

Scientific Article

Outcomes and patterns of care in a nationwide cohort of pediatric medulloblastoma: Factors affecting proton therapy utilization

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Abstract

Purpose: We examined national outcomes and patterns of care for pediatric patients with medulloblastoma (MB) in a large observational cohort.

Methods and materials: Using the National Cancer Database, we evaluated the clinical features and survival outcomes of patients diagnosed with MB. The association between intervention, covariables, and outcome was assessed in a multivariable Cox analysis and through logistic regression analysis. Survival was estimated using the Kaplan-Meier method.

Results: Among the 4032 patients in the National Cancer Database with pediatric brain tumors, 1300 patients met the inclusion criteria of histologic diagnosis, receipt of chemotherapy and radiation, and age ≤ 18 years. The median age and follow-up were 8.4 years and 4.5 years, respectively. Five-year survival was 79.0%. In the univariate analysis, inferior outcome (overall survival) was associated with rural residence (hazard ratio [HR], 2.78; 95% confidence interval [CI], 1.47–5.29; $P < .01$) and histology (large cell; HR, 1.78; 95% CI, 1.08–2.94; $P < .05$). In multivariable analysis, both remained significant predictors of survival (large cell: HR, 1.68; $P < .05$; rural residence: HR, 2.74; $P < .01$). In 2013, the utilization rate of proton therapy (23% of patients) in the United States surpassed intensity modulate radiation therapy (16%), more frequently for patients with higher income ($P < .05$) or more favorable insurance status ($P < .05$).

Conclusions: As one of the largest data sets on pediatric MB, the observed variations in treatment intervention and survival outcomes may represent a target for further research.

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Introduction

Pediatric medulloblastomas (MBs) are a subcategory of embryonal tumors that arise from the posterior fossa. Five histological classifications of MB are currently

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recognized by the World Health Organization^{1,2}: classic, anaplastic, large cell, desmoplastic or nodular, and MB with extensive nodularity. The mean overall incidence of pediatric MB is 6.0 per 1,000,000 persons,^{3,4} but there is a discrepancy among reported studies, especially by histology, location, and age at diagnosis (adult vs pediatric).^{3,5}

Treatment for newly diagnosed pediatric MB begins with surgery, both as a means to improve outcome and to confirm the tumor type. Current guidelines recommend radiation therapy as part of treatment for all pediatric MBs in children older than 3 to 4 years at diagnosis. For younger children, delaying or omitting radiation therapy may be preferable to maximally preserve neurocognitive function.⁶⁻⁸ Multiagent chemotherapy is a standard component after radiation therapy for all pediatric patients.^{7,9,10} Radiation therapy modality for pediatric MBs consists of 2- and 3-dimensional conformal radiation therapy (CRT), intensity modulated radiation therapy (IMRT), or proton beam therapy (PBT). Although PBT is not shown to have increased survival or outcomes for pediatric MBs,¹¹ it may offer fewer side effects and may be considered the gold standard for MB treatment in the modern era. Its utilization, however, has not been well characterized in the modern literature.^{12,13}

In addition to type of tumor, histology, and genetic effects, other factors may affect the long-term outcomes of patients with cancer. Two factors that have been studied more extensively, outside of cancer type/modality and treatment factors, include the effect of race^{14,15} and socioeconomic status¹⁶ on survival rate. For example, Al-Refaei et al analyzed the impact of ethnicity on the prognosis of patients with gastric adenocarcinoma.¹⁷ Although they identified ethnic differences in both prognosis and treatment of gastric adenocarcinoma, their research did not address whether biologic or socioeconomic disparities accounted for the differences in outcomes. Kinlock et al analyzed the North Carolina Central Cancer Registry for race-based disparities in treatment waiting times for patients with prostate cancer.¹⁸ Their analysis uncovered a longer wait time between diagnosis and treatment for black men with prostate cancer compared with white men. Other studies have been conducted to look for socioeconomic disparities and their impact on cancer outcomes using the National Cancer Database (NCDB).¹⁹⁻²² To the best of our knowledge, data are limited on the impact of social disparities on receipt of radiation modality for pediatric MB.²³

Our research aims were to use the NCDB to study the impact of disparities in access to care for patients with cancer, specifically pediatric patients with MB, has on receipt of radiation therapy modality as well as factors that affect survival. In particular, we examined the relationship between clinical and sociodemographic parameters, with use of advanced radiation therapy modality. Our hypothesis was that utilization of PBT has increased significantly over the past several years, but disparities in access to this care exist.

Methods and materials

Data source

The NCDB, a national hospital-based oncology database, was used to conduct a retrospective cohort study of pediatric patients with MB. As a joint project of the American College of Surgeons Commission on Cancer and the American Cancer Society, the NCDB is a prospectively collected registry for 1500 hospitals, representing 75% of all cancers diagnosed in the United States, and has accumulated data on approximately 29 million cancer cases.

Captured variables include basic demographics (eg, age, race/ethnicity, and sex), socioeconomic characteristics, cancer staging, treatment course, comorbid conditions, and vital status.

Study patients

The CONSORT diagram in [Figure 1](#) shows the study exclusion criteria that were used to define the cohort. Patients were included based on histology for MB, age <19 years (pediatric), and receipt of both radiation and chemotherapy. Tumor histology and classification were based on ICD-O-3 morphology codes. Listed under the section for MB, histology was further divided into MB not otherwise specified (classical), desmoplastic, and large cell. After excluding patients (per CONSORT diagram, [Fig 1](#)), we analyzed a descriptive set of 1300 patients in our study. A total of 143 patients were identified as receiving radiation therapy but not chemotherapy, and 299 patients were listed as receiving chemotherapy but not radiation therapy. A total of 216 patients were listed as receiving neither chemotherapy nor radiation therapy or had incomplete data with regard to chemotherapy or radiation treatment and were therefore excluded. In accordance with NCDB participant user file data use agreements, the survival analysis was limited to patients diagnosed before 2010 (2004-2009) to allow at least 5 years of follow-up for all patients, thus excluding 517 patients and leaving a survival analysis of 783 patients.

Study variables

All variables studied were encoded in the NCDB data set for brain tumors. Study variables for patient characteristics and disparity of treatment modalities were analyzed by radiation modality—whether the patient received 2- or 3-dimensional CRT, IMRT, or PBT. Factors analyzed included sex, race, Charlson-Deyo comorbidity score, insurance status, education, distance traveled from treating facility, and histology.

For the survival analysis, the same variables for treatment modality were analyzed, as well as young age

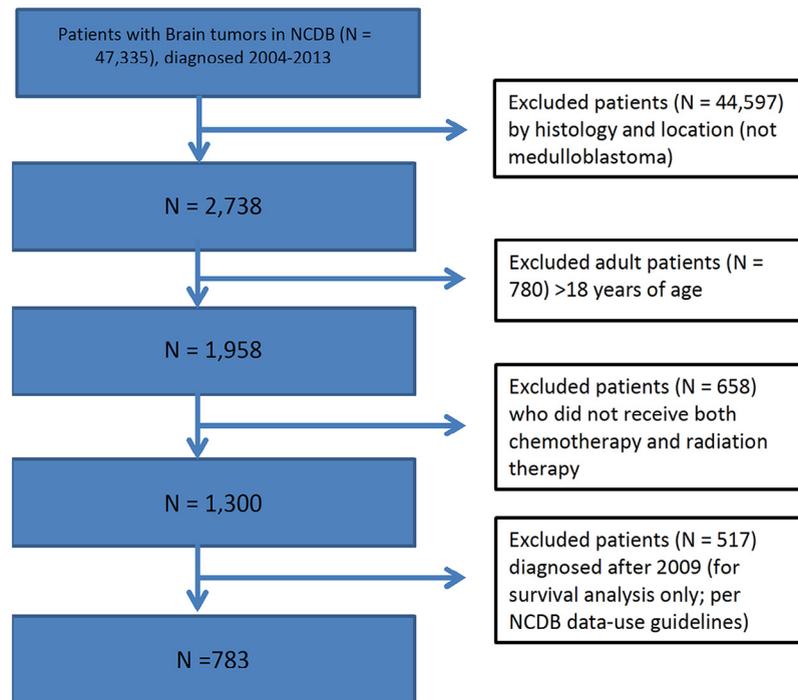


Figure 1 CONSORT diagram.

(<3 years). Due to the relatively low number of pediatric patients in the United States, several variables that would be very useful in an analysis of outcomes were made unavailable by the NCDB to maintain patient data de-identification. These variables included type of treatment facility, staging and grading information, molecular subtypes, and most information regarding surgical data.

Statistical analysis

Categorical and continuous variable distributions were presented with standard descriptive statistics. χ^2 tests were used to compare the sociodemographic and clinical characteristics of the cohort by insurance status. Socio-economic variables were placed in a logistic regression analysis to determine the effect on receipt of PBT. Individual variables that were statistically significant were included in a multivariable logistic regression analysis. Unadjusted associations of individual covariates with survival were described with univariate Cox proportional hazards models. A multiple Cox proportional hazards model then was fitted to estimate the hazard ratios (HRs) associated with variables for access and disparity of care and other covariates with respect to overall survival (OS) and their 95% confidence intervals (CIs). The covariates considered for inclusion in the model included age, sex, race, Charlson-Deyo comorbidity score, and socioeconomic status indicators (ie, income and education level),

histology, and tumor location. All positive (statistically significant) variables in the univariate analysis were placed in the multivariable analysis to determine their relationship with OS.

Kaplan-Meier survival curves were created for the entire cohort. OS was calculated in months from the date of diagnosis to the date of last contact or confirmed death.

All statistical analyses were performed with STATA 12.1 statistical software (StataCorp, College Station, TX). For all statistical testing, a 2-sided significance level of $P < .05$ was used.

Results

Descriptive statistics

As seen in [Table 1](#), of the 1277 patients involved in this study who met the criteria for diagnosis (by histology) and age (<18 years) and received both radiation therapy and chemotherapy, 64.8% were male and 35.2% were female. A total of 23 patients were excluded for analysis of factors that affect radiation therapy modality due to radiation therapy treatment other than 2- or 3-dimensional, IMRT or PBT. The average age of patients in this study was 8.44 years old (range, 0-18 years; standard deviation, 4.4) and the median follow-up was 4.5 years. The median total dose of radiation therapy delivered was 54.0 Gy.

Table 1 Patient characteristics according to radiation therapy modality

Parameter	Patients (n)	Radiation Therapy Modality			P-value
		2D/3D (%)	IMRT (%)	PBT (%)	
Overall	1277	1003 (78.54%)	157 (12.29%)	117 (9.16%)	n/a
Sex					
Male	827 (64.8%)	658 (65.6%)	105 (66.9%)	64 (54.7%)	.055
Female	450 (35.2%)	345 (34.4%)	52 (33.1%)	53 (45.3%)	
Race					
White	1012 (79.3%)	799 (79.7%)	129 (82.2%)	84 (71.8%)	.001 ^a
Black ^a	155 (12.1)	124 (12.4%)	21 (13.4%)	10 (8.6%)	
Other	110 (8.6%)	80 (8.0%)	7 (4.5%)	23 (19.7%)	
Charlson-Deyo Comorbidity Score					
0	1212 (94.9%)	950 (94.7%)	148 (94.3%)	114 (97.4%)	.346
1	43 (3.4%)	33 (3.3%)	8 (5.1%)	2 (1.7%)	
2	22 (1.7%)	20 (2.0%)	1 (0.6%)	1 (0.9%)	
Education (% Not High School Graduate in Patients' ZIP Code)					
≥21%	242 (19.3%)	198 (20.2%)	26 (16.6%)	18 (15.8%)	.007 ^a
13%-20.9%	316 (25.2%)	252 (25.7%)	47 (29.9%)	17 (14.9%)	
7%-12.9%	383 (30.6%)	300 (30.6%)	48 (30.6%)	35 (30.7%)	
<7%	311 (24.8%)	231 (23.6%)	36 (22.9%)	44 (38.6%)	
Median Household Income (in Patients' ZIP Code)					
< \$30,000	159 (13.1%)	130 (13.6%)	24 (15.9%)	5 (4.6%)	.028 ^a
\$30,000-35,999	212 (17.5%)	164 (17.2%)	32 (21.2%)	16 (14.8%)	
\$36,000-45,999	344 (28.4%)	275 (28.9%)	40 (26.5%)	29 (26.9%)	
≥ \$46,000	497 (41.0%)	384 (40.3%)	55 (36.4%)	58 (53.7%)	
Distance from Treating Radiation Therapy Facility					
<12.5 miles	408 (32.0%)	314 (31.3%)	55 (35.0%)	39 (33.3%)	.231
12.5-50 miles	488 (38.2%)	397 (39.6%)	56 (35.7%)	35 (29.9%)	
≥50 miles	381 (29.8%)	292 (29.1%)	46 (29.3%)	43 (36.8%)	
Insurance Status					
Private/Other Insurance	837 (67.4%)	647 (66.5%)	99 (63.9%)	91 (79.8%)	.010 ^a
Medicaid/Uninsured	405 (32.6%)	326 (33.5%)	56 (36.1%)	23 (20.2%)	
Histology					
Classic/NOS	1084 (84.9%)	852 (85.0%)	132 (84.1%)	100 (85.5%)	.989
Desmoplastic	116 (9.1%)	90 (9.0%)	16 (10.2%)	10 (8.6%)	
Large Cell	77 (6.0%)	61 (6.1%)	9 (5.7%)	7 (6.0%)	
Urban/Rural County					
Metropolitan county	1030 (83.1%)	805 (82.7%)	124 (80.5%)	101 (89.4%)	p = 0.266
Urban county	185 (14.9%)	146 (15.0%)	28 (18.2%)	11 (9.7%)	
Rural county	25 (2.0%)	22 (2.3%)	2 (1.3%)	1 (0.9%)	

2D, 2-dimensional; 3D, 3-dimensional; IMRT, intensity modulated radiation therapy; NOS, not otherwise specified; PBT, proton beam therapy.

^a Statistically significant.

Disparities in receipt of radiation therapy modality

Table 1 depicts the various parameters associated with radiation therapy modality. Patients who were white (PBT, 72% vs 2-/3-dimensional, 80% vs IMRT, 82%; $P < .001$) were more likely to receive PBT compared with patients who were black (PBT, 9% vs 2-/3-dimensional, 12% vs IMRT, 13%; $P < .001$). Other socioeconomic factors, higher education (upper quartile: 39% PBT vs 24% 2-/3-dimensional vs 23% IMRT; lower quartile: 16% PBT vs 20% 2-/3-dimensional vs 17% IMRT; $P = .007$) and higher median household income (upper quartile:

54% PBT vs 40% 2-/3-dimensional vs 36% IMRT; lower quartile: 5% PBT vs 14% 2-/3-dimensional vs 16% IMRT; $P = .028$) were more likely to receive PBT compared with 2-/3-dimensional CRT or IMRT. Lastly, type of insurance affected the likelihood of a patient receiving PBT, with patients who possessed private insurance (80% PBT vs 67% 2-/3-dimensional vs 64% IMRT; $P = .010$) most likely to receive PBT compared with those with Medicaid or no insurance (20% PBT vs 34% 2-/3-dimensional vs 36% IMRT; $P = .010$).

Socioeconomic factors were included in a logistic regression analysis to analyze radiation modality correlations (Table 2). Race was not a significant predictor of recep-

Table 2 Logistic regression analysis for factors that affect likelihood of receipt of PBT

Prognostic Factor	OR	P-value	OR (multivariable)	P-value
Race				
White	1.00 (Ref.)			
Black	0.76	.432		
Other	2.92	<.001 ^a		
Age (years)				
3-18	1.00 (Ref.)			
<3	0.16	.071		
Median Household Income				
<\$30,000	1.00 (Ref.)		1.00 (Ref.)	
\$30,000-35,999	2.51	.078	2.21	.14
\$36,000-45,999	2.84	.035 ^a	2.82	.045 ^a
≥\$46,000	4.07	.003 ^a	2.94	.044 ^a
Education (% Not HS Graduate in Patients' ZIP Code)				
≥21%	1.00 (Ref.)		1.00 (Ref.)	
13%-20.9%	0.71	.32	0.56	.130
7%-12.9%	1.25	.46	0.92	.820
<7%	2.05	.015 ^a	1.27	.535
Insurance Status				
Private Insurance/Other	1.00 (Ref.)		1.00 (Ref.)	
Uninsured/Medicaid	0.49	0.003 ^a	0.70	0.168
Histology				
Classic/NOS	1.00 (Ref.)			
Desmoplastic	0.93	0.83		
Large Cell	0.98	0.97		
Urban/Rural County				
Metropolitan County	1.00 (Ref.)			
Urban County	0.58	0.098		
Rural County	0.38	0.35		

HS, high school; OR, odds ratio; PBT, proton beam therapy; Ref, reference group.

^a Statistically significant.

tion of PBT. When compared with the lowest income bracket (<\$30,000), a median income of >\$36,000 was correlated with greater odds of receiving PBT (odds ratio [OR], 2.84, $P = .035$; OR, 4.07, $P = .003$). Uninsured or Medicaid status was associated with a 0.49 OR of receiving PBT compared with private insurance/Medicare ($P = .003$). Education (by high school diploma) was a significant predictor of PBT use as well, with the highest educated regions being most likely to receive PBT (OR, 2.05; $P = .015$). Interestingly, young age (<3 years) was associated with a decreased likelihood of receipt of PBT (OR, 0.16; $P = .071$) but with borderline significance.

Histology was not correlated to any increased or decreased likelihood of receipt of PBT, which supports the observation that socioeconomic factors affect the likelihood of PBT. In multivariable logistical regression analysis, education and insurance status were no longer significant predictors of likelihood of receiving PBT; however, income remained a significant predictor. PBT utilization for pediatric MB increased between 2004 (0.7% of patients in this study were treated with PBT) and 2013 (23.4% of patients; see [Supplemental Fig S1](#)).

Survival analysis

The 5-year OS for the patients in the entire cohort was 79.0% ([Fig 2](#)). In the unadjusted univariate analysis ([Table 3](#)), large cell histology was associated with decreased OS (67.8% for 5-year survival; HR, 1.78; 95% CI, 1.08-2.94; $P = .024$) compared with the entire cohort, whereas desmoplastic histology was associated with better outcomes (87.4% 5-year survival; HR, 0.74; 95% CI, 0.40-1.36; $P = .34$) ([Fig 3](#)). Receipt of a radiation boost was not significantly associated with better or worse outcomes (HR, 1.12; 95% CI, 0.81-1.55; $P = .48$). Metropolitan, urban, and rural county of residence was a significant predictor of outcome for patients with MB. Patients from a rural residence were associated with much poorer outcomes (HR, 2.78; $P = .002$) and a decreased 5-year survival (62.7% vs 79.3% for metropolitan; 82.7% for urban counties; Wilcoxon test $P = .007$).

When urban/rural residence and histology were combined into a multivariable analysis, both variables remained significant predictors of outcome ([Table 4](#)) with minimal changes in the associated HRs.

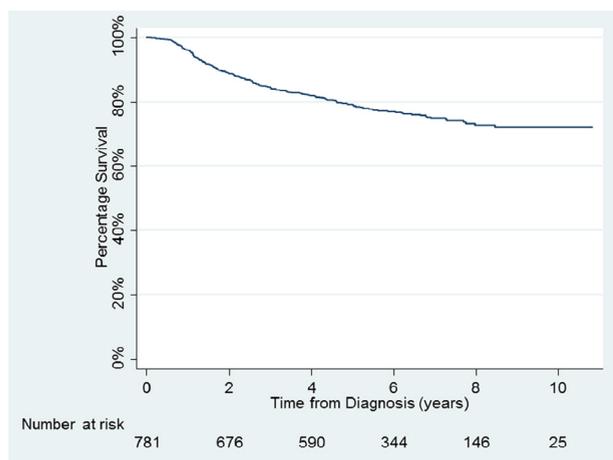


Figure 2 Overall survival for the entire cohort. The 5-year overall survival was 79.0% for all pediatric patients with medulloblastoma.

Discussion

In our current study of more than 750 pediatric patients with MB, we discovered disparities in the radiation therapy modality utilized and variations in national outcomes on the basis of histology. The 5-year OS rate for the studied population was 79%, which is slightly better than the nationally published standards from prospective trials on MB (range, 69.2%-76.1%).²⁴⁻²⁶ Univariable and multivariable Cox analyses identified histology (with large cell histology possessing the poorest prognosis) and rural residence as significant predictors of outcomes. We postulate that poorer outcomes for patients who reside in rural communities may be due to a lack of access to necessary care or potentially delayed diagnosis and subsequent treatment.

In addition to type of tumor, histology, and genetic effects, other factors may affect long-term outcomes for patients with cancer. Two factors that affect survival rate that have been studied more extensively, outside of cancer type/modality and treatment factors, include race^{17,19,20,27} and socioeconomic status.²⁸ These factors have been shown to have profound effects across medicine (eg, through pain management).²⁹⁻³¹ Additionally, analyses of racial and socioeconomic factors in cancer survival have been used within the NCDB and the Surveillance, Epidemiology, and End Results database and may be a reasonable surrogate for predicting outcomes.^{17,20} For example, Fedewa et al performed a similar analysis of the NCDB for uterine cancer and showed that black race and worse insurance status were both associated with poorer outcomes.¹⁹ Ward et al analyzed the Iowa Cancer registry database to determine factors that affect patients who do not receive treatment and found that race and insurance type affected whether a patient was likely to receive standard treatment.²⁸ Additional studies have demonstrated that insurance type, as analyzed by private insurance, Medicare, Medicaid, and no insurance, may be a more significant predictor of outcome than standard clinical parameters.^{21,22}

Table 3 Univariate analysis for overall survival

Prognostic Factor	Univariate Analysis	
	HR (95% CI)	P-value
Radiation Therapy Modality		
2D/3D-CRT	1.00 (Ref.)	
IMRT	0.82 (0.46-1.48)	.52
Proton	0.99 (0.41-2.40)	.98
Sex		
Male	1.00 (Ref.)	
Female	0.82 (0.60-1.12)	.21
Race		
White	1.00 (Ref.)	
Black	1.15 (0.74-1.78)	.54
Other	0.77 (0.42-1.41)	.39
Age (y)		
3-18	1.00 (Ref.)	
< 3	1.06 (0.59-1.90)	.85
Charleston-Deyo Comorbidity Score		
0	1.00 (Ref.)	
1	1.42 (0.73-2.78)	.31
2	1.11 (0.35-3.46)	.86
Insurance Status		
Private/Other	1.00 (Ref.)	
Uninsured/Medicaid	0.95 (0.69-1.30)	.74
Education (% NOT HS Graduate in Patients' ZIP Code)		
≥21%	1.00 (Ref.)	
13%-20.9%	1.18 (0.75-1.85)	.49
7%-12.9%	1.17 (0.75-1.82)	.50
<7%	0.99 (0.62-1.59)	.96
Median Household Income (Patients' ZIP Code)		
<\$30,000	1.00 (Ref.)	
\$30,000-35,999	0.70 (0.41-1.18)	.18
\$36,000-45,999	0.68 (0.42-1.09)	.11
≥\$46,000	0.82 (0.53-1.27)	.38
Distance from Facility		
<12.5 miles	1.00 (Ref.)	
12.5-50 miles	0.96 (0.69-1.37)	.81
≥50 miles	1.16 (0.80-1.67)	.44
Histology^a		
Classic/NOS	1.00 (Ref.)	
Desmoplastic	0.74 (0.40-1.36)	.34
Large Cell	1.78 (1.08-2.94)	.024 ^a
Reception of Radiation Boost		
Boost	1.00 (Ref.)	
No boost	1.12 (0.81-1.55)	.48
Urban/Rural County		
Metropolitan county	1.00 (Ref.)	
Urban county	0.74 (0.47-1.18)	.21
Rural county	2.78 (1.47-5.29)	.002 ^a

2D, 2-dimensional; 3D, 3-dimensional; CI, confidence interval; CRT, conformal radiation therapy; HR, hazard ratio; HS, high school; IMRT, intensity modulated radiation therapy; NOS, not otherwise specified; PBT, proton beam therapy; Ref., reference group.

^a Statistically significant.

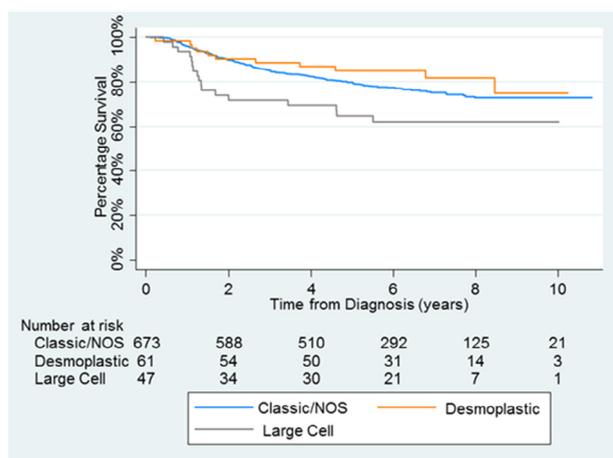


Figure 3 Overall survival by tumor histology. The 5-year overall survival of patients with classic/not otherwise specified histology was 79.0% versus 87.4% for patients with desmoplastic histology versus 67.8% for patients with large cell histology. ($P < .01$, Wilcoxon test).

In the current study, although we have demonstrated increasing utilization of PBT in patients with MB (see [Supplemental Fig S1](#)), there continues to be dramatic underutilization of PBT in this population. Although proton beam radiation therapy has not been shown to have increased survival or outcomes for pediatric medulloblastomas,¹¹ it does have decreased side effects in pediatric brain tumors.^{12,13} Thus, pediatric MBs are a well-accepted indication for proton therapy because the American Society of Radiation Oncology includes all pediatric solid malignancies in its model policy for payor coverage.

In the descriptive analysis that was used to determine the factors affecting the likelihood of receiving PBT, multiple factors led to decreased utilization. These included race, insurance status, and socioeconomic status (household income and education quartile). Patients of white race and with private insurance were much more

likely to receive PBT than black, uninsured (0 patients received PBT), or Medicaid patients, respectively. Further analysis was conducted using logistic regression analysis. Increased odds of PBT utilization were found to be associated with private insurance or Medicare and better socioeconomic status (in particular, median income and education). This suggests that access to and funding for PBT for pediatric brain tumors for less fortunate, uninsured patients currently may be limited. Many other studies have found that education level,¹⁶ insurance status,²¹ median household income,¹⁵ and race¹⁸ are important surrogates for disparate access to much needed care across a variety of conditions.²⁸ Given that this population of pediatric patients may already be at risk for poorer developmental outcomes, access to radiation therapy that may be able to mitigate this side effect is especially important.

Recent analysis by Kann et al analyzed the differing effects of deferred radiation therapy on survival through the NCDB data set (ie, rates of omission of radiation therapy).³² With a median follow-up of 4.8 years and a studied age group of 3 to 8 years, the researchers discovered that these low rates of radiation therapy utilization were associated with a detriment to survival in this age group (in addition to more advanced disease and treatment at low-volume centers). Interestingly, the only parameters associated with the omission of radiation therapy were younger age and year of diagnosis. In contrast with our study, Kann et al analyzed predominantly based on age (3-8 years) without significant analysis for disparity of care (specifically the use of proton therapy). Second, Kann et al did not analyze for outcomes based on histology or urban/rural disparities, both parameters that were found to be important in the current study.

Survival analysis and factors that affect outcomes were analyzed in the Cox analysis. Although this analysis does provide a strong link between histologic diagnosis and prognosis, there are many limitations to the data contained within the data set that must be addressed. First, although the multivariable analysis was adjusted for measured covariates, we were unable to control for unknown confounders and unreported prognostic factors, such as the extent of surgical resection and initial tumor size, which are both indicative of outcomes.³³ Second, another limitation of the data set is the limited follow-up. Given the relatively young age of the study population and the testable outcome parameter of OS, the limited follow-up does not allow for an accurate analysis of survival after 5 years. Third, the NCDB does not report toxicity of treatment or secondary treatments, which would be helpful in risk stratifying the patients most appropriate for specific radiation therapy modalities. For example, a patient with a larger tumor that is adjacent to a critical structure and who underwent a subtotal resection may be more likely to receive PBT rather than a 2-/3-dimensional CRT technique.

Table 4 Multivariable analysis for overall survival

Prognostic Factor	Multivariate Analysis	
	HR (95% CI)	P-value
Histology^a		
Classic/NOS	1.00 (Ref.)	
Desmoplastic	0.77 (0.42-1.42)	.40
Large Cell	1.69 (1.01-2.83)	.048 ^a
Urban/Rural County		
Metropolitan county	1.00 (Ref.)	
Urban county	0.75 (0.47-1.19)	.22
Rural county	2.73 (1.44-5.20)	.002 ^a

CI, confidence interval; HR, hazard ratio; NOS, not otherwise specified; Ref., reference group.

^a Statistically significant.

Conclusions

In this study, we confirm the national outcomes of pediatric patients with MB who undergo standard adjuvant chemoradiation after surgical resection. With large patient numbers that exceed those of single prospective trials, the NCDB has proven to be a powerful tool to demonstrate significant disparities in survival outcomes in a relatively uncommon disease and may help generate hypotheses for novel treatment strategies. We recommend that national efforts are made to increase access to PBT when indicated for pediatric patients.

Acknowledgments

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Supplementary data

Supplementary material related to this article can be found at <https://doi.org/10.1016/j.adro.2017.07.007>.

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