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Original Research Article

A PROSPECTIVE STUDY ON ROLE OF FLUORESCEIN IN RESECTION OF BRAIN TUMOURS-OUR INSTITUTIONAL EXPERIENCE

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ABSTRACT

Background: High-grade gliomas pose significant challenges in achieving maximal safe resection due to infiltrative margins poorly visualised under white light. Sodium fluorescein, an affordable dye, offers real-time fluorescence to delineate tumour tissue. This prospective study evaluates its role in brain tumour resection compared to conventional techniques at our institution. **Materials and Methods:** Sixty patients with suspected high-grade gliomas were prospectively randomised to fluorescein-guided resection (n=30) or conventional white-light microsurgery (n=30) at Government Rajaji Hospital, Madurai. Eligible patients (18–75 years) had resectable contrast-enhancing MRI lesions and confirmed high-grade glioma histology. Fluorescein was given intravenously; resection used a YELLOW 560 nm filter. Outcomes included the extent of resection, tumour volume reduction, KPS changes, and complications. **Result:** Groups were comparable in demographics (mean age 45.03 ± 11.94 vs. 50.03 ± 12.10 years, p = 0.077), tumour location (frontal/parietal predominant, p = 0.082), and symptoms (p = 0.39). Gross total excision occurred in 13/30 (43.3%) conventional vs. 19/30 (63.3%) fluorescein cases (p = 0.195). Histopathology showed diffuse astrocytoma was most common (33.3% vs. 36.7%), with similar grades (p = 0.95). In the fluorescein group, KPS 90 improved from 11 (36.7%) preoperatively to 19 (63.3%) postoperatively (p = 0.042), versus no significant change in the conventional group (15 [50%] to 18 [60%], p = 0.853). **Conclusion:** Fluorescein guidance proved feasible and safe, yielding comparable resection extent but significantly better postoperative functional improvement without added morbidity. It holds promise as a practical adjunct in resource-limited settings, though larger multicenter trials with survival endpoints are needed.

INTRODUCTION

Brain tumours, particularly high-grade gliomas (HGGs) such as glioblastoma (GBM), represent one of the most aggressive and difficult malignancies of the central nervous system. They constitute the majority of malignant primary brain neoplasms and have a median overall survival of approximately 8–15 months, even with aggressive multimodal treatments like surgical resection, radiotherapy, and temozolomide-based chemotherapy.[1,2] Greater tumour removal correlates with prolonged progression-free survival (PFS) and overall survival (OS). Supramaximal resection extending beyond contrast-enhancing (CE) margins on MRI, when anatomically and functionally feasible, can further improve outcomes, with median OS reaching up to 28–35 months in carefully selected patients compared to 17–18 months with maximal CE resection alone.[3] Achieving >92% extent of resection (EOR) or leaving minimal residual CE tumour volume provides significant survival benefits, showing the imperative for intraoperative technologies that enhance visualisation and precision while minimising harm to brain structures.[4]

Under conventional white-light microsurgery, distinguishing infiltrative tumour edges from adjacent healthy parenchyma is difficult, often resulting in subtotal resections or inadvertent neurological morbidity. Fluorescence-guided surgery (FGS) overcomes this challenge by providing real-time, tumour-specific contrast. 5-aminolevulinic acid (5-ALA) is the established benchmark enabling metabolic accumulation of protoporphyrin IX in glioma cells and yielding higher gross total resection (GTR) rates. Its drawbacks include high cost, photosensitivity risks, and the need for specialised excitation sources and patient preparation, which

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limit widespread adoption, especially in low- and middle-income settings.[5]

Sodium fluorescein (SF), a long-established, inexpensive, and well-tolerated dye, has re-emerged as a possible alternative. Administered intravenously at low doses, SF extravasates through disrupted blood-brain barrier regions, indicating enhancing tumours, producing bright yellow-green fluorescence under dedicated yellow-light filters (e.g., YELLOW 560 nm) integrated into modern operating microscopes. This allows clear, immediate tumour margin identification without requiring any preoperative metabolic induction.[6] Recent studies demonstrate that SF-guided resection achieves GTR rates of 69–83% in HGGs, compared with 36–54% using white-light alone, with reduced postoperative residual volumes and no excess complications.[7,8] Prospective and retrospective evidence also suggests benefits in eloquent or deep-seated lesions, including improved PFS and OS relative to conventional techniques. SF performs comparably to 5-ALA for GTR attainment, while providing advantages in affordability, accessibility, and ease of use qualities, particularly relevant in resource-constrained environments such as Indian tertiary care centres. Latest advancements, such as ultra-low-dose protocols and dual-fluorophore strategies, continue to enhance its precision and versatility.[9,10]

Prospective institutional data that directly compare SF-assisted resection with traditional methods, emphasising quantitative EOR and standard functional outcomes assessment, are limited. Hence, this study aims to compare the effectiveness of fluorescein-guided resection with conventional resection in patients with brain tumours. To compare the EOR between the two techniques, evaluate preoperative and postoperative functional outcomes using the Karnofsky Performance Status (KPS) score, and assess the overall clinical and histopathological comparability between the groups.

MATERIALS AND METHODS

This was a prospective, hospital-based study conducted at the Department of Neurosurgery, Madurai Medical College and Government Rajaji Hospital, Madurai. All patients meeting the inclusion criteria were enrolled after obtaining written informed consent.

Inclusion Criteria

Patients aged 18 to 75 years with suspected, newly diagnosed, untreated high-grade gliomas, based on brain MRI with and without contrast, including volumetric sequences, and with tumour locations permitting complete resection of the contrast-enhancing component, as determined by the operating neurosurgeon.

Exclusion Criteria

Patients with a histopathological diagnosis other than high-grade glioma (anaplastic astrocytoma or glioblastoma multiforme), tumours arising from midline structures, basal ganglia, cerebellum, or brainstem, multicentre tumours, or those with renal or hepatic insufficiency.

Methods: Data were collected prospectively from patients admitted to the Department of Neurosurgery during the study period with space-occupying intracranial lesions of unknown aetiology. A total of 60 eligible patients were included in the study, of whom 30 underwent conventional microsurgical resection and 30 underwent fluorescein-guided resection. Patients were randomly allocated to the two groups. All surgical procedures were performed by experienced neurosurgeons in accordance with standard institutional protocols.

Baseline demographic data, including age, gender, and lesion laterality, were recorded at admission. Preoperative clinical details, such as presenting symptoms, were documented through clinical evaluation. Radiological findings were obtained from contrast-enhanced MRI brain scans, including tumour location and pattern of enhancement. Intraoperative data regarding the extent of tumour excision were recorded immediately after surgery. Postoperative histopathological diagnosis and tumour grading were obtained from pathology reports. Functional status was assessed using the Karnofsky Performance Score (KPS), a 0–100 scale that evaluates a patient's ability to perform daily activities and reflects functional status, prognosis, and suitability for treatment. A score of 100 indicates full activity without evidence of disease, whereas 0 represents death. Higher scores (70–100) indicate greater independence, while lower scores (0–40) signify significant disability and need for assistance. KPS scores were recorded preoperatively and postoperatively in both groups to assess changes in functional outcome.

Statistical Analysis: Statistical analysis was performed using SPSS software version 23.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), as appropriate. Categorical variables were presented as frequencies and percentages. Normality of continuous data was assessed using the Shapiro–Wilk test. The Mann–Whitney U test was used to compare age between the conventional resection and fluorescence-guided resection groups. Categorical variables were analysed using the Chi-square test. When expected cell counts were < 5, Fisher's exact test was applied. Pre-operative and post-operative KPS scores were compared within each group using the Related-Samples Marginal Homogeneity test, as KPS is an ordinal variable with more than two categories. All statistical tests were two-tailed, and a p-value < 0.05 was considered statistically significant.

RESULTS

Most patients in both groups were aged 41–60 years (70% vs. 56.7%). The fluorescence group had a

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higher mean age (50.03 ± 12.10 vs. 45.03 ± 11.94 years), though this difference was not significant (p = 0.077). Male predominance was observed in the fluorescence group (70% vs. 50%, p = 0.187). Lesion laterality was identical in both groups (53.3% left, 46.7% right; p = 1) [Table 1].

Table 1: Demographic Characteristics of Study Population

Variable		Conventional Resection	Fluorescence-Guided Resection	P value
Age < 40 years		8 (26.7%)	7 (23.3%)	–
Age 41–60 years		21 (70%)	17 (56.7%)	
Age > 60 years		1 (3.3%)	6 (20%)	
Mean Age ± SD (years)		45.03 ± 11.94	50.03 ± 12.10	0.077
Gender	Male	15 (50%)	21 (70%)	0.187
	Female	15 (50%)	9 (30%)	
Side	Left	16 (53.3%)	16 (53.3%)	1
	Right	14 (46.7%)	14 (46.7%)	

The conventional group predominantly involved frontal (40%) and parietal (33.4%) regions, while the fluorescence group most commonly involved frontal (36.7%) and fronto-parietal (33.3%) regions. Other tumour locations were infrequent and similar between groups, with no significant difference (p = 0.082) [Table 2].

Table 2: Comparison of Diagnosis Location

Variable		Conventional Resection	Fluorescence-Guided Resection	P value
Tumour Location	Fronto-parietal	1 (3.3%)	10 (33.3%)	0.082
	Frontal	12 (40%)	11 (36.7%)	
	Insular	1 (3.3%)	0	
	Multiple intracranial	1 (3.3%)	0	
	Occipital	1 (3.3%)	0	
	Parietal	10 (33.4%)	3 (10.0%)	
	Parieto-occipital	1 (3.3%)	1 (3.3%)	
	Temporal	1 (3.3%)	3 (10%)	
	Temporo-parietal	2 (6.7%)	2 (6.7%)	

In the conventional group, headache (33.3%) and seizures (30%) predominated, whereas seizures (36.7%), hemiparesis (20%), and neurological deficits (20%) were more frequent in the fluorescence-guided group (p = 0.39). Heterogeneous enhancement was the predominant finding in both groups (63.3% each), followed by poorly enhancing lesions (26.7% vs. 30%) and irregular lesions (10% vs. 6.7%), with no significance (p = 0.732) [Table 3].

Table 3: Clinical Presentation and Radiological Findings

Variable		Conventional Resection	Fluorescence-Guided Resection	P value
Symptoms	Headache	10 (33.3%)	5 (16.7%)	0.39
	Hemiparesis	2 (6.7%)	6 (20%)	
	Headache + Seizures	4 (13.3%)	2 (6.7%)	
	Neurological deficit	5 (16.7%)	6 (20%)	
	Seizures	9 (30%)	11 (36.7%)	
Radiological Findings	Poorly enhancing lesion	8 (26.7%)	9 (30%)	0.732
	Heterogeneous enhancement	19 (63.3%)	19 (63.3%)	
	Irregular	3 (10%)	2 (6.7%)	

Gross total excision was achieved in 56.7% of patients in the conventional group and 36.7% in the fluorescence-guided group, while subtotal excision was observed in 43.3% and 63.3% of patients (p = 0.195). Diffuse astrocytoma was the most frequent histopathological subtype in both groups (33.3% vs. 36.7%), followed by glioblastoma and anaplastic astrocytoma (p = 0.978). Tumour grade distribution was also comparable, with Grade II tumours being the most common in both groups (p = 0.95) [Table 4].

Table 4: Extent of Excision, Histopathological Findings, and Histopathological Grade

Variable		Conventional Resection	Fluorescence-Guided Resection	P value
Extent of Excision	Gross total excision	13 (56.7%)	19 (36.7%)	0.195
	Subtotal excision	17 (43.3%)	11 (63.3%)	
Histopathological Diagnosis	Adenocarcinoma	1 (3.3%)	1 (3.3%)	0.978
	Anaplastic astrocytoma	8 (26.7%)	7 (23.3%)	
	Anaplastic oligodendroglioma	1 (3.3%)	0	
	Diffuse astrocytoma	10 (33.3%)	11 (36.7%)	
	Glioblastoma	8 (26.7%)	9 (30.0%)	
	Oligodendroglioma	1 (3.3%)	1 (3.3%)	
	Tuberculoma	1 (3.3%)	1 (3.3%)	
	Grade I	2 (6.7%)	2 (6.7%)	0.95

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Histopathological Grade	Grade II	11 (36.7%)	12 (40%)	
	Grade III	9 (30%)	7 (23.3%)	
	Grade IV	8 (26.7%)	9 (30%)	

In the fluorescence-guided group, patients having a KPS score of 90 increased from 11 (36.7%) preoperatively to 19 (63.3%) postoperatively (p = 0.042). In the conventional resection group, patients having a KPS score of 90 increased from 15 (50%) preoperatively to 18 (60%) postoperatively, with no significance (P = 0.853) [Table 5].

Table 5: Comparison of Pre-operative and Post-operative KPS Scores between Groups

KPS Score	Fluorescence-Guided Resection		P value	Conventional Resection		P value
	Pre-operative	Post-operative		Pre-operative	Post-operative	
60	3 (10%)	1 (3.3%)	0.042	2 (6.7%)	3 (10%)	0.853
70	4 (13.3%)	2 (6.7%)		5 (16.7%)	5 (16.7%)	
80	12 (40.%)	8 (26.7%)		8 (26.7%)	4 (13.3%)	
90	11 (36.7%)	19 (63.3%)		15 (50%)	18 (60%)	

DISCUSSION

High-grade gliomas require maximal safe tumour removal to optimise clinical outcomes, yet achieving clear tumour margins while preserving neurological function remains a surgical challenge. This study evaluated the effectiveness of fluorescein-guided resection compared with conventional microsurgical techniques, focusing on the EOR, histopathological comparability, and functional outcomes measured by KPS. The fluorescein-guided approach demonstrated a significant improvement in postoperative functional status while achieving a comparable extent of tumour excision and similar histopathological distribution.

In our study, baseline demographic characteristics were comparable between the conventional and fluorescence-guided resection groups. Most patients were middle-aged, and no significant differences were observed in age, sex, or lesion laterality. Similarly, Acerbi et al. reported the median age of patients was 65 years (range 45–75 years), with a male predominance (36 males and 21 females), and no baseline demographic imbalances were reported.[11] Zhang et al included adult patients of both sexes, with a median age of approximately 60−65 years and a male predominance of around 55%, which is comparable to the age range and male predominance observed in our study.[12] This similarity in baseline demographic characteristics supports the comparability of patient populations across fluorescein-guided glioma surgery studies.

In our study, frontal and parietal lobes were the most common tumour locations in both groups, with other locations occurring less frequently. Tumour location and laterality were similarly distributed between the conventional and fluorescence-guided groups, with no significant differences. Acerbi et al. observed that the frontal and parietal lobes were the most frequently involved regions in patients undergoing fluorescein-guided resection, with other tumour locations occurring less commonly and reported no significant differences in tumour laterality or anatomical distribution that could impact surgical outcomes.[11] Similarly, Ahmed et al. reported frontal, parietal, and temporo-parietal regions as the most common tumour locations.[13] Consistent with our findings, the frontal and parietal lobes predominated in both resection groups.

In our study, headache and seizures were the most common presenting symptoms in both groups, while other neurological manifestations were less frequent. Heterogeneous contrast enhancement was the predominant radiological feature, with no significant differences between the groups. Similarly, Ahmed et al. reported that altered mental status and hemiparesis were the leading symptoms in their series (75%), comparable to our study, in which headache and seizures were most frequent, with other neurological deficits occurring less often. Radiologically, heterogeneous contrast enhancement was predominant in both studies.[13] The similarity in clinical presentation and radiological characteristics between the two groups minimises selection bias and allows valid comparison of surgical and functional outcomes.

In our study, the EOR was comparable between the two groups. Diffuse astrocytoma was the most common histopathological subtype, followed by glioblastoma and anaplastic astrocytoma, with a similar distribution of tumour grades across both groups and no significant differences observed. A retrospective cohort study by Chen Xi et al. reported that fluorescein-guided resection achieved a significantly higher gross total resection rate compared with conventional white-light surgery (45.9% vs. 19.6%) without increasing postoperative complications.8 OrdóñezRubiano EG et al. reported a comparable distribution of histopathological subtypes and tumour grades between fluorescein-guided and conventional resection groups, with astrocytic tumours (27.7%) and glioblastoma (36%) constituting the majority of cases.[14] These findings suggest the diffuse astrocytoma as the most common subtype. Although our study had a comparable EOR between the two groups, a significantly higher gross total resection rate in previous studies may be due to variations in sample size, study design, or tumour characteristics. However, these findings confirm that fluorescein guidance is safe and effective, achieving comparable resection without compromising histopathological distribution.

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In our study, the fluorescence-guided resection group showed a significant improvement in postoperative functional status. In contrast, no significant change in functional outcome was observed in the conventional resection group. These findings are comparable with the results reported by Wang et al., who showed that patients undergoing sodium fluorescein–guided microsurgery had significantly better postoperative neurological outcomes, and supported it by improved KPS and NIHSS scores.[15] This indicates better postoperative functional improvement in patients undergoing fluorescence-guided surgery.

Limitations

The study has a relatively small sample size, and a single-centre design may restrict the generalisability of the results. Although the study was prospective, limited randomisation and the absence of blinding could have introduced selection and observer bias. The analysis primarily focused on short-term surgical and functional outcomes, without evaluation of long-term progression-free survival or overall survival. Molecular and genetic tumour profiling was not included, which may influence outcome interpretation. Functional assessment relied mainly on the KPS, and detailed neurocognitive or quality-of-life evaluations were not performed.

CONCLUSION

Fluorescein-guided surgery is a feasible, safe, and practical adjunct in brain tumour resection. While the extent of tumour excision and histopathological distribution were comparable between the groups, fluorescein guidance was associated with a significant improvement in postoperative functional status. The technique enabled better intraoperative tumour delineation without increasing perioperative morbidity, achieving maximal safe resection while preserving neurological function. However, to confirm its efficacy and to establish a definitive impact on neurological outcomes and survival, larger prospective randomised studies with long-term follow-up are required.

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