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Recommendations for the organisation of care in paediatric radiation oncology across Europe

Janssens, Geert O; Timmermann, Beate; Laprie, Anne; Mandeville, Henry; Padovani, Laetitia; Chargari, Cyrus; Journy, Neige; Kameric, Lejla; Kienesberger, Anita; Brunhofer, Melanie; Kozhaeva, Olga; Gasparotto, Chiara; Kearns, Pamela; Boterberg, Tom; Lievens, Yolande; Vassal, Gilles

DOI:

[10.1016/j.ejca.2019.03.003](https://doi.org/10.1016/j.ejca.2019.03.003)

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Document Version

Publisher's PDF, also known as Version of record

Citation for published version (Harvard):

Janssens, GO, Timmermann, B, Laprie, A, Mandeville, H, Padovani, L, Chargari, C, Journy, N, Kameric, L, Kienesberger, A, Brunhofer, M, Kozhaeva, O, Gasparotto, C, Kearns, P, Boterberg, T, Lievens, Y & Vassal, G 2019, 'Recommendations for the organisation of care in paediatric radiation oncology across Europe: a SIOPE-ESTRO-PROS-CCI-Europe collaborative project in the framework of the JARC' European Journal of Cancer, vol. 114, pp. 47-54. <https://doi.org/10.1016/j.ejca.2019.03.003>

[Link to publication on Research at Birmingham portal](#)

Publisher Rights Statement:

Checked for eligibility: 13/05/2019

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<https://doi.org/10.1016/j.ejca.2019.03.003>

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Current Perspective

Recommendations for the organisation of care in paediatric radiation oncology across Europe: a SIOPE–ESTRO–PROS–CCI-Europe collaborative project in the framework of the JARC[☆]



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Received 19 February 2019; accepted 4 March 2019

Available online 3 May 2019

[☆] SIOPE-affiliated countries (<https://www.siope.eu/about-siope/members/>), plus Albania, Estonia and Montenegro.

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KEYWORDS

Paediatric;
Radiotherapy;
Standards of care;
Recommendations;
Radiation oncology;
Paediatric oncology;
Childhood cancer;
SIOPE

Abstract Disparities in survival and long-term side-effects from paediatric cancer are observed across European Society for Paediatric Oncology (SIOPE)–affiliated countries. The Joint Action on Rare Cancers (JARC) is a project supported by the European Union and member states aiming to formulate recommendations on rare cancers, including paediatric malignancies, to reduce inequalities and to improve health outcomes. Most paediatric cancers are treated by a combination of systemic agents, surgery and/or radiotherapy. Radiotherapy for children is becoming increasingly complex because of the growing availability of new modalities and techniques and the evolution in molecular biology. These added challenges have the potential to enhance disparities in survival and side-effects between countries, but also among centres in the same country. To tackle radiotherapy-related inequalities, representatives of SIOPE, European Society for Radiotherapy and Oncology, Paediatric Radiation Oncology Society and Childhood Cancer International–Europe defined ‘standard’ and ‘optional’ levels to deliver Good Clinical Practice–compliant treatment in paediatric radiation oncology with a focus on patient-related care, education and training. In addition, more than 250 paediatric radiotherapy centres across the SIOPE-affiliated countries have been mapped. For a better understanding of resources in paediatric radiotherapy, JARC representatives are working on an online survey for paediatric radiation oncologists of each centre in SIOPE-affiliated countries. The outcome of this survey will give an insight into the strengths and weaknesses of paediatric radiotherapy across SIOPE-affiliated countries and can be relevant for European Reference Networks in terms of collaboration pathways and referrals in paediatric radiotherapy.

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1. Introduction

Close collaboration among professionals in paediatric haematology and oncology has resulted in a significant survival benefit over the last decades [1]. Despite these efforts, disparities in survival rates of more than 20% and long-term side-effects are a reality across Europe [2–6]. To reduce these inequalities and to improve health outcomes in European countries, a project entitled ‘European Standards of Care for Children with Cancer’ had been initiated with the support of the European Union (EU) [7,8]. This project consolidated the ideal requirements for centres specialised in the treatment of children with cancer across Europe.

Annually, in countries affiliated to SIOPE Europe, almost 25,000 new patients aged 0–19 years are diagnosed with cancer of whom more than 4000 will die because of disease progression or disease-related toxicity (Table 1) [9]. Most paediatric cancers are treated by a combination of systemic agents, surgery and/or

radiotherapy (RT), making paediatric radiation oncologists core medical members of the childhood cancer treatment team. Historically, RT for children was delivered using a standard-treatment-for-all approach. Nowadays, with the growing availability of new modalities and techniques, RT for children is becoming particularly complex and requires an individual approach. In addition, there has been a marked increase in the understanding of the molecular biology of paediatric cancers, and in addition, the potential late effects of RT on normal organ structure and function are being recognised and quantified in relation to the treatment given.

The **Joint Action on Rare Cancers (JARC)** is a multistakeholder collaborative project supported by the EU and member states, which aims to formulate policy recommendations on rare cancers, including paediatric malignancies [10]. For RT-related issues in paediatric malignancies (Work Package 9 [WP9]), there is involvement from strategic partners including SIOPE (and its QUARTET¹ project), Childhood Cancer International–Europe (CCI-Europe), European Society for Radiotherapy and Oncology (ESTRO) and Paediatric Radiation Oncology Society (PROS). To achieve the best possible outcomes for children, treatment centres should meet an appropriate level of standards and have access to continuously updated ‘best practice’ information. A recent survey in the context of

Table 1
Childhood cancer incidence and mortality in SIOPE-affiliated countries: 2018 (source: Globocan).

Type of cancer (age: 0–19 years)	Incidence	Mortality
Haematologic malignancies	9938	1643
Brain tumours	3184	1168
Solid tumours	7467	1503
Total	24,240	4314

SIOPE, European Society for Paediatric Oncology.

¹ Quality and Excellence in Radiotherapy and Imaging for Children and Adolescents with Cancer across Europe in Clinical Trials.

this project demonstrated that general guidelines for paediatric radiation oncology are available in only three (France, Germany and United Kingdom [UK]) of 30 European countries responding to the survey.

Representatives of the strategic partners defined ‘standard’ and ‘optional’ levels to deliver Good Clinical Practice (GCP)–compliant treatment in paediatric radiation oncology. Given the complexity of paediatric radiation oncology, the list of items will focus on patient care, education and training, as well as the organisation of patient-related research.

2. European Standards of care for paediatric radiation oncology

2.1. Patient care

2.1.1. Tumour board

2.1.1.1. Standard. Patients with newly diagnosed tumours, treatment response evaluations or any suspicion of progression should be discussed in a multidisciplinary team meeting, which registers treatment decisions including the indication for RT, timing of treatment and requirement for concomitant treatment modalities. Team meetings should be scheduled on a weekly basis and consist of all core medical specialists, including at least one paediatric oncologist, radiation oncologist and (neuro)surgeon, with additional support from a radiologist, a nuclear medicine physician and a pathologist. To allow specialists working at distance from the board room, a remote conferencing system ideally should be available (Table 2–A).

2.1.1.2. Optional. To enhance the quality of the discussion for specific patient groups, other specialists such as surgeons, neurologists, ophthalmologists, endocrinologists and/or clinical geneticists may join.

2.1.2. Radiotherapy consultation

2.1.2.1. Standard. Within an informational talk with the family and the patient, the paediatric radiation oncologist discusses the indication for radiation therapy in the context of the disease and/or other treatment modalities. He or she explains the procedure related to RT (fixation, imaging, anaesthesia and treatment), the potential acute and late side-effects and the logistics related to the RT process. When a significant RT dose to the ovaries or testes is expected, referral for fertility preservation should be considered and discussed with the family. Typically, both parents (or legal guardians) are involved. It is recommended to fully inform children from the age of 12–14 years or depending on the individual stage of development. To explain RT to children, informal booklets, textbooks, apps or movies are available, adapted for different age groups. Guided tours of the department can be reassuring for children,

helping to familiarise them with the new surroundings. Outside working hours, a 24-h on-call service is essential to manage emergencies or complications, if necessary, via colleague paediatric oncologists. To cover holiday periods or weekends, at least two radiation oncologists with knowledge of paediatric tumours are available (Table 2–B).

2.1.2.2. Optional. Play specialists (or equivalent personnel) prepare and support the child before and during RT, using a variety of techniques which can include mini-computed tomography (CT), magnetic resonance imaging (MRI) and/or linear accelerator (LINAC). Play specialists have been shown to significantly reduce the requirement for anaesthesia in young children [11]. Ideally, age-adapted environments should be available, which may include a playground for children.

2.1.3. Radiotherapy treatment preparation

2.1.3.1. Standard. To obtain optimal daily reproducibility during RT, the department is able to use fixation tools (thermoplastic mask, neck support, vacuum mattress and body cast), individually manufactured by experienced radiation therapists (RTTs) or mould room technicians. Three-dimensional CT-based treatment planning is required for optimal geometrical and anatomical information. In the era of advanced diagnostic imaging, software and knowledge on clinical image processing, in particular for coregistration, a central review of treatment plans (e.g. QUARTET) is needed. Before RT treatment planning starts, the RTT or dosimetrist is instructed about the positioning of the child, the concerned body region and specific dose constraints to maximise target dose coverage and to reduce the risk of late effects. When a clinically significant benefit is expected with advanced photon techniques, proton beam therapy or brachytherapy, the patient should be referred to a specialised centre defined as the relevant partnering reference institution if not available in-house. To maximise the chances of compliance from the child, longer time slots are needed for preparation. In cases where there is a lack of compliance of a child, especially for those aged 3 years or younger, the department can prepare treatment with the patient being under anaesthesia (Table 2–C).

2.1.3.2. Optional. State-of-the-art RT departments implement 4D information when motion of the target volume is expected and rely on MRI or positron-emission tomography (PET)–CT images to prepare the RT process. Besides conventional highly conformal RT, intensity-modulated RT and proton beam therapy are being used in an increasing number of paediatric patients and are accessible via defined cooperation

Table 2
Patient care.

Workflow and goals	Personnel	Equipment
A. Tumour board	Standard or mandatory	Standard or mandatory
Diagnosis + staging primary tumour, recurrence	Multidisciplinary team	Board room
Treatment protocol	Paediatric oncologist, (neuro)surgeon, radiation oncologist	Remote conferencing system available
Response on treatment	Supported by	
Registration	Radiologist, (nuclear medicine physician), pathologist (Bi)weekly Optional Neurologist Ophthalmologist Endocrinologist Clinical geneticists	Optional
B. RT Consultation	Standard or mandatory	Standard or mandatory
Discussion on RT procedure (fixation, imaging, anaesthesia)	At least 2 radiation oncologists with knowledge on paediatric tumours	Child-friendly environment
Discussion on potential acute late side-effects	24-h on-call service, if necessary via cooperation	Informational booklet, textbook, app or movie
Discussion on logistics related to RT	Reference network for fertility preservation Optional Play specialist or equivalent	Guided tour in the department Optional Healing environment Play area for children Mini-CT/MRI/LINACS
C. Treatment preparation	Standard or mandatory	Standard or mandatory
Fixation (mask, neck support, body cast, vacuum mattress)	Dedicated RTTs (mould room, CT and PET, MRI if applicable)	Mould room with dedicated tools for fixation
Image acquisition	RTT with knowledge of clinical image processing (coregistration)	CT
Image coregistration	RTT with interest in paediatric oncology	Access to MRI, when indicated
RT planning	Radiation oncologist with knowledge on paediatric tumours Clinical physicist (Paediatric) anaesthesiologist	Software for image fusion (MR–PET–CT) 3D delineation system 3D treatment planning system for photons–electrons Anaesthesia equipment Reference network for brachytherapy Reference network for advanced photon therapy Reference network for proton therapy Access to QUARTET or central review of RT plans (study patients) Child-friendly environment
RT QA (intern)		Optional (4D) CT (4D) PET-CT (4D) MRI (Rotational) IMRT–IMPT Stereotactic RT 3D treatment planning system for protons Reanimation unit for paediatrics Brachytherapy operation equipment
RT QA (extern)		Standard or mandatory Photon–electron therapy
D. RT treatment delivery	Standard or mandatory	Standard or mandatory
Delivery of conformal radiotherapy	RTT with affinity for children	Photon–electron therapy
To respect onset of RT following international guidelines	Radiation oncologist, weekly or biweekly patient contact	Patient position verification tools with correction protocols
To respect overall treatment time	Paediatric oncologist available Anaesthesiologist	Easy access to paediatric oncology unit (e.g. concomitant treatment) Anaesthesia equipment Adapted time slots to treat children Child-friendly environment

Table 2 (continued)

Workflow and goals	Personnel	Equipment
	Optional	Optional Daily online position correction protocols Cone beam CT scan Image-guided RT Adaptive RT Stereotactic RT Proton therapy MRI-guided RT Brachytherapy
E. Follow-up after RT	Standard or mandatory	Standard or mandatory
Awareness of late side-effects of treatment	Radiation oncologist	Child-friendly environment
	Optional Paediatric nurse	Registration of late toxicity Optional LATER multidisciplinary outpatient clinic

CT, computed tomography; PET, positron-emission tomography; RT, radiotherapy; RTT, radiation therapist; MRI, magnetic resonance imaging; LINAC, linear accelerator; QA, quality assurance; IMRT, intensity modulated radiation therapy; IMPT, intensity modulated proton therapy; LATER, late effects after childhood cancer.

pathways, whereas the indications for stereotactic ablative RT or brachytherapy remain limited.

2.1.4. Radiotherapy treatment delivery

2.1.4.1. Standard. With the exception of a limited number of indications (e.g. flank RT), opposing photon beams are avoided, and highly conformal RT should be the standard of care. Regardless of any study participation, it is recommended to respect the defined timing for the start of RT and overall treatment duration, as mentioned in the treatment protocols. In the RT treatment room, at least one RTT or healthcare provider has particular affinity with paediatric patients. Patient position verification protocols using laser, light field and X-ray systems are essential to assure target coverage and to reduce the RT dose to normal structures. Time slots are adapted to the compliance of the child. In case of lack of compliance, the department can deliver RT with the patient being under general anaesthesia within the time restrictions of the tumour protocol (Table 2–D).

2.1.4.2. Optional. Daily positioning verification by X-ray, cone beam CT or MRI scans with online corrections can facilitate a reduction in margins around the clinical target volume and consequently limit normal tissue exposure to RT.

2.1.5. Radiotherapy follow-up

2.1.5.1. Standard. Awareness of late side-effects caused by RT after a childhood cancer treatment is important. Routine follow-up visits and systematic registration of moderate to severe long-term side-effects are key for management of late toxicities, improving understanding and directing strategies of prevention for childhood cancer survivors and future generations (Table 2–E).

2.1.5.2. Optional. Participation by the radiation oncologist in a multidisciplinary outpatient clinic is preferred, given the complexity of side-effects due to the different

treatment modalities observed in a significant number of long-term survivors.

2.2. Education and training

2.2.1. Standard

The low incidence and high number of different paediatric tumour types, combined with an increasing body of new molecular information, requires basic education and refresher courses at regular intervals. Basic education can be obtained during paediatric oncology courses, some of them even dedicated to radiation oncology, or by spending a time period in a reference centre for paediatric (radiation) oncology. International organisations such as PROS, SIOPE, ESTRO, American Society for Radiation Oncology (ASTRO) and national societies such as the UK Children's Cancer and Leukemia Group offer educational courses to refresh the knowledge on paediatric (radiation) oncology. Moreover, a significant number of patients in daily practice will not fit the existing guidelines. In such situations, radiation oncologists treating paediatric patients should rely on an (inter)national network of experts. Consequently, attending teaching courses and meetings is recommended at least once every two years. In addition, SIOPE is working on an online textbook that will define the 'gold standard' per tumour type and summarise ongoing studies per disease site and reference radiation oncology specialists across Europe. All radiation oncologists involved in paediatric oncology will be encouraged to register for this online tool. Furthermore, SIOPE is planning to organise (bi)monthly courses on specific topics in paediatric oncology with room for discussion on individual cases (Table 3).

2.2.2. Optional

In many countries, discussions are ongoing to propose a minimal level of expertise, or number of cases treated

Table 3
Education and training.

Goals	Personnel	Equipment
To get knowledge on the ‘gold standard’ in paediatric RT	Standard or mandatory Need for basic education in paediatric radiation oncology by	Standard or mandatory SIOPE/ESTRO (online) textbook with ‘gold standard’ policy per disease across EU
To ask for expert opinions on difficult cases	Paediatric oncology courses dedicated to radiation oncologists such as	Access by registration (free membership)
To get access to a (inter) national network	ESTRO or –PROS course	Chapters edited by RT chairs from SIOPE working groups
To obtain a certification in paediatric oncology	ESTRO–ASTRO congress	Expiration date: 2 y
	SIOPE annual meetings	Web-conference system for online courses by experts on difficult cases
	National courses on paediatric RT (certification)	
	Molecular biology for the paediatric radiation oncologist (certification)	
	Training at a reference centre for paediatric (radiation) oncology	
	Refresher courses	
	Mandatory (with certificate)	
	Optional	Optional
	Defining a minimum level of expertise	Defining a minimum number of cases treated per institution

ASTRO, American Society for Radiation Oncology; ESTRO, European Society for Radiotherapy and Oncology; PROS, Paediatric Radiation Oncology Society; RT, radiotherapy; SIOPE, European Society for Paediatric Oncology.

per institution, given the rare and diverse range of tumours faced in paediatric oncology.

2.3. Patient-related research

2.3.1. Standard

Centres are encouraged to participate and include patients in ongoing and therapy-optimising study protocols and (interdisciplinary) registries and/or adhere to (inter)national guidelines. Registries should focus on locoregional failure, survival, dose prescription, dose to organs at risk and late toxicity items. Indeed, central registration of outcomes and toxicities is of utmost importance to demonstrate progress in the reduction of inequalities across SIOPE-affiliated countries, which is the main purpose of this project (Table 4).

2.3.2. Optional

Data managers can support physicians with the administrative burden.

3. Discussion

Across countries affiliated with SIOPE, significant disparities in survival and the severity of long-term side-effects are observed [2–7]. Although the reasons for these disparities may be multifactorial, differences in the organisation of complex multidisciplinary care and education on rare diseases, such as paediatric cancers, are probably among the most important explanations. To

tackle the issue of disparities related to RT, in this article, representatives of SIOPE, PROS, ESTRO and CCI-Europe defined a list with ‘standard’ and ‘optional’ levels to deliver GCP-compliant treatment in paediatric radiation oncology focussing on patient care, education and training, as well as the organisation of patient-related research.

Roughly one in three children diagnosed with cancer will undergo RT with curative intent during their disease course [12]. As the vast majority of paediatric cancer clinics in Europe diagnose less than one hundred new patients annually, an associated radiation oncologist will treat on average of 1 or maybe 2 or 3 similar cases per year. With the growing availability of new modalities and techniques and the evolution in molecular biology, RT for children is becoming increasingly complex and requires an individualised approach. These added challenges for paediatric radiation oncologists have the potential to enhance disparities in survival and side-effects between countries but also among centres in the same country. Consequently, national discussions on requirements for a minimum number of cases or patients per treating institution (ranging from 5 to up to 50 children treated with RT per year) are ongoing. Although consensus on a minimum number of patients is far from reached, it may be obvious that centres treating a higher number of patients will benefit from their aggregated experiences. High-volume centres may have the opportunity to generate better techniques for

Table 4
Research.

Goals	Personnel	Equipment
Participation in open study protocols of all kinds	Standard or mandatory Radiation oncologists with access to study protocols	Standard or mandatory Data registration platform (also off-protocol)
Participation in surveys	Ethical committee	
Registration of outcome (including late toxicity)	Optional Data managers	Optional

challenging scenarios and to establish a dedicated team that can participate in specialist meetings and educational activities [13–15].

For a better understanding of resources in paediatric RT, SIOPE mapped more than 250 paediatric RT centres across SIOPE-affiliated countries. Currently, JARC WP9 representatives are working on an online survey for paediatric radiation oncologists in each centre, focussing on the standard and optional levels of organisation of patient care, education and clinical research. The outcome of this survey will give an insight into the strengths and weaknesses of paediatric RT across SIOPE-affiliated countries and can be relevant for European Reference Networks in terms of collaboration pathways and referrals in paediatric RT.

4. Conclusions

With the increasing degree of complexity of RT for paediatric cancers, establishing appropriate structures is crucial to reduce disparities in survival rates and in the severity of long-term side-effects. This European initiative would like to encourage treating institutions to create the appropriate environment for children receiving radiation therapy by defining fundamental structures and processes related to patient care, education and training, and the organisation of patient-related research.

Role of contributors

G.J. and G.V. contributed to manuscript concept and design. All contents of this manuscript were formulated by a group of experts in the field of paediatric (radiation) oncology. All authors edited, reviewed and approved the final version of the report.

Conflict of interest statement

None declared.

Funding

This research was supported by the joint action ‘724161/JARC’ which has received funding from the European Union’s Health Programme (2014–2020).

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