Pineocytomas are uncommon tumors that are believed to arise from parenchymal cells of the pineal gland, and account for 0.4–1.0% of all intracranial tumors. Given the relative rarity of these tumors and the challenges associated with successful surgery in this region, the current literature is limited to case reports and small series. Studies that examine surgical or radiotherapeutic outcomes often combine pineocytomas with other pineal region tumors of different histologies. These limitations make it difficult to discern the best course of action for treating these tumors based on the experiences of any single center or practitioners. In small patient series, reported rates of tumor control are variable. Thus, no consensus currently exists regarding the best treatment goals for patients with pineocytoma. Management approaches described in the literature include surgery with a goal of GTR, STR alone, biopsy procedure followed by radiosurgery, and chemotherapy. Gross-total resection is limited by the difficult location of these tumors and the potential of serious neurological and endocrinological complications. Given the lack of detailed knowledge of the potential benefit of aggressive resection, the risk-benefit ratio of these efforts is unclear.
To assess the value of aggressive resection, we systematically reviewed the published literature to evaluate the effect of the extent of resection and radiotherapy on tumor control in patients with pineocytoma. Our objective was to answer 3 questions: 1) Does surgical debulking improve tumor control more than a biopsy procedure and radiation therapy? 2) Does GTR improve tumor control compared with STR in addition to radiation therapy? 3) Does the addition of radiation to STR improve tumor control?

Methods

Article Selection

A comprehensive systematic review of the literature was conducted on tumor control and PFS after treatment of pineocytoma, pooling data from the existing English-language literature. Articles were identified during a PubMed search using Boolean searches with key words “pineocytoma” alone and in combination with the key words “treatment,” “mortality,” and “morbidity.” After reviewing these articles, a thorough review of all referenced sources was also performed.

All references that contained disaggregated data specifically addressing tumor control or reporting progression with adequate follow-up data in patients who had undergone surgery (biopsy procedure or resection) of histologically confirmed pineocytoma were included in our analysis. Any paper that did not provide some follow-up data on these patients with follow-up imaging was excluded, as these studies would not facilitate Kaplan-Meier analysis.

Data Extraction

The median largest tumor dimension and median tumor volume were not reportable or analyzable in our analysis because studies did not consistently report either value. Data were first stratified into 3 groups based on extent of resection data presented in each reference; these 3 groups were biopsy, STR, and GTR. Data were then stratified based on treatment with or without radiation therapy.

Tumor control data were included if adequate radiographic follow-up data were presented and stated in the study, demonstrating evidence of recurrence or continued tumor control. Time to progression was defined as time from diagnosis to radiographic evidence of progression. Progression-free survival was calculated at the 1- and 5-year time points. Studies that did not present patient data in a way that these variables could reliably be determined were excluded from further analysis.

Statistical Analysis

The Pearson chi-square test was used to analyze for differences in preoperative categorical factors, including sex and hydrocephalus. The Fisher exact test was used if there were < 5 values per cell. Analysis of variance was used to evaluate statistical differences in preoperative continuous factors, including age. Kaplan-Meier estimates were used to generate time-to-progression curves. Differences in time to progression were analyzed by the log-rank test. Cox proportional hazard modeling was used to assess for differences in PFS adjusting for differences in preoperative variables. Analyses were carried out using the statistical software package SPSS version 16.0 (SPPS Inc.).

Results

Clinical Characteristics of Included Patients

The literature search yielded a total of 64 references meeting our inclusion criteria, containing disaggregated data on 166 patients with pineocytoma (Table 1). There was a slight male preponderance (52%), and the median age was 30 years. The most common presenting symptom was headache (75%) followed by nausea (35%) and visual changes (25%). The majority of patients (65%) had evidence of hydrocephalus on presentation. Most tumors were of conventional histology (73%). Of the 146 patients with data describing extent of resection, 30 (21%) underwent a biopsy procedure, 55 (38%) underwent STR, and 61 (42%) underwent GTR. Twenty-eight percent of patients underwent postprocedure treatment with either fractionated radiotherapy or stereotactic radiosurgery. Follow-up ranged from 3 to 165 months in these studies.

<table>
<thead>
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<th>Variable (no. of cases)</th>
<th>Value (%)</th>
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<tr>
<td>sex (166)</td>
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<tr>
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</tbody>
</table>
Tumor control after pineocytoma surgery

Does Surgical Debulking Improve Tumor Control Compared with Biopsy and Radiation?

To determine if resection improved tumor control, we compared rates of progression in patients who underwent biopsy (with or without radiation therapy) with those who underwent resection (GTR or STR, with or without radiation therapy). There were no statistically significant differences between the 2 groups regarding sex (p = 0.8, chi-square test) or age (p = 0.06, ANOVA). Preoperative hydrocephalus was noted more frequently in patients undergoing resection than in patients undergoing biopsy alone (71 vs 50%, respectively; p < 0.05, chi-square test). Resection reduced the overall reported rate of progression compared with biopsy with or without radiation therapy (6.3 vs 17.8%, respectively; p < 0.05, chi-square test). The 1- and 5-year PFS rates for the resection group compared with the biopsy group were 97 and 90% (1 year), and 89 and 75% (5 years), respectively, which represented a statistically significant improvement using Kaplan-Meier analysis (p < 0.05, log-rank test; Fig. 1).

Does GTR Improve Tumor Control Compared with STR in Addition to Radiation Therapy?

To determine if subtotal surgical tumor debulking followed by adjuvant radiation therapy provided similar tumor control as GTR, rates of treatment failure were compared between patients who underwent GTR without radiation therapy versus those who underwent STR with subsequent radiation. Forty-nine patients underwent GTR and 21 underwent STR followed by radiation therapy. There were no statistically significant differences between the groups regarding sex (p = 0.4, chi-square test), age (p = 0.9, ANOVA), or presence of hydrocephalus (p = 0.08, Fisher exact test). No tumor recurrences were reported in those patients who underwent GTR, which represented a significant improvement compared with patients receiving STR as well as radiation (0 vs 9.5%, respectively; p < 0.05, chi-square test). The 1- and 5-year PFS rates for the GTR group versus the group undergoing STR combined with radiation therapy were 100 and 94% (1 year), and 100 and 84% (5 years), respectively, which represented a statistically significant improvement using Kaplan-Meier analysis (p < 0.05, log-rank test; Fig. 2).

Does the Addition of Radiation to STR Improve Tumor Control?

In an analysis limited to published data on patients who received STR, we determined the effect of postoperative adjuvant radiation therapy on tumor control. Of the 34 patients reported to undergo STR, 21 received postoperative radiotherapy, whereas 13 did not. There were no significant differences in sex (p = 0.2, Fisher exact test), age (p = 0.8, ANOVA), or preoperative rates of hydrocephalus between the 2 groups (p = 0.6, Fisher exact test). Subtotal resection alone was associated with a similar rate of recurrence compared with treatment with STR followed by adjuvant radiotherapy (7.7 vs 11%, respectively; p = 0.86, chi-square test). The 1- and 5-year PFS rates for the STR group versus the STR and radiotherapy group were 100 and 94% (1 year), and 100 and 81% (5 years), respectively, which was not a significantly significant difference using Kaplan-Meier analysis (p = 0.83, log-rank test; Fig. 3).

Discussion

Despite the growing literature on this uncommon lesion, there is no current consensus on how to best manage these lesions, or the expected outcomes following surgery and/or radiotherapy, with published tumor control rates ranging from 67 to 100% depending on the therapeutic strategy used. Due to the rarity of these tumors, it has been difficult to provide accurate information regarding rates of occurrence. In this study, we systematically reviewed the published pineocytoma literature to attempt to better understand the expected outcomes after surgery for

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Fig. 1. Graph showing a statistically significant difference (p < 0.05) in tumor control rates over time between patients treated using resection compared with those treated using a biopsy procedure and radiation therapy (XRT).

Fig. 2. Graph showing a statistically significant difference (p < 0.05) in tumor control rates over time between patients treated using GTR compared with those treated using STR and postoperative radiation therapy.
pineocytoma with or without postoperative radiation therapy. Our analysis suggests that aggressive resection with the goal of GTR is the best treatment for patients with pineocytomas, which based on the limited existing literature provides tumor control rates suggesting that GTR is curative. A comparative survival analysis suggested that STR with adjuvant postoperative radiation is not able to replace GTR, as tumor control rates are clearly better with more aggressive surgery.

Further analysis in this study suggested that postoperative adjuvant radiotherapy after STR does not significantly add to tumor control rates compared with STR alone. Together with the inability of STR with radiotherapy to replace GTR, these data suggest that pineocytoma is a relative radioresistant lesion, and in the absence of better evidence suggesting radiotherapy is beneficial for this lesion, the data suggest that there is a minimal role for conventional fractionated radiation treatment either as the sole or adjuvant treatment for pineocytoma.

Although these findings represent a helpful summary of the published literature on this topic, an analysis of published data are only as good as its composite studies and may reflect source study biases. It is impossible for us to control for the quality of the data reported in the literature, and an overly stringent definition of “tumor recurrence” in some studies may overestimate rates of tumor control. Furthermore, subjectively defined variables, such as histological grade, extent of resection, and the adequacy of radiation therapy likely vary between studies, and we cannot independently confirm the validity of these definitions in other groups’ publications. Furthermore, our use of Kaplan-Meier analysis largely precludes the use of formal meta-analysis, including the calculation of a Q-statistic that allows the determination of how heterogeneous the data are. The inability to study these using meta-analytic methods prevents us from addressing this limitation in a statistically meaningful way. Finally, due to the diverse range of data presentation, the number of variables able to be studied and controlled for is limited. Variables that might be of interest that are inconsistently presented across studies cannot be reviewed.

**Conclusions**

In this paper, we report the results of a summary of the published literature on tumor control rates of pineocytomas after treatment with various modalities. Given the relatively rarity of this tumor, this study aims to accurately describe outcome characteristics using a data set that would be difficult to accumulate at a single center treating this tumor. Our analysis suggests that obtaining GTR is the foundation of treatment of these tumors and suggests that the role of radiation-based therapy for pineocytoma is limited.

**Disclosure**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**Author contributions to the study and manuscript preparation** include the following. Conception and design: AT Parsa, AJ Clark, ME Ivan, ME Sughrue, D Aranda. Acquisition of data: ME Sughrue, D Aranda, AJ Kane. Analysis and interpretation of data: AT Parsa, AJ Clark, ME Sughrue, I Yang, SJ Han, AJ Kane. Drafting the article: ME Sughrue, I Yang. Critically revising the article: AT Parsa, AJ Clark, ME Ivan, ME Sughrue, I Yang, SJ Han, AJ Kane. Reviewed final version of the manuscript and approved it for submission: AT Parsa, AJ Clark, ME Ivan, ME Sughrue, I Yang, D Aranda, SJ Han, AJ Kane. Statistical analysis: SJ Han. Study supervision: AT Parsa.

**References**


![Graph showing a nonstatistically significant difference (p = NS) in tumor control rates over time between patients treated using STR alone and those treated using STR and postoperative radiation therapy.](image-url)
Tumor control after pineocytoma surgery


