

# Gamma Knife Radiosurgery for Pineal Region Tumor

**Pineal region tumors** (PTs) represent extremely rare pathologies, characterized by highly heterogeneous histological patterns. Most of the available evidence for Gamma Knife radiosurgical (GKS) treatment of PTs arises from multimodal regimens, including GKS as an adjuvant modality or as a salvage treatment at recurrence. We aimed to gather existing evidence on the topic and analyze single-patient-level data to address the efficacy and safety of primary GKS. This is a systematic review of the literature (PubMed, Embase, Cochrane, Science Direct) and pooled analysis of single-patient-level data. A total of 1054 original works were retrieved. After excluding duplicates and irrelevant works, we included 13 papers (n = 64 patients). An additional 12 patients were included from the authors' original series. A total of 76 patients reached the final analysis; 56.5% (n = 43) received a histological diagnosis. Confirmed lesions included pineocytoma WHO grade I (60.5%), pineocytoma WHO grade II (14%), pineoblastoma WHO IV (7%), pineal tumor with intermediate differentiation WHO II/III (4.7%), papillary tumor of pineal region WHO II/III (4.7%), germ cell tumor (2.3%), neurocytoma WHO I (2.3%), astrocytoma WHO II (2.3%) and WHO III (2.3%). Presumptive diagnoses were achieved in the remaining 43.5% (n = 33) of cases and comprised of pineocytoma (9%), germ cell tumor (6%), low-grade glioma (6%), high-grade glioma (3%), meningioma (3%) and undefined in 73%. The mean age at the time of GKS was 38.7 years and the mean lesional volume was  $4.2 \pm 4$  cc. All patients received GKS with a mean marginal dose of  $14.7 \pm 2.1$  Gy (50% isodose). At a median 36-month follow-up, local control was achieved in 80.3% of cases. Thirteen patients showed progression after a median time of 14 months. Overall mortality was 13.2%. The median OS was not reached for all included lesions, except high-grade gliomas (8mo). The 3-year OS was 100% for LGG and pineal tumors with intermediate differentiation, 91% for low-grade pineal lesions, 66% for high-grade pineal lesions, 60% for germ cell tumors (GCTs), 50% for HGG, and 82% for undetermined tumors. The 3-year progression-free survival (PFS) was 100% for LGG and pineal intermediate tumors, 86% for low-grade pineal, 66% for high-grade pineal, 33.3% for GCTs, and 0% for HGG. Median PFS was 5 months for HGG and 34 months for GCTs. The radionecrosis rate was 6%, and cystic degeneration was observed in 2%. Ataxia as a presenting symptom strongly predicted mortality (odds ratio [OR] 104, p = .02), while GCTs and HGG histology well predicted PD (OR: 13, p = .04). These results support the efficacy and safety of primary GKS treatment of PTs. Further studies are needed to validate these results, which highlight the importance of the initial presumptive diagnosis for choosing the best therapeutic strategy <sup>1)</sup>.

Seventeen PRT patients with negative pathology who underwent GKS were retrospectively studied. Nine patients had further whole-brain and spinal cord radiotherapy and chemotherapy 6-9 months after GKS. Sixteen of 17 cases were followed up over a mean of 33.3 months. The total response rate was 75%, and the control rate was 81.3%. No obvious neurological deficits or complications were attributable to GKS. The findings indicate that GKS may be an alternative strategy in selected PRT patients who have negative pathological diagnoses, and that good outcomes and quality of life can be obtained with few complications <sup>2)</sup>.

<sup>1)</sup>

Gagliardi F, De Domenico P, Garbin E, Snider S, Mortini P. Primary Gamma Knife Radiosurgery for pineal region tumors: A systematic review and pooled analysis of available literature with histological stratification. J Pineal Res. 2023 Dec;75(4):e12910. doi: 10.1111/jpi.12910. Epub 2023 Sep 13. PMID:

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2)

Wang P, Mao Q, Wang W, Zhou LX, Liu YH. Gamma knife surgery for pineal region tumors: an alternative strategy for negative pathology. *Arq Neuropsiquiatr*. 2014 Feb;72(2):129-35. doi: 10.1590/0004-282x20130217. PubMed PMID: 24604367.

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