–14]. However, current use of low-dose 3D protocols remains unknown, and it remains unclear whether technical acquisition settings have been fully optimised in all centres.

The objective of this paper was to collect current technical acquisition parameters from paediatric CBCT protocols throughout SIOPE affiliated radiotherapy departments for brain/head and abdominal sites as well as summarizing the literature that reports paediatric CBCT protocols.

Methods and material

A literature search was first conducted in August 2022 with the aim to summarise published paediatric CBCT protocols for IGRT. The Medline database (PubMed) was used to create a search string based on an adapted PICO diagram² (PEO = Population (children), exposure (IGRT with CBCT), outcome (CBCT protocols for children)) with relevant MeSH terms and text words. This yielded a total of 196 papers, of which, 113 papers were excluded based on the abstract and title. A total of 22 papers were included after full text review for data extraction upon consensus by two authors (DEØ, ABA).

We then conducted a survey via the SIOPE network of paediatric radiation oncologists and collected data from 6 September to 22 October 2022. The survey was sent to 246 centres across 35 SIOPE affiliated countries. Responders consented to participate and to be contacted by email. The survey consisted of three parts: 1) demographic information, 2) CBCT settings for brain/head sites, and 3) CBCT settings for abdominal sites. Full survey details are in [appendix A](#). These two sites of interest were chosen as they are very different in anatomy and visualisation requirements. Acquisition and set-up protocols were asked for both sites, with two additional questions addressing the use of 4D CBCT and motion management for abdominal sites. The survey was reviewed by the SIOPE ROWG prior to distribution.

Duplicate responses were removed. If ranges for quantitative parameters (e.g. current-exposure time, mAs) were reported, two protocols for the lowest and the top value of the range were generated. CBCT protocols reporting < 10 projections were removed from analysis, assuming reporting error, because this was too few projections to reconstruct a CBCT image. Suspected reporting errors were clarified with responders; however, this was only possible if consent to be contacted had been given.

Technical exposure settings were assessed with descriptive statistics and compared between brain/head and abdominal protocols using the unpaired two-samples Wilcoxon test to establish if protocols differed significantly between body sites, vendors, modality (proton/photon), centres reporting use of dose-reduction strategies, and centres using motion management strategies. Pearson correlation was performed to evaluate association between total mAs exposure and number of projections to establish if dose contributions came from higher mAs settings per projection, or a greater number of projections. Set-up parameters

were evaluated with descriptive statistics. Statements from free text questions were categorised according to common themes and the count per category was reported. Consensus for coding was agreed by two authors (DEØ, ABA). Free text answers from questions containing an option for “Other, please specify” are detailed in [Appendix B](#).

Results

Our literature search revealed 22 out of 196 papers with detailed paediatric CBCT protocols for IGRT. Papers were divided into three subgroups (optimisation studies, reported protocols and dose calculation studies). Only 7 papers were focused on optimisation of the paediatric CBCT protocol. A full overview of the included papers is shown in [Table 1](#). It is evident that tube voltage (kVp) settings are more consistent across protocols than other settings, e.g., mAs. mAs settings vary a lot in some studies. This might be explained by the fact, that these included had multiple anatomical sites. The heterogenous CBCT settings and acquisition parameters, suggest that consensus is lacking. Four out of seven optimisation studies reported using bowtie filter as a part of their protocol. Ten studies reported protocols, but the majority are from a single institution, where they likely use the same protocol. We found that multiple anatomical sites were addressed in the protocol papers, and that most studies were focused on thorax and abdomen. All optimisation studies addressed and assessed registration accuracy, but only 4/7 assessed visual image quality.

We received responses from 50/246 centres across 25/35 European countries. 44/50 centres treated with photons and 10/50 with protons (4 centres treated with both). Patients treated per year (p/y) were divided into intervals: <10p/y: 11 centres, 11–25p/y: 12 centres, 26–50p/y: 12 centres, 51–100p/y: 7 centres, 101–150p/y: 7 centres, >150p/y: 2 centres. Distribution of manufacturers and imaging modalities are shown in [Fig. 1a-b](#). Varian was the most common vendor and kV CBCT was the most used imaging modality amongst the centres. Centres who used kV CBCT as the only imaging modality were 14/50 (28 %) for brain/head, and 13/50 (26 %) for abdomen. “Other” imaging modalities are specified in [Appendix B](#).

Technical settings for brain/head and abdominal sites were reported by 30/50 and 31/50 centres respectively. 9/30 centres reported multiple CBCT protocols for brain/head sites and 10/31 centres for abdominal sites, with protocols adapted based on various factors including age, weight, treatment modality or manufacturer, body size, or as a specific low-dose protocol. In total, 48 brain/head protocols and 53 abdomen protocols were reported.

[Fig. 2](#) shows the distribution of frequency of CBCT use ([Fig. 2a](#)) and tube voltage settings (kVp, [Fig. 2b](#)). Most protocols were used daily (brain/head = 28/48 (58 %) and abdomen = 33/53 (62 %)). There was greater consistency in kVp settings for brain/head sites than abdominal sites, where 37/48 (77 %) of brain protocols used 100kVp compared to 18/53 (34 %) of abdominal protocols ([Fig. 2b](#)).

Further technical exposure settings are shown in [Fig. 3](#). A significantly higher mAs exposure was reported for abdominal protocols than for brain/head protocols ([Fig. 3a](#), $p < 0.001$), but the number of projections was consistent ([Fig. 3b](#), $p = 0.207$). Across all brain/head and abdominal protocols, total mAs exposure and number of projections showed a moderate positive correlation ($r = 0.48$, $p < 0.001$), and the median (interquartile range) of calculated mAs per projection was 0.20 (0.10–0.34) and 0.76 (0.30–1.25) mAs for the brain/head and abdomen protocols respectively. This indicates that dose optimisation between body sites is performed by adjusting mAs rather than number of projections.³ A significant difference ($p < 0.01$) in field of view (FOV) size

² PICO diagrams are commonly used for systematic literature searches, e.g., Cochrane Meta-analyses. PICO = Population, Intervention, Comparison and Outcome. Depending on the scientific field and question the PiCO diagram can be customized and adapted to fit the research question better. <https://www.cochranlibrary.com/about/pico-search>.

³ The number of projections is customizable to an extent, depending on manufacturer configurations of projection frame rate and speed of rotation. Linacs commonly have a maximum speed of 1 revolution per minute for safety reasons.

Table 1
Protocols extracted from the literature and grouped by the purpose of the study.

Author, year	Anatomy	Age (years)	Vendor	kVp	mAs	No. of projections	Bowtie Filter used	Image quality evaluation	Registration evaluation
OPTIMISATION STUDY									
Bryce-Atkinson, 2021 [9]	Mixed sites	6–13	Elekta	120	18–460.8	180–360	✓	✓	✓
Olch, 2021 [7]	HN, thorax, Pelvis	–	Varian	80–125	50–1080	–	–	–	✓
Bryce-Atkinson, 2020 [22]	Mixed sites	1–16	Elekta	100	5–32	200	✓	✓	✓
Huang, 2019 [26]	–	–	Varian	80	100	–	✓	–	✓
Alcorn, 2019 [8]	CNS	1–20	Elekta	100	31.5	183	x	✓	✓
Rao, 2019 [23]	Abdomen	1.5–9.2	Elekta	100–120	31.5–63	315	x	–	✓
De Jong, 2014 [27]	CSI	–	Elekta	–	10–32 mA, 10–40 ms [†]	–	✓	✓	✓
REPORTED PROTOCOLS									
Yuan, 2022 [28]	HN	–	Elekta	100	18.2	182	–	–	–
Sheikh, 2022 [16]	Mixed sites	0–18	Hitachi*	100	–	–	–	–	–
Uh, 2021 [29]	Abdomen/pelvis	1–23	Hitachi*	90–125	10–60	–	✓	–	–
Huijskens, 2019 [30]	Abdomen, thorax	2–18	Elekta	120	10 mA, 10–40 ms [†]	180–760	–	–	–
Guerreiro, 2019 [31]	Abdomen	1–8	Elekta	100	16 mA, 10 ms [†]	–	–	–	–
Huijskens, 2018 [32]	Abdomen, thorax	8.6–17.9	Elekta	120	10 mA, 10 or 40ms [†]	180–760	–	–	–
Guerreiro, 2018 [33]	Abdomen	1–8	Elekta	100	16 mA, 10 ms [†]	–	–	–	–
Huijskens, 2018 [34]	Abdomen, thorax, spine	2.2–17.8	Elekta	120	10 mA, 10 ms [†]	–	–	–	–
Huijskens, 2017 [35]	Abdomen, CSI, thorax	2–18	Elekta	120	10 mA, 10 or 40ms [†]	180–760	–	–	–
Huijskens, 2015 [36]	Abdomen, thorax, spine	1.6–17.8	Elekta	–	–	–	✓	–	–
DOSE CALCULATION STUDY									
Dzierma, 2018 [18]	Abdomen, thorax	5–17	Siemens	121	200–700	200–360	–	–	–
Son, 2017 [37]	Mixed sites	5	Varian	100–125	72–720	360–655	✓	–	–
Kim, 2016 [38]	Abdomen	5	Varian	125	40–80 mA, 10–25 ms [†]	650–700	✓	–	–
Deng, 2012 [10]	Abdomen, CNS	2.75–6	Varian	60–125	80 mA, 13–25 ms [†]	–	✓	–	–
Ding, 2010 [20]	HN, thorax, pelvis	2.6	Varian	100–125	10–80 mA, 20–25 ms [†]	–	✓	–	–

✓ = yes, x = no, - = not specified, * = protons centre, † = mAs per projection, otherwise total mAs is reported directly from the study or by calculation from the reported number of projections and mAs per projection, CSI = craniospinal irradiation, HN = head and neck, CNS = central nervous system.

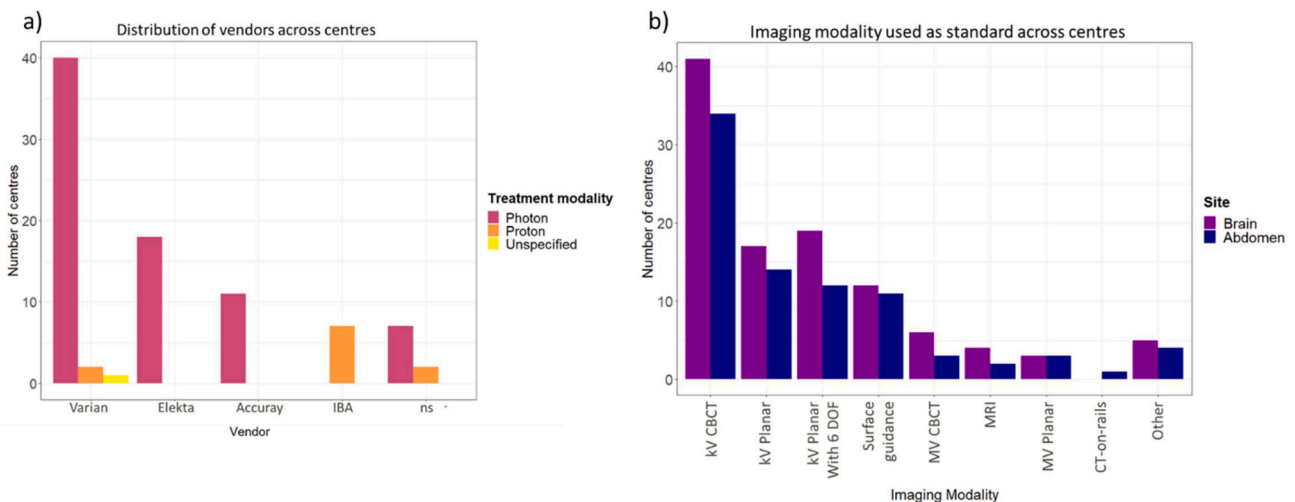


Fig. 1. a) Distribution of IGRT manufacturers used, 24/50 centres had multiple treatment machines and of these, 13/50 centres had ≥ 2 manufacturers. b) Distribution of imaging modality used as standard in paediatric IGRT. 42/50 and 35/50 centres used kV CBCT as standard for the brain/head and abdomen, respectively. Both plots show number of centres out of 50 centres in total. Note that multiple manufacturers/imaging modalities could be selected by each centre. ns = not specified, kV = kilovoltage, MV = megavoltage, 6 DOF = 6 degrees of freedom, MRI = magnetic resonance imaging.

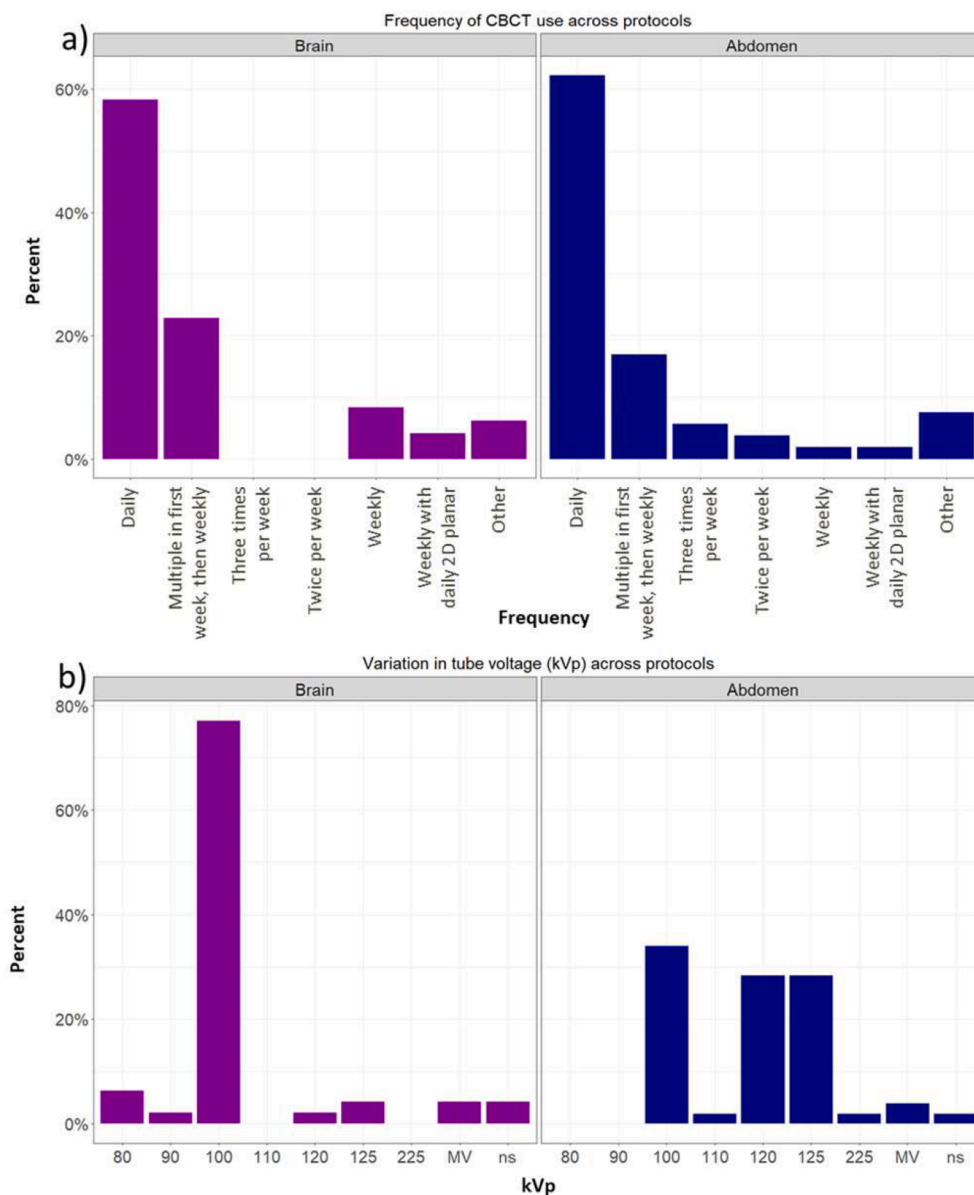


Fig. 2. A) distribution of cbct frequency across protocols, indicating how often a particular protocol is implemented b) distribution of kVp setting used across protocols, where MV indicates megavoltage CBCT was used and ns = not specified. $n = 48$ brain/head and $n = 53$ abdomen protocols.

was found between sites, likely due to the increased FOV variation in abdominal protocols. Significantly higher doses were reported for abdominal protocols ($p < 0.001$), in agreement with reported higher mAs exposure and larger FOV. For brain/head protocols, 27/48 (56 %) used full-fan bowtie filters, 3/48 (6 %) used half-fan, and 16/48 (33 %) used no filter. There was less consistency in abdominal protocols, as 22/53 (41 %) used full-fan, 17/53 (32 %) used half-fan and 13/53 (25 %) had no filter. Bowtie filter type was unreported in 2/48 (4 %) and 1/53 (2 %) of brain/head and abdomen protocols respectively. Note that in Varian systems, the bowtie filter type is linked with field of view, where full-fan mode is limited to < 24 cm [16].

Maximum number of CBCTs allowed in a single fraction was inconsistently reported. The most common maximum of CBCTs were for brain/head protocols 2 (11/48, 23 %) or 3 CBCTs (11/48, 23 %), and for abdominal protocols 2 CBCT (11/53, 21 %). However, this was overall largely unreported in 14/48 (29 %) of brain/head and 22/53 (42 %) of abdominal protocols.

Overall, greater consistency amongst brain/head protocols was observed for all technical exposure parameters compared to abdominal

protocols.

A wide variation in computer tomography dose index (CTDI) for the protocols was reported, spanning a reported dose range from 0.32 to 67.7 mGy for brain/head protocols and 0.27–119.7 mGy for abdominal protocols. Dose was significantly higher ($p < 0.01$) in brain protocols from Varian systems than Elekta systems, but not significantly different ($p = 0.68$) for abdominal protocols. There was no significant difference in dose between photon and proton modalities (brain: $p = 0.43$, abdominal: $p = 0.85$). Table 2 lists the exposure settings reported to achieve different dose ranges. It is evident that low-dose protocols were more frequently used for brain/head than abdominal sites, with the largest proportion of abdominal protocols falling within the highest dose range (> 10 mGy).

35 different set-up protocols were reported for each anatomical site (brain/head and abdomen). Consensus was reached in the method used for on-treatment CT-CBCT image registration for patient set-up, with 31/35 (89 %) brain/head protocols and 28/35 (80 %) abdominal protocols using automatic registration with manual adjustments. This was followed by automatic matching only for 3/35 (9 %) brain/head and 5/

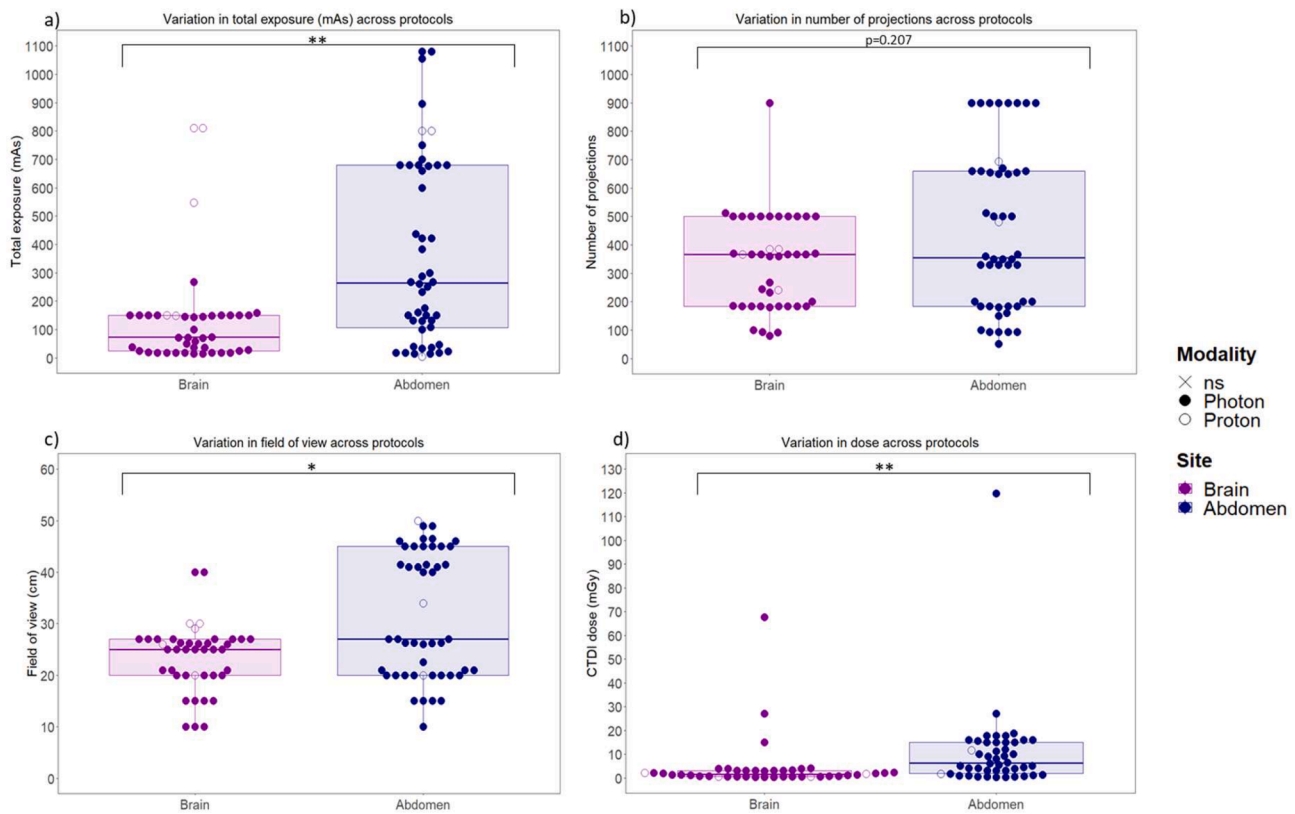


Fig. 3. Exposure settings per CBCT scan. **a)** Distribution of total mAs exposure reported across all protocols (n = 42 brain/head, n = 49 abdomen), **b)** Distribution of number of projections reported across protocols (n = 44 brain/head, n = 49 abdomen), **c)** Distribution of field of view (FOV) reported across protocols (n = 42 brain/head, n = 48 abdomen), **d)** Distribution of dose reported across protocols (n = 42 brain/head, n = 46 abdomen), dose reported as computer tomography dose index (CTDI) dose. Note that unspecified values were excluded from analysis. ns = not specified. **indicates highly significant (p < 0.001) differences between brain/head and abdomen protocols, *indicates significant differences (p < 0.01) between brain/head and abdomen protocols.

Table 2
Summary of exposure settings applied to achieve CBCT scans.

	No. protocols	kVp	mAs	No. projections	FOV
Brain/Head protocols					
0 ≤ 1 mGy	17	100 (100–100)	18.4 (18.0–42.1)	185 (183–366)	26.0 (20.0–27.0)
1 ≤ 2 mGy	10	100 (100–100)	71.0 (40.3–130.5)	369 (367–471)	26.0 (25.0–27.0)
2 ≤ 5 mGy	12	100 (100–100)	149.0 (144.8–150.0)	369 (198–500)	25.0 (21.0–26.1)
5 ≤ 10 mGy	0	–	–	–	–
≥ 10 mGy	1	100 (100–100)	150.0 (150.0–150.0)	500 (500–500)	10.0 (10.0–10.0)
Abdominal protocols					
0 ≤ 1 mGy	9	100 (100–100)	18.3 (18.0–33.0)	183 (180–330)	20.0 (20.0–21.0)
1 ≤ 2 mGy	3	100 (100–100)	108.0 (74.0–454.0)	693 (447–797)	38.5 (32.8–44.3)
2 ≤ 5 mGy	8	115 (100–120)	167.5 (150.0–252.5)	200 (143–538)	26.7 (25.0–32.0)
5 ≤ 10 mGy	9	120 (100–125)	361.0 (283.0–478.1)	367 (330–500)	33.7 (23.4–41.0)
≥ 10 mGy	15	125 (120–125)	680.0 (668.0–725.0)	655 (415–785)	45.0 (41.5–46.0)

Protocols within dose ranges from low dose <2 mGy, to higher dose >10 mGy. MV CBCT protocols and protocols where dose was unreported were excluded from analysis and the number of protocols sampled in each dose range is shown. kVp, mAs, number of projections and field of view are all reported as median (interquartile range).

35 (14 %) abdomen protocols.

In brain/head protocols, the anatomy considered by the registration algorithm varied: 22/35 (63 %) used bony anatomy only, 11/35 (31 %) used a two-step match on bone, then soft tissue. In contrast, only 7/35 (20 %) of abdominal protocols considered bony anatomy only, with the majority (24/35, 69 %) performing a two-step match on bone then soft tissue.

The most common set-up correction procedure across both sites was to correct for both translations and rotations (19/35, 54 % of brain/head protocols and 18/35, 51 % of abdomen protocols). This was followed by correction of translations only in 13/35 (37 %) brain/head and 11/35 (31 %) abdominal protocols. Just 1/35 (3 %) abdominal protocol

corrected rotations only.

The median (interquartile range) for set-up tolerances for both anatomical sites were similar, brain/head protocols: 1.5 (1.0–3.0) mm / 1.0 (0.2–2.3)° and abdominal protocols: 1.5 (0.8–3.0) mm / 1.0 (0.2–2.0)°. For abdominal protocols, only 3/31 (10 %) centres reported that 4D CBCT was used at their institution.

There was no consensus on the use of motion management strategies in abdominal sites, as most centres reported no strategy (36 %) and 30 % of the centres gave no response, (Fig. 4). Use of motion management strategies was not significantly associated with a reported dose (p = 0.88), suggesting that the possible improvement in image quality achieved through motion management strategies was not linked to use of a

Motion Management strategies

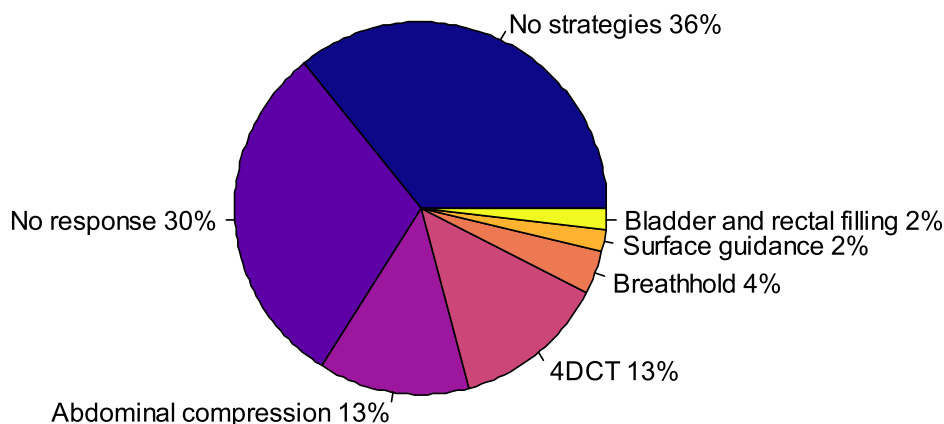


Fig. 4. Distribution of motion management strategies among all centres (n = 50). Note this was only addressed for abdominal protocols.

low-dose protocol.

Strategies aiming to reduce dose were reported by 35/50 (70 %) centres for brain/head sites and 30/50 (60 %) centres for abdominal sites. The most common strategies for both sites were to reduce exposure settings (brain/head: 19/49 (39 %), and abdominal: 19/49 (39 %)) followed by avoiding CBCT (brain/head: 7/49 (14 %) and abdominal: 3/49 (6 %)) (Table A1 in appendix B). Centres reporting that they implemented reduced exposure settings had significantly lower dose abdominal protocols ($p < 0.05$), but not brain/head protocols ($p = 0.83$). However, brain/head protocols overall were significantly lower in dose than abdominal protocols, suggesting that reported protocols already consider the differences in imaging need between the two sites.

Limitations to implementing CBCT were reported by 31/50 (63 %) centres. 11/50 (22 %) reported “No limitations”. Due to this low overall response rate, it is difficult to define major obstacles to CBCT optimisation (see Table A2 Appendix B). A comment that was repeated was the obstacle of body size variation and dose optimisation, e.g., that dose reduction may give good image quality in younger (smaller) patients but may not be sufficient in older (larger) patients.

Discussion

To our knowledge, this is the first survey in paediatric IGRT including specific technical settings for CBCT across European radiotherapy centres. CBCT is widely used and, typically, daily. However, large variations in technical acquisition parameters exist, with a greater consistency for brain/head sites compared to abdominal sites. Our systematic literature search revealed that few papers focusing on paediatric IGRT reported their protocol. In the 22 papers where protocols were reported, little consensus was observed and only seven papers focused on optimisation. Though it has been shown that low-dose CBCT for IGRT is feasible for paediatric patients, this was not mirrored in the survey with only 19 (39 %) centres reporting having optimised exposure settings for paediatric patients. Consequently, there is an urgent unmet need for implementing optimised paediatric IGRT protocols in clinical practice.

Reliable setup verification ensures safe delivery of radiotherapy. However, standardisation is challenging in a heterogenous patient population such as paediatric patients. Paediatric patients differ in many ways, e.g., age, body-size, and diagnosis. Many of them are also expected to become long-term survivors and state-of-the-art techniques are essential for minimizing late-effects [26]. It has been demonstrated that quality assurance (QA) in radiotherapy trials improve outcomes [27–31]. An

increasing focus on ensuring high quality in paediatric radiotherapy trials has given rise to QUARTET (Quality and Excellence in Radiotherapy and Imaging for Children and Adolescents with Cancer across Europe in Clinical Trials) [32–33]. QUARTET is a centralised external radiotherapy QA programme that supports clinical radiotherapy trials for children and adolescents across Europe. The mission is to ensure equity for high quality of radiotherapy plans across Europe for paediatric patients. Likewise, in 2008 paediatric radiologists launched the ImageGently campaign to increase awareness of “one-size does not fit all” in radiological procedures such as CT-scans [34]. Multiple protocols for CT-scan settings – for children and adolescents – guided by body-size and age have been suggested through the initiative [35–38]. Furthermore, Nagy et al recently published a systematic approach to reduce the imaging dose in paediatric CT-scans [39].

Previous surveys on the use of paediatric IGRT across diagnoses and institutions have reported a great variance in the applications for children, use of child-specific protocols, use of imaging modalities and frequency of acquisition. These surveys have together been pivotal in demonstrating the need for paediatric IGRT guidelines [12–14]. The present survey complements this published work by focusing on 3D IGRT performed with CBCT and collecting the technical parameters for contrasting sites: the brain/head and the abdomen.

We identified some limitations in our study. Only 29 centres out of 50 responding centres replied to all the questions, 30 replied with brain/head protocols and 31 with abdomen protocols. We acknowledge that the survey was very technical in its focus and hence, labour intensive for the centres to provide full and complete answers. It was recommended to consult the physicist responsible for paediatric RT at the institution, and this added complexity for the responders in a busy clinical work schedule. Another limitation is that only technical acquisition and registration parameters were addressed. We recognise that image quality is an essential part of IGRT optimisation, however, we believe this would be better addressed in a workshop enabling e.g., peer-review of image quality for different age groups and body sizes of patients.

From the literature review we found that low-dose CBCT for abdominal sites has been shown to be appropriate in clinical practice (cf. Table 1) [22–23,40–41,7–9]. A simulation study suggested that increasing dose holds limited benefit to image quality due to the presence of *dose-independent* anatomical noise from abdominal motion [9,23]. Interestingly, whilst the literature focused predominantly on body sites, the results from our survey (cf. Table 2) showed that low-dose protocols are primarily used for brain/head sites, suggesting that recommendations from optimisation studies have not yet widely

reached clinical practice in abdominal sites. Based on our survey and review, we propose to make dose-optimised paediatric CBCT protocols more accessible to all institutions by using a decision tree for imaging modality and frequency as suggested by Hua et al, in addition to the following steps [14]:

Minimize the dose by minimizing mAs.

- This can be done safely and easily and is already applied in daily clinical practice in some institutions (cf. Table 2 and [9]).

Always use a bow-tie filter to minimize dose exposure.

- Both the survey and the literature review suggest that bow-tie filters are under-used though they can easily be implemented in clinical practice (cf. Table 1 and [22]).

Develop a strategy for motion management in paediatric patients.

- A motion management strategy can improve clinical accuracy and create more consistent images for IGRT [9].

In conclusion low-dose CBCT protocols for paediatric patient exist in the literature but have not yet been widely adopted; we hope our survey will raise awareness of this unmet need and encourage wider implementation of dose-optimised protocols. The survey itself do not ensure that the reported protocols are fully optimised, and the literature regarding this is somewhat scarce.

As radiotherapy is under constant development, it is likely that new imaging technologies can further improve the balance between imaging dose and quality, and protocol optimisation should be seen an integral part of continuous quality improvement. The importance of quality assurance in paediatric radiotherapy clinical trials is already recognised, with groups such as QUARTET. We hope that IGRT protocols, complete with technical details and QA recommendations, will be included in such efforts.

Funding

This survey was done on behalf of The European Society of Paediatric Oncology (SIOPE) Radiation Oncology Working Group (ROWG).

MVM and DEØ was supported by the Danish Childhood Cancer Foundation (grant no 2015–9) and the Danish Cancer Society (ID: R248-A14714). MA acknowledge the support from Engineering and Physical Sciences Research Council (EPSRC), UK (grant number EP/T028017/1). ABA was supported by a SU2C-CRUK Pediatric Cancer New Discoveries Challenge Team Grant (grant no SU2C#RT6186).

CRedit authorship contribution statement

Daniella Elisabet Østergaard: Conceptualization, Methodology, Software, Data curation, Investigation, Writing – original draft. **Abigail Bryce-Atkinson:** Conceptualization, Methodology, Software, Data curation, Investigation, Writing – original draft. **Mikkel Skaarup:** Conceptualization, Writing – review & editing. **Bob Smulders:** Conceptualization, Writing – review & editing. **Lucy Siew Chen Davies:** Conceptualization, Writing – review & editing. **Gillian Whitfield:** Conceptualization, Writing – review & editing. **Geert O. Janssens:** Conceptualization, Writing – review & editing. **Lisa Lyngsie Hjalgrim:** Conceptualization, Writing – review & editing, Supervision. **Ivan Vogelius Richter:** Conceptualization, Writing – review & editing, Supervision. **Marcel van Herk:** Writing – review & editing, Supervision. **Marianne Aznar:** Conceptualization, Writing – review & editing, Supervision. **Maja Vestmø Marald:** Conceptualization, Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors are grateful for the critical input and endorsement by the steering committee members of the SIOPE Europe Radiation Oncology Working Group.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.radonc.2023.109963>.

References

- [1] Oeffinger KC, Mertens AC, Sklar CA, Kawashima T, Hudson MM, Meadows AT, et al. Chronic health conditions in adult survivors of childhood cancer. *N Engl J Med* 2006;355:1572–82. <https://doi.org/10.1056/NEJMsa060185>.
- [2] Suh E, Stratton KL, Leisenring WM, Nathan PC, Ford JS, Freyer DR, et al. Late mortality and chronic health conditions in long-term survivors of early-adolescent and young adult cancers: a retrospective cohort analysis from the Childhood Cancer Survivor Study. *Lancet Oncol* 2020;21:421–35. <https://linkinghub.elsevier.com/retrieve/pii/S1470204519308009>.
- [3] Palmer JD, Tsang DS, Tinkle CL, Olch AJ, Kremer LCM, Ronckers CM, et al. Late effects of radiation therapy in pediatric patients and survivorship. *Pediatr Blood Cancer* 2021;68. <https://doi.org/10.1002/pbc.28349>.
- [4] Dawson LA, Sharpe MB. Image-guided radiotherapy: rationale, benefits, and limitations. *Lancet Oncol* 2006;7:848–58. <https://linkinghub.elsevier.com/retrieve/pii/S1470204506709044>.
- [5] Crehange G, Mirjole C, Gauthier M, Martin E, Truc G, Peignaux-Casasnovas K, et al. Clinical impact of margin reduction on late toxicity and short-term biochemical control for patients treated with daily on-line image guided IMRT for prostate cancer. *Radiother Oncol* 2012;103:244–6.
- [6] Lundgaard AY, Hjalgrim LL, Rechner LA, Josipovic M, Joergensen M, Aznar MC, et al. TEDDI: radiotherapy delivery in deep inspiration for pediatric patients - A NOPHO feasibility study. *Radiation Oncol* 2018;13.
- [7] Olch AJ, Alaei P. How low can you go? A CBCT dose reduction study. *J Appl Clin Med Phys* 2021;22:85–9.
- [8] Alcorn SR, Zhou XC, Bojchko C, Rubo RA, Chen MJ, Dieckmann K, et al. Low-Dose Image-guided pediatric CNS radiation therapy: final analysis from a prospective low-dose cone-beam CT protocol from a multinational pediatrics consortium. *Technol Cancer Res Treat* 2020;19:1533033820920650.
- [9] Bryce-Atkinson A, De Jong R, Marchant T, Whitfield G, Aznar MC, Bel A, et al. Low dose cone beam CT for paediatric image-guided radiotherapy: image quality and practical recommendations. *Radiother Oncol J Eur Soc Ther Radiol Oncol* 2021;163:68–75.
- [10] Deng J, Chen Z, Roberts KB, Nath R. Kilovoltage imaging doses in the radiotherapy of pediatric cancer patients. *Int J Radiat Oncol Biol Phys* 2012;82:1680–8.
- [11] Zhang Y, Yan Y, Nath R, Bao S, Deng J. Personalized assessment of kV cone beam computed tomography doses in image-guided radiotherapy of pediatric cancer patients. *Int J Radiat Oncol Biol Phys* 2012;83:1649–54.
- [12] Alcorn SR, Chen MJ, Claude L, Dieckmann K, Ermoian RP, Ford EC, et al. Practice patterns of photon and proton pediatric image guided radiation treatment: results from an International Pediatric Research consortium. *Pract Radiat Oncol* 2014;4:336–41.
- [13] Wall V, Marignol L, ElBeltagi N. Image-guided radiotherapy in paediatrics: a survey of international patterns of practice. *J Med Imaging Radiat Sci* 2018;49:265–9. <https://linkinghub.elsevier.com/retrieve/pii/S1939865417303867>.
- [14] Hua C, Vern-Gross TZ, Hess CB, Olch AJ, Alaei P, Sathiaselan V, et al. Practice patterns and recommendations for pediatric image-guided radiotherapy: a Children's Oncology Group report. *Pediatr Blood Cancer*. 2020;67. <https://doi.org/10.1002/pbc.28629>.
- [15] Washio H, Ohira S, Funama Y, Ueda Y, Morimoto M, Kanayama N, et al. Dose reduction and low-contrast detectability using iterative CBCT reconstruction algorithm for radiotherapy. *Technol Cancer Res Treat*. 2022;21:153303382110673. <https://doi.org/10.1177/15330338211067312>.
- [16] Sheikh K, Liu D, Li H, Acharya S, Ladra MM, Hrinivich WT. Dosimetric evaluation of cone-beam CT-based synthetic CTs in pediatric patients undergoing intensity-modulated proton therapy. *J Appl Clin Med Phys* 2022;23:e13604.
- [17] Hess CB, Thompson HM, Benedict SH, Seibert JA, Wong K, Vaughan AT, et al. Exposure risks among children undergoing radiation therapy: considerations in the era of image guided radiation therapy. *Int J Radiat Oncol Biol Phys* 2016;94:978–92.
- [18] Alaei P, Spezi E, Reynolds M. Dose calculation and treatment plan optimization including imaging dose from kilovoltage cone beam computed tomography. *Acta Oncol (Madr)* 2014;53:839–44. <https://doi.org/10.3109/0284186X.2013.875626>.

- [19] Dzierma Y, Mikulla K, Richter P, Bell K, Melchior P, Nuesken F, et al. Imaging dose and secondary cancer risk in image-guided radiotherapy of pediatric patients. *Radiat Oncol* 2018;13:168.
- [20] Ding GX, Munro P, Pawlowski J, Malcolm A, Coffey CW. Reducing radiation exposure to patients from kV-CBCT imaging. *Radiother Oncol J Eur Soc Ther Radiol Oncol* 2010;97:585–92.
- [21] Ding GX, Coffey CW. Radiation dose from kilovoltage cone beam computed tomography in an image-guided radiotherapy procedure. *Int J Radiat Oncol Biol Phys* 2009;73:610–7.
- [22] Bryce-Atkinson A, de Jong R, Bel A, Aznar MC, Whitfield G, van Herk M. Evaluation of ultra-low-dose paediatric cone-beam computed tomography for image-guided radiotherapy. *Clin Oncol* 2020;32.
- [23] Rao AD, Lee J, Fu W, Nicholas S, Alcorn SR, Moore J, et al. Precision of 2 low-dose abdomen/pelvis cone beam computed tomography protocols for alignment to bone and soft tissue in pediatric patients receiving image guided radiation therapy. *Pr Radiat Oncol*. 2019;9:e307–13.
- [24] Ciardo D, Alterio D, Jereczek-Fossa BA, Riboldi M, Zerini D, Santoro L, et al. Set-up errors in head and neck cancer patients treated with intensity modulated radiation therapy: quantitative comparison between three-dimensional cone-beam CT and two-dimensional kilovoltage images. *Phys Medica* 2015;31:1015–21. <https://linkinghub.elsevier.com/retrieve/pii/S1120179715003269>.
- [25] Windmeijer C, Bel A, De Jong R, Balgobind B, Collaboration G, Rasch C, et al. PO-1018 Current status of pediatric image-guided radiation therapy in Europe: an international survey. *Radiother Oncol* 2019;133.
- [26] Landier W, Skinner R, Wallace WH, Hjorth L, Mulder RL, Wong FL, et al. Surveillance for late effects in childhood cancer survivors. *J Clin Oncol* 2018;36:2216–22. <https://doi.org/10.1200/JCO.2017.77.0180>.
- [27] Weber DC, Tomsej M, Melidis C, Hurkmans CW. QA makes a clinical trial stronger: evidence-based medicine in radiation therapy. *Radiother Oncol* 2012;105:4–8. <https://linkinghub.elsevier.com/retrieve/pii/S0167814012003593>.
- [28] Ohri N, Shen X, Dicker AP, Doyle LA, Harrison AS, Showalter TN. Radiotherapy protocol deviations and clinical outcomes: a meta-analysis of cooperative group clinical trials. *JNCI J Natl Cancer Inst* 2013;105:387–93. <https://doi.org/10.1093/jnci/djt001>.
- [29] Kron T, Fox C, Ebert MA, Thwaites D. Quality management in radiotherapy treatment delivery. *J Med Imaging Radiat Oncol* 2022;66:279–90. <https://doi.org/10.1111/1754-9485.13348>.
- [30] Kelly SM, Turcas A, Corning C, Bailey S, Cañete A, Clementel E, et al. Radiotherapy quality assurance in paediatric clinical trials: first report from six QUARTET-affiliated trials. *Radiother Oncol* 2023;182:109549. <https://linkinghub.elsevier.com/retrieve/pii/S0167814023000877>.
- [31] Chang D, Moore A, van Dyk S, Khaw P. Why quality assurance is necessary in gynecologic radiation oncology. *Int J Gynecol Cancer* 2022;32:402–6. <https://doi.org/10.1136/ijgc-2021-002534>.
- [32] Kelly SM, Effeney R, Gaze MN, Bernier-Chastagner V, Blondeel A, Clementel E, et al. QUARTET: a SIOP Europe project for quality and excellence in radiotherapy and imaging for children and adolescents with cancer. *Eur J Cancer* 2022;172:209–20. <https://linkinghub.elsevier.com/retrieve/pii/S0959804922003276>.
- [33] de Rojas T, Clementel E, Giralt J, Cruz O, Boterberg T, Kortmann R-D, et al. Radiotherapy practice for paediatric brain tumours across Europe and quality assurance initiatives: current situation, international survey and future perspectives. *Eur J Cancer* 2019;114:36–46. <https://linkinghub.elsevier.com/retrieve/pii/S0959804919302199>.
- [34] Goske MJ, Applegate KE, Boylan J, Butler PF, Callahan MJ, Coley BD, et al. The image gently campaign: working together to change practice. *Am J Roentgenol* 2008;190:273–4. <https://doi.org/10.2214/AJR.07.3526>.
- [35] Boylan JK. Image Gently® at 10 Years. *J Am Coll Radiol* 2018;15:1193–5. <https://linkinghub.elsevier.com/retrieve/pii/S1546144018302527>.
- [36] Frush DP, Strauss KJ. Image gently: getting it right. *J Am Coll Radiol* 2017;14:575–6. <https://linkinghub.elsevier.com/retrieve/pii/S1546144017303058>.
- [37] Sammer MBK, Frush DP. Image Gently™ Includes “Image IntelliGently. *J Am Coll Radiol*. 2023 <https://linkinghub.elsevier.com/retrieve/pii/S1546144023006269>.
- [38] Moore QT, Frush DP. Image gently: interdisciplinary collaboration for analysis of radiation-related data to improve pediatric radiography. *J Am Coll Radiol* 2021;18:1469–70. <https://linkinghub.elsevier.com/retrieve/pii/S1546144021005421>.
- [39] Nagy E, Tschauner S, Schramek C, Sorantin E. Paediatric CT made easy. *Pediatr Radiol* 2022;53:581–8. <https://doi.org/10.1007/s00247-022-05526-0>.
- [40] De Jong R, Lens E, Van Herk M, Alderliesten T, Kamphuis M, Dávila Fajardo R, et al. OC-0282: optimizing cone-beam CT presets for children to reduce imaging dose illustrated with craniospinal axis. *Radiother Oncol [Internet]* 2014;111:S109–10. <https://linkinghub.elsevier.com/retrieve/pii/S016781401530387X>.
- [41] Huang Y, Du Y, Li C, Wang H, Zu Z, Feng Z, et al. Pediatric cone beam CT on Varian Halcyon and TrueBeam radiotherapy systems: radiation dose and positioning accuracy evaluations. *J Radiol Prot Off J Soc Radiol Prot* 2019;39:739–48.