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Original Article

Re-irradiation of locally recurrent pediatric intracranial ependymoma: Experience of the French society of children's cancer

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ABSTRACT

Purpose: This study aimed to evaluate retrospectively the clinical results of re-irradiation for children with a locally recurrent brain ependymoma.
Methods: 33 full-dose re-irradiations were delivered to 31 children with a recurrent brain ependymoma after a standard treatment. Each child was followed up with clinical and MRI examinations. We evaluated overall survival, local recurrence free-survival and short term toxicity according to CTCAE 4.0 scale.
Results: With a median follow-up of 37 months (range, 0 to 107), median local recurrence free-survival was 31 months (range, 2 to 63) and median overall survival was 34 months (range, 3 to 63). It was significantly higher in patients who underwent surgery first, compared with re-irradiation only. Cumulated dosimetric data were available for 22 patients. On average, maximal BED to brain stem was 106,2 $Gy_{\alpha/\beta 3}$ (±35,4) for infratentorial re-irradiation. No acute toxicity grade >2 was reported and 1 case of brain radionecrosis treated successfully with steroids was reported after radiosurgery.
Conclusion: Local recurrence of brain ependymoma can be treated with full-dose re-irradiation, which can be hypofractionated with an acceptable short term toxicity in spite of high total doses delivered to OARs, especially brain stem.

Introduction

In children, ependymoma is the third most frequent malignant brain tumor. The tumor is frequently intracranial, located in the posterior fossa in 2/3 of cases [1,2]. The prognosis of WHO grade II or III ependymoma is poor, with an overall survival (OS) of 50–85% at 5 years, and a progression free survival of 23–70% at 5 years [3].

The cornerstone of the treatment in newly diagnosed ependymoma is surgery followed by radiotherapy. A complete resection is associated with a better prognosis for non-metastatic children [4]. Adjuvant radiotherapy, with a total dose of 54 to 59.4 Gy, significantly improves the overall survival rate and is currently considered as a standard of treatment [5].

In spite of these treatments, a third of the patients relapse, often locally. The median time before relapse is between 13–25 months [4], but it can occur later, up to 80 months. Systemic treatment has a limited efficacy, especially in macroscopic disease [6]. Thus, treatment consists then of another maximal surgical resection sometime followed by a second adjuvant irradiation. Indeed, a few retrospective, non randomized studies, showed the feasibility of such approach and a possible benefit in OS [7–11]. No prospective study has validated the re-irradiation in the context of relapsed intracranial ependymoma. However, given the literature data, this strategy is regularly proposed in multidisciplinary medical meetings in France.

There is no consensus on these re-irradiation modalities, neither on dose, nor fractionation, nor technique. Furthermore, usual dose constraints to brain stem or cervical medulla has to be widely overtaken.

The aim of this study was to retrospectively evaluate the clinical results (OS, PFS, short-term toxicity) of cerebral re-irradiations achieved in reference French pediatric radiotherapy centers and to contribute to define the optimal modalities of this treatment.

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Patients and method

Clinical, radiological and dosimetric files of children irradiated in France for an ependymoma have been registered on a web platform dedicated to clinical research (the PEPPI study) [12–14]. We included every file concerning children re-irradiated for a brain relapse.

Population

Between November 2006 and December 2013, 31 children younger than 18 (median age 6 years) received 33 re-irradiations (two children were re-irradiated twice) for a local relapse of cerebral ependymoma in 9 French reference pediatric radiotherapy centers. The median age at diagnosis was 6 years (range 1–15). Twenty-two patients (71%) were boys, and 9 patients (29%) were girls. Twenty-three patients (74%) were treated for a supratentorial tumor, and 8 (26%) for an infratentorial tumor. In 27 cases (87%), tumors were classified grade 3 according to WHO classification in 27 cases (87%) and grade 2 in 4 cases (13%).

Treatment

Initial and relapse treatment were discussed at the reference center pediatric oncology multidisciplinary tumor board. Initial adjuvant radiotherapy was delivered with standard modalities (60 Gy/60 fractions bifractionated, or 59,4Gy/33 fractions, or 54 Gy/30 fractions), with or without a craniospinal irradiation (CSI). At local relapse, therapeutic strategy was discussed again in multidisciplinary meetings. The indication, dose and irradiation techniques were proposed on a case by case basis, depending on resection quality and localization. The techniques used included conformal radiation therapy, intensity modulated radiotherapy (IMRT), fractionated stereotactic radiotherapy or radiosurgery. Follow-up was performed every 3 months with clinical examination and cerebromedullar MRI.

Data

Clinical data collected were overall survival (OS), local recurrence free survival (LRFS) and short term toxicity following the CTCAE 4.0 scale. Cerebral radionecrosis was assessed on clinical and radiological arguments. We retrieved data on radiation technique, prescribed dose, fractionation, and maximal dose to OARs when it was available. Considering the heterogeneity between the treatments, the doses delivered to target volumes and OARs have been converted into Biologically Equivalent Dose (BED) using Barendsen formula [15]:

$$BED = nxdx\left[1 + \frac{d}{\alpha/\beta}\right]$$

For greater clarity, cumulated doses delivered to OAR were also converted in isoeffective dose (EQD2) following linear quadratic formula:

$$EQD2 = nxdx\frac{d + \frac{\alpha}{\beta}}{2 + \frac{\alpha}{\beta}}$$

n: number of fractions; d: dose per fraction; $\alpha/\beta = 3$ for normal tissue and 2 for medulla; $\alpha/\beta = 10$ for tumor.

Cumulative dosimetric data were obtained by adding the maximal doses of both courses of treatment, based on a "worst-case scenario". When dosimetric data of both irradiations were available in DICOM-RT format, a cumulative dosimetry was obtained using the Artiview software (Aquilab™).

Given the different doses and fractionation delivered in our population, the treatments have been classified in 4 groups depending on median dose delivered to PTV (BED >40 $Gy_{\alpha/\beta10}$, >45 $Gy_{\alpha/\beta10}$, >50 $Gy_{\alpha/\beta10}$, >55 $Gy_{\alpha/\beta10}$) and in 3 groups depending on fractionation: normofractionated (≤2 Gy/fraction), hypofractionated (2–6 Gy/fraction) or very hypofractionated (>6 Gy/fraction).

Statistical analysis

PFS and OS from the end of re-irradiation were estimated using the Kaplan–Meier method. Significance testing ($\alpha = 0{,}05$) was performed on the basis of the log-rank and the Cox model. The whole analysis was led with the XLSTAT software.

Results

The initial irradiations of the 31 patients were delivered between April 2000 and September 2012, always following a surgical resection, which was considered complete in 27 cases (87%) and incomplete in 4 cases (13%). In 28/31 cases (90%), radiotherapy had been delivered with fractions of 1.8 Gy, for a median total dose of 57.6 Gy (range, 48.6 to 61). Three children (10%) had received a bifractionated protocol with 60 Gy delivered in 60 fractions. Twenty-five patients received localized radiotherapy and 6 received CSI due to a double localization.

The CTV, i.e. the relapse site, was localized inside the field of radiotherapy in 27 cases (81.8%) and on the edge of the field in 6 cases (18.2%). Two patients (6.1%) experienced a synchronous medullar relapse.

Among the 33 re-irradiations, 26 (79%) were delivered after a surgical resection. The surgical resection was considered complete in 21/26 cases (81%), subcomplete in 2/26 patients (8%) and incomplete in 3/26 patients (12%).

The median time between the 2 courses of radiotherapy was 29 months (range, 3 to 120). The average PTV volume was 12 cc ($\sigma = 15$). The technique used was IMRT in 18 cases (55%), stereotactic radiotherapy in 10 cases (30%), radiosurgery in 4 cases (12%), and conformal radiotherapy in 1 case (3%). The re-irradiation was associated with a CSI in 4 cases/33 (12%). Average dose was 34.9 Gy_{EQD2} (±12.9), and average BED was 49.4 $Gy_{\alpha/\beta10}$ (±11.5). The fractionation was normal in 11 cases (33%), high in 13 cases (39%) and very high in 9 cases (27%). There was no significant difference of PTV volume according to technique or fractionation. Details about doses and fractionation appear in Table 1.

With a median follow up of 37 months (range, 0 to 107), the median LRFS was 31 months (range, 2 to 63) (Fig. 1A). The median overall survival was 34 months (range, 3 to 63). Overall survival rate was 70% at 1 year (95%CI, 54 to 86) and 48% at 3 years (95% CI, 26 to 71) (Fig. 1B). Eight patients were alive in complete remission (26%), 8 were alive with progressive disease (26%), 14 were deceased (45%) and 1 was lost of follow-up (3%).

The median LRFS was 39 months (range, 2 to 63) in the group of patients that underwent surgical resection before the re irradiation versus 9 months (range, 3 to 15) in the group of patients treated with radiotherapy only ($p = 0{,}004$) (Fig. 1C). There was also a significant difference for OS: in the group of resected patients, the median OS was 63 months (range, 6 to 63) versus 9 months (range, 3 to 32) in the other group (Fig. 1D). There was a trend for a better survival in the group of patients treated with a high fractionation (Fig. 1E and F). No significant difference of survival was found according to the total dose delivered or to the association with a CSI. The results of univariate and multivariate analyses appear in Table 2.

Table 1
Details about technique and prescribed doses.

Technique	Dose/fraction	Prescription isodose	N. of fractions	Total dose to PTV	EQD2 dose to PTV	BED to PTV	CSI
RT3D	1,8	–	25	45	44,25	53,1	No
IMRT	1	–	54	54	49,5	59,4	Yes
IMRT	1,5	–	33	49,5	47,4375	56,925	No
IMRT	1,8	–	15	27	26,55	31,86	Yes
IMRT	1,8	–	27	48,6	47,79	57,348	Yes
IMRT	1,8	–	28	50,4	49,56	59,472	No
IMRT	1,8	–	30	54	53,1	63,72	No
IMRT	1,98	100	30	59,4	59,301	71,1612	No
IMRT	3,5	100%	10	35	39,375	47,25	Yes
IMRT	3,5	100	10	35	39,375	47,25	No
IMRT	3,5	100%	10	35	39,375	47,25	No
IMRT	4	–	8	32	37,33	44,8	No
IMRT	5	100%	5	25	31,25	37,5	No
IMRT	5	100%	5	25	31,25	37,5	No
IMRT	5,1	100%	10	51	64,175	77,01	No
IMRT	6	100%	6	36	48	57,6	No
IMRT	8	100	3	24	36	43,2	No
IMRT	8	80%	3	24	36	43,2	No
IMRT	6	–	3	18	24	28,8	No
SRT	1,8	100	20	36	35,4	42,48	No
SRT	1,8	–	25	45	44,25	53,1	No
SRT	1,8	100	30	54	53,1	63,72	No
SRT	3,5	100%	10	35	39,375	47,25	No
SRT	4	80%	9	36	42	50,4	No
SRT	4,4	80%	10	44	52,8	63,36	No
SRT	4,5	–	6	27	32,625	39,15	No
SRT	5	80%	5	25	31,25	37,5	No
SRT	6	80%	5	30	40	48	No
SRT	8	80%	3	24	36	43,2	No
RS	18	–	1	18	42	50,4	No
RS	18	–	1	18	42	50,4	No
RS	18	50%	1	18	42	50,4	No
RS	18	50%	1	18	42	50,4	No

RT3D: three-dimensional conformational radiotherapy; IMRT Intensity-Modulated Radiotherapy SRT: Stereotactc Radiotherapy; RS: Radiosurgery; NF: normofractionated (≤2 Gy/fraction); HF: hypofractionated (2–6 Gy/fraction); VHF: very hypofractionated (>6 Gy/fraction); CSI: CranioSpinal Irradiation.

The dosimetry for the OARs was known for 20 of 31 initial irradiations, and for 24 of 33 re-irradiations. The maximal doses to each important OAR have been summarized in 22 cases with a worst-case scenario, the results appear in Table 3. A cumulative dosimetry was realized in 9 cases. Average dosimetric values to brain stem were: Dmax 91,5 Gy_{EQD2} (5,8–226,7), D2 cc 82,6 Gy_{EQD2} (4,3–185,8), V115 Gy_{EQD2} 13,4% (0–97,1) et V59 Gy_{EQD2} 7,5 cc (0–18,4).

Toxicity could be evaluated in 25 patients (68%). Acute toxicities during re-irradiation were asthenia grade 1 or 2 in 3 cases (11%), cerebellar ataxia in 5 cases (19%), headache grade 1 or 2 in 3 cases (11%), pituitary insufficiency in 1 patient (4%) and cognitive disorder in 1 case (4%). No hearing or visual impairment, no case of acute myelitis was described. One patient re-irradiated with radiosurgery with a cumulated BED of 185,7 $Gy_{\alpha/\beta 3}$ maximum dose to brainstem was treated successfully with steroids for an asymptomatic radionecrosis diagnosed 3 months after the re-irradiation.

Out of 9 patients for whom precise dosimetric and volumetric data were known thanks to DICOM RT plans fusions, 2 suffered from cerebellar ataxia further to the re-irradiation. Average cumulated doses to PTV were respectively 117,4 Gy_{EQD2} and 208,7 Gy_{EQD2}, and cumulated maximal doses to PTV were respectively 122,6 Gy_{EQD2} and 226,7 Gy_{EQD2}.

Discussion

This multicentric retrospective study on 31 patients shows that re irradiation is feasible for local recurrent intracranial ependymoma with acceptable short-term toxicity. It confirms the results of other retrospective studies carried out mainly on smaller samples [8–10,15,16–19], or in the retrospective study of Merchant [7] that described 38 patients treated with re-irradiation, 18 of them for a non metastatic disease. Of this population, 6 patients were treated with radiosurgery, with 4 cases of radiation necrosis and 1 toxic death and 1 long-term survivor. Thirteen patients were treated with focal fractionation radiotherapy with a better short term tolerance, and 10 of them had no evidence of disease, with a median follow up of 30 months. An early study from Tsang et al. reported the long-term outcomes of 101 children treated with re-irradiation for a local and/or distant recurrence of ependymoma [11]. Children were treated at RT2 with normofractionated radiotherapy, with a median dose of 54 Gy. A CSI was administered as part of RT2 in 54% of cases. The re-irradiation offered the possibility of long-term disease control in some patients. It was well-tolerated for most patients, with a 10-year cumulative incidence of radiation necrosis grade 3 or higher at 7.9%. A few recent studies offered to treat those patients with proton therapy with similar results [20,21].

In our study, the modalities of treatment were heterogeneous, but there was a majority of hypofractionated treatments, with IMRT or stereotactic technique. This treatment seems to be safe, since no toxicity of grade >2 has been reported, except of one case of symptomatic radiation necrosis after radiosurgery. Nevertheless, Hoffman et al. recently reported short-term results of 12 cases of hypofractionated adjuvant re-irradiation for local intracranial recurrences of ependymoma, with 6 cases of radiation necrosis, 3 requiring a symptomatic management with bevacizumab and steroids [10].

One strength of our study is the calculation of Biologically Equivalent Dose (BED) for target volumes and OARs as well as the isoeffective dose (EQD2). The evaluation of the toxicity is

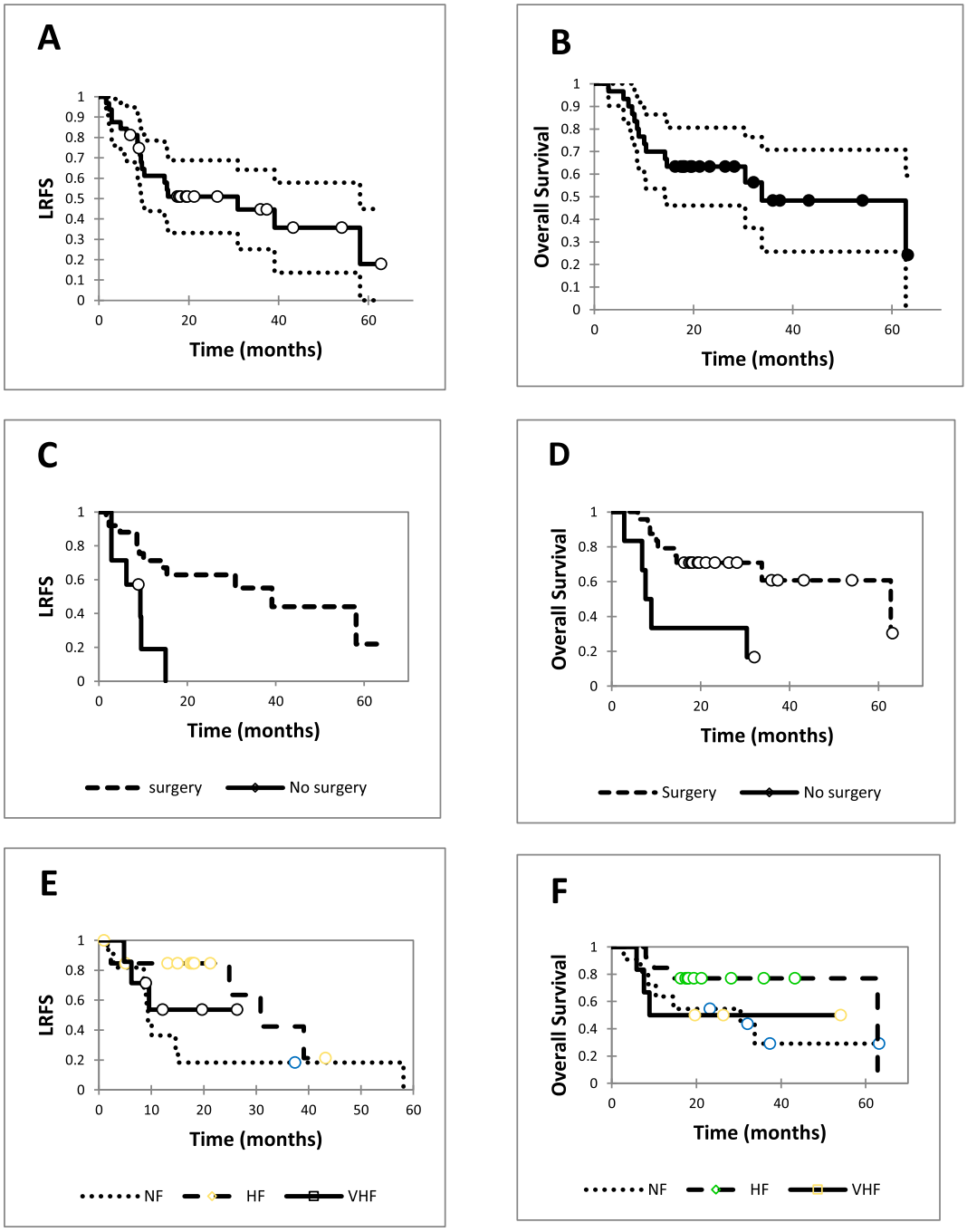

Fig. 1. Local Recurrence-Free Survival (1A). Overall Survival (1B). Local Recurrence-Free Survival and Overall Survival with or without surgery (1C and 1D). Local recurrence-free Survival and Overall Survival according to fractionation (1E and 1F).

Table 2
Uni- and multivariate analyses of the effects of prognostic factors on the overall survival and the local control.

	Local control		Overall survival	
Variable	Univariate p	Adjusted p	Univariate p	Adjusted p
Surgery before RT	0,004	0,008	0,005	0,010
BED >45 Gy	0,286	0,868	0,813	0,494
Fractional:				
- NF	0,165		0,367	
- HF		0,228		0,597
- VHF		0,233		0,774
Associated CSI	–	–	0,884	0,633

RT: Radiotherapy; BED: Biological Equivalent Dose; NF: normofractionated; HF: hypofractionated; VHF: Very hypofractionated; CSI: Craniospinal irradiation.

Table 3
Average of cumulative maximal doses received by OARs (RT1 + RT2).

OAR	All (n = 22)	Supratentorial RT (n = 16)	Infratentorial RT (n = 6)
Brain Stem			
D_{EQD2}	86,29 ± 43,64	106,20 ± 21,19	13,87 ± 26,44
$BED_{\alpha/\beta3}$	130,57 ± 64.34	155,95 ± 35,46	23,97 ± 44,73
Spinal cord			
D_{EQD2}	38,63 ± 29,33	38,63 ± 29,33	–
$BED_{\alpha/\beta2}$	69,89 ± 51,80	69,89 ± 51,80	–
R internal ear			
D_{EQD2}	25,88 ± 20,37	33,46 ± 16,64	0,64 ± 0,40
$BED_{\alpha/\beta3}$	46,82 ± 34,02	59,24 ± 26,69	1,26 ± 0,78
L internal ear			
D_{EQD2}	37,01 ± 29,15	47,97 ± 23,54	0,45 ± 0,20
$BED_{\alpha/\beta3}$	64,19 ± 47,83	81,45 ± 38,01	0,90 ± 0,40
Hypophysa			
D_{EQD2}	10,10 ± 11,28	11,82 ± 10,83	7,25 ± 12,46
$BED_{\alpha/\beta3}$	17,40 ± 19,31	19,83 ± 18,56	12,95 ± 21,62
Optic chiasm			
D_{EQD2}	17,42 ± 20,93	20,78 ± 21,90	8,71 ± 17,08
$BED_{\alpha/\beta3}$	29,91 ± 35,55	35,14 ± 37,02	15,29 ± 29,50
R optic nerve			
D_{EQD2}	6,01 ± 9,00	5,21 ± 4,05	7,62 ± 15,54
$BED_{\alpha/\beta3}$	10,48 ± 15,34	9,12 ± 7,09	13,49 ± 27,22
L optic nerve			
D_{EQD2}	5,35 ± 7,80	4,88 ± 4,40	6,28 ± 12,93
$BED_{\alpha/\beta3}$	9,36 ± 13,19	8,67 ± 7,99	10,88 ± 22,11
R lens			
D_{EQD2}	2,93 ± 4,62	2,47 ± 2,70	3,85 ± 7,54
$BED_{\alpha/\beta3}$	5,33 ± 8,18	4,54 ± 4,83	7,07 ± 13,67
L lens			
D_{EQD2}	5,80 ± 13,46	6,95 ± 15,79	3,05 ± 5,00
$BED_{\alpha/\beta3}$	9,89 ± 22,03	11,52 ± 25,49	5,68 ± 9,13

The values are expressed on average followed by the standard deviation.

complicated by the previous treatments, including iterative surgical resections. Nevertheless, the treatment seemed well tolerated, in spite of high doses to OARs, particularly for brainstem. Recommendations in the French group for the maximal median dose on the whole brain stem should not exceed 54 Gy with a usual fractionation ≤2 Gy. The V59 should stay beyond 10 cc, and a maximal dose of 64 Gy is tolerated [22]. Indelicato and al suggest that, in pediatric population, the parameters of V55Gy and maximum brainstem dose may be the principal indicators to consider [23]. In this re-irradiation study, standard dose constraints on brainstem have been overtaken with a good short-term clinical tolerance, matching with the data of the literature [8]. We are actually lacking the recommendations concerning dose constraints to respect in this context of reirradiation, in particular for a pediatric population. Two publications report cases of children re-irradiated for diffuse intrinsic pontine glioma for a total dose of 74 Gy on brain stem, without short-term severe toxicity [24,25]. For the cervical medulla, the risk of developing a myelopathy is estimated at 25% for a BED ranging from 102 to 181,5 Gy [26], but we didn't identify any case of myelopathy in our population. The same has been true for internal ears, which were re-irrradiated without any acute clinical consequence. A hypothesis for this tolerance could be the time between the two irradiations [27]. In our study, the most frequent toxicity was cerebellar ataxia in patients without any troubles before reirradiation, with 5 cases observed with a cumulated dose on posterior fossa above 117 Gy_{EQD2} and a median time between the two irradiation of 33 months (10–78). Indeed, we know the radiation-induced necrosis can be expected at cumulative normalized total doses >102 Gy [28]. That is why it seems essential to delineate the cerebellum as a whole-part organ, especially as its irradiation would be predictive for neurocognitive impairment [29]. However, we cannot recommend any dose constraint in this context, since tumor progression would have also certainly led to the same symptoms. Finally, the worst and the most frequent side effect reported in the literature is the radionecrosis, which seems very frequent when the re-irradiated volume increases [30], or when the re-irradiation is delivered in a single session, as is the case for only one patient in our series. These correlated data argue for dose fractionation.

The results of our study in term of local control and overall survival are similar to those reported in the literature (Table 4) but bring new insight as they use recent techniques, dose equivalences and describe good brainstem tolerance except one transient brainstem radionecrosis. If we consider the subgroup of patients treated after complete surgical resection, the results get close to those presented by Bouffet et al. [8]. Therefore, a surgery as complete as possible must be systematically discussed at the relapse.

Bouffet et al. showed that re-irradiation could improve the overall survival [8]. Indeed, they described the outcomes of 47 children treated for an intracranial recurrence of ependymoma. 29 patients were treated with surgical resection and/or chemotherapy, and 18 with full-dose reirradiation. There was a significant improvement of overall survival in the group of patients treated with adjuvant radiotherapy. We lack prospective data, but local treatment with complete surgery and adjuvant radiotherapy seems to be the best strategy at the moment. Nevertheless, the modalities of an optimal re-irradiation are not defined yet on dose, fractionation and technique. Messahel et al. have shown a trend to a better local control for children re-irradiated with a dose superior to 45 Gy [18]. Bouffet et al. also insisted on the importance of full-dose re-irradiation (54–59 Gy) [8]. It is surprising not to find this dose relationship on our population. The heterogeneity of the treatment schemes may be the cause. The optimal fractionation also remains to be defined. Radiosurgery should be used only for stereotactic re-irradiation of small residual tumors. Indeed, there is a major risk of radionecrosis in this particular context of re-irradiation, and local control and overall survival are reduced. This is confirmed by the results of Merchant et al. [7]. Normofractionated radiotherapy with an optimal total dose (54–59,4 Gy) has been the standard protocol retained by published studies, but our results open the door to a reasonable hypofractionation, which seems to offer a local control to the least equivalent, a satisfactory clinical tolerance, and a better comfort for these young patients, since it decreases the number of sessions of treatment. A stereotactic technique would be preferred to spare the OARs as much as possible. Few authors recently addressed hypofractionated approaches in recurrent intracranial ependymoma with comparable results [31,32].

Lastly, the association of the local re-irradiation with a CSI is discussed in the literature. The studies of Bouffet and Merchant yielded a benefit in overall survival with an adjuvant CSI to the dose of 36 Gy [7,8]. Tsang et al. showed that it reduces the incidence of distant failure after RT2, particularly in individuals with 1q gain [11]. Messahel et al. showed that this benefit concerned only the children of more than 3 years [18]. This benefit is not significant in our study, and our very small group does not allow concluding, as 4 children underwent CSI. The indication of CSI must be actually individually discussed by taking into account the expected profit and the expected toxicity, in particular for most young children. It could be specified according to molecular subgroups of each tumor [33].

The variety of modalities of the re-irradiation in our study reflects the rapid evolution of techniques as IMRT and SRS in this period of time. The practices in France are going to be harmonized in the future, and patients with a tumor volume at relapse <30 cm^3 are now included in the prospective phase II clinical trial SBRT

Table 4
Clinical results of studies on recurrent cerebral ependymoma in pediatric population.

Reference	N	Surg.	Modalities	Tolerance	Clinical response
Stafford, Cancer 2000[17]	12		12 RS	2 RN	Median OS 3,4 y PFS at 3 y: 68%
Combs, BMC Cancer, 2006[14]	7	–	7 RTNF 20–60 Gy	No tox grade >2	OS at 3 y: 83% OS at 5 years: 50%
Merchant IJROBP 2008[6]	38	+	6 RS 15–18 Gy 13 RTNF 54–59 Gy 19 CSI	5 RN 1 toxic death	PFS >1 y
Liu, Ped Blood Cancer, 2009[15]	6	+	6 RVHF 3 × 8 Gy or 3 × 10 Gy	3 radiation necrosis (50%)	OS et PFS at 28 months: 100%
Zacharoulis, Childs Nerv Syst 2010[3]	24	+/–	19 RTNF 50–70 Gy including 4 CSI 36 Gy 5 not reported	Satisfactory short term tolerance	Median PFS 15 months OS at 5 y: 16%
Bouffet, IJROBP 2012[4]	18	+	18 RTNF 54–59 Gy including 4 CSI 36 Gy	Satisfactory short term tolerance Neurocognitive toxicity	OS at 3 y with RT: 81% OS at 3 y without RT: 7%
Hoffmann, J Neurooncol. 2014[10]	12	+	12 HF: 3x 8 Gy	6 radiation necrosis (50%)	OS at 2 y 71%
Tsang, IJROBP 2017[9]	101	+	NF: 54 Gy (36–59.4)	7 radiation necrosis grade ≥3 (10-year cumulative incidence 7,9%)	Median OS: 75 months Median PFS: 27.3 months
Our study	33	+/–	11 RTNF 5 RTHF 17 RTVHF/RS	No tox >grade 2 1 RN	OS at 1 y: 70%; at 3 y: 48% LRFS at 1 y: 61%; at 3 y: 45%

N: number of patients; Surg.: surgery; RT: radiotherapy, NF: normofractionated, HF: hypofractionated; VHF: very hypofractionated; RS: radiosurgery; CSI: craniospinal irradiation; LRFS; progression-free survival, OS: overall survival.

(NCT 02013297) that delivers SRS on the residue with 3 fractions of 8 Gy or 5 fractions of 5 Gy. The study protocol does not authorize a cumulative dose higher than 115 Gy to any point of the brain or the brain stem [34].

Conclusion

Local recurrence of ependymoma is frequent. In the current state of knowledge, it should be treated with a maximal surgical resection, followed with full-dose re-irradiation, which can be hypofractionated. The association with a CSI has to be individually discussed by taking into account the age of the patient. With an acceptable short-term tolerance, in spite of high total doses to OARs, brainstem tolerance was good and this strategy of treatment offers a curative perspective.

Conflict of interest statement

No conflict of interest.

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