Upfront Frameless Hypofractionated Gamma Knife Radiosurgery

- Upfront frameless hypofractionated gamma knife radiosurgery for large posterior Fossa metastases
- Feasibility of fractionated gamma knife radiosurgery in the management of newly diagnosed Glioblastoma
- Benefits of image-guided stereotactic hypofractionated radiation therapy as adjuvant treatment of craniopharyngiomas. A review

Upfront Frameless Hypofractionated Gamma Knife Radiosurgery

Clinical Applications

- Large brain metastases
- Skull base meningiomas
- Vestibular schwannomas
- Selected recurrent gliomas
- Arteriovenous malformations (AVMs)

Advantages

- Improved patient comfort (frameless setup)
- High conformality and dose precision
- Reduced radiation-related toxicity via fractionation
- Suitable for outpatient treatment

Example Case

- A 62-year-old patient with a 3.5 cm right frontal **meningioma** near the motor cortex is treated with:
  - `'Upfront frameless hypofractionated Gamma Knife radiosurgery'`
  - `'Regimen'`: 5 sessions, 5 Gy per session
  - `'Outcome'`: Well-tolerated, no motor deficit or significant edema

Notes

- Hypofractionation is especially beneficial when the lesion is near critical structures (e.g., optic chiasm, brainstem).
- Frameless platforms rely on high-resolution MRI, cone-beam CT, and real-time motion tracking for precision.

Retrospective Single-center Observational cohort studies

A retrospective single-center observational cohort study, of Koç University Hospital assesses the efficacy and safety of upfront HF-GKRS for treatment-naïve large pf-METs. 40 patients with 42 posterior fossa metastases received HF-GKRS from October 2017 to June 2024. Patients eligible for the study were 18 years or older, had histologically confirmed malignancy, large pf-METs (> 4 cm3), and a minimum of two follow-up MRI scans. The primary outcome was local control (LC), with secondary assessments of distant intracranial failure (DICF), intracranial progression-free survival (PFS), overall survival (OS), and toxicity. LC was achieved in 88.1% of pf-METs over a median follow-up of 6 months (mean: 13.7 months). LC rates at 6, 12, and 24 months were 95.8%, 95.8%, and 74.5%, respectively. Local failure (LF) occurred in 11.9% of cases, with a median recurrence time of 12 months. DICF was noted in 35% of patients, while no cases of LMD were reported. Intracranial PFS rates at 6, 12, and 24 months were 54.1%, 39.0%, and 16.7%, respectively, with a median PFS of 8 months. Symptomatic hydrocephalus developed in one patient (2.5%). Controlled primary tumor status (HR: 0.17, p = 0.036) was significantly associated with lower risk of death, while no other parameters were predictive of LC, DICF, or intracranial PFS. HF-GKRS demonstrates strong efficacy and safety as a primary treatment for selected, treatment-naïve large pf-METs over a relatively short follow-up duration. Further studies are warranted to refine patient selection, fractionation, and dosing strategies for this challenging population [1)].

 Strengths Focused population: Patients with large (>4 cm³) and untreated pf-METs—a subgroup typically excluded or underserved in many radiosurgical trials.

Use of modern frameless HF-GKRS: Demonstrates applicability of advanced mask-based Gamma Knife systems in posterior fossa tumors.

Well-defined outcomes:

Local Control (LC) was primary,

DICF, PFS, OS, and toxicity as secondary outcomes.

Reasonable follow-up for local control metrics, with:

LC at 6 and 12 months = 95.8%,

LC at 24 months = 74.5%.

Low toxicity: Only one patient (2.5%) developed symptomatic hydrocephalus.

Relevant statistical analysis: Hazard ratio (HR) used to identify prognostic factors—controlled primary tumor was statistically significant (HR: 0.17, p = 0.036).

⚠ Limitations

Retrospective study design: Prone to selection and reporting biases; causal inference is limited.

Small sample size: 40 patients with 42 lesions restricts statistical power, especially in multivariate analyses.

Single center: Results may not generalize to other institutions with different patient populations or radiosurgical techniques.

Short median follow-up (6 months) for assessing long-term outcomes like radionecrosis or brainstem toxicity.

No control arm: No comparison with surgery, whole-brain RT, or single-fraction GKRS.

Incomplete exploration of dosimetric variables (e.g., dose per fraction, BED, target coverage, OAR sparing).

 Clinical Implications

This study supports frameless hypofractionated GKRS as a feasible upfront treatment for:

Large posterior fossa metastases,

Patients unsuitable for surgery or single-fraction SRS due to size/location.

Importantly:

High local control can be achieved,

Toxicity is low, despite the critical location,

Patient selection (primary tumor control) remains key to outcome.

 Conclusion

This retrospective analysis offers promising evidence that upfront frameless HF-GKRS is an efficacious and safe non-invasive treatment for large, treatment-naïve posterior fossa metastases. However, due to design and size limitations, prospective multicenter trials with longer follow-up and comparative arms are needed to optimize fractionation schedules, patient selection criteria, and outcome prediction models.

1)
Samanci Y, Aydin S, Düzkalir AH, Askeroglu MO, Peker S. Upfront frameless hypofractionated gamma knife radiosurgery for large posterior Fossa metastases. Neurosurg Rev. 2025 May 15;48(1):418. doi: 10.1007/s10143-025-03572-4. PMID: 40372490.