Cohort Study

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Awake brain mapping by direct cortical stimulation; technical note to get higher resection rate and low morbidity in low-grade glioma patients

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Introduction: Direct cortical stimulation has been used for brain mapping and localization of eloquent areas in awake patients. This simplified technique is to provide the positive areas, which can be preserved if the tumor or lesions are involved eloquent areas.
Objective: The main objective of this study is to determine whether direct cortical stimulation in awake brain mapping for low-grade glioma patients increases the rate of resection or not.
Method: The authors present a retrospective study between 2020 to 2022 that includes 35 cases in a single center, to get higher resection rate, and their consequences in awake craniotomy in low-grade glioma patients. Here, two neurosurgeons were involved and the minimum follow-up was 12 months.
Results: The authors achieved 80% removal of tumors. To get higher resection rate we emphasized negative mapping with prior anatomical analysis to understand functional realignment. Stimulation-related complications will be thoroughly discussed with a potential future direction to minimize the issues. The authors used PROMIS score to measure patients physical and mental health status and kernofsky score to measure performance status before and after successful surgery. The authors found three cases of transient deficit in repetitive stimulation. Repeated stimulation to identify the eloquent areas with low voltage frequency is a good option. Numbness in the face related to stimulation may continue for 6 weeks.
Conclusion: Functional realignment in shifted brain and edema can be seen while doing cortical and subcortical stimulation. Most of the stimulation from low to high for language mapping may vary from patient to patient. For safe removal of low-grade glioma a steep learning curve is needed to find out the negative areas, though the authors emphasize positive mapping of areas to secure the maximum eloquence.

Keywords: awake brain mapping, direct cortical stimulation, low-grade glioma

Introduction

The most frequent primary brain tumors are gliomas[1]. The best course of treatment for gliomas now relies on maximum safe resection, which has been demonstrated to have a considerable impact on patients with high-grade or low-grade gliomas in terms of progression-free survival[2]. However, due to gliomas' infiltrative nature, it is not always possible to remove the tumor completely while maintaining the functionality of the cerebral cortex's expressive structures and subcortical white matter tracts. The surgical management of diffuse low-grade gliomas, particularly those that are found in so-called 'eloquent areas', is increasingly using intraoperative cortical and subcortical brain mapping during awake surgery. A rising number of studies regard this treatment as the gold standard intraoperative strategy for the surgical excision of low-grade gliomas of the left dominant hemisphere[3–5]. Surgery for all of these patients is intended to achieve onco-functional balance, which entails a gross complete resection with a low risk of morbidity. There may be significant morbidity associated with the radical removal of insular gliomas. In order to maximize the extent of tumor removal and reduce postoperative morbidities, it is suggested that brain mapping techniques can be utilized to detect the eloquent areas of the brain with adequate precision intraoperatively[6,7].

Awake craniotomy is a useful surgical technique that can be used safely to locate and maintain functioning regions of the brain during the excision of primary brain tumors. Recent research has

HIGHLIGHTS

- Direct cortical stimulation has been used for brain mapping and localization of eloquent areas in awake patients.
- This simplified technique is to provide the negative areas.
- Functional realignment in shifted brain and edema can be seen while doing cortical stimulation.

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shown that awake craniotomy combined with intraoperative electrical brain mapping is a reliable technique to reduce the risk of long-term deficit during surgery for tumors located within expressive areas[8,9]. This technique allowed for the expansion of surgical indications in areas that were previously thought to be inoperable while maintaining quality of life, particularly in the case of infiltrative tumors like low-grade gliomas[10]. On the other hand, it might be argued that maintaining functional sites would result in less tumor removal. To the best of our knowledge, there have only been two other publications where the degree of resection was directly compared between 'traditional' and awake surgeries[10]. Even though both studies found that intraoperative mapping improved the extent of resection, the comparison was done with a control group rather than the same patients.

A shift in perspective from a modular narrative of brain organization to a meta-network perspective resulted from the development of new surgical techniques that make it possible to trace the connections within the brain. Increased understanding of the connectome results in improved risk-benefit ratios for surgery; improved awake intraoperative surgery; improved pre-operative information allowing optimal surgical task selection in accordance with patient preferences; development of oncological resection surgery with disconnection; and individual multiphase surgical strategy will enable surgical resection in those 'eloquent' areas in accordance with a localizationist dogma[11]. The purpose of this research is to provide informations particularly techniques to get higher resection rate and low morbidity related to direct cortical stimulation in low-grade glioma patients.

Objective

The main objective of this study is to determine whether direct cortical stimulation in awake brain mapping for low-grade glioma patients increases the rate of resection or not.

Method

We present a retrospective study between 2020 to 2022 that includes 35 cases in a single center, to get higher resection rate, and their consequences in awake craniotomy in low-grade glioma patients. Here, two neurosurgeons were involved. Our anesthesia was sleep-awake-sleep and the minimum follow-up was 6 months. The work has been reported in line with the strengthening the reporting of cohort, cross-sectional, and case–control studies in surgery (STROCSS) criteria[12].

Table 1

Clinical characteristics of the patients

Age/Sex	Clinical features	Location	Glioma (grading)	Complications	Tumor removal (%)
40/Male	Seizure, hemiperesis	Right frontal	Grade2	Hand numbness	90
42/Female	Seizure, aphasia	Left frontal	Grade1	Transient arm weakness	80
38/Male	Seizure, arm weakness	Left frontal	Grade2	None	95
46/Female	Aphasia	Left frontotemporal	Grade1	None	90
31/Male	Headache	Left temporal	Grade1	Transient sensory aphasia	90
39/Male	Seizure	Left insular	Grade2	Hand numbness	70
41/Female	Hemiplegia	Right frontal	Grade1	Persistent arm weakness (improved leg weakness)	85
47/Male	Seizure	Right temporal	Grade1	None	80
30/Male	Headache	Right frontal	Grade2	Left arm numbness	75
36/Male	Headache, aphasia	Left frontal	Grade1	None	80
41/Male	Headache	Right frontal	Grade1	None	85
37/Female	Seizure	Right temporal	Grade2	Persistent seizure needed amygdalohippocampectomy	75
48/ Male	Headache, vomiting	Right fronto-parietal	Grade1	None	70
29/Male	Seizure	Right parietal	Grade1	None	80
30/Male	Aphasia	Left insular	Grade2	Dysphasia	80
38/Male	Seizure	Right frontal	Grade1	None	90
42/Male	Headache	Right temporal	Grade2	Peroperative Seizure	85
41/Male	Headache	Right frontal	Grade1	None	90
27/Female	Aphasia	Left frontal	Grade1	Peroperative Seizure	70
49/Male	Headache	Right frontal	Grade1	None	80
55/Male	Seizure	Left frontal	Grade1	None	75
43/Female	Seizure	Right frontal	Grade2	Peroperative Seizure	80
34/Male	Headache	Right parietal	Grade1	None	80
26/Male	Seizure	Left insular	Grade1	Dysphasia	70
45/Male	Seizure	Left temporal	Grade1	None	75
39/Male	Seizure	Left frontal	Grade1	Hand weakness	75
47/Male	Headache	Left temporo-parietal	Grade2	None	75
40/Male	Seizure	Left frontal	Grade1	None	80
35/Male	Seizure	Right frontal	Grade1	None	80
43/Male	Seizure	Left temporal	Grade1	Speech difficulty	75
55/Male	Aphasia, acalculia	Left angular gyrus	Grade2	Dysphasia	75
54/Male	Seizure	Right insular	Grade2	None	75
33/Female	Headache	Left insular	Grade2	None	70
34/Male	Seizure	Right frontal	Grade1	None	80
45/Male	Headache	Right frontal	Grade2	None	80

Results

Table 1 shows the clinical characteristics of the patients of our study. Here, maximum number of patients (18) had seizure and headache (12). Among all patients, 22 patients had grade 1 glioma and 13 patients had grade 2 glioma. See the Table 1 below.

Figure 1 shows the percentage of tumor removal of the patients. Here, we removed 80% of the tumors among the patients and 20% were residual. See the figure below.

Figure 2 shows the transient deficits found among the patients in repetitive stimulation. We found three cases (8.75%) of transient deficit in repetitive stimulation. Repeated stimulation to identify the eloquent areas with low voltage frequency is a good option. See the details in the figure below.

Figure 3 shows the preoperative and postoperative PROMIS Global- 10 scores of the patients in our study. Here, the preoperative and postoperative global physical health T-scores are respectively. And, the preoperative and postoperative global mental health T-scores are respectively. See the figure below.

Figure 4 shows patients performance status according to the kernofsky scores before and after surgery. Here, the higher the score the better the performance status is. The average preoperative score was 30%, which become 80% after the successful surgery of the patients. See the figure below.

Discussion

The surgical treatment of low-grade gliomas has seen significant change in the last 10 years[13,14]. It has been shown that improvements in intraoperative functional mapping techniques in awake patients significantly increase the indications for surgical resection while lowering the risk of long-term disability for low-grade gliomas situated within the so-called eloquent areas, traditionally thought to be inoperable[15].

In the current investigation, we confirm that direct cortical stimulation, which has been used to map the brain and pinpoint expressive regions in conscious patients, has improved functional outcomes Figure 5. We think that identifying the eloquent areas with low voltage frequency by repetitive stimulation is a suitable choice.

In a study of 1460 surgical resections for gliomas, including 522 low-grade gliomas, reveals that the incidence of persistent neurological damage has lowered to 4.1% with the use of intraoperative electrical mapping[16]. It is interesting to note that a prior study from 1994 to 2003 (analysis of 834 gliomas, including 358 low-grade gliomas) revealed a similar rate of sequelae of 4.2% against a mean of 19% of definite damage in cases when intraoperative electrical mapping was not employed[10]. Such data support the rising use of an intrasurgical approach of functional mapping in recent years as well as the validity of awake mapping to maintain the quality of life of patients who have undergone surgery for a low-grade glioma. The long-term quality of life of patients with adult low-grade gliomas improved as a result of the identification of the functional region[17,18].

Low-grade glioma is a well-known example of an invasive, ill-defined lesion. As a result, the scope of resection is reduced to prevent lasting deficit when the tumor is found in presumably eloquent areas based only on anatomic criteria. In the current work, we focused on negative mapping with prior anatomical analysis to comprehend functional realignment in order to achieve a greater resection rate. Because it is now recognized that tumor cells can enter brain tissue far from the boundaries of the tumor picture without resulting in permanent deficiency, a method based on intrasurgical awake imaging allowed for the maximization of the amount of glioma excision beyond the visual limits of the tumor. Because of the mechanisms of brain plasticity that have been widely studied in situations of slow-growing lesions like low-grade gliomas, even within 'crucial' areas, intraoperative awake mapping opens the door to a greater degree

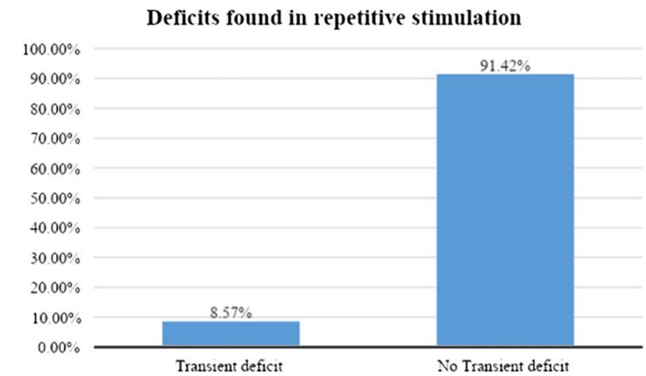

Figure 2. Deficits found in repetitive stimulation.

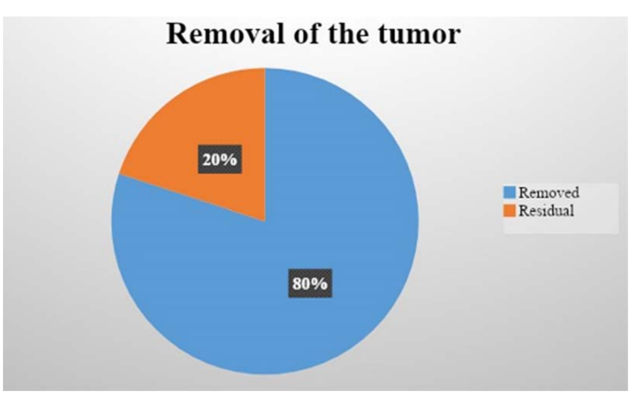

Figure 1. Percentage of tumor removal.

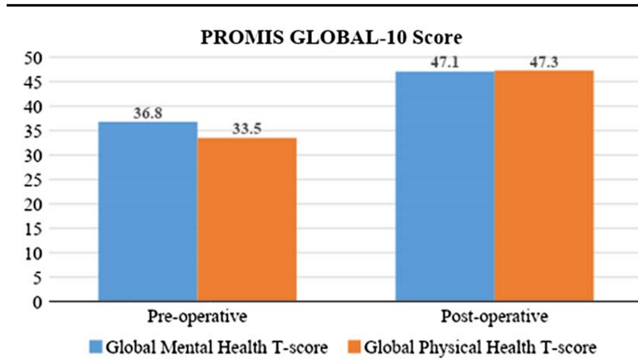

Figure 3. Patients health status according to the PROMIS GLOBAL-10 score.

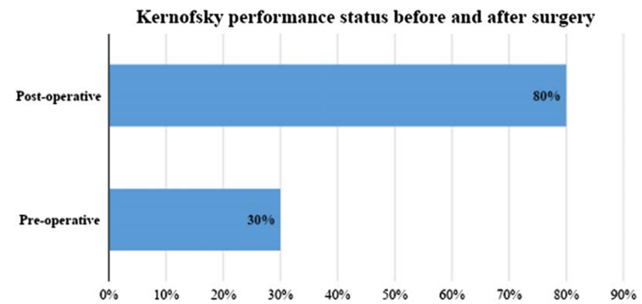

Figure 4. Patients performance status according to the kernofsky scores before and after surgery.

of resection than that determined only by anatomic criteria. According to a study, direct electrical stimulation during low-grade glioma resection improves the quality of the tumor resection process and lowers the risk of complications, which may have an effect on survival[10]. The quality of life and brain function of patients were preserved compared to before surgery because all patients were working, despite the fact that lesion removal was optimized because no margin was left around the eloquent structures detected by electrostimulation[16].

The primary objective of surgery for low-grade gliomas is to optimize the degree of resection, which neurosurgeons must keep in mind. Despite the paucity of trials, there is mounting evidence that more thorough tumor excision may lengthen patients' lives by preventing the anaplastic transition from occurring[19]. So it may be argued that intraoperative mapping combined with the preservation of expressive cortical and subcortical regions might result in a lesser degree of excision. To the best of our knowledge, traditional and awake techniques have never directly compared the degree of glioma eradication[10]. In high-grade glioma[11], repeat surgery represents a safe and efficient therapeutic approach to enhance overall survival while preserving quality of life in patients with diffuse low-grade glioma.

For right insular glioma we preferred transopercular approach in awake craniotomy, which is preferred to get higher resection rate by Duffau *et al.*[20]. In order to provide a safe treatment, it is imperative that patients remain aware throughout the process

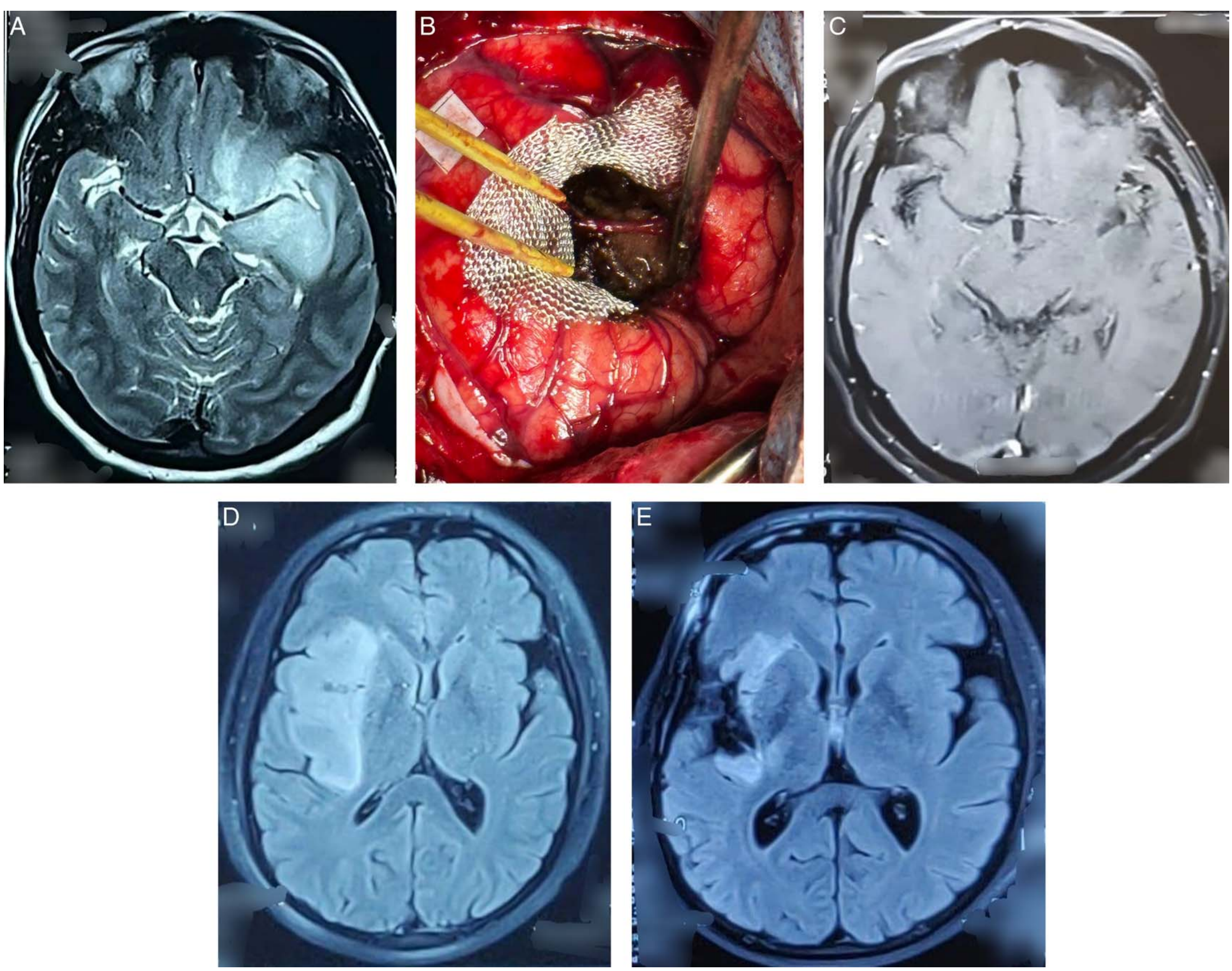

Figure 5. A: Preoperative T2 MRI image of left insular glioma. B: Peroperative resection of glioma (transopercular) with preservation of MCA branches. C: Postoperative MRI of insular glioma. D: Preoperative FLAIR image of right insular glioma. E: Postoperative FLAIR image of resected glioma.

and that the temporalis muscle, the surgical site, and the scalp lobe receive painkillers and local anesthetics[20]. It is crucial to use local anesthetics like ropivacaine efficiently during an active craniotomy. However, large doses of ropivacaine can be given safely during awake craniotomy, as reported by Sato *et al.*[21]. They employed a total dose of up to 5.0 mg/kg in an awake craniotomy with repeated anesthetic administration, resulting in a safe surgery.

According to a recent study, expression profiling of aberrant miRNAs offers important insights into the etiology of glial tumors and may be used to identify biomarkers and therapeutic targets for miRNAs[22].This is especially true for a variety of CNS illnesses, such as the extremely difficult problem of brain tumors. Through their ability to target a wide variety of genes, miRNAs are essential in determining the traits and actions of tumor cells. They actively contribute to controlling the process of cellular differentiation and altering the level of aggressiveness displayed by brain tumors[23]. Due to its complex involvement, it is possible that the dysregulation of particular microRNAs can serve as a useful predictor of clinical outcome[23]. According to another study, gliomas of the dominant insula represent a challenging subgroup of cerebral gliomas[24]. The use of intraoperative brain mapping is a technique that maximizes tumor resection with a fair degree of accuracy while also accurately localizing and protecting neurological functions. In the study, most patients tolerate this treatment well, though not all do, and there are no known long-term complications[24]. Moreover, when performed by a skilled practitioner, cranial chord excision for lesions in expressive regions is a safe, efficient way to treat lesions during pregnancy that does not affect the course of the pregnancy[25].

We do acknowledge, however, that electrostimulation still carries a small chance of false positives. Although the specificity of cortico-subcortical electrical mapping is still a matter of concern, we have shown that awake mapping permits an increase in the degree of resection while maintaining brain function.

Limitation of the study

There are some limitations of this study. It was a retrospective study and the number of cases reported are small. As well as it was a single center study. In future, more investigations with larger sample and multicenter analysis can strengthen the outcome of this study.

Conclusion

Functional realignment in shifted brain and edema can be seen while doing cortical and subcortical stimulation. Most of the stimulation from low to high for language mapping may vary from patient to patient. For safe removal of low-grade glioma a steep learning curve is needed to find out the negative areas, though we emphasize positive mapping of areas to secure the maximum eloquence (Fig. 5).

Ethical approval

Ethical approval for this study (ERC-BBS/0041/23/2023) was provided by the Ethics Research Committee of Bangladesh Bioethics Society, Dhaka, Bangladesh on 15 September 2023.

Consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

All authors equally contributed to the analysis and writing of the manuscript.

Conflicts of interest disclosure

There are no conflicts of interest.

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Not applicable.

Provenance and peer review

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References

[1] Farina P, Lombardi G, Bergo E, *et al*. Treatment of malignant gliomas in elderly patients: a concise overview of the literature. Biomed Res Int 2014; 2014:734281.

[2] Della Puppa A1, De Pellegrin S, d'Avella E, *et al*. 5-aminolevulinic acid (5-ALA) fluorescence guided surgery of high-grade gliomas in eloquent areas assisted by functional mapping. Our experience and review of the literature. Acta Neurochir (Wien) 2013;155:965–72.

[3] De Witt Hamer PC, Robles SG, Zwinderman AH, *et al*. Impact of intraoperative stimulation brain mapping on glioma surgery outcome: a meta-analysis. J Clin Oncol 2012;30:2559–65.

[4] Yordanova YN, Moritz-Gasser S, Duffau H. Awake surgery for WHO Grade II gliomas within "noneloquent" areas in the left dominant hemisphere: toward a "supratotal" resection. Clinical article. Journal of neurosurgery 2011;115:232–9.

[5] Kim SS, McCutcheon IE, Suki D, *et al*. Awake craniotomy for brain tumors near eloquent cortex: correlation of intraoperative cortical

mapping with neurological outcomes in 309 consecutive patients. Neurosurgery 2009;64:836–346.
[6] Bertani G, Fava E, Casaceli G, *et al*. Intraoperative mapping and monitoring of brain functions for the resection of lowgrade gliomas: technical considerations. Neurosurg Focus 2009;27:E4.
[7] Bello L, Gallucci M, Fava M, *et al*. Intraoperative subcortical language tract mapping guides surgical removal of gliomas involving speech areas. Neurosurgery 2007;60:67–82.
[8] Chang EF, Potts MB, Keles GE, *et al*. Seizure characteristics and control following resection in 332 patients with low-grade gliomas. J Neurosurg 2008;108:227–35.
[9] Duffau H. Intraoperative cortico-subcortical stimulations in surgery of low-grade gliomas. Expert Rev Neurother 2005;5:473–85.
[10] Duffau H, Lopes M, Arthuis F, *et al*. Contribution of intraoperative electrical stimulations in surgery of low grade gliomas: a comparative study between two series without (1985-96) and with (1996-2003) functional mapping in the same institution. J Neurol Neurosurg Psychiatry 2005;76:845–51.
[11] Motomura K, Ohka F, Aoki K, *et al*. Supratotal resection of gliomas with awake brain mapping: maximal tumor resection preserving motor, language, and neurocognitive functions. Front Neurol 2022;13:874826.
[12] Mathew G, Agha R. for the STROCSS Group. STROCSS 2021: strengthening the reporting of cohort, cross-sectional and case-control studies in surgery. Int J Surg 2021;96:106165.
[13] Mandonnet E, Pallud J, Clatz O, *et al*. Computational modeling of the WHO grade II glioma dynamics: principles and applications to management paradigm. Neurosurg Rev 2008;31:263–9.
[14] Mandonnet E, Jbabdi S, Taillandier L, *et al*. Preoperative estimation of residual volume for WHO grade II glioma resected with intraoperative functional mapping. Neuro Oncol 2007;9:63–9.
[15] Pouratian N, Asthagiri A, Jagannathan J, *et al*. Surgery insight: the role of surgery in the management of low-grade gliomas. Nat Clin Pract Neurol 2007;3:628–39.
[16] Pouratian N, Mut M, Jagannathan J, *et al*. Lowgrade gliomas in older patients: a retrospective analysis of prognostic factors. J Neurooncol 2008;90:341–50.
[17] Carrabba G, Fava E, Giussani C, *et al*. Cortical and subcortical motor mapping in rolandic and perirolandic glioma surgery: impact on postoperative morbidity and extent of resection. J Neurosurg Sci 2007;51: 45–51.
[18] Duffau H. Repeated awake surgical resection(s) for recurrent diffuse low-grade gliomas: Why, when, and how to reoperate? Front Oncol 2022;12: 947933.
[19] Shaw EG, Berkey B, Coons SW, *et al*. Recurrence following neurosurgeondetermined gross-total resection of adult supratentorial low-grade glioma: results of a prospective clinical trial. J Neurosurg 2008; 109:835–41.
[20] Duffau H. Awake mapping with transopercular approach in right insular-centered low-grade gliomas improves neurological outcomes and return to work. Neurosurgery 2022;91:182–90.
[21] Sato T, Okumura T, Nishiwaki K. Preanesthesia scalp blocks reduce intraoperative pain and hypertension in the asleep-awake-asleep method of awake craniotomy: a retrospective study. J Clin Anesth 2020;66: 109946.
[22] Beylerli O, Gareev I, Sufianov A, *et al*. The role of microRNA in the pathogenesis of glial brain tumors. Noncoding RNA Res 2022;7:71–6.
[23] Beylerli O, Encarnacion Ramirez MJ, Shumadalova A, *et al*. Cell-Free miRNAs as non-invasive biomarkers in brain tumors. Diagnostics (Basel) 2023;13:2888.
[24] Alimohamadi M, Shirani M, Shariat Moharari R, *et al*. Application of awake craniotomy and intraoperative brain mapping for surgical resection of insular gliomas of the dominant hemisphere. World Neurosurg 2016;92:151–8.
[25] Mofatteh M, Mashayekhi MS, Arfaie S, *et al*. Awake craniotomy during pregnancy: a systematic review of the published literature. Neurosurg Rev 2023;46:290.