Hypofractionated Gamma Knife radiosurgery for brain metastases

- Evaluation of clinical and volumetric outcomes following adaptive gamma knife radiosurgery for brain metastases
- Hypo-Fractionated Radiotherapy to the Cavity for Resected Brain Metastases: A UK Series
- Efficacy and safety of stereotactic radiosurgery for large cystic brain metastases: a comparison with and without cyst aspiration via Ommaya reservoir
- Spot-Scanning Confocal Photon Beams for Hypofractionated Brain Radiosurgery
- Radiosurgery of benign intracranial lesions. Indications, results , and perspectives
- Upfront frameless hypofractionated gamma knife radiosurgery for large posterior Fossa metastases
- Post-operative hypofractionated stereotactic radiotherapy for brain metastases from lung and breast cancer in patients without prior WBRT: a retrospective dose escalation study
- Fraction-variant beam orientation optimization for spatiotemporal fractionation schemes

---

Fractionated Gamma Knife radiosurgery (GKS) represents a feasible option for patients with large brain metastases (BM). However, the dose-fractionation scheme balanced between local control and radiation-induced toxicity remains unclear. Therefore, Kim et al. conducted a dose-escalation study using fractionated GKS as the primary treatment for large (> 3 cm) BM.

The exclusion criteria were more than 3 lesions, evidence of leptomeningeal disease, metastatic melanoma, poor general condition, and previously treated lesions. Patients were randomized to receive 24, 27, or 30 Gy in 3 fractions (8, 9, or 10 Gy per fraction, respectively). The primary endpoint was the development of radiation necrosis assessed by a neuroradiologist blinded to the study. The secondary endpoints included the local progression-free survival (PFS) rate, change in tumor volume, development of distant intracranial progression, and overall survival.

Between September 2016 and April 2018, 60 patients were eligible for the study, with 46 patients (15, 17, and 14 patients in the 8-, 9-, and 10-Gy groups, respectively) available for analysis. The median follow-up duration was 9.6 months (range 2.5-25.1 months). The 6-month estimated cumulative incidence of radiation necrosis was 0% in the 8-Gy group, 13% (95% confidence interval [CI] 0%-29%) in the 9-Gy group, and 37% (95% CI 1%-58%) in the 10-Gy group. Being in the 10-Gy group was a significant risk factor for the development of radiation necrosis ($p = 0.047$; hazard ratio [HR] 7.2, 95% CI 1.1-51.4). The 12-month local PFS rates were 65%, 80%, and 75% in the 8-, 9-, and 10-Gy groups, respectively. Being in the 8-Gy group was a risk factor for local treatment failure ($p = 0.037$; HR 2.5, 95% CI 1.1-29.6). The mean volume change from baseline was a 47.5% decrease in this cohort. Distant intracranial progression and overall survival did not differ among the 3 groups.

In this dose-escalation study, 27 Gy in 3 fractions appeared to be a relevant regimen of fractionated GKS for large BM because 30 Gy in 3 fractions resulted in unacceptable toxicities and 24 Gy in 3 fractions was associated with local treatment failure [1)].

McTyre et al considered candidates for fractionated GKRS if they had 1 or more of the following indications: a benign tumor >10 cc in volume or abutting the optic pathway, a vestibular schwannoma

with the intent of hearing preservation, or a tumor previously irradiated with single-fraction GKRS. The immobilization device used for all patients was the Extend system (Leksell Gamma Knife Perfexion, Elekta, Kungstensgatan, Stockholm).

They identified 34 patients treated with fractionated GKRS between August 2013 and February 2015. There were a total of 37 tumors treated including 15 meningiomas, 11 pituitary neuroendocrine tumors, 6 brain metastases, 4 vestibular schwannomas, and 1 hemangioma. At last follow-up, all 21 patients treated for perioptic tumors had stable or improved vision and all 4 patients treated for vestibular schwannoma maintained serviceable hearing. No severe adverse events were reported.

Fractionated GKRS was well tolerated in the treatment of large meningiomas, perioptic tumors, vestibular schwannomas with intent of hearing preservation, and reirradiation of previously treated tumors [2].

1)
Kim KH, Kong DS, Cho KR, Lee MH, Choi JW, Seol HJ, Kim ST, Nam DH, Lee JI. Outcome evaluation of patients treated with fractionated Gamma Knife radiosurgery for large (> 3 cm) brain metastases: a dose-escalation study. J Neurosurg. 2019 Aug 16:1-10. doi: 10.3171/2019.5.JNS19222. [Epub ahead of print] PubMed PMID: 31419791.
2)
McTyre E, Helis CA, Farris M, Wilkins L, Sloan D, Hinson WH, Bourland JD, Dezarn WA, Munley MT, Watabe K, Xing F, Laxton AW, Tatter SB, Chan MD. Emerging Indications for Fractionated Gamma Knife Radiosurgery. Neurosurgery. 2016 Mar 9. [Epub ahead of print] PubMed PMID: 26963331.