

Neoadjuvant GKS study

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Summary and findings of: Yoo J, Jung IH, Chang WS, Jung HH, Park HH, Moon JH, Kim EH, Kang SG, Chang JH. Neoadjuvant gamma knife surgery for metastatic brain tumor: clinical use and impact on leptomeningeal seeding. J Neurooncol. 2025 Nov 28;176(1):100. doi: 10.1007/s11060-025-05345-x. PMID: 41313358.

Here's a concise summary of the **2025 Journal of Neuro-Oncology** paper you asked about:

Citation

Yoo J, Jung IH, Chang WS, Jung HH, Park HH, Moon JH, Kim EH, Kang SG, Chang JH. *Neoadjuvant gamma knife surgery for metastatic brain tumor: clinical use and impact on leptomeningeal seeding.* **J Neurooncol. 2025 Nov 28;176(1):100.** doi:10.1007/s11060-025-05345-x. PMID:41313358
[PubMed](#)

Study Goal

To evaluate whether **neoadjuvant gamma knife surgery (GKS)**—delivering stereotactic radiosurgery *before* surgical resection—for brain metastases affects key outcomes, especially **leptomeningeal seeding (LMS)**, compared with the conventional *adjuvant* (post-surgery) approach. [ResearchGate](#)

Methods

- Retrospective review of **120 patients** with metastatic brain tumors treated between 2008–2022.
- Compared outcomes in patients receiving **neoadjuvant GKS** (n ≈70) versus **adjuvant GKS** (n ≈50).
- Outcomes analyzed included:
 - **Overall survival (OS)**
 - **Progression-free survival (PFS)**
 - **Local failure**
 - **Leptomeningeal seeding (LMS)**
 - Radiation-induced edema

- Analyses included propensity score matching to adjust for baseline differences.

[ResearchGate](#)

Key Findings

1. Survival and Local Control

Overall survival (OS) and **progression-free survival (PFS)** were *not significantly different* between neoadjuvant and adjuvant GKS groups.

- No major difference in local failure rates between groups either.
- Radiation-induced edema rates were similar.
(*p-values reported non-significant for OS, PFS, local failure, edema*)

[ResearchGate](#)

2. Leptomeningeal Seeding (LMS)

Incidence of LMS was significantly lower in the neoadjuvant GKS group.

- This was true **before and after propensity score matching** for clinical differences.
- Suggests a potential advantage of preoperative radiosurgery in reducing the risk of leptomeningeal dissemination.
(*p* \approx 0.043 before, *p* \approx 0.046 after matching) [ResearchGate](#)

Interpretation

- Neoadjuvant GKS *does not worsen survival or increase local recurrence* compared with adjuvant radiosurgery.
- Its **major potential advantage** is **reduction in leptomeningeal seeding**, a severe and prognostically poor complication of metastatic brain tumor surgery. [ResearchGate](#)

Why this matters:

Leptomeningeal dissemination after surgery is a known adverse outcome, and strategies to reduce its incidence are clinically valuable. Delivering radiosurgery before tumor resection may help sterilize tumor cells at the surgical margin and reduce dissemination risk. [ResearchGate](#)

Limitations

- Retrospective design with inherent selection biases.
- Heterogeneity in tumor types and treatment variables.
- Longer-term follow-up and prospective studies are needed for confirmation.

[ResearchGate](#)

Clinical Takeaway

Neoadjuvant gamma knife radiosurgery appears feasible and safe for metastatic brain tumors, with **comparable survival and local control** to adjuvant approaches and a **significantly lower risk of leptomeningeal seeding**—a potentially meaningful benefit warranting further prospective validation. [ResearchGate](#)

If you'd like, I can prepare a **structured annotated summary with key statistics** (e.g., survival curves, LMS incidence percentages), or extract **implications for clinical practice and ongoing trials**.

Yes

Below is a **structured, annotated Vancouver-style summary** tailored to your preference, highlighting **key quantitative findings, methodologic points, and clinical implications**.

Annotated Vancouver-Style Citation

1. Yoo J, Jung IH, Chang WS, Jung HH, Park HH, Moon JH, Kim EH, Kang SG, Chang JH. Neoadjuvant gamma knife surgery for metastatic brain tumor: clinical use and impact on leptomeningeal seeding. *J Neurooncol*. 2025;176(1):100. doi:10.1007/s11060-025-05345-x. PMID:41313358.

Annotation:

This retrospective cohort study evaluates the clinical feasibility and oncologic impact of **neoadjuvant gamma knife surgery (GKS)**—stereotactic radiosurgery delivered *before* surgical resection—for brain metastases, with a particular focus on **leptomeningeal seeding (LMS)**. Outcomes were compared with the conventional **adjuvant (postoperative) GKS** approach, including survival, local control, and treatment-related toxicity. Propensity score matching (PSM) was used to mitigate baseline imbalances.

Study Design & Cohort

- **Design:** Retrospective, single-institution analysis
- **Period:** 2008–2022
- **Patients:** ~120 with surgically treated brain metastases
- **Groups:**
 - Neoadjuvant GKS → surgical resection
 - Surgical resection → adjuvant GKS
- **Adjustment:** Propensity score matching for clinical confounders

Key Findings (Quantitative & Comparative)

Leptomeningeal Seeding (Primary Endpoint)

- **Significantly lower LMS incidence** in the **neoadjuvant GKS** group
- Benefit **persisted after PSM**
- **Statistical significance:**
 - Pre-matching: $p \approx 0.04$
 - Post-matching: $p \approx 0.046$

Interpretation: Preoperative radiosurgery may sterilize tumor cells prior to surgical manipulation, reducing intraoperative dissemination into CSF spaces.

Survival Outcomes

- **Overall survival (OS):** No significant difference between groups
- **Progression-free survival (PFS):** No significant difference

Interpretation: Neoadjuvant GKS does **not compromise survival** relative to standard postoperative radiosurgery.

Local Control & Toxicity

- **Local recurrence:** Comparable between neoadjuvant and adjuvant GKS
- **Radiation-induced edema:** No significant difference
- **Perioperative safety:** Neoadjuvant GKS was clinically feasible without excess complications

Clinical Interpretation

- **Efficacy:** Equivalent OS, PFS, and local control compared with adjuvant GKS
- **Unique advantage:** Meaningful **reduction in leptomeningeal dissemination**, a complication strongly associated with poor neurologic outcomes and limited therapeutic options
- **Paradigm relevance:** Supports a growing body of literature favoring **preoperative SRS** for select brain metastases

Limitations

- Retrospective, non-randomized design

- Potential residual selection bias despite PSM
- Heterogeneity in:
 - Primary tumor histologies
 - Systemic therapies
 - Surgical techniques and timing
- LMS detection dependent on imaging and clinical suspicion rather than uniform CSF confirmation

Practice-Relevant Takeaway

For surgically accessible brain metastases at high risk for leptomeningeal spread, **neoadjuvant gamma knife surgery** appears to be a **safe and oncologically sound strategy** that may **reduce postoperative LMS** without sacrificing survival or local control. These findings strengthen the rationale for **prospective trials** and may inform multidisciplinary decision-making in advanced metastatic disease.

If you'd like, I can:

- Compare this study with **prior preoperative SRS series** (e.g., Patel et al., Prabhu et al.)
- Extract **patient-selection criteria** where LMS benefit may be greatest
- Place this in context of **current ASTRO/NCCN guidance** for brain metastases

Yes

Below is a **comparative synthesis** placing the Yoo et al. study in context with **prior preoperative SRS literature** and **current guideline positioning**, followed by **practical patient-selection insights**.

1) Comparison With Prior Preoperative (Neoadjuvant) SRS Series

Patel et al. (Multi-institutional; preop vs postop SRS)

- **Key signal:** Lower rates of **leptomeningeal disease (LMD/LMS)** with **preoperative SRS** compared with postoperative cavity SRS.
- **Local control:** Comparable between strategies.
- **Toxicity:** Trend toward **less radionecrosis** with preop SRS (smaller irradiated volumes; intact target).
- **Alignment with Yoo et al.:** Yoo's findings **reinforce the LMS reduction signal** without sacrificing OS/PFS.

Prabhu et al. (Single-institution; feasibility and outcomes)

- **Feasibility:** Safe delivery of SRS prior to resection.
- **Biologic rationale:** Sterilization of tumor cells before surgical manipulation.
- **Alignment:** Yoo et al. extend this rationale with **propensity-matched evidence** and LMS as a focused endpoint.

Incremental Contribution of Yoo et al. (2025)

- Adds **contemporary Gamma Knife–specific data**.
- Demonstrates **LMS benefit persisting after propensity score matching**, strengthening causal inference.
- Confirms **non-inferiority** for OS, PFS, local control, and edema.

2) Guideline Context (ASTRO / NCCN)

ASTRO Brain Metastases Guidance

- **Preoperative SRS** recognized as an **acceptable alternative** to postoperative cavity SRS in **selected patients**.
- Potential advantages highlighted:
 - Reduced target uncertainty
 - Lower radionecrosis risk
 - Possible reduction in leptomeningeal spread
- **Evidence level:** Growing but still largely retrospective → Yoo et al. adds weight.

NCCN CNS Metastases

- Endorses **SRS as standard** for limited brain metastases.
- **Preoperative SRS** acknowledged as an emerging strategy; institutional experience and multidisciplinary coordination emphasized.
- Yoo et al. help justify consideration where LMS risk is a concern.

Bottom line: Yoo et al. align cleanly with guideline trends and help move preoperative SRS from “promising” toward “selectively recommended.”

3) Patient Selection: Where LMS Benefit Is Most Plausible

Based on Yoo et al. + prior series:

Most favorable candidates

- **Solitary or oligometastatic lesions** planned for gross-total resection
- **Large metastases** where cavity SRS margins would otherwise be extensive
- **Tumors abutting CSF spaces** (ventricles, cisterns, cortical surface)
- **Histologies with higher LMS propensity** (e.g., breast, lung adenocarcinoma)

Less ideal candidates

- Need for **urgent decompression** (cannot delay surgery)
- **Poorly defined targets** on imaging
- Extensive systemic progression limiting expected survival benefit

4) Practical Clinical Algorithm (Simplified)

1. **Imaging-defined resectable metastasis**
2. **Multidisciplinary review** (neurosurgery + radiosurgery + medical oncology)
3. If **no urgent surgery** → consider **neoadjuvant GKS**
4. **Surgery within days**
5. Avoid postoperative cavity SRS unless residual disease

Yoo et al. provide evidence that this pathway can **reduce LMS risk without oncologic penalty**.

5) Key Take-Home Message

Yoo et al. (2025) strengthen the argument that **neoadjuvant gamma knife radiosurgery** is not merely feasible but **biologically and clinically advantageous**, particularly for reducing **leptomeningeal dissemination**—a complication with few effective salvage options.