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EANS-EANO guidelines on the extent of resection in gliomas

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Abstract

Intense efforts are employed to optimize neurosurgical resection of gliomas in different clinical scenarios. However, the level of evidence employed toward personalized treatment decisions is still moderate. Therefore, a joint task force was created by the European Association for Neurosurgical Societies (EANS) and the European Association of Neuro-Oncology (EANO) in order to provide interdisciplinary guidance on the extent of resection (EOR) in glioma surgery. This task force assessed the data on the EOR in gliomas, evaluated the level of evidence, and composed recommendations. The EOR is determined routinely by postoperative magnetic resonance imaging. Since EOR may be associated with survival and may have an impact on epilepsy, neurocognition, quality of life, neurological status, and also on planning of radiation and pharmacotherapy (evidence classes I-IV), recommendations of different levels can be made for the resection of newly diagnosed glioblastomas (level A), recurrent glioblastomas (level C), newly diagnosed (level B) and recurrent (good practice point) IDH mutant gliomas, ependymomas in children (level B) and adults (good practice point) as well as World Health Organization CNS grade 1 tumors (good practice point). We hereby report the outcome of this collaborative effort by the joint task force between EANS and EANO.

Key Points

- Newly diagnosed (level A) and recurrent (level C) glioblastomas should be resected completely, whenever safely possible. In glioblastoma IDH wild type, complete resection is defined as removal of all contrast-enhancing tumor on postoperative magnetic resonance imaging.
- Newly diagnosed (level B) and also recurrent (good practice point) IDH mutant gliomas should be resected to prolong survival and improve epilepsy.
- Newly diagnosed and recurrent ependymomas should be resected in children (level B) and adults (good practice point).

This first joint guideline of the European Association for Neurosurgery (EANS) and the European Association for Neuro-Oncology (EANO) on the extent of resection (EOR) in gliomas aims at assessing the role of EOR in different glioma types in different clinical situations. In general, there is still little evidence from controlled clinical trials leading to wide variations of surgical procedures worldwide. Since EOR is associated with prognosis and has a strong impact on the neurological condition of the patients,[1] standardized operating procedures addressing the required EOR in glioma surgery might be very helpful. These guidelines will address surgery of the most common glioma subtypes according to the current World Health Organization (WHO) classification and respect standard clinical situations like de novo gliomas and recurrences. To accomplish this aim, the EANS and the EANO assembled a task force of experts in glioma surgery, but also in neighboring neurooncologically relevant fields, to provide a comprehensive, multidisciplinary approach to this issue.

Methods

The joint EANS and EANO task force was nominated by the EANS and EANO executive boards and represents the fields of neurosurgery, neurology, radiation oncology, medical oncology, neuroradiology, and neuropathology including molecular

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pathology. The topics of this guideline were distributed among the authors according to their scientific profile and clinical profession. The review process for literature was determined among all authors as follows: The Medline database as well as the Cochrane Library, Embase-Ovid, Cancer Net, and Science Citation Index from January 2000 until September 2024 were searched. Sensitive and specific keywords as well as combinations of keywords were used. The main keywords were glioma, glioblastoma, astrocytoma, oligodendroglioma, IDH mutant, IDH wild type, recurrent, surgery, EOR, prognosis, progression, and survival in various combinations. Additional keywords were used in the specific chapters of this guideline. All types of clinical and basic science articles in all languages represented by the members of the task force were considered. Exclusion criteria were publications not listed in PubMed or being written in languages not represented by members of the task force.

The consensus process followed a structured, multistep approach. Each tumor entity and clinical scenario was assigned to a subgroup of experts according to their clinical and scientific background. Drafts were prepared and then circulated among all authors. The full panel reviewed the drafts in iterative rounds of written feedback, followed by a dedicated consensus conference. Discrepancies were resolved by discussion until unanimous agreement was reached. No recommendation was dropped because of lack of consensus. After discussing different evidence rating systems, the scientific evidence was rated into classes I-IV, and recommendations were labeled as levels A-C, according to the guidelines of the European Federation of Neurological Societies (Table 1), which have traditionally been used in guidelines prepared by the EANO.[2] In cases when sufficient evidence for a recommendation level A-C was not available, the task force offered advice as "good practice point." To address the associations of EOR with patient-related outcome parameters like survival or neurocognition in general and, additionally, the relevance of EOR in specific clinical situations, respectively, for specific entities, we subdivided the recommendations into "general" and "specific" recommendations. The rating of evidence and labeling of recommendations was performed in a final consensus conference of the task force. This process ensured that recommendations reflected a multidisciplinary and pan-European consensus. Natural language processing tools driven by artificial intelligence have not been used in this guideline.

General Recommendations

Neuroradiological Assessment of EOR

Following surgery, the EOR should be evaluated by magnetic resonance imaging (MRI) within 24-48 h to minimize potential interference from postoperative changes.[1,3] The postoperative MR images should be carefully compared to the preoperative MRI scans, employing an MR protocol that, for the purpose of identifying residual tumor, should include, at a minimum, standard MR sequences. These are, for nonenhancing gliomas, T2-weighted or fluid-attenuated inversion recovery (FLAIR) images, while for potentially contrast-enhancing gliomas, T1-weighted sequences with and without the application of intravenous gadolinium-based contrast agent are essential to assess the extent of tumor resection.[1,3,4] The incorporation of diffusion-weighted imaging helps distinguish postoperative ischemia from residual tumor tissue.[3,5] Moreover, differentiating between residual nonenhancing tumor tissue and perifocal edema can pose challenges. Therefore, it is recommended to conduct a follow-up MRI examination 12 weeks after surgery in this situation. Any remaining FLAIR/T2 hyperintensities at this timepoint are highly suspicious of residual nonenhancing tumor components. The addition of advanced MR sequences (eg diffusion-weighted imaging, perfusion-weighted imaging, MR spectroscopy or ^{18}F-fluoro-ethyl-L-tyrosine (FET)—positron emission tomography) to the standard MR protocol could also be beneficial in this regard.[3,6,7]

The completeness of tumor resection can be described either by the percentage of tumor removal or, preferably, by the absolute residual postoperative tumor volume (good practice point).

How to define EOR and, in particular, how to classify different types of incomplete resections is currently under intense discussion. The common term "gross total resection" has been challenged since it is not precisely defined and describes a more subjective impression of having the tumor removed without obvious remnants. In this guideline, we prefer to use the terminology and classification defined by Karschnia et al (see Table 2).[9]

Supramaximal (or supramarginal or supratotal) resection is conceptualized by the resection of nonenhancing, presumably tumor-infiltrated tissue beyond the visible tumor borders of both contrast-enhancing and nonenhancing gliomas as identified on MRI.[8]

In contrast, the category *complete resection* entails the complete removal of contrast-enhancing tumor tissue in glioblastomas, IDH wild type, while in gliomas, IDH mutant regardless of the WHO CNS grade, it necessitates the complete resection of both contrast-enhancing and T2/Flair-hyperintense tumor.[9] Within this guideline, the term "complete resection" will be used instead of "gross total resection." According to a definition by Karschnia et al, the term *near total resection* refers to a reduction of 95%-99% and

Table 1. Evidence classes and recommendations

Evidence	
Class I	Prospective randomized trial (PRT) or review of PRTs
Class II	Prospective matched pair cohort studies
Class III	Any controlled trial (incl. retrospective controls)
Class IV	Uncontrolled studies, case series, case reports, expert opinion
Recommendation	
Level A	One class I or at least two class II studies
Level B	One class II or overwhelming class III evidence
Level C	At least two class III studies
Good practice point	Only class IV evidence

According to Brainin et al.[2]

residual contrast-enhancing tumor volume of ≤1 cm^3 in glioblastomas, IDH wild-type.[9] In the case of gliomas, IDH mutant WHO CNS grades 2-4, it requires a reduction of 90%-99% and a residual Flair/T2-hyperintens tumor volume of ≤5cm^3.[9]

Regarding the presence of substantial residual tumor postsurgery, a threshold of at least 80% removal and ≤5cm^3 of residual contrast-enhancing tumor tissue is indicative of *subtotal resection* in glioblastomas, IDH wild type. For gliomas, IDH mutant WHO CNS grades 2-4, achieving at least 40% removal and ≤25cm^3 of residual FLAIR/T2-hyperintense tumor tissue defines the category of subtotal resection. This is in contrast to the category *partial resection*, where a lesser EOR is attained. If surgery is conducted solely for obtaining a tissue-based diagnosis without the intention of reducing significant tumor volume, the term *biopsy* should be used.[9]

Associations of EOR with Survival

Overall survival (OS) and progression-free survival (PFS) are the most crucial endpoints for the assessment of any oncological therapy. However, PFS and—even more—OS are influenced by a variety of factors in a multidisciplinary treatment setting. For this reason, it is challenging to assess the effect of a single therapy on survival. There are only very small numbers of prospective trials to investigate the role of resection in gliomas and there is only one single randomized, controlled trial with PFS as a survival endpoint.[10] In this study, Stummer et al showed a significantly increased PFS of patients with glioblastoma who were operated on after oral application of 5-aminolaevulinic acid (5-ALA). In the 5-ALA group, the percentage of patients without residual tumor was significantly higher than in the control group, which corresponded to increased PFS at 6 months (class I).

There are also limited numbers of prospective, in part randomized trials with limited patient numbers comparing different cohorts.[11–15] They show a trend toward longer survival with complete resection or higher EOR (class II).

By far most studies are retrospective and were performed at a single center or a small number of centers. All grades of gliomas have been covered using different study designs. In many studies of patients with low-grade (1, 2) gliomas, astrocytic and oligodendroglial tumors were mixed in a single series. Furthermore, heterogeneous, sometimes not quantified definitions of EOR were used. The evidence class of these studies is predominantly IV, some series can be assigned to class III.[16–18] Some retrospective studies selected a semiquantitative approach showing better PFS or OS with higher extents of resection (class III).[19–21]

All together, independent from study design and evidence class, the majority of these studies confirm an association of EOR with survival. The association of complete resection with PFS is based on class I evidence; the association with OS is only supported by class III evidence. There is still no clear agreement on semiquantitative approaches; any recommendations for thresholds of EOR are based on retrospective data only. More details will be provided in the "special recommendations" sections for individual clinical situations.

Effects of EOR on Neurocognition

Neurocognition is an important functional clinical outcome in patients diagnosed with gliomas. Thus, it came not only into the focus of research but also has been increasingly implemented in the clinical routine of specialized centers in the last decade and the development of adapted test batteries for cognitive assessment is ongoing. However, the best available evidence regarding EOR and its association with cognitive function in glioma patients is class III, although neurocognition has been reported to be an independent predictor for progression-free- and OS.[22,23]

Extent of resection and its effect on neurocognition as a main outcome have been addressed in adult patients with "high-grade glioma (HGG)" and "low-grade glioma (LGG)." One meta-analysis investigated the effect of tumor resection on changes in different cognitive functions in patients with glioma after surgery. Complex attention, language, learning, and memory tasks were positively affected by surgery, whereas it had a negative impact on the performance of executive functions (evidence class III).[24,25]

Table 2. Terminology for extent of resection[8] (modified)

	Glioblastoma (contrast enhancing)	Glioma WHO CNS grades 2-4 (noncontrast enhancing)
Supramaximal resection	Resection of noncontrast-enhancing (CE) volume beyond CE tumor	Resection of non-hyperintense volume beyond FLAIR hyperintense volume
Complete resection (= gross total resection)	Complete resection of CE tumor volume	Complete resection of FLAIR hyperintense volume
Near total resection	Residual CE volume ≤1 cm^3 or reduction of 95%-99% of CE	Resection of at least 90% of FLAIT hyperintense tumor and residual FLAIR hyperintense volume ≤5 cm^3
Subtotal resection	Residual CE volume ≤5 cm^3 or reduction of 80%-95% of CE	Resection of more than 40% of FLAIR hyperintense tumor and residual FLAIR hyperintense volume ≤25 cm^3
Partial resection	Reduction of less than 80% contrast-enhancing tumor	Reduction of less than 40% of FLAIR hyperintensity
Biopsy	No tumor reduction	No tumor reduction

Considering cognitive and behavioral outcomes, nonrandomized single-center studies of increasing EOR in both LGG and HGG show a decline in neurocognitive function immediately after surgery with a return to baseline at follow-up, except for memory, particularly in patients with gliomas in the dominant hemisphere (evidence class IV).[26–28] However, in LGG patients no negative association of EOR with impaired neurocognition in the mid-term follow-up (6-12 months) was found.[29–31] The main affected domains after surgery were attention, working memory, and executive functioning.[32,33]

Awake craniotomy with intraoperative functional testing is routinely used to preserve language function in tumors localized in or next to eloquent regions. One meta-analysis and some retrospective data regarding awake resection of HGG and LGG in eloquent regions showed that neuropsychological function can be preserved despite increased EOR, again with short-term declines regarding language, executive functioning, attention, and memory functions immediately after surgery, returning to baseline during follow-up, except for psychomotor speed (evidence class III).[28,34–38]There is one multicenter study evaluating prospectively EOR and neurocognition in glioblastoma. Recruitment has been finished; follow-up is still ongoing (NOA-19, DKRS00010162).

In recent years, return to work (RTW) as an additional functional outcome has been increasingly investigated.[39,40] The percentage of patients with a glioma able to RTW varies between tumor types.[41] A retrospective series found that 52% and 63% of patients returned to work after 1 and 2 years and described a positive association of EOR and RTW in LGG patients, being significant between biopsy and resection in LGG 1 year after surgery. Additional factors were previous sick leaves, older age, and lower functional level (evidence class IV).[42,43]

As a clinical consequence, awake craniotomies should be considered to increase EOR while preserving cognitive functioning in patients with gliomas located in eloquent regions (recommendation level C), and resection of LGG should be considered superior to biopsy in terms of neurocognitive functioning (good practice point).

Effects of EOR on Health-Related Quality of Life

Health-related quality of life (HRQoL) is impaired in glioma patients independently of tumor type. A recent meta-analysis including 15 randomized controlled trials showed that baseline HRQoL variables are independent prognostic factors for PFS and OS (evidence class II).[44] EOR and its association with HRQoL are often secondary endpoints in ongoing clinical trials.[45] The development of postoperative neurologic and cognitive deficits and its association with EOR plays an important role regarding HRQoL, as new postoperative deficits, such as new motor deficits, language deficits, or unsteadiness and/or ataxia have been identified as independent predictors of decline in HRQoL.[46]

To date, no data from randomized controlled trials exist focusing on HRQoL and EOR as the primary outcome. Currently, one trial investigating the aforementioned relation is ongoing (NCT05399524).[47] Data from prospective trials in patients with glioblastomas like the ANOCEF trial, with a post hoc assessment of EOR and HRQoL, show that partial resection is superior to biopsy with less severe deterioration of HRQoL in elderly patients, while incomplete re-resection in patients with recurrent glioblastoma was associated with higher impairment due to increased motor dysfunction and decreased global health status (evidence class III).[14,48]

Some prospective observational monocenter studies in patients with "HGG" and "LGG" showed that greater EOR in patients with glioblastoma was associated with less decline in HRQoL in the further disease trajectory.[49,50] In a systematic review regarding EOR and functional outcomes in patients with LGG, complete resection was positively associated with RTW within 12 months of surgery. However, further patient-reported outcomes (HRQoL) were not included in the quantitative analysis because of insufficient data.[51] In a retrospective evaluation of HGG, EOR was not associated with a change in HRQoL after multivariate analysis.[52]

In summary, HRQoL predominantly depends on postoperative neurologic and cognitive deficits and is, therefore, strictly related to the quality of resection. There is no evidence that higher EOR is associated with reduced HRQoL (evidence class III).

Associations of EOR with Epilepsy

Seizures complicate the clinical course of 25% to 80% of patients with gliomas and glioneuronal tumors.[53] The epilepsy surgery experience suggests that long-term freedom from seizures requires identification and removal of the epileptogenic zone, which usually corresponds to the tumor and a variable amount of surrounding cortices. From an epilepsy surgery perspective, seizure control in tumor cases therefore requires at least a complete tumor resection ("lesionectomy") and often removal of additional tissues.[54] These latter operations may be regarded as supramaximal resections. Additionally, there is some influence of tumor location on epilepsy control after surgery.[55]

Most tumor epilepsy surgeries are performed in heavily selected patients presenting with longstanding medication-refractory epilepsy and gangliogliomas, dysembryoplastic neuroepithelial tumors (DNETs), or other so-called LEATs (long-term or low-grade epilepsy-associated tumors).[54,56–59]

Diffuse gliomas often also present with epilepsy, which—however—is rarely pharmacoresistant. A meta-analysis of 1379 cases with WHO CNS grade 2 described superior epilepsy control following complete versus subtotal resection.[60] Carstam et al used the more recent neuropathological classification paradigms and investigated 130 patients with IDH-mutant lower-grade (WHO CNS grades 2 and 3) gliomas. These authors described a significant correlation between the EOR (treated as a continuous variable) and freedom from seizures (Engel class 1a/ILAE1), regardless of 1p/19q deletion status.[61]

Pallud et al reviewed 1006 patients with IDH wild-type glioblastomas and found a statistically significant association between lack of seizure control and a complete or supramaximal resection versus biopsy only.[62] The authors also obtained some evidence that partial resections might have a beneficial effect and that supramaximal surgery may result in better epilepsy outcomes than complete resections. Borger and co-workers reported superior seizure control

following lobectomies (ie supramaximal resections) versus complete resections for temporal lobe glioblastomas.[63]

Incomplete glioma resections may also have some beneficial effects on seizure control. Complete resections are rarely possible for patients with insular gliomas. Nevertheless, the pooled average rate of freedom from seizures in patients with epilepsy from insular glioblastomas was 79.6% in a recent meta-analysis.[64] Ius et al investigated 155 WHO CNS grade 2 gliomas and described an 85% EOR and a 15 cm^3 residual tumor volume threshold for optimal seizure control.[65] Similar figures (80%-91% and 19 cm^3) have also been reported by others.[66,67]

All studies describe and analyze retrospective and often selected cohorts, sometimes without controls (mixed class III and IV evidence). Medication-resistant epilepsy is often not accounted for, and seizure outcomes are assessed at variable time points. Many studies have not used the modern molecular tumor classification paradigms and proper epilepsy outcome measures such as the Engel or ILAE scale. Nevertheless, there appears to be substantial evidence that EOR correlates with postoperative seizure control in a similar manner across histologies. The best results are seen after supramaximal resections and—in cases with pharmacoresistant epilepsy—surgeries aiming at the removal of a predefined epileptogenic zone (recommendation level C).

Effects of EOR on Neurological Function

The effect of EOR on neurological function has been inconsistently investigated in the available clinical trials. Some studies included neurological function as secondary endpoints, but with different assessment methods.

A prospective randomized clinical trial enrolling patients with contrast-enhancing gliomas amenable to radiologically complete resection found that more patients in the intraoperative MRI group had complete tumor resection (23 [96%] of 24 patients) than did in the control group (17 [68%] of 25, $P=.023$).[12] Postoperative rates of new neurological deficits did not differ between patients in the intraoperative MRI group (3 [13%] of 24) and controls (2 [8%] of 25, $P=1.0$).

In a secondary analysis of the pivotal phase III trial on the value of fluorescence-guided resection using 5-ALA of malignant glioma, neurological function in the 2 treatment arms was specifically investigated.[10,68] The incidence of adverse effects (AEs) was balanced, with AEs reported in 58.7% of patients in the 5-ALA group and 57.8% of patients in the control group, as was the incidence in the subgroup of neurological AEs (5-ALA vs control, 42.8% vs 44.5%; $P=.74$). Grades 3 and 4 (categorized according to the CommonToxicity Criteria) neurological AEs were also balanced (7.0% vs 5.2%; $P=.49$). However, a higher rate of neurological deterioration at 48 h after resection was seen using the NIH-SS score: 0.5 ± 2.6 versus 0.0 ± 2.3 in the 5-ALA and control groups, respectively. Although no longer significantly different at 7 days after surgery, the number of patients with deterioration of the NIHSS score still tended to be slightly higher in the 5-ALA arm. Three months after surgery, the number of patients showing deterioration compared with their preoperative condition did not differ significantly. The risk was higher in patients with deficits unresponsive to steroids. Patients with complete resections had a significantly prolonged time to neurological deterioration (with stable or increased use of steroids), compared with patients with incomplete resections.

The French multicenter randomized phase III RESECT study compared the results associated with 5-ALA fluorescence and with white-light conventional microsurgery in patients with glioblastoma managed according to the current standards of care.[69] In this trial, a total of 171 patients were assigned to the 5-ALA fluorescence group ($n=88$) or to the placebo group ($n=83$). The proportion of complete resections was significantly higher in the 5-ALA fluorescence group (53/67, 79.1%) than in the placebo group (33/69, 47.8%; $P=.0002$). The proportion of patients with a worsened neurological status 3 months postoperatively (9/68, 13.2% [5-ALA group]; 9/70, 12.9% [placebo group], $P=.95$) was similar between groups (evidence class II). A propensity score matched cohort study by Gerritsen et al. found a positive correlation of awake craniotomy, EOR, and better neurological outcome analyzing 536 patients with glioblastoma (evidence class II).[70] A systematic review and meta-analysis evaluating resection rates and neurological outcome after resection of the contrast-enhancing tumor in diffuse gliomas bordering eloquent areas using electrophysiology and 5-ALA fluorescence found a low rate of persistent neurological decline at postoperative day 90 of 4.6%.[71]

Overall, it may be concluded that the early neurological impairment with modern neurosurgical techniques aiming at complete resection (with most data available for 5-ALA) is commonly transient and restricted to the postoperative period and outweighed by the PFS and OS benefits. This is particularly true for patients with a limited prognosis. Future studies should implement standardized assessment tools for neurological function, such as the Neurologic Assessment in Neuro-Oncology (NANO) scale.[72]

Effects of EOR on Radiotherapy Planning and Pharmacotherapy

Radiotherapy is a core treatment modality in the management of adult-type diffuse gliomas.[1] For patients with glioblastoma, radiotherapy to a total dose of 60 Gy in 30 fractions with concurrent and maintenance temozolomide (TMZ) is the standard treatment.[73] Postoperative radiotherapy utilizes modern external beam radiation therapy techniques such as intensity-modulated radiation therapy and volumetric modulated arc therapy, which increase dose conformity; however, target volumes may vary significantly among institutions. According to the European Society for Radiotherapy & Oncology and European Association of Neuro-Oncology (ESTRO-EANO) guidelines, the gross tumor volume (GTV) delineation should be based on the resection cavity (if present) plus any residual enhancing tumor on contrast-enhanced T1-weighted MRI, without inclusion of peritumoral edema (ESTRO-EANO Guidelines).[74]The clinical target volume (CTV) is defined as the GTV plus a 15 mm margin to account for microscopic spread. The radiation therapy oncology group recommends a 2-phase treatment, where the initial CTV typically includes postoperative cavity and contrast-enhancing residual tumor with peritumoral edema (GTV) plus a 20 mm margin, followed by a boost field defined as postoperative cavity T1 contrast-enhancing residual tumor plus a 20 mm margin.[75] For patients with grades 2-3 gliomas, the CTV

includes postoperative cavity and any residual tumor (enhancing and nonenhancing) plus 10-15 mm margin to be applied in all directions.[76,77] These definitions per se point at the high importance of EOR for radiation planning.

Furthermore, approximately half of all patients with glioblastoma develop macroscopically rapid early progression between surgery and postoperative radiotherapy, which is associated with poorer outcomes.[78] Tumor growth is observed more frequently in patients undergoing subtotal and partial resection and, together with increased edema, this is likely to have an impact on radiotherapy planning, resulting in increased GTV and CTV volumes. Significant changes in resection cavity volume and edema size may occur between immediate postoperative MRI and pre-radiotherapy MRI with an impact on target delineation and clinical outcome, as well as during RT, with an overall trend toward decreased cavity size for those who underwent complete tumor resection.[79–83]

In patients with diffuse IDH-mutant LGG, EOR has traditionally had an impact on the timing of RT followed by chemotherapy: younger patients without neurological deficits undergoing complete resection can be managed through observation alone. In contrast, early focal RT (50.4-54 Gy in 1.8 Gy fractions) should be considered for patients with incomplete resection and/or for patients aged >40 years.[1] In addition, cavity changes after GTR may result in smaller irradiated target volumes and normal brain volumes.

In summary, standard chemoradiation following complete resection in patients with glioblastoma is associated with longer PFS and OS. Cavity changes observed after GTR and before RT may have an impact on target delineation in patients with glioblastoma and IDH-mutant gliomas, resulting in reduction of target volumes (good practice point).

Specific Recommendations

EOR in Newly Diagnosed Glioblastoma IDH Wild Type

Across the literature, a consistent pattern emerged demonstrating a positive association between greater EOR and improved survival outcomes in patients with IDH wild-type glioblastoma. Fluorescence-guided surgery using 5-aminolevulinic acid (5-ALA) was shown to enhance the EOR and subsequent PFS outcomes compared to conventional surgery alone (evidence class I).[10] A subsequent study, evaluating the same study data set focused on OS, confirmed a significant positive correlation between complete resection and survival.[84] In the French RESECT study, which also randomized patients in a 5-ALA versus white light arm (see above), PFS and OS did not differ significantly, which may be explained by low patient numbers.[69] Another German study evaluated the role of intraoperative MRI in a prospective randomized manner.[12] A significantly higher percentage of complete resections by using intraoperative MRI could be confirmed as well as a significant increase in PFS. However, the total number of patients was also low, 3/49 patients had tumors other than glioblastoma, and there were no data for OS (evidence class II). A randomized study on elderly patients over 70 years (ANOCEF) revealed no significant difference in OS comparing debulking and resection; however, there was no neuroradiological resection control, and total numbers of patients was 101 only (evidence class I).[48]

Whereas these prospective studies used a binary design, defining the groups according to complete/incomplete resection (or any surgery versus biopsy in the ANOCEF), several retrospective studies defined resection thresholds other than complete resection without any residual contrast enhancement. These thresholds had been relevant for increased PFS and OS (evidence class III).[19,21] Using a data set of 500 patients, Sanai et al developed a staged prediction model showing an improved survival beginning at an EOR level as low as 78%.[21]

The up-to-date largest retrospective cohort was published by the RANO (Radiological Assessment in Neuro-Oncology) Resect group in 2023.[16] Volumetric EOR and survival were assessed in 1008 patients from 7 high-volume centers in Europe and USA. Patients were stratified to volumetrically defined cohorts. As expected, "complete" resection was associated with improved OS compared to "near total," "subtotal," or "partial" resection. Interestingly, "supramaximal" resection including noncontrast-enhancing brain volumes around the contrast-enhancing tumor (see Table 2), was associated with even better OS compared to complete resection (evidence class III).

The question of which tools should be employed to achieve maximum safe resection was addressed by Roder et al.[85] Within a prospective multicenter study, 314 patients from 11 centers were included in a center-specific MRI and a 5-ALA group comparing these resection techniques. In the MRI arm, 81% complete resections (less than 0.175 cm^3 residual tumor) were achieved, compared to 78% in the 5-ALA arm. Median PFS and OS were comparable in both groups; no residual contrast enhancement (0 cm^3) was a significant favorable prognostic parameter, especially in patients with *MGMT* promoter-unmethylated tumors.

A large number of further studies using retrospective analyses yielded similar results, unequivocally supporting the positive effect of complete resection on survival in patients with newly diagnosed glioblastoma; defining maximum safe resection as the aim of resection (recommendation level A).

EOR in Recurrent Glioblastoma

The vast majority of glioblastomas recur despite intensive multimodal and multidisciplinary treatment, including extensive cytoreduction and concomitant radio-chemotherapy. Treatment options at radiological recurrence include another cytoreductive surgery, re-challenge with radiation therapy, and salvage pharmacotherapy. Repeat surgery removes the tumor mass and has the benefit of gaining tumor tissue for additional histopathological and molecular genetic analysis. However, this potential benefit for local control comes at the price of the risk of new neurological deficits, wound healing difficulties, and medical complications, potentially delaying additional regional and systemic therapies. Overall, how far another resection influences survival is a matter of an ongoing debate.

There is one randomized controlled trial on repeat surgery still ongoing (RESURGE study, NCT02394626). One post hoc analysis from a multicenter trial on dose-dense TMZ and many retrospective single- and multicentric data were reported. The post hoc analysis by Suchorska et al investigated the outcome associations of repeat surgery in the 105

patients of the DIRECTOR trial, in which the patients were randomized for 2 different regimes of TMZ at glioblastoma recurrence.[14] The 71 patients who received surgery at recurrence showed no significant prolongation of PFS compared to the 34 who did not (11.4 months vs 9.8 months, *P*=.633). In a subgroup analysis, the authors then re-stratified those 59 patients who had post-surgery imaging available according to whether or not a complete resection of contrast-enhancing tumor was achieved. The 40 patients with complete resection had a significantly longer post-progression survival (PRS) time compared to patients with incomplete resections (12.9 months vs 6.5 months, *P*=.001) and also achieved a better quality of life. In contrast, incomplete resection was even numerically inferior to no resection in terms of PRS (6.5 months vs 9.8 months, *P*=.052; evidence class II).

A retrospective multicenter analysis including 503 patients receiving re-resection in 20 centers revealed an OS of 25 months and a post-recurrence survival (PRS) of 11.9 months. Karnowski performance score (KPS), EOR at first surgery, and chemotherapy were relevant factors for survival and the complication rate was 8%.[86] Furtak et al performed a matched cohort analysis on 35 patients with re-operated recurrent glioblastoma matched to 35 non-re-operated patients using propensity score matching.[87] OS was significantly longer in patients with multiple surgeries compared to those with only one surgery (528 vs 297 days, respectively; *P*=.002; evidence class II).

More recent studies, such as the report by Karschnia and the RANO resect group as well as the bicentric analysis by Behling et al, also focus on PRS.[16,88] Reporting on 355 patients with recurring IDH wild-type glioblastoma, of whom 151 received another surgery and 204 did not, Behling reports a median PRS of all patients of 9 months (95% CI: 8.0-10.0).[88] PRS with complete resection was 12 months (95% CI: 9.7-14.3, *n*=81), incomplete resection 11 months (95% CI: 8.9-13.1, *n*=70), and without resection 7 months (95% CI: 06-08, *n*=204), which might represent the indication bias. In the report by the RANO resect group, patients undergoing re-resection had a median PRS of 11 ± 0.7 months compared to 7 ± 0.5 months without second surgery (*P*=.001).[89] However, only patients with a contrast-enhancing tumor volume of ≤1cm^3 after repeat surgery had a survival benefit compared to patients without repeat surgery. In another retrospective study, Mukherjee et al reported on 312 patients, of whom 145 received additional surgeries and 167 did not.[90] Median PRS was 10.8 months and 6.9 months in the reoperated and non-reoperated groups, respectively (log-rank test: *P*=.02). Both reports are rated as evidence class III.

Similarly, a majority of retrospective analyses show a positive correlation of repeat surgeries and survival using various study designs.[90–107]

However, the meta-analysis by Gorlia et al failed to show a survival benefit of repeat surgery or showed that a major part of the observed difference in OS between those with repeat surgery and those without is attributed to patient selection.[108,109]

One also might consider that there could be more confounding factors in pretreated patients, which makes the interpretation of retrospective data on patients with re-resection difficult. For example, a more benign nature of the underlying glioblastoma might lead to a longer survival and to more discussion time about repeat surgery. Hence, the current evidence allows a level C recommendation to perform complete resection in recurrent glioblastoma whenever safely possible. Evidence for the survival benefit of subtotal resection is weak and controversial. Similarly, and as depicted by the RANO resect group, there is yet no evidence that supramaximal resection is associated with prolonged survival and improved outcome.[89]

EOR in IDH Mutant Glioma

A Norwegian near-randomized study demonstrated that a strategy of resection was superior to biopsy in patients with LGGs (evidence class II).[110] This also holds true when only analyzing IDH mutant gliomas.[111] Although the studies lacked volumetric data on EOR (or residual tumor volume), accumulating data suggest that it is not merely about "any resection": In another pseudorandomized study, a survival benefit was only seen when residual tumor volume was less than 15 mL.[112] The change in policy that has occurred in many centers, moving toward more active surgical treatment, can be achieved without an increase in morbidity and with a favorable functional outcome.[113]

Two influential papers concerning EOR and survival were published in 2008. One landmark paper was published by Smith and colleagues, analyzing patients with LGGs undergoing resection with volumetric methods.[114] This study demonstrated a clear and stepwise association of EOR with survival, but with a particularly good outcome when complete resection was achieved. Another study from Shaw et al studied a low-risk group (younger than 40 years, good performance, and neurosurgeon-determined complete resection) and showed that a residual tumor of >1cm^3 was a negative prognostic predictor. Additionally, this study depicted some interesting findings. First, neurosurgeon-determined "complete resection" is not valid as 39% of 216 patients included had larger tumor remnants.[115] Second, in this more homogeneous cohort of tumors with a high degree of "resectability" and where no adjuvant treatment was given, a clear association of progression (a clear increase in T2w signal) or transformation (new contrast enhancement) was seen with larger tumor remnants. Interestingly, a similar concept of "failed complete resection" was used in the study from Coburger et al, published in 2016.[116] Analyzing 288 patients, a complete resection, guided by intraoperative MRI, was associated with prolonged PFS compared to intended subtotal resection or "failed complete resection." A French study from 2013 by Capelle et al analyzed a total of 1097 patients with a supratentorial LGG. Deep-seated (eg thalamic) lesions and gliomatosis were excluded. Similarly to Smith et al,[114] the authors found a clear step-wise association between EOR and survival.[117]

New information started to emerge following the WHO 2016 classification, when the LGGs subtypes were no longer subject to histopathological characteristics alone, and cleaner subgroups were created based upon molecular markers with IDH mutation and 1p19q codeletion.[118] For patients with IDH-mutant gliomas of WHO CNS grade 2, Wijnenga et al provided data indicating that the role of EOR/residual tumor volume may be different in IDH-mutant astrocytoma versus oligodendroglioma.[119] In contrast to oligodendrogliomas, in astrocytomas any small remnant is

associated with inferior survival.[119] Rossi et al also included WHO CNS grade 3 gliomas.[120] This study largely focused on supramaximal resection and demonstrated an association between supramaximal resection and prolonged survival, also when compared to a complete resection. This association was observed for both astrocytomas and oligodendrogliomas of WHO CNS grades 2 and 3.

Hervey-Jumper et al, studying patients with IDH-mutant WHO CNS grade 2 gliomas, included large exploratory and validation cohorts.[121] An interactive prognostic model employing different parameters showed that a minimum resection ratio of 75% and 80% improved OS and PFS, respectively. Of note, supramaximal resection was only associated with improved survival in patients with astrocytoma.

Overall, the literature from the molecular era indicates that complete resection of IDH mutant gliomas should be the goal of surgery (evidence class II; recommendation level B). However, the role of EOR may differ between IDH-mutant astrocytomas and oligodendroglioma. There is a strong and consistent outcome association with complete resection in IDH mutant astrocytomas,[119,121–123] while in patients with oligodendrogliomas the results are mixed,[121,123–126] potentially because chemoradiotherapy is more active in the latter.

EOR in Recurrent IDH Mutant Gliomas

There is a lack of high-quality studies evaluating EOR in relation to survival in patients with IDH mutant gliomas, as all the observational studies have the inherent limitation of selection bias. For recurrent gliomas with IDH mutation, the selection bias is further aggravated, as no more than 50% undergo re-operation despite long-term follow-up.[113127] Data from the pre-molecular era indicate a benefit of complete resection over partial resection.[128] Most studies are, however, small and without information concerning IDH mutation and 1p19q codeletion (evidence class IV).[129,130]

There are, however, some studies with available IDH mutation status. Shofty et al even tried to reduce the selection bias by comparing those re-operated with a group that were offered re-operation but declined further surgery. According to their findings, undergoing repeated surgery was beneficial with prolonged survival.[127] Grau and colleagues found that in IDH mutant WHO CNS grade 2 gliomas later undergoing resection for suspected malignant transformation, posttransformation survival was beneficial in the group undergoing complete resection.[131]

Consequently, reoperation is a reasonable option, especially when a complete removal seems possible (good practice point). However, selection bias represents a significant limitation of all above-mentioned studies.

EOR in Circumscribed Astrocytic Gliomas, Glioneuronal, and Neuronal Tumors

The current 2021 WHO classification lists a variety of rare circumscribed astrocytic gliomas, glioneuronal, and neuronal tumors. The more frequent histologies include pilocytic astrocytoma, pleomorphic xanthoastrocytoma (PXA), subependymal giant cell astrocytoma (SEGA), central neurocytoma, ganglioglioma, and DNET. Adult patients account for a minority of cases. These tumors often follow a relatively benign clinical course and frequently present with long-standing or even drug-resistant epilepsy.[56,132] From an epilepsy surgery perspective, many of the tumors can be classified as LEATs (long-term or low-grade epilepsy-associated tumors, see above).[56]

Yahanda et al reported a multicenter comparative experience with 284 patients with WHO CNS grade 1 gliomas and glioneuronal tumors (mean age: 21 years; 46.8% pilocytic astrocytomas, 27.5% gangliogliomas, 14.1% DNETs). Complete and near-total resections correlated with a significantly better OS (5 years: 96% vs 88%) and also PFS (5 years: 89% vs 78%) possibly reflecting primarily findings in the pilocytic astrocytoma subcohort.[133] Jungk et al published 58 patients with supra- (46.6%) and infratentorial pilocytic astrocytoma in adults. Complete resection was independently associated with longer PFS in the multivariate analysis.[134] Similarly, EOR was the only significant predictor of recurrence-free survival in the large series (N=499, 136>21 years) by Kulac et al.[135] EOR was prognostic in a recent analysis of 865 patients from SEER (Surveillance, Epidemiology, and End Results Program of the National Cancer Institute) (all >20 years),[136] but not in the National Cancer Database (N=3057, all >18 years). However, EOR was not reported in 69.7% of the latter cohort.[137]

Pleomorphic xanthoastrocytomas are assigned to the WHO CNS grades 2 or 3 based on mitotic counts. A recent systematic review identified 325 published patients. Median OS was 209 and 49 months for grades 2 and 3 tumors, respectively. A complete resection ("gross total resection") was linked to better PFS and OS.[138] Contradictory findings have also been published. Rodrigues et al analyzed 346 grade 2 and 62 grade 3 PXA patients from the SEER database and found no correlation between survival and EOR.[139]

Subependymal giant cell astrocytomas are very benign lesions. Nguyen and co-workers analyzed the SEER data and found no evidence that EOR is associated with survival; however, any surgery versus no surgery was correlated with better OS.[140]

Most gangliogliomas are also benign; however, some patients suffer recurrences and a few even succumb to their disease. A history of long-term epilepsy is predictive of a very benign clinical course.[56,141,142] Varshneya et al searched the National Cancer Database and found no association between degree of resection and OS among 198 adults with gangliogliomas (91.4% "low grade").[143] Yust-Katz and co-workers reported 67 adults from their institution (92.5% "low grade") and described better recurrence-free survival and OS following complete rather than partial resection.[144] Extent of resection heavily impacts tumor recurrence and patient survival in cases with non-benign gangliogliomas.[141] A recent study of 381 (147 ≥ 21 years) DNETs from the SEER database found no correlation between EOR and survival or recurrence; however, against the background of a 98% 5-year OS rate.[140]

Central neurocytomas are rare intraventricular (third and lateral ventricles) tumors. More aggressive ("atypical") tumors can probably be characterized based on increased proliferative activity. Formal thresholds have, however, not been defined.[132] Xie et al reported 101 patients (64.4% categorized as atypical) and found significantly better overall and PFS following complete versus partial resection.

Postoperative radiotherapy was found to be linked to better survival after incomplete surgeries but not to the degree seen after complete resections.[145] Dutta et al studied 868 patients from the National Cancer Database with neurocytomas (71.7% ventricular). Extent of resection was associated with better OS in the univariate but not in the multivariate analysis.[146] Kweh et al identified 101 published cases with extraventricular neurocytomas. Complete resection was associated with significantly better overall and recurrence-free survival.[147]

There are only evidence of class IV data about the role of any EOR in these entities. However, the available evidence suggests some correlation between EOR and tumor recurrence and patient survival across histologies, which supports complete resections as the surgical standard for circumscribed astrocytic gliomas, glioneuronal, and neuronal tumors (good practice point). The benefit of a complete resection may appear to be minor in patients with benign tumors, for example, SEGAs, DNETs, and most gangliogliomas. However, many cases should nevertheless have complete resections for epilepsy control (see also above). A more aggressive surgical strategy should also be considered in cases (eg in gangliogliomas) not presenting with long-term epilepsy, which may follow a more adverse clinical course (good practice point).

EOR in Ependymoma

Ependymomas comprise 1.8% of all primary CNS tumors and 6.8% of all glioma.[148] They represent a very heterogeneous group of tumors from rather benign subependymomas to very aggressive and often deadly childhood ependymomas of the posterior fossa. The site of occurrence of ependymoma varies depending on the age of the patient. In children, approximately 90% of cases occur in the intracranial region, while in adults, about 65% of cases originate in the spinal cord. The histopathological variants that had been separately described in the 2016 version are no longer listed as subtypes of ependymoma, after it had been recognized that papillary, tanycytic, or clear cell morphology has no clinical value by itself.[149] A recent molecular classification has distinguished 10 subgroups of ependymomas that appear to reflect more precisely than histology alone the biological, clinical, and histopathological heterogeneity across the major anatomical compartments, age groups, and tumor grades and have represented the basis for the update of WHO classification from 2016 to 2021. According to the 2021 WHO classification of CNS tumors,[150] ependymomas should be classified according to a combination of histological and molecular features across 3 tumor locations: supratentorial, infratentorial, and spinal. Molecularly defined posterior fossa A (PFA) ependymomas have a poor prognosis compared with that of posterior fossa B (PFB) ependymomas in children.[151] Ependymal tumors of the spinal cord comprise 4 distinct tumor types in all age classes.[149]

Surgery is considered the first and crucial step of standard treatment in all ependymoma entities. However, evidence classes differ strongly between the pediatric and adult population. Prospective studies on the management of ependymoma patients have been performed mainly in children, while only retrospective series are available for adult patients.[152] The HIT 88/89 and HIT 91 prospective non-randomized studies showed a significant survival advantage of children receiving a complete resection compared to incompletely resected patients (estimated PFS after 3 years: 83.3% vs 38.5%).[153] This was confirmed in a larger retrospective series evaluating the HIT database (134 patients), clearly describing residual tumor volume as a predictor of shorter event-free and OS.[154] In adults, several clinical parameters such as age, sex, tumor location, pathologic grade, extent of tumor removal, and postoperative adjuvant treatment have all been evaluated as possible prognostic factors.[155] In most studies, EOR has emerged as one of the most significant predictors of outcome.[156–158]

Currently, there is no standard salvage treatment for recurrent ependymomas. Most recurrences develop within the first 2 years from diagnosis. Data from the German multicenter E-HIT-REZ-2005 study (non-randomized) examined the role of local therapy and the efficacy of chemotherapy in 53 children and adolescents with recurrent ependymomas. The authors concluded that the EOR was the most important predictor of survival at relapse.[159]

In summary, the evidence for a survival benefit by complete resection in newly diagnosed ependymomas is class II for children and class IV for adults. In the recurrent situation there is also class II evidence for children and class IV for adults. Therefore, a recommendation level B for complete resection can be made in children for newly diagnosed and recurrent ependymomas, whereas for adults there is only a recommendation as a good practice point in both situations.

Summary and Discussion

Extent of resection appears to have a prognostic role in almost all glioma entities and in most clinical situations. This is best documented in newly diagnosed glioblastoma IDH wild type (class I evidence) and leads to the recommendation of efforts at complete resection (defined by postoperative MRI) whenever safely possible (level A). The cumulative evidence for recurrent glioblastoma is lower (class III), justifying a recommendation level C only for complete resection whenever safely possible. In newly diagnosed IDH mutant gliomas, there is class II evidence for a beneficial role of resection on survival (recommendation level B); however, the degree of resection in each case still is a matter of debate. There is growing evidence that complete resection should be intended in astrocytic tumors and that in 1p/19q co-deleted tumors safe resection with minimal risk might be a better strategy due to the good response to medical therapy of these tumors (good practice point). Like in glioblastoma, the evidence level for surgery in patients with recurrent IDH-mutant tumors is low (class IV) justifying a recommendation for resection as a good practice point. In well-circumscribed, mostly WHO CNS grade 1 tumors, resection offers a cure and should be employed as a therapy of choice. However, despite a plethora of studies, the evidence level is low enabling only a recommendation as a good practice point. In the mixed entity of ependymoma, the recommendation level for resection as the only or first step of treatment differs in children and adults. Whereas in children there is evidence class II by systematic prospective studies

Table 3. List of studies on EOR in Gliomas (evidence levels I and II)

First Author	Title	Evidence level	Primary endpoint	Key finding
Stummer et al[10]	Fluorescence-guided surgery with 5-aminolevulinic acid for resection of malignant glioma: a randomised controlled multicentre phase III trial	I	PFS 6 months after 5-ALA guided surgery	CR rate 65% vs 36% ($P<.0001$), PFS 41 vs 21% ($P=.0003$)
Picart et al[69]	Use of 5-ALA fluorescence-guided surgery versus white-light conventional microsurgery for the resection of newly diagnosed glioblastomas (RESECT study): a French multicenter randomized phase III study	I	PFS and OS after 5-ALA-guided surgery	CR 79% in 5-ALA group vs 48% ($P=.0002$). No difference in PFS and OS
Laigle-Donadey et al[48]	Surgery for glioblastomas in the elderly: an Association des Neuro-oncologues d'Expression Française (ANOCEF) trial	I	OS in eldery pats.	OS 5.6 mo after surgery vs 3.7 mo ($P=.03$)
Timmermann et al[153]	Combined postoperative irradiation and chemotherapy for anaplastic ependymomas in childhood: results of the German prospective trials HIT 88/89 and HIT 91	I	PFS after surgery in children with ependymoma	3-year PFS 83% after CR vs 38% after incomplete resection, EOR the only significant prognostic factor
Vuorinen et al[11]	Debulking or biopsy of malignant glioma in elderly people—a randomised study.	II	OS in the elderly	2.7-fold longer OS after craniotomy ($P=.035$)
Senft et al[12]	Intraoperative MRI guidance and extent of resection in glioma surgery: a randomised, controlled trial.	II	Rate of CR w/o MRI	96% CR in MRI group vs 68%, no difference in PFS ($P=.023$)
Eyüpoglu et al[13]	Supra-complete surgery via dual intraoperative visualization approach (DiVA) prolongs patient survival in glioblastoma	II	EOR, rate of supramaximal resection	Supracomplete resection using DiVA in 30/105 GBM pts.
Suchorska et al[14]	Suchorska B, Weller M, Tabatabai G, et al. Complete resection of contrast-enhancing tumor volume is associated with improved survival in recurrent glioblastoma-results from the DIRECTOR trial.	II	PFS and PRS w/o surgery	CR improves PRS (12.9 vs 6.5 mo, $P=.0001$)
Wu et al[15]	3.0-T intraoperative magnetic resonance imaging-guided resection in cerebral glioma surgery: interim analysis of a prospective, randomized, triple-blind, parallel-controlled trial	II	EOR w/o intra-OP MRI	CR with intra-OP MRI 86% vs 48% ($P<.001$)
Roder et al[85]	Intraoperative MRI-guided resection is not superior to 5-aminolevulinic acid guidance in newly diagnosed glioblastoma: a prospective controlled multicenter clinical trial	II	CR using intra-OP MRI vs 5-ALA	No superiority of any method
Furtak et al[87]	Survival after reoperation for recurrent glioblastoma multiforme: A prospective study.	II	OS w/o surgery	528 vs 297 days after re-operation ($P=.0004$)
Jakola et al[110]	Comparison of a strategy favoring early surgical resection vs a strategy favoring watchful waiting in low-grade gliomas	II	5-year-OS surgery vs STX biopsy	Comparison of regional cohorts with different regimes, 5 year-OS 74% after surgery vs 60% after biopsy ($P=.03$)
Smith et al[114]	Role of extent of resection in the long-term outcome of low-grade hemispheric gliomas.	II	EOR and outcome	OS was predicted by EOR (HR 0.972, $P<.001$)
Shaw et al[115]	Recurrence following neurosurgeon-determined gross-total resection of adult supratentorial low-grade glioma: results of a prospective clinical trial.	II	EOR and outcome	Direct correlation of EOR and recurrence rate
Gerritsen et al[70]	Effect of awake craniotomy in glioblastoma in eloquent areas (GLIOMAP): a propensity score-matched analysis of an international, multicentre, cohort study.	II	EOR and outcome after awake craniotomy	Fewer neurological deficits ($P=.019$), longer OS ($P=.0005$), longer PFS ($P=.006$)

Abbreviations: DR = complete resection, PRS = post-recurrence survival, mo = months.

leading to a recommendation level B, in adults surgical resection can only be recommended as a good practice point.

Recently, the discussion about the degree of resection, particularly in glioblastoma, has been intensified. There still is class I evidence for complete resection of contrast-enhancing

Table 4. List of Recommendations

There is a clear indication for efforts at complete resection (removal of all contrast-enhancing tumor) in patients with newly diagnosed glioblastomas, whenever safely possible (level A)
Re-resection is a valid option in patients with recurrent glioblastomas and should be taken into consideration whenever safely possible and when a complete resection of all contrast-enhancing volume appears feasible (level C)
IDH mutant gliomas should undergo maximal safe resection to prolong survival and improve epilepsy (level B). However, the role and extent of resection might differ by integrated histology, since oligodendrogliomas offer a good response to chemotherapy (good practice point).
In patients with recurrent IDH mutant gliomas, re-resection is a valid option and should be considered when safely possible (good practice point).
Despite evidence for class IV only, resection offers a cure in well-circumscribed intracerebral tumors of WHO CNS grade 1 and should therefore be therapy of first choice (good practice point).
Ependymomas represent a complex entity in children and adults. The recommendation level for resection is B for children and a good practice point for adults with newly diagnosed and recurrent tumors.

tumor only. On the other hand, retrospective data of high quality (class III) meanwhile show positive prognostic associations of stepwise near total or subtotal resections, and there is also the observation of potentially improved survival of supramaximal compared to the usually intended complete resection. Thus, overall, the gradual EOR, respectively, residual tumor volume is an important point worth to be addressed prospectively. Moreover, there is also growing information that epigenetic and molecular glioma subtypes might influence surgical decisions. This also needs to be addressed prospectively in the near future.

A list of published studies on glioma resection evidence class I and II is stated in Table 3. Current clinical trials can be found by searching www.clinicaltrials.com. A summary of recommendations is provided in Table 4.

Keywords

glioblastoma | glioma | prognosis | resection | surgery | survival

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Data availability

The data underlying this article are available in PubMed.

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