

Electrocorticography and navigated transcranial magnetic stimulation–tailored supratotal resection for epileptogenic low-grade gliomas

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OBJECTIVE Epilepsy is commonly associated with low-grade gliomas (LGGs), impacting patients' well-being. While resection is the primary treatment, seizures can persist postoperatively in 27%–55% of cases. The authors aimed to evaluate an electrocorticography (ECoG) and navigated transcranial magnetic stimulation (nTMS)–tailored supratotal resection (ETT-SpTR) for LGG in controlling seizures, preserving neurological function, and enhancing treatment effectiveness.

METHODS The authors retrospectively analyzed a prospectively enrolled cohort of patients with LGG presenting with epileptic seizures with ictal/interictal activity on electroencephalography (EEG) who underwent resective surgery. The authors performed preoperative nTMS to identify functional cortical areas. ECoG was used to guide the removal of the high-risk epilepsy cortical areas (HREAs). Patients were divided into two groups: group I, the control group, underwent gross-total resection alone, whereas group II patients underwent removal of HREAs identified by ECoG (ETT-SpTR). Resection avoided functionally eloquent areas as identified on nTMS, checked with cortical mapping. Postoperative seizure outcome was assessed using the Engel classification.

RESULTS Fifteen patients who underwent LGG resection between January and July 2023 were included. Among 24 identified nTMS-positive points, none were included in the resection. Overall, 73.3% of patients (11/15) showed positive intraoperative ECoG, with better outcomes in group II (85.7% Engel class IA) than in group I (25% Engel class IA) at the follow-up ($p = 0.02$, OR 0.5 [95% CI 0.035–7.10], RR 0.19 [95% CI 0.03–1.2]). Seizure control was significantly better in group II, with no notable differences in postoperative transient neurological deficits between the two groups ($p = 0.45$). No permanent neurological deficits were observed during follow-up. Statistical analysis revealed significant differences between the two groups ($p < 0.05$).

CONCLUSIONS This preliminary study affirms the predictive value of TMS for postoperative neurological status and safety in epileptic patients. Intraoperative ECoG effectively identified peritumoral HREAs. ETT-SpTR significantly improved epileptic outcomes, preserving functions without permanent neurological worsening. Additional resection targets the HREAs in the temporal, frontal, and parietal lobes.

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KEYWORDS LGG; low-grade glioma; supratotal resection; TMS; transcranial magnetic stimulation; epilepsy

EPILEPSY is prevalent in 40%–70% of glioma patients, especially those with low-grade gliomas (LGGs).^{1,2} Despite guidelines recommending antiepileptic drugs after the first seizure,³ their side effects and limited efficacy pose challenges. Resection, particularly gross-total resection (GTR),^{4,5} is the most effective approach for

seizure control, but 27%–55% of LGG patients still experience seizures postoperatively.^{4,6} Despite encouraging data on supratotal resection (SpTR) regarding overall survival (OS) and epileptological outcomes in these patients, there is still no clear and shared definition of SpTR in the literature.

ABBREVIATIONS DTI = diffusion tensor imaging; ECoG = electrocorticography; EEG = electroencephalography; ETT-SpTR = ECoG-nTMS–tailored SpTR; GTR = gross-total resection; HGG = high-grade glioma; HREA = high-risk epilepsy area; iECoG = intraoperative ECoG; LGG = low-grade glioma; nTMS = navigated TMS; OS = overall survival; QOL = quality of life; rMT = resting motor threshold; rTMS = repetitive TMS; SEEG = stereo-EEG; SpTR = supratotal resection; TMS = transcranial magnetic stimulation.

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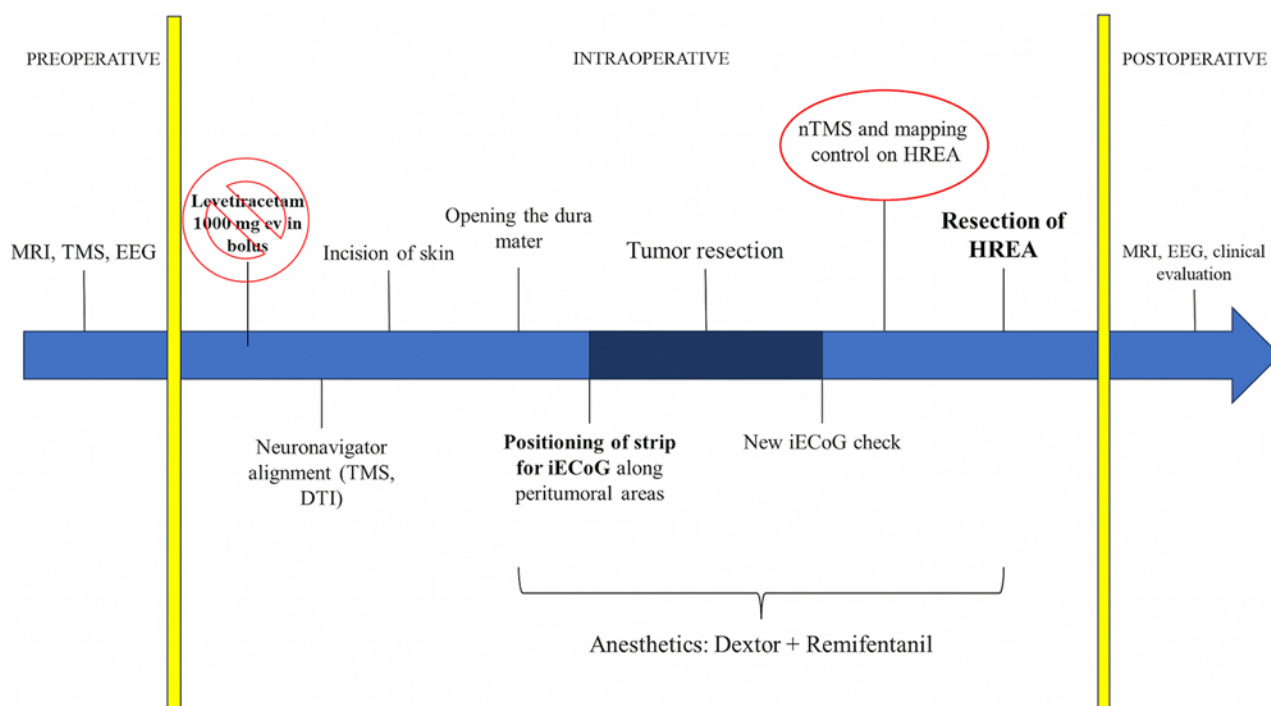


FIG. 1. Schematic representation of our workflow. ev = endovenous. Figure is available in color online only.

Molecular studies indicate peritumoral cortex involvement in high-risk epilepsy areas (HREAs) in LGG.^{1,7,8} Identifying these areas remains challenging, with techniques like video-electroencephalography (EEG) and stereo-EEG (SEEG) being time-consuming for these oncological patients. Electrocorticography (ECoG) emerged as a more immediate application, guiding resection based on research trends.^{9–11}

In this study, we evaluated the reliability of ECoG-navigated transcranial magnetic stimulation (nTMS)-tailored supratotal resection (ETT-SpTR) in identifying HREAs while preserving functional areas in LGG patients with epilepsy. The primary objective was functional preservation, and nTMS, combined with intraoperative monitoring, is a crucial technique in achieving this goal. The research aims to contribute to improved surgical strategies for epilepsy management in LGG patients.

Methods

We retrospectively analyzed a series of prospectively enrolled patients with intracranial LGG and epileptic seizures as the onset symptom undergoing resection at our center. We considered epileptic seizures to be all phenomena in which a clinical manifestation was correlated with ictal/interictal EEG abnormalities. Figure 1 summarizes each step of the method we used.

Preoperative MRI

All patients underwent MRI at our center using a 3T MRI unit (Ingenia 3T, Philips Medical Systems) with the standard oncological protocol.¹² Diffusion tensor imaging

(DTI) sequences were performed for white matter tract reconstruction.

Preoperative TMS

Preoperative functional cortical areas were defined using TMS with a figure-of-eight coil (Galileo NetBrain Neuronavigator 9000, EB Neuro Corp.). A volumetric T1-weighted MR image was used to build a patient's 3D brain model. We consider the resting motor threshold (rMT) as minimal TMS intensity to obtain a motor evoked potential of 50 μ V, registered at the right first dorsal interosseus muscle, in approximately 50% of 5–10 consecutive trials.¹³ We adopted a monophasic pulse stimulation to investigate motor areas and a biphasic pulse stimulation with fixed intensity above the rMT for testing language and calculation function.

For mapping the motor cortex, we measured the amplitudes of the motor evoked potentials evoked in muscles contralateral to the stimulation. Then, we delineated a map of the scalp sites from which responses are obtained for each muscle of interest. We considered points localized in the frontal, prefrontal, and postcentral cortices.

The language task consisted of the DO80 naming test,⁴⁶ whereas the calculation task required simple single-step arithmetic operations. Before each repetitive TMS (rTMS) mapping, the patient performed the "baseline" task (i.e., completed without rTMS perturbation) to remove all incorrect answers from the stimulation sequence. Then, rTMS perturbation consisted of trains-of-5 pulses at 5 Hz with an intensity of 100% of the first dorsal interosseus muscle rMT, delivered simultaneously with the pictures' presentations, showing the DO80 naming test for language

or arithmetic operations for calculation.¹⁴ For the language function, 90 trains were applied over the left perisylvian cortices, while the calculation function was mapped on 70 spots, distributed over parietal, temporal, frontal, and prefrontal cortices.

Seizure Preoperative Management

Patients underwent preoperative EEG, with inclusion criteria limited to patients exhibiting interictal or ictal activity during preoperative recording. For EEG recording, screw-type needle electrodes were positioned on the scalp according to the international 10–20 system (C3', Cz, C4', and Fz). A neurophysiology expert interpreted the EEG traces. Electrographic and electroclinical seizures were defined according to Hirsch's criteria.¹⁵ Antiepileptic therapy with levetiracetam was initiated at a standard dosage of 500 mg twice daily.¹⁶

Intraoperative Setting of ETT-SpTR

Preoperative MRI with DTI sequences and TMS data were loaded in the neuronavigation system (StealthStation 8, Medtronic), aiming to enable constant monitoring of the distance between functional structures and resection margins during surgery.

A perioperative levetiracetam bolus before surgical incision and after induction was not administered to observe interictal activity on intraoperative ECoG (iECoG). After opening the dura mater, the anesthetic regimen involved dexmedetomidine and remifentanyl, avoiding propofol to prevent the suppression of the ECoG trace (burst suppression¹⁷).

We used Cz'-Fz, C3'-Fz, C4'-Fz, and C3'-C4' montages for ECoG. A four-contact subdural strip (Wyler electrodes, AD-Tech Medical Instrument Corp.) was placed on the exposed cortical surface. Raw EEG was visually scored, and seizures were defined following Hirsch's criteria¹⁵ for electrographic and electroclinical events.

The ECoG strip was positioned in multiple exposed cortical areas along the planned GTR margins. ECoG recording was performed before, during, and at the end of resection. The decision to include an ECoG area with epileptiform activity (HREA) in the resection margins was based on the risk of neurological deficits; thus, the functionality of the cortical area was defined based on nTMS, tractography, and direct cortical stimulation (DCS). We did not extend the resection to cortical areas positive on ECoG when these were functional.

After identifying the HREA with iECoG, we assessed its location relative to the altered signal in the FLAIR sequences using the neuronavigation system.

At the opening the dura mater, we checked the localization of any nTMS-positive point over the exposed cortical area with the neuronavigation probe. We calculated the distance, classified as less or more than 1 cm, from any nTMS-positive points to the margins of resection. After this, we proceeded with DCS. In cases of discrepancies between the two techniques, we considered the data from DCS, which is the gold standard for cortical mapping. In awake surgery, the Penfield technique used low-frequency stimulation for motor, language, and calculation cortical

mapping (0.5–3 mA). An expert speech therapist guided patients during stimulation.

For asleep surgery, DCS was performed according to the Taniguchi paradigm, with high-frequency stimulation, investigating only motor function and monitoring with electromyography. The language function was monitored with cortico-cortical evoked potentials,¹⁸ which checked the integrity of the arcuate fasciculus during the resection with stimulation (Broca's area) and a recording (Wernicke's area) strip.

We sent the removed tissue to the laboratory for histological examination, which was classified according to the 2021 WHO classification.¹⁹

We divided our study population into two groups: group I, patients undergoing GTR of the glioma (control group), and group II, patients undergoing ETT-SpTR. Early postoperative MRI was performed to define the degree of glioma resection.²⁰ Cases of GTR of the glioma were included in the study. After discharge, follow-up was conducted with clinical and electroencephalographic monitoring and radiological assessment. Engel classification²¹ was used to define epileptological outcomes. The postoperative functional outcome was the percentage of neurological deficits that worsened, improved, or emerged postoperatively. We calculated the incidence of these deficits in both groups. We assessed the statistically significant difference in the percentages between the two groups, using comparison tests and calculating the odds ratio and relative risk.

Patients whose postoperative histological report did not confirm the suspicion of LGG, those without seizures confirmed by EEG, and those with partial resection of the LGG were excluded from the study, as were patients who died during follow-up.

We assessed the efficacy of ETT-SpTR in extratemporal regions. In group II, we calculated the percentages of LGG and the ECoG-positive area resected for each cerebral lobe. We computed the epileptogenic outcome for both temporal and extratemporal areas, taking into account the location of the resected ECoG-positive area, and expressed the values as percentages, calculating the statistical difference.

Statistical Analysis

Measurement data are expressed as mean $\pm$ SD. ANOVA or the Student t-test was used to assess statistical differences between the two groups. Qualitative data were analyzed using the chi-square test or Fisher's exact test. A p value < 0.05 was considered statistically significant. In the present study, odds ratios and relative risks were calculated to assess the statistical significance of associations. Odds ratios were used to measure the strength of association between categorical variables, while relative risks were calculated to estimate the risk of an event in one group compared with the another. These methods were chosen to accurately assess the significance of relationships between the analyzed variables.

Results

We included 15 patients between January and July 2023 diagnosed with LGG undergoing GTR, with seizures as

TABLE 1. Population characteristics

	Value
No. of patients	15
Age, yrs	
Mean $\pm$ SD	48.73 $\pm$ 18.39
Range	23–74
Sex	
Male	8 (53.3)
Female	7 (46.7)
Type of seizure	
Generalized	6 (40)
Focal	9 (60)
Site of LGG	
Temporal lobe	9 (60)
Frontal lobe	4 (26.7)
Parietal lobe	2 (13.3)
Type of surgery	
Awake	3 (20)
Asleep	12 (80)
Side of LGG	
Lt	7 (46.7)
Rt	8 (53.3)
Pathology profile:	
Oligodendroglioma, 1p-19q codeleted, WHO grade 2	6 (40)
Astrocytoma, WHO grade 2	9 (60)
Group	
I	8 (53.3)
II	7 (46.7)

Values are presented as the number of patients (%) unless stated otherwise.

the presenting symptom (Table 1). Eight were male, and 7 were female (53.3% vs 46.7%). The mean age was 48.73 ± 18.39 years (range 23–74 years; median 56 years). There were 8 patients (53.3%) in group I and 7 (46.7%) in group II. All patients in the study were started on levetiracetam 500 mg twice daily at the diagnosis of seizures. Preoperative EEG traces showed interictal activity in all patients. In 4 patients (26.6%), the lesion was located in the frontal region; in 2 patients (13.3%), it was parietal; and in the remaining 9 patients (60%), it was temporal. We performed awake surgery in 3 patients (20%) and asleep resection in the remaining 12 patients (80%). Resection was performed on the left side in 7 patients (46.7%) and on the right side in 8 patients (53.3%). Six oligodendrogliomas (1p-19q codeleted, WHO grade 2; 40%) and 9 astrocytomas (WHO grade 2; 60%) were diagnosed. Eleven patients (73.3%) had positive ECoG: 4 in group I and 7 in group II. In all cases, the HREA was extratumoral and outside the FLAIR-altered signal on preoperative MRI. In all group II patients, interictal anomalies in the ECoG trace disappeared after resection. ECoG results were negative in 4 group I patients; in the remaining 4 group I patients, the epileptiform cortical area was not included in the resection because it was functional. None of the group I patients showed complete regression of interictal anomalies on postresection EEG. The follow-up was at least 10 months (range 10–14 months). Six of 7 group II patients (85.7%)

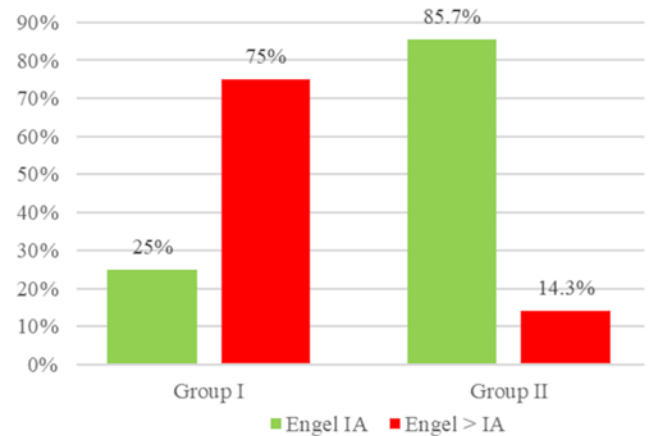


FIG. 2. Seizure outcome. In group I (control group, GTR), complete seizure control (Engel class IA) was achieved in 25% of cases. In group II (ETT-SpTR), seizure control was achieved in 85.7% of cases ($p = 0.02$). Figure is available in color online only.

remained seizure free after surgery and during follow-up (Engel class IA), while only 2 group I patients (25%) had Engel class IA outcomes; the remaining 6 patients (75%) experienced epileptic seizures during follow-up (Engel class IIA–IVB outcomes). Seizure control was achieved by 25% of group I patients and 85.7% of group II patients ($p = 0.02$, OR 0.5 [95% CI 0.035–7.10], RR 0.19 [95% CI 0.03–1.2]; exact probability according to Fisher: 0.04, t -value 2.44, $p < 0.05$) (Fig. 2).

In group I, we observed the postoperative functional outcome. No patient (0%) experienced improvement in neurological status, 7 patients (87.5%) had a stable neurological examination, and 1 patient (12.5%) had worsening neurological deficits. In group II, 1 (14.2%) patient experienced neurological improvement, 4 patients (57.2%) had neurological stability, and 2 patients (28.6%) had worsening neurological status. The difference between the two groups did not show statistical significance ($p = 0.45$, OR 2.8 [95% CI 0.19–40.06], RR 2.28 [95% CI 0.25–20.13]) (Table 2).

In group II, we observed 4 temporal LGGs (57.1%) and 3 frontal LGGs (42.9%). Among patients in the same group, the resected HREA comprised 3 temporal lobes (42.9%), 3 frontal lobes (42.9%), and 1 parietal lobe (14.3%). These data imply that the lobe of origin of the LGG did not correspond in all cases to the lobe where the HREA was located. During follow-up, seizure control (Engel class IA) was achieved in all 3 patients (100%) with temporal ECoG and in 3 patients (75%) with extratempo-

TABLE 2. Postoperative neurological outcome in groups I and II

Neurological Outcome	No. of Patients (%)	
	Group I	Group II
Improvement	0 (0)	1 (14.3)
Stability	7 (87.5)	4 (57.1)
Worsening	1 (12.5)	2 (28.6)

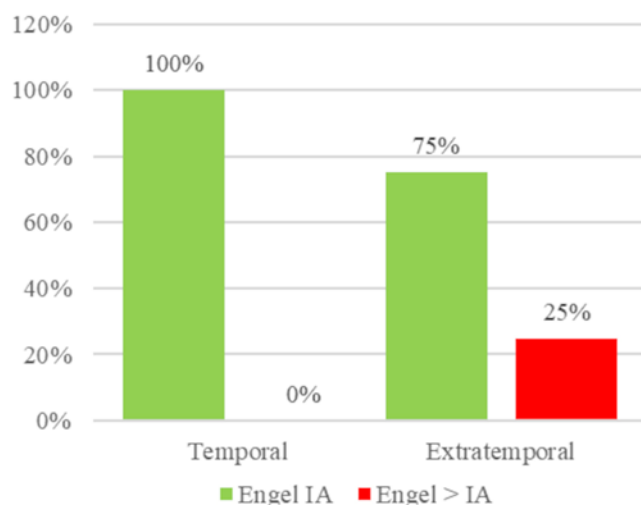


FIG. 3. Seizure outcome in group II patients (ETT-SpTR), subdivided by ECoG location. All patients with LGGs in the temporal lobe achieved Engel class IA outcomes, whereas 75% of patients with LGGs outside the temporal lobe achieved Engel class IA outcomes. Figure is available in color online only.

ral ECoG ($p = 0.38$, OR 0.33 [95% CI 0.001–11.34], RR 0.41 [95% CI 0.022–7.71]) (Fig. 3).

We performed nTMS and verified the findings using DCS in all patients. Table 3 reports all the positive nTMS points identified on the cortex exposed after craniotomy for each patient. After opening the dura mater, we exposed 24 positive nTMS points in all 15 patients. Ten of these 24 (41.7%) were positive motor points, 8 (33.3%) were positive language points, 5 (20.8%) were positive calculation points, and 1 (4.2%) was a positive somatosensory point.

We never directly included nTMS-positive points in the resection. We found a distance of less than 1 cm in only 3 patients (20%), the same individuals in whom we observed a new postoperative neurological deficit. In all 3 of these patients, the neurological deficit was transient, with complete recovery of functions during the follow-up. No postoperative deficit was recorded in patients in whom the distance of positive nTMS points was greater than 1 cm from the resection margins.

Discussion

Our preliminary work observed how ETT-SpTR is a safe and effective technique for improving functional and epileptogenic outcomes for patients with LGG. Specifically, we preoperatively investigated the patient's eloquent areas with TMS to preserve them intraoperatively. Additionally, we searched for HREAs in the peritumoral cortex using iECoG, thereby expanding the resection to an SpTR. Consequently, we observed a lower rate of epileptic seizures in the long-term follow-up compared with GTR, with no change in the rate of postoperative neurological deficits. In our case series, we treated LGG in temporal, frontal, and parietal regions, achieving comparable results regarding epileptological outcomes.

Therapeutic development in the last decades prolonged the OS of patients with LGG (15–17 years),^{22,23} and GTR is the benchmark surgical treatment²⁴ (Fig. 4). Recent systematic reviews and meta-analyses have proven that SpTR prolongs progression-free survival and OS for LGGs^{25,26} and high-grade gliomas (HGGs)^{24,27} more than GTR. The concept of SpTR is still being defined, and the aim is to consider resection beyond the visible tumor margins on MRI (for LGGs, the T2-FLAIR hypersignal). Based on this lack of a definition, we have adopted the definition of SpTR as a functional concept linked to the physiologi-

TABLE 3. Characteristics of exposed nTMS point for each patient

Patient No.	Total No. of nTMS Points Exposed	Motor Points	Language Points	Calculation Points	Somatosensory Points	Distance From Resection Margins, cm	New Postop Deficit	Follow-Up
1	3	3	0	0	0	<1	Hemiparesis	Complete recovery
2	1	1	0	0	0	>1	None	NA
3	0	0	0	0	0	NA	None	NA
4	2	2	0	0	0	>1	None	NA
5	0	0	0	0	0	NA	None	NA
6	2	0	1	1	0	<1	Partial aphasia	Complete recovery
7	3	0	3	0	0	<1	None	NA
8	2	2	0	0	0	<1	Hemiparesis	Complete recovery
9	2	0	0	1	1	>1	None	NA
10	1	0	0	1	0	>1	None	NA
11	3	0	2	1	0	>1	None	NA
12	2	2	0	0	0	>1	None	NA
13	0	0	0	0	0	NA	None	NA
14	2	0	1	1	0	>1	None	NA
15	1	0	1	0	0	>1	None	NA

NA = not applicable.

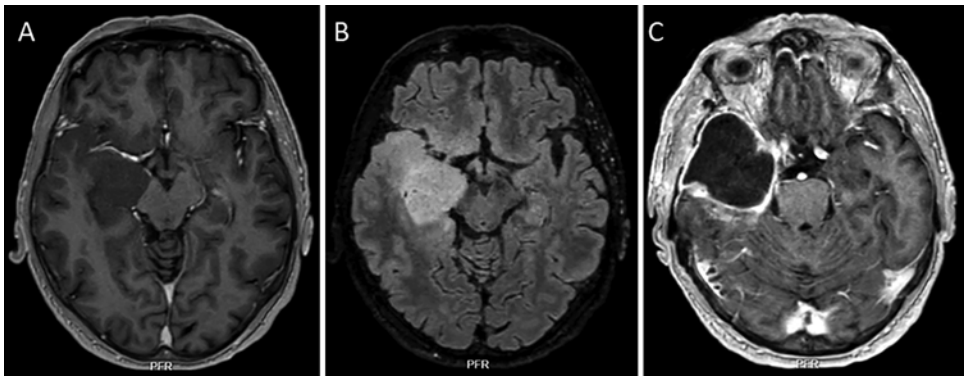


FIG. 4. Contrast-enhanced T1-weighted (A), FLAIR (B), and contrast-enhanced T1-weighted (C) MR images showing GTR of the LGG.

cal and pathological connectivity of brain parenchyma. In defining the SpTR, we aim to improve patients' quality of life (QOL), allowing for a longer OS. The main goals to improve the QOL are avoiding new neurological deficits and curing the seizures, which are the primary presenting symptom in more than 90% of LGGs,^{7,28} primarily as focal seizures (45%–95%).⁶

Given that approximately 27%–55% of postoperative patients with LGG experience recurrent epileptic seizures^{4,10,29,30} requiring pharmacological treatment, studying techniques that enable a more radical tumor resection and address peritumoral areas involved in associated epileptogenesis becomes crucial.⁷ Intraoperative ECoG is one of the most used techniques for this purpose. To our knowledge, no studies in the literature have reported the rate of epilepsy persistence after GTR of LGGs due to extratumoral foci in an adult population, perhaps because of the low accuracy of iECoG in finding the extratumoral foci. Few papers have addressed this surgical technique in the literature (Table 4). Yao et al. analyzed whether iECoG was reliable in determining whether to extend the resection of epileptogenic LGGs to the temporal pole, but the analysis focused solely on this area rather than the entire peritumoral cortex.¹⁰ Zweiphenning et al. investigated exclusively temporal areas with iECoG, as well.⁹ Robertson et al. investigated iECoG reliability in a heterogeneous pediatric population (LGG and HGG).³¹

Indeed, the ETT-SpTR is a resection technique for LGGs beyond the visible tumor margins on MRI, involv-

ing the removal of areas that might not appear to be tumor related but exhibit indirect signs of tumoral infiltration/alteration of the normal neuroglial cytoarchitecture caused by the tumor. Based on recent studies on the cytoarchitectural changes in the peritumoral cortex of LGGs underlying associated epilepsy,^{7,8} we have adopted, as indirect signs to reach the SpTR, those nontumoral areas exhibiting rhythmic and repetitive signs of intraoperative interictal ECoG activity (HREAs). Thus, we spared any eloquent areas identified by nTMS during the resection. Our study analyzed the ETT-SpTR of LGGs to preserve patient functions, improve epileptic outcomes, and increase QOL.

Surgery

Resection provides seizure control ranging from 36% to 100% in patients with LGGs.^{32,33} Literature reviews^{25,26} have identified the extent of resection as the primary predictor of postoperative seizure control.^{26,30,34–36} After GTR, the persistence of epileptic seizures at 12 months postoperatively ranges from 27% to 55%.^{4,10,29,30} This variability could be related to whether or not the HREA is involved in the resection. The main challenge in glioma surgery is that independent HREAs can be nested within extratumoral cortical areas substantially devoid of tumor.⁷

Similarly, SpTR⁶ has been proposed for better seizure control,^{25,26} even with a second surgery.^{34,36} This hypothesis is based on potentially removing presumed epileptogenic areas through SpTR beyond abnormalities defined

TABLE 4. Review of the literature

Authors & Year	No. of Patients	Results	Conclusion	Limits
Yao et al., 2018 ¹⁰	108	74.07% Engel class IA	ECoG accurately localizes the epileptogenic area in LGG	ECoG-guided resection extended only to the temporal pole
Robertson et al., 2019 ³¹	41	66.06% Engel class IA	ECoG-guided resection does not improve the epileptogenic outcome	Pediatric population, heterogeneous (HGG & LGG), unclear data on EOR
Zweiphenning et al., 2022 ⁹	78	67% Engel class IA in the HFO group; 90% in spike-isolated group	HFO-guided tailoring of epilepsy surgery was not noninferior to spike-guided tailoring on intraop ECoG	Only temporal lobe

EOR = extent of resection; HFO = high-frequency oscillation.

by MRI.³⁵ Using ETT-SpTR for LGG to identify HREA could improve postoperative seizure control, avoiding a second surgery and the excessive resection of functional areas.^{37,38} However, previous series have yielded variable results.

As our data suggest, cases we classified as group II had a better epileptological outcome than those undergoing only GTR. We did not extend resection in group I either because ECoG positivity was not found or because the positive area was functional for the patient. The ECoG strip was placed along the entire peritumoral cortex, with multiple placement attempts before and after resection, allowing us to study the peritumoral area accurately despite the limited number of electrodes on the strip. ECoG was positive in 11 of the 15 patients (73.3%), so it is a high-sensitivity technique to identify HREAs. Our results affirm that the identified and removed HREA always had an interictal-type electrical correlate.

As an additional analysis, we did not observe differences in terms of epileptogenic outcomes in patients in group II with positive temporal or extratemporal ECoG areas. Based on our knowledge, this work is the first in the literature that observes how ECoG-guided resection can be successfully applied to both peritumoral temporal and extratemporal areas.

Navigated TMS

Navigated TMS has been increasingly used over the years to preserve function in patients undergoing neurosurgical procedures. Several studies have sought to assess the application of nTMS in epilepsy surgery.^{39–41} Invasive intracranial electrodes for SEEG stimulate the pathological epileptogenic network, provide highly effective identification,⁴⁰ and map functionally eloquent areas. Otherwise, SEEG is an invasive procedure reserved for epileptic patients for whom the primary goal is to identify the epileptic focus in the presurgical evaluation. Mapping eloquent areas is a secondary purpose of SEEG for presurgical planning in these patients. Applying this examination in oncological patients with suspected glioma (which could also be WHO grade 3 or 4 on histological examination) is not commonly practiced.

Moreover, SEEG does not have the primary objective of cortical mapping, as it is an invasive procedure; DCS remains the gold standard for this purpose. Therefore, we did not subject our patients to this examination during preoperative planning. Therefore, TMS cannot replace intracranial electrodes or strips in identifying the epileptogenic focus in complex epilepsy cases, but it can still be valuable in noninvasively identifying eloquent areas in preoperative planning for these patients. Despite common concerns regarding the application of TMS in epileptic patients, all relevant studies confirm its safety.^{39,41} The rate of seizures in epileptic patients during TMS was described as less than 1%.⁴² In our study, no seizures occurred during TMS, confirming its safety.

Our study used nTMS to orient the craniotomy and the cortical mapping. However, we could assess the accuracy of nTMS-positive points in predicting postoperative neurological deficits since they were never included in the resection. In cases of nTMS-positive points and negative

results on DCS, we extended the resection to the margins of these points without ever encompassing them. Our data confirm that nTMS is a valid predictor for postoperative new neurological deficits. No nTMS-positive points were included in the area resection, and no permanent postoperative neurological deficits were found, even in cases in which the distance between the positive nTMS point and resection margins was less than 1 cm, confirming previous findings in the literature.^{43,44} All new-onset postoperative neurological deficits were transient in every case, with complete functional recovery during follow-up. Our patients have a long life expectancy,⁴⁵ so preserving their QOL after surgery is a priority. However, although focal postoperative neurological deficits can be strongly disabling, it is essential to note that these patients have a time window for complete recovery in cases of partial and transient functional deficits.

The absence of a difference between the two groups regarding the incidence of postoperative neurological deterioration is evidence that the surgical intervention did not result in any distinction in terms of function preservation for the patient. Both functional and oncological objectives remained primary goals in all surgeries.

Limitations

Our preliminary work is limited by the small number of patients and the limited follow-up period. Future studies are needed to confirm our results. Intraoperative ECoG is a feasible technique to identify HREAs, but it has low accuracy (73.3% of patients with positive iECoG), another study limitation. In light of greater accuracy, we could accurately define the percentage of persistent epilepsy post-GTR of LGGs precisely due to extratemporal foci. Another limitation of our study is that we did not examine our patients with magnetoencephalography. Future studies could compare the accuracy of iECoG with MEG in identifying HREAs in oncological patients.

Conclusions

Our study affirms that ETT-SpTR for LGGs improves epileptic and functional outcomes, enhancing patients' QOL. We confirmed the predictive value and safety of nTMS. Intraoperative ECoG is a high-sensitivity technique to identify HREA. The resected peritumoral HREA was found in temporal regions and other lobes. Future directions include expanding cohorts and extending follow-up for comprehensive insights.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Battista. Acquisition of data: Battista, Parenti, Gadda, Amadori. Analysis and interpretation of data: Battista, Gadda, Amadori. Drafting the article: Battista, Amadori.

Critically revising the article: Muscas, Bonaudo, Gadda, Martinelli, Carrai, Amadori, Grippo, Della Puppa. Reviewed submitted version of manuscript: Amadori, Grippo. Approved the final version of the manuscript on behalf of all authors: Battista. Statistical analysis: Battista, Amadori. Administrative/technical/material support: Amadori. Study supervision: Amadori.

Supplemental Information

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