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Survival and pattern of failure after postoperative radiation therapy for medulloblastoma in adult patients

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Aim. To present the results of postoperative radiotherapy in 27 adult patients with medulloblastoma and to design future management strategies.
Material and methods. 27 patiens with medulloblastoma were treated between 1984 and 2000, of whom 26 received craniospinal irradiation (median 33.6 Gy) with a boost to the posterior fossa (55 Gy). No patient received chemotherapy at primary treatment. Pattern of failure, overall survival (OS), disease free survival (DFS) and survival after recurrence (SAR) were analysed. Age, tumour location, desmoplasia in histology examination, extent of resection, shunt presence, performance and neurologic status were included in a univariate analysis in order to assess possible factors influencing overall survival. The disease stage was disregarded because of insufficient initial staging.
Results. Actuarial 5- and 10- year OS rates were 55% and 44%, respectively. Actuarial 5- and 10- year DFS rates were 44% and 31% respectively. In univariate analysis age was the only significant prognostic factor for OS. For patients less than 30 years of age 5-year OS rate was 40%, for elders – 90%, p=0.004. A tendency to improve OS was observed with better performance and neurologic status, and location in the cerebellar hemisphere, whilst the presence of shunt and gross total resection worsened OS without statistical significance.
Tumour recurred in 17 (63%) patients. Ten relapses (59%) occurred within the first 2 years of follow up. Seven recurrences were in the posterior fossa, either alone (3 patients) or both in the posterior fossa and other sites (4 patients). Other relapses occurred either alone or in 2 or more sites such as: the supratentorial region (3 patients), the spine (4 patients), outside the CNS (6 patients). The median SAR was 12 months (1-35 months). Mean SAR for patients receiving chemotherapy at relapse was 19 months, whilst for patients treated without chemotherapy the mean SAR was 5 months. A tendency for longer SAR was observed when recurrence occurred later after primary treatment. Mean SAR for patients relapsed after 3 years was 16 months, whilst for patients relapsed within 3 first years it was 9.5 months.
Conclusions. Results are poor, but similar to those cited in literature. Results should be related to the presence of prognostic factors, especially the initial extent of disease. The frequency of recurrences in the posterior fossa and outside the CNS is similar. Accurate initial staging could differentiate patients for whom the use of chemotherapy or implementation of new radiotherapy techniques is meaningful. The majority of relapses were observed within the first 2 years. Older patients have better overall survival.

Ocena wyników i przyczyn niepowodzeń pooperacyjnego napromieniania dorosłych chorych na rdzeniaka płodowego

Cel. Ocena wyników pooperacyjnej radioterapii 27 dorosłych chorych na rdzeniaka płodowego (medulloblastoma).
Materiał i metoda. Poddano analizie 27 chorych na rdzeniaka płodowego, leczonych napromienianiem w II Zakładzie Teleradioterapii Centrum Onkologii im. M. Skłodowskiej-Curie, w latach 1984-2000. Dwudziestu sześciu chorych napromieniono na oś mózgowo-rdzeniową (mediana – 33,6 Gy), podwyższając dawkę na tylny dół czaszki do 55 Gy. Jeden chory był napromieniony paliatywnie na mózg. Chorym nie podawano chemioterapii jako pierwotnego leczenia. Przeprowadzono analizę niepowodzeń leczenia, przeżycia całkowitego, przeżycia bez nawrotu choroby i przeżycia po wznowie (PPW). Oceny czynników rokowniczych dokonano w analizie jednowymiarowej, włączając wiek, stan ogólny, stan neurologiczny, zakres resekcji, lokalizację guza (robak versus półkula móżdżku), obecność desmoplazji i obecność zastawki w komorze mózgu. Do analizy nie włączono stopnia zaawansowania ze względu na brak wykonywania wszystkich obowiązujących badań wyjściowych (rezonans rdzenia kręgowego i punkcja lędźwiowa).

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Wyniki. Przeżycie 5- i 10-letnie wyniosło odpowiednio 55 oraz 44%. Prawdopodobieństwo 5- i 10-letniego przeżycia bez nawrotu choroby wynosiło odpowiednio 44 i 31%. Wiek okazał się jedynym istotnym czynnikiem prognostycznym w analizie jednowymiarowej. Pięcioletnie przeżycie całkowite dla chorych w wieku poniżej 30 lat wynosiło 40%, a dla chorych w wieku 30 i więcej lat 90% (p=0,004). Obserwowano tendencję do poprawy przeżycia chorych w dobrym stanie ogólnym i neurologicznym, z lokalizacją guza w półkuli móżdżku, natomiast obecność zastawki i radykalizm operacji pogarszały przeżycie (bez znamienności statystycznej).
U 17 chorych stwierdzono wznowę. 10 wznów (59%) wystąpiło w ciągu pierwszych 2 lat obserwacji. Stwierdzono 7 niepowodzeń leczenia w zakresie tylnego dołu czaszki, jako jedyne miejsce (3) lub z towarzyszącymi przerzutami (4). Niepowodzenia odległe wystąpiły w jednej lub wielu lokalizacjach: nadnamiotowo (3), rdzeń kręgowy (4), poza CSN (6). Mediana PPW wynosiła 12 miesięcy (przedział: 1-35 miesięcy). Średnia PPW chorych leczonych chemicznie z tego powodu wyniosła 19 miesięcy, a chorych nie leczonych cytostatykami – 5 miesięcy. Obserwowano tendencję do dłuższego PPW, im wznowa pojawiała się później od pierwotnego leczenia. Gdy wznowę stwierdzano w ciągu pierwszych 3 lat obserwacji, średnie PPW wynosiło 9.5 miesiąca, a w przypadkach, gdy wznowę stwierdzono później, średnie PPW wynosiło 16 miesięcy.
Wnioski. Wyniki pooperacyjnego napromieniania chorych na rdzeniaka płodowego są niezadowalające. Ich ocenę utrudnia brak wyjściowego zaawansowania choroby. Częstość niepowodzeń miejscowych i odległych jest podobna. Do większości nawrotów dochodzi w pierwszych 2 latach obserwacji. Starsi chorzy mają lepsze rokowanie.

Key words: medulloblastoma, radiotherapy
Słowa kluczowe: rdzeniak płodowy

Introduction

Modulloblastoma, as an infratentorial primitive neuroectodermal tumour, remains one of the most intriguing diseases studied and treated by the multidisciplinary oncology team because of its unique characteristics and apparent radiocurability. This tumour occurs most commonly in children, very rarely in adults. Standard therapy consists of maximal resection compatible with good neurologic outcome and postoperative craniospinal irradiation (CSI) with a boost to the posterior fossa using conventional fractionation schemes. The role of chemotherapy is still debated.

The main aim of this study is to present the results of postoperative radiotherapy in 27 patients with medulloblastoma treated at the 2nd Department of Radiation Oncology of The M. Sklodowska-Curie Memorial Cancer Center (MSCMCC) and Institute of Oncology in Warsaw. The second aim is to design future management strategies basing upon our own experiences and published data.

Materials and methods

The records of 27 patients referred for radiotherapy to the 2nd Department of Radiation Oncology of the MSCMCC between January 1984 and June 2000 were reviewed.

There were 22 male and 5 female patients, mean age – 28 yrs. The most common presenting symptoms were headache, gait imbalance, nausea, vomiting, ataxia, dysmetria, nystagmus, and cranial nerve dysfunction. Performance status evaluated according to WHO score was 0 in 2 patients, I in 18, II in 3 and III in 4 patients. Neurologic status evaluated according to the EORTC\MRC score (Table I) [1] was I in 15 patients, II in 8 patients, and III in 4. All patients had histopathologic diagnosis of medulloblastoma. Desmoplasia was present in 5 cases.

The tumour was located in the vermis in 7 patients, in the vermis and 4th ventricle in 6 pts. Seven pts. had infiltration limited to the cerebellar hemispheres. In 4 cases the tumour invaded both the vermis and the cerebellar hemisphere. Two tumours were located in the cerebellopontine angle. One patient had a midline lesion that extended into the brainstem. Tumour size was not routinely recorded.

The mean interval from operation to onset of radiotherapy was 39 days (range: 20-82 days).

The extent of resection was mainly based on the surgeon's assessment at the time of the operation. Two patients underwent partial resection, 9 – a subtotal resection and 16 – a gross total resection.

Seven patients required a shunt before radiation therapy, one shunt was placed during radiotherapy because of hydrocephalus.

In this retrospective material no patient had undergone complete staging before treatment, incl. no MRI of the spine and no CSF samples for cytological analysis. None of the patients were found to have metastases (in view of such incomplete diagnosis).

All patients received radiation therapy. The median dose given to the posterior fossa was 55.0 Gy (range: 30.0-60.8 Gy), and 33.6 Gy to the craniospinal fields (range: 26.4-40.0 Gy). One patient was treated with palliative intent, without spinal irradiation. For all but two patients receiving hyperfractionated CSI to 30 Gy with 1.2 Gy per fraction twice a day, doses per fraction were 1.6-2.0 Gy (median:1.8).

High-energy photons (Co60, X6 and X15 MV) and electrons (15 to 22 MeV) were employed. A three dimensional treatment planning system was used for 4 patients only – treated after 1996.

The average duration of the treatment course was 70 days (range: 12-124 days).

Table I. EORTC/MRC Neurologic Deficits Score [1]

1. Absence of any neurologic deficit detectable
2. Minor neurologic deficits; without any impairment of normal activity
3. Neurologic deficits leading to some impairment of normal activity (paresis, minor mental changes)
4. Serious neurologic deficits leading to disability to care for himself: paralysis, aphasia, serious mental (emotional and/or cognitive) changes
5. Any communication with patient impossible

None of the patients received chemotherapy at primary treatment. One patient received lomustine (CCNU) during the last week of radiotherapy, because of a suspicion of bone metastases, not confirmed by complementary examination carried out at the end of the treatment. Nine patients received chemotherapy at recurrence.

Overall survival (OS) and disease free survival (DFS), measured from the onset of radiotherapy, were calculated using the Kaplan-Meier method.

Univariate analysis (UA) using the log rank test was performed in order to assess possible prognostic factors for OS. The following factors were included in the UA: age, extent of resection, performance status, neurologic status, tumour location (vermis vs cerebellar hemisphere), desmoplasia in histology examination and shunt presence.

Results

Mean follow up was 60.7 months (range: 5-204 months). Minimum follow-up for alive patients was 17 months.

The tolerance of radiotherapy was good. Only moderate early complications (erythema, alopecia, leukopoenia at 2000-3000 (11 pts.), mild diarrhoea (2 pts.)) were observed. One patient developed hydrocephalus and received the planned dose after shunting. Eighteen patients received corticoids during radiotherapy. No severe late complications were observed in the studied group.

No patients developed secondary malignancies.

Actuarial 5- and 10- year OS rates were 55% and 44%, respectively (Figure 1). Actuarial 5- and 10- year DFS rates were 44% and 31% respectively (Figure 2). Twelve patients died.

In the univariate analysis age was the only significant prognostic factor for OS. For patients younger than 30 years (17 cases) and with age ≥30 years (10 cases) 5--year OS rates differed significantly (40% and 90% respectively, p=0.004) (Figure 3). We observed a trend towards improved OS with better performance and neurologic status and location in the cerebellar hemisphere, whilst the presence of shunt and gross total resection worsened OS without statistical significance. Table II shows results of UA for all analysed variables.

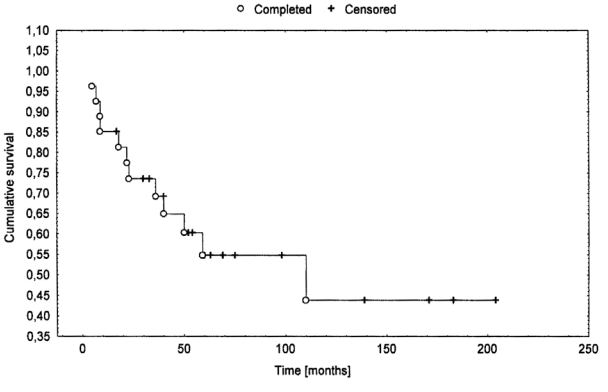

Figure 1. Overall survival of 27 patients with medulloblastoma estimated by the Kaplan-Meier method

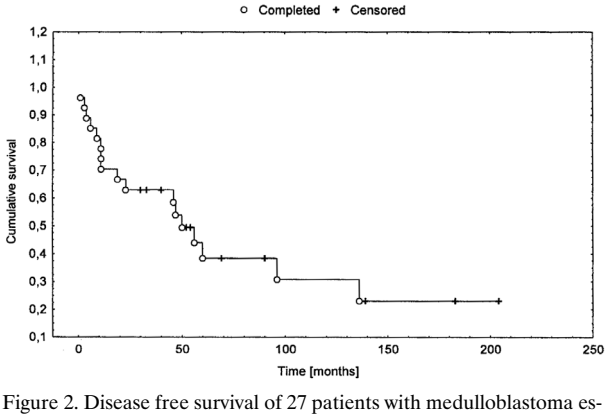

Figure 2. Disease free survival of 27 patients with medulloblastoma estimated by the Kaplan-Meier method

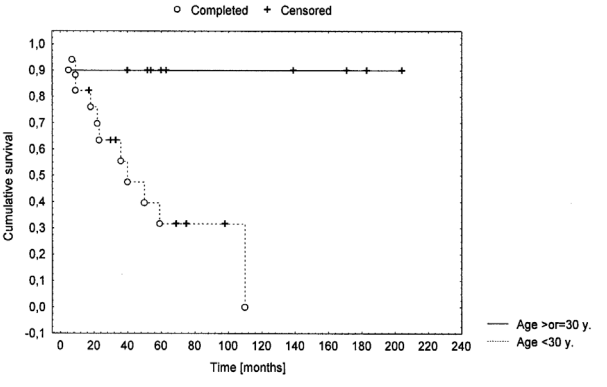

Figure 3. Overall survival of 27 patients with medulloblastoma according to age (p=0.004)

Table II. Prognostic factors for overall survival in univariate analysis

Variable	5-year survival	P-value in log rank test
Age:		
< 30 years	32%	0.004
≥30 years	90%	
Extent of resection		
Gross total resection	48%	0.58
Subtotal, partial and biopsies	67%	
Performance status		
0-I	58%	0.20
II-III	43%	
Neurologic status		
I	60%	0.25
II-IV	47%	
Location		
Cerebellar hemisphere	64%	0.41
Vermis	48%	
Shunt		
Present	31%	0.17
Absent	65%	
Desmoplasia		
Present	53%	0.81
Absent	55%	

The multivariate analysis was not performed because of a limited number of patients.

17 (63%) patients recurred. Ten relapses (59%) occurred within the first 2 years of follow-up, 2 (11.7%) between 3 and 4 years, 3 (17.5%) between 4 and 5 years, 1 (5.9%) after 5 years, and 1 (5.9%) after 11 years. Seven recurrences were found in the posterior fossa, either alone (3 pts.) or in both posterior fossa and other sites (4 pts.). Metastatic relapses occurred either alone or in 2 or more sites, such as the supratentorial region (3 pts.), the spine (4 pts.) or outside the CNS (6 pts.). In 5 cases there was insufficient staging to localise the recurrence. Recurrences outside the CNS were located in bones (6 pts.), lymph nodes (1 pts.) and lung (1 pts.). One supratentorial relapse was due to a geographic miss by excess blocking of the orbital region.

The median survival after recurrence (SAR) was 12 months (range: 1 – 35 months). Treatment for recurrence included surgery in 3 patients, while radiation therapy was given to 6 patients, including radiosurgery for one. Eight patients were treated by chemotherapy – this was associated with longer SAR. Mean SAR for patients receiving chemotherapy at relapse was 19 months (range: 7-34 months), whilst for patients treated without chemotherapy the mean SAR was 5 months (range 1-17 months). A tendency towards longer SAR was also observed when the recurrence occurred later after primary treatment. Mean SAR for patients relapsed after 3 years was 16 months, whilst for patients relapsed within 3 first years the mean SAR was 9.5 months.

Discussion

Our results concerning the survival of 27 patients with medulloblastoma are similar to the outcomes reported by other authors, ranging from 52% to 68% at 5 years and from 25% to 64% at 10 years [2-12].

The main problem in the evaluation of results in our study is related to an unknown distribution of prognostic factors caused by insufficient staging. As is stated in literature the extent of the disease is significantly associated with the length of survival. Early failures are attributed to poor prognosis – "high risk" patients being primarily characterised by the presence of leptomeningeal metastases (M1-4 stage) (Table III) [13]. Other poor prognostic factors include partial resection of the tumour, age below 3 years and brainstem invasion [2-5].

The dose delivered to the neuraxis and the posterior fossa is a crucial problem. In this study patients were fractionated conventionally to median dose of 55 Gy to the posterior fossa and 32 Gy to the spine. The total and fractional doses were delivered acc. to literature recommendation. Contemporary protocols recommend 36 Gy to the craniospinal axis and 54-56 Gy to the posterior fossa, 1.8-2 Gy per fraction, using 3-dimensional treatment planning system.

Reduced dose neuraxis irradiation (23.4 Gy vs. 36 Gy) is associated with an increased risk of relapse [14]. Survival did correlate with the dose to the cranial field with threshold dose of 30 Gy [15]. The results are also worse when the dose given to the posterior fossa is less than 50 Gy, however higher doses (72 Gy, 1 Gy twice daily) did not improve survival [9, 16-18].

Leptomeningeal failure is a common component of failure and occurs in the posterior fossa, as well as in the spine. Posterior fossa recurrence (as a component of failure) occurs in 55-71% [2, 3, 5]. Seven patients (58% of known locations of failures) in our study relapsed in the posterior fossa. Isolated tumour bed failure occurred in 3 (25%) cases, others report 22% -50% [2, 3, 5]. The spine was affected in 4 (33%) cases, as compared to 20%-38% in literature [2, 5, 9]. Isolated supratentorial recurrence is a rarely observed event (12%) and is commonly caused by an inadequate dose to the region of the cribriform plate [9]. Among 3 relapses diagnosed in this region, observed in our study, there was one relapse caused by geographic miss. It is important to properly cover the subfrontal cribriform plate region by an elective dose, and avoid excessively generous eye blocks. The quality of medulloblastoma radiotherapy technique definitely correlates with the outcome.

It is worth to consider some issues in the technical conduct of CSI for medulloblastoma. There is a need to change the spinal-spinal and cranial-spinal junction every 10 Gy, while to determine the inferior margin of the field the saggital MRI images should be used for proper location of the caudal sac. Treatment plan includes irradiation of the entire subarachnoid space extending to the spinal ganglia located in the intervertebral foramina. The entire posterior fossa should be exposed to the full dose [19]. The preferred cranio-spinal junction is at the lowest point in the neck with exclusion of the shoulders in the lateral cranial field, which results in a higher dose to the cervical

Table III. Chang Harisiadis classification system for cerebellar medulloblastoma [13]

T1	<3 cm in greatest dimension
T2	≥3 cm
T3a	≥3 cm with extension into the aqueduct of Sylvius and\or into foramen of Luschka
T3b	≥3 cm with unequivocal extension into the brainstem
T4	≥3 cm with extension up past the aqueduct of Sylvius and\or down past the foramen magnum
M0	No evidence of subarachnoid or hematogenous metastasis
M1	Microscopic tumour cells found in cerebrospinal fluid
M2	Gross nodular seeding demonstrated in the cerebellar or cerebral subarachnoid space, or in the 3rd or lateral ventricles
M3	Gross nodular seeding in spinal subarachnoid space
M4	Metastasis outside the cerebrospinal axis

spinal cord, but the doses received by the thyroid gland, mandible, pharynx and larynx are lower [20].

There is a consensus that prolonged treatment time influences the results. John O. Charco et al. [10] have demonstrated that for patients with radiotherapy duration less than 45 days the posterior fossa control was 89% at 5 years, as compared with 68% for those treated longer (p=0.01). Similarly freedom from relapse at 5 years was 76% and 43%, respectively (p=0.04).

The average duration of irradiation in our group of patients was 70 days. That is so because before 1996 brain and spine irradiation was performed in two stages successively. Without appropriate initial staging we cannot conclude to what extent this worsened the results.

Interpretation of the univariate analysis concerning prognostic factors is also strongly compromised by the absence of data concerning the initial extent of the disease. Additionally, the size of the group is small – a common problem in one-centre studies on adult medulloblastoma. Christian Carrie et al. [12] identify postoperative performance status as a prognostic factor. Complete resection is of no benefit if it results in poor postoperative performance status. It may be the reason of our surprising results with no significant worsening of survival with larger tumour resection.

Some authors claim that the presence of desmoplasia in tumour is a positive prognostic factor and the presence of a shunt is a negative prognostic factor [2, 3, 6, 7]. We did not arrive at this relation, maybe because of a small number of events.

There is a very interesting rule, referred to as Colin's law, which can be of help to estimate the chance of cancer cure in children and young adults. It is also applicable to medulloblastoma patients. The cure could be assured if patients survived their age and 9 months beyond diagnosis [21]. Patients with later recurrence had a longer SAR. Additionally, medulloblastoma occurring in older patient is slightly less aggressive. There was longer survival among older patients. Medulloblastoma is an exceptional brain neoplasm where older age of the patient does not worsen survival [4].

Benefits of chemotherapy are still controversial, as most studies are not conclusive. Results of surgery and radiotherapy can be improved by the positive impact of chemotherapy in decreasing the risk of extraneural metastases by the use of chemotherapy in more advanced cases [2]. Good results have been reported using cisplatinum in the "high risk" population and using the 8/1 (VCR, BCNU, procarbazine, Hydrea, cisplatinum, aracytin C, cyclophamine) regimen in the M7 protocol [12]. In M0 patients receiving chemotherapy before CSI, the risk of neuraxis progression seems to increase with the duration of chemotherapy [11]. Many institutions prefer to use of chemotherapy after CSI or at recurrence, only because radiotherapy is a "gold standard" and it is risky to delay the onset of proper treatment, especially in adults. There was an observed benefit of treating recurrences with chemotherapy in this study. This statement has limitations because of a retrospective character of the study. When recurrence is less aggressive, there appears a chance to convey the treatment.

New approaches of treating medulloblastoma are being investigated, including dose escalation with stereotactic or conformal techniques, either as primary treatment or at relapse. Radiosurgery appears to reduce the proportion of first failures occurring locally when it is as a part of initial management [22].

To summarise, accurate staging is necessary to identify all sites of disease and to assess the risk of recurrence, allowing appropriate decisions concerning therapy. In "high risk" patients the results of surgery and radiotherapy can be improved by chemotherapy, especially decreasing the risk of extraneural metastases [2]. A study concerning the implementation of new radiotherapy methods could be also carried out for patients with increased risk of local failure.

It is tempting to speculate that improvements in imaging and treatment may alter the results.

Conclusions

1. Reported results of conventional postoperative radiotherapy for medulloblastoma patients are poor, but similar as stated in literature.
2. All treatment results for medulloblastoma patients should be related to the presence of prognostic factors, especially to the initial extent of the disease.
3. The frequency of recurrences in the posterior fossa and outside the CNS is similar. Accurate initial staging could differentiate patients, in whom the use of chemotherapy or implementation of new radiotherapy techniques is meaningful.
4. Most of the relapses were observed within the first 2 years, but observation of late recurrences requires a long follow-up period.
5. Older patients show better overall survival.

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References

1. Karim ABF, Bleehan NM. A randomized trial on efficacy of radiation therapy of the cerebral gliomas. Joint EORTC\MRC Protocol No 22845\br 4, Appendix II, 1986.
2. Merchant TE, Wang MH, Haida T et al. Medulloblastoma: long-term results for patients treated with definitive radiation therapy during the computed tomography era. *Int J Radiat Oncol Biol Phys* 1996; 36: 29-35.
3. Prados MD, Warnick RE, Wara WM et al. Medulloblastoma in adults. *Int J Radiat Oncol Biol Phys* 1995; 32: 1145-1152.
4. Jenkin D, Shabanah MA, Shail EA et al. Prognostic factors for medulloblastoma. *Int J Radiat Oncol Biol Phys* 2000; 47: 573-584.
5. Frost PJ, Laperriere NJ, Shun Wong C et al. Medulloblastoma in adults. *Int J Radiat Oncol Biol Phys* 1995; 32: 951-957.

6. Bloom HJ, Bessell EM. Medulloblastoma in adults: a review of 47 patients treated between 1952 and 1981. *Int J Radiat Oncol Biol Phys* 1990; 18: 763--772.
7. Khafaga Y, Kandil AE, Jamshed A et al. Treatment results for 149 medulloblastoma patients from one institution. *Int J Radiat Oncol Biol Phys* 1996; 35: 501-506.
8. Skołyszewski J, Gliński B. Results of postoperative irradiation of medulloblastoma in adults. *Int Phys J Radiat Oncol Biol* 1989; 16: 479-482.
9. Wara WM, Le QTX, Sneed PK et al. Pattern of recurrence of medulloblastoma after low-dose craniospinal radiotherapy. *Int Phys J Radiat Oncol Biol* 1994; 30: 551-556.
10. DelCharco JO, Bolek TW, McCollough WM et al. Medulloblastoma: time-dose relationship based on a 30-year review. *Int J Radiat Oncol Biol Phys* 1998; 42: 147-154.
11. Hartsell WF, Gajjar A, Heideman RL et al. Patterns of failure in children with medulloblastoma: effects of preirradiation chemotherapy. *Int J Radiat Oncol Biol Phys* 1997; 39: 15-24.
12. Carrie C, Lasset C, Blay JY et al. Medulloblastoma in adults: survival and prognostic factors. *Radioter Oncol* 1993; 29: 301-307.
13. Chang CH, Housepian EM, Herbert C. An operative staging system and a megavoltage radiotherapeutic technique for celebellar medulloblastomas. *Radiology* 1969; 93:1351-1359.
14. Thomas PRM, Deutsch M, Kepner JL et al. Low-stage Medulloblastoma: final analysis of trial comparing standard-dose with reduced-dose neuraxis irradiation. *J Clin Oncol* 2000; 18: 3004-3011.
15. Bouffet E, Gentet JC, Doz F et al. Metastatic medulloblastoma: the experience of the French Cooperative M7 Group. *Eur J Cancer* 1994; 30: 1478-1483.
16. Silverman CL, Simpson JR. Cerebellar medulloblastoma: the importance of posterior fossa dose to survival and patterns of failure. *Int J Radiat Oncol* 1982; 8: 2023-2027.
17. Berry MP, Jenkin RDT, Keen CW et al. Radiation treatment for medulloblastoma. *J Neurosurg* 1981; 55: 43-51.
18. Prados MD, Edwards MSB, Chang SM et al. Hyperfractionated craniospinal radiation therapy for primitive neuroectodermal tumors: results of a phase II study. *Int J Radiat Oncol Biol Phys* 1999; 43: 279-285.
19. Carrie C, Alapetite C, Mere P et al. Quality control of radiotherapeutic treatment of medulloblastoma in a multicentric study: The contribution of radiotherapy technique to tumor relapse. *Radiol Oncol* 1992; 24: 77-81.
20. Narayana A, Jeswani S, Paulino AC. The cranial-spinal junction in medulloblastoma: does it matter? *Int J Radiat Oncol Biol Phys* 1999; 44: 81-84.
21. Hershatter BW, Halperin EC, Cox EB. Medulloblastoma: the Duke experience. *Int J Radiat Oncol Biol Phys* 1986; 12: 1829-1837.
22. Hodgson DC, Goumnerova LC, Loeffler JS, et al. Radiosurgery in the management of pediatric brain tumors. *Int J Radiat Oncol Biol Phys* 2001; 50: 929-935.

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