Published in final edited form as:

Am J Clin Oncol. 2014 February ; 37(1): 1–7. doi:10.1097/COC.0b013e31826b9cf0.

Long-term Outcomes and Role of Chemotherapy in Adults With Newly Diagnosed Medulloblastoma

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Abstract

Objective—To assess the survival and role of adjuvant chemotherapy in adult medulloblastoma.

Methods—We reviewed outcomes of 66 patients (aged 18 y or more; median age, 33 y) with medulloblastoma. Forty-four (67%) patients had M0 disease, 9 had M1-M4, and 13 had MX. Thirty-one patients each for whom risk stratification was available were classified as high risk or standard risk. Fifty-six patients had histologic results: classic histology was the most common (n = 46 [84%]), followed by desmoplastic (n = 9), and large cell/anaplastic (n = 1). Overall survival (OS) and progression-free survival (PFS) were estimated with Kaplan-Meier curves and log-rank tests. Cox regression analysis was used to compare recurrences.

Results—Median follow-up was 6.7 years. The estimated 5-year OS and PFS were 74% and 59%, respectively. High-risk versus standard-risk classification was associated with worse OS (61% vs. 86%; $P = 0.03$) and recurrence (hazard ratio, 2.56; $P = 0.05$) and a trend for worse PFS (49% vs. 69%; $P = 0.13$). Gross total resection was associated with improved OS ($P = 0.03$) and a trend toward improved PFS ($P = 0.09$). No chemotherapy benefit could be demonstrated for the group as a whole. For high-risk patients with classic histology (n = 25), chemotherapy was associated with a trend for improvement in 5-year PFS from 36% to 71% ($P = 0.10$) and in 5-year OS from 49% to 100% ($P = 0.08$).

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Presented at the American Society for Therapeutic Radiology and Oncology 52nd Annual Meeting, San Diego, CA, October 31–November 4, 2010.

The authors declare no conflicts of interest.

Conclusions—In adult patients with medulloblastoma, the extent of resection and risk classification predicts the outcome. These results suggest a chemotherapy benefit for high-risk patients with classic histology.

Keywords

brain tumors; chemotherapy; radiation oncology; radiotherapy

Medulloblastoma is the most common pediatric brain tumor but has a much lower incidence in adults, accounting for only about 1% of brain tumors in the older age group.¹ Furthermore, well-known differences in medulloblastoma exist between adults and pediatric patients.²⁻⁵ Some institutions have reported 5-year overall survival (OS) for adults as high as 84%, whereas other analyses, including a recent update from the Surveillance, Epidemiology and End Results (SEER) program within the National Cancer Institute, showed a 5-year OS of only 65%.^{6,7} The data have also varied about the effects of residual disease, metastatic disease, adjuvant chemotherapy, histologic subtype, and tumor location on patient outcomes.^{1-3,8-11}

Chemotherapy plays an important role in pediatric medulloblastoma, both allowing reduced craniospinal radiation dose for average-risk patients^{12,13} and improving survival of high-risk patients.^{14,15} The role of chemotherapy in adult treatment is less clear. Most centers favor full-dose (36 Gy) craniospinal irradiation without chemotherapy for standard-risk patients, because adults have generally completed physical growth and have more difficulty tolerating chemotherapy. Chemotherapy is often added to the treatment of high-risk adults on the basis of pediatric outcomes data,^{14,15} but little is known about its effects in these patients.

We therefore conducted a retrospective study of adult medulloblastoma patients treated at our tertiary care academic medical center from 1969 to 2008 to review outcomes, prognostic factors, and the role of chemotherapy in these patients.

METHODS

After obtaining approval from the Mayo Clinic Institutional Review Board, we retrospectively reviewed medical records of all patients seen at our institution who had medulloblastoma and were aged 18 years or older at diagnosis. In accordance with Minnesota state law, we also obtained authorization from all living patients to review their medical records for research purposes. Only patients seen at the time of initial diagnosis of medulloblastoma were included. Medical charts were reviewed to abstract data on demographics, clinical presentation, and treatment/tumor characteristics (including metastatic [M] stage, extent of surgery, chemotherapy, and radiotherapy). Pathologic findings were also reviewed for all patients with available slides. The World Health Organization classification was used to categorize the histologic types of medulloblastoma. Disease stage was based on the findings of Chang et al,¹⁶ and patients were classified as having either standard-risk or high-risk disease.⁶

Statistical Analysis

Statistical analyses were performed using JMP software (version 8.0 statistical package; SAS Institute Inc., Cary, NC). Survival analyses included OS and progression-free survival (PFS). OS was defined as time from diagnosis to death or last follow-up and calculated using the Kaplan-Meier method. PFS was defined as time from diagnosis to disease progression (based on either imaging or pathologic diagnosis), death, or last follow-up. Patient subsets were compared using the log-rank test.

The following variables were assessed for their prognostic value: metastatic (M) stage (M0 vs. M⁺), risk stratification (standard risk vs. high risk), sex, location (central vs. lateral), extent of surgery (gross total resection [GTR] vs. subtotal resection [STR] or biopsy), pathology (desmoplastic vs. classic), total radiation dose ≥ 55 versus < 55 Gy, and use of chemotherapy. We also assessed the effects of chemotherapy in different patient subsets (high-risk stratification, STR or biopsy, central location, lateral location, M⁺, male sex, female sex, and histologic type). With high-risk patients, we attempted to determine whether any particular histology benefited from use of chemotherapy. PFS and OS were characterized by different time periods and compared for the subset of patients staged with magnetic resonance imaging (MRI) compared with those who were not. Cox regression analysis was used to calculate hazard ratios (HRs) for death and recurrence for the following variables: risk stratification, sex, M stage, location, extent of resection, use of chemotherapy, pathology, and radiation dose. Separate calculations were made to obtain HRs for any recurrence, for recurrence in the posterior fossa, and for recurrence in the distant central nervous system (CNS), defined as anywhere in the CNS except the posterior fossa. Patients with recurrent disease were assessed for patterns of failure and median time to recurrence from initial diagnosis. Survival time from recurrence was calculated as time from recurrence to death or last follow-up.

RESULTS

Patient and Tumor Characteristics

Table 1 summarizes characteristics of all 66 patients, who had a median age of 33 years. Median follow-up was 6.7 years (range, 0.2 to 30.3 y). Thirty-one patients presented with midline tumors, 34 patients had lateral tumors, and 1 patient had no information available regarding tumor location. Forty-four patients had M0 disease, 1 had M1 disease, 1 had M2 disease, 5 had M3 disease, and 2 had M4 disease. Thirteen patients were classified as MX because the spine was either not evaluated (n = 6) or because the medical record contained no information about such evaluation (n = 7). Three patients seen after 1990 were classified with M0 disease if they had a negative MRI of the spine but results were not available for a lumbar puncture. Thirty-one patients were defined as having standard-risk medulloblastoma, 31 had high-risk disease, and 4 did not have enough information for risk classification. Fifty-six of the 66 patients had pathologic specimens available for review: classic histology was most common (n = 46 [84%]), followed by desmoplastic (n = 9) and large cell/anaplastic (n = 1) (Table 1).

Surgical Treatment

Forty patients underwent GTR as defined by either the operative note or the postoperative computed tomography or MRI scan. Eighteen patients had an STR, and 7 patients had only a biopsy. Information was not available for 1 patient.

Radiotherapy

Of the 66 patients, 64 patients had information available about the use of radiotherapy at diagnosis. Sixty-one of these 64 patients had irradiation of the craniospinal axis with or without a posterior fossa boost. One patient had whole-brain irradiation alone (50 Gy). Two patients did not receive radiotherapy at diagnosis. One such patient presented with metastatic disease to the leptomeninges and a vertebral body and received chemotherapy alone after a biopsy. The other had a complicated postoperative course after an STR and died before receiving additional therapy.

For patients with data available on their radiotherapy, the median dose to the craniospinal axis was 36 Gy (range, 23.4 to 45.9 Gy), to the whole brain was 36 Gy (range, 23.4 to 55.8 Gy), and to the posterior fossa was 55 Gy (range, 30 to 72 Gy).

Chemotherapy

Twenty-eight patients received chemotherapy after surgery. Of the 22 patients for whom data were available on chemotherapy sequencing, 13 (59%) had chemotherapy delivered subsequent to (with or without concurrent) irradiation. Of the 2 patients with M4 disease, 1 patient received cyclophosphamide, etoposide, and cisplatin before craniospinal radiotherapy, followed by thiotepa, carmustine, and ultimately high-dose chemotherapy with stem cell support. The other patient with M4 disease received cyclophosphamide, etoposide, and cisplatin after a biopsy procedure. This patient died before a planned treatment of high-dose chemotherapy with stem cell support. The remaining 7 patients with information on sequencing of therapy had chemotherapy before (with or without concurrent) irradiation. Six of these 7 patients received a platinum-containing regimen; 1 patient received lomustine alone. These chemotherapeutic agents are summarized in Table 1.

Survival Analysis

The estimated 5-year OS and PFS for all patients were 74% and 59%, respectively (Fig. 1). Five-year and 10-year PFS for patients meeting criteria for standard risk were 69% and 59%, respectively, compared with 49% and 38%, respectively, for those classified as high risk (Fig. 2). Five-year OS for patients classified as standard risk was 86% compared with 61% for those classified as high risk (Fig. 3).

Estimates of PFS and OS for different subsets of patients are displayed in Table 2. Patients with standard-risk disease had significantly better OS ($P = 0.03$) and a trend toward better PFS ($P = 0.13$). A similar result was found for patients with GTR for OS ($P = 0.03$) and PFS ($P = 0.09$). No significant differences were observed for sex, location, or pathology. HRs for death and recurrence are reported in Table 3. There was no difference in OS or disease free survival (DFS) by age when using a cutoff of 25 or 30 years.

Effect of Adjuvant Chemotherapy

Chemotherapy did not improve PFS or OS for the group as a whole, nor did it significantly improve results for the group of 31 patients with high-risk disease (Figs. 4A, B). In patients with desmoplastic histology ($n = 9$), the use of chemotherapy was associated with decreases in 5-year PFS (50% vs. 100%; $P = 0.06$) and OS (50% vs. 100%; $P = 0.04$). For the group of patients with both high-risk and classic histology ($n = 25$), chemotherapy was associated with a decreased risk of relapse in the posterior fossa ($P < 0.01$) and with a trend for improvement in OS (100% vs. 49% at 5 y; $P = 0.08$) and PFS (71% vs. 36%; $P = 0.10$) (Figs. 4C, D). Chemotherapy was not associated with any improvement in recurrence or survival for standard-risk patients with classic histology. No significant benefit was found for the use of chemotherapy in the other factors that were tested. Two patients who presented with standard-risk disease received chemotherapy in addition to low-dose (< 36 Gy to craniospinal axis) irradiation. Both were alive without disease recurrence at the time of last follow-up (1 at 4 mo and 1 at 50 mo).

Metastatic Disease Beyond the CNS

Two patients presented with M4 disease. One was found to have metastasis to bone after undergoing GTR for a tumor. He subsequently underwent chemotherapy followed by irradiation and ultimately had treatment with high-dose chemotherapy and stem cell support. He has had no evidence of recurrent disease and was still alive 81 months after diagnosis. The other patient had metastatic disease to the leptomeninges and a vertebral body. He was treated with chemotherapy alone after undergoing a biopsy, and died within 7 months.

Treatment Era

OS and PFS did not differ significantly for different time periods (Fig. 5). Patients treated after the median year of diagnosis (1993) did not have a significantly different OS compared with that of patients treated during the earlier time period ($P = 0.69$). Similarly, no significant difference was found for patients staged with or without an MRI (Fig. 6).

Recurrent Disease

Recurrent disease developed in 19 patients at a median time from diagnosis of 3.2 years (range, 0.5 to 14 y). The patterns of treatment failure for the entire group are listed in Table 4. The most common location of recurrence was the posterior fossa. High-risk disease ($P < 0.01$) and extent of resection ($P = 0.06$) correlated with failure in the distant CNS. High-risk disease was also associated with a higher risk of any type of recurrence ($P = 0.05$).

DISCUSSION

Medulloblastoma has a much lower incidence in adults than in children and may represent a biologically and clinically distinct entity. Reports of adult medulloblastoma are often limited by small numbers. A SEER database report found a 5-year OS of 65%.⁶ Some small reports have also found 5-year OS rates of $< 70\%$.^{3,17,18} Other larger reports from single institutions have indicated somewhat better results. For example, Coulbois et al¹⁹ found a 5-year OS of 81% in a population of 22 patients with adult medulloblastoma. This result is consistent with an OS of 83% in 36 patients reported by Chan et al.¹ In a report from the M.D. Anderson

Cancer Center, 28 patients had a 5-year OS of 84%.⁷ A large, updated French multicenter experience involving 253 patients had a reported 5-year OS of 72%.²⁰ Our results appear to be similar to those in that report, as our patients had a 5-year OS of 74% and a 5-year DFS of 59%.

Similar to the findings of published pediatric series, our findings indicate that risk stratification is a predictor of prognosis in patients with medulloblastoma. However, various experiences with small groups of patients have found different results. Prados et al⁸ defined a group of poor-risk patients as those with < 75% removal of tumor, metastatic disease, and brainstem or leptomeningeal invasion. These patients had worse OS and DFS compared with those of other patients. However, other authors have not found a difference in outcome by risk stratification.⁷ Some series have demonstrated the prognostic significance of M stage or extent of surgery.^{1,3,21} Riffaud et al²¹ defined high risk as having less than a GTR or as having disseminated disease. Such patients had a 5-year OS of 71% compared with a rate of 85% in standard-risk patients. In a French multicenter experience, high-risk versus standard-risk patients had significantly worse OS (65% vs. 77%).²² Similarly, our experience shows a significantly worse outcome for high-risk patients in terms of OS as well as in terms of the risk of recurrence. Although we could not demonstrate M stage as an individual prognostic factor, extent of surgery (STR or biopsy vs. GTR) did predict for OS. Our inability to detect a difference by M status may have been related to the fact that 13 of 66 patients were staged as MX.

Histologic type may be important in medulloblastoma. In pediatric cases, the large cell/anaplastic type has been shown to portend a poor prognosis.²³ Histology may be similarly important for adults with medulloblastoma.²⁴ In our patients, our review of pathologic findings determined that only 1 patient had large cell/anaplastic type. Thus, anaplastic histology seems to be rare in adults. We could not identify any difference in outcomes between desmoplastic and classic histologies. However, it should be noted that the numbers of patients with different histologies is small in this report, which may have made it difficult to identify significant differences.

We investigated the importance of radiation dose to the craniospinal axis, the whole brain, and the posterior fossa. In a previous report from our institution, patients had improved 10-year OS with a posterior fossa dose of 50 Gy or more, or with whole-brain irradiation, or with the use of spinal irradiation.²⁵ Other authors have also reported a dose response for irradiation of the posterior fossa in adults.^{22,26,27} In the current study, we found no relation between radiation doses given to patients and their ultimate survival or recurrence. This may be due to a change in our practice that resulted in the use of full craniospinal irradiation and a posterior fossa boost (usually > 50 Gy) in most patients.

The role of adjuvant chemotherapy in adult medulloblastoma is controversial. In children, there has been a growing interest in reducing the radiation dose to the craniospinal axis for patients with standard-risk disease.²⁸ The addition of chemotherapy may allow for a reduced craniospinal dose when treating children with standard-risk medulloblastoma.^{12,13} It is not known whether this approach would work for adults as well. In the French multicenter experience,²⁰ a lower dose to the spine was predictive of worse OS. However, in patients

with standard-risk disease who received both low-dose (< 34 Gy) craniospinal irradiation and chemotherapy, there was no difference in survival compared with that for standard-risk patients receiving higher doses. In our experience, 2 patients with standard-risk disease were treated with low-dose (< 36 Gy) craniospinal irradiation and chemotherapy. At last follow-up, both patients were alive without disease progression. Many clinicians are concerned about the ability of adults to tolerate the acute side effects of the chemotherapy regimens used in pediatric trials. Thus, we are reluctant to recommend low-dose craniospinal irradiation. Prospective trials are needed to assess whether low-dose craniospinal irradiation with chemotherapy can be used safely in adults and whether the additional chemotherapy toxicity is worth the small craniospinal irradiation dose reduction for adults.

There may also be a role for systemic therapy for standard-risk patients even with higher doses of radiation. Data from the Primitive Neuroectodermal Tumour trial-3 (PNET-3) of patients with M0-M1 disease showed an improvement in event-free survival with the addition of chemotherapy before radiotherapy.¹⁵ The benefits of chemotherapy in that trial were limited to the group with complete resection. It is unclear whether this potential benefit of additional chemotherapy in low-risk patients exists for adults with standard-risk disease.^{21,22} In the French multicenter experience, chemotherapy was not associated with improved survival for standard-risk patients.²² In our series, we observed no association with the use of systemic therapy and improved outcomes for the group as a whole or for patients with standard-risk disease.

Systemic chemotherapy has been shown to improve outcomes for pediatric patients with high-risk characteristics.^{14,29} However, the role of chemotherapy in adults with high-risk disease is not clear. For example, in the large French series, chemotherapy did not increase the survival of high-risk patients.²² Others have suggested that chemotherapy may improve the results for patients with high-risk disease such that they have a prognosis similar to that for standard-risk patients.^{30,31} Brandes et al³⁰ published results from a prospective trial in adults with medulloblastoma. Ten patients with low-risk (T1-T3a with no residual or M0) disease received radiotherapy alone after surgery and 26 with high-risk disease were treated with chemotherapy before irradiation. The 5-year OS and PFS was 80% and 80%, respectively, in the low-risk group compared with 73% and 69%, respectively, in the high-risk group. These authors noted that there was no significant difference in OS or PFS between the group with low-risk disease and the group with high-risk disease.

Our data showed an association of chemotherapy with a reduction in posterior fossa recurrence for patients with high-risk disease (> 1.5 cm³ residual or M⁺) and classic histology. There was also a trend toward better OS and PFS in this small group of patients. Desmoplastic histology is associated with more favorable outcomes and may be less likely to benefit from additional treatment intensification. This suggestion of improved results in the high-risk subset with classic histology warrants further investigation in future studies.

In a recent report analyzing data from 1973 to 2004 in the SEER database, Lai⁶ suggested that outcomes for patients with medulloblastoma have improved over time. We also attempted to examine the outcomes by treatment era for adult patients with medulloblastoma. We found no significant difference in outcomes over the period

investigated in this paper or for patients staged with or without an MRI. One possible reason for why we were unable to detect a difference in outcome over time may relate to the small sample size of our patient cohort. It could be possible that statistically significant results were not found because of this limitation.

In conclusion, both the extent of surgical resection and high-risk disease are prognostic factors for adult patients with medulloblastoma. Survival for adults with standard-risk medulloblastoma is excellent and mirrors that reported in pediatric series. In high-risk patients with classic histology, survival is poor but may be improved by the addition of chemotherapy.

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FIGURE 1. Survival after diagnosis of medulloblastoma. Kaplan-Meier estimates of progression-free survival (PFS) and overall survival (OS) for 66 adult patients from the time of diagnosis.

FIGURE 2.

Progression-free survival (PFS) of adult medulloblastoma patients by risk group. Kaplan-Meier estimates of PFS for 31 standard-risk adult patients compared with that for 31 high-risk patients ($P = 0.13$).

FIGURE 3.

Overall survival (OS) of adult medulloblastoma patients by risk group. Kaplan-Meier estimates of OS for 31 standard-risk patients compared with that for 31 high-risk patients ($P = 0.03$).

FIGURE 4.

Effects of chemotherapy in select subgroups of adult medulloblastoma patients. A and B, Kaplan-Meier estimates for progression-free survival (PFS) ($P = 0.46$) and overall survival (OS) ($P = 0.36$) for 31 high-risk patients treated with or without chemotherapy. C and D, Kaplan-Meier estimates for PFS ($P = 0.10$) and OS ($P = 0.08$) with both high-risk and classic histology ($n = 25$) with ($n = 14$) or without ($n = 11$) chemotherapy. Chemo indicates chemotherapy; No chemo, no chemotherapy.

No. at Risk										
1969-1979	8	8	8	7	6	6	6	6	5	5
1980-1989	21	19	19	18	16	13	12	12	12	11
1990-1999	17	17	16	15	14	14	13	13	11	11
2000-2008	20	15	15	14	13	10	9	7	4	0

FIGURE 5. Overall survival (OS) of adult medulloblastoma patients by time period treated. No significant difference in OS was found among groups of patients treated in 1969 to 1979, 1980 to 1989, 1990 to 1999, or 2000 to 2008 ($P = 0.65$).

FIGURE 6.

Overall survival of adult medulloblastoma patients staged with or without magnetic resonance imaging (MRI). No significant difference was demonstrated for medulloblastoma patients staged with MRI ($n = 44$) over those not staged with MRI ($n = 22$) ($P = 0.46$).

TABLE 1**Characteristics of 66 Patients With Medulloblastoma**

Characteristics	N (%)
Risk stratification (n = 62)	
High risk	31 (50)
Standard risk	31 (50)
Sex	
Male	37 (56)
Female	29 (44)
Age (y)	
18-25	18 (27)
26-35	27 (41)
36-45	11 (17)
> 45	10 (15)
Location (n = 65)	
Lateral	34 (52)
Central	31 (48)
Metastatic stage	
0	44 (67)
1	1 (2)
2	1 (2)
3	5 (8)
4	2 (3)
X	13 (20)
Chemotherapy regimen (n = 63)	
Cyclophosphamide with cisplatin-based regimens	16 (24)
Chemotherapy, unknown type	4 (6)
Cisplatin based	5 (8)
Cyclophosphamide, etoposide, cisplatin, thiotepa, carmustine (ultimately HDCSCS)	1 (2)
Cyclophosphamide based	1 (2)
Lomustine alone	1 (2)
None	35 (56)
Surgery (n = 65)	
Biopsy only	7 (11)
Subtotal resection	18 (28)
Gross total resection	40 (62)
Radiation (n = 64)	
Spinal	61 (95)
Whole brain alone	1 (2)
None	2 (3)
Pathology (n = 56)	
Classic	46 (82)

Characteristics	N (%)
Desmoplastic	9 (16)
Anaplastic	1 (2)

HDCSCS indicates high-dose chemotherapy with stem cell support.

TABLE 2
Estimates of OS and PFS in Different Subgroups of 66 Patients With Medulloblastoma

Characteristics	PFS			OS		
	5-Year (%)	10-Year (%)	P	5-Year (%)	10-Year (%)	P
Risk group (N = 62)						
Standard (n = 31)	69	59	0.13	86	77	0.03
High (n = 31)	49	38		61	49	
Sex (N = 66)						
Male (n = 37)	55	49	0.69	70	59	0.77
Female (n = 29)	64	48		77	68	
Metastatic stage (N = 53)						
M0 (n = 44)	61	51	0.34	77	70	0.22
M ⁺ (n = 9)	45	NA		76	48	
Location (N = 65)						
Lateral (n = 34)	61	61	0.21	79	66	0.15
Medial (n = 31)	59	40		70	62	
Surgery (N = 65)						
GTR (n = 40)	65	52	0.09	84	73	0.03
STR or biopsy only (n = 25)	49	40		57	47	
Chemotherapy (N = 63)						
Yes (n = 28)	60	50	0.85	79	59	> 0.99
No (n = 35)	58	46		68	62	
Pathology (N = 55)						
Desmoplastic (n = 9)	71	48	0.51	71	71	0.67
Classic (n = 46)	56	46		73	60	

GTR indicates gross total resection; M⁺, evidence of metastatic disease; M0, no metastases present; OS, overall survival; PFS, progression-free survival; STR, subtotal resection.

TABLE 3

HRs for Death and Recurrence in 66 Patients With Medulloblastoma

Characteristics	Death		Recurrence (Any)		Recurrence (PF)		Recurrence (Distant CNS)	
	HR	P	HR	P	HR	P	HR	P
High risk (n = 31) vs. standard risk (n = 31)	2.37	0.03	2.56	0.05	1.51	0.49	∞	<0.01
Male (n = 37) vs. female sex (n = 29)	1.11	0.77	1.02	0.96	0.67	0.49	1.22	0.79
M ⁺ (n = 9) vs. M0 (n = 44)	1.90	0.25	1.98	0.27	0	0.07	4.91	0.06
Central (n = 31) vs. lateral location (n = 34)	1.73	0.15	1.03	0.96	0.81	0.72	3.07	0.16
STR or biopsy (n = 25) vs. GTR (n = 40)	2.19	0.04	1.85	0.12	2.13	0.20	5.38	0.03
No chemotherapy (n = 25) vs. chemotherapy (n = 28)	1.00	> 0.99	1.02	0.97	3.10	0.11	0.92	0.91
PF dose <55 Gy (n = 26) vs. 55 Gy (n = 28)	0.93	0.87	1.07	0.89	1.63	0.44	0.50	0.41
CSA dose <36 Gy (n = 17) vs. 36 Gy (n = 37)	0.84	0.70	1.31	0.61	2.40	0.20	0.48	0.49
WB dose <36 Gy (n = 10) vs. 36 Gy (n = 44)	0.61	0.40	0.60	0.47	1.02	0.98	0	0.12
Desmoplastic (n = 9) vs. classic (n = 46)	0.77	0.66	1.09	0.89	0.48	0.44	2.35	0.34

CNS indicates central nervous system; CSA, craniospinal axis; GTR, gross total resection; HR, hazard ratio; M0, no metastases present; M⁺, evidence of metastatic disease; PF, posterior fossa; STR, subtotal resection; WB, whole brain.

TABLE 4

Sites of Disease Recurrence in Adult Patients With Medulloblastoma

Location	N
Posterior fossa	12
Brain *	3
Bone marrow	1
Spinal axis	6
Intraperitoneal	1

*
Excluding posterior fossa.