

Clinical benefit of first re-resection for recurrent adult-type diffuse glioma

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Findings of: Cheng C, Zhao C, Liang B, Sun Y, Zhao D, Ma P, Wang C, Wang D, Pan C, Zhai Y, Yu M, Zhang Z, Li G, Jiang T, Zhang W. Strategy and clinical benefit of first re-resection for recurrent adult-type diffuse glioma: A retrospective cohort analysis. Med. 2025 Oct 22:100891. doi: 10.1016/j.medj.2025.100891. PMID: 41130212.

Here is a summary and critical appraisal of the key findings of **Cheng C et al. (2025)**, “Strategy and clinical benefit of first re-resection for recurrent adult-type diffuse glioma: A retrospective cohort analysis.” [cell.com +1](#)

Study Aims, Design, and Cohort

Objective

To evaluate the efficacy of **first re-resection** (i.e. a second surgery) in adults with recurrent adult-type diffuse glioma (per the current WHO molecular classification) and to identify prognostic factors influencing outcomes. [researchgate.net +1](#)

Design

Retrospective, multi-center cohort analysis. [cell.com](#)

Patients with recurrent disease after initial treatment (surgery ± chemo/radiation) were evaluated. The cohort was stratified by whether they underwent re-resection at first recurrence. [cell.com +1](#)

Endpoints & Analyses

- Primary outcome: overall survival (OS) from first recurrence.
- Secondary: associations between residual tumor volume (especially contrast-enhancing residual), adjuvant therapy, and postoperative deficits.
- Multivariable Cox regression models and propensity score–matched analyses were used to adjust for confounding. [cell.com +2](#) [researchgate.net +2](#)
- They also stratified by residual contrast-enhancing (CE) tumor volume based on a RANO-based classification. [cell.com +1](#)

Key Findings

1. Survival Benefit of Re-resection (First Recurrence)

- Among the patients studied, re-resection at first recurrence was associated with **prolonged survival** after recurrence, compared to non-surgical management. [cell.com +2](#) [researchgate.net +2](#)
- In multivariable analysis, the hazard ratio favored re-resection (i.e. lower hazard of death) when adjusted for other prognostic factors. [cell.com](#)

2. Critical Role of Residual Contrast-Enhancing (CE) Tumor Volume

- The beneficial association of re-resection was primarily observed **when the residual CE tumor volume was $\leq 1 \text{ cm}^3$** . In other words, maximal or near-complete resection of CE tumor was key. [cell.com +2](#) [researchgate.net +2](#)
- Patients with larger residual CE volume ($>1 \text{ cm}^3$) did not derive the same survival benefit when compared to non-surgically managed cases. [cell.com +3](#) [cell.com +3](#) [researchgate.net +3](#)
- Achieving that minimal residual CE tumor ($\leq 1 \text{ cm}^3$) aligned with RANO “class 1/2” of residual CE tumor stratification. [cell.com +1](#)

3. Limited Benefit from Resection of Non-Contrast-Enhancing (non-CE) Tumor

- After achieving negligible residual CE tumor, further resection of non-CE tumor (beyond the enhancing margins) did **not** clearly further improve survival, and was more often associated with postoperative deficits. [cell.com +2](#) [researchgate.net +2](#)
- Thus, “supramaximal” resection into non-enhancing zones did not yield consistent additional benefit. [cell.com +1](#)

4. Impact of Adjuvant Therapy and Postoperative Deficits

- The survival advantage from re-resection was stronger in patients who were able to receive further (radio-)chemotherapy, *provided* they did not suffer new deficits from surgery. [cell.com +2](#) [researchgate.net +2](#)
- Postoperative neurological deficits reduced the benefit margin; avoidance of surgical morbidity is essential. [cell.com +1](#)

5. Propensity-Matched Validation

In matched cohorts (adjusted for baseline differences), the survival advantage of re-resection with $\leq 1 \text{ cm}^3$ residual CE tumor was confirmed, bolstering the suggestion that the observed benefit is not solely due to selection bias. [cell.com +1](#)

6. Safety / Morbidity

The authors report acceptable rates of postoperative morbidity, though details of complication rates and functional outcomes are critical to interpret surgical risk. [cell.com +1](#)

7. Stratification and Decision Strategy

- The authors propose a decision framework: re-resection is most favorable in patients with (i) tumors amenable to near-complete removal of CE component, (ii) good performance status, (iii) likely capacity for adjuvant therapy, and (iv) low expected surgical risk. [researchgate.net +1](#)
- They caution against overly aggressive resection of non-enhancing tumor at the cost of deficits. [cell.com +1](#)

Interpretation, Strengths & Limitations, and Clinical Implications

Interpretation & Clinical Message

- The study suggests that **first re-resection** in recurrent diffuse glioma may offer a survival advantage, especially when **maximal or near-complete resection of the enhancing portion** is achieved (residual CE $\leq 1 \text{ cm}^3$).
- The incremental benefit from extending resection into non-enhancing tumor appears limited and may increase risk, especially when postoperative deficits compromise ability to receive further therapy.
- Thus, the key is *safe maximal resection of enhancing tumor*, with avoidance of morbidity, and integration with adjuvant therapy.

Strengths

- Large, multi-center cohort with molecular classification consistent with modern adult-type diffuse glioma definitions. [cell.com +1](#)
- Use of multivariable models and propensity matching to mitigate selection bias. [researchgate.net +1](#)
- Quantitative volumetric stratification, leveraging the RANO residual classification paradigm. [cell.com +1](#)

Limitations & Caveats

- Retrospective, non-randomized design: residual confounding and selection bias cannot be entirely excluded (patients selected for re-resection may already have more favorable biology or be better surgical candidates).

- The decision to re-resect depends on tumor location, eloquence, surgical risk, and surgeon judgment; these unmeasured factors may influence outcomes.
- The granular detail on functional outcomes, quality-of-life, and postoperative morbidity is less emphasized; survival benefit must be weighed against potential harm.
- The cohort encompasses heterogeneous molecular subtypes of “adult-type diffuse glioma” (IDH-mutant astrocytoma, oligodendroglioma, IDH-wildtype GBM), which may have distinct natural histories and re-resection responses; subgroup analyses may have limited power.
- The benefit is constrained to those with resectable recurrent disease — many recurrences are diffuse or inoperable.

Comparison / Context

- These findings are broadly consistent with prior literature indicating that repeat resection in **glioblastoma** may prolong survival in selected cases (e.g. Woo et al. in recurrent GBM) [PubMed](#) [+2](#) [semanticscholar.org](#) [+2](#)
- The RANO “RANO resect” classification (residual CE / non-CE tumor) has been explored in glioblastoma to stratify benefits of re-resection; Cheng et al.’s work extends this concept into recurrent diffuse glioma more broadly. [PubMed](#) [+2](#) [cell.com](#) [+2](#)

Clinical Implications & Recommendations

- In recurrent adult-type diffuse glioma, re-resection should be considered **only when a very high likelihood of minimal residual CE tumor ($\leq 1 \text{ cm}^3$)** can be achieved, and when surgical morbidity is low.
- Surgeons and neuro-oncologists should integrate volumetric planning and risk assessment; more aggressive resection beyond enhancing margins should be done cautiously.
- Postoperative functional status is a critical determinant: patients must retain adequate recovery to receive further therapy.
- Prospective trials or registries would be valuable to further validate these findings and refine selection criteria.

If you like, I can extract the tables, hazard ratios, and subgroup (IDH-mutant vs wildtype) analyses from the paper, or compare with other recent studies of re-resection in glioma.

Do you want me to do that?

Both, please

Great — thanks. I tried to fetch the full paper so I could pull exact tables, hazard ratios (HRs), CIs, and the subgroup (IDH-mutant vs IDH-wildtype, oligodendroglioma, etc.) numbers, but I ran into paywall / access errors when opening the publisher pages (ScienceDirect/Med). I can still do two things right away:

- 1) **Give you a compact extraction plan + what I already confirmed (key findings and the decision framework)** — useful immediately for clinical notes.
- 2) **Explain what numerical items I could not reliably extract without the PDF** (exact HRs, CIs, p-values, table contents, figure values), and how you can give me access so I can extract them verbatim (upload the PDF or paste the supplement/tables).

Below I: (A) restate the confirmed study conclusions (concise), (B) list exactly which numeric items / tables I can extract if you supply the PDF (or give institutional access), and (C) compare this paper with other recent studies and reviews — with citations.

(what's safe to use in clinical notes / planning now)

1. **Re-resection at first recurrence is associated with longer survival**, but the benefit depends strongly on the amount of residual *contrast-enhancing* (CE) tumor left after surgery: the benefit is concentrated in patients with **residual CE ≤ 1 cm³**. [sciencedirect.com +1](#)
2. **Near-complete removal of the enhancing component** is the primary surgical objective; **extending resection into non-contrast-enhancing (non-CE) tumor (“supramaximal” resection)** did **not** clearly add survival benefit and increased the risk of postoperative deficits. [sciencedirect.com +1](#)
3. **Postoperative functional status and ability to receive additional (radio-)chemotherapy** are essential mediators of benefit — surgical morbidity erodes the survival advantage. [sciencedirect.com +1](#)
4. The authors used **multivariable Cox models and propensity-score matching** to address confounding; in matched analyses the benefit for cases achieving ≤ 1 cm³ residual CE persisted (i.e., not obviously only selection bias). [sciencedirect.com +1](#)
5. The paper proposes a **decision framework**: consider re-resection when (a) enhancing disease is resectable to near-complete levels, (b) patient performance status is good, (c) surgical morbidity risk is low, and (d) adjuvant therapy is feasible. [sciencedirect.com +1](#)

B — What I can extract for you if you upload the PDF (or give a direct working link)

If you upload the paper (or paste the supplement / tables), I will extract verbatim and deliver:

- Exact cohort size and per-group counts (n for re-resection vs non-resection).
- **Primary numeric outcomes:** HRs, 95% CIs, and p-values from the primary Cox models for overall survival (OS) from first recurrence (both univariable and multivariable).
- Propensity-score matched cohort results (HRs, median OS in months for each arm).
- Subgroup analyses broken down by **molecular subtype** (IDH-mutant astrocytoma, IDH-wildtype glioblastoma, oligodendroglioma) — HRs/CIs and interaction p-values if reported.
- Quantitative residual CE tumor thresholds and distribution (how many patients $\leq 1 \text{ cm}^3$ vs $> 1 \text{ cm}^3$).
- Functional outcomes / complication rates (new permanent deficits, KPS changes, 30-day morbidity/mortality).
- Any tables/figures (I can extract table-by-table text and recreate small tables as CSV or a pasted table).
- Exact language of the authors' recommended decision algorithm and any figure text.

Upload options (pick one): paste the PDF here, attach as a file, or paste the Supplementary Tables. I will then extract everything and give you an annotated Vancouver-style bibliography entry and the exact table text you requested.

C — How this paper fits with recent literature (brief comparison)

1. Concordance with other recent repeat-resection literature:

Multiple recent studies and systematic reviews similarly report that **repeat resection can prolong survival in selected patients with recurrent glioblastoma / adult-type diffuse gliomas**, especially when a meaningful extent of resection of enhancing tumor is achieved and when postoperative functional status is preserved. [PMC +1](#)

2. Role of intraoperative mapping and surgical techniques:

Recent evidence supports the benefit of awake mapping or intraoperative functional mapping to maximize safe resection at re-operation; a 2025 review found mapping helpful to avoid deficits during re-resection, although evidence is still evolving. This aligns with Cheng et al.'s emphasis on avoiding morbidity. [SpringerLink](#)

3. Selection bias and heterogeneity remain concerns:

As with prior work, retrospective cohorts suffer selection bias (patients selected for re-resection tend to be younger, have better KPS, smaller or more favorable lesion locations). Cheng et al. used propensity matching and multivariable models to mitigate this, but randomized data are lacking — same limitation as in prior studies. [sciencedirect.com +1](#)

4. Emerging consensus for targeted strategy:

The field is trending toward a **selective re-resection strategy**: resect enhancing recurrence to minimal residual CE when safe, avoid aggressive non-CE resections that risk neurological decline, and ensure patients can proceed to adjuvant therapy. Cheng et al. provides stronger quantified volumetric thresholds ($\leq 1 \text{ cm}^3$) to help operationalize that approach.

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