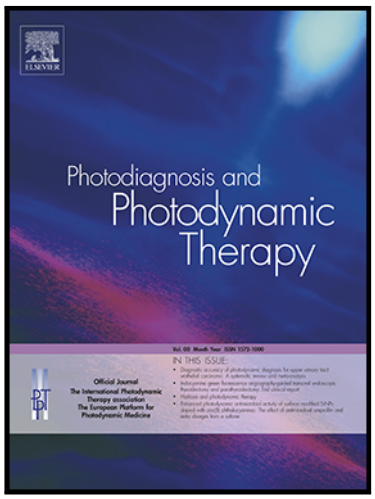

Combined 5-Aminolevulinic Acid Fluorescence and Intraoperative Ultrasound Enhance Resection and Functional Outcomes in High-Grade Glioma Surgery

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Highlights

- 5-ALA + ioUS improves HGG surgery outcomes
- It boosts GTR, cuts 6-month recurrence, aids recovery
- 5-ALA + ioUS is safe for better HGG prognosis

Combined 5-Aminolevulinic Acid Fluorescence and Intraoperative Ultrasound Enhance Resection and Functional Outcomes in High-Grade Glioma Surgery

Running title: High-Grade Glioma Surgery

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Abstract

Objective: This study aimed to evaluate the clinical efficacy of combining 5-aminolevulinic acid (5-ALA) fluorescence with intraoperative ultrasound (ioUS) for microsurgical resection of high-grade gliomas (HGGs).

Methods: In this single-centre retrospective cohort study, 228 patients with HGG were grouped based on the surgical approach: 122 underwent 5-ALA + ioUS-guided resection, whereas 106 received conventional microsurgery (control). Outcomes included gross total resection (GTR) rates, tumour recurrence at 3–6 months, postoperative Karnofsky Performance Status (KPS) scores, intraoperative haemorrhage value and operation time, length of hospital stay and complications.

Results: The 5-ALA + ioUS group achieved significantly higher GTR rates (91.0% vs 74.5%; $P < 0.001$) and lower recurrence rates at both 3 months (4.1% vs 12.3%; $P = 0.027$) and 6 months (9.0% vs 23.6%; $P = 0.002$) than the control group. Functional recovery (the KPS) improved more substantially in the 5-ALA + ioUS group at 1 month (85.9 vs 77.6; $P < 0.001$) and 6 months (90.9 vs 82.5; $P < 0.001$) postoperatively. Intraoperative haemorrhage (255.9 vs 338.5 mL), operation time (2.6 vs 3.4 h) and hospital stay (14.8 vs 20.4 days) were significantly

reduced (P < 0.001 for all) in the 5-ALA + ioUS group compared with the control group. Complication rates did not differ significantly between the groups (P = 0.104).

Conclusion: This retrospective study suggests that the combination of 5-ALA and ioUS may improve GTR, reduce early recurrence, enhance functional recovery and optimise surgical efficiency in HGG resection. Prospective studies are warranted to confirm these results.

Keywords: gliomas, 5-aminolevulinic acid, ultrasonography, margins of excision, Karnofsky Performance Status

Introduction

Maximal safe resection is important for improving survival in patients with intracranial gliomas, particularly high-grade gliomas (HGGs), including glioblastomas (GBMs) [1]. Recent evidence has highlighted that a greater extent of resection (EOR) is correlated with improved progression-free survival (PFS) and overall survival (OS) in HGGs [2,3]. However, achieving this goal is challenging due to the tumour's infiltrative nature, indistinct margins and frequent involvement of eloquent brain regions [4]. Incomplete resection leaves residual tumour, which leads to recurrence, whereas excessive resection risks permanent neurological deficits, affecting survival [5].

These challenges have spurred the development of intraoperative adjuvant technologies to enhance the visualisation of tumour tissues, such as 5-aminolevulinic acid (5-ALA) fluorescence, intraoperative ultrasound (ioUS) and intraoperative magnetic resonance imaging (MRI). By inducing protoporphyrin IX (PpIX) fluorescence in malignant glioma cells, 5-ALA

enables real-time microscopic visualisation of tumour tissues [6]. Previous studies have shown that 5-ALA considerably increases complete resection rates and 6-month PFS in HGGs compared with conventional microsurgery [6,7]. However, 5-ALA remains a challenge as a diagnostic method because tissue autofluorescence interferes with PpIX signals in cases where tumours emit only weak signals, and non-tumorous lesions, including inflammatory sites, tend to emit PpIX fluorescence [8]. Intraoperative ultrasound provides real-time dynamic structural imaging directly at the surgical site [9]. It compensates for brain shift, aids lesion localisation and helps detect residual tumour with advantages in portability, cost and repeatability [9,10]. Previous studies have observed that complete tumour resection of gliomas was increased when ioUS was used [11].

Crucially, these two tools possess complementary strengths: 5-ALA excels at detecting surface microscopic infiltration, and ioUS provides real-time structural guidance and compensates for shifts. Their synergistic combination holds considerable promise for maximising tumour detection while minimising functional risk beyond the capability of any single modality [12]. Pepa et al. [12] conducted a retrospective study to evaluate whether the integration of 5-ALA with ioUS improved residual tumour identification in GBMs. A total of 230 patients with GBM underwent 5-ALA- and/or ioUS-guided surgeries. The results showed that the combination of the two techniques achieved the best outcomes in terms of EOR [12]. Similarly, Aibar-Durá et al. [13] analysed data from 72 patients who underwent HGG resection at a single hospital and found that combining 5-ALA and ioUS enhanced diagnostic accuracy for HGG resection. However, comprehensive evidence regarding the impact of combined 5-ALA and ioUS on functional recovery, surgical efficiency and overall clinical outcomes in HGG surgery remains

limited.

This study aims to address these critical knowledge gaps by investigating the clinical outcomes of combining 5-ALA fluorescence and ioUS in patients undergoing microsurgical resection for HGGs, with a specific focus on resection efficacy, functional recovery and surgical efficiency.

Methods

Patients

This single-centre retrospective study was approved by the ethics committee of our hospital in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients.

In this retrospective study, data from patients who underwent HGG resection between 1 January 2019 and 31 December 2023 at our hospital were collected. The inclusion criteria were as follows: (1) patients undergoing glioma surgery for the first time; (2) patients with pathological confirmation of HGG (World Health Organization grades III–IV) [14] and follow-up longer than 6 months; (3) patients aged 18 years or older; and (4) glioma considered suitable for complete surgical resection. Patients were excluded if they had severe comorbidities, extracranial metastasis or recurrent gliomas.

The patients were grouped according to the surgical procedure: (1) 5-ALA- and ioUS-guided surgeries (5-ALA + ioUS group) and (2) conventional microsurgical procedures (control group).

Clinical characteristics and surgical procedures

Patients' age, sex, weight and period from tumour diagnosis to surgery were

retrospectively recorded. The location and size of the tumour in each patient were preoperatively identified using contrast-enhanced brain MRI.

All surgeries were microsurgical resections conducted using an OPMI Pentero 800 microscope (Carl Zeiss, Oberkochen, Germany) under general anaesthesia. Electrophysiological monitoring (Nicolet Endeavor CR, Cardinal Health, Dublin, Ireland) and a neuronavigation system were used in all cases.

For patients in the 5-ALA + ioUS group, 5-ALA (Medac GmbH, Wedel, Germany) was administered 3–5 h before surgery at a dose of 20 mg per kilogram of body weight. Following dural opening, the tumour location and boundaries were visualised using the Pentero 800 surgical microscope. The microscope was equipped with a dedicated filter set for fluorescence excitation at a wavelength of 400-410 nm (blue light) to visualize the protoporphyrin IX (PpIX) fluorescence. Concurrently, ioUS was employed for real-time localisation. The ioUS findings were correlated with preoperative MRI to precisely delineate the tumour's spatial position and anatomical margins. Once concordance between the ioUS and preoperative MRI findings was established, tumour resection was initiated. Under microscopic visualisation with blue light (400-410 nm) excitation, 5-ALA-induced PpIX accumulation enabled real-time fluorescence-guided resection. The tumour tissues were distinctly demarcated into areas of strong, solid pink-red fluorescence, vague or patchy pink fluorescence, and no fluorescence. The intensity of PpIX fluorescence has been shown to positively correlate with tumour cell density [8]. A sample from a region of solid pink-red fluorescence was sent for intraoperative frozen section pathology, which confirmed the diagnosis of HGG. Resection then proceeded, guided by ioUS and the 5-ALA fluorescence patterns. The surgical goal was to remove all areas of strong

fluorescence. However, in eloquent brain areas identified by intraoperative electrophysiological monitoring, even if strong fluorescence was present, resection was either not performed or was limited to avoid permanent neurological deficits, adhering to the principle of maximal safe resection. Surgeons continued the dissection until reaching the margins, where fluorescent tissues disappeared. At this point, ioUS was repeated to confirm the absence of residual sonographic tumour tissue. All resected tumour specimens were subsequently sent for definitive postoperative histopathological examination.

For the control group, microsurgical resection was performed solely based on preoperative MRI and computed tomography imaging guidance, without the use of ioUS or 5-ALA.

All surgical procedures were performed by a team of experienced neurosurgeons at our hospital. Contrast-enhanced brain MRI was performed again to evaluate residual tumour tissue. Radio-chemotherapy was started as determined by consultation with hospital oncologists.

Evaluations

Tumour recurrence rate: Patients were followed up for 6 months to evaluate tumour recurrence by repeating contrast-enhanced brain MRI examinations. Tumour recurrence was defined as the appearance of new contrast-enhancing mass lesions on postoperative brain MRI, exhibiting features suggestive of high-grade malignancy such as haemorrhage, necrosis or cystic formations. Recurrence rates were assessed at 3 and 6 months postoperatively.

Gross total resection (GTR) rate: This was defined as the absence of any residual contrast enhancement in T_1-weighted sequences on early (<72 h) postoperative MRI [15]. All other cases with detectable residual enhancement were classified as partial resection. GTR rates were analyzed for the entire cohort and subsequently by histopathological subtype.

The Karnofsky Performance Scale (KPS): This scale is widely used to assess the functional status of patients with cancer. The KPS is an objective evaluation index scored from 0 to 100, with higher scores indicating a better condition [16]. The KPS score was assessed at three key time points: preoperatively (baseline), 1 month postoperatively and 6 months postoperatively.

Other evaluations: Haemorrhage volume and operation duration were obtained from surgical records. Postoperative complications, including intracranial infection, postoperative seizure, disturbance of consciousness and muscle weakness, were recorded.

Statistical analysis

Data analysis was performed using SPSS Statistics software (version 22.0). Categorical data were presented as numbers and percentages, and continuous data were presented as mean ± standard deviation if normally distributed or as median and confidence interval if skewed. Categorical variables were compared using the χ^2 test or Fisher's exact test, and continuous variables were compared using a Student's *t*-test or the Mann–Whitney *U* test. To assess the impact of histopathological heterogeneity on the primary outcome, a prespecified subgroup analysis of GTR rates was performed for the major tumor subtypes (glioblastoma, anaplastic astrocytoma, and anaplastic oligodendroglioma). A P-value of <0.05 was considered statistically significant.

Results

A total of 228 patients with HGGs (145 men and 83 women) who met the inclusion criteria were analysed in this study. Among them, 122 patients (53.51%) underwent 5-ALA- and ioUS-

guided surgeries (5-ALA + ioUS group), including 74 men and 48 women, with a mean age of 53.12 years (range 23–77 years). The remaining 106 patients (46.49%) underwent conventional microsurgical procedures (control group), including 71 men and 35 women, with a mean age of 54.89 years (range 20–76 years). All patients successfully completed the surgical operation. There were no statistically significant differences in baseline characteristics between the two groups (Table 1). Specifically, the mean tumor largest diameter was comparable between the control group (56.62 ± 10.31 mm, range 31-90 mm) and the 5-ALA + ioUS group (57.70 ± 10.79 mm, range 35-95 mm; P = 0.442). Furthermore, the proportion of tumors located in eloquent brain areas was similar between the control group (48/106, 45.28%) and the 5-ALA + ioUS group (59/122, 48.36%; P = 0.698), indicating a comparable surgical challenge profile in terms of functional preservation.

Postoperative tumor recurrence was significantly lower in the 5-ALA + ioUS group compared to the control group at both 3 months (5/122 [4.10%] vs 13/106 [12.26%]; P = 0.027) and 6 months (11/122 [9.02%] vs 25/106 [23.58%]; P = 0.002) (Table 2).

Intraoperatively, both the haemorrhage volume and operation time were significantly reduced in the 5-ALA + ioUS group compared to the control group (P < 0.001 for both, Table 2). The GTR rate was also significantly higher in the 5-ALA + ioUS group (111/122, 90.98%) than in the control group (79/106, 74.53%) (P < 0.001). Furthermore, the length of hospital stay was significantly shorter in the 5-ALA + ioUS group (P < 0.001). The occurrence of postoperative complications was comparable between the two groups (P = 0.104), with intracranial infection remaining the most frequent complication (occurring in 7/122 patients in the 5-ALA + ioUS group and 9/106 patients in the control group).

Preoperative KPS scores were comparable between the two groups (control: 75.66 ± 9.01 vs 5-ALA + ioUS: 75.25 ± 10.73; P = 0.754, Table 1, Figure 1). Postoperative KPS scores were significantly higher in the 5-ALA + ioUS group than in the control group at both the 1-month (85.93 ± 10.24 vs 77.64 ± 10.51 points; P < 0.001) and 6-month follow-ups (90.89 ± 10.93 vs 82.55 ± 8.58 points; P < 0.001, Figure 1). The magnitude of improvement in KPS scores from baseline to 6 months postoperatively was also significantly greater in the 5-ALA + ioUS group (15.64 ± 9.50 points) than in the control group (6.89 ± 11.20 points; P < 0.001). These results consistently indicate that the 5-ALA + ioUS intervention is associated with significantly better functional recovery, as measured by the KPS.

Given the heterogeneity in tumor histology within our cohort, we conducted a subgroup analysis to evaluate the GTR rates according to the major pathological subtypes. The distribution of subtypes between the two groups was comparable (Table 1). As detailed in Table 3, the 5-ALA + ioUS group consistently demonstrated higher GTR rates compared to the control group across all subtypes. The absolute difference in GTR rates was most pronounced in glioblastomas (GBMs), where the combined modality achieved a GTR rate of 89.29% versus 67.86% in the control group (P = 0.021). A strong trend towards higher GTR rates with the combined approach was also observed in anaplastic astrocytomas (AA, 92.31% vs 72.73%) and anaplastic oligodendrogliomas (AO, 94.12% vs 78.57%), although these differences did not reach statistical significance in our cohort, likely due to the smaller sample sizes in these subgroups. This stratified analysis indicates that the benefit of 5-ALA and ioUS guidance in achieving maximal resection is applicable to the common high-grade glioma subtypes and is not solely driven by a single histology.

Discussion

Our retrospective study demonstrates that the combined use of 5-ALA fluorescence and ioUS considerably enhances the surgical management of HGGs. Compared with conventional microsurgery guided solely by preoperative imaging, the 5-ALA + ioUS approach achieved higher rates of GTR, substantially reduced tumour recurrence at 6 months, improved functional recovery, decreased intraoperative haemorrhage and operative time and shortened hospital stay without increasing postoperative complications. These findings underscore the synergistic potential of integrating complementary intraoperative technologies to overcome the inherent challenges of glioma resection.

The most notable outcome in our study is the markedly higher GTR rate achieved with the combined modality (5-ALA + ioUS). This finding aligns with and extends the work of Pepa et al. [12], whose retrospective analysis of 230 patients with GBM demonstrated that the combination of 5-ALA and ioUS yielded the highest EOR compared with either technique alone or conventional surgery. Similarly, Aibar-Durán et al. [13] reported enhanced diagnostic accuracy for HGG resection when combining these tools. Our results support the complementary value of integrating 5-ALA fluorescence and ioUS in HGG surgery. Crucially, the benefit of the combined technique on the GTR rate was consistent across the major histopathological subtypes (glioblastoma, anaplastic astrocytoma, and anaplastic oligodendroglioma), as detailed in our subgroup analysis. The observed improvements in GTR and functional recovery are likely related to the combined advantages of both modalities: 5-ALA enables direct microscopic visualisation of viable tumour cells through porphyrin

metabolism [6,16,17], whereas ioUS provides real-time, deep-seated structural guidance, compensates for brain shift and assists in detecting subcortical residual tumour not visible under the microscope [9,10]. Although our findings suggest potential cooperation between these two techniques, the independent contribution of ioUS cannot be excluded.

Previous studies have shown that GTR is a major factor contributing to improved OS and PFS in patients with gliomas [18,19]. In the current study, a considerably lower 6-month recurrence rate was observed in the 5-ALA + ioUS group compared with the control group. This finding reinforces the direct clinical benefit of achieving higher GTR rates in the 5-ALA + ioUS group. However, longer-term follow-up is needed to determine whether the observed advantage in recurrence rate at 6 months translates into substantial improvements in OS.

Beyond improving resection completeness, our study also reveals a major functional advantage associated with the 5-ALA + ioUS approach. Patients in the 5-ALA + ioUS group exhibited substantially better functional recovery than those in the control group, as evidenced by considerably higher KPS scores at both 1 and 6 months postoperatively. Crucially, the improvement in KPS scores from baseline to 6 months was also markedly greater in the 5-ALA + ioUS group than in the control group. The KPS is a well-validated prognostic indicator in neuro-oncology, with higher scores correlating strongly with better survival and quality of life [16,20]. The superior functional recovery observed likely stems from two key factors inherent to the combined technique: first, the enhanced visualisation provided by 5-ALA and ioUS allows for more precise dissection along tumour–brain interfaces, potentially minimising unnecessary damage to eloquent functional pathways adjacent to the tumour; second, the ability to confidently identify residual tumour using both modalities may reduce the need for

exploratory dissection in critical areas, thereby preserving neurological function. Although previous studies focused primarily on the effects of 5-ALA and ioUS on EOR and survival [12,13], our results provide evidence that the 5-ALA + ioUS combination also translates into tangible benefits for patients' functional status and recovery trajectory.

Our findings also demonstrate notable improvements in surgical efficiency and resource utilisation. Both intraoperative blood loss and operation time were considerably lower in the 5-ALA + ioUS group than in the control group. This improvement is likely attributable to the enhanced tumour visualisation provided by the combined use of 5-ALA fluorescence and ioUS, which allows surgeons to rapidly and accurately delineate tumour boundaries and distinguish tumour tissues from normal brain tissues. As a result, less time is spent identifying tumour margins or managing unexpected bleeding from unclear anatomy, contributing to more efficient and safer resections [21]. Furthermore, the considerably short hospital stay in the 5-ALA + ioUS group compared with the control group represents a substantial clinical and economic benefit. The most common complication, intracranial infection, occurred slightly less frequently in the 5-ALA + ioUS group than in the control group (4/65 vs 6/59), though this difference was not statistically significant. Critically, the achievement of higher GTR rates without a corresponding increase in complications underscores the safety profile of the combined approach when performed by experienced teams.

The GTR rate was primarily influenced by tumour location relative to eloquent brain areas rather than tumour volume. Tumours involving motor, language or other functionally critical regions often cannot be completely resected in order to preserve neurological function. High-grade gliomas frequently involve eloquent brain regions such as motor or language areas, and

their boundaries with normal brain tissue are indistinct [22]. Tumour cells may infiltrate along white matter tracts or perivascular spaces, making it difficult to achieve total resection without risking considerable neurological deficits, including hemiplegia or aphasia. Therefore, incomplete resection is an inherent limitation in glioma surgery, reflecting the balance between maximising tumour removal and preserving neurological function. This characteristic underscores the clinical challenge of achieving GTR even with advanced intraoperative guidance techniques.

The present study has several limitations. First, the retrospective single-centre design and the heterogeneous histology of the cohort may restrict the statistical power and hinder the drawing of strong conclusions, limiting the generalisability of the findings. Although our subgroup analysis suggested a consistent benefit across subtypes, the sample size for individual non-GBM subtypes remained modest, preventing definitive conclusions for each specific histology. Second, the follow-up period was limited to 6 months for recurrence and functional outcomes. Longer-term follow-up is essential to determine whether the observed advantages in recurrence rate at 6 months could translate into considerable improvements in OS and long-term functional status. Third, our study did not specifically analyse non-enhancing HGGs, as false-negative 5-ALA responses may occur in non-enhancing lesions. Finally, while the inclusion of various HGG subtypes enhances the generalizability of our findings to the real-world clinical spectrum of HGGs, it also introduces histological heterogeneity as a potential confounding factor. Future prospective randomised studies with larger, and ideally histologically stratified, cohorts are warranted to validate our findings.

Conclusion

In conclusion, within the limitations of this retrospective study, our results suggest that the combined intraoperative use of 5-ALA fluorescence and ioUS may improve the surgical management of HGGs by potentially increasing GTR rates, reducing early tumour recurrence and enhancing postoperative functional recovery. However, the independent contributions of 5-ALA and ioUS cannot be distinguished in this study, and a prospective randomised trial comparing 5-ALA + ioUS with 5-ALA alone, ioUS alone, and surgery alone is needed to validate these findings.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the declaration of Helsinki.This study was conducted with approval from the Ethics Committee of The First Medical Center of Chinese PLA General Hospital.

Competing Interest

The authors declare that they have no competing interests.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Consent for publication

The manuscript is not submitted for publication or consideration elsewhere.

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Figure legend

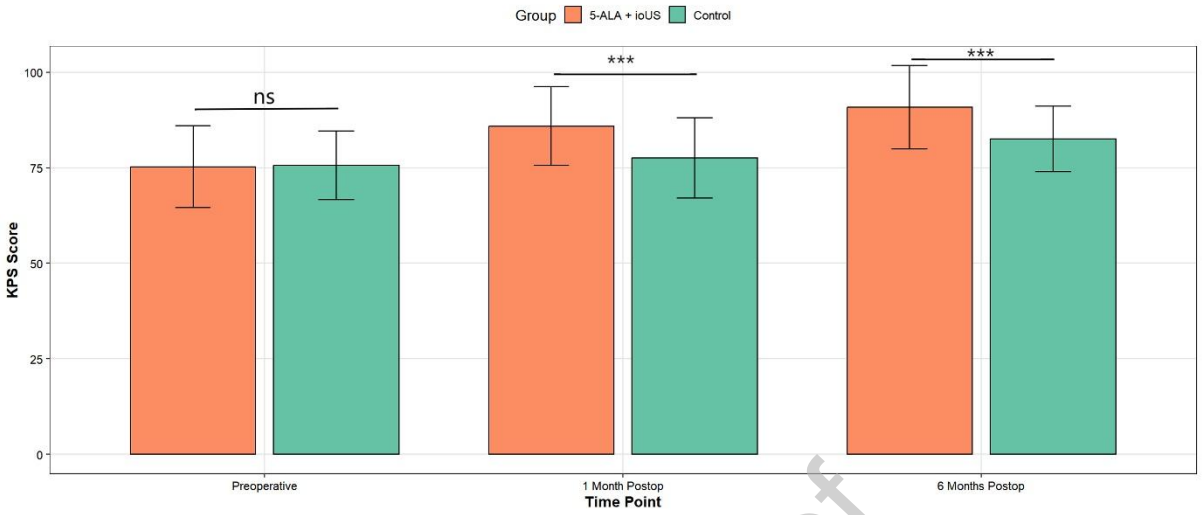

Figure 1. Comparison of Karnofsky Performance Status (KPS) scores between the Control group and the 5-ALA + ioUS group at three time points: preoperative, 1 month postoperative, and 6 months postoperative. Data are presented as mean ± standard deviation. ***P < 0.001, ns, not significant. Error bars represent standard deviations. Statistical significance was determined by appropriate tests comparing the two groups at each time point.

Table 1 Baseline characteristics in patients from both groups

Characteristics	Control group (n=106)	5-ALA + ioUS group (n=122)	P values
Age, years, mean ± SD	54.89 ± 12.10	53.12 ± 12.85	0.281
Gender, n (%)			0.452
Males	71 (66.98)	74 (60.66)	
Females	35 (33.02)	48 (39.34)	
Weight, kg, mean ± SD	61.5 ± 7.2	62.8 ± 8.1	0.185
Preoperative KPS score, mean ± SD	75.66 ± 9.01	75.25 ± 10.73	0.754
Disease duration, month, mean ± SD	5.18 ± 1.59	5.24 ± 1.61	0.776
Tumor in eloquent area, n (%)	48 (45.28)	59 (48.36)	0.698
Tumor side, n (%)			0.538
Left	50 (47.17)	54 (44.26)	
Right	54 (50.94)	64 (52.46)	
Both	2 (1.89)	4 (3.28)	
Tumor location, n (%)			0.421
Frontal	47 (44.34)	55 (45.08)	
Parietal	11 (10.38)	13 (10.66)	
Temporal	36 (33.96)	38 (31.15)	
Others	12 (11.32)	16 (13.11)	
Pathological type, n (%)			0.901
Anaplastic astrocytoma	20 (18.87)	24 (19.67)	
Anaplastic oligodendroglioma	25 (23.58)	31 (25.41)	
Glioblastoma	50 (47.17)	56 (45.90)	
Others	11 (10.38)	11 (9.02)	
WHO classification, n (%)			0.823
III	47 (44.34)	57 (46.72)	
IV	59 (55.66)	65 (53.28)	

Characteristics	Control group (n=106)	5-ALA + ioUS group (n=122)	P values
IDH 1/2 mutation, n (%)	8 (7.55)	11 (9.02)	0.812
Tumor biggest diameter, mm, mean ± SD (range)	56.62 ± 10.31 (31-90)	57.70 ± 10.79 (35-95)	0.442

Note: SD, standard deviation; IDH, isocitrate dehydrogenase. Eloquent areas were defined as regions involving motor, sensory, language, visual cortex, basal ganglia, or internal capsule, as determined by preoperative MRI and/or functional neuroimaging. Other tumor location included occipital lobe, thalamus, insula, and basal ganglia areas.

Table 2 Intraoperative and postoperative comparisons between 2 groups

Variables	Control group (n=106)	5-ALA + ioUS group (n=122)	P values
Hemorrhage volume, mL, mean ± SD	338.49 ± 76.58	255.90 ± 63.44	< 0.001
Duration of operation, h, mean ± SD	3.42 ± 0.64	2.58 ± 0.57	< 0.001
Hospital stays, d, mean ± SD	20.42 ± 5.70	14.78 ± 2.99	< 0.001
Postoperative complication, n (%)	18 (16.98)	12 (9.84)	0.104
Gross total resection, n (%)	79 (74.53)	111 (90.98)	< 0.001
Tumor recurrence, n (%)			
3-month recurrence	13 (12.26)	5 (4.10)	0.027
6-month recurrence	25 (23.58)	11 (9.02)	0.002

Note: SD, standard deviation

Table 3 Subgroup analysis of gross total resection rates by histopathological subtype

Pathological Subtype	Group	n	Gross Total Resection, n (%)	P value
Glioblastoma (GBM)	Control	28	19 (67.86%)	0.021
	5-ALA + ioUS	30	26 (89.29%)	
Anaplastic Astrocytoma (AA)	Control	11	8 (72.73%)	0.332
	5-ALA + ioUS	13	12 (92.31%)	
Anaplastic Oligodendroglioma (AO)	Control	14	11 (78.57%)	0.325
	5-ALA + ioUS	17	16 (94.12%)	
Other subtypes	Control	6	5 (83.33%)	1.000*
	5-ALA + ioUS	5	4 (80.00%)	

Note: GTR, gross total resection. P value calculated using Fisher's exact test due to small sample size.

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the declaration of Helsinki.This study was conducted with approval from the Ethics Committee of The First Medical Center of Chinese PLA General Hospital.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval

of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Competing Interest

The authors declare that they have no competing interests.