ISPNO 2024 Philadelphia

Clinical results, acute and early late toxicity after proton radiotherapy for pediatric medulloblastoma, retrospective analysis

Barbora Ondrova[1], David Sumerauer[2], Michal Zapotocky[2], Stanislava Hederova[3], Filip Jadrijevic-Cvrlje[4], Zdenek Pavelka[5], Irena Vlahova[6], Michal Andrlik[1], Vladimir Vondracek[1], Lucie Landova[2]

[1] Proton Therapy Center Czech, Prague, [2] University Hospital Motol, Prague, [3] Pediatric University Hospital, Bratislava, Slovakia, [4] Childrens hospital, Zagreb, Croatia, [5] University Hospital Brno, Brno, [6] UMHAT ,Tsaritsa Yoanna-ISUL, Sofia, Bulgaria

Introduction

- Craniospinal irradiation with boost to primary tumor site (and metastatic sites) is current radiotherapy standard for most patients diagnosed with medulloblastoma (MB). This treatment is effective, but survivors frequently develop long-term toxicity affecting the quality of life. Proton radiotherapy has the same efficacy compared to conventional photon-based techiques, but might achieve lower risk of toxicity.
- We retrospectivelly analyzed our cohort of patients irradiated for MB in our institution, using IMPT (intensity modulated proton therapy) between May 2013 and December 2023.
- Eighty patients (50 male, 30 female, median age at radiotherapy 8 years /range 3-17/) with primary or recurrent MB (not previously irradiated) were treated and included into analysis.
- Neoadjuvant, concurrent and adjuvant systemic treatment was applied according to the protocol selected by the pediatric oncologist.
- 36 patients were treated for high-risk MB (mostly metastatic), 44 pts for SR disease.
- Methylation subgrouping was not done in all cases, thus we decided not to show this data here and further analysis is planned.

Results

- All but one patients completed their treatment, acute toxicity including hematological was mild (Table 2) and lead to treatment interruption in seven cases.
- With a median of follow-up 39,6 months (range 3-119) 62 pts were in complete remission, 3 pts alive with disease, 14 died from disease progression and one died from complication (intracranial hemorrhage).

Toxicity

- Two secondary malignancies potentially associated with IMPT (thyroid cancer, radiation induced high-grade glioma).
- Endocrionopathy – see table 3
- One case of severe brainstem necrosis with persistent neurological deficit, treated with corticosteroids and bevacizumab
- In two cases, there was a combination of disease progression and brainstem necrosis found in autopsy.
- Due to lack of data, we were not able to analyze cognitive functions and quality of life.

Conclusion

- Proton radiotherapy using IMPT for craniospinal irradiation in MB is feasible, treatment outcomes and toxicity are encouraging, although a longer follow-up is needed.

Table 1 - Group characteristics

Sex	Female	30 pts	37,5%
	Male	50 pts	62,5%
Risk group	Standard risk	44 pts	55,0%
	High risk	36 pts	45,0%
M-status	M0	50 pts	62,5%
	M1	12 pts	15,0%
	M2	10 pts	12,5%
	M3	8 pts	10,0%
Dose to craniospinal axis	23.4 GyE	43 pts	53,8%
	30.6 GyE	5 pts	6,3%
	36 GyE	28 pts	35,0%
	Other	4 pts	5,0%
Neoadjuvant chemotherapy	Yes	16 pts	20,0%
	No	64 pts	80,0%
Concurrent chemotherapy	Yes	61 pts	76,3%
	No	19 pts	23,8%
Anesthesia	Yes	30 pts	37,5%
	No	50 pts	62,5%
Posterior fossa syndrome	Yes	20 pts	25,0%
	No	60 pts	75,0%
Disease status	CR	62 pts	77,5%
	AWD	3 pts	3,8%
	DOD	14 pts	17,5%
	DOC	1 pts	1,3%

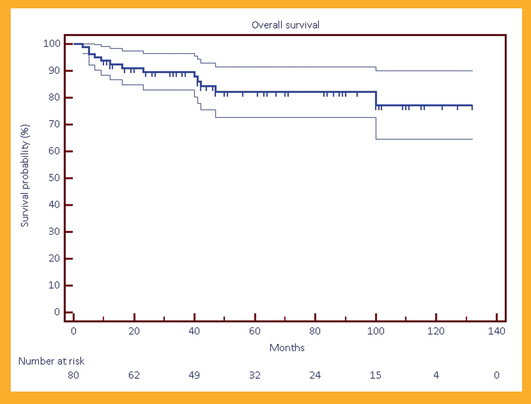
CR – complete resmission, AWD – aliwe with disease, DOD – died of disease, DOC – died from complication

Table 2 - Acute toxicity (excl. hemathological) (CTCAE 4.03)

Dermatitis	G1	48 pts	60,0%
	G2	32 pts	40,0%
Dysphagia	G0	61 pts	76,3%
	G1	14 pts	17,5%
	G2	3 pts	3,8%
	G3	2 pts	2,5%
Anorexia	G0	28 pts	35,0%
	G1	46 pts	57,5%
	G2	6 pts	7,5%
Headache	G0	50 pts	62,5%
	G1	26 pts	32,5%
	G2	4 pts	5,0%
Nausea / vomiting	G0	15 pts	18,8%
	G1	27 pts	33,8%
	G2	38 pts	47,5%

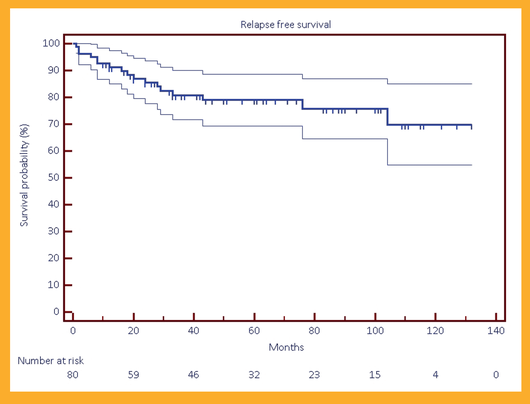
Table 3 - Late toxicity (CTCAE 4.03)

Hypothyroidism	G0	58 pts	72,5%
	G1	1 pts	1,3%
	G2	21 pts	26,3%
Growth-hormon deficit	G0	57 pts	71,3%
	G1	4 pts	5,0%
	G2	19 pts	23,8%
Sex-hormones deficit	G0	67 pts	83,8%
	G1	1 pts	1,3%
	G2	3 pts	3,8%
	G3	9 pts	11,3%
Hearing	G0	68 pts	85,0%
	G1	9 pts	11,3%
	G2	2 pts	2,5%
	G3	1 pts	1,3%



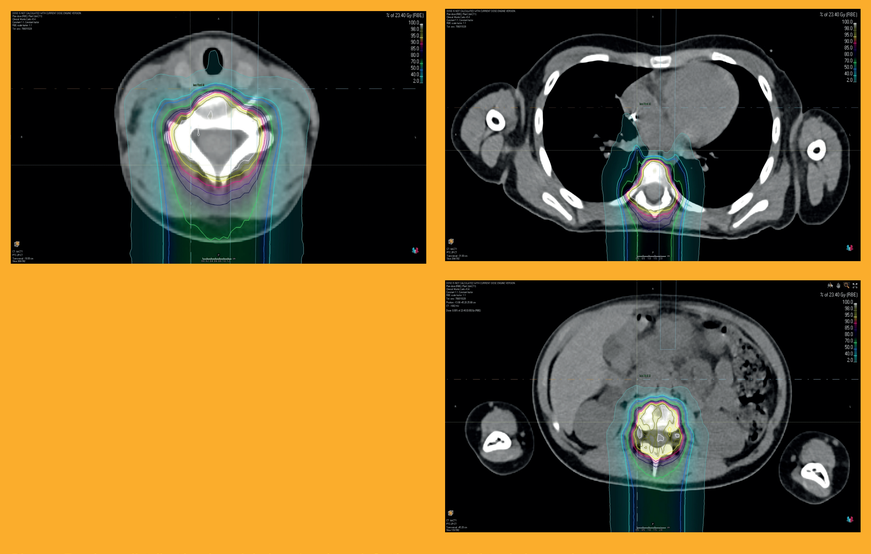
Picture 1
– Overall survival (OS)

Median OS not achieved,
2-yers OS 89,6% + 3,5%,
3-years OS 89,6% + 3,5%,
4-years OS 82,1% + 4,8%

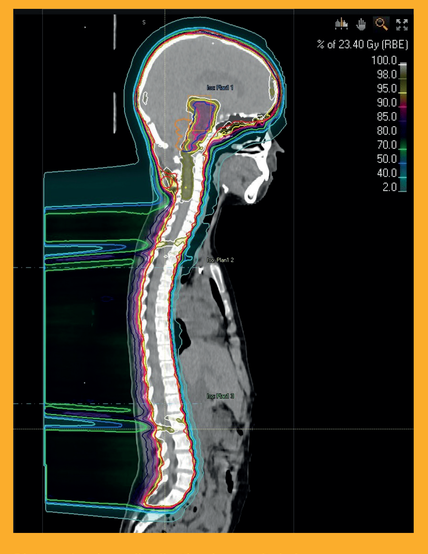


Picture 2
– Relapse free survival

Median RFS not achieved,
2-years RFS 85,5% + 4,1%,
3-years RFS 80,8% + 4,7%,
4-years RFS 79% + 4,9%



Picture 3 – dose distribution in axial view (neck up left, thorax up right, abdomen bottom right)



Picture 4 – dose distribution in saggital view, whole vertebrae in the PTV

PROTON THERAPY CENTER CZECH