

Comparative Dosing of Bevacizumab for Radiation Necrosis: Impact of Tumor Type on Edema Response

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Abstract

Purpose

Bevacizumab is an effective treatment for radiation necrosis; dose dependent radiographic and edema response data are lacking.

Methods

Multicenter, retrospective cohort study of adult patients with primary central nervous system tumors or brain metastases who received bevacizumab for radiation necrosis between June 2021 and July 2024. Patients were grouped by bevacizumab dose (7.5 mg/kg vs 10 mg/kg administered every three weeks). Primary outcome was edema response, assessed by a blinded neuro-oncologist. Secondary outcomes included contrast enhancing disease response, clinical response, adverse events, treatment discontinuation, and re-dosing for recurrent radiation necrosis. Analyses were performed with and without adjustment for tumor type.

Results

104 patients were included (7.5 mg/kg, n = 53; 10 mg/kg, n = 51). Edema response differed between dosing groups in unadjusted analyses ($p = 0.032$), favoring the 7.5 mg/kg cohort; however, this association was attenuated after adjustment for tumor type. Contrast enhancing disease response did not differ between groups in either unadjusted or adjusted analyses ($p = 0.43$). Clinical response was higher in the 7.5 mg/kg group (65.2% vs 37.8%, $p = 0.013$). Tumor type differed significantly between cohorts ($p < 0.001$), with more primary CNS tumors in the 10 mg/kg group. Rates of adverse events, treatment discontinuation, and re-dosing were similar.

Conclusions

While lower-dose bevacizumab was associated with greater edema reduction in unadjusted analyses, this effect was attenuated after accounting for tumor type. Importantly, 7.5 mg/kg dosing appeared sufficient for achieving edema control and contrast enhancing disease response. These findings support an individualized approach to bevacizumab dosing in radiation necrosis and highlight the need for prospective, tumor-stratified studies.

Introduction

Radiation necrosis of central nervous system (CNS) tissue is a serious complication following brain radiation, typically developing 6 months to 3 years after radiation therapy is completed[1–5]. The volume of irradiated areas and total radiation dose are the most predictable risk factors. There are many

theories for radiation necrosis development, and while the exact mechanism is unknown, a vascular mechanism is widely accepted. Increased capillary permeability causing extracellular edema is thought to be the cause of radiation necrosis while endothelial dysfunction, tissue hypoxia, and subsequent necrosis maintain this process[6–8]. Due to this proposed mechanism of action, early vascular endothelial growth factor (VEGF) blockade is thought to be a potential strategy to control cerebral edema related to radiation necrosis by decreasing vascular permeability[9].

Current management of radiation necrosis often involves the use of dexamethasone to alleviate symptoms. However, long-term use of steroids is problematic due to associated adverse events including musculoskeletal, endocrine/metabolic, gastrointestinal, cardiovascular, and immunologic[10]. Bevacizumab is a recombinant human monoclonal antibody that binds VEGF, preventing it from binding to its receptors on endothelial cells[9, 11, 12]. This plays a major role in angiogenesis and regulates vascular permeability, making it an optimal drug to treat radiation necrosis. As a result of its vascular mechanism of action, dose-dependent adverse events of bevacizumab can arise including thrombosis, gastrointestinal perforation, impaired wound healing, and hemorrhage[13–16]. There are also known risks of rebound radiation necrosis following discontinuation of anti VEGF therapy as multiple studies have reported. However, whether the rate of recurrence is dose-dependent has not been evaluated[17, 18].

Bevacizumab has emerged as an effective treatment for radiation necrosis across a range of primary and metastatic brain tumor populations, with reported benefits including reductions in edema, contrast enhancement, corticosteroid requirements, and neurologic symptoms[19–24]. Published experience, however, reflects substantial heterogeneity in dosing, with regimens ranging from low-dose approaches such as 2.5 mg/kg and fixed low-dose schedules to more conventional doses of 5–7.5 mg/kg, and up to higher doses of 10–15 mg/kg[14, 23, 25–28]. Despite this variability, prior studies have generally shown radiographic and clinical improvement across dosing strategies, and the limited comparative data available have not demonstrated a consistent advantage for higher-dose bevacizumab over lower-dose approaches in the treatment of radiation necrosis. Collectively, these findings suggest that bevacizumab efficacy in radiation necrosis may not be strongly dose dependent within commonly used ranges, underscoring the need for larger, indication-specific studies to clarify the lowest effective dose and better individualize therapy.

Bevacizumab has been extensively studied in glioblastoma (GBM), where it is commonly administered at 10 mg/kg every 2 weeks, a regimen established in early trials of recurrent disease and reinforced by studies such as the BELOB trial[29, 30]. As a result, this dosing strategy became adopted into practice for high-grade gliomas and has often been extrapolated to other CNS indications, including radiation necrosis, despite differences in underlying biology and treatment goals. This historical precedent likely contributes to ongoing variability in bevacizumab dosing and underscores the need for indication-specific dose optimization.

This study will address the gap in the literature regarding optimal bevacizumab dosing by comparing the two most common doses utilized, 7.5 mg/kg and 10 mg/kg both administered every 3 weeks, using a large patient population. This study will also aim to evaluate differences in radiation necrosis recurrence and safety outcomes between the two dosing strategies.

Materials and Methods

This study was a multi-center, retrospective chart review of adult patients with either primary central nervous system (CNS) tumors or brain metastases from secondary malignancies who were treated with bevacizumab at Mayo Clinic Enterprise locations between June 29, 2021, and July 31, 2024. Patients prescribed “bevacizumab,” for a diagnosis of radiation necrosis were identified retrospectively from Mayo Clinic’s Electronic Health Record (EHR) using SlicerDicer™. Data was de-identified for analysis and stored in REDCap[31, 32]. This study was approved by the Mayo Foundation Institutional Review Board and performed in accordance with the ethical standards of the 1964 Declaration of Helsinki with adherence to all relevant regulations of the US health insurance portability and accountability act. Data were collected from existing medical records and analyzed in a de-identified manner. Only patients who had provided authorization for the use of their medical records for research purposes were included; patients who declined Minnesota Research Authorization were excluded prior to data collection. All participants provided the required consent/authorization for inclusion in research in accordance with institutional policies and applicable ethical standards. Those not treated with bevacizumab specifically for radiation necrosis were manually excluded. Radiation necrosis can be difficult to differentiate from recurrent disease without biopsy; we utilized a combination of clinical judgement, pattern of enhancement, timing of onset from radiation exposure and perfusion imaging to guide diagnosis. Patients were eligible for inclusion regardless of prior bevacizumab exposure. Prior bevacizumab use was permitted if it had occurred at least 6 months before bevacizumab initiation for radiation necrosis or, when administered for tumor control, if it was given on a dosing schedule different from the radiation necrosis treatment regimen included in this analysis. Only bevacizumab doses administered specifically for radiation necrosis were included in the study analyses.

For the primary analysis, patients were divided into two groups: those receiving 7.5 mg/kg of bevacizumab and those receiving 10 mg/kg. Patients treated with bevacizumab 10 mg/kg every 2 weeks were excluded because this dosing schedule is commonly used in recurrent glioblastoma and was considered less representative of bevacizumab prescribing specifically for radiation necrosis. Both treatment groups received bevacizumab every 3 weeks; dosing was at the provider’s discretion. The primary outcome measured was radiographic edema response classified according to the following groups: (1) increase of edema, > 105% of baseline; (2) constant edema, 75%-105% of baseline; (3) slight decrease of edema, 25%-75% of baseline; (4) large decrease of edema, < 25% of baseline.

Secondary endpoints included radiographic contrast enhancing disease response, adverse events between dosing groups such as arterial/venous thromboembolism, hemorrhage, gastrointestinal perforation, and other treatment-related toxicities. Contrast enhancing disease response defined as the

best imaging outcome following completion of the bevacizumab treatment as assessed by a blinded neuro-oncologist on the study team. Contrast enhancing disease responses were categorized as follows: Complete response (CR) if imaging changed related to radiation necrosis completely resolves, partial response (PR) if imaging changed related to radiation necrosis improved to where there was 25% or greater decrease in contrast enhancement but not complete resolution, stable disease (SD) if there was less than 25% decrease in contrast enhancement or no more than 20% increase, or progressive radiation necrosis if there was greater than 20% increase in contrast enhancement despite bevacizumab administration. Patients who had missing imaging were classified as unknown. Additional outcomes included treatment discontinuation due to toxicity, evidence of clinical improvement/response as documented in provider notes (defined as improvement in patient's presenting CNS symptoms), and the need for re-dosing due to recurrence of radiation necrosis.

Descriptive statistics are reported by dose group as frequencies and percentages for categorical data and either means and standard deviations or medians and interquartile ranges for continuous data. Differences in categorical variables, including contrast enhancing disease response and safety outcomes, were tested using Chi-square or Fisher's exact tests, as appropriate. Differences in continuous variables were tested using equal variance two-sample t-tests or Wilcoxon rank sum tests, as appropriate for the distribution. Efficacy outcomes were additionally compared between dose groups using multivariable methods to adjust for tumor type (primary CNS tumor or brain metastasis); multivariable logistic regression was used to assess clinical response and dichotomized edema response, Cochran-Mantel-Haenszel testing was used to assess contrast enhancing disease response and 4-level edema response. All analyses were performed using SAS version 9.4 software (SAS Institute, Inc.; Cary, NC).

Results

Baseline Demographics and Clinical Characteristics

A total of 104 adult patients met inclusion criteria, with 53 patients receiving bevacizumab 7.5 mg/kg and 51 patients receiving 10 mg/kg (Figure 1). Overall, the cohort had a mean age of 59.3 years and was predominantly White and non-Hispanic. Baseline age, sex distribution, weight, race, and ECOG performance status were similar between treatment groups (Table 1).

Tumor type differed significantly between dosing cohorts ($p < 0.001$). Patients with primary CNS tumors were more likely to receive bevacizumab 10 mg/kg (84.3% vs 43.4%), whereas the 7.5 mg/kg group more frequently included patients with brain metastases from extracranial primaries such as lung, breast, and melanoma.

The median number of bevacizumab doses administered was four in both cohorts, although the interquartile range was wider in the 10 mg/kg group (IQR 3–9 vs 3–4; $p = 0.011$) (Table 2). Prior bevacizumab exposure for radiation necrosis ($n=8$) or tumor-control ($n=4$) was numerically more common in the 10 mg/kg group (17.6% vs 5.7%), although this difference was not statistically significant

($p = 0.073$). Other treatment-related factors, including concomitant steroid use, anticoagulation, systemic therapy, radiation characteristics, and time from radiation to bevacizumab initiation, were similar between groups. Among patients receiving dexamethasone, the median dexamethasone dose at bevacizumab initiation was 12 mg/day (IQR 8-16) in the 7.5 mg/kg cohort and 10 mg/day (IQR 5-16) in the 10 mg/kg cohort ($p=0.16$). The median time from dexamethasone initiation to bevacizumab initiation was 7.0 months (IQR 2.3-12.8) and 4.8 months (IQR 1.4-8.1), respectively ($p=0.13$).

Efficacy

Given the significant imbalance in tumor type between groups, an adjusted analysis accounting for tumor type (dichotomized as primary CNS and brain metastasis) was performed (Table 3). To further explore the impact of tumor type on edema response, count of patients with edema decrease was stratified by tumor type and bevacizumab dose (Figure 2). Edema response, the primary endpoint, differed significantly between dosing strategies in unadjusted analyses ($p = 0.032$), although the difference was not statistically significant after adjustment for tumor type ($p = 0.082$) (Table 3). Based on the distribution in Table 3, patients receiving bevacizumab 7.5 mg/kg had a greater proportion of edema reduction (combined slight and large decrease) compared with those receiving 10 mg/kg. Similarly, a greater proportion of patients in the 7.5 mg/kg group achieved a large decrease in edema (<25% of baseline). When edema response was dichotomized to evaluate large reductions versus all other categories, the unadjusted difference was significant ($p = 0.015$), but this association was attenuated and no longer statistically significant after adjustment for tumor type ($p = 0.057$).

Contrast enhancing disease response did not differ significantly between dosing groups in unadjusted analyses ($p = 0.43$) (Table 3). In the 7.5 mg/kg group, 32.7% of patients achieved a complete or partial response, 61.5% had stable disease, and 5.8% experienced progression. Similarly, in the 10 mg/kg cohort, 29.5% achieved a complete or partial response, 59.1% had stable disease, and 11.4% experienced progression. After adjustment for tumor type, there remained no significant association between bevacizumab dose and contrast enhancing disease response.

Clinical response differed between treatment groups, with patients receiving 7.5 mg/kg more likely to have documented clinical improvement compared with those receiving 10 mg/kg (65.2% vs 37.8%, $p = 0.013$), although this difference was not significant after adjustment for tumor type ($p = 0.054$) (Table 3).

Safety

Rates of serious adverse events, including thromboembolism, hemorrhage, and gastrointestinal perforation, were low and did not differ significantly between dosing groups ($p > 0.99$) (Table 3). Hemorrhagic events included cerebral hemorrhage and gastrointestinal bleeding, while thromboembolic complications included deep vein thrombosis, pulmonary embolism, ischemic stroke, and lacunar infarction. One gastrointestinal perforation and one case of grade 3 hypertension were observed. Other reported toxicities included transient fever/chills, severe fatigue, and Brown-Sequard syndrome. No new safety signals were identified, and treatment discontinuation due to toxicity remained uncommon.

Discussion

This retrospective, enterprise-wide analysis evaluated two commonly used bevacizumab dosing strategies for radiation necrosis, with edema response as the primary endpoint. In unadjusted analyses, bevacizumab 7.5 mg/kg was associated with significantly greater reductions in edema, whereas contrast enhancing disease response did not differ between dosing strategies. However, after adjustment for tumor type, the observed association between bevacizumab dose and edema response was attenuated, suggesting that underlying tumor biology may partially account for the apparent dose–response relationship.

The difference between unadjusted and adjusted findings is clinically and biologically informative. The unadjusted results suggest a potential dose-dependent effect of bevacizumab on vascular permeability and edema reduction, which is consistent with its mechanism of action as a VEGF inhibitor[9]. However, the attenuation of this effect after adjustment indicates that tumor type is a critical confounder, likely reflecting inherent differences in vascular characteristics, blood–brain barrier disruption, and baseline edema burden between primary CNS tumors and metastatic lesions[33–35]. These findings highlight the importance of distinguishing between true pharmacologic dose effects and differences arising from underlying disease biology.

An additional consideration in interpreting these findings is prior bevacizumab exposure. Although prior bevacizumab use was numerically more common in the 10 mg/kg cohort than in the 7.5 mg/kg cohort (17.6% vs 5.7%), this difference was not statistically significant. Prior bevacizumab exposure occurred in a minority of patients and included both tumor-directed therapy and treatment for recurrent radiation necrosis. Because prior anti-VEGF therapy may influence subsequent radiographic or clinical responses, some residual confounding remains possible. However, the substantially greater imbalance in tumor type between cohorts likely represents a more important source of confounding and may better explain the attenuation of treatment effects observed after adjustment.

Corticosteroid exposure may influence response to bevacizumab in patients with radiation necrosis. However, baseline corticosteroid use appeared generally similar between cohorts. Median dexamethasone dose at bevacizumab initiation was 12 mg/day (IQR 8–16) in the 7.5 mg/kg cohort and 10 mg/day (IQR 5–16) in the 10 mg/kg cohort ($p = 0.16$). Likewise, the median interval from dexamethasone initiation to bevacizumab initiation did not differ significantly between groups (7.0 vs 4.8 months, $p = 0.13$). These findings suggest that differences in corticosteroid management were unlikely to be the primary driver of the observed outcomes, although residual confounding related to cumulative corticosteroid exposure cannot be excluded.

Consistent with the edema findings, greater edema reduction in unadjusted analyses was observed in the 7.5 mg/kg cohort, which also demonstrated higher clinical response rates. This alignment may reflect shared underlying factors influencing both radiographic and symptomatic improvement rather than a direct dose effect. Clinical outcomes may be influenced by treatment tolerability, cumulative exposure, prior bevacizumab use, and differences in tumor type and symptom etiology. Additionally,

milder toxicities, such as fatigue or hypertension, which were not systematically captured, may have disproportionately impacted patients receiving higher doses, thereby attenuating perceived clinical benefit. The persistence of tumor-type imbalance further complicates interpretation of clinical outcomes, as patients with brain metastases may derive more rapid symptomatic benefit from reductions in vasogenic edema compared with those with primary CNS tumors.

The observed tumor-type imbalance between dosing cohorts likely reflects real-world prescribing patterns. Patients with primary CNS tumors were more likely to receive higher-dose bevacizumab, consistent with historical dosing practices established in glioblastoma, where 10 mg/kg every 2 weeks has been widely utilized[29, 30]. This practice pattern appears to persist when bevacizumab is used for radiation necrosis, despite mechanistic differences between tumor progression and treatment-related injury. As demonstrated in this analysis, such prescribing patterns introduce confounding that can meaningfully influence observed treatment effects if not accounted for.

The safety profile observed in this study was consistent with the known toxicities of bevacizumab. Serious adverse events were uncommon and included hemorrhagic, thromboembolic, gastrointestinal, and hypertensive complications. Given the retrospective design and low event frequency, meaningful comparisons between dose groups were limited. Importantly, no new safety signals emerged, suggesting that both 7.5 mg/kg and 10 mg/kg dosing strategies remain generally well tolerated when used for radiation necrosis.

Taken together, these results support a more nuanced, goal-directed approach to bevacizumab dosing in radiation necrosis. While lower doses may be associated with greater edema reduction in unadjusted analyses, the lack of a robust association after adjustment suggests that dose alone may not be the primary driver of response. These findings suggest that bevacizumab dosing in radiation necrosis should be individualized based on tumor biology rather than extrapolated from glioblastoma dosing paradigms. Prospective studies incorporating tumor stratification and edema-focused endpoints are needed to refine optimal, indication-specific dosing strategies.

The strengths of this study include its relatively large sample size and blinded radiographic assessment. However, several limitations should be acknowledged. This study is limited by its retrospective design, potential selection bias, and the absence of randomization in bevacizumab dosing. Radiation necrosis was diagnosed using clinical and radiographic criteria rather than routine histopathologic confirmation, and some patients may have had mixed treatment effect and tumor progression. Nevertheless, this reflects contemporary clinical practice, as histopathologic confirmation is not routinely pursued in many patients due to procedural risk, lesion location, patient comorbidities, and the availability of advanced imaging modalities that are commonly used to support diagnostic decision-making. Furthermore, detailed corticosteroid exposure, lesion volumetrics, and standardized neurocognitive assessments were not consistently available. Given the heterogeneous study population and limited power for subgroup analyses and rare adverse event detection, these findings should be considered hypothesis-generating and validated in prospective, tumor-stratified studies.

Conclusion

In conclusion, this retrospective analysis demonstrates that bevacizumab dosing is associated with differences in edema response in unadjusted analyses, but this relationship is attenuated after accounting for tumor type, while contrast enhancing disease response does not differ between dosing strategies. These findings suggest that underlying tumor biology plays a critical role in shaping observed treatment effects, and that apparent dose-response relationships may be confounded by differences in patient populations. Taken together 7.5 mg/kg dosing achieved similar radiographic outcomes and did not appear inferior after accounting for tumor type. Prospective, tumor-stratified studies incorporating edema-focused and patient-centered endpoints are needed to better define optimal dosing strategies in this heterogeneous population.

Declarations

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Author Contributions:

SES, ML and US conceptualized the idea and designed the research. SES, ML, MB, AN, JW, AV and NK performed data collection. SES, US, KC and CMH analyzed the data. SES, ML, JB, CMH, JT, SS, GH, JW, AV, NK, SC, BN, JC, JU, DL, SK, MR, SG and US played an important role in interpreting the results and writing the manuscript.

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Data availability: Individual patient level data will be made available upon request.

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Tables

Table 1: Demographic Characteristics

Bevacizumab dose				
	7.5 mg/kg (N=53)	10 mg/kg (N=51)	Total (N=104)	P-value
Age (years), Mean (SD)	61.0 (12.35)	57.6 (14.34)	59.3 (13.41)	0.204 ¹
Sex, n (%)				0.072 ²
Male	25 (47.2)	33 (64.7)	58 (55.8)	
Female	28 (52.8)	18 (35.3)	46 (44.2)	
Weight (kg), Mean (SD)	85.2 (23.15)	86.3 (21.53)	85.7 (22.27)	0.807 ¹
Race, n (%)				0.100 ³
Asian	3 (5.7)	0 (0.0)	3 (2.9)	
Black or African American	3 (5.7)	1 (2.0)	4 (3.8)	
White	45 (84.9)	50 (98.0)	95 (91.3)	
Unknown	2 (3.8)	0 (0.0)	2 (1.9)	
Baseline ECOG, n (%)				0.098 ³
0	9 (24.3)	5 (29.4)	14 (25.9)	
1	13 (35.1)	4 (23.5)	17 (31.5)	
2	12 (32.4)	2 (11.8)	14 (25.9)	
3	2 (5.4)	4 (23.5)	6 (11.1)	
4	1 (2.7)	2 (11.8)	3 (5.6)	
Missing	16	34	50	
Tumor type, n (%)				<.001 ³
Breast	8 (15.1)	0 (0.0)	8 (7.7)	
Lung	14 (26.4)	2 (3.9)	16 (15.4)	
Melanoma	4 (7.5)	2 (3.9)	6 (5.8)	
Brain	23 (43.4)	43 (84.3)	66 (63.5)	
Other	4 (7.5)	4 (7.8)	8 (7.7)	
¹ Equal variance two sample t-test; ² Chi-Square p-value; ³ Fisher Exact p-value;				

Table 2: Treatment Related Factors

	Bevacizumab Dose		
	7.5 mg/kg (N=53)	10 mg/kg (N=51)	P-value
Number of bevacizumab doses, Median (IQR)	4 (3, 4)	4 (3, 9)	0.011 ¹
Concomitant anticoagulation, n (%)	10 (18.9)	10 (19.6)	0.924 ²
Concomitant steroid use, n (%)	41 (77.4)	44 (86.3)	0.239 ²
Median dexamethasone dose at bevacizumab initiation, mg/day (IQR)	12 (8, 16)	10 (5, 16)	0.16 ¹
Time from dexamethasone initiation to bevacizumab initiation, months (IQR)	7.0 (2.3, 12.8)	4.8 (1.4, 8.1)	0.13 ¹
Concomitant systemic therapy, n (%)	24 (45.3)	19 (37.3)	0.406 ²
Prior bevacizumab therapy, n (%)	3 (5.7)	9 (17.6)	0.073 ²
Prior immunotherapy, n (%)	12 (22.6)	5 (9.8)	0.077 ²
Radiation Dose (Gy)			0.100 ¹
Missing	3	9	
Median (IQR)	45 (27, 60)	56 (35, 60)	
Radiation Type, n (%)			0.757 ³
Whole brain radiation	1 (1.9)	0 (0.0)	
Gamma knife	7 (13.2)	5 (9.8)	
SRS	15 (28.3)	13 (25.5)	
Other	30 (56.6)	33 (64.7)	
Time from radiation to bevacizumab (months)			0.118 ¹
Missing			
Median (IQR)	1	1	
	11.7 (7.1, 21.9)	9.0 (3.3, 17.0)	
¹ Wilcoxon rank sum p-value; ² Chi-Square p-value; ³ Fisher Exact p-value;			

Table 3: Efficacy and Safety

	Bevacizumab Dose			
	7.5 mg/kg (N=53)	10 mg/kg (N=51)	P-value	Tumor type- adjusted p-value
Edema response, n (%)			0.032 ¹	0.082 ³
Increase of edema	0 (0.0)	3 (6.8)		
Constant edema	7 (13.7)	10 (22.7)		
Slight decrease of edema	15 (29.4)	17 (38.6)		
Large decrease of edema	29 (56.9)	14 (31.8)		
Missing	2	7		
Contrast enhancing disease response, n (%)			0.431 ¹	0.779 ³
Complete response (CR)				
Partial response (PR)	1 (1.9)	3 (6.8)		
Stable disease (SD)	16 (30.8)	10 (22.7)		
Progression of disease	32 (61.5)	26 (59.1)		
Missing	3 (5.8)	5 (11.4)		
	1	7		
Clinical response, n (%)			0.013 ²	0.054 ⁴
Yes	30 (65.2)	14 (37.8)		
No	16 (34.8)	23 (62.2)		
Missing	7	14		
Adverse events⁶, n (%)	n=10	n=9	>0.999 ¹	-
Thromboembolic events	4 (40)	3 (33.3)		
Hemorrhage	3 (30)	2 (22.2)		
Gastrointestinal perforation	0 (0.0)	1 (11.1)		
Other	3 (30)	3 (33.3)		
Bevacizumab stopped due to adverse effects, n (%)	9 (17.0)	8 (15.7)	0.858 ²	-
Bevacizumab re-dosed due to radiation necrosis recurrence, n (%)	12 (22.6)	6 (11.8)	0.143 ²	-

¹Fisher Exact p-value; ²Chi-Square p-value; ³Cochran-Mantel-Haenszel p-value; ⁴Logistic regression parameter p-value; ⁵Edema response classified according to the following groups: (1) increase of edema, >105% of baseline; (2) constant edema, 75%-105% of baseline; (3) slight decrease of edema,

25%-75% of baseline; (4) large decrease of edema, <25% of baseline; ⁶Adverse event type is reported for the 19 patients with adverse event documented in the medical record.

Figures

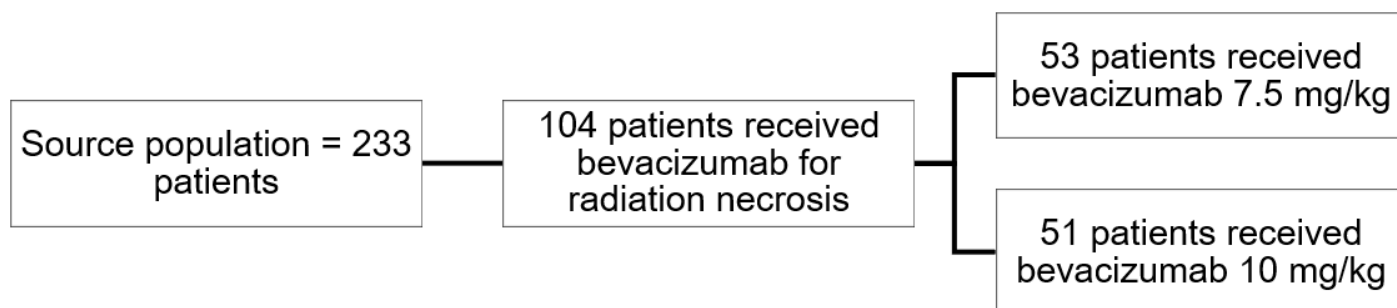


Figure 1

Study Population

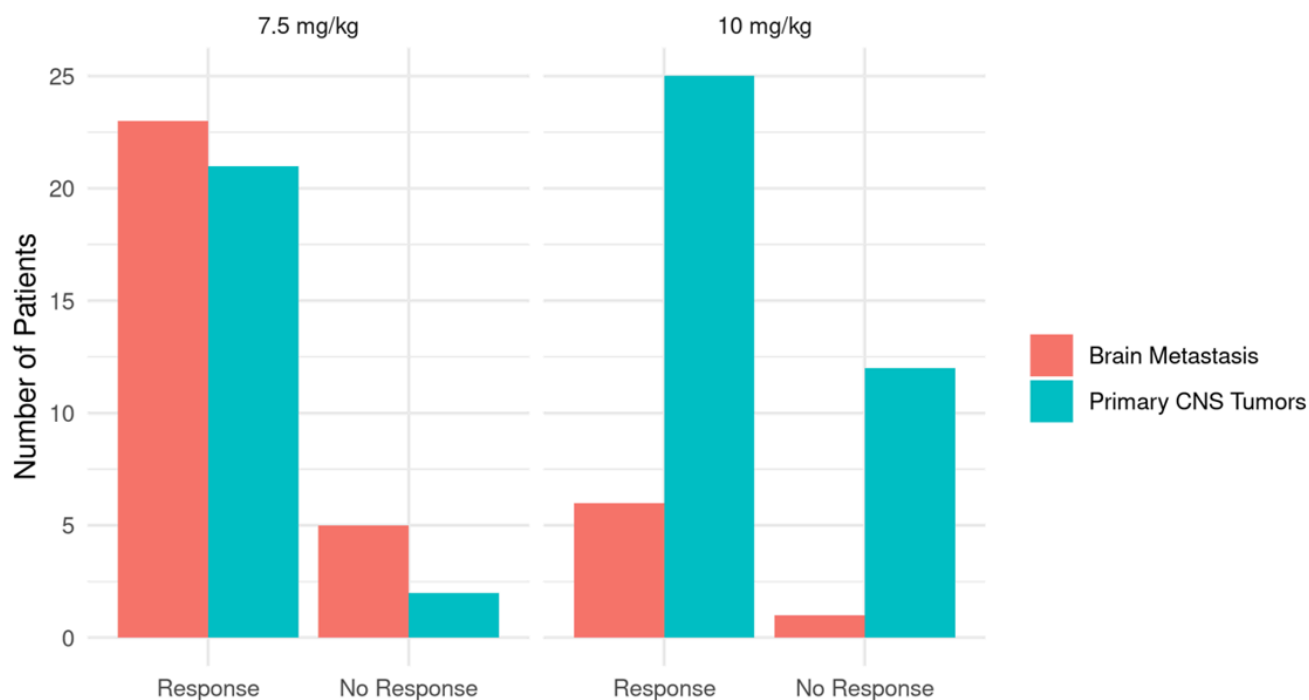


Figure 2

Counts of edema reduction (slight decrease [25% decrease from baseline] or better) stratified by bevacizumab dose and tumor type