Neoadjuvant gamma knife surgery for metastatic brain tumor: clinical use and impact on leptomeningeal seeding

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Aims and scope

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Abstract

Purpose

This study aimed to compare leptomeningeal seeding (LMS) incidence, local failure rates, and survival outcomes between neoadjuvant and adjuvant gamma knife surgery (GKS) in patients with brain metastases.

Methods

We retrospectively analyzed 120 patients treated at a single institution from 2008 to 2022. Overall survival (OS), progression-free survival (PFS), LMS occurrence, local failure, and key clinical prognostic variables were compared between the neoadjuvant and adjuvant GKS groups.

Results

Seventy patients received neoadjuvant GKS, while 50 received adjuvant GKS. Baseline differences in

primary tumor origin, preoperative Karnofsky Performance Score, and extracranial metastasis were statistically significant. No significant differences were observed in OS ($p = 0.21$), PFS ($p = 0.27$), radiation induced edema ($p = 0.219$) or local failure ($p = 0.19$) between groups. LMS incidence was significantly lower in the neoadjuvant group ($p = 0.043$), with this advantage maintained after propensity score matching ($p = 0.046$).

Conclusions

Neoadjuvant GKS yields survival and local failure outcomes comparable to adjuvant GKS, while significantly reducing the risk of LMS. These findings support the potential clinical advantage of neoadjuvant GKS in the management of brain metastases.

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

References

1. Arvold ND, Lee EQ, Mehta MP et al (2016) Updates in the management of brain metastases. Neuro Oncol 18(8):1043–1065. https://doi.org/10.1093/neuonc/now127

Article PubMed PubMed Central Google Scholar

2. Fox BD, Cheung VJ, Patel AJ, Suki D, Rao G (2011) Epidemiology of metastatic brain tumors. Neurosurg Clin N Am 22(1):1–6. https://doi.org/10.1016/j.nec.2010.08.007

Article PubMed Google Scholar

3. Hatiboglu MA, Akdur K, Sawaya R (2020) Neurosurgical management of patients with brain metastasis. Neurosurg Rev 43(2):483–495. https://doi.org/10.1007/s10143-018-1013-6

Article PubMed Google Scholar

4. Patchell RA, Tibbs PA, Regine WF, Dempsey RJ, Mohiuddin M, Kryscio RJ, Markesbery WR, Foon KA, Young B (1998) Postoperative radiotherapy in the treatment of single metastases to the brain: a randomized trial. JAMA 280(17):1485–1489. https://doi.org/10.1001/jama.280.17.1485

Article PubMed Google Scholar

5. Kocher M, Soffietti R, Abacioglu U et al (2011) Adjuvant whole-brain radiotherapy versus

observation after radiosurgery or surgical resection of one to three cerebral metastases: results of the EORTC 22952–26001 study. J Clin Oncol 29(2):134–141. https://doi.org/10.1200/JCO.2010.30.1655

Article PubMed Google Scholar

6. Chang EL, Wefel JS, Hess KR et al (2009) Neurocognition in patients with brain metastases treated with radiosurgery or radiosurgery plus whole-brain irradiation: a randomised controlled trial. Lancet Oncol 10(11):1037–1044. https://doi.org/10.1016/S1470-2045(09)70263-3

Article PubMed Google Scholar

7. Aoyama H, Shirato H, Tago M et al (2006) Stereotactic radiosurgery plus whole-brain radiation therapy vs stereotactic radiosurgery alone for treatment of brain metastases: a randomized controlled trial. JAMA 295(21):2483–2491. https://doi.org/10.1001/jama.295.21.2483

Article PubMed Google Scholar

8. Brown PD, Ballman KV, Cerhan JH et al (2017) Postoperative stereotactic radiosurgery compared with whole brain radiotherapy for resected metastatic brain disease (NCCTG N107C/CEC.3): a multicentre, randomised, controlled, phase 3 trial. Lancet Oncol 18(8):1049–1060. https://doi.org/10.1016/S1470-2045(17)30441-2

Article PubMed PubMed Central Google Scholar

9. Udovicich C, Ng SP, Tange D, Bailey N, Haghighi N (2022) From postoperative to preoperative: A case series of hypofractionated and Single-Fraction neoadjuvant stereotactic radiosurgery for brain metastases. Oper Neurosurg (Hagerstown) 22(4):208–214. https://doi.org/10.1227/ONS.0000000000000101

Article Google Scholar

10. Yoo J, Cha YJ, Park HH, Park M, Joo B, Suh SH, Ahn SJ (2022) The extent of necrosis in brain metastases may predict subtypes of primary cancer and overall survival in patients receiving craniotomy. Cancers (Basel) 14(7). https://doi.org/10.3390/cancers14071694

11. Ho DE, Imai K, King G, Stuart EA (2011) MatchIt: nonparametric preprocessing for parametric causal inference. J Stat Softw 42(8)

12. Palmer JD, Perlow HK, Matsui JK et al (2022) Fractionated pre-operative stereotactic radiotherapy for patients with brain metastases: a multi-institutional analysis. J Neurooncol 159(2):389–395. https://doi.org/10.1007/s11060-022-04073-w

Article PubMed Google Scholar

13. Udovicich C, Ng SP, Tange D, Bailey N, Haghighi N (2022) From postoperative to preoperative: A case series of hypofractionated and Single-Fraction neoadjuvant stereotactic radiosurgery for brain metastases. Oper Neurosurg 22(4):208–214. https://doi.org/10.1227/ONS.0000000000000101

Article PubMed Google Scholar

14. Ucgul AN, Tugcu AO, Erpolat OP (2025) Neoadjuvant stereotactic radiosurgery for brain metastases: current evidence and clinical perspectives. Biomol Biomed 26(3):377–382. https://doi.org/10.17305/bb.2025.12890

Article PubMed PubMed Central Google Scholar

15. Prabhu RS, Patel KR, Press RH, Soltys SG, Brown PD, Mehta MP, Asher AL, Burri SH (2019) Preoperative vs postoperative radiosurgery for resected brain metastases: A review. Neurosurgery 84(1):19–29. https://doi.org/10.1093/neuros/nyy146

Article PubMed Google Scholar

16. Lehrer EJ, Kowalchuk RO, Ruiz-Garcia H, Merrell KW, Brown PD, Palmer JD, Burri SH, Sheehan JP, Quninoes-Hinojosa A, Trifiletti DM (2022) Preoperative stereotactic radiosurgery in the management of brain metastases and gliomas. Front Surg 9:972727. https://doi.org/10.3389/fsurg.2022.972727

Article PubMed PubMed Central Google Scholar

17. Asher AL, Burri SH, Wiggins WF, Kelly RP, Boltes MO, Mehrlich M, Norton HJ, Fraser RW (2014) A new treatment paradigm: neoadjuvant radiosurgery before surgical resection of brain metastases with analysis of local tumor recurrence. Int J Radiat Oncol Biol Phys 88(4):899–906.

https://doi.org/10.1016/j.ijrobp.2013.12.013

Article PubMed Google Scholar

18. Takami H, Nassiri F, Moraes FY et al (2020) A phase II study of neoadjuvant stereotactic radiosurgery for large brain metastases: clinical trial protocol. Neurosurgery 87(2):403–407. https://doi.org/10.1093/neuros/nyz442

Article PubMed Google Scholar

19. Diehl CD, Shiban E, Straube C et al (2019) Neoadjuvant stereotactic radiosurgery for intracerebral metastases of solid tumors (NepoMUC): a phase I dose escalation trial. Cancer Commun (Lond) 39(1):73. https://doi.org/10.1186/s40880-019-0416-2

Article PubMed Google Scholar

20. Li YD, Coxon AT, Huang J et al (2022) Neoadjuvant stereotactic radiosurgery for brain metastases: a new paradigm. Neurosurg Focus 53(5):E8. https://doi.org/10.3171/2022.8.FOCUS22367

Article PubMed PubMed Central Google Scholar

21. Patel KR, Burri SH, Asher AL et al (2016) Comparing preoperative with postoperative stereotactic radiosurgery for resectable brain metastases: A Multi-institutional analysis. Neurosurgery 79(2):279–285. https://doi.org/10.1227/NEU.0000000000001096

Article PubMed Google Scholar

22. Patel KR, Burri SH, Boselli D et al (2017) Comparing pre-operative stereotactic radiosurgery (SRS) to post-operative whole brain radiation therapy (WBRT) for resectable brain metastases: a multi-institutional analysis. J Neurooncol 131(3):611–618. https://doi.org/10.1007/s11060-016-2334-3

Article PubMed Google Scholar

23. Patel AR, Nedzi L, Lau S et al (2018) Neoadjuvant stereotactic radiosurgery before surgical resection of cerebral metastases. World Neurosurg 120:E480–E487. https://doi.org/10.1016/j.wneu.2018.08.107

Article PubMed Google Scholar

24. Goldberg SB, Schalper KA, Gettinger SN et al (2020) Pembrolizumab for management of patients with NSCLC and brain metastases: long-term results and biomarker analysis from a non-randomised, open-label, phase 2 trial. Lancet Oncol 21(5):655–663. https://doi.org/10.1016/S1470-2045(20)30111-X

Article PubMed PubMed Central Google Scholar

25. Tawbi HA, Forsyth PA, Algazi A et al (2018) Combined nivolumab and ipilimumab in melanoma metastatic to the brain. N Engl J Med 379(8):722–730. https://doi.org/10.1056/NEJMoa1805453

Article PubMed PubMed Central Google Scholar

26. Palmisciano P, Ferini G, Khan R, Bin-Alamer O, Umana GE, Yu K, Cohen-Gadol AA, El Ahmadieh TY, Haider AS (2022) Neoadjuvant stereotactic radiotherapy for brain metastases: systematic review and meta-analysis of the literature and ongoing clinical trials. Cancers (Basel) 14(17). https://doi.org/10.3390/cancers14174328

27. Routman DM, Yan E, Vora S et al (2018) Preoperative stereotactic radiosurgery for brain metastases. Front Neurol 9:959. https://doi.org/10.3389/fneur.2018.00959

Article PubMed PubMed Central Google Scholar

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Contributions

JY, I-H.J: Contributed to data collection, analysis, and interpretation. Drafted the initial version of the manuscript and was involved in manuscript review and editing.; WSC, HHJ, HHP: Assisted with data collection and analysis. Participated in manuscript drafting and critically revised the manuscript.; JHM, EHK, S-G.K: Provided supervision and contributed to the conceptualization and design of the study. Assisted with data interpretation and reviewed the manuscript for important intellectual content.; JHC: Led the conceptualization and design of the study. Provided overall supervision, secured funding, and critically reviewed the final manuscript.

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Ethics declarations

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Institutional Review Board of Severance Hospital, Yonsei University College of Medicine (IRB 4-2023-0105). Patient information was anonymized and de-identified before the analysis.

Consent to participate

Consent from participants was waived due to the retrospective nature of the study.

Consent to publish

Consent to publish was waived as this was a retrospective study with all patients anonymized.

Competing interests

The authors declare no competing interests.

Additional information

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Supplementary information

Below is the link to the electronic supplementary material.

Supplementary Material 1

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