SIOP 2023
INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY
OTTAWA, CANADA | OCTOBER 11-14, 2023

Irradiation of paediatric patients with impt using controlled inspiration – feasibility, acute and early late toxicity – results from the proton therapy center in prague

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Background and Aims

Radiotherapy to the thorax/mediastinum carries the risk of severe acute and late toxicities in long-term survivors. Proton bream radiotherapy (PBRT) with controlled breathing reduces the dose to organs at risk, minimizing adverse effects. We evaluated the feasibility, toxicity and therapeutic outcomes in pediatric patients treated at our center.

Methods

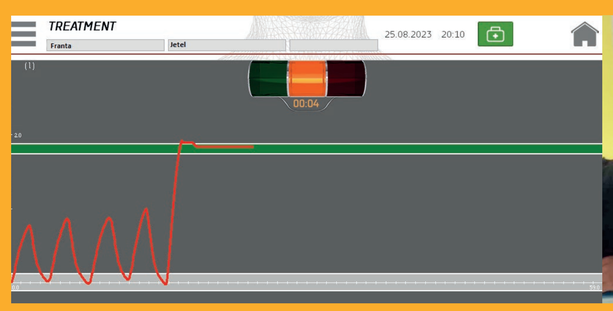
Between August 2018 and December 31st, 2022, 19 pediatric patients (21 courses of irradiation, 2 re-irradiated patients is STS group) underwent PBRT with pencil beam scanning and controlled inspiration. 19 courses were radical and 2 were palliative re-irradiation. All patients received initial training, followed by fixation and the planning CT.

Patient No	Sex	Age	Time of follow-up / months	Treatment protocol	Histology	Treatment volume	Dose / GyE	No of fraction	Acute toxicity	Late toxicity greater than G2	Disease status
1	M	18	53	EuroNet-PHL-C1 TG3	Hodgkin Lymphoma	neck, suclavicular, mediastinum	29,8	16	oesophagus G1, skin G1	none	CR
2	F	17	43	EuroNet-PHL-C1 TG1	Hodgkin Lymphoma	mediastinum	29,8	16	oesophagus G1, skin G1	none	CR
3	F	17	42	EuroNet-PHL-C1 v TG-2	Hodgkin Lymphoma	mediastinum, bilateral neck, supraclavicular bilat, axila left, hilus left	29,8	16	skin G1, oesophagus G2	none	CR
4	M	16	28	EuroNet-PHL-C1, TG-3	Hodgkin Lymphoma	bilateral neck and supraclavicular region, mediastinum	29,8	16	skin G1, oesophagus G1	none	CR
5	M	18	30	EuroNet-PHL-INterim Tre-atment Guidelines 2013-1-27	Hodgkin Lymphoma	neck left, supra a infraklavicular region bilat, mediastinum	29,8	16	Leu G2	none	CR
6	M	16	37	EuroNet-PHL-C2	Hodgkin Lymphoma	bilateral neck, supra a infraclavicular region, mediastinum, axilla bilat, bilateral hilus, supra and infradiafragmatical nodes	19,8	11	no significant toxicity	none	CR
7	F	19	29	EuroNet-PHL-C1 TG2	Hodgkin Lymphoma	neck, supraclavicular, mediastinum	29,8	16	no significant toxicity	none	CR
8	F	14	24	EuroNet-PHL C2 TL3	Hodgkin Lymphoma	bilateral neck, supra a infraclavicular region, mediastinum, left axila, bilateral hilus, pleura, spleen, paraaortic lymph nodes, left ilic nodes	19,8	11	oesophagus G1, Leu G1, Lymfo 2-3	none	CR
9	M	12	20	Euronet PHL-C2	Hodgkin Lymphoma	neck, supra and infraclavicular, bilateral axila, mediastinum, retroperitoneal nodes, liver hilus, spleen	19,80	11	salivary glands G1	none	CR
10	M	16	17	Euro-NetPHL-C1	Hodgkin Lymphoma	supra and infraclavicular region	19,8	11	upper GIT G2	none	PD / marginal relapse
11	M	17	3	EuroNet-PHL-C2 interim - TL2	Hodgkin Lymphoma	supraclavicular region, lower neck, mediastinum, bilateral hilar nodes	19,8	11	lung G1, oesophagus G1	none	CR
12	M	19	3	EuroNet-PHL-C2 TL2	Hodgkin Lymphoma	bilateral neck and supraclavicular reagion, mediastinum	19,8	11	no significant toxicity	none	CR
13	M	15	3	EuroNet-PHL-C2 interim - TL2	Hodgkin Lymphoma	bilateral lower neck, mediastinum, retrosternal and pretracheal nodes, right hilus	19,8	11	skin G1, oesophagus G1	none	CR

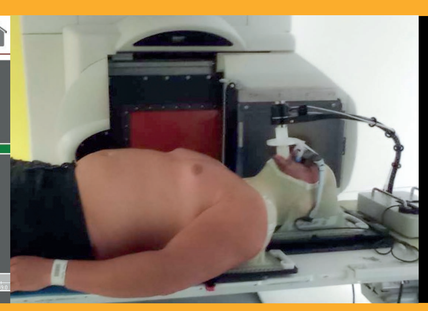
The patients with STS received 45–59.4 GyE to the chest, upper abdominal wall, diaphragm, epigastrium, or mediastinum, with a median follow-up of 13 months. There were eight courses in total with two re-irradiations. Three patients died due to metastatic disease progression, one patient is alive with disease progression, and two patients are in complete remission (CR).

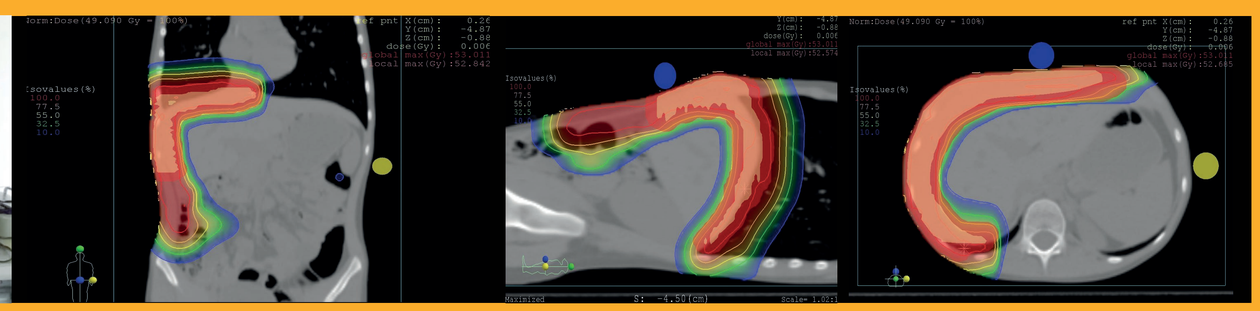
Patients with HL underwent irradiation to the mediastinum and other sites. Six patients received 29.8 GyE and seven patients received 19.8 GyE. All patients are currently alive (median follow-up: 29 months), with 12 patients in CR and one with marginal relapse.

Patient No	Sex	Age	Time of follow-up / months	Treatment protocol	Histology	Treatment volume	Dose / GyE	No of fraction	Whole lung irradiation	WLI - source	WLI - dose / GyE	Acute toxicity	Late toxicity greater than G2	Progression	Site of progression	Disease status
1	F	14	50	none	spindle cell sarcoma	right chest wall	54	30	no	NA	NA	skin G2	none	yes	chest wall metastases	PD
2	M	16	53	EuroEwing 2008	Ewing sarcoma	chest wall and sternum, intrathoracic propagation	55,8	31	yes	photons	18	skin G1, lung G1	none	no	NA	CR
3	M	11	18	none	spindle cell sarcoma	right chest wall and diaphragm	59,4	33	yes	photons	15	upper GIT G2, skin G1, mucouse membrane G2 , Neu G3, Wbc G2	none	yes	recurrence infrahepatally	DOD
4	F	16	8	EuroEwing 2012	undifferentiated sarcoma	left chest wall	45	25	yes	protons	15	lung G1, oesophagus G2, skin G1	none	yes	lung metastases	DOD
5	M	13	2	none	spindle cell sarcoma	recurrence infrahepatally	50	25	yes	photons	15	upper GIT G2, Hb G2, Wbc G1	none	yes	multiple metastases	DOD
6	M	18	3	EpSSG NRSTS 2005	synovial sarcoma	pleural and mediastinal metastases	54	27	no	NA	NA	skin G1, lung G1, oesophagus G1	none	yes	local and distal progression	DOD
7	F	15	20	EpsSG RMS 2005	undifferentiated rhabdomyosarcoma	mediastinum, axila, supracavicullar region, lungs	59,4	33	no	NA	NA	skin G2, oesophagus G1, lung G1	none	no	NA	CR
8	F	18	9	none	spindle cell sarcoma	right 11th and 12th rib infiltration, right paracardial region	50	20	no	NA	NA	skin G1	none	yes	distal progression	PD



Picture showing the screen at the moment of controlled inhalation


Patient with HL in the treatment position


Treatment volume and isodoses (STS of the chest wall and diaphragm)

Results

- The age of patients ranged from 11–19 years (median 16). Median follow-up was 21.9 months (3–53 months). Six patients had soft tissue sarcomas (STS), 13 had Hodgkin lymphoma (HL). Disease status and toxicity were assessed from March 1, 2023, using the RTOG scale for acute and late toxicities.
- As the treatment protocols (dose, volumes) and expected treatmets outcomes differs significantly in both groups, we analysed results of patients with soft tisue sarcomas and Hodgkin lymphomas separately, see tables.
- No acute or late toxicity above grade 2 occurred in our cohort, but follow-up duration is limited.

Conclusion

- Pediatric patients can undergo proton radiotherapy using IMPT technique and controlled breathing with low acute toxicity. No significant late toxicity has been observed even if very large volumes were radiated, but longer follow-up is needed. Relapse rate is very low especially in HL group, and there are no signs of higher risk of local or marginal recurrences in both groups compared to photon irradiation. Proton radiotherapy is appropriate for selected patients requiring mediastinal or chest wall irradiation.

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