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# Decision making and surgical modality selection in glioblastoma patients: an international multicenter survey

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## Abstract

**Purpose** Due to the lack of consensus on the management of glioblastoma patients, there exists variability amongst surgeons and centers regarding treatment decisions. Though, objective data about the extent of this heterogeneity is still lacking. We aim to evaluate and analyze the similarities and differences in neurosurgical practice patterns.

**Methods** The survey was distributed to members of the neurosurgical societies of the Netherlands (NVVN), Europe (EANS), the United Kingdom (SBNS) and the United States (CNS) between January and March 2021 with questions about the selection of surgical modality and decision making in glioblastoma patients.

**Results** Survey respondents (224 neurosurgeons) were from 41 countries. Overall, the most notable differences observed were the presence and timing of a multidisciplinary tumor board; the importance and role of various perioperative factors in the decision-making process, and the preferred treatment in various glioblastoma cases and case variants. Tumor boards were more common at academic centers. The intended extent of resection for glioblastoma resections in eloquent areas was limited more often in European neurosurgeons. We found a strong relationship between the surgeon's theoretical survey answers and their actual approach in presented patient cases. In general, the factors which were found to be theoretically the most important in surgical decision making were confirmed to influence the respondents' decisions to the greatest extent in practice as well.

**Discussion** This survey illustrates the theoretical and practical heterogeneity among surgeons and centers in their decision making and treatment selection for glioblastoma patients. These data invite further evaluations to identify key variables that can be optimized and may therefore benefit from consensus.

**Keywords** Glioblastoma · Decision making · Safe resection · Biopsy · Survey

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## Introduction

Guidelines for the management of neurosurgical disease have been published by national and international neurosurgical societies in partnership with other specialties. Despite these widely accepted guidelines, neurosurgeons practice patterns differ within an institution, and amongst centers nationally and internationally based upon a surgeon's individual expertise and preference. The neurosurgical management of brain tumors requires a balance of neurosurgical guidelines with patient specific characteristics and the surgeon's individual experience to determine the optimal treatment. Surgeons decide on whether to operate, the extent of resection (ranging from no surgery, biopsy, debulking, to maximal safe resection), the use of mapping techniques (e.g. awake craniotomy) [1, 2], the use of surgical adjuncts (e.g. fluorescence) [3] and the use of additional imaging (e.g. fMRI, intraoperative MRI, intraoperative ultrasound, DTI) [4–9]. Factors that could influence the surgeon's decision range from the patient's age, comorbidities and preference, the preoperative functioning and morbidity of the patient, to the size, location and eloquence of the tumor [10–13]. The neurosurgical field is still divided on a number of these factors, examples of which are: how aggressive one should operate on glioblastoma (GBM) patients, the added value of mapping techniques in GBMs in or near eloquent areas, and if one should be restrained with performing a resection among elderly GBM patients (and should opt for biopsy instead for example) [14–21].

The heterogeneity in decision making and treatment selection between surgeons and centers that differ in experience, affiliation and region has yet to be assessed objectively and globally.

This survey aims to evaluate the various layers of onco-neurosurgical decision making in both a theoretical and practical setting with special attention for multidisciplinary tumor boards, the patient-related and tumor-related factors that play a role in the decision-making process, the factors that influence the defensiveness/aggressiveness of the surgeon's approach, and his or her approach in selected cases which represent various subgroups of GBM patients. This survey will give insight in the neurosurgical practices for the treatment of these patients on a global scale and the reasons behind the similarities and differences between surgeons and why they make the choices they make. The goal is to conduct a contemporary benchmark assessment that will serve as a first step in reaching practice consensus in GBM patients for certain variables.

## Methods

### Survey design

The questionnaire was constructed by the ENCRAM Research Consortium [22]. Questions were aimed to evaluate the local decision making and surgical modality selection in glioblastoma cases, especially regarding absence/presence multidisciplinary boards and its timing, attitude towards glioblastoma surgery (e.g. distinction between relatively aggressive or defensive), factors influencing this attitude in specific cases (e.g. tumor location, patient age) and factors influencing the decision between biopsy and resection. A sizable part of the survey focused on evaluating the respondent's choice and rationale for a surgical modality in example cases of different subgroups of glioblastoma patients. The target audience included consultant neurosurgeons (attendings) and neurosurgery fellows in neuro-oncology. These providers were divided in 3 groups: neurosurgery consultants/attendings with > 5 years as experience as a neurosurgeon after their residency, neurosurgery consultants/attendings with < 5 years as experience as a neurosurgeon after their residency, and neurosurgery fellows. Additional baseline characteristics included country, gender, number of glioma resections performed and place of practice (academic, non-academic, private practice). Academic centers are institutes that include both a teaching hospital and medical school and provide mostly specialized tertiary care. Non-academic centers are community hospitals that provide mostly secondary care to the community. Private practices are institutes that are paid for and owned by investors rather than by governments (United Kingdom: medical care that is not part of the National Health Service, NHS).

### Survey dispersal

The survey was made available by a link to the online LimeSurvey questionnaire platform (LimeSurvey GmbH, Hamburg, Germany) and were distributed twice by electronic mailing lists of the Congress of Neurological Surgeons (CNS) and the Dutch Neurosurgical Association (NVVN) with Mailchimp (Atlanta, GA, USA). It was included twice in the monthly newsletter of the European Association of Neurological Societies (EANS) and distributed among the members of the British Society of Neurological Surgeon (SBNS) by mail. Participation in the survey was voluntary and without remuneration. Response rate was 5.0% among CNS members, 2.7% among SBNS members and 16.0% among NVVN members. Response rate among EANS members could not be assessed due to

the nature of the survey's dispersal. The survey was open for entries between January and March 2021.

## Statistical analysis

Survey data were exported for further data analysis on March 6th, 2021 from LimeSurvey into an Excel file and analyzed using R version 4.0.3 (the R foundation, Vienna, Austria). Data were grouped according to the baseline characteristics gender, WHO region, type of institute, surgeon training level and the number of glioma resections the surgeon had performed. Overall response differences were analyzed using the  $\chi^2$  test for proportions with the Marascuillo procedure and Bonferroni correction for multiple testing. For responses with an observed count of < 10 and/or expected count of < 5 the Fisher's exact test was used. Categorical survey responses were further analyzed for different subgroups using multivariate logistic (logit) regression with type of institute and region (Europe/US) as the two independent variables. Continuous survey outcomes were analyzed using multinomial linear regression. For variables with > 2 response options, dummy coding was used for processing responses into dichotomous variables. For questions that allowed multiple answers, the McFadden MNL model was used as a mixed effects model to analyze subgroup responses. Univariate logistic regression was used to further analyze the case responses with reported factor importance and region (Europe/US) as the independent variables. Statistical significance was set at 5%.

## Results

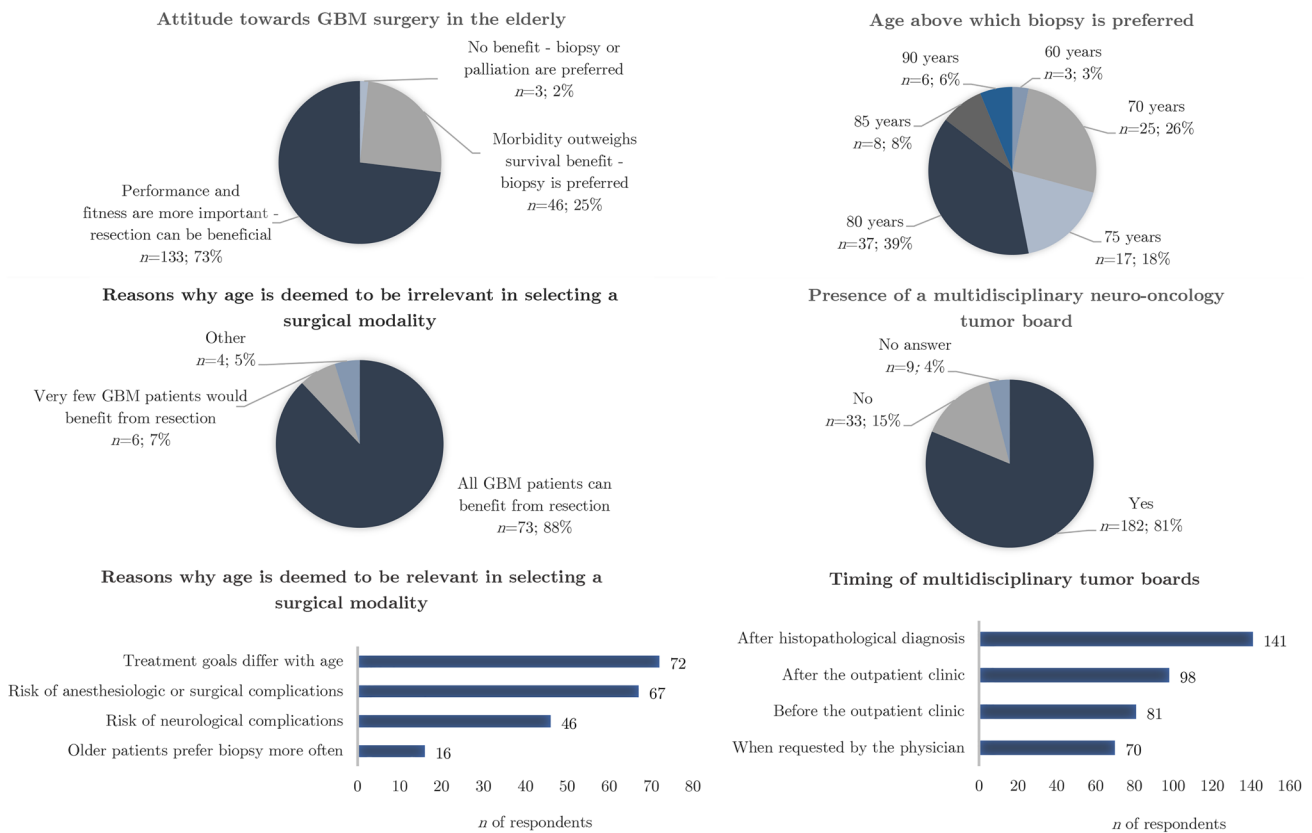
We obtained a total of 224 responses from 41 countries. Table S1 (Data Supplement) shows the baseline characteristics of the respondents. 202 survey participants were male (90.2%) and 22 participants were female (9.8%).

Thirty-seven percent of the responses originated from the United States and Canada ( $n=83$ ), 7.6% from Latin America ( $n=17$ ), 40.6% from Europe ( $n=91$ ), 3.1% from the Eastern Mediterranean Region ( $n=7$ ), 4.5% from South-East Asia ( $n=10$ ), 4.9% from the Western Pacific ( $n=11$ ) and 2.2% from the African Region ( $n=5$ ) (Table S1, Figure S1, Data Supplement). These countries included (absolute  $n$  of responses in parentheses): American Samoa (1), Argentina (4), Australia (3), Austria (2), Belgium (5), Brazil (2), Canada (6), Chile (1), China (1), Colombia (4), Czech Republic (1), Egypt (1), Finland (1), France (3), Germany (7), Greece (2), India (5), Indonesia (3), Iran (1), Ireland (1), Italy (5), Jordan (1), Mexico (4), Nepal (2), the Netherlands (24), Nigeria (1), Pakistan (1), Peru (2), Philippines (1), Portugal (3), Romania (3), Serbia (3), South Africa (4), South Korea (3), Spain (2), Sudan (3), Switzerland (1), Taiwan

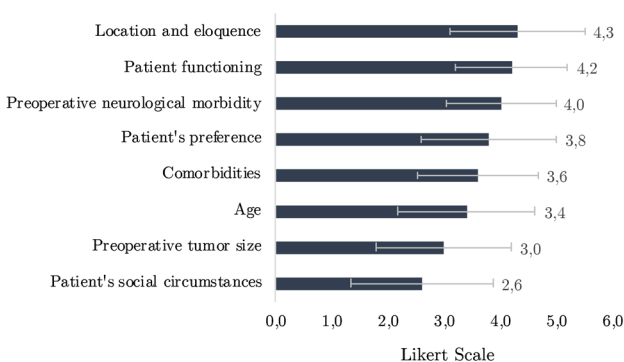
(1), Turkey (2), United Arab Emirates (1), United Kingdom (26) and the United States (77). 62.9% of participants was appointed at an academic practice/university hospital ( $n=141$ ), 19.2% worked at a non-academic practice/community hospital ( $n=43$ ), 14.3% was appointed at a private practice ( $n=32$ ) and 4.2% selected "other" as their current appointment ( $n=8$ ). The majority of survey respondents concerned consultant neurosurgeons with > 5 years of practice after finishing their fellowship (82.6%,  $n=185$ ), 13.4% still had less than 5 years of experience ( $n=30$ ). 3.6% of respondents were currently appointed as neurosurgical fellow ( $n=8$ ), and one respondent was still in her residency. Experience with glioma surgery differed between respondents: 24.6% had performed less than 100 glioma resections ( $n=55$ ), 51.3% had performed between 100 and 500 resections ( $n=115$ ) and 24.1% had performed more than 500 resections ( $n=54$ ).

## General decision making

Overall responses were significantly different for 7 of the 8 questions (Table S2, Data Supplement). Multivariate subgroup analyses for academic vs. non-academic/private practice respondents and European vs. US neurosurgeons were significant for 3 of the 8 questions. Two hundred and twenty-four neurosurgeons reported on the decision making in GBM patients at their center. At a majority of centers, a multidisciplinary neuro-oncology tumor board was present (81.3%,  $p<0.0001$ , Fig. 1), and significantly more often at academic centers (OR = 8.05,  $p=0.0021$ ). The most common timing of this board was after the definitive histopathological diagnosis (77.5%,  $p<0.0001$ ). European respondents reported more often the presence of a tumor board prior to the outpatient clinic (OR = 4.78,  $p<0.0001$ ), while their US colleagues more often held a tumor board after the histopathological diagnosis (OR = 0.28,  $p=0.0051$ ). Respondents indicated on a Likert scale the extent to which various factors influence their decision when choosing a treatment modality for GBM patients (a rating of 1 meaning not important at all and 5 meaning very important). Tumor location and eloquence was rated the most important factor (mean 4.3), followed by preoperative patient functioning (mean 4.2), preoperative neurological morbidity (mean 4.0), patient's preference (mean 3.8), comorbidities (mean 3.6), patient's age (3.4), preoperative tumor size (mean 3.0) and the patient's social circumstances (mean 2.6) (Fig. 2). Among the respondents who rated "age" an important or very important factor in their decision making (Likert scale 4 or 5), the reason for this was most commonly that the treatment's goals differ for younger and older GBM patients (74.2%), followed by an increasing risk of anesthesiologic or surgical complications with increasing age (69.1%), increasing risk of neurological complications with increasing age (47.4%) and that older



**Fig. 1** Significant differences—General decision making and attitude towards GBM surgery in the elderly

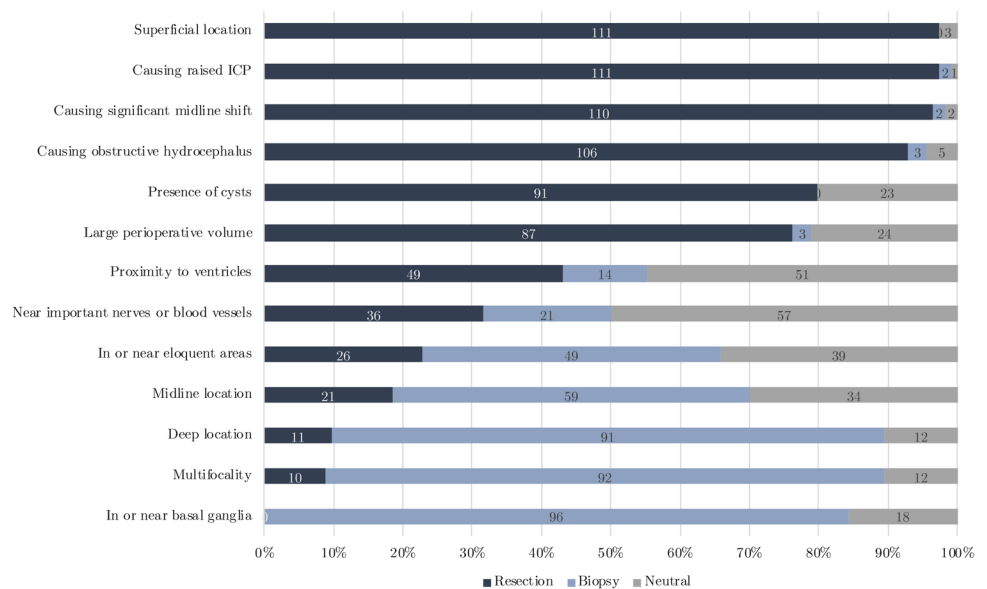


**Fig. 2** Impact of perioperative factors on surgical modality selection in GBM patients

patients more often prefer a biopsy (16.5%). Moreover, the patient's age above which they would be more inclined to choose a biopsy rather than a resection was for the majority of respondents 80 years old (38.1%), (Fig. 1). Overall, the majority of respondents agreed that the patient's age should be approached relatively since performance and fitness are ultimately more important, and that resection followed by adjuvant therapy is usually the best choice in GBM patients (71.5%),  $p < 0.0001$ ). However, almost a quarter of

respondents (24.7%) reported that in their opinion, in older GBM patients the risk of morbidity outweighs the potential survival benefit and that biopsy followed by adjuvant therapy is usually the best choice for these patients. Moreover, respondents were asked to indicate whether various perioperative factors would, in their opinion, warrant a more aggressive (i.e. resection) or defensive (i.e. biopsy) approach which are illustrated in Fig. 3. Survey responses for all questions were further analyzed to evaluate the impact of the surgeon's experience [in glioma surgery] on their answers (Table S3). The only significant difference was regarding attitude towards glioblastoma surgery in elderly patients: experienced neurosurgeons more often agreed with the statement that in older patients, the risk of morbidity outweighs survival benefit and that biopsy is often the best choice. Less experienced colleagues however found fitness and performance more important and were more inclined to perform a resection. For these perioperative factors, no significant differences were observed in the subgroup analyses for academic vs. non-academic/private practice surgeons. Though, US colleagues were slightly less defensive when tumors were located in or near eloquent areas (biopsy; OR = 0.22;  $p = 0.0020$ ).

**Fig. 3** Impact of tumor related factors on surgical modality selection in GBM patients



### Glioblastoma patient cases

Respondents were asked to select their preferred treatment modality in four different GBM cases. Response options were: best supportive care, chemotherapy/radiotherapy only, biopsy, debulking, maximum resection without mapping, and maximum resection with mapping. Biopsy, debulking and maximum resection were followed by adjuvant therapy. If respondents selected debulking or maximum resection (with or without mapping) as their treatment of preference, they were asked to indicate whether they would use one or more surgical adjuncts or additional imaging. After completion of the original patient case, respondents were asked if their approach would change in various case variants (more aggressive, same approach, or more defensive), in which one or more perioperative factors were altered (while the rest of the case remained the same). More aggressive and more defensive indicate that the surgeon would choose a *treatment modality* which would be more aggressive (“up the ladder”) or more defensive (“down the ladder”), respectively. Consequently, respondents who preferred a maximum resection with mapping or best supportive care in the original case could not be more aggressive or more defensive in the case variants, respectively. Moreover, the results were further analyzed to evaluate respondents from which initial treatment group switched their approach when the case variant was presented. With regression analysis, an additional analysis was performed to investigate if this switch was in line with the respondent’s earlier reported Likert scale rating for this particular factor, and if there were any differences between European and US surgeons. The results of these responses are summarized in Tables 1, 2 and Fig. 4A–D.

### Case 1

The clinical details of case 1 are described in the text box of Fig. 4A.

The majority of respondents preferred maximum resection with mapping (56.1%) significantly more often than maximum resection without mapping (38.7%,  $p = 0.0022$ ) and debulking (5.2%,  $p < 0.0001$ ) (Table 1, Fig. 4). No respondents preferred a biopsy, chemotherapy or radiotherapy only or best supportive care.

In case variant 1 (elderly patient), a majority of respondents who preferred maximum resection with mapping and without mapping chose the same approach (with mapping: 73.4%, without mapping: 84.3%) ( $p < 0.0001$ ) (Table 1). Though, a slight majority of respondents who preferred debulking chose to be more defensive (57.1%). Regression analysis showed that respondents who had reported the factor age as important or very important earlier in the survey were indeed more defensive in case variant 1 when the patient was older (OR = 4.89, 95% CI 1.84–13.00,  $p = 0.0015$ ) (Table 1).

In case variant 2 (ASA III, KPS 60), the majority of respondents who preferred maximum resection with mapping in the original case or debulking reported to be more defensive in this case variant (maximum resection with mapping: 59.2%, debulking: 57.1%), while respondents who preferred maximum resection without mapping chose the same approach more often (54.9%) (Table 1). Overall, there was no significant difference between the same approach and a more defensive approach ( $p = 0.2736$ ). There was a nonsignificant relationship with earlier reported Likert scales on patient functioning (OR = 2.43,



**Table 1** (continued)

Case	Response options	Response (%)	P value	Case variant 1 Patient 75 y/o	Case variant 2 ASA I, KPS 100, MMSE 30/30	
<p><b>Case 3</b> n=153</p> <p>Male, 44 y/o</p> <p>Past medical history: hypertension, ICD placement in 2016 for persistent ventricular arrhythmias following acute myocardial infarctions in 2012 and 2016.</p> <p>History and physical: worsening headache for 4 months and personality changes, sometimes disoriented and apathic according to partner. No vision problems.</p> <p>Neurological examination: normal. KPS: 70. MMSE: 21/30.</p> <p>MRI + Gd: large multifocal contrast-enhancing lesion in both frontal lobes and corpus callosum. Inhomogeneous aspect with presence of both cysts and solid parts. Developing biventricular hydrocephalus.</p> <p>Which surgical treatment would you prefer in this case?</p> <p>NB: for adjuncts, select one or more answers</p>	<ul style="list-style-type: none"> <li>• Maximum resection with mapping                             <ul style="list-style-type: none"> <li>○ No adjuncts</li> <li>○ Intraoperative ultrasound</li> <li>○ Intraoperative MRI</li> <li>○ Functional MRI</li> <li>○ DTI</li> <li>○ Fluorescence</li> </ul> </li> <li>• Maximum resection without mapping                             <ul style="list-style-type: none"> <li>○ No adjuncts</li> <li>○ Intraoperative ultrasound</li> <li>○ Intraoperative MRI</li> <li>○ Functional MRI</li> <li>○ DTI</li> <li>○ Fluorescence</li> </ul> </li> <li>• Debulking followed by adjuvant therapy                             <ul style="list-style-type: none"> <li>○ No adjuncts</li> <li>○ Intraoperative ultrasound</li> <li>○ Intraoperative MRI</li> <li>○ Functional MRI</li> <li>○ DTI</li> <li>○ Fluorescence</li> </ul> </li> <li>• Biopsy followed by adjuvant therapy</li> <li>• Chemotherapy or radiotherapy only</li> <li>• Best supportive care</li> </ul>	<p>1 (0.65)<sup>c</sup></p> <p>0</p> <p>0</p> <p>0</p> <p>0</p> <p>0</p> <p>1</p> <p>13 (8.5)<sup>c</sup></p> <p>3</p> <p>2</p> <p>4</p> <p>3</p> <p>2</p> <p>6</p> <p>40 (26.1)<sup>b</sup></p> <p>11</p> <p>12</p> <p>2</p> <p>2</p> <p>4</p> <p>11</p> <p>90 (58.8)<sup>a</sup></p> <p>2 (1.3)<sup>c</sup></p> <p>7 (4.6)<sup>c</sup></p>	<p><sup>a/b/c</sup>&lt;0.0001*</p> <p><sup>a/e</sup>&lt;0.0001*</p> <p><sup>b/c</sup>&lt;0.0001*</p>	<p>Same 1 (100.0)</p> <p>↓ 0</p> <p>↑ 1 (7.7)</p> <p>Same 7 (53.8)</p> <p>↓ 5 (38.5)</p> <p>↑ 0</p> <p>Same 12 (38.7)</p> <p>↓ 19 (61.3)</p> <p>↑ 0</p> <p>Same 55 (69.6)</p> <p>↓ 24 (30.4)</p> <p>↑ 0</p> <p>Same 1 (100.0)</p> <p>↓ 0</p> <p>↑ 0</p> <p>Same 7 (100.0)</p>	<p>Same 1 (100.0)</p> <p>↓ 0</p> <p>↑ 1 (7.7)</p> <p>Same 10 (76.9)</p> <p>↓ 2 (15.4)</p> <p>↑ 4 (11.1)</p> <p>Same 24 (66.7)</p> <p>↓ 2 (5.6)</p> <p>↑ 16 (20.3)</p> <p>Same 60 (75.9)</p> <p>↓ 3 (3.8)</p> <p>↑ 0</p> <p>Same 1 (100.0)</p> <p>↓ 0</p> <p>↑ 5 (71.4)</p> <p>Same 2 (28.6)</p>	
Case	Response options	Response (%)	P value	Case variant 1 Patient 45/y/o	Case variant 2 Right temporal No aphasia	Case variant 3 GCS 15, ASA I, KPS 100
<p><b>Case 4</b> n=152</p> <p>Female, 76 y/o</p> <p>Past medical history: hypertension, bilateral peripheral arterial occlusive disease (PAOD) Fontaine III since 2010, cataract</p> <p>History and physical: significant concentration problems and receptive aphasia. Morning sickness and frequent vomiting since last week. Two epileptic seizures last 3 days, treated with intranasal midazolam.</p> <p>Neurological examination: E3V4M6 with severe receptive aphasia, right-sided hemi-neglect and gait imbalance. KPS: 60.</p> <p>MRI + Gd: contrast-enhancing lesion in the left parieto-temporal lobe with extensive edema, possibly near Wernicke's area. Suspected GBM.</p> <p>Which surgical treatment would you prefer in this case?</p> <p>NB: for adjuncts, select one or more answers</p>	<ul style="list-style-type: none"> <li>• Maximum resection with mapping                             <ul style="list-style-type: none"> <li>○ No adjuncts</li> <li>○ Intraoperative ultrasound</li> <li>○ Intraoperative MRI</li> <li>○ Functional MRI</li> <li>○ DTI</li> <li>○ Fluorescence</li> </ul> </li> <li>• Maximum resection without mapping                             <ul style="list-style-type: none"> <li>○ No adjuncts</li> <li>○ Intraoperative ultrasound</li> <li>○ Intraoperative MRI</li> <li>○ Functional MRI</li> <li>○ DTI</li> <li>○ Fluorescence</li> </ul> </li> <li>• Debulking followed by adjuvant therapy                             <ul style="list-style-type: none"> <li>○ No adjuncts</li> <li>○ Intraoperative ultrasound</li> <li>○ Intraoperative MRI</li> <li>○ Functional MRI</li> <li>○ DTI</li> <li>○ Fluorescence</li> </ul> </li> <li>• Biopsy followed by adjuvant therapy</li> <li>• Chemotherapy or radiotherapy only</li> <li>• Best supportive care</li> </ul>	<p>18 (11.8)<sup>c</sup></p> <p>2</p> <p>3</p> <p>1</p> <p>3</p> <p>3</p> <p>9</p> <p>31 (20.4)<sup>b</sup></p> <p>8</p> <p>8</p> <p>6</p> <p>4</p> <p>4</p> <p>11</p> <p>56 (36.8)<sup>a</sup></p> <p>17</p> <p>8</p> <p>6</p> <p>4</p> <p>5</p> <p>16</p> <p>21 (13.8)<sup>c</sup></p> <p>0</p> <p>26 (17.1)<sup>b</sup></p>	<p><sup>a/b</sup> 0.0005*</p> <p><sup>a/c</sup>&lt;0.0001*</p> <p><sup>b/c</sup> 0.1472</p>	<p>Same 14 (100.0)</p> <p>↓ 0</p> <p>↑ 5 (17.9)</p> <p>Same 23 (82.1)</p> <p>↓ 0</p> <p>↑ 26 (63.4)</p> <p>Same 15 (36.6)</p> <p>↓ 0</p> <p>↑ 13 (68.4)</p> <p>Same 6 (31.6)</p> <p>↓ 0</p> <p>↑ 15 (57.7)</p> <p>Same 11 (42.3)</p>	<p>Same 14 (100.0)</p> <p>↓ 0</p> <p>↑ 6 (21.4)</p> <p>Same 22 (78.6)</p> <p>↓ 0</p> <p>↑ 31 (75.6)</p> <p>Same 10 (24.4)</p> <p>↓ 0</p> <p>↑ 13 (68.4)</p> <p>Same 5 (26.3)</p> <p>↓ 1 (5.3)</p> <p>↑ 22 (84.6)</p> <p>Same 4 (15.4)</p>	<p>Same 14 (100.0)</p> <p>↓ 0</p> <p>↑ 6 (21.4)</p> <p>Same 22 (78.6)</p> <p>↓ 0</p> <p>↑ 23 (56.1)</p> <p>Same 18 (43.9)</p> <p>↓ 0</p> <p>↑ 6 (26.4)</p> <p>↓ 0</p> <p>↑ 24 (92.3)</p> <p>Same 2 (7.7)</p>

95% CI 0.90–6.54,  $p = 0.0798$ ) and comorbidities (OR = 1.67, 95% CI 0.84–3.32,  $p = 0.1465$ ) (Table 1).

In case variant 3 (right frontal tumor without hemiparesis), the majority of respondents who preferred maximum resection with mapping or without mapping indicated that they would choose the same approach (maximum resection with mapping: 96.1%, without mapping: 90.2%), whereas a slight majority of respondents who preferred debulking indicated they would be more aggressive in this case variant (42.9%) (Table 1). Overall, most respondents chose the same approach as in the original case ( $p < 0.0001$ ). European and US neurosurgeons did not differ in treatment preferences for all three case variants.

### Case 2

The clinical details of case 2 are described in the text box of Fig. 4B.

The majority of respondents preferred maximum resection without mapping (71.7%) significantly more often than maximum resection with mapping (13.2%,  $p < 0.0001$ ) and debulking (11.2%,  $p < 0.0001$ ) (Table 1, Fig. 4). Two respondents preferred a biopsy, 1 respondent preferred chemotherapy or radiotherapy only and two respondents preferred best supportive care.

In case variant 1 (younger patient), a majority of respondents who preferred maximum resection with mapping, without mapping or debulking chose the same approach (maximum resection with mapping: 100%, without mapping: 92.7%, debulking: 58.3%) ( $p < 0.0001$ ) (Table 1). Regression analysis showed that respondents who had reported the factor “age” as important or very important earlier in the survey were indeed more aggressive in case variant 1 when the patient was younger (OR = 7.53, 95% CI 1.63–34.70,  $p = 0.0096$ ) (Tables 1, 2).

In case variant 2 (ASA III, KPS 60), the majority of respondents who preferred maximum resection with mapping in the original case chose the same approach (62.5%), as did respondents who originally preferred maximum resection without mapping (59.4%) (Table 1). Overall, a majority of respondents chose the same approach for this case variant and the original case ( $p = 0.0012$ ). Regression analysis showed a significant relationship with earlier reported Likert scales on patient functioning (OR = 4.52, 95% CI 1.28–15.98,  $p = 0.0192$ ) and comorbidities (OR = 2.89, 95% CI 1.37–6.09,  $p = 0.0054$ ) (Table 2).

In case variant 3 (11 mm midline shift), the majority of respondents who preferred maximum resection with mapping, without mapping and debulking indicated that they would choose the same approach (maximum resection with mapping: 93.8%, without mapping: 92.7%, debulking: 66.7%) (Table 1). Overall, most respondents chose the same approach as in the original case ( $p < 0.0001$ ). European and

US neurosurgeons did not differ in treatment preferences for all three case variants.

### Case 3

The clinical details of case 3 are described in the text box of Fig. 4C.

The majority of respondents preferred a biopsy (58.8%) significantly more often than debulking (26.1%,  $p < 0.0001$ ) and maximum resection (with mapping: 0.65, without mapping: 8.5%;  $p < 0.0001$ ) or chemotherapy/radiotherapy only (1.3%) or best supportive care (4.6%) ( $p < 0.0001$ ) (Table 1, Fig. 4). European respondents were more likely to choose biopsy for this case than their US colleagues (OR = 3.52, 95% CI 1.63–7.59,  $p = 0.0014$ ).

In case variant 1 (elderly patient), a majority of respondents who preferred maximum resection without mapping or biopsy chose the same approach (maximum resection without mapping: 53.8%, biopsy: 69.6), while 61.3% of the respondents who preferred debulking chose a more defensive approach (Table 1). Overall, the majority of respondents prefers the same approach for the case variant as in the original case ( $p < 0.0001$ ). Regression analysis showed that respondents who had reported the factor age as important or very important earlier in the survey were indeed more defensive in case variant 1 when the patient was older (OR = 2.22, 95% CI 1.05–4.68,  $p = 0.0358$ ) (Table 2).

In case variant 2 (ASA III, KPS 60), the majority of respondents who preferred biopsy in the original case chose the same approach in this case variant (75.9%), as did the respondents who preferred maximum resection without mapping (76.9%) or debulking (66.7%). Notably, a majority of respondents who preferred best supportive treatment in the original case now indicated to be more aggressive (71.4%) (Table 1). Overall, a majority of respondents chose the same approach for this case variant and the original case ( $p < 0.0001$ ). Regression analysis showed no relationship with earlier reported Likert scales on patient functioning (OR = 1.10, 95% CI 0.37–3.58,  $p = 0.8764$ ) and comorbidities (OR = 0.79, 95% CI 0.34–1.85,  $p = 0.5964$ ) (Table 1).

### Case 4

The clinical details of case 4 are described in the text box of Fig. 4D.

The majority of respondents preferred debulking (36.8%) significantly more often than maximum resection without mapping (20.4%) or best supportive care (17.1%) ( $p = 0.0005$ ), and also significantly more often than maximum resection with mapping (11.8%) or biopsy (16.4%) ( $p < 0.0001$ ). (Table 1, Fig. 4). European respondents were

more defensive and were more likely to prefer best supportive care (OR = 9.24, 95% CI 3.00–28.47,  $p = 0.0001$ ), while US respondents were more aggressive and more often chose maximum resection without mapping (OR = 0.28, 95% CI 0.11–0.69,  $p = 0.0060$ ).

In case variant 1 (younger patient), a majority of respondents who preferred maximum resection with or without mapping chose the same approach (maximum resection with mapping: 100%, without mapping: 82.1%). In contrast, a majority who originally preferred debulking, biopsy or best supportive care chose to be more aggressive in this situation (debulking: 63.4%, biopsy: 68.4%, best supportive care: 57.7%) (Table 1). Overall, there was no significant difference between a more aggressive approach (46.1%) or the same approach (53.9%) for this case variant ( $p = 0.2129$ ). Regression analysis showed a nonsignificant relationship with earlier reported Likert scales on age (OR = 1.74, 95% CI 0.85–3.56,  $p = 0.1306$ ) (Table 2).

In case variant 2 (right temporal tumor, no aphasia), the majority of respondents who preferred maximum resection with or without mapping in the original case chose the same approach in this case variant (maximum resection with mapping: 100%, without mapping: 78.6%). Similar to variant 1, the respondents who preferred debulking or biopsy in the original case reported more often to be more aggressive in this situation (debulking: 75.6%, biopsy: 68.4%), as did the respondents who preferred best supportive care earlier (84.6%) (Table 1). Overall, a majority of respondents chose to be more aggressive in this case variant ( $p = 0.0337$ ). Regression analysis showed a significant relationship with earlier reported Likert scales on patient functioning (OR = 4.52, 95% CI 1.28–15.98,  $p = 0.0192$ ) and comorbidities (OR = 2.89, 95% CI 1.37–6.09,  $p = 0.0054$ ) (Table 2).

In case variant 3 (11 mm midline shift), similar to variants 1 and 2, the majority of respondents who were already aggressive in the original case choose the same approach in this situation (maximum resection with mapping: 100%, without mapping: 78.6%). The majority of respondents who were slightly more defensive in the original case choose to be more aggressive in this case variant (debulking: 56.1%, biopsy: 68.4%, best supportive care: 92.3%) (Table 1). Overall, there was no significant difference between a more aggressive approach (51.6%) or the same approach (48.4%) for this case variant ( $p = 0.6094$ ). Regression analysis showed a very slight nonsignificant relationship with the earlier reported Likert scores on preoperative functioning (OR = 1.08, 95% CI 0.40–2.91,  $p = 0.8862$ ) and comorbidities (OR = 1.54, 95% CI 0.76–3.11,  $p = 0.2310$ ). Furthermore, European respondents were more likely to choose a more aggressive approach for variant 3 (OR = 2.96, 95% CI 1.31–6.69,  $p = 0.0088$ ) (Table 2).

## Discussion

### Key results

This survey is the first to investigate the local neurosurgical practices regarding treatment modality selection and decision making in GBM patients on a global scale. These practice variations were evaluated both on a theoretical and practical level (using patient cases) and further analyzed using multiple regression analyses for region, affiliation, and various perioperative factors' Likert scores.

We found a significant heterogeneity among surgeons and centers regarding their local decision-making practices as well as their surgical treatment preferences in glioblastoma patients. For the majority of the survey questions, the responses were significantly different between respondents. Overall, the most notable differences were observed for questions about the presence of a multidisciplinary neuro-oncology tumor board, the timing of this board, the importance of various perioperative factors in the decision-making process, the role and meaning of various perioperative factors in this process (aggressive vs. defensive approach), the reasons why the patient's age does or does not play a role in this process, how aggressive the treatment for GBM patients in general should be, the respondent's preferred treatment in various GBM cases, and the respondent's adaptation to multiple case variants. Subgroup analyses for affiliation using multivariate regression showed that multidisciplinary boards are more common at academic centers, whereas the analysis for region indicated that European neurosurgeons more commonly discuss the patient at these boards prior to the outpatient clinic. On the other hand, their US colleagues more commonly discuss the patient at these boards after the histopathological diagnosis. We do not have a clear explanation for this finding, although the highly centralized organization of hospitals and healthcare in Europe might play a role which may deem pre-clinic assessment and discussion of cases necessary.

Multivariate regression further showed that in some cases, US colleagues are slightly more aggressive in their surgical attitude: they are less likely to perform a biopsy when the tumor is located in or near eloquent areas, and more likely to have a more aggressive approach in patient cases 3 and 4. Moreover, the surgeon's reported importance of various perioperative factors does often correspond with their case responses: in the case variants, respondents who had earlier in the survey rated the factor or factors that were altered important in their decision were more likely to change their approach.

## Interpretation and comparison with the literature

We observed various significant differences between surgeons and centers in a theoretical and practical setting.

First, the difference in aggressiveness/defensiveness of European vs. US neurosurgeons which we observed in our results. The theoretical part of the survey showed that European neurosurgeons were almost five times less likely to have a neutral attitude towards the factor ‘tumor located in or near eloquent areas’ and were more than two times more likely to choose a biopsy in these cases. Their US colleagues however were more often neutral about this factor or preferred a resection (which could be both STR or GTR). To the best of our knowledge, the difference in attitude between EU and US neurosurgeons has not been reported in the previous literature. We would like to underline that our survey only studied the surgeon’s preoperative attitude, which may not always reflect the intraoperative attitude (or surgical result) adequately. Surgeons who aim for GTR not always reach this goal and sometimes decide intraoperatively to go for STR instead. Furthermore, note that the observed differences in aggressiveness of attitude do not have any relationship with differences in skill level.

When evaluating the practical part of the survey, two cases included patients with an eloquent tumor (case 1: right frontoparietal causing hemiparesis; case 4: left parietotemporal causing aphasia). When analyzing these case responses, there is no significant difference in case 1 between European and US neurosurgeons, but for case 4 there is: US neurosurgeons were almost four times as likely to select ‘maximum resection without mapping’ as their preferred option, whereas European neurosurgeons were more than nine times more likely to select ‘best supportive treatment’ as their preferred choice. The fact that there is only a significant difference between EU/US neurosurgeons in case 4 and not in case 1 is of particular interest. One possible cause may be the fact that in case 1 almost 95% of respondents chose an aggressive approach (maximum resection with or without mapping). This in turn might be explained by the fact that the patient was in much better condition in case 1 than in case 4 (medical history, KPS, GCS, neurological examination), for which the responses were relatively evenly distributed between a very defensive approach (best supportive treatment) and a very aggressive one (maximum resection). The combined results on these cases might indicate that in young patients in good condition with eloquently located tumors, both European and US neurosurgeons opt for an aggressive approach. However, when a patient is older, has a suboptimal condition or has a significant amount of neurological morbidity, European colleagues on average become more defensive, while their US colleagues still prefer an aggressive approach (on average, according to the practical part of our survey). Our data did provide us with a possible

reason of this observation. Although we did not observe a difference in the theoretical importance of the factor “age” between European vs US neurosurgeons, the difference of the factor “Patient functioning (KPS)” was significant. Europeans were more inclined to deem this factor more important in their decision making. This might explain why they would have a slightly more defensive attitude in older patients with a suboptimal KPS. However, since the differences between European and US colleagues are relatively small these findings need to be validated in a second dataset.

Moreover, we further analyzed the data to evaluate if the factors that influence the surgeon’s decision-making are the same in theory and practice. As mentioned above, case 1 described a relatively young and fit patient. Altering the patient’s age or the location of the tumor does not significantly change the responses. However, when altering the ASA score (I–III) and KPS (100–60), a majority of respondents chooses a more defensive approach. This indicates that in fit patients, even when the tumor is located in or near eloquent areas, an overwhelming majority of surgeons still prefer to be relatively aggressive and that the preoperative functioning of the patient is for them more important than either the patient’s age or the tumor’s location. This is partly in line with the reported Likert scores, in which the factor “location and eloquence” was rated with a mean of 4.3, “patient functioning” with a mean of 4.2 and “age” with a mean of 3.4. It is worth mentioning that even though the tumor in this case is eloquently located, almost 40% of respondents strives for maximum resection *without* mapping, which underlines the fact that mapping techniques are still not standard of care for these patients in all centers. The responses of case 2 are in line with case 1: age seems to be of lesser relevance than patient functioning. In case 3, the patient is young but has a much worse overall functioning and neurological performance with the scan showing a classic butterfly glioma. Almost three-quarters of the respondents now choose to be more defensive and opt for debulking or biopsy instead. Increasing the patient’s age to 75 makes the respondents’ preferred approaches more defensive, more so in those who first preferred debulking. Improving the patient’s fitness to ASA I/KPS 100/MMSE 30/30 makes their approaches slightly more aggressive (almost 20%), more so from those who first preferred biopsy. Note that the increase in defensive approaches in the case of an older patient was larger than the increase in aggressive approaches in the case of a fitter patient. In this case, the location of the tumor (butterfly glioma) shows to be the decisive factor. In case 4, the patient is of older age, has an extensive past medical history, significant neurological morbidity (severe receptive aphasia) and suboptimal functioning and GCS (E3M6V4, KPS 60). Approximately a third of all respondents preferred an aggressive approach (maximum resection), a third chose to be more defensive (biopsy, best supportive care), and a

**Table 2** Treatment modality selection in selected GBM cases – Regression analyses

Case variant	Approach	Response (%)	<i>P</i> value	Adjusted OR for neurosurgeons who rated this factor important (4–5 Likert Scale) vs. neutral or unimportant (1–2–3) (95% CI)	<i>P</i> value	Adjusted OR for European vs. US neurosurgeons (95% CI)	<i>P</i> Value
<b>Case 1 Base</b>	Max Rx, mapping +	87 (56.1) <sup>a</sup>	0.0022 <sup>*a/b</sup>	NA		0.80 (0.39–1.66)	0.5572
	Max Rx, mapping –	60 (38.7) <sup>b</sup>	<0.0001 <sup>*a/c</sup>			0.28 (0.051–1.49)	0.1340
	Debulking	8 (5.2) <sup>c</sup>	<0.0001 <sup>*b/c</sup>			0.59 (0.28–1.26)	0.1747
Case 1 Variant 1	More aggressive	8 (6.0)	<0.0001 <sup>*a/b</sup>			NA	
Older patient (75 years old)	Same	102 (76.1) <sup>b</sup>				0.64 (0.24–1.69)	“
Factor: Age	More defensive	24 (17.9) <sup>a</sup>		4.89 (1.84–13.00)	0.0015*	1.56 (0.59–4.09)	0.3707
Case 1 Variant 2	More aggressive	1 (0.75)	0.2736 <sup>a/b</sup>			NA	
ASA III, KPS 60	Same	62 (46.3) <sup>b</sup>				0.53 (0.24–1.14)	“
Factor: Preoperative functioning <sup>†</sup>	More defensive	71 (53.0) <sup>a</sup>		2.43 (0.90–6.54) <sup>†</sup>	0.0798	1.90 (0.88–4.12)	0.1021
Factor: Comorbidities <sup>††</sup>				1.67 (0.84–3.32) <sup>††</sup>	0.1465		
Case 1 Variant 3	More aggressive	7 (5.2) <sup>a</sup>	<0.0001 <sup>*a/b</sup>	NA		NA	
Right frontal, no hemiparesis	Same	121 (90.3) <sup>b</sup>					
Factor: Location and eloquence	More defensive	6 (4.5)					
Factor: Preoperative morbidity							
<b>Case 2 Base</b>	Max Rx, mapping +	20 (13.2) <sup>b</sup>	<0.0001 <sup>*a/b</sup>	NA		0.84 (0.24–2.93)	0.7894
	Max Rx, mapping –	109 (71.70) <sup>a</sup>	<0.0001 <sup>*a/c</sup>			0.81 (0.35–1.92)	0.6397
	Debulking	17 (11.2) <sup>b</sup>	<0.0001 <sup>*b/c</sup>			1.70 (0.49–5.85)	0.4027
	Biopsy	3 (2.0) <sup>c</sup>				NA	
	CTx/RTx	1 (0.66) <sup>c</sup>				NA	
	Best supportive care	2 (1.3) <sup>c</sup>				NA	
Case 2 Variant 1	More aggressive	14 (10.9) <sup>a</sup>	<0.0001 <sup>*a/b</sup>			0.98 (0.30–3.13)	0.9677
Younger patient (45 years old)	Same	114 (89.1) <sup>b</sup>				1.02 (0.32–3.29)	“
Factor: Age	More defensive	0		7.53 (1.63–34.70)	0.0096*		
Case 2 Variant 2	More aggressive	6 (4.9)	0.0012 <sup>*a/b</sup>			NA	
ASA III, KPS 60	Same	74 (57.8) <sup>b</sup>				0.47 (0.21–1.05)	“
Factor: Preoperative functioning <sup>†</sup>	More defensive	48 (37.5) <sup>a</sup>		4.52 (1.28–15.98) <sup>†</sup>	0.0192*	2.13 (0.95–4.78)	0.0656
Factor: Comorbidities <sup>††</sup>				2.89 (1.37–6.09) <sup>††</sup>	0.0054*		
Case 2 Variant 3	More aggressive	10 (7.8) <sup>a</sup>	<0.0001 <sup>*a/b</sup>	NA		0.61 (0.13–2.87)	0.5299
Midline shift (11 mm)	Same	116 (90.6) <sup>b</sup>				1.64 (0.35–7.74)	“
Factor: None	More defensive	2 (1.6)					
<b>Case 3 Base</b>	Max Rx, mapping +	1 (0.65) <sup>c</sup>	<0.0001 <sup>*a/b</sup>	NA		NA	
	Max Rx, mapping –	13 (8.5) <sup>c</sup>	<0.0001 <sup>*a/c</sup>			NA	
	Debulking	40 (26.1) <sup>b</sup>	<0.0001 <sup>*b/c</sup>			0.50 (0.22–1.14)	0.0999
	Biopsy	90 (38.8) <sup>a</sup>				3.52 (1.63–7.59)	0.0014*
	CTx/RTx	2 (1.3) <sup>c</sup>				NA	
	Best supportive care	7 (4.6) <sup>c</sup>				NA	
Case 3 Variant 1	More aggressive	5 (3.8)	<0.0001 <sup>*a/b</sup>				
Older patient (75 years old)	Same	84 (63.2) <sup>b</sup>				1.12 (0.51–2.48)	“
Factor: Age	More defensive	44 (33.1) <sup>a</sup>		2.22 (1.05–4.68)	0.0358*	0.89 (0.40–1.97)	0.7743

**Table 2** (continued)

Case variant	Approach	Response (%)	<i>P</i> value	Adjusted OR for neurosurgeons who rated this factor important (4–5 Likert Scale) vs. neutral or unimportant (1–2–3) (95% CI)	<i>P</i> value	Adjusted OR for European vs. US neurosurgeons (95% CI)	<i>P</i> Value		
<b>Case 3 Variant 2</b>									
ASA I, KPS 100, MMSE 30/30	More aggressive	26 (19.8) <sup>a</sup>	<0.0001 <sup>*a/b</sup>	1.10 (0.37–3.58) <sup>†</sup>	0.8764	1.19 (0.46–3.09)	0.7162		
	Same	98 (74.8) <sup>b</sup>				0.84 (0.32–2.17)	“		
Factor: Preoperative functioning <sup>†</sup>	More defensive	7 (5.3)				0.79 (0.34–1.85) <sup>††</sup>	0.5946		
<b>Case 4 Base</b>									
	Max Rx, mapping +	18 (14.1) <sup>b</sup>	0.0003 <sup>*a/b</sup>	NA		0.56 (0.20–1.59)	0.2783		
	Max Rx, mapping –	31 (24.2) <sup>b</sup>	<0.0001 <sup>*a/c</sup>			0.28 (0.11–0.69)	0.0060 <sup>*</sup>		
	Debulking	56 (43.8) <sup>a</sup>	0.1472 <sup>b/c</sup>			1.14 (0.59–2.20)	0.7051		
	Biopsy	21 (16.4) <sup>c</sup>				0.81 (0.32–2.02)	0.6481		
	CTx/RTx	0				9.24 (3.00–28.47)	0.0001 <sup>*</sup>		
	Best supportive care	26 (20.3) <sup>b</sup>							
<b>Case 4 Variant 1</b>									
Younger patient (45 years old)	More aggressive	59 (46.1) <sup>a</sup>	0.2129 <sup>a/b</sup>	1.74 (0.85–3.56)	0.1306	2.31 (1.02–5.20)	0.0436 <sup>*</sup>		
	Same	69 (53.9) <sup>b</sup>				0.43 (0.19–0.98)	“		
	More defensive	0							
<b>Case 4 Variant 2</b>									
Right temporal, no aphasia	More aggressive	72 (56.3) <sup>a</sup>	0.0337 <sup>*a/b</sup>	1.72 (0.66–4.51) <sup>†</sup>	0.2680	1.72 (0.77–3.83)	0.1833		
Factor: Location and eloquence <sup>†</sup>	Same	55 (43.0) <sup>b</sup>				0.90 (0.37–2.23) <sup>††</sup>	0.8276	0.58 (0.26–1.29)	“
Factor: Preoperative morbidity <sup>††</sup>	More defensive	1 (0.078)							
<b>Case 4 Variant 3</b>									
GCS 15, ASA I, KPS 100	More aggressive	66 (51.6) <sup>a</sup>	0.6094 <sup>a/b</sup>	1.08 (0.40–2.91) <sup>†</sup>	0.8862	2.96 (1.31–6.69)	0.0088 <sup>*</sup>		
Factor: Preoperative functioning <sup>†</sup>	Same	62 (48.4) <sup>b</sup>				1.54 (0.76–3.11) <sup>††</sup>	0.2310	0.34 (0.15–0.76)	“
Factor: Comorbidities <sup>††</sup>	More defensive	0							

*Max Rx* maximum resection, *Mapping +* with mapping, *Mapping –* without mapping, *CTx* chemotherapy, *RTx* radiotherapy, *GCS* Glasgow Coma Scale, *ASA* American Society of Anesthesiologists score, *KPS* Karnofsky Performance Score, *MMSE* Mini Mental State Examination, *NB* the modalities biopsy, debulking, maximum resection without mapping and maximum resection with mapping include adjuvant chemoradiotherapy

third was in between (debulking). Lowering the patient's age, changing the tumor's location to the right temporal lobe without causing aphasia or improving the patient's performance all led almost half of the respondents to choose a more aggressive approach. All factors were relatively similar

in their capacity to change the respondent's preferred treatment: tumor location and eloquence did so to the greatest extent followed by preoperative functioning and age (which is in accordance with the reported mean Likert scores). Thus, the factors which were found to be the most important

**Case 1**

Male, 36 y/o

Past medical history: blank

History and physical: decreased strength and coordination in the left upper extremity for 3 months. No headache, no nausea, no vomitus. Prefers an aggressive resection.

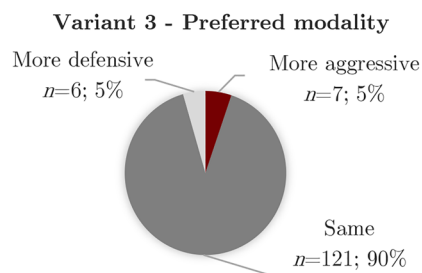
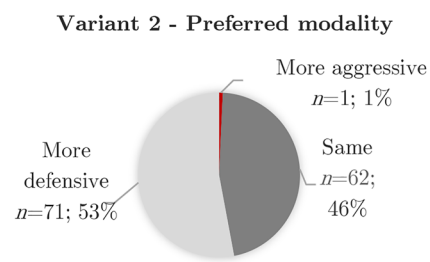
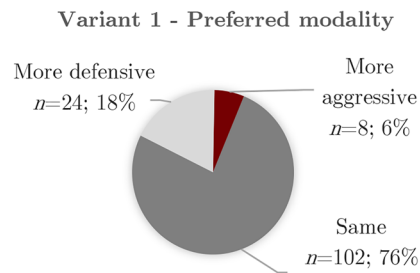
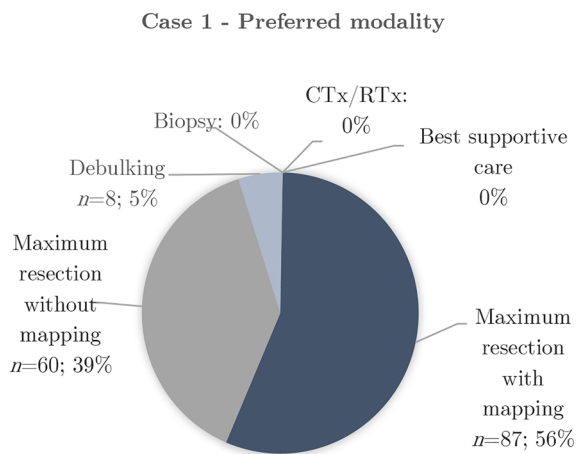
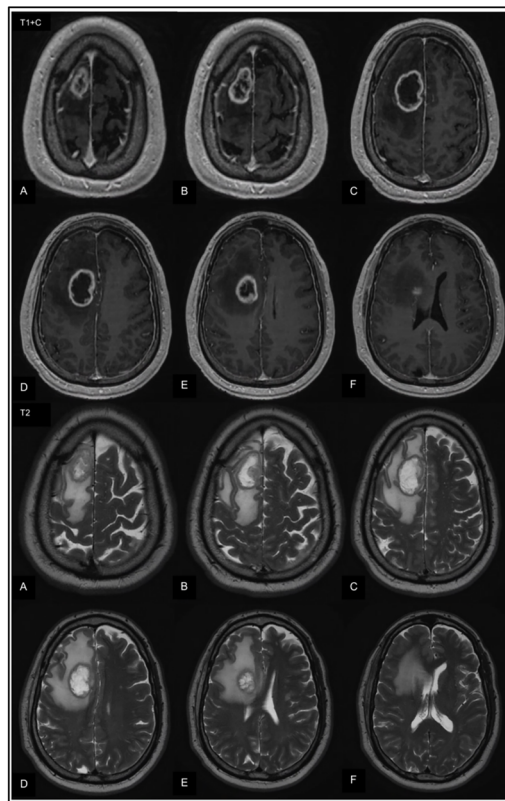
Neurological examination: Barré +/-, left-sided hemiparesis MRC grade 4. KPS: 100. MMSE: 30/30.

MRI + Gd: space-occupying lesion with contrast enhancement and extensive perifocal edema in the right frontoparietal region, suspected primary high-grade glioma

Which surgical treatment would you prefer in this case?

NB: for adjuncts, select one or more answers

Case variants: 1) older patient (75 years old); 2) ASA III, KPS 60; 3) right frontal tumor, no hemiparesis



**Fig. 4** Treatment modality selection in various GBM cases

**Case 2**

Female, 75 y/o

Past medical history: blank

History and physical: headache for 2 months, incidental finding on MRI.

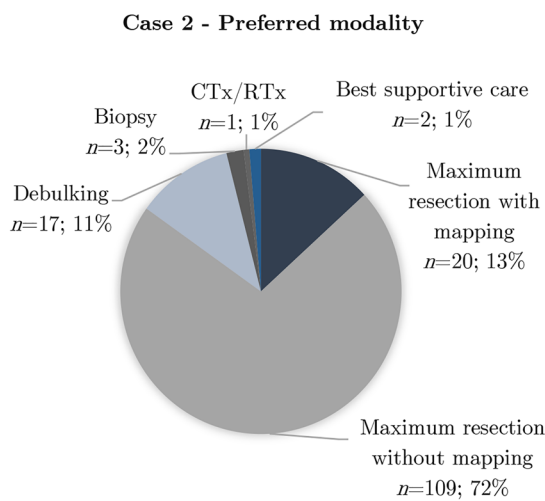
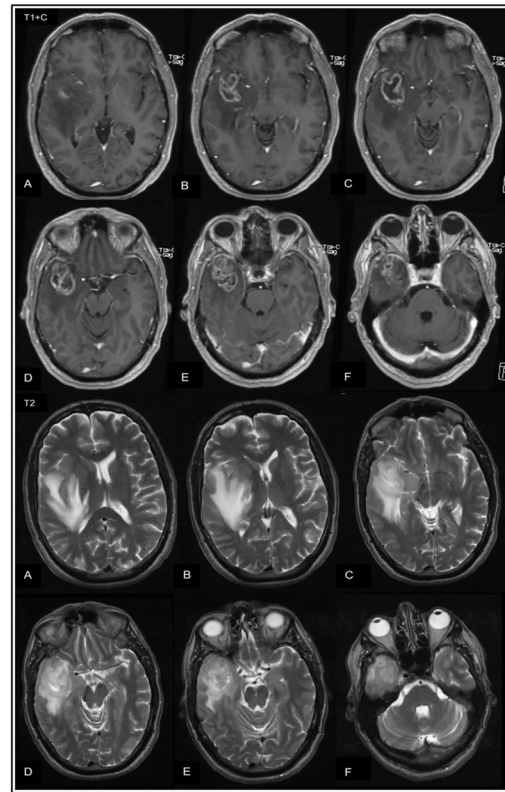
Neurological examination: normal. KPS: 100. MMSE: 30/30.

MRI + Gd: space-occupying lesion in the right temporal lobe. Irregular contrast enhancement, suspected for glioblastoma.

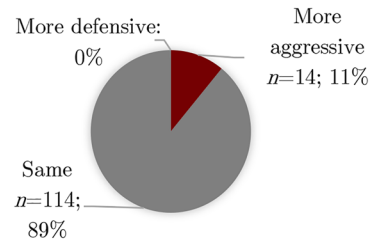
Which surgical treatment would you prefer in this case?

NB: for adjuncts, select one or more answers

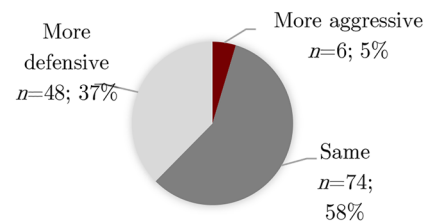
Case variants: 1) younger patient (45 years old); 2) ASA III, KPS 60; 3) midline shift (11 mm)



**Variant 1 - Preferred modality**



**Variant 2 - Preferred modality**



**Variant 3 - Preferred modality**

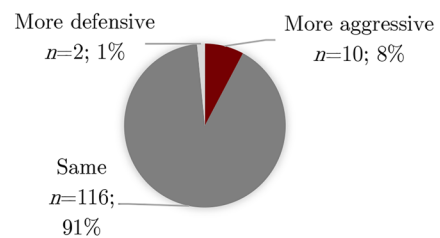


Fig. 4 (continued)

**Case 3**

Male, 44 y/o

Past medical history: hypertension, ICD placement in 2016 for persistent ventricular arrhythmias following acute myocardial infarctions in 2012 and 2016.

History and physical: worsening headache for 4 months and personality changes, sometimes disoriented and apathic according to partner. No vision problems.

Neurological examination: normal. KPS: 70. MMSE: 21/30.

MRI + Gd: large multifocal contrast-enhancing lesion in both frontal lobes and corpus callosum. Inhomogeneous aspect with presence of both cysts and solid parts. Developing biventricular hydrocephalus.

Which surgical treatment would you prefer in this case?

NB: for adjuncts, select one or more answers

Case variants: 1) older patient (75 years old); 2) ASA I, KPS 100, MMSE 30/30

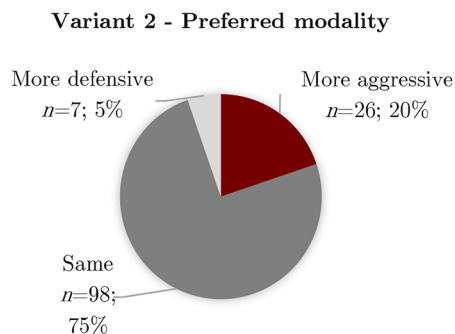
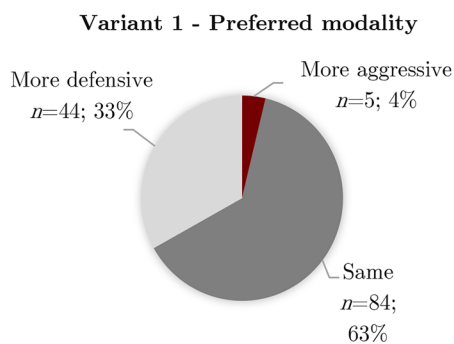
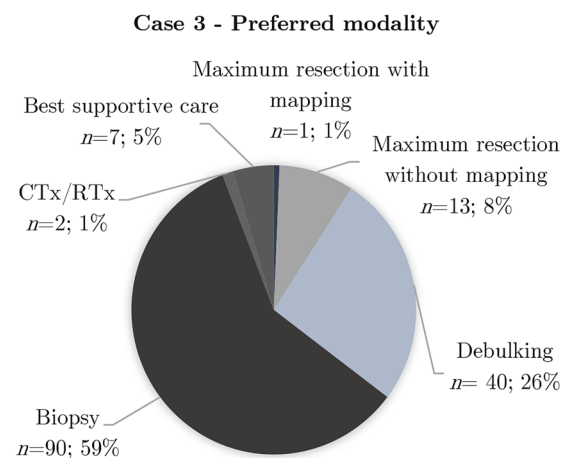
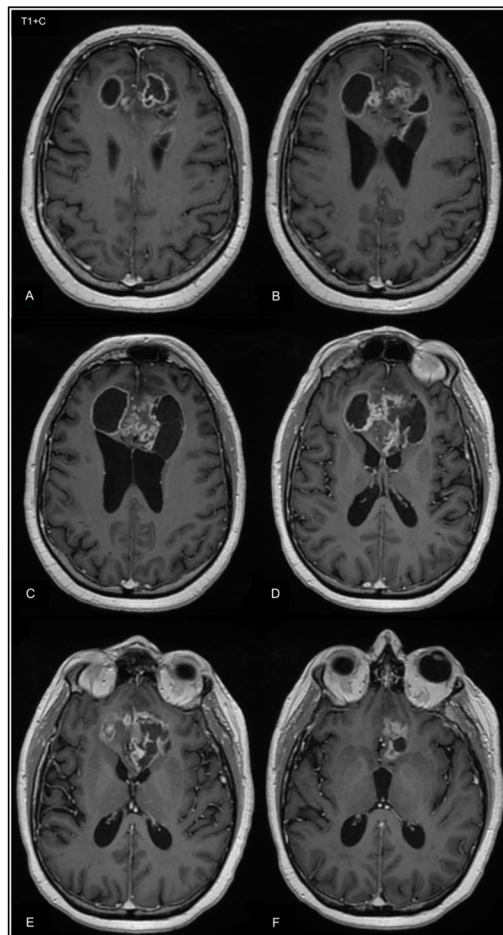


Fig. 4 (continued)

**Case 4**

Female, 76 y/o

Past medical history: hypertension, bilateral peripheral arterial occlusive disease Fontaine III since 2010, cataract

History and physical: significant concentration problems and receptive aphasia. Morning sickness and frequent vomiting since last week. Two epileptic seizures last 3 days, treated with intranasal midazolam.

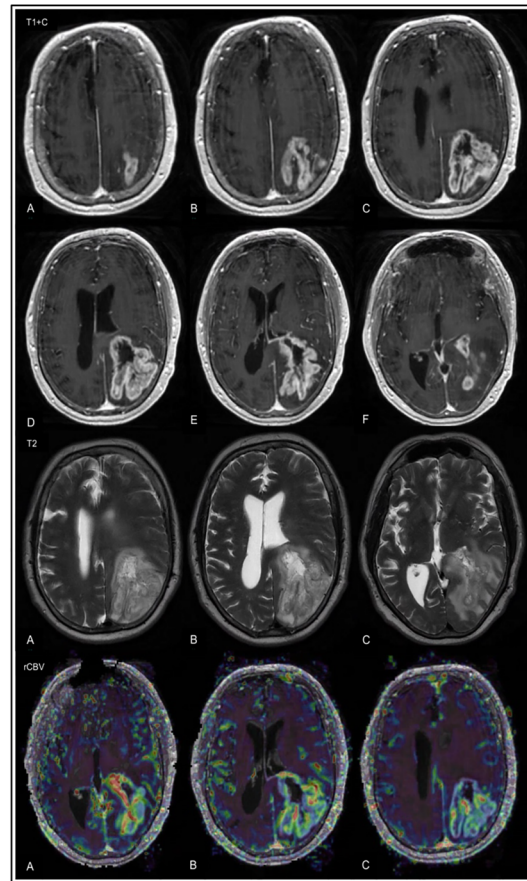
Neurological examination: E3V4M6, severe receptive aphasia, right-sided hemi-neglect, gait imbalance. KPS: 60.

MRI + Gd: contrast-enhancing lesion in the left parieto-temporal lobe with extensive edema, possibly near Wernicke's area. Suspected GBM.

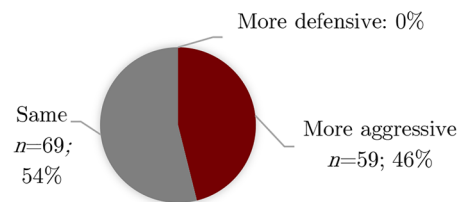
Which surgical treatment would you prefer in this case?

NB: for adjuncts, select one or more answers

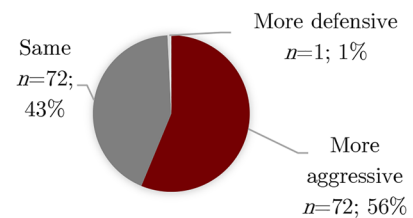
Case variants: 1) younger (45 years old); 2) right temporal tumor, no aphasia; 3) GCS 15, ASA I, KPS 60



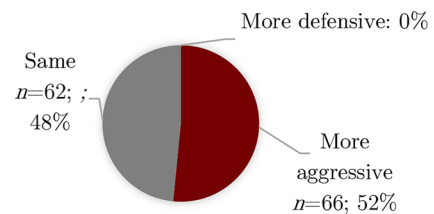
**Variant 1 - Preferred modality**



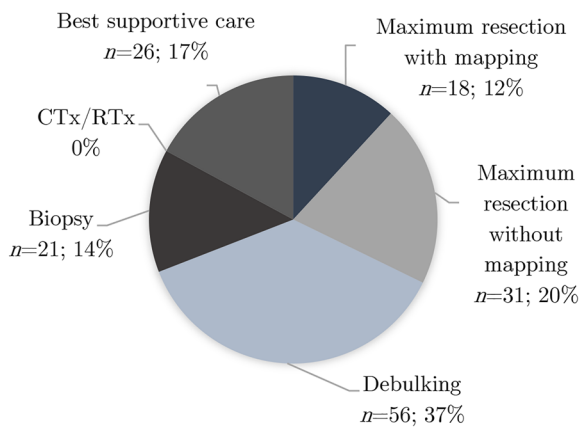
**Variant 2 - Preferred modality**



**Variant 3 - Preferred modality**



**Case 4 - Preferred modality**



**Fig. 4** (continued)

in theory were confirmed to influence the respondents' decisions to the greatest extent in practice as well.

While guidelines exist on the management of neurosurgical disease, neurosurgical practices and treatment selection in brain tumor patients vary significantly depending on a surgeon's preferred approach which results in varied behaviors (biopsy and resection). Recently, Müller et al. published their results on a novel method to compare surgical decisions between two Dutch academic hospitals in GBM patients using probability brain maps [23]. In those two similar cohorts –the biopsy percentage differed significantly (21% vs. 40%,  $p=0.002$ ). The location and volume of the tumor, nor the patient's age and condition could explain this difference. Moreover, there was significant variation in the extent of tumor removal: one team more often resected tumor in the right caudate nucleus and anterior limb of the right internal capsule than the other team. They conclude that these differences may be related to a difference in risk/benefit decision making. Though, it remains unclear on which objective basis this would be.

### Limitations and strengths

A notable limitation of a survey-based study such as this is sampling bias, while 224 neurosurgeons from 41 countries were surveyed, there are surgeons and centers that were not included in the study. In particular, the respondents skewed towards western countries from high-income countries. In addition, surgical decision making may reflect a center's culture on the surgeon's responses. Second, we did not have the depth of data to analyze the potential influence of the center's culture on the surgeon's responses. Third, our data did not allow for an additional analysis of the type of mapping (e.g. awake vs. asleep, subcortical vs. cortical). Important strengths of this study include the survey's global distribution, the survey's combination of theory and practice, the detail and variance in the patient cases, and the subgroup analyses between EU and US neurosurgeons and academic versus non-academic centers.

### Conclusions and future directions

This survey demonstrates the heterogeneity in local practices and preferences between surgeons and centers with regard to decision making and treatment modality selection in GBM patients. The lack of objective data and clinical guidelines has caused global variability since no consensus has been reached on a wide array of critical perioperative decisions. A large consistency however between factors influencing the theoretical and practical decision-making exercises has been demonstrated. The results of this study mark the importance

for additional research that addresses critical aspects of these processes. Further research could focus on the use of machine learning to create an algorithm incorporating the most important preoperative factors (e.g. location and eloquence, age, KPS, NIHSS) from which the optimum strategy in each case would be rendered (e.g. biopsy, debulking, maximum resection with or without mapping). This would serve as a tool for neurosurgeons to help them with their decision making. It would also be interesting to correlate the findings from this survey with responses from anesthesiologists and trained assessors of eloquent areas such as neuro-linguists and neurophysiologists. A third potential topic would be the difference in decision making in low-income versus high-income countries and its effect on best practices.

The current study may serve as a first step towards future large-scale research efforts to identify essential factors that can be optimized and may therefore benefit from consensus, consequently streamlining the decision-making process. This will provide the neurosurgical field with the required quantity, quality and depth of data on which practical guidelines can be based in order to focus on identifying the optimal treatment for subgroups of GBM patients.

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**Data availability** The datasets generated during and analysed during the current study are not publicly available due to ethical reasons, but are available from the corresponding author on reasonable request.

**Code availability** R code is available from the corresponding author on reasonable request.

### Declarations

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** This article does not contain any studies with human participants or animals performed by any of the authors.

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