The Impact of Social Determinants on Receipt of Adjuvant Radiation Nationally Following Atypical Meningioma Surgery

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Abstract

Purpose:

We aimed to identify socioeconomic gaps in the administration of adjuvant radiotherapy for patients with atypical meningioma and secondarily to determine differences in survival between patients receiving radiation and those not receiving radiation at 12 and 60 months.

Methods:

The National Cancer Database was queried for patients receiving atypical meningioma surgery between 2004 and 2019. Statistical analyses were performed to assess the association between receipt of adjuvant radiation and social determinants. Secondarily, KM curves were used to compare overall patient survival between those that received radiation and those that did not.

Results:

Adjuvant radiation was less likely to be administered to patients over 65 (95% CI =0.53- 22 0.77) and more likely to be administered to males (95% CI =1.07-1.38). Compared to the Southern USA, patients were more likely to receive radiotherapy in the Northeastern (95% CI 24 =1.40–2.05), Midwestern (95% CI =1.06-1.54), and Western parts of the USA (95% 25 CI =1.31-2.00). Patients residing furthest from their facility were less likely to receive radiation (95% CI =0.65-0.98). Insured patients were more likely to receive radiation (p = 0.048) than uninsured patients. On multivariate analysis, no differences were found between racial groups regarding adjuvant radiation. For patients unstratified, radiation was shown to improve survival at 12 and 60 months.

Conclusion:

Disparities exist in the administration of adjuvant radiotherapy for atypical meningioma. Patients over 65, women, those residing in the southern USA, those living further from their facilities and uninsured patients are less likely to receive radiation than their counterparts.

Introduction

Meningioma is a common intracranial tumor, accounting for at least one-third of all adult primary neoplasms of the CNS during the period from 2005-2019 in the United States[1-3]. The WHO classification system for CNS tumors, most recently updated in 2021, identifies meningiomas as a single tumor type arrayed along a spectrum of 15 subtypes (based on histological and molecular characteristics), all of which can belong to any of 3 grades (encapsulating behavior and prognosis)[4].

The incidence of atypical meningiomas (WHO grade 2, AMs) has increased in recent years[5]. This is due to changes in grading of meningiomas, most notably including “brain invasion” as a primary grading criterion[6]. AMs have recurrence rate of up to 48% in 10 years[7], so many institutions have advocated
for adjuvant radiotherapy (ART) after attempted gross total resection (GTR)\[8, 9\]. A growing body of evidence suggests that ART prolongs overall survival and reduces the likelihood of local recurrence \[10, 11\]. This has prompted organizations such as the EANO to currently recommend that AMs be treated with surgery followed by adjuvant RT unless the latter is otherwise contraindicated by relevant medical factors (Evidence Class 2, Recommendation Level B) \[14\].

Considering this evolving treatment paradigm, we sought to identify current socio-economic gaps in receipt of radiation in this patient population on a national scale in hopes of improving equitable access and AM patient outcomes.

Here we identify patient and institution-level factors influencing the rates of ART administration after resection of AMs. We then characterize the association of adjuvant RT with overall survival in various patient groups of interest.

**Methods**

**Study Population**

The National Cancer Database (NCDB) from the American College of Surgeons and the American Cancer Society was queried for patients with atypical meningioma localized to the cerebral, spinal, and NOS meninges (ICD code 9539/1) who underwent surgical intervention. Only primary tumors were included. If the patient had multiple primary tumors, only the first tumor was included. Patients were included regardless of whether or not they received radiation. For those patients receiving radiation, only phase I radiation data was included. Only radiation treatment limited to one or more sub-sites of the brain was included, patients receiving radiation to the whole brain and meninges were excluded. Patients with tumors occurring outside the meninges were excluded. Patients were also excluded if their tumors did not carry the histology of meningioma. Institutional Review Board approval was not required to perform this study as the database contains only de-identified records.

**Variables**

Age at diagnosis, race/ethnicity, sex, facility location, Great Circle Distance and primary payor were examined as independent variables in relation to receipt of radiation following surgery on atypical meningioma. Age at diagnosis was categorized into those 65 or younger and those over 65 at diagnosis. Race/Ethnicities were grouped into Hispanic White, Non-Hispanic White, Non-Hispanic Black, Asian/Pacific Islander, American Indian/Aleutian/Eskimo, and Other. Sex was categorized into male and female. Facility types were categorized as Community Cancer Program/Other, Comprehensive Community Cancer Program, Integrated Network Cancer Program Academic/Research Program, and Not Available. Facility locations were grouped into the Northeast, Midwest, West, South, Not Available. The Great Circle Distance was defined as the distance in miles between the patient’s residence and the hospital that reported that case and was grouped into 0 – 6.2, >6.2 – 15.2, >15.2 – 40.1, >40.1 – 2570.7, and Not Available. Primary Payor was categorized as Private, Medicaid, Medicare/Other
Government, and Not Insured/Unknown. Only the variables listed above, sourced from the NCDB database were used to obtain data.

**Statistical Analysis**

Descriptive statistics were performed for all variables to establish the quantity of people from each group and the percent from each group who underwent radiation therapy as opposed to not (Table 1). Next, a univariate association was performed using a $\chi^2$ test to determine the association of each covariate with the receipt or radiation or lack thereof. Univariate logistic regression was then used to determine the statistical significance of the trends. Finally, a backward elimination model was used to generate a multivariate logistic regression to examine the relationship of each of the variables with the receipt of radiation therapy. Adjustments were made for facility type, facility location, primary site of tumor, age at diagnosis, sex, race, primary payor, median income by quartiles, high school education, Great Circle Distance, Charlson-Deyo score, year of diagnosis because these factors had been found to be statistically significant in the univariate analysis. All analyses were performed using SAS 9.4 (SAS Institute, Inc) and SAS macros developed by the Biostatistics and Bioinformatics and Winship Research Informatics Shared Resources at Winship Cancer Institute in Atlanta, Georgia.

**Results**

**Participant Demographics**

8654 AM patients were identified within the NCDB based on the above criteria. As seen in Table 1 regarding the demographics of the population 14% received radiation, 37.9% were over the age of 65, 43.5% were male and 78.5% were white. Academic/research facilities saw 45.5% of patients. 20.8% of patients were treated in the Northeast, 28.5% in the South, 24.8% in the Midwest and 13.8% in the West with data unavailable for the remaining 11.8%. Patients were evenly distributed in terms of distance from their home to the facility that reported their case (22.4 – 22.6% for each category of known Great Circle Distances) with 52% patients residing in metro areas with populations of more than 1 million. Most patients had private insurance (45.0%), with 39.8% having Medicare/Other Government, 8.4% with Medicaid and 6.8% being uninsured/not known (Table 1).

**Table 1.** Descriptive Statistics for patients receiving surgery for atypical meningioma.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Level</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation</td>
<td>Yes</td>
<td>1202</td>
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<tr>
<td></td>
<td>No</td>
<td>7362</td>
</tr>
<tr>
<td>Facility Type</td>
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</tr>
<tr>
<td></td>
<td>Comprehensive Community Cancer Program</td>
<td>1937</td>
</tr>
<tr>
<td></td>
<td>Academic/Research Program</td>
<td>3893</td>
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<tr>
<td></td>
<td>Integrated Network Cancer Program</td>
<td>1573</td>
</tr>
<tr>
<td></td>
<td>Not Available</td>
<td>1010</td>
</tr>
<tr>
<td>Facility Location</td>
<td>Northeast</td>
<td>1778</td>
</tr>
<tr>
<td></td>
<td>South</td>
<td>2475</td>
</tr>
<tr>
<td></td>
<td>Midwest</td>
<td>2122</td>
</tr>
<tr>
<td></td>
<td>West</td>
<td>1179</td>
</tr>
<tr>
<td></td>
<td>Not Available</td>
<td>1010</td>
</tr>
<tr>
<td>Age at Diagnosis</td>
<td>&gt;65</td>
<td>3247</td>
</tr>
<tr>
<td></td>
<td>&lt;=65</td>
<td>5317</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>3729</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>4835</td>
</tr>
<tr>
<td>Race</td>
<td>White</td>
<td>6723</td>
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<tr>
<td></td>
<td>Black</td>
<td>1196</td>
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<tr>
<td></td>
<td>Others/Unknown</td>
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<tr>
<td>Primary Payor</td>
<td>Not Insured/Unknown</td>
<td>579</td>
</tr>
<tr>
<td></td>
<td>Private</td>
<td>3854</td>
</tr>
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</table>
## Primary Outcome

In our population of 8654, 14% of patients received ART. Based only on variables that were found to be statistically significant on univariate analysis, multivariate analysis was performed to assess differences in the receipt of radiation following atypical meningioma surgery between groups (Table 2).

It was found that in comparison to patients 65 and younger, patients over 65 were less likely to receive radiation (OR = 0.64; 95% CI =0.53-0.77, p = <0.001), and compared to female patients, males were more
likely to receive radiation (OR = 1.21; 95% CI = 1.07 – 1.38, p = 0.002). Compared to the Southern United States, patients were more likely to receive radiation in the Northeastern (OR = 1.70; 95% CI = 1.40 – 2.05), Midwestern (OR = 1.28; 95% CI = 1.06 – 1.54), and Western parts of the United States (OR = 1.62; 95% CI = 1.31 – 2.00), type 3 p-value = 0.013. Compared to patients 6.2 miles or less from the facility that reported their case, patients 40.1 - 2570.7 miles away were less likely to receive radiation (OR = 0.80; 95% CI = 0.65 – 0.98). Compared to uninsured patients/patients with unknown insurance status, patients with any kind of insurance were more likely to receive radiation p = 0.048: Private (OR = 1.44; 95% CI = 1.08 – 1.94), Medicaid (OR = 1.54; 95% CI = 1.09 – 2.17), Medicare/Other Government insurance (OR = 1.56; 95% CI = 1.13 – 2.16). No statistical differences between racial groups in terms of radiation was found when non-Hispanic white was used as baseline (p = 0.160) in the multivariate analysis. However, it should be noted that the univariate regression demonstrated that compared to non-Hispanic white patients, non-Hispanic black patients were less likely to receive radiation (OR = 0.78; 95% CI = 0.64 - 0.94) and Asian/Pacific Islanders were more likely to receive radiation (OR = 1.36; 95% CI = 1.03 – 1.79) (Table 1).

Table 2: Multivariate Logistic Regression
<table>
<thead>
<tr>
<th>Covariate</th>
<th>Level</th>
<th>N</th>
<th>Odds Ratio (95% CI)</th>
<th>OR P-value</th>
<th>Type3 P-value</th>
</tr>
</thead>
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<tr>
<td>Age at Diagnosis</td>
<td>&gt;65</td>
<td>3247</td>
<td>0.64 (0.53-0.77)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
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<tr>
<td></td>
<td>&lt;=65</td>
<td>5317</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Race/Hispanic</td>
<td>Hispanic White</td>
<td>466</td>
<td>0.79 (0.58-1.07)</td>
<td>0.131</td>
<td>0.160</td>
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<tr>
<td></td>
<td>Non-Hispanic Black</td>
<td>1183</td>
<td>0.84 (0.68-1.03)</td>
<td>0.091</td>
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<tr>
<td></td>
<td>Hispanic Black</td>
<td>13</td>
<td>0.39 (0.05-3.10)</td>
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<td></td>
<td>Asian/Pacific Inslander</td>
<td>358</td>
<td>1.14 (0.85-1.51)</td>
<td>0.381</td>
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<tr>
<td></td>
<td>American Indian, Aleutian, or Eskimo</td>
<td>29</td>
<td>1.40 (0.56-3.49)</td>
<td>0.473</td>
<td></td>
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<tr>
<td></td>
<td>Other</td>
<td>258</td>
<td>0.72 (0.49-1.07)</td>
<td>0.104</td>
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<tr>
<td></td>
<td>Non-Hispanic White</td>
<td>6257</td>
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<td>-</td>
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<tr>
<td>Sex</td>
<td>Male</td>
<td>3729</td>
<td>1.21 (1.07-1.38)</td>
<td>0.002</td>
<td>0.002</td>
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<td></td>
<td>Female</td>
<td>4835</td>
<td>-</td>
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<tr>
<td>Facility Type</td>
<td>Community Cancer Program/Other</td>
<td>151</td>
<td>1.51 (0.98-2.31)</td>
<td>0.061</td>
<td>0.013</td>
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<tr>
<td></td>
<td>Comprehensive Community Cancer Program</td>
<td>1937</td>
<td>1.02 (0.85-1.21)</td>
<td>0.861</td>
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<tr>
<td></td>
<td>Integrated Network Cancer Program</td>
<td>1573</td>
<td>1.26 (1.07-1.50)</td>
<td>0.007</td>
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</tr>
<tr>
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<td>Academic/Research Program</td>
<td>3893</td>
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<td>-</td>
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</table>
### Radiation=Yes

<table>
<thead>
<tr>
<th>Covariate</th>
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<th>N</th>
<th>Odds Ratio (95% CI)</th>
<th>OR P-value</th>
<th>Type3 P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facility Location</td>
<td>Northeast</td>
<td>1778</td>
<td>1.70 (1.40-2.05)</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Midwest</td>
<td>2122</td>
<td>1.28 (1.06-1.54)</td>
<td>0.010</td>
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</tr>
<tr>
<td></td>
<td>West</td>
<td>1179</td>
<td>1.62 (1.31-2.00)</td>
<td>&lt;.001</td>
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<tr>
<td></td>
<td>South</td>
<td>2475</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Great Circle Distance</td>
<td>&gt;6.2, &lt;=15.2</td>
<td>1922</td>
<td>1.07 (0.89-1.29)</td>
<td>0.465</td>
<td>0.053</td>
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<td></td>
<td>&gt;15.2, &lt;=40.1</td>
<td>1925</td>
<td>0.89 (0.74-1.08)</td>
<td>0.247</td>
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<tr>
<td></td>
<td>&gt;40.1, &lt;=2570.7</td>
<td>1923</td>
<td>0.80 (0.65-0.98)</td>
<td>0.031</td>
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<tr>
<td></td>
<td>&gt;=0, &lt;=6.2</td>
<td>1934</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Primary Payor</td>
<td>Private</td>
<td>3854</td>
<td>1.44 (1.08-1.94)</td>
<td>0.015</td>
<td><strong>0.048</strong></td>
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<tr>
<td></td>
<td>Medicaid</td>
<td>720</td>
<td>1.54 (1.09-2.17)</td>
<td>0.015</td>
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<tr>
<td></td>
<td>Medicare/Other Government</td>
<td>3411</td>
<td>1.56 (1.13-2.16)</td>
<td>0.007</td>
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<td></td>
<td>Not Insured/Unknown</td>
<td>579</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

* Number of observations in the original data set = 8564. Number of observations used = 8564.

** Backward selection with an alpha level of removal of .05 was used. No variables were removed from the model.

**Secondary Outcome**

Overall patient survival, defined as months from date of surgery to death or last follow up, was analyzed. For all patients unstratified, those who received radiation had increased survival at 12 months (92.9 vs 97.9%) and at 60 months (78.6% vs 85.5%) compared to those who did not (Fig 1a). Stratified by sex, both men and women who received radiation had improved survival at both time points (Fig 1b). When stratified by age, patients 65 and under who received radiation had better overall survival than their age
mates who did not at 12 months (96.8% vs 98.7%), but not at 60 months. Interestingly, older patient patients (> 65) had longer survival times at both 12 months (96.2% vs 86.8%) and at 60 months (70.9% vs 62.3%) if they received radiation as opposed to those who did not (Fig 1c).

Patients in the Southern region of the United States (region of the US that demonstrated less chance of receiving radiation on multivariate analysis) who received radiation had improved survival compared to other patients in the same region who did not at 12 months (97.6% vs 91.7%), and at 60 months (82.1% vs 74.1%). This was also seen in all other regions of the US as well (97.9% vs 92.2% at 12 months and 84.9% vs 77.6% at 60 months) (Fig 1d). Most notably, stratified by insurance status, Medicaid patients who received radiation did not have improved survival compared to Medicaid patients who did not receive radiation at both time points. However, uninsured patients who received radiation had statistically significant improved survival compared to other uninsured patients who did not receive radiation at 12 months (100% vs 96.5%) and at 60 months (100% vs 87.2%) (Fig. 1e).

**Discussion**

Inequities in access to health care because of race, sex, age, insurance status, etc. have previously been described for a variety of neurosurgical and non-neurosurgical conditions, e.g., adjuvant chemoradiotherapy in glioblastoma[12] and adjuvant chemotherapy in breast cancer[13]. This report is, to our knowledge, the first investigation of disparities in access to and delivery of ART for WHO grade 2 AMs.

**Key Results**

**Impact of patient characteristics on the primary outcome**

Using non-Hispanic whites as a reference group, we found no significant association between race (including Black and Hispanic and the administration of ART) in our multivariate analysis, despite an association between black race and decreased rates of ART and Asian/Pacific Islander race and increased rates of ART in the univariate analysis. This finding possibly highlights that differences in ART may not be inherent to race itself, but due to the confounding socioeconomic factors that differ between racial groups. These differences are in line with previous studies in the US that have revealed racial minorities may suffer from worse outcomes compared to white Americans in multiple metrics, including rates of neurosurgical intervention and mortality, many of which may stem from poor initial access to care[14, 15].

We found that both female sex and age >65 had a significant negative association with the likelihood of receiving ART. Taken together, these two findings suggest a major potential area for improvement in patient outcomes given that meningiomas are more common in women than in men and have a predilection for diagnosis in an older population, with an over 2.5-to-1 female-to-male sex ratio and median age of 66 for diagnoses occurring between 2015-2019 in the US[3]. Given the continual
improvement in delivery of RT to limit long-term side effects[16, 17], administration of RT in an older population is feasible as patient overall survival continues to improve as well[18].

Lastly, our study suggests that insurance status does affect receipt of RT as no insurance or unknown insurance (NI-UI) demonstrated a significant negative association of receiving ART. Relative to the NI-UI group, all other groups had roughly equal level of access to radiotherapy. Of note, those with Medicaid/Medicare were slightly more likely than even those with private insurance, a finding which underscores the importance of expanding population-wide healthcare access to at least some form of insurance. Previous reports in the general medical literature have echoed such a conclusion[19].

**Impact of facility characteristics on primary outcome**

Using a Great Circle Distance (GCD) of < 6.2 miles from the facility as a reference point, we found a significant negative association between patient-facility distance > 40.1 miles and administration of ART. This suggests that those living in underserved areas may suffer deficits in their ability to access care for AMs. This finding corroborates recent findings from the NCI/NIH[20] and for which various solutions have been suggested including creating relationships between care providers and local community members[21]. While lack of access in rural areas is not surprising, we also found that patients in all other regions (Northeast, Midwest, and West) were significantly more likely to receive ART than patients in the South. There could be myriad reasons for this finding, including lower levels of higher education attainment and decreased access to primary care[22, 23]. Future studies should aim to investigate potential causes for these differences in region and distance from facilities, including the implications of living in more rural areas on access to neurosurgical care for atypical meningioma. Given that in 2020, six of the top ten states in the NCDB database were in age-adjusted cancer mortality were in the “South”[24], access to appropriate therapy once a diagnosis has been made is likely one part of the region’s lagging approach to cancer care.

**Secondary outcomes**

Our study suggests that use of ART in AMs is associated with increased time to recurrence and overall survival, which fits with most reports in the literature[8, 25]. RT may have side effects, including impairments in long-term neurological functioning, radiation necrosis, and a very small increased risk of other cancers, but our report of improved OS across all subgroups in our study at a national level adds further evidence to the more judicious use of ART.

**Limitations**

The major limitation of our study, inherent to the NCDB, is our dataset’s use of meningioma classification schemes that do not take into account the most recent WHO 2021 updates for meningioma classification. As a result, what is classified in our database as an atypical meningioma may now be
classified differently. The length of the timespan also makes it such that our work does not consider changes in management paradigms over time. Another limitation of our data is that only a small proportion of the patients in our database (14%) underwent radiation therapy. While we attempted to account for confounding variables, we recognize the potential for missed factors that may have contributed to decisions to radiate or not to radiate. Lastly, we realize there has been a gradual progression in care of meningiomas amongst providers over the 2-decade time span of the data collection, particularly at academic centers as new data regarding the use of radiation has been published, the adoption of which would be difficult to adequately characterize from this data set. This may be particularly true of areas that have only recently adopted the use of adjuvant RT which may not be adequately represented in the collected data available to our group.

Generalizability

Given that this study drew on a national database of AM cases over a time span of almost two decades, the results are generalizable to trends in care in the US.

Conclusion

Disparities in access to care will always be undesirable, particularly in purported high income and resource countries like the United States where therapies should be available and effective for prevalent and treatable conditions like meningiomas. We demonstrate gaps in the current state of care and radiation administration for atypical meningiomas, particularly for women, the elderly, the uninsured, those in rural areas, and those in the South.

Declarations

Funding

This study did not receive any funding or financial support.

Competing Interests: The authors have relevant financial or non-financial interests to disclose.

Author Contributions

All authors contributed to study conception and design. Data analysis was performed by Xiaojie Zhi. The first draft of the manuscript was written by Zvipo Chisango and Obiadada Ugochukwu and all authors have commented on previous versions of the manuscript. All authors have read and approved the final manuscript.

Data Availability

The data analyzed for this study is from the National Cancer Database and is available upon request from the American College of Surgeons.
Ethics Approval and Consent to Participate

This study analyzed anonymized, aggregate data and did not require IRB approval or consent to participate.

Consent to Publish

The authors affirm that no individual person's data is included in this manuscript in any form.

References


**Figures**
Figure 1

Kaplan-Meier Curves demonstrating the relationship between receipt of adjuvant radiation therapy and overall survival to 5 years following atypical meningioma surgery. *(Fig 1a).* For all patients unstratified, radiation improved survival at both time points. *(Fig 1b).* Stratified by sex, patients receiving radiation showed improved survival at 12 months and at 60 months. *(Fig 1c).* Patients 65 years old and over had improved survival at 12 months and 60 months following radiation and those under 65 had improved
survival at 12 months but not at 60 months. (Fig 1d). Stratified by facility location, no statistically significant differences were noted between patients who received radiation and those who did not at either 12 or 60 months. (Fig 1e). Stratified by insurance status, Medicaid patients did not benefit from adjuvant radiation, but uninsured patients did.