

# Neurocytomas: Long-term experience of a single institution

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There is a lack of studies reporting on outcomes of control and treatment toxicities for neurocytomas. A 25-year retrospective review of a tertiary center's experience with neurocytomas was completed to report on these outcomes. All cerebral neurocytoma cases (19 patients; median age, 31 years; range, 18–62 years; 18 intraventricular and 1 extraventricular) treated between 1984 and 2009 were analyzed, including central pathology and radiology reviews. Median follow-up was 104.5 months (range, 0.75–261.7 months). Primary treatment was surgery alone ( $n = 18$  patients), followed by surgery and adjuvant radiotherapy ( $n = 1$ ). The crude local control rate after surgery was 68% for all cases (cerebral neurocytomas) and 74% for central neurocytomas. Salvage therapies included further surgery ( $n = 4$ ), radiation ( $n = 3$ ), and chemotherapy ( $n = 1$ ). Ten-year Kaplan-Meier overall and relapse-free survival rates were 82% and 62% and 81% and 57%, respectively, for all cases and for central neurocytomas only. The median overall survival and relapse-free survival were 104.5 and 79.3 months, respectively, for all cases and for central neurocytomas. Ten patients had grade 3/4 toxicity, and 1 patient had a grade 5 perioperative hemorrhage that resulted in death 23 days after surgery. Late grade 3/4 toxicities occurred in 9 patients. Three patients had permanent grade 2 motor or cognitive deficits. We provide the first report outlining toxicities and survival outcomes in a series of 19 patients. Our experience suggests that initial surgery provides durable local control rates in two-thirds of patients, with low risk for significant permanent deficits. Salvage therapy with surgery and/or radiation provides durable local control in tumors that recur after surgery.

**Keywords:** atypical neurocytoma, central neurocytomas, cerebral neurocytomas, extraventricular neurocytoma, management, rare tumors, toxicities.

Neurocytomas are rare World Health Organization (WHO) grade II neuronal tumors, which were first identified as histologically distinct entities in 1982.<sup>1</sup> They likely have an incidence of less than 1% given that a range of 0.1%–0.5% has been reported.<sup>2–6</sup> These tumors occur most commonly within the ventricles, with a generally favorable prognosis as a result of indolent growth,<sup>1</sup> with no documented cases of malignant transformation.

Neurocytomas can occur outside of the ventricle, and such occurrences are now classified by WHO as extraventricular neurocytomas (EVNs) given differences in their location and wider spectrum in their morphologic appearance compared with intraventricular neurocytomas.<sup>7</sup>

Extraventricular locations such as the occipital lobe, parietal lobe, temporal lobe, frontal lobe, hypothalamus, cerebellum, pons, spinal cord, cauda equina, and retina have been reported.<sup>8</sup> Cerebral neurocytoma is also part of the nomenclature most often used to refer collectively to central neurocytomas and EVNs and is less commonly interchangeable as a term for EVN alone.<sup>1,2</sup>

Management of neurocytomas has been guided by retrospective case reports, institutional case series, and meta-analyses of institutional experiences.<sup>9,10</sup> Surgery is the primary modality of initial intervention<sup>11</sup>; with watchful waiting (surveillance) not documented as a common primary option. Despite the indolent nature of these tumors, most patients are symptomatic at presentation, with increased intracranial pressure due to mass effect or hydrocephalus, and thus require intervention rather than surveillance. The optimal utilization/timing of radiation in these tumors remains unclear.<sup>11</sup> This is a crucial question given that the indolence of these tumors results in prolonged survivorships in a

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younger patient population in their productive years. The potential late sequelae of radiation are well documented—of particular concern for young patient cohorts are possible deleterious impacts on the neurocognitive and endocrine systems and risk for second malignancies, issues common to other low-grade primary neoplasms.<sup>12</sup>

We report our 25-year experience in managing neurocytoma, including patterns of treatment and toxicities experienced by our patients compared with the published literature. Chromosomal changes have been previously noted in these tumors,<sup>13</sup> but the frequency and prognostic importance remain undetermined. We hypothesized that 1p and 19q loss of heterozygosity may correlate with patterns of outcome.

## Materials and Methods

After research ethics board approval, records of all sequential patients with a diagnosis of neurocytoma treated at the London Health Sciences Centres in London, Canada, between January 1, 1984, and January 1, 2008, were reviewed. Adults (age  $\geq 18$  years) with a pathological or serial radiographic confirmation of cerebral neurocytomas were included. Over this period, the WHO classification schemes for CNS tumors were used. There were 3 cases that had external review of their diagnoses at the time of diagnosis. Central pathology and radiology reviews were performed. For tumors with sufficient tissue, analysis by fluorescence in situ hybridization (FISH) was completed for 1p and 19q loss of heterozygosity (LOH).

Data abstracted from each patient's medical record included: sex; date of first symptoms; date of first CT or MRI scan that showed tumor; symptoms at presentation; and duration, date, and age at tissue diagnosis; location of presentation; tumor location; presence of calcification or enhancement on the preoperative scan; tumor size; extent of tumor resection based on imaging or surgical record (gross-total resection [GTR] or subtotal resection [STR]); KPS at presentation; pathological details, including features associated with atypical neurocytoma<sup>14</sup>; timing, number, type, and intent of surgery; timing of radiotherapy; radiation dose and technique; toxicity of treatments; date of tumor progression; pathology at progression; treatment at progression; and last known status.

Radiotherapy was considered adjuvant therapy if it was given immediately or within 4 months after initial surgery without evidence of progression and was considered salvage therapy if the patient was initially observed and treated for clinical or radiographic progression postsurgery. The date of progression was confirmed retrospectively based on radiology review as radiographic worsening of CT or MRI scans, or described as worse by the reporting neuro-radiologist, or based on symptomatic deterioration consistent with tumor progression. The survival, site, and time of first recurrence and documented grade higher than III acute and late ( $>3$  months) toxicities were collected as end

points. Toxicity was scored retrospectively using the Common Toxicity Criteria for Adverse Events version 3.0.<sup>15</sup> Local control was defined as the absence of any tumor regrowth or progression on imaging and excluded the patient who died in the perioperative period. Survival was calculated from date of diagnosis, and local control was calculated from date of first surgery. The Kaplan-Meier method was used to estimate cause-specific, relapse-free, and overall survival for both cerebral neurocytomas (central + extraventricular) and central neurocytomas alone (exclusion of the extraventricular case).

## Results

Twenty neurocytoma patients were identified from our initial review. One patient presumed to have neurocytoma based on radiographic imaging and without histological diagnosis was excluded from this analysis. This 74-year-old asymptomatic patient was found to have an incidental 3.5-cm enhancing, calcified tumor in the right lateral ventricle on CT. He was followed with serial imaging every 6 months until his time of death from intercurrent disease 5 years later.

The remaining 19 patients all had tissue confirmation and formed the basis of this report. Images were available for central radiology review in 9 cases, and tissue was available for central pathology review in 12 cases. The median follow-up was 104.5 months (range, 0.75–261.7 months). There were 9 male and 10 female patients, the median age was 31 years (range, 18–62 years), and the median KPS was 90 (range, 60–100). Headache (50%) and papilledema (55%) were the most common presenting symptoms (others included cognitive changes, parathesias, tinnitus, seizures, weakness, disequilibrium, visual changes, and nausea/vomiting) and signs (others included memory, papilledema, visual deficits, ataxia, and paresis) with a median duration of symptoms prior to diagnosis of 6.7 months (range, 2–36 months). Seizures were uncommon, with only 3 (15%) patients affected.

In 18 of the patients, the neurocytomas were central (within the ventricles), and in 1 patient the tumor was extraventricular (temporal lobe). The neurocytomas occurred most commonly in the lateral ventricles with involvement of the third ventricle in 7 of 18 patients. The median tumor size was 4.2 cm (range, 1.5–8.6 cm) with 95% of the tumors enhanced, 56% calcified, and 45% cystic.

There was no discordance between the central pathology reviews of the 12 cases available for central review compared with initial pathology results. All (100%) of the tumors were positive for synaptophysin and expression of glial fibrillary acidic protein (GFAP). All cases showed GFAP expression and were interpreted as reactive except for 1 case with small foci of tumor cells that showed GFAP expression. Presence of 1 or more high-risk features was used as an atypical classification in order to correlate to the risk of recurrence. Seven patients (37%) had at least 1 atypical feature: 2 (10%) had necrosis or mitosis  $\geq 3/10$  high-power fields

**Table 1.** Summary of the 6 patients with progression according to primary treatment received, time to progression, type of salvage, time to salvage treatment, and last known survival

	Tumor Profile	Primary Treatment	Time to first Progression (mo)	Salvage Treatment and Time to Salvage (mo)	Last Known Status
1	Atypical	STR	27.1	1. 2nd STR:1 2. Chemo:11 3. GTR : 1	Alive, no disease
2	Atypical	STR	10.1	1. RT: 18	Alive, stable disease
3	Typical	STR	188	1. RT: 45	Alive, stable disease
4	Atypical	STR + RT	97.4	1. GTR:1.5	Alive, no disease
5	Typical	STR	4.1	1. No salvage	Died with disease
6	Atypical	GTR	89.8	1. RT:33 2. GTR: 1	Alive, stable disease

Abbreviation: RT, radiotherapy; STR, subtotal resection; GTR; gross-total resection.

present, 3 (15%) had nuclear atypia or Ki-67 > 2%, and only 1 patient (5%) had endothelial proliferation. Atypical features were associated with a higher rate of recurrence (4/7 [68%] with atypical features had recurrence vs. 2/13 [15%] without after initial surgery). Two of the 3 cases of atypical neurocytomas that did not show relapse had GTR as initial treatment; the patient who underwent STR for a 6-cm atypical neurocytoma had no documented progression at 19 months of follow-up.

FISH analysis was successfully completed on 10 tumor samples from 8 patients (2 patients had sufficient tissue from initial and recurrent tumor tissue for analysis). None had combined 1p and 19q codeletions, and 3 had an isolated 1p deletion. One of the tumors with 1p deletions was in a patient with EVN, whose initial tissue had had no deletions; however, analysis of the subsequent recurrent disease showed the 1p deletion. This patient recurred 89 months after GTR and required salvage surgery, as the cystic component of the recurrent tumor was not responsive to radiation. The second patient with 1p deletion remained well 21 months after GTR. The third patient noted as having 1p deletion underwent STR but died of a primary unknown carcinoma (adenocarcinoma) shortly thereafter. Among the 5 patients with no deletions, 2 recurred after initial surgery, and both were subsequently successfully salvaged with further surgery or radiation.

All of the patients ( $n = 19$ ) received surgery as primary treatment (GTR: 10, STR: 9). The tumor size ranges for patients undergoing GTR and STR were 1.5 cm–6 cm and 5.5 cm–8.5 cm, respectively.

Surgical interventions were craniotomy, shunt, ventriculostomy, biopsy, extraventricular drain, stereotactic biopsy, and incision and drain, with a median number of 2 interventions (range, 1–7). Craniotomy for definitive resection was the most frequent intervention (68%). Four (14%) patients required a shunt, 2 (7%) had an extraventricular drain, and 3 (11%) had a third ventriculostomy. No adjuvant radiation was delivered post-GTR. In 1 patient with an STR, adjuvant radiotherapy was delivered (whole brain radiation of 54 Gy in 30 fractions), with complete resolution of the tumor in size and

enhancement. This patient recurred after 97.4 months, received GTR as salvage, and was well at last follow-up (145 months after initial surgery).

The crude local control rate after surgery was 68% for cerebral neurocytomas, with 6/19 patients (excluding 1 patient who died perioperatively) progressing after their initial surgery, and 74% for central neurocytomas. The crude local control rate was 44% after STR ± radiotherapy, with median time to progression of 27.1 months (range, 4.1–188 months) compared with 90% after GTR with time to recurrence of 89.8 months for the single case. The 10-year crude local control rate for atypical neurocytomas was 42% versus 83% for typical neurocytomas.

Of the 6 patients who relapsed, 5 had an initial STR, while one had a GTR (Table 1). The time to relapse had a wide range, at 4, 10, 27, 90, 97, and 188 months. In 4 patients (67%), the recurrences were asymptomatic, with an increase in the size of residual tumor (83%) or enhancement (50%) noted on imaging. Symptoms at recurrence included headaches, cognitive changes, and instability. There was KPS change in 2 patients (33%) as a result of their relapse. Salvage therapy was either or a combination of surgery, radiation, and chemotherapy in the 6 patients who demonstrated intracranial progression after initial surgery. Median time to salvage treatment from time of relapse was 12.5 months (range, 1–45 months). The most common salvage treatment was surgery ( $n = 4$ ), with 3 patients receiving salvage radiotherapy and 1 patient receiving salvage chemotherapy. The 3 patients who received salvage radiation were treated with focal radiation to 50–54 Gy/25–30. One patient who had atypical EVN with a large cystic component progressed during salvage radiation noted with imaging showing a stable solid component but growth within the cystic part. He required further salvage surgery a month later. The other patients have had local control of their tumors at 26 and 39 months after radiation. One patient received salvage chemotherapy with procarbazine/CCNU (lomustine)/vincristine for 3 cycles and was then switched to temozolomide. There was initial radiographic response and progression shortly after, at which time she had

GTR. At 109 months of follow-up, she was well with no disease.

At the time of last known follow-up, 12 patients were alive with no evidence of disease, and 5 were alive with stable disease. Two patients (11%) died during the follow-up period from causes not directly related to the tumor. For cerebral neurocytomas, the 10-year Kaplan-Meier overall, cause-specific, and relapse-free survival rates were 82%, 95%, and 62%, respectively, with median overall survival and relapse-free survival of 104.5 and 79.3 months, respectively. The Kaplan-Meier overall and relapse-free survival rates were 81% and 57%, respectively, for cases of central neurocytomas.

Acutely after surgery, 10 patients had grades 3/4 toxicity (grade 3 = 7, grade 4 = 3) and 1 patient had a grade 5 perioperative hemorrhage resulting in death 23 days after surgery. The most common acute toxicity was a motor deficit, and 1 patient required mobility aids as a result of this acute toxicity for 2 months but did not have permanent motor deficits. Three patients required prolonged admission for rehabilitation after surgery. Late toxicity was observed in 9 patients (grade 3 = 8; grade 4 = 1) after surgery alone. The most common late toxicity was a cognitive deficit. At the time of last follow-up, 3 (GTR = 2, STR = 1) patients had permanent motor ( $n = 1$ ) or cognitive deficits ( $n = 2$ ) affecting their activities of daily living, but none required any aids (grade 2), thus KPS was likely 70-80 compared with the cohort without late toxicity, where KPS was 90-200 at last follow-up. The patient with the motor deficit underwent a GTR and developed foot numbness. One of the documented permanent cognitive deficits occurred in a patient who underwent GTR but had also sustained head injury secondary to a motor vehicle accident. The EVN patient who had multiple resections was documented as having cognitive effects affecting schoolwork after his second surgery (STR). There were no documented grade 3 or 4 acute or late toxicity after adjuvant/salvage radiotherapy or chemotherapy. Two of 4 patients who underwent radiation had formal testing by the Mini-Mental State Examination (MMSE). While 1 of the 2 had short-term memory difficulties predating salvage radiation, the MMSE testing score was stable at 30/30 for both patients. There was no documented grade 3 or 4 acute or late toxicity after adjuvant/salvage radiotherapy or chemotherapy.

## Discussion

Almost 30 years after recognition as histologically distinct tumors, neurocytomas remain enigmatic. We reviewed survival, local control, and toxicities in 19 patients with neurocytomas treated at our tertiary care center. Our center serves a population of approximately 1 million and, considering 19 patients diagnosed in the last 25 years, results in an annual incidence of 0.8%, which is comparable to the published literature,<sup>5</sup> highlighting the rarity of the tumor. It is possible that we

may not have captured all neurocytomas treated at our institution; however, central review of low-grade glioma in our institution in other contexts did not yield such cases.<sup>16</sup>

One of the strengths of our study was review of central pathology and radiology as well as FISH analysis. This is important, as the literature suggests the variability of classification and grading of gliomas,<sup>17</sup> and our results can be interpreted confidently as being applicable to neurocytoma. The absence of 1p/19q LOH acted as another confirmatory test by distinguishing it from oligodendroglioma, which can appear histologically very similar.<sup>10</sup> Perry et al.<sup>18</sup> reported 2 cases of EVN with 1p19q deletion, which would have made the distinction from oligodendroglioma difficult, especially given that they are extraventricular and hence should remain an important part of the differential of tumors in young patients.<sup>19</sup> Single deletions have been previously reported in the literature, with 1p deletion a more common occurrence among neurocytomas.<sup>13</sup> Our finding of 3 patients with 1p deletion is consistent with the literature. The change in LOH status occurred in our patient with EVN, who had an aggressive clinical course given his recurrence after GTR and nonresponse to salvage radiotherapy. Rodriguez et al. reported an association between codeletion and aggressive EVN tumor behavior.<sup>20</sup> Change in LOH status in recurrent neurocytomas has not been previously reported to the best of our knowledge and raises the question of whether FISH analysis in the recurrent setting may be useful in selecting patients for more aggressive therapies such as adjuvant chemotherapy or radiotherapy.

There is no general consensus on management of neurocytomas. Our review suggests that the extent of surgery is influenced by size, with smaller tumors having an increased likelihood of GTR. Several influential retrospective reviews have suggested the importance of adjuvant treatment for local control without impact on survival. However, our study results suggest that the timing of radiation does not play a role in survival outcomes. The largest review comes from the Mayo Clinic, as reported by Leenstra et al., with management recommendations based on their long-term outcomes and comparative analysis of outcomes with extent of resection and atypical features.<sup>10</sup> A key limitation of their study was the lack of toxicity profile. In fact, most of the large studies ( $n > 10$ ) (Table 2) reported have been limited to survival  $\pm$  control rates data. To the best of our knowledge, this is the first large ( $n = 20$ ) study that reports on long-term survival, control rates, and toxicity outcomes. Prolonged survival was observed with a median exceeding 8 years, with a 10-year survival rate of 82%. Long duration of tumor control was observed, with 10-year progression-free survival of 62%, and appeared dependent on extent of resection (10-year local control STR = 40% vs. 90% for GTR), which appears to be influenced by tumor size, with timing of radiation a nondeterminant of survival. Our rates of survival and control are similar to those of some major retrospective reviews (Table 2) despite the fact that adjuvant radiotherapy was not commonly used.

**Table 2.** Some of the Major Retrospective Series on Neurocytomas ( $n > 10$ )

Author/Year	N	Treatment (n) (primary)	Crude Survival/Outcomes	F/U (median)	Complications	Comments
Current study/2010	20	GTR: 10 STR: 8 STR/RT: 1 Surveillance: 1	10 yr OS: 82% 10 yr LC: 61% Relapse-free survival: 62%	104.5 mo	Acute grade 3/4: 10/19 Acute grade 5: 1/19 Late grade 3/4: 9/19 perm deficits: 4/19	No 1p 19q
Leenstra et al. <sup>10</sup> /2007	45	GTR (15) STR (14) GTR/RT (4) STR/RT (7) GTR/RT/CH (2) STR/RT/CH (1) Bx/RT (2)	10 y OS: 83% 10 y LC: 60%	10 y	N/A	Review of cases from 1971 No 1p19q 1/3 recurred (GTR/STR)  Med RT, 55.8 Gy
Figarella-Branger et al. <sup>21</sup> /1992	20	GTR (9) STR (11) RT (13)	14/20 alive	0.5–9 y	N/A	
Kim et al. <sup>22</sup> /1996	13	GTR (6) STR (7) RT (8)	12/13 alive 2/5 pts: GTR recurred 2 pts: GTR/RT stable 3 pts: STR alone stable 5 pts: STR/RT stable	1.1–9 y	N/A	
Sharma et al. <sup>23</sup> /2006	20	GTR (14) STR (6) All alive pts received adjuvant RT	15/20 OS: 66.7% No local failures during f/u period	6–72 Med: 32 mo	Postop deaths: 5 (25%) No other toxicity reported	No discussion of grade 5 toxicity
Schild <sup>6</sup> /1997	32	GTR (5) STR (14) GTR/RT (5) STR/RT (8) GTR/RT/CHT (2) STR/RT/CHT (2)	5 yr OS: 81%, LC: 79% GTR: 5 yr LC 100% 5 yr OS 80% STR/RT: 5 yr LC 100% STR: 5 yr LC 50%		N/A	Salvage RT (3)
MacKenzie <sup>24</sup> /1999	15	GTR (8) STR (5) Bx/obs (2) RT (5)	OS: 93.3% LC: 71.4%	72.8 (13–255)	N/A	
Soylemezoglu et al. <sup>25</sup> /1997	36	GTR (34) Bx/RT (2)	OS: 89.7% 8/36 recurred	46.9 (0.5–204)	2 postop death	
Fujimaki et al. <sup>26</sup> /1997	10	STR/RT (9) STR (1)	OS: 100% LC: 100%	90 (23–160)		

Abbreviations: F/U, follow-up; OS, overall survival; LC, local control; Bx, biopsy; RT, radiotherapy; CHT, chemotherapy; pts, patients; N/A, not applicable; GTR, gross-total resection; STR, subtotal resection.

In very indolent tumors, STR may produce significant local control even though the tumor may eventually progress.

With regard to the adjuvant treatment debate, a 2002 analysis of published institution reports of 504 patients from 91 centers concluded that adjuvant radiation was beneficial after incomplete resection.<sup>11</sup> The debate arises given that the extent of resection influences local control only but not survival, and the impact of symptomatic recurrences is not well established in the literature. The largest single institution review has suggested postoperative radiation for improved local control for atypical neurocytomas known to have a higher risk of recurrence, and our findings of a disproportionate rate of recurrence among atypical neurocytomas would support this recommendation.<sup>10</sup> Rades et al. analyzed 85 atypical cases published in the literature and found that adjuvant radiation improved both local control and survival in patients who underwent STRs. There was no added benefit of adjuvant radiation for complete resections of atypical neurocytomas. These results were limited by the fact that there was no central pathology review, and analysis was of preexisting published data from multiple institutions.<sup>27</sup>

Our results show that surgery alone produced durable local control with minimal adverse toxicity. While there were 3 patients with grade 2 permanent deficit, one of the deficits was in a patient with brain injury, which acted as a confounder for the cognitive deficits. Surgery is an essential element in these patients, as it provides not only histological confirmation but symptomatic relief of increased intracranial pressure, which is common among these patients. While the extent of resection has been suggested to have a survival benefit in low-grade gliomas,<sup>28,29</sup> it has not been established as a determinant of survival for neurocytomas.<sup>10</sup> The more recent studies suggest better tumor control and survival as well as fewer perioperative deaths likely as a result of improvement in surgical techniques and improved postoperative care. Resection of deep-seated tumors is difficult, but the high rate of resection and low frequency of permanent deficits in our patients likely reflect improved surgical techniques. Chen et al. support our finding of good functional outcomes after surgery.<sup>29</sup> However, Lee et al.<sup>9</sup> showed some increased risk with salvage surgery.

Given that there was only a single case of adjuvant radiation, we are unable to comment on the role of immediate postoperative radiation for local control, other than to note that the lack of it does not appear to adversely impact control or survival (Table 2). Attempting to summarize the broad range of outcome data from different series is difficult; nevertheless, we suggest that our control and survival rates are comparable to primary surgery alone, with radiotherapy deferred to the salvage setting.

The avoidance of adjuvant treatment and/or delayed treatments helps minimize toxicity in a population with

indolent tumors and does not appear to have any adverse impact on survival. This is in clear contrast to some of the larger case series, where the majority of the patients underwent adjuvant treatments. The largest single institutional experience, from the Mayo Clinic, as reported by Leenstra et al.,<sup>10</sup> shows that 35% of their patients received adjuvant radiation as part of their initial management but that one-third of their patients recurred, and survival rates are similar to our study. They proposed patient selection on the basis of atypical neurocytomas for consideration of adjuvant therapy. Our results support that atypical neurocytomas are at higher risk of recurrence, with a poor local control rate of 42%; however, given that there is no impact on survival, it would not be unreasonable to delay radiation until progression/recurrence, particularly among those patients with GTR.

Potential neurocognitive toxicity secondary to radiation is always of concern with anticipated prolonged survivorships. Radiation is known to be effective in treatment of low-grade gliomas and remains a therapeutic option for these patients.<sup>25</sup> Extrapolation of long-term toxicity to the setting of other low-grade primary cerebral neoplasms, like neurocytoma, seems reasonable. The salvage radiation in our patients used doses  $\leq 2$  Gy and modern focal radiation techniques shown to reduce risk of late neurotoxicity among patients with low-grade glioma.<sup>12,32-36</sup> Neurocognitive testing (MMSE) was available for 2 of 4 patients who received adjuvant or salvage radiation, and both patients demonstrated no impairment over time after treatment.

Our review confirms that GTR of neurocytoma is associated with durable long-term control, excellent disease-free survival, and a low rate of long-term deficits and should be the preferred initial therapy. Patients with STR and no adjuvant treatment were successfully salvaged with surgery or radiation at the time of clinical and radiographic progression, with good long-term function after salvage suggesting that careful surveillance alone after STR may be a safe strategy. While one-third of our patients recurred, with the majority of recurrences within 2.5 years of surgery, the sporadic recurrences at prolonged intervals (e.g., 15 years) emphasizes the importance of ongoing surveillance in these groups of patients and mirrors patterns of recurrences for low-grade gliomas.<sup>27</sup>

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