

Neurosurgeons' perspective on surgical treatment of glioblastoma: Practices, beliefs and willingness to randomize in surgical trials

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Abstract

Background. The optimal extent of resection for glioblastoma remains debated, with high-level evidence from randomized controlled trials (RCTs) notably scarce. We aimed to evaluate international surgical practices, perceived quality of evidence, and feasibility of future RCTs through an international survey of neurosurgeons.

Methods. An international survey was distributed via European Organization for Research and Treatment of Cancer (EORTC), European Association of Neurosurgical Societies (EANS), Congress of Neurological Surgeons (CNS), and national societies. We used descriptive statistics to summarize surgical practices and univariate analysis and multivariate regression to identify demographic or institutional factors associated with clinical decision-making.

Results. Responses were received from 328 neurosurgeons across 38 countries. Participation was predominantly from Europe (81.1%), with 12.2% from North America. Most participants (82.9%) practiced in academic centers. While 60.4% identified supramarginal resection (SMR) as the optimal surgical goal, 37.8% aim for complete resection of enhancing tumor (CRET). Overall, 90.2% viewed the evidence for CRET as strong, compared to 63.1% for SMR. Despite these views, 72.6% expressed willingness to randomize patients between CRET and SMR, while 49.4% would be willing to randomize between partial resection and biopsy, if CRET is not feasible. Despite differences in individual practice, willingness to participate in RCTs remained consistent across geographic regions. The incomplete overlap between case-based decisions and general willingness to randomize highlights the importance of case-specific nuances. A paradox was observed where perceived weak evidence correlated with lower willingness to randomize ($P < .001$).

Conclusion. There is substantial global willingness among neurosurgeons to participate in surgical RCTs for glioblastoma. These findings provide a foundation for designing future international trials to resolve long-standing controversies regarding optimal surgical strategy for glioblastoma.

Key Points

- 72.6% of surgeons are willing to randomize between CRET and supramarginal resection.
- Regional practice variations do not preclude global trial participation.
- Results confirm sufficient clinical equipoise for future surgical glioblastoma RCTs.

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Importance of the Study

While the association between extent of resection and survival in glioblastoma is well-documented, the neuro-oncological community lacks Class I evidence to define the “optimal” surgical goal. This study addresses a critical barrier to high-level evidence: surgeon equipoise. By surveying a global cohort of 328 neurosurgeons, we revealed a significant disconnect between perceived evidence strength and the willingness to randomize, particularly regarding supramarginal resection. The findings are pivotal for 3 reasons: first, they quantify the

international willingness to participate in surgical (randomized controlled trials) RCTs; second, they identify regional practice variations that could influence trial recruitment; and third, they highlight a “knowledge paradox” where perceived weak evidence correlates with lower trial participation. These insights provide a strategic roadmap for cooperative groups to design feasible, well-powered surgical trials that can finally move glioblastoma management from expert-opinion-based practice to evidence-based standards.

The field of oncological neurosurgery is often characterized by a scarcity of high-level evidence, partly due to the limited number of randomized controlled trials (RCTs).¹⁻⁵ For an RCT to be ethically and practically feasible, a state of clinical and scientific equipoise is necessary, meaning there is genuine uncertainty regarding the comparative therapeutic merits of the interventions being tested.⁶ There is no widespread consensus among neurosurgeons on the optimal surgical management of glioblastoma, and neurosurgeons typically have specific—at times dogmatic—practices in clinical management and decision-making. Performing an RCT would require a willingness to put these aside and to embrace the clinical uncertainty. In a large international multicenter survey focusing on decision-making and surgical modality selection in patients with glioblastoma, significant variability among surgeons and centers in local decision-making practices and surgical treatment preferences was observed.⁷ This finding may also correlate with how neurosurgeons perceive evidence in surgical neuro-oncology, specifically regarding their engagement with clinical trials and views on randomization. Another survey examined considerations for a surgical RCT for patients with diffuse low-grade gliomas (DLGG).⁸ This survey was prompted by a shift toward upfront maximal safe resection for DLGGs without clear evidence from an RCT. Over half of the respondents (54%) believed that a surgical RCT for DLGGs would not be ethical, and nearly 70% did not believe that equipoise, defined here as the state of genuine uncertainty about the benefits or harms of different treatments, actually exists. The main barriers to performing RCTs appear to be the neurosurgeons' perceptions of safety and existing evidence.⁸

Both surveys demonstrate a wide variety in clinical decision-making regarding when choosing among observation (for low-grade glioma only), biopsy, and maximal resection. Both underscore a common theme: despite the existence of guidelines, significant variations in neurosurgical practice persist for glioblastoma and DLGG, stemming from a lack of high-level evidence or broad consensus on certain critical decisions. Specifically in glioblastoma, there is ongoing debate on whether supramarginal resection (SMR) should be the preferred approach over complete resection of enhancing tumor (CRET). Also in cases where CRET is not feasible, there is currently no clear evidence showing that partial resection (PR) provides survival benefit over biopsy alone. Thus, higher-level evidence is needed to better inform surgical treatment of glioblastoma. The

acceptance and willingness of the broader community to perform randomized clinical trials in the setting of surgical treatment of glioblastoma is unknown.

We designed a survey to evaluate neurosurgeons' stances and habits regarding various aspects of glioblastoma surgery, particularly focusing on known controversies regarding the ideal extent of resection to be aimed for. The goal of this survey was to better understand themes of controversy, estimate neurosurgeons' perception of evidence, assess equipoise, and ultimately evaluate openness to performing RCTs in different contexts in glioblastoma surgery.

Methods

Survey Design and Distribution

The study employed a survey that was internationally distributed to neurosurgeons. The survey was conceptualized and drafted by JD, AJ, and AM, after which it was reviewed and refined by all members of the Neurosurgery Committee of the European Organization for Research and Treatment of Cancer (EORTC) Brain Tumor Group. The survey was distributed as a Google Forms link (Google, SF, USA) through the EORTC, European Association of Neurosurgical Societies (EANS), and Congress of Neurological Surgeons (CNS), through the Belgian, Spanish, British German, and French national societies, as well as through individual neurosurgeons from the USA, Europe and Australia. The survey was open from September 24, 2024 until February 7, 2025.

The questions assessed demographics of participating neurosurgeons; current surgical practices in glioblastoma surgery (such as general strategies and adjuncts used), opinions on the evidence for and applicability of CRET and SMR, willingness to randomize patients in hypothetical clinical trial scenarios; and approaches to multifocal glioblastoma. Six cases, representing various situations that test the answers to the general questions made earlier, were presented at the end of the survey, along with an open question asking what the respondent felt was the main unaddressed controversy in glioblastoma surgery. A shorter survey version that omitted the specific question on multifocal glioblastoma and the cases with multifocal glioblastoma was the main survey circulated through CNS. The survey questions can be found in the [supplementary data](#).

A waiver of requirement for formal approval was obtained from the UZ Brussel ethics board board, since the study involved an anonymous survey of healthcare professionals and did not involve patients or clinical interventions. Informed consent was implied by the voluntary completion and submission of the survey. All data were collected and analyzed anonymously, except where participants specifically opted to provide contact details for further collaboration.

Statistical Analysis

Survey responses were exported from Google Forms into Excel for initial data cleaning and preparation, and duplicate entries were removed. In case of duplicate entries with different responses from the same surgeon, the first fully completed survey was retained. All analyses were conducted using R, version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria), with a significance level of $P \leq .05$. Descriptive statistics were used to summarize participant demographics, general surgical practices, opinions on key procedures, and willingness to participate in clinical trials. Categorical and ordinal variables were summarized as frequencies and percentages.

All pairwise associations between categorical variables were assessed using Chi-square or Fisher's exact tests. When expected cell counts were < 5 , Monte Carlo simulation with 10,000 iterations was applied. For 2×2 categorical comparisons, odds ratios (ORs) with 95% confidence intervals (CI) were included. For larger contingency tables, Cramér's V was reported to indicate the strength of association. P -value were corrected for multiple comparisons using Benjamini-Hochberg. It needs to be noted that, due to the large number of comparisons, there is an increased risk of false positives, even with BH correction. Therefore, the analyses were considered exploratory rather than confirmatory, aiming at identifying potential associations to guide further modeling.

Multiple logistic regression models were used for dichotomous outcomes. For ordinal outcomes, cumulative ordinal logistic regression models (proportional odds models) were applied using the same set of respondent and institution-level predictors. ORs and 95% CI were obtained by exponentiating regression coefficients. Statistical significance was assessed using Wald tests on the log-odds scale. Results are reported as ORs with 95% CIs and corresponding P -value. Statistical significance was set at $P < .05$.

For the response evaluation to cases, general versus case-specific willingness to randomize were assessed using chi-square tests and Cramér's V. For Cases 1-3, willingness to randomize SMR vs CRET was cross-tabulated against case-specific willingness. For Cases 4-6, willingness to randomize between PR and biopsy was used. Preferred surgical approach versus case-specific preference was similarly examined by chi-square and Cramér's V; for Cases 1 and 3, ORs with 95% CI were calculated comparing SMR/FLAIR versus CRET. Evidence perception and career stage were each cross-tabulated against case-specific willingness using chi-square; evidence perception analyses were conducted for Cases 1-3, and career-stage analyses for Cases 1-4.

Logistic regression was performed for Cases 1 and 2. Predictors included general willingness (ordinal: No=1, Undecided=2, Yes=3), surgical goal (binary: CRET=0, SMR/FLAIR=1), and career stage (ordinal). Results are reported as ORs with 95% CIs and Wald P -value; model fit was evaluated using McFadden's pseudo- R^2 . For Cases 5 and 6 ($n=289$), each case contained 2 randomization questions addressing biopsy versus resection and resection of one versus all lesions. General multifocal surgical attitude (5 categories) and general PR/biopsy willingness were each cross-tabulated against case-specific willingness using chi-square and Cramér's V, and preferred approach versus willingness was examined by chi-square. McNemar's test was used for paired comparisons of Case 5 versus Case 6 responses within each question type. For all case-level, a two-sided $P < .05$ threshold was applied throughout without correction for multiple comparisons.

Results

Descriptive Analysis

The study population is presented in Table 1. A total of 328 neurosurgeons completed the survey (Figure 1). Of these, 56 (17.6%) were female, 268 (81.8%) were male, and 4 (1.2%) preferred not to disclose their gender. Respondents were practicing in Europe (81.1%), followed by North America (12.2%), Asia (2.7%), Oceania (2.1%), and South America (1.8%). At the regional level, Western Europe accounted for the largest proportion of participants (34.1%), followed by Southern Europe (24.1%) and Northern Europe (18.9%). Smaller proportions originated from Northern America (11.3%), Eastern Europe (4.0%), and other regions including Australia and New Zealand, Central America, Eastern Asia, Southern Asia, and Western Asia.

Most surgeons practiced in academic centers (244/328; 74.4%), followed by combined academic/nonacademic affiliations (28/328; 8.5%) and exclusively private or public non-academic affiliations (56/328; 17.1%). Career stages of participants, as well as the number of glioma or other intrinsic brain tumors operated on yearly by the responding surgeons, are listed in Table 1.

Technical adjunct use during glioblastoma surgery was common: neuronavigation was used by 98.5% of respondents (323/328), 79.6% are using neuromonitoring, including awake surgery (261/328), 83.2% use fluorescence (273/328), while ultrasound was used by 60.4% (198/328). In total, 35.3% (115/328) use Positron Emission Tomography (PET)-scan in the pre- or postoperative assessment of glioblastoma. Most respondents (270/328, 83.2%) perform awake surgery in less than 20% of glioblastoma cases.

Regarding optimal surgical goals in glioblastoma surgery, 194/328 (59.1%) consider SMR or FLAIRectomy the optimal goal, whereas 124/328 (37.8%) prefer CRET.

To establish the overall goals of surgery among respondents, we asked in what percentage of patients with glioblastoma they considered CRET would be possible, with response options starting at 30% or less and increasing in 10% increments. 46.3% (152/328) replied that this would be possible in 70-80% of patients with glioblastoma, with an additional 18.9% (62/328) estimating this in the 90%-100%

Table 1. Study population demographics. Values are presented as numbers with percentages in parentheses. *P*-value represent results of Chi-square tests comparing distributions between different career stages. Fisher's exact test was applied for 2×2 tables with low expected frequencies. The table includes demographic variables (gender, continent, institution type), surgical experience (annual number of glioma brain tumor operations, maximum surgical goal), use of technical adjuncts (neuronavigation, neuromonitoring, awake surgery, fluorescence guidance, ultrasound, PET), and assessments of evidence supporting complete removal of contrast-enhancement (CRET) and supramarginal resection (SMR). Additionally, respondents' attitudes toward multifocal glioblastoma (39/328 answered the survey version where this specific question as well as the cases pertaining to multifocal GBM were omitted) and willingness to randomize between different surgical approaches (CRET vs. SMR, partial resection [PR] vs. biopsy) are shown. A significance level of *P* < .05 was considered statistically significant

	<5 years (N=70)	5-10 years (N=72)	10-20 years (N=116)	>20 years (N=70)	Total (N=328)	<i>P</i> -value
Gender						0.034
Male	50 (71.4%)	54 (75.0%)	102 (87.9%)	62 (88.6%)	268 (81.7%)	
Female	19 (27.1%)	16 (22.2%)	13 (11.2%)	8 (11.4%)	56 (17.1%)	
Prefer not to disclose	1 (1.4%)	2 (2.8%)	1 (0.9%)	0 (0.0%)	4 (1.2%)	
Continent						0.253
Asia	1 (1.4%)	1 (1.4%)	5 (4.3%)	2 (2.9%)	9 (2.7%)	
Europe	60 (85.7%)	52 (72.2%)	97 (83.6%)	57 (81.4%)	266 (81.1%)	
North America	9 (12.9%)	15 (20.8%)	9 (7.8%)	7 (10.0%)	40 (12.2%)	
Oceania	0 (0.0%)	3 (4.2%)	2 (1.7%)	2 (2.9%)	7 (2.1%)	
South America	0 (0.0%)	1 (1.4%)	3 (2.6%)	2 (2.9%)	6 (1.8%)	
Institution						0.811
Academic	50 (71.4%)	58 (80.6%)	87 (75.0%)	49 (70.0%)	244 (74.4%)	
Combined, with academic	6 (8.6%)	4 (5.6%)	11 (9.5%)	7 (10.0%)	28 (8.5%)	
Private or public non-academic	14 (20.0%)	10 (13.9%)	18 (15.5%)	14 (20.0%)	56 (17.1%)	
Operations of intrinsic brain tumor patients, per surgeon per year						0.028
20 or less	20 (28.6%)	13 (18.1%)	11 (9.5%)	13 (18.6%)	57 (17.4%)	
21-50	24 (34.3%)	19 (26.4%)	41 (35.3%)	26 (37.1%)	110 (33.5%)	
51-75	9 (12.9%)	23 (31.9%)	27 (23.3%)	15 (21.4%)	74 (22.6%)	
76-100	6 (8.6%)	11 (15.3%)	10 (8.6%)	7 (10.0%)	34 (10.4%)	
101-150	6 (8.6%)	2 (2.8%)	17 (14.7%)	6 (8.6%)	31 (9.5%)	
More than 150	5 (7.1%)	4 (5.6%)	10 (8.6%)	3 (4.3%)	22 (6.7%)	
Optimal surgical goal in GBM surgery						0.219
Debulk and obtain tissue for diagnosis	1 (1.4%)	2 (2.8%)	1 (0.9%)	2 (2.9%)	6 (1.8%)	
Perform a supramarginal resection (clear margin around contrast-enhancement)	38 (54.3%)	40 (55.6%)	43 (37.1%)	38 (54.3%)	159 (48.5%)	
Perform FLAIRectomy	8 (11.4%)	7 (9.7%)	17 (14.7%)	7 (10.0%)	39 (11.9%)	
Remove all contrast-enhancement	23 (32.9%)	23 (31.9%)	55 (47.4%)	23 (32.9%)	124 (37.8%)	
Use of technical adjuncts						
1) Use of Neuronavigation						0.577
No	2 (2.9%)	0 (0.0%)	2 (1.7%)	1 (1.4%)	5 (1.5%)	
Yes	68 (97.1%)	72 (100.0%)	114 (98.3%)	69 (98.6%)	323 (98.5%)	
2) Use of Neuromonitoring						0.489
Yes	55 (78.6%)	57 (79.2%)	97 (83.6%)	52 (74.3%)	261 (79.6%)	
No	15 (21.4%)	15 (20.8%)	19 (16.4%)	18 (25.7%)	67 (20.4%)	
3) Awake Surgery, %						0.939
Less than 20%	57 (81.4%)	60 (83.3%)	94 (81.0%)	59 (84.3%)	270 (82.3%)	
More than 20%	13 (18.6%)	12 (16.7%)	22 (19.0%)	11 (15.7%)	58 (17.7%)	
4) Use of Fluorescence guidance						0.874
Yes	58 (82.9%)	58 (80.6%)	97 (83.6%)	60 (85.7%)	273 (83.2%)	
No	12 (17.1%)	14 (19.4%)	19 (16.4%)	10 (14.3%)	55 (16.8%)	
5) Use of Ultrasound						0.363
Yes	42 (60.0%)	41 (56.9%)	77 (66.4%)	38 (54.3%)	198 (60.4%)	
No	28 (40.0%)	31 (43.1%)	39 (33.6%)	32 (45.7%)	130 (39.6%)	

Table 1. Continued

	<5 years (N=70)	5-10 years (N=72)	10-20 years (N=116)	>20 years (N=70)	Total (N=328)	P-value
Use of PET						0.934
No	47 (67.1%)	47 (66.2%)	73 (63.5%)	44 (62.9%)	211 (64.7%)	
Yes	23 (32.9%)	24 (33.8%)	42 (36.5%)	26 (37.1%)	115 (35.3%)	
Evidence for CRET						0.107
Very weak	0 (0.0%)	1 (1.4%)	0 (0.0%)	0 (0.0%)	1 (0.3%)	
Rather weak	1 (1.4%)	1 (1.4%)	4 (3.4%)	4 (5.7%)	10 (3.0%)	
Neutral	4 (5.7%)	3 (4.2%)	7 (6.0%)	7 (10.0%)	21 (6.4%)	
Rather strong	26 (37.1%)	30 (41.7%)	57 (49.1%)	31 (44.3%)	144 (43.9%)	
Extremely strong	39 (55.7%)	37 (51.4%)	48 (41.4%)	28 (40.0%)	152 (46.3%)	
Evidence for SMR						0.601
Very weak	2 (2.9%)	2 (2.8%)	2 (1.7%)	2 (2.9%)	8 (2.4%)	
Rather weak	4 (5.7%)	5 (6.9%)	17 (14.7%)	11 (15.7%)	37 (11.3%)	
Neutral	21 (30.0%)	17 (23.6%)	26 (22.4%)	12 (17.1%)	76 (23.2%)	
Rather strong	30 (42.9%)	37 (51.4%)	56 (48.3%)	38 (54.3%)	161 (49.1%)	
Extremely strong	13 (18.6%)	11 (15.3%)	15 (12.9%)	7 (10.0%)	46 (14.0%)	
Attitude towards multifocal glioblastoma (n=289)						0.877
NA (were not presented with the question)					39	
I don't perform biopsy and go for immediate radiochemotherapy instead	1 (1.6%)	1 (1.7%)	1 (1.0%)	0 (0.0%)	3 (1.0%)	
I remove the largest, most symptomatic lesion only, going for maximal resection of this lesion	15 (24.6%)	16 (26.7%)	25 (23.8%)	18 (28.6%)	74 (25.6%)	
I tend to attempt remove every lesion, going for maximal resection	6 (9.8%)	3 (5.0%)	9 (8.6%)	8 (12.7%)	26 (9.0%)	
I tend to debulk large lesions without insisting on maximal resection	7 (11.5%)	12 (20.0%)	21 (20.0%)	12 (19.0%)	52 (18.0%)	
I tend to favor biopsy and rarely perform resection	32 (52.5%)	28 (46.7%)	49 (46.7%)	25 (39.7%)	134 (46.4%)	
Willingness to randomize between CRET and SMR						0.616
No	10 (14.3%)	13 (18.1%)	21 (18.1%)	9 (12.9%)	53 (16.2%)	
Undecided	4 (5.7%)	9 (12.5%)	14 (12.1%)	10 (14.3%)	37 (11.3%)	
Yes	56 (80.0%)	50 (69.4%)	81 (69.8%)	51 (72.9%)	238 (72.6%)	
Willingness to randomize between PR and Biopsy						0.232
No	31 (44.3%)	31 (43.1%)	35 (30.2%)	27 (38.6%)	124 (37.8%)	
Undecided	6 (8.6%)	12 (16.7%)	14 (12.1%)	10 (14.3%)	42 (12.8%)	
Yes	33 (47.1%)	29 (40.3%)	67 (57.8%)	33 (47.1%)	162 (49.4%)	

range. When asking about the percentage of glioblastoma patients where SMR can be performed (options here were never, 5%-10%, 20%-40% or >50% of cases), 45.7% (150/328) estimate this is possible in 20%-40% of patients, while 39.3% (129/328) estimate that this option is limited to only 5%-10% of patients. (Figure 2).

Perceived evidence strength for CRET was rated as "rather strong" or "extremely strong" by 296/328 (90.2%), while for SMR it was rated "rather strong" or "extremely strong" by 207/328 (63.1%) (Figure 2).

A survey version where the specific question about attitude in multifocal glioblastoma as well as the cases

pertaining to multifocal glioblastoma was omitted was filled out by 39/328 participants. In dealing with multifocal glioblastoma, 134/289 (46.49%) of respondents tended to favor biopsy, 74/289 (25.6%) would remove the largest symptomatic lesion only, 52/328 (18.0%) would debulk the largest lesion without insisting on maximal resection, and 26/328 (9.0%) would attempt to remove all lesions. Three respondents (3/328, 1.0%) would opt for immediate radiochemotherapy without any surgical intervention.

Most respondents were willing to randomize patients eligible for both procedures between CRET and SMR (238/328, 72.6%), with 53/328 (16.2%) unwilling and 37/328

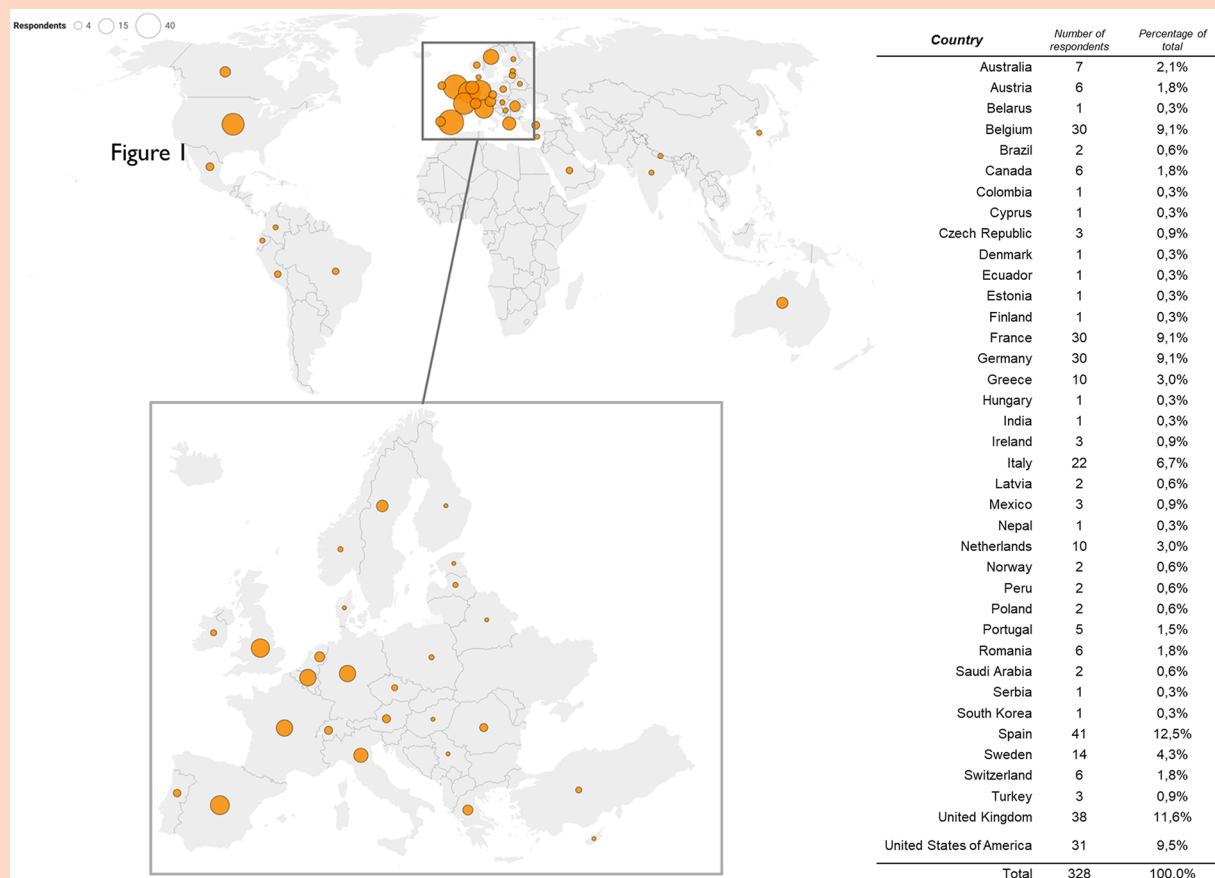


Figure 1. Respondents per country. The size of each dot represents the number of respondents. Created with Datawrapper.com.

(11.3%) undecided. When complete resection was not feasible, 162/328 (49.4%) were willing to randomize between PR and biopsy, 124/328 (37.8%) were unwilling, and 42/328 (12.8%) were undecided. This distribution as well as correlations through logistic regression are illustrated in Figure 3 (top).

Correlative Analysis

Correlation Between Perception of Evidence and Willingness to Randomize.—There was a statistically significant relationship between perceived strength of evidence for SMR and willingness to randomize between complete resection and SMR. When clinicians believe the evidence for SMR is already very strong, they are more reluctant to randomize patients. When the evidence is perceived as neutral, surgeons are most willing to randomize, but if evidence is perceived as very weak, clinicians are least likely to randomize ($P=.0001$) (Figure 5, top).

Exploration of Associations between Respondent Characteristics and Reported Practices.—After exclusion of 6 respondents who selected a debulking-only approach to obtain tissue for diagnosis and 4 respondents who preferred not to disclose their gender, further analyses included 318 participants. Significant associations were observed between demographic

characteristics, practice patterns, technology adoption, and surgical preferences, with detailed results provided in [Supplementary Table S1](#). In brief, regional origin was associated with center type, fluorescence and PET use, and multifocal management strategies. Academic and high-volume centers showed higher neuromonitoring and ultrasound adoption, and surgeons holding SMR as the optimal goal rated the supporting evidence as stronger and were more willing to randomize.

Associations between Surgeon Characteristics and Glioblastoma Surgical Practices and Attitudes.—To identify surgeon characteristics associated with glioblastoma surgical practices, perceptions of evidence, and attitudes toward randomization, multiple regression analyses for nine key outcomes were performed. These included:

1. Optimal surgical goal
2. Perceived evidence strength for CRET
3. Perceived evidence strength for SMR
4. Willingness to randomize between CRET and SMR
5. Willingness to randomize between PR and biopsy
6. Estimated feasibility of performing SMR
7. General practice in multifocal glioblastoma (categorized as biopsy vs. resection)
8. Proportion of glioblastoma patients undergoing awake surgery
9. Estimated feasibility of performing CRET

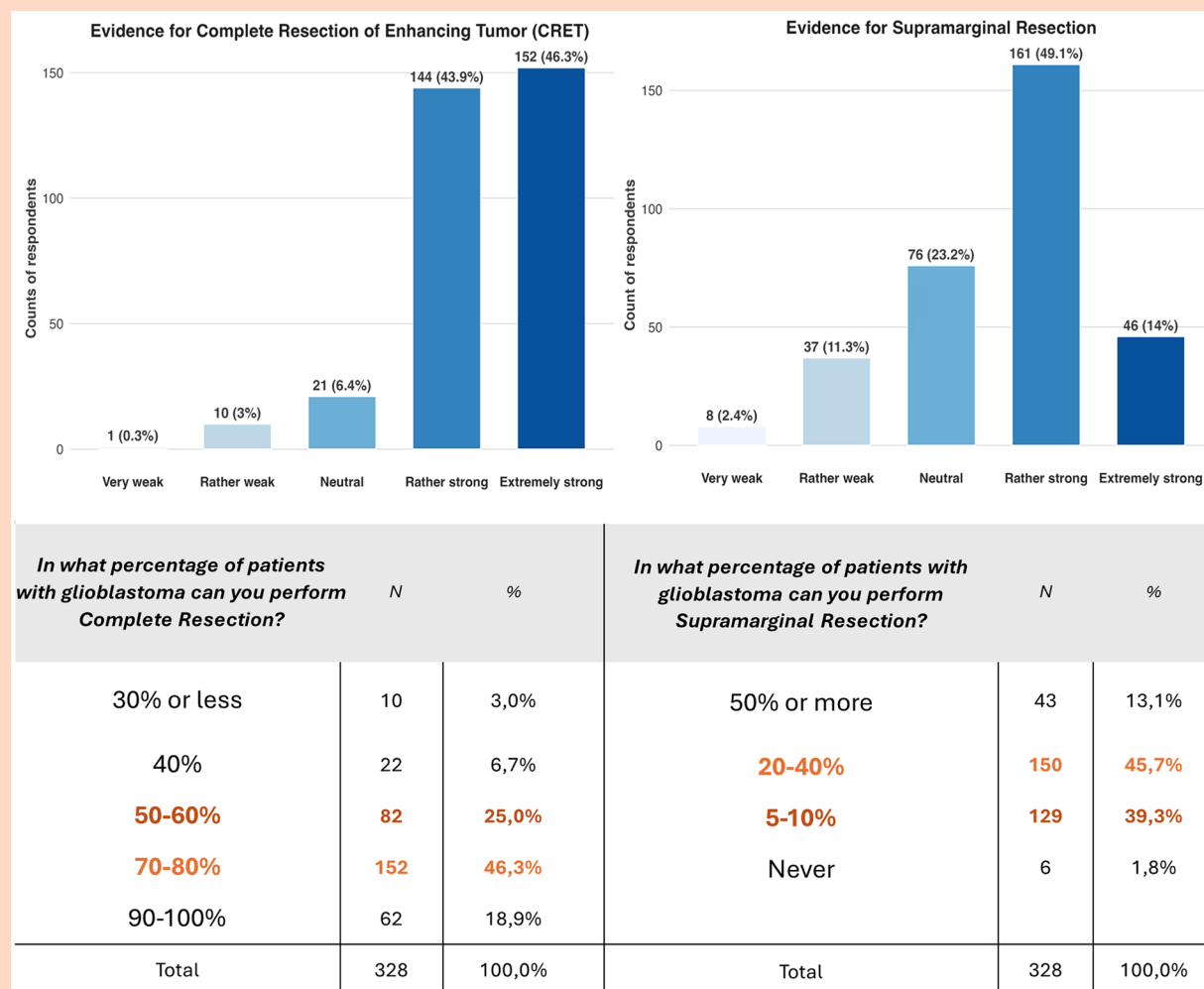


Figure 2. Top: Perceived evidence strength for Complete Resection of Enhancing Tumor (CRET) (left) and Supramarginal resection (SMR) (right). Values are presented as numbers with percentages in parentheses. Bottom: Estimation by respondents of feasibility of Complete Resection of Enhancing Tumor (CRET) (left) and Supramarginal resection (SMR) (right).

Predictor variables included continent, gender, type of center, career stage, annual brain tumor surgical volume, optimal goal in glioblastoma surgery, percentage of awake surgery, use of technical adjuncts (ultrasound, neuromonitoring, fluorescence, neuronavigation), and the use of PET. Reference categories were: European, Male, academic center, 10-20 years career stage, annual volume of 21-50 intrinsic brain tumor cases, maximal goal: CRET, fluorescence guidance = yes, neuromonitoring = yes, awake surgery <20% and no PET use.

A logistic regression was conducted to examine factors associated with neurosurgeons' **optimal surgical goal in glioblastoma**, comparing preference for FLAIRectomy/SMR versus complete resection of contrast enhancement (CRET). Career stage was a strong predictor: surgeons early in their careers (<5 years) were more likely to prefer SMR (OR 2.35, 95% CI, 1.19-4.75, $P=.015$) compared to those 10-20 years post-training, as were surgeons 5-10 years (OR 2.15, 95% CI, 1.10-4.30, $P=.028$) and >20 years post-training (OR 2.24, 95% CI, 1.16-4.45, $P=.018$). Lower annual brain tumor surgical volume (equal to or <20) was associated with lower odds of preferring SMR (OR 0.46, 95% CI, 0.22-0.94, $P=.036$), as was not using intraoperative neuromonitoring (OR 0.42, 95% CI,

0.22-0.79, $P=.008$). The remaining characteristics were not significant (all $P>.05$) (Figure 3, bottom left).

A cumulative ordinal logistic regression was performed to identify factors associated with clinicians' **perceived strength of evidence for CRET**. Respondents from North America (OR=0.28, 95% CI, 0.12-0.65, $P=.003$) and from other regions outside Europe (OR=0.30, 95% CI, 0.10-0.85, $P=.024$) were significantly less likely to rate the evidence as stronger compared with European respondents. No other variables were significantly associated with perceived evidence strength (all $P>.10$). These findings suggest that regional differences, rather than demographic or institutional factors, may influence clinicians' perceptions of the evidence supporting CE resection (Figure 3, bottom right).

Potential predictors associated with **perceived evidence for SMR** were also evaluated using cumulative ordinal logistic regression. Female respondents (OR=0.54, 95% CI, 0.31-0.93, $P=.028$), more frequently performing awake surgery (OR=0.55, 95% CI, 0.31-0.98, $P=.042$), and an annual brain tumor surgical volume equal to or less than 20 patients (OR=0.45, 95% CI, 0.23-0.86, $P=.015$), were significantly less likely to report higher perceived evidence (Supplementary Figure 1).

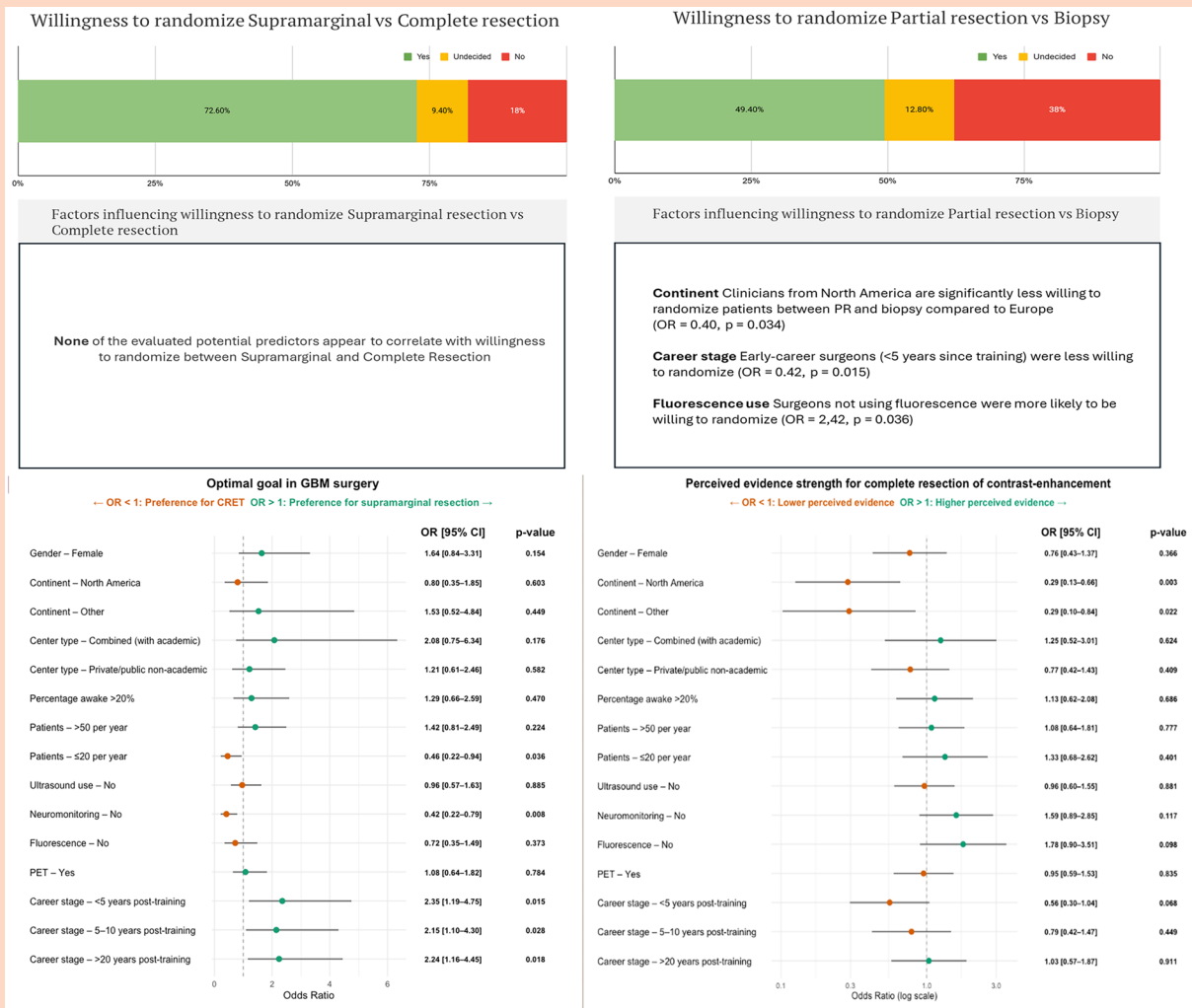


Figure 3. Top: Willingness to randomize in two scenarios. The potential influencing factors were evaluated through logistic regression and include continent, type of center, surgeon gender, surgical volume, use of awake surgery, neuromonitoring, fluorescence use (OR: Odds Ratio) Bottom left: factors associated with surgeons' maximal surgical goal in glioblastoma patients. Forest plot showing odds ratios (OR) and 95% confidence intervals (CI) for predictors of preferring FLAIRectomy/supramarginal resection versus complete resection of contrast-enhancing tissue. Bottom right: factors associated with perceived evidence for complete resection of contrast enhancement: Forest plot showing odds ratios (OR) and 95% confidence intervals (CI) for predictors of perceived evidence for resection of contrast enhancement. ORs >1 (turquoise) indicate higher likelihood of choosing supramarginal resection, while ORs <1 (orange) indicate lower likelihood and thus higher preference for CRET. Predictors included gender, continent, center type, career stage, percentage of awake surgery, annual patient volume, and use of technical adjuncts (ultrasound, neuromonitoring, fluorescence, PET). Right columns display OR [95% CI] and P -value. Significant predictors ($P < .05$) reflect independent associations after adjustment for all other variables.

Results from logistic regression analysis of factors influencing surgeons' **willingness to randomize patients between complete resection and SMR and between PR and biopsy** are illustrated in [Figure 3](#) (top).

Evaluation of factors associated with management preferences in patients with multifocal glioblastoma (resection strategies versus conservative management by biopsy or immediate radiochemotherapy) through logistic regression revealed that surgeons from continents outside Europe and North America were significantly more likely to favor resection compared with European surgeons (OR 4.64, 95% CI, 1.26–22.9, $P = .033$). Other predictors were not significantly associated with practice preference. Forest plots of logistic regression for factors associated with

proportion of glioblastoma patients undergoing awake surgery, estimated feasibility of performing CRET, estimated feasibility of performing SMR are shown in the [supplementary data](#).

Cases and Correlations

Six cases were presented to survey respondents: 3 exploring supramarginal versus complete resection in unifocal GBM (Cases 1–3), and three addressing resection versus biopsy in non-resectable or multifocal scenarios (Cases 4–6). For each case, willingness to randomize patients was correlated with demographic, attitudinal, and practice-related variables.

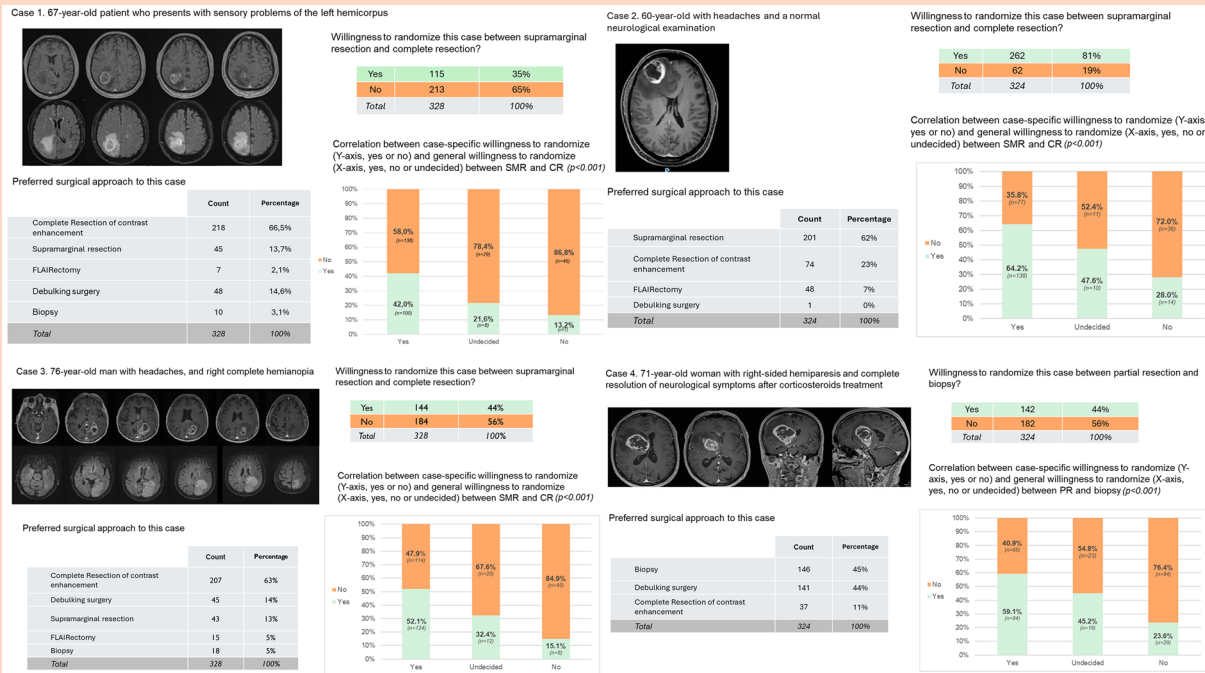


Figure 4. Illustration, summary of responses and correlation with general willingness to randomize of cases potentially eligible for supramarginal resection (SMR) vs complete resection (CR) (Case 1 to 3) or partial resection (PR) vs biopsy (Case 4).

Supramarginal Vs. Complete Resection in Unifocal GBM (Cases 1-3).—Overall willingness to randomize patients between CRET and SMR differed substantially across the 3 first cases: 35% (115/328) for Case 1 (eloquent-area tumor with sensory deficit), 81% (262/324) for Case 2 (non-eloquent parietal tumor, no deficit), and 44% (144/328) for Case 3 (occipital tumor with hemianopia). There is no complete overlap but nevertheless a strong correlation between general willingness to randomize and case-specific willingness to randomize CRET vs SMR in all applicable cases (Case 1: 42.0% vs. 13.2%; $\chi^2 = 19.1$, Cramér's $V = 0.24$, Case 2: 92.3% vs. 32.7%; $\chi^2 = 98.6$, $V = 0.55$, Case 3: 52.1% vs. 15.1%; $\chi^2 = 26.3$, $V = 0.28$) (Figure 4).

The preferred surgical approach showed even stronger associations. In Case 1, surgeons favoring SMR or FLAIRectomy were markedly more willing to enroll than CRET-preferring surgeons ($\chi^2 = 81.0$, $V = 0.50$; OR 12.4, 95% CI, 5.5-27.8). In Case 2, the pattern inverted: CRET-preferring surgeons were more willing than SMR/FLAIR-preferring surgeons (91.9% vs. 77.9%; $\chi^2 = 23.2$, $V = 0.27$). In Case 3, the preferred approach again favored willingness to randomize among SMR/FLAIR-preferring surgeons ($\chi^2 = 47.7$, $V = 0.38$; OR 3.58, 95% CI, 1.87-6.85) (Supplementary Figure 4).

Logistic regression confirmed these patterns. For Case 1, general willingness to pursue SMR (OR 2.26, $P < .001$) and holding SMR as a surgical goal (OR 1.86, $P = .015$) were independent positive predictors of willingness to randomize between CRET and SMR. For Case 2, general willingness remained a strong positive predictor (OR 5.64, $P < .001$), while preference for SMR was a negative predictor (OR 0.28, $P = .002$).

Perceived evidence strength showed a notable paradox in Case 2: surgeons who rated current SMR evidence as neutral were the most willing to enroll (96.0%), whereas those who

rated it as extremely strong were the least willing (56.5%; $\chi^2 = 30.0$, $V = 0.30$) (Figure 5, bottom). Career stage was a significant correlate only in Case 3, where early-career surgeons (<5 years post-training) were most willing (57.1%), mid-career surgeons (10-20 years) least so (34.5%), and those with >20 years at an intermediate level (42.9%; $\chi^2 = 9.5$, $P = .023$, $V = 0.17$).

Resection Vs. Biopsy in Non-Resectable or Multifocal Scenarios (Cases 4-6)

Case 4: Incompletely Resectable GBM

Willingness to randomize between PR and biopsy in a non-completely resectable GBM (71-year-old with steroid-responsive hemiparesis) was 43.8% (142/324). General willingness to randomize between PR and biopsy was the dominant correlate ($\chi^2 = 35.6$, $V = 0.33$): 59.1% in surgeons who were generally willing versus 23.6% among those generally unwilling (Figure 5). Preferred surgical approach did not reach significance ($\chi^2 = 4.4$, $P = .11$), suggesting that equipoise in this scenario is distributed more evenly across surgical preference groups.

Cases 5-6: Multifocal GBM

Among respondents that were presented with the multifocal cases ($n = 289$), willingness to randomize to biopsy versus resection was 45.3% (131/289) for Case 5 (53-year-old, 2 lesions, no deficit) and 43.9% (127/289) for Case 6 (61-year-old, 2 lesions, dominant-hemisphere dysphasia); these rates were not significantly different (McNemar $P = .67$). Willingness to randomize between resection of one versus all lesions diverged substantially: 47% (135/289) in Case 5 versus 60% (173/289) in Case 6 (McNemar $P < .001$), indicating a frontal and closeby multifocality influences decision-making and surgical preference (Supplementary Figure 5).



Preferred approach in multifocal GBM management consistently correlated with willingness to randomize between resection and biopsy: biopsy-favoring surgeons were most willing to enroll in both Case 5 (57.5%; $\chi^2 = 19.1$, $P<.001$, $V=0.26$) and Case 6 (56.7%; $\chi^2 = 17.8$, $P=.001$, $V=0.25$). There was similar albeit somewhat weaker association in Case 5 ($\chi^2 = 8.5$, $P=.014$, $V=0.17$) and Case 6 ($\chi^2 = 10.2$, $P=.006$, $V=0.19$). Preferred surgical approach correlated significantly with one-versus-all willingness in both Case 5 ($\chi^2 = 12.3$, $P=.016$, $V=0.21$) and Case 6 ($\chi^2 = 17.0$, $P=.002$, $V=0.24$), while preferred approach did not predict biopsy/resection willingness in Case 6 ($P=.24$). A summary of the responses to the open question "What do you consider to be an unaddressed controversy in glioblastoma surgery?" is provided as a [supplementary file](#).

Discussion

The paucity of RCTs in surgical neuro-oncology, particularly for glioblastoma (glioblastoma), often leaves clinicians relying on lower-level evidence and personal or institutional practice to make clinical decisions for patient management. Our survey shows that the perception of evidence strength for CR is very high, with 93% of respondents valuing the evidence as strong. This aligns with the actual evidence base for CR, which is indeed relatively strong since it is based on results from secondary analyses of prospective and randomized trials, also supported by rigorously studied retrospective series.^{2,3,9-11} Although 61% of respondents graded evidence for SMR as strong or extremely strong, the

evidence for SMR is currently graded as low quality due to the lack of RCTs, despite strong retrospective signals.¹²⁻¹⁵ Trials that randomize between CR and SMR are currently ongoing or in development.^{16,17} Perception of evidence base for biopsy vs resection in patients where complete resection cannot be realistically obtained was not evaluated in the survey, but the current evidence in this context is also low since no randomized studies on the topic have been performed. Results from retrospective series point toward the absence of survival benefit for PR in glioblastoma.¹⁸⁻²² Whether there is indeed no survival benefit and whether PR provides benefit in terms of improvement or stability of neurological function would need to be determined in an RCT.

Distinct patterns in surgical practice driven by both experience and environment are seen in the survey results. A majority of respondents (59.1%) favor SMR or "FLAIRectomy" over the traditional goal of complete resection of CRET, suggesting a shifting paradigm in the neurosurgical community. However, this preference is not uniform. Logistic regression identified that surgeons in their early careers (<5 years) are significantly more likely to pursue SM than their mid-career colleagues. This may reflect recent shifts in training curricula that increasingly emphasize extended resections and the use of advanced intraoperative adjuncts. It could, however, also reflect attitudes associated with career stage and experience. Younger surgeons would typically have had less experience with the negative clinical consequences of surgeries that were overly aggressive and therefore would be more prone to taking this risk. In a survey study on clinical decision making and expected length of survival, senior surgeons (and anesthesiologists) were found to be more risk-averse than their junior colleagues.²³ Research into surgical decision-making also showed that novices tend to interpret intraoperative information strictly at the level of pathology and physiology while more experienced surgeons employ a "Reconciliation Cycle" that takes a more holistic approach by incorporating and often prioritizing quality of life, thereby modulating the urge for aggressive resection.²⁴

The survey did not go into detail of definitions of SMR. For this reason, SMR and FLAIRectomy were analyzed together. Definitions in literature do vary, however: some define this as a 1 cm margin beyond CE, in other cases, it is defined as 1 cm margin beyond CE or until the next sulcus.^{16,17} The RANO Resect group defines supramaximal resection as a complete absence of CE combined with a small volume (<5 cm³) of NCE. FLAIRectomy is defined as complete resection of the FLAIR-hyperintense area.²⁵ A difficulty remains that the term implies anatomical boundaries, while functional boundaries are a crucial determinant of potential extent of resection, since functional deficits postoperatively also carry with them worse prognosis.^{26,27} Our survey shows that awake surgery is not often employed in the context of glioblastoma, despite its potential to optimize the "onco-functional balance" and potentially enable more frequent SMR.¹⁴

The use of intraoperative adjuncts—specifically neuro-monitoring and ultrasound—proved to be a strong independent predictor of preferring SMR. This aligns with the practical necessity of these tools when pushing resection boundaries beyond visible tumor margins. The finding of strong regional differences rather points toward the role of

practice characteristics, ie the high-volume academic centers in our sample are more often situated in European regions and are more likely to have access to and utilize advanced technologies. Consequently, the "regional" differences observed may essentially reflect disparities in resource availability and center volume rather than fundamental disagreements on surgical philosophy. This distinction is relevant for trial design, as it suggests that variability in practice may be more amenable to standardization through protocolized access to technology than to changes in individual surgical beliefs.

A key objective of this study was to assess the "willingness to randomize" as a proxy for clinical equipoise. We observed a robust willingness (72.6%) to randomize patients between CRET and SMR. From a methodological perspective, this level of stated willingness suggests that a large-scale randomized trial comparing CRET and SMR is feasible, particularly in high-volume centers where both strategies are routinely considered. Willingness to randomize between PR and biopsy was 49.4%, which most likely indicates a deeply engrained belief in the value of cytoreduction even when maximal resection is not possible. Notably, surgeons who perform awake surgery more frequently (>20% of cases) were less willing to randomize in the PR vs. biopsy scenario ($P = .034$), possibly because these surgeons are more committed to attempting resection whenever feasible. Clinicians who perceived the existing evidence for SMR as "neutral" were the most willing to randomize, illustrating the principle of clinical equipoise. Those who viewed the evidence as "extremely strong" (indicating a fixed preference) or "very weak" were significantly less willing to participate. The reluctance among those viewing evidence as "weak" is counterintuitive and is an apparent paradox but likely stems from ethical concerns or perceived futility; if a surgeon believes a technique has very weak support, they may consider it unethical to test it against a standard of care. This finding highlights that reluctance to randomize does not arise solely from strong conviction in one strategy but may also reflect ethical discomfort when the available evidence is perceived as insufficient.

The case scenarios presented at the end of the survey expose a certain disconnect between general (more abstract) willingness and case-based (concrete) decision-making. While 72.6% of surgeons expressed general willingness to randomize between SMR and CRET, this number fluctuated when presented with specific clinical cases. For example, in a case that could be considered a straightforward indication for SMR, almost 36% of respondents who expressed general willingness to randomize between SMR and CRET were not willing in this specific case. Conversely, 28% of respondents who were not willing to randomize in general expressed being willing in this specific case. This indicates that the specifics of each case scenario play a role in decision-making and can change opinions in both directions and will strongly influence actual recruitment. In general, it appears that the surgeons' willingness to randomize patients between CRET and SMR is driven by an interplay of baseline surgical philosophy, case-specific preferences, and the presence of clinical equipoise. In Case 1, holding SMR as the primary surgical goal correlated with more willingness to randomize, while in the non-eloquent scenario of Case 2, a preference for SMR was rather a significant negative predictor (OR

0.28), indicating that CRET-preferring surgeons would be the primary drivers of enrollment in such cases. The apparent “equipoise paradox” regarding the perception of existing evidence is also apparent in specific cases. Practitioners who viewed the current evidence for SMR as neutral were overwhelmingly willing to participate (96.0%), whereas those who rated the evidence as extremely strong were the least willing (56.5%). Ultimately, these results emphasize a fundamental challenge in surgical trial recruitment: strong personal conviction functionally eliminates clinical uncertainty, thereby reducing the perceived necessity of a trial and directly hindering patient enrollment.

The case scenarios also show a strong preference for resection as opposed to biopsy, even in/close to eloquent areas and in cases with multifocal GBM. Willingness to randomize between STR and biopsy was notably lower than between SMR and Complete Resection (CR), indicating that a trial randomizing between resection and biopsy in patients where complete resection cannot be achieved will most likely be more challenging. This finding of deeply engrained beliefs despite absence of evidence makes such a trial even more important.

Reassuringly, a large proportion of surgeons are willing to randomize. These findings suggest that future surgical RCTs should carefully define inclusion criteria and stratification variables to account for clinically meaningful heterogeneity across patients and scenarios.

This study has its limitations. First, the survey-based methodology may lead to an overestimation of the willingness to randomize in clinical practice, as stated preferences do not always fully translate into actual bedside decision-making. Furthermore, an intent to reach a specific extent of resection, whether it be complete resection or SMR, does not always translate into actually achieving this result, which is something that should be accounted for when calculating sample sizes and evaluating feasibility of a trial. Another limitation is that the data reflects a selection bias toward surgeons from academic and high-volume centers and displays regional imbalances. Consequently, the observed heterogeneity within Europe likely reflects underlying differences in local training, resources, and healthcare systems rather than continental geography alone. Finally, another important limitation here is that the surgeon's opinion of whether randomization is justified does not always mean that the patient agrees. To address this, another survey study is currently being conducted to evaluate patients' willingness to be randomized in specific scenarios.

Conclusion

This international survey confirms that while the neurosurgical management of glioblastoma varies by region, institution, and surgeon experience, a widespread willingness exists to subject these differences to rigorous scientific testing. The strong preference for SMR among younger surgeons and those in high-tech, high-volume centers contrasts with a preference for complete resection of contrast enhancement in other settings. This divergence highlights the need for comparative-effectiveness research. With over 70% of neurosurgeons willing to randomize between standard and SMR and almost 50% willing to randomize between PR and biopsy in cases where complete resection is not

possible, there appears to be room for definitive surgical RCT to address the uncertainty in the optimal surgical management of glioblastoma.

Supplementary Material

Supplementary material is available online at *Neuro-Oncology Advances* (<https://academic.oup.com/nao>).

Keywords

clinical equipoise | extent of resection (EOR) | glioblastoma | supramarginal resection | surgical randomized controlled trials (RCTs)

Author Contributions

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Conflict of Interest Statement

JD has received honoraria for advisory board participation from Miltenyi, Servier. ELR. has received research grants from Bristol Meyers Squibb (BMS), and honoraria for lectures or advisory board participation or consulting from Bayer, Biodexa/Sitoxi, Janssen, Leo Pharma, Pierre Fabre, Roche, Seattle Genetics, and Servier. GM received honoraria for lectures, consultation, or advisory board participation from Brainlab, Accuray, Servier, Astra-Zeneca, Pfizer, and Novocure. MP has received honoraria for lectures, consultation, or advisory board participation from the following for-profit companies: Bayer, Bristol-Myers Squibb, Novartis, Gerson Lehrman Group (GLG), CMCCcontrast, GlaxoSmithKline, Mundipharma, Roche, BMJ Journals,

MedMedia, Astra Zeneca, AbbVie, Lilly, Medahead, Daiichi Sankyo, Sanofi, Merck Sharp & Dome, Tocagen, Adastra, Gan & Lee Pharmaceuticals, Janssen, Servier, Miltenyi, Böhlinger-Ingelheim, Telix, Medscape, OncLive, Medac, Nerviano Medical Sciences, and ITM Oncologics GmbH. MW has received research grants from Novartis, Quercis and Versameb, and honoraria for lectures or advisory board participation or consulting from Anheart, Bayer, Curevac, Medac, Neurosense, Novartis, Novocure, Orbus, Pfizer, Philogen, Roche and Servier. LL, PK, RPA, MDJ, ES, MS, JG, JVDV, TP, MMJW, AJ, AM report no potential conflicts of interest.

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Ethics Approval Statement

A waiver of requirement for formal approval was obtained from the UZ Brussel ethics board, since the study involved an anonymous survey of healthcare professionals and did not involve patients or clinical interventions. Informed consent was implied by the voluntary completion and submission of the survey. All data were collected and analyzed anonymously, except where participants specifically opted to provide contact details for further collaboration. For those participants who chose to provide contact information for follow-up, data were handled in accordance with GDPR/standard data protection guidelines.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon well-founded request.

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