# Unveiling the Efficacy of Gamma Knife Radiosurgery for Tectal Plate Gliomas

**Nülifer Kilic Durankus, MD** *, **Yavuz Samanci, MD** ‡§, **Ali Haluk Düzkalir, MD** §, **Selcuk Peker, MD** ‡§

*Department of Radiation Oncology, Koc University School of Medicine, Istanbul, Turkey; ‡Department of Neurosurgery, Koc University School of Medicine, Istanbul, Turkey; §Department of Neurosurgery, Gamma Knife Center, Koc University Hospital, Istanbul, Turkey

**Correspondence:** Selcuk Peker, MD, Department of Neurosurgery, School of Medicine, Koç University, Davutpaşa Cd. No: 4, Zeytinburnu, Istanbul, 34010, Turkey.
Email: peker@selcukpeker.com

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**BACKGROUND AND OBJECTIVES:** Tectal plate gliomas (TPGs) are midbrain tumors that grow slowly and have a benign clinical course. Most TPGs are low-grade astrocytomas, but they can encompass various histological tumor types. Gamma Knife radiosurgery (GKRS) is being explored as a potentially safe and effective treatment option for TPGs, although research in this area is limited. This study aims to evaluate GKRS's efficacy and safety in patients with TPG and provide a comprehensive review of existing literature on the topic.

**METHODS:** This retrospective, single-center study included 48 patients with consecutive TPG who underwent GKRS between September 2005 and June 2022. Patients diagnosed with TPGs based on radiological or tissue-based criteria and who had a minimum follow-up period of 12 months were eligible for inclusion. The primary end points were local control and the absence of GKRS-associated or tumor-associated mortality and morbidity.

**RESULTS:** During a median follow-up of 28.5 months (range, 12-128), the radiological assessment showed tumor control in all cases, with 16.7% achieving a complete response and 68.8% achieving a partial response. Pseudoprogression occurred in 6.2% of cases, with onset ranging from 3 to 8 months. Clinical outcomes revealed no permanent neurological deterioration, with symptoms improving in 14.6% of patients and remaining stable in the others. One patient in the pseudoprogression group experienced transient Parinaud syndrome. One patient died during follow-up because of unrelated causes. The mean survival time after GKRS was 123.7 months. None of the clinical, radiological, or radiosurgical variables showed a correlation with partial/complete response, clinical improvement, or overall survival.

**CONCLUSION:** There is limited research available on the management of TPGs, and this study presents the largest patient cohort treated with GKRS, along with a substantial follow-up duration. Despite its limitations, this study demonstrates the efficacy and low-risk profile of GKRS for TPGs.

**KEY WORDS:** Brainstem, Gamma Knife radiosurgery, Low-grade astrocytoma, Tectal plate glioma, Tectum

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Tectal plate gliomas (TPGs) are a specific type of glioma belonging to the midbrain glioma group that grow slowly and rarely cause neurological deficits.[1] Most TPGs comprise low-grade astrocytomas, although they encompass various histological tumor types. These tumors often lead to obstructive hydrocephalus, increased intracranial pressure, and/or Parinaud syndrome because of their proximity to the cerebral aqueduct.[2,3]

**ABBREVIATIONS: CR,** complete response; **ETV,** endoscopic third ventriculostomy; **HR,** hazard ratio; **PD,** progressive disease; **PR,** partial response; **RT,** radiotherapy; **SD,** stable disease; **SRS,** stereotactic radiosurgery; **TPG,** tectal plate glioma; **TRIC,** treatment-related imaging change; **VPS,** ventriculoperitoneal shunt.

Given their indolent nature, the management approach for most TPGs involves close radiological observation after cerebrospinal fluid (CSF) diversion.[4] However, in cases where tumors show radiological progression, alternative treatment modalities such as surgery, chemotherapy, or radiotherapy (RT) may be used. Among these options, stereotactic radiosurgery (SRS) using Gamma Knife radiosurgery (GKRS) has been identified in small case series as a safe and promising approach for managing TPGs that necessitate intervention beyond mere observation.[5,6]

Because of the low incidence of TPGs, there is limited literature available on the efficacy of GKRS. Therefore, this study aimed to evaluate the efficacy and safety of GKRS in patients with TPGs and to review the relevant literature on this topic.

# METHODS

## Ethics Statement

This retrospective study, which used prospectively managed data, received ethical approval from the Institutional Review Board of Koc University (2022.022.IRB1.017). Before participation, informed consent was obtained from all individuals.

## Eligibility and Demographic Data

This study was conducted at a single center and included a total of 48 consecutive patients who underwent GKRS for TPGs between September 2005 and June 2022. Data for the study were obtained from patient charts and neuroimaging databases. Eligible participants included those with radiology-based or tissue-based diagnoses of TPGs who received up-front or adjuvant GKRS and had a minimum follow-up period of 12 months. The exclusion criteria included high-grade glioma and tumor extension beyond the tectal region. In cases where histological confirmation was not available, the diagnosis of TPGs was made based on typical radiological findings, including the presence of a focal, well-circumscribed, bulbous lesion deforming the quadrigeminal plate above the cerebral aqueduct, which appeared isodense or hypointense on T1-weighted images and hyperdense on T2-weighted MR images.[3]

Table 1 presents a summary of the patient and disease characteristics. The median age at diagnosis was 14 years, varying from 5 to 64 years. Among the included patients, 21 (43.7%) were male and 27 (56.3%) were female. Most patients (81.3%) initially exhibited clinical signs and symptoms of intracranial hypertension, with headache being the most frequent (81.3%), followed by nausea/vomiting (10.4%). Other recorded symptoms, some of which were also associated with hydrocephalus, included eye movement disorders (16.7%) and ataxia (16.7%). A CSF diversion procedure was performed in 37 (77.1%) patients, with 13 receiving an endoscopic third ventriculostomy and 24 undergoing ventriculoperitoneal shunt placement. The diagnosis of TPGs was based on histopathology in 9 patients while the remaining patients were diagnosed based on MRI. Among patients who underwent tumor biopsy (n = 1) or surgery (n = 8), pilocytic astrocytoma World Health Organization grade I was the most common histological tumor type (66.7%). Gadolinium enhancement was observed in 9 individuals, representing 18.8% of the cohort.

## Radiosurgical Technique

GKRS were performed by means of various Leksell Gamma Knife models (Elekta Instrument AB), including 4C (2005-2012), Perfexion (2012-2017), and Icon™ (2017-2022). Before the procedure, local scalp anesthesia was administered, and a Leksell frame was applied. Fluid-attenuated inversion recovery (FLAIR), T2-weighted, and contrast-enhanced T1-weighted sequences were obtained, and sedation was used when necessary. After Gamma Knife Icon, all MR sequences were acquired without a stereotactic frame. Tumor volume was calculated by contouring the lesion on each slice and matching T2-weighed, FLAIR, and contrast-enhanced T1-weighted axial MR images. For postoperative cases, tumor volume was the resection cavity, postoperative enhanced area on contrast-enhanced T1-weighted MR images, and abnormal T2-weighted and FLAIR area.[7] No margin was added to the target volume. The median age at the time of GKRS treatment was 16 years, varying from 7 to 68 years. The median time to GKRS treatment was 13.5 months (range, 1-201). The most common indication for GKRS was up-front treatment (45.8%), followed by tumor progression (37.5%). The median tumor volume was 1.7 $cm^3$ (range, 0.6-13.6). The median marginal dose was 12 Gy (range, 11-14) to 40%–55% isodoses.

## Follow-Up and Study End Points

The follow-up of the patients was carried out by a neurosurgeon who evaluated symptoms or signs, neurological function, and the Karnofsky performance scale score. These assessments were used to decide whether additional intervention was necessary. Complications were defined as the emergence of new deficits not present before GKRS. Imaging follow-up was performed at 6-month intervals during the first year and annually thereafter. These follow-up MRIs were then compared with baseline MR images, and changes in tumor size were classified into different categories: progressive disease (PD) if there was a volume increase of more than 25% or the appearance of new lesions, stable disease (SD) for volume changes less than 25%, partial response (PR) if there was a volume reduction of more than 25%, and complete response (CR) if all lesions disappeared.[4]

The primary efficacy end point was tumor control after SRS, which was defined as SD, PR, or CR. Local failure was defined as PD sustained in at least 2 imaging follow-ups. Recurrence was described as the emergence of a previously unidentified tumor or the growth of treated tumor tissue. The primary safety end point focused on evaluating the absence of SRS-related or tumor-related mortality and morbidity during the follow-up period. Adverse events were categorized using the Common Terminology Criteria for Adverse Events version 5.[8]

## Statistical Analysis

The univariate analysis included reporting the median (range) for continuous variables and the number (%) for categorical variables. The variables included in the univariate analysis were chosen based on their clinical relevance and their potential to impact the outcomes of interest through a combination of clinical experience and existing literature on TPGs and GKRS. Any variable having a significant univariate test was selected as a candidate for the multivariate analysis. The Kaplan-Meier method was used for survival analysis. A 2-tailed *P*-value <.05 was deemed to be significant. Statistical analyses were conducted using IBM SPSS statistics version 29 software (IBM Corporation).

# RESULTS

## Radiological Outcome

The patients were followed for a median duration of 28.5 months, varying from 12 to 128 months. Tumor control was achieved in all cases after GKRS, with 16.7% exhibiting a CR, 68.8% showing a PR, and 14.6% demonstrating SD. Figure illustrates an example patient with PR. Pseudoprogression was observed in 3 (6.2%) cases, occurring between 3 and 8 months after GKRS. Among these cases, 2 patients received up-front GKRS while the other had a residual growth of a Grade II astrocytoma. Notably, none of the pre-GKRS and GKRS variables correlated with PR/CR or pseudoprogression (Table 2). The summarized data for all patients can be found in Table 1.

**TABLE 1. Summary of the Study Cohort (n = 48) Treated With Gamma Knife Radiosurgery for Tectal Plate Glioma**

| Variable | n (%) | Median (range) |
|---|---|---|
| Sex | | |
| Female | 27 (56.3) | |
| Male | 21 (43.7) | |
| Age at diagnosis, y | | 14 (5-64) |
| Diagnosis | | |
| Histology | 9 (18.8) | |
| Radiology | 40 (83.3) | |
| Signs and symptoms at diagnosis | | |
| Headache | 39 (48.1) | |
| Ataxia | 9 (11.1) | |
| Diplopia | 8 (9.9) | |
| Dizziness | 8 (9.9) | |
| Impaired vision | 5 (6.2) | |
| Nausea/vomiting | 5 (6.2) | |
| Other | 7 (8.6) | |
| Tumor surgery | | |
| Open surgery | 8 (16.7) | |
| Biopsy | 1 (2.1) | |
| None | 39 (81.3) | |
| CSF diversion surgery | | |
| VPS | 24 (50) | |
| ETV | 13 (27.1) | |
| None | 11 (22.9) | |
| Pathology | | |
| Pilocytic astrocytoma (grade I) | 6 (7.4) | |
| Fibrillary astrocytoma (grade II) | 3 (3.7) | |
| N/A | 39 (48.1) | |
| Age at GKRS, y | | 16 (7-68) |
| Initial diagnosis to GKRS, mo | | 13.5 (1-201) |
| Reason for GKRS | | |
| Up-front | 22 (45.8) | |
| Progression | 18 (37.5) | |
| Residual growth | 5 (10.4) | |
| Recurrence | 2 (4.2) | |
| Residual | 1 (2.1) | |
| Pre-GKRS headache | 39 (81.3) | |
| Pre-GKRS vision problems | 13 (27.1) | |
| Pre-GKRS Karnofsky Performance Status Scale | | 90 (50-100) |
| Tumor volume, $cm^3$ | | 1.7 (0.6-13.6) |
| Contrast enhancement | 9 (18.8) | |
| Marginal dose, Gy | | 12 (11-14) |
| Isodose, % | | 50 (40-55) |
| Follow-up period, months | | 28.5 (12-128) |
| Post-GKRS symptoms | | |
| Stable | 41 (83.4) | |
| Improved | 7 (14.6) | |
| Radiological outcome | | |
| PR | 33 (68.7) | |
| CR | 8 (16.7) | |
| Stable | 7 (14.6) | |
| Pseudoprogression | 3 (6.2) | |

CR, complete response; CSF, cerebrospinal fluid; ETV, endoscopic third ventriculostomy; GKRS, Gamma Knife radiosurgery; N/A, not available; PR, partial response; VPS, ventriculoperitoneal shunt.

### Clinical Outcome

Pre-GKRS symptoms improved in 14.6% of patients and remained stable in the rest. No patients showed any permanent neurological deterioration during the follow-up period. One patient with pseudoprogression experienced a transient Parinaud syndrome that recovered within 3 months with short-term, low-dose steroid use. One patient was deceased during the follow-up because of unrelated causes. The mean survival time after GKRS was 123.7 months. Median survival was not reached in the study cohort. Notably, none of the pre-GKRS and GKRS variables correlated with clinical improvement or overall survival (Table 2).

## DISCUSSION

There is limited research available on the management options for TPGs, and this study has the most substantial TPG patient cohort treated using GKRS, accompanied by a substantial follow-up duration (Table 3).

TPGs are generally indolent with a favorable prognosis, and managing them has always been challenging because of their critical location and benign characteristics.[9] CSF diversion procedures are commonly performed for accompanying hydrocephalus, and most patients (77.1%) in our cohort received at least one CSF diversion procedure before GKRS. Although CSF diversion and regular MRI scans are often recommended, it is important to note that up to 86% of untreated TPGs may progress during follow-ups.[10,11] The optimal treatment for progressing or recurrent tectal gliomas is controversial. More aggressive management, including surgery, chemotherapy, or RT, may be necessary for rapidly growing or atypical tumors.[12] Surgery is rarely used but can be considered for larger or progressive tumors, often followed by adjuvant therapy. TPG surgery carries significant risks and potential complications; however, newer techniques like fully endoscopic approaches offer safer options.[4,13-15] Chemotherapy is commonly used as adjuvant therapy, but its use is limited because of the indolent nature of most TPGs and the lack of studies demonstrating its efficacy.

RT is occasionally used in the treatment of TPGs when observation alone is no longer sufficient. Compared with other options, RT is considered safe and effective. However, significant side effects such as necrosis and steroid dependency were observed with fractionated external beam RT in brainstem tumors.[16,17] In a phase III study by Mandell et al,[18] various toxicities, including objective hearing loss, were reported. Although advanced radiation delivery methods such as 3-dimensional conformal RT and intensity-modulated RT have enhanced treatment precision, they may still result in unintended exposure of healthy tissues to low to moderate radiation doses, leading to an elevated risk of radiation-induced side effects.[19] Some studies emphasize the potential for long-term toxic effects and the early onset of cellular senescence in brain cells because of exposure to low doses of radiation.[20] To overcome these effects, focal RT approaches such as SRS and proton radiation are now commonly used with other treatments or after surgery.[21] Among these approaches, GKRS stands out for its precise targeting, minimal impact on surrounding healthy tissues, and cost-effectiveness as a first-line treatment option in TPGs.

The number of studies on GKRS for TPGs is particularly restricted.[22] Kihlstrom et al[6] reported 7 TPG cases treated with doses varying from 14 to 35 Gy. Most tumors responded well to treatment while severe radiation-induced edema and complications occurred in 2 patients with higher (35 Gy) marginal doses.

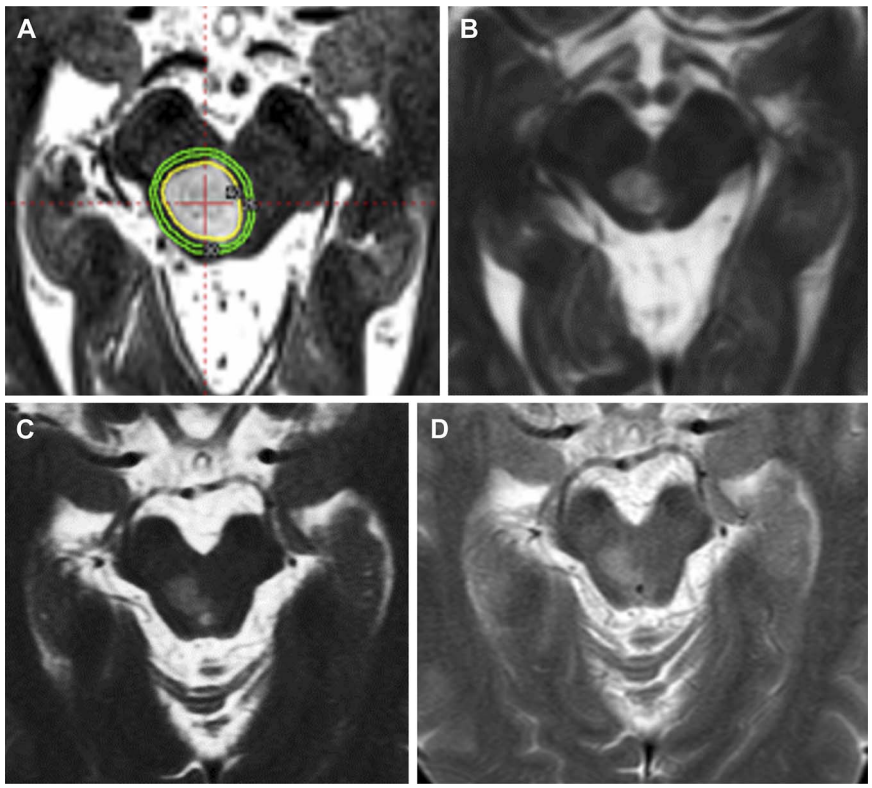


**FIGURE.** **A**, *A 52-year-old female patient with a 1 cm$^3$ tectal glioma. The tumor was irradiated with a marginal dose of 11 Gy to the 40% isodose line. The tumor demonstrated a partial response and was stable at* **B**, *1 year,* **C**, *2 years, and* **D**, *4 years after Gamma Knife radiosurgery.*

**TABLE 2. Cox Regression Analysis for Radiological and Clinical Outcomes**

| | Univariate | | |
|---|---|---|---|
| **Parameter** | ***P*** | **HR** | **95% CI for HR** |
| Parameters related to partial/complete response | | | |
| Age at Gamma Knife radiosurgery | .836 | 1.002 | 0.982–1.023 |
| Time to Gamma Knife radiosurgery | .880 | 1.001 | 0.993–1.008 |
| Sex | .740 | 1.114 | 0.590–2.102 |
| Tumor surgery before Gamma Knife radiosurgery | .667 | 1.190 | 0.538–2.632 |
| Histological grade | .634 | 1.139 | 0.666–1.947 |
| Contrast enhancement | .693 | 0.847 | 0.371–1.933 |
| Tumor volume | .566 | 0.964 | 0.851–1.092 |
| Marginal dose | .159 | 1.310 | 0.899–1.908 |
| Parameters related to pseudoprogression | | | |
| Age at Gamma Knife radiosurgery | .860 | 1.006 | 0.937–1.081 |
| Time to Gamma Knife radiosurgery | .686 | 1.004 | 0.984–1.025 |
| Sex | .769 | 1.433 | 0.130–15.809 |
| Tumor surgery before Gamma Knife radiosurgery | .699 | 1.611 | 0.144–18.039 |
| Histological grade | .364 | 1.894 | 0.477–7.522 |
| Contrast enhancement | .689 | 1.641 | 0.145–18.637 |
| Tumor volume | .982 | 1.005 | 0.661–1.528 |
| Marginal dose | .948 | 1.053 | 0.228–4.866 |
| Parameters related to clinical improvement | | | |
| Age at Gamma Knife radiosurgery | .499 | 0.977 | 0.912–1.046 |
| Time to Gamma Knife radiosurgery | .996 | 1.000 | 0.982–1.018 |
| Headache before Gamma Knife radiosurgery | .737 | 1.438 | 0.173–11.988 |
| Visual symptoms before Gamma Knife radiosurgery | .097 | 4.002 | 0.777–20.619 |
| Histological grade | .380 | 1.616 | 0.554–4.716 |
| Karnofsky Performance Status | .289 | 0.965 | 0.903–1.031 |
| Contrast enhancement | .209 | 3.102 | 0.530–18.141 |
| Tumor volume | .295 | 1.097 | 0.922–1.306 |
| Marginal dose | .074 | 2.041 | 0.932–4.468 |
| Maximum dose | .356 | 1.134 | 0.896–1.480 |
| Partial/complete response | .799 | 1.318 | 0.158–11.025 |
| Parameters related to overall survival | | | |
| Age at Gamma Knife radiosurgery | .776 | 1.017 | 0.904–1.144 |
| Time to Gamma Knife radiosurgery | .582 | 0.961 | 0.833–1.108 |
| Histological grade | .712 | 0.071 | 0–89010.147 |

**TABLE 2. Continued.**

| Parameter | Univariate | | |
|---|---|---|---|
| | *P* | HR | 95% CI for HR |
| Karnofsky Performance Status | .862 | 1.126 | 0.298–4.257 |
| Tumor volume | .433 | 0.049 | 0–91.932 |
| Partial/complete response | .767 | 27.392 | 0–9.218E+10 |
| Adverse radiation effects | .951 | 442 514.472 | 5.116E+184 |

HR, hazard ratio.

The authors stated that SRS was effective for deeply located low-grade gliomas, but caution was advised against doses exceeding 14 Gy to avoid uncontrolled radiation-induced changes. In our study, the median marginal dose was 12 Gy (range, 11-14), which aligns with the suggested treatment dosage. Weintraub et al[23] demonstrated the effects of GKRS on pediatric patients with glioma, including only 8 TPG cases. The results at the final follow-up showed a median volume decrease of 86% in 7 (88%) patients, with CR observed in 3 (38%) patients. Hadjipanayis et al[24] investigated GKRS in 12 low-grade astrocytomas, with only 2 located in the tectum. Both patients had undergone partial resection before GKRS. One patient was treated for tumor recurrence, and the tumor showed volume reduction during an 87-month follow-up. The tumor in the other patient remained stable for 12 months without significant volume changes. Boëthius et al[25] reported 19 pilocytic astrocytoma cases, with 12 in the brainstem. Despite using a low marginal dose, the study achieved tumor control in all cases, with 85% demonstrating modest tumor volume reduction after GKRS. Yen et al[26] reported beneficial effects of GKRS on 20 patients with brainstem gliomas, of which 13 were tectal. Four patients experienced CR, 4 showed a reduction of >50% and 3 experienced tumor shrinkage varying from 25% to 50%. However, PD occurred in 2 patients at 5 and 36 months of follow-up, with 1 patient succumbing to tumor growth after failed fractionated RT after GKRS with a low marginal dose of 5 Gy. In their 2 series focusing on GKRS for

**TABLE 3. Summary of Studies in Which Gamma Knife Radiosurgery Was Used for the Treatment of Tectal Gliomas**

| Study | n | Median age (y) | Median volume ($cm^3$) | Median marginal dose (Gy) | Median follow-up (mo) | Local control (%) | Overall survival (%) | Adverse radiation effect (%) |
|---|---|---|---|---|---|---|---|---|
| Kilhstrom et al,[6] 1994 | 7 | 13 | 4.1 | 18 | 48 | 85.7 | 100 | 28.6 |
| Weintraub et al,[23] 1999 | 8 | 8.5 | 1.6 | 15.2 | 74 | 87.5 | 100 | 0 |
| Hadjipanayis et al,[24] 2002 | 2 | 25.5 | 4.5 | 14 | 49.5 | 100 | 100 | 0 |
| Boethius et al,[25] 2002 | 12[a] | 7.9 | 1.7 | 10.5 | 60.6 | 100 | N/A | 75 |
| Yen et al,[26] 2007 | 13 | 15 | 1.5 | 15 | 70 | 92.3 | 92.3 | 0 |
| Kano et al,[27] 2009 | 6[a] | 34.5 | 6.2 | 11.5 | 83.3 | 33.3 | 83.3 | N/A |
| Kano et al,[28] 2009 | 13[a] | 10.5[b] | 2.1[b] | 14.5[b] | 55.5[b] | 96[b] | 98[b] | 10[b] |
| El-Shehaby et al,[5] 2015 | 11 | 22 | 4.5 | 12 | 40 | 100 | 100 | 36.4 |
| Present study, 2023 | 48 | 16 | 1.7 | 12 | 28.5 | 100 | 97.9 | 0 |

N/A, not available.
[a]Mixed brainstem lesions.
[b]Whole cohort.

pilocytic astrocytoma, Kano et al[27,28] included 19 patients with brainstem tumors without specifying precise locations. They reported 1-year and 5-year progression-free survival rates of 83.9% and 31.5% for adults and 91.7% and 70.8% for children, respectively. El-Shehaby et al[5] reported a recent GKRS case series for TPGs, including 5 pilocytic astrocytomas and 6 nonpilocytic astrocytomas. Tumor volumes varied from 1.2 to 14.7 cc, with a median of 4.5 cc. The marginal dose was reported as 11–14 Gy, with a median of 12 Gy. The authors observed CR in 6 tumors. In their study, Gagliardi et al[29] investigated 39 patients with low-grade gliomas, including 6 TPGs. Although not reported separately, 57.7% of cases exhibited volume reduction, with a median decrease of 33.3% at the last follow-up. Notably, clinical improvement was seen in 52.4% of the patients. In a recent meta-analysis on low-grade TPGs, Gagliardi et al[22] also stated that tectal location was a positive predictive factor for PR or CR ($P$ = .003) and a negative predictive factor for treatment-related imaging changes (TRICs) ($P$ = .002) after GKRS.

Conventional RT literature describes various postradiation reactions, and similar reactions are also seen after GKRS for TPGs. GKRS patients have more TRICs than studies involving RT, likely due to improved neuroimaging sensitivity.[22] Clinically significant TRICs are generally mild, often manifesting as temporary worsening of preexisting symptoms or emergence of transient disturbances, particularly related to gaze alterations caused by focal edema.[5,6] Similarly, one of our patients with pseudoprogression experienced transient Parinaud syndrome that resolved with steroid use. Severe conditions such as signs of increased intracranial pressure are rare.[5] Increased contrast enhancement does not necessarily indicate tumor progression as it is often attributable to TRICs.[29] Radiation-induced pseudoprogression, seen in 36% of cases in a systematic review, involves emergence or exacerbation of contrast enhancement and/or edema on the FLAIR sequence during the subacute RT phase.[30] We also observed 3 pseudoprogressions, followed by spontaneous resolution, except one in which we used a low-dose steroid for Parinaud's syndrome. Rarely, cystic degeneration and radiation necrosis were also reported in the literature.[22]

### Limitations

Although our study represents the largest series of patients with TPG treated with GKRS, it is imperative to acknowledge the limitations. The small cohort size and shorter median follow-up and events limited the statistical power of our analysis and including patients with no histological confirmation might introduce confounding factors. Nevertheless, it is worth noting that in current neurosurgical practice, patients with clinical and radiological indications of a TPG are frequently managed without undergoing biopsy or surgery.[10] Furthermore, it is important to consider that the patients in our series predominantly had smaller tumors, which may introduce a potential selection bias in the obtained results.

## CONCLUSION

The management of TPGs necessitates a careful evaluation of different treatment options. The available evidence suggests that GKRS can achieve tumor control and produce favorable outcomes regarding tumor response and survival. However, it is important to consider individual patient characteristics and tumor factors when determining the most appropriate treatment approach for TPGs. A multidisciplinary approach is essential to tailor the treatment strategy to each patient's specific needs.

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