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Original Article

Surgery Section

Intra-axial Supratentorial Tumours Resection under Fluorescein Guidance with 560 nm Yellow Filter: A Cross-sectional Study

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ABSTRACT

Introduction: Excision of intra-axial tumours with maximal resection and minimal deficits is one of the intricate procedures in neurosurgery. Fluorescence-guided Surgery (FGS) helps in better identification of tumour tissue and allows Maximal Safe Resection (MSR) of high-grade brain tumours. Sodium fluorescein dye, when injected intravenously, gets concentrated in High-grade Glioma (HGG) tissue due to a disrupted Blood-Brain Barrier (BBB), thus aiding in MSR, Extent of Resection (EOR), and Gross Total Resection (GTR).

Aim: To assess the effectiveness of intraoperative use of sodium fluorescein in achieving MSR and GTR.

Materials and Methods: This was a cross-sectional study conducted on 30 patients with HGG who underwent surgery between January 2021 and May 2023 at SDM College of Medical Sciences, Dharwad, Karnataka, India. Two groups of 15 patients each were divided into those operated with the use of Fluorescein Sodium (FS) and those without FS. FS was administered at a dose of 5 mg/kg at the time of craniotomy. The primary endpoint was the number of patients with Histopathological Examination (HPE)-confirmed HGGs showing no contrast-enhancing tumour in the immediate postoperative Magnetic Resonance Imaging (MRI). Secondary endpoints included residual tumours on postoperative MRI, Focal Neurological Deficits (FND), and FS-related toxicity. The association between FS status and recurrence at different treatment time points was assessed using the Pearson Chi-square test. Recurrence rates were compared in each FS group using the Cochran Q test. Statistical significance was set at a 5% level (p-value <0.05).

Results: Homogeneous or heterogeneous yellow-green fluorescence was observed on the tumour tissue in all 15 patients (100%). Of the 15 patients where FS was used, two showed lesion recurrences at six months, and 13 showed recurrences at 12 months. Among the 15 patients where FS was not used, 11 showed recurrences at six months, and four showed recurrences at 12 months. This indicates that MSR, GTR, and EOR can be improved using FS intraoperatively during tumour resection.

Conclusion: Based on the results, fluorescein dye with a 560 nm yellow filter under a highly illuminated microscope can help achieve better tumour resection with minimal injury to surrounding eloquent areas. It can be utilised as an ideal adjunct for tumour resection rather than with a microscope alone.

Keywords: Glioma, Gross total resection, Indocyanine green, Maximal safe resection, Sodium fluorescein

INTRODUCTION

For years, surgeons have been intrigued by the intraoperative labeling of brain tumours or vascular malformations. Improved MSR and GTR have been observed by using fluorescence intraoperative imaging techniques to detect tumours or vascular malformations at the time of surgery. Recently, fluorescence-guided tumour resection techniques have gained great interest as they enhance tumour tissue during excision [1]. HPE of the frozen section traditionally aids in intraoperative diagnosis to assess the tumour type with grade and monitor surrounding tissue for MSR and GTR, considered the gold standard. There are various agents available for intraoperative fluorescence, with the most commonly used ones being 5-ALA (5-Aminolevulinic acid), FS, and ICG (Indocyanine green) [2]. It is important to note that the cost of FS is lower compared to 5-ALA and ICG, which is significant for populations with lower socio-economic status, while yielding similar results and outcomes [1]. 5-ALA , a precursor of haemoglobin that stimulates porphyrin production in tumour cells, significantly increases the EOR leading to improved Progression-Free Survival (PFS) at six months [3-7]. Limiting factors for the widespread use of 5-ALA include the need for oral administration of the drug 2.5 to 3.5 hours before anaesthesia induction, the requirement to avoid direct patient exposure to sunlight or strong room light for 24 hours post-administration due to the risk of skin sensitisation, and the high cost of 5-ALA [1,2].

Sodium fluorescein (the sodium salt of fluorescein) is another fluorophore being used. In the wavelength range from 540 to 690 nm, this biomarker emits fluorescent radiation. FS is available as a water-soluble dye and is extensively used for ophthalmological procedures with minimal side-effects [8-11]. Sodium fluorescein becomes concentrated in cerebral areas where the BBB is disrupted. The invasiveness of tumourous lesions disrupts the continuity of the BBB, altering the permeability of blood vessels. This alteration allows fluorescein to concentrate specifically at the tumour site, enabling clearer delineation of the tumour tissue if a dedicated filter is present on the surgical microscope, potentially leading to increased MSR, EOR, and GTR rates [12].

It is also worth noting that fluorescein costs less than 5-ALA and can be easily administered via intravenous injection at the initiation of anaesthesia. Further support for FS use comes from ophthalmological surgeries, where its utilisation has been reported with few side-effects [8-11]. While studies are demonstrating the utility of FS in glioma excision, there is limited literature from smaller Indian cities lacking adequate infrastructure [13,14]. This study is significant as it was conducted in tier two cities where infrastructure availability and the feasibility of using FS are limited. Therefore, this study aimed to review the application of sodium fluorescein intraoperatively for intra-axial brain tumours and evaluate the effectiveness of intraoperative sodium fluorescein use in achieving MSR and GTR.

MATERIALS AND METHODS

This cross-sectional study was conducted at SDM College of Medical Sciences, Dharwad, Karnataka, India. The study period

planned was between January 2021 to May 2023. The retrospective analysis of the data was carried out after obtaining ethical committee clearance, which coincided with the end of the follow-up period for our last case in the study (3rd January 2024 to 5th February 2024). An ethical committee clearance certificate (SDMIEC/2023/575) was obtained for this study.

Inclusion criteria: Individuals with HGG confirmed by gadolinium-enhanced MRI, informed consent about the off-label use of FS, normal renal function tests, and no known allergy to FS were included in the study.

Exclusion criteria: Patients with deranged renal function tests, the paediatric population, extra-axial and infratentorial tumours, and vascular malformations were excluded from the study.

Sample size: The study population comprised patients who underwent surgery at the institute, with a sample size of 30. The patients were divided into two groups of 15 each: one group operated with the use of FS and the other group without FS.

Study Procedure

All patients underwent preoperative and postoperative contrast-enhanced MRI. Sodium fluorescein was intravenously injected at a dose of 5 mg/kg at the beginning of the craniotomy to observe fluorescence in the tumour tissue [15]. The tumour was excised with the assistance of FS-induced fluorescence, observed through a separate filter on the operating microscope (KINEVO 900 ZEISS). Parameters such as MSR, EOR, and GTR are directly linked to the outcome, particularly recurrence-free survival. EOR and GTR were evaluated based on complete excision of tumour margins displaying fluorescence and postoperative MRI indicating no residual tumour [13,16,17]. MSR was assessed by complete tumour excision with minimal or no postoperative FND. Data were retrieved from the medical records register within the department.

STATISTICAL ANALYSIS

The collected data were analysed using IBM Statistical Package for Social Sciences (SPSS) statistical software version 23.0. Descriptive statistics, including frequency and percentages, were calculated for categorical variables. The association between the status of FS and recurrence status at different treatment time points was assessed using the Pearson Chi-square test. The recurrence rate was compared in each FS group using the Cochran Q test. Statistical significance was set at a 5% level ($p<0.05$).

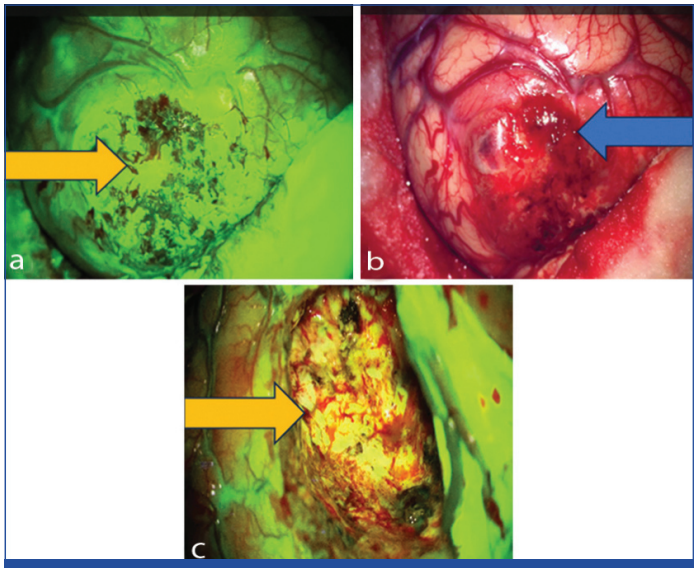
RESULTS

This study included 30 patients who underwent surgery for high-grade supratentorial gliomas. Out of the 30 patients, 15 underwent glioma excision with FS guidance, while the remaining 15 did not use FS but were operated under the microscope with high magnification. Both the FS-guided and non FS-guided groups were comparable in terms of sex, age (between 19-65 years), preoperative KPS (>70 was included) (Karnofsky performance scale) [18], and tumour location [Table/Fig-1] [18].

Parameters		Without FS	With FS
Gender	Male	10	10
	Female	5	5
Tumour location	Frontal	6	5
	Temporal	4	5
	Parietal	3	3
	Occipital	2	2

[Table/Fig-1]: Gender distribution and tumour location.

Approximately, half an hour after craniotomy, all tumours in the SF-guided group exhibited a uniform and moderate yellow fluorescence when viewed through the yellow 560 nm filter [Table/Fig-2]. The fluorescence was sensitive enough to detect the tumour border while preserving the cerebral cortex. There were no side-effects, allergic responses, or postoperative neurological impairments associated with the SF-guided surgery, and tumour fluorescence remained stable for an average of about 4 to 5 hours.



[Table/Fig-2]: Showing enhancement of the tumour area intraoperatively and tumour bed free of enhancement indicating GTR. Orange arrows are at the antero-medial aspect of the tumour and blue arrows are at the postero-lateral aspect of the tumour. a) Intraoperative image showing the tumour under a microscope with fluorescence; b) Intraoperative image showing the tumour under a microscope without fluorescence; c) Intraoperative image showing the excised tumour cavity under a microscope.

In both the FS-guided and non FS-guided groups, the early postoperative MRI did not show significant differences [Table/Fig-3,4]. At six months postsurgery, out of the 15 patients in the FS group, only two showed recurrence (13.33%), whereas in the non FS group, 11 patients (73.33%) showed recurrence [Table/Fig-3]. At

Recurrence at	Without FS, n (%)	With FS, n (%)	n (%)		Chi-square	p-value
Baseline (immediate postoperative)						
Yes	0	0	0		-	1.0000
No	15 (100)	15 (100)	30	(100)		
6 months						
Yes	11 (73.33)	2 (13.33)	13 (43.33)		10.9950	0.0010*
No	4 (26.67)	13 (86.67)	17 (56.67)			
12 months						
Yes	15 (100)	15 (100)	30 (100)		-	1.0000
No	0	0	0			
Total	15 (100)	15 (100)	30 (100)			

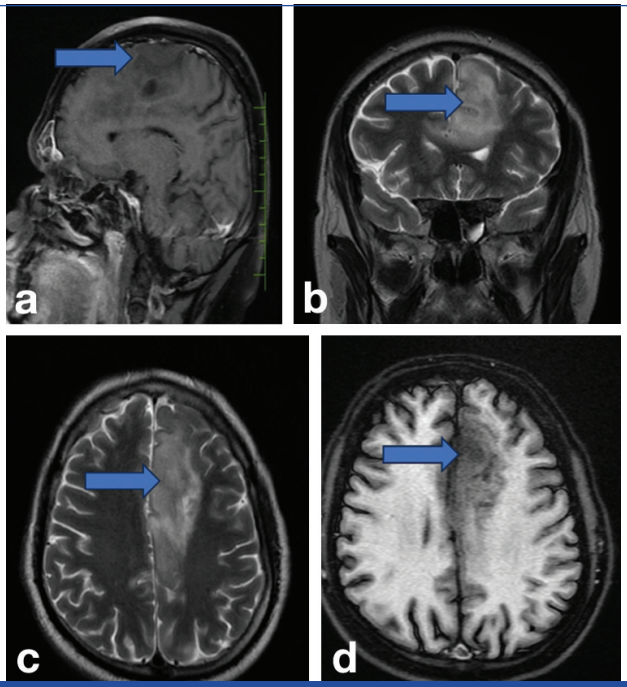
[Table/Fig-3]: Comparison of two groups (Without FS and with FS) with recurrence rates at different treatment times.
A statistical significance was set at a 5% level of significance ($p<0.05$) employing the Pearson chi-square test

Groups	Recurrence	Baseline n (%)	6 months n (%)	12 months n (%)	Cochran Q	p-value
Without FS	Yes	0	11 (73.33)	15 (100)	24.1333	0.0001*
	No	15 (100)	4 (26.67)	0		
With FS	Yes	0	2 (13.33)	15 (100)	26.5333	0.0001*
	No	15 (100)	13 (86.67)	0		

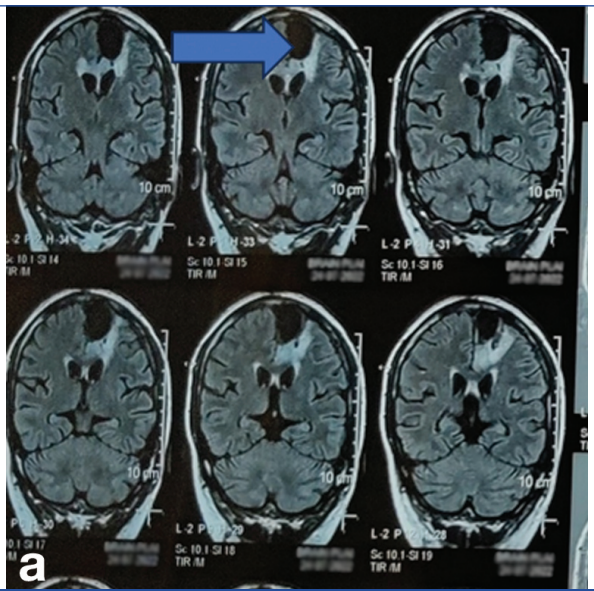
[Table/Fig-4]: Comparison of different treatment times with recurrence rate in two groups (Without FS and With FS).
A statistical significance was set at a 5% level of significance (p<0.05) employing the Cochran Q test

12 months of postsurgery follow-up scans, the recurrences were the same in both groups (100%).

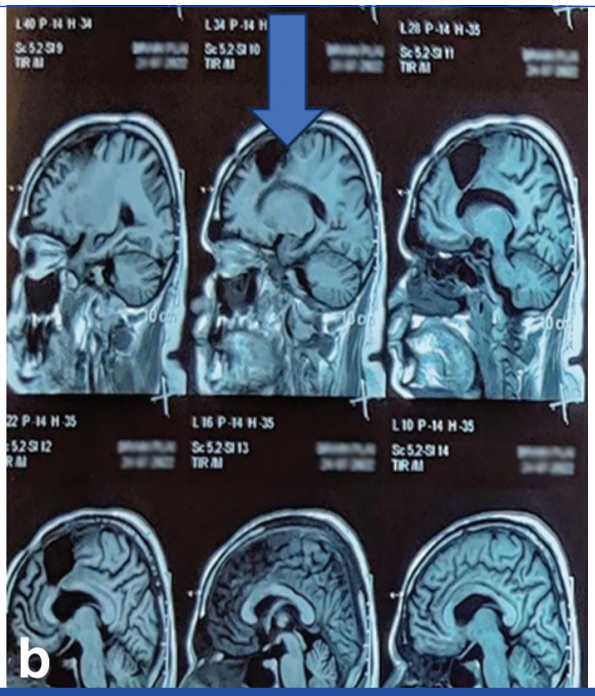
This suggests that utilising FS intraoperatively during tumour resection can improve MSR, EOR, and GTR. The MRI comparison pre- and postoperatively, as shown in [Table/Fig-5,6a-c], illustrates the GTR. Given the lower proportion of early recurrence in the FS group at six months, FS can be considered a safe alternative for excising gliomas, thereby enhancing the quality of life and Overall Survival (OS) of patients.



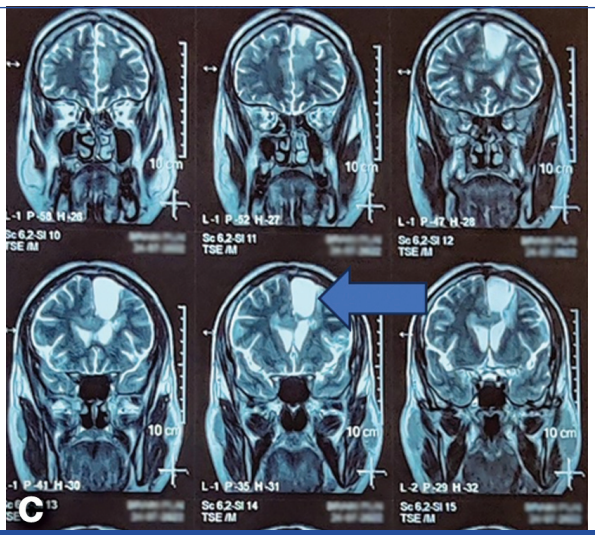
[Table/Fig-5]: Preoperative MRI images showing left frontal lesion depicted by an arrow mark. a) T1W sagittal image showing the tumour in left frontal region; b) T2W coronal image showing tumour in the left frontal region; c) T2W axial image showing tumour in the left frontal region; d) T1W axial image showing the tumour in the left frontal region.



[Table/Fig-6a]: Postoperative MRI showing GTR of the lesion depicted by an arrow mark. a) T1W coronal image showing the excised tumour cavity.



[Table/Fig-6b]: T1W sagittal image showing excised tumour cavity.



[Table/Fig-6c]: T2W coronal image showing excised tumour cavity.

DISCUSSION

The results of this study demonstrate that the resection of gliomas can be enhanced with the use of FS. The outcomes were better in the group where FS was utilised, as evidenced by a smaller number of recurrences at six months postoperation, thereby extending the lives of patients with HGGs post-excision compared to those where FS was not used. This indicates that using FS leads to improved outcomes at a lower cost compared to ALA in terms of PFS, GTR, and potentially MSR.

In many cases, tumour removal relies solely on tactile differentiation and visual signals to guide the resection of various ICSOLs. Technical advancements aim to bridge this gap. Tools to aid MSR include a microscope, intraoperative MRI, USG, and neuro-navigation. FGS has evolved alongside these tools, with FS gaining interest among

neurosurgeons. In most ICSOLs, such as HGGs, metastases, and haemangioblastomas, FS has been shown to assist in tumour excision [15,19-24]. While FS fluorescence can be observed without a microscope at high doses, the use of a particular filter helps reduce the dose and decrease the incidence of dose-related complications [25].

Shinoda J et al., resented the first retrospective study of 32 patients treated with fluorescein but without a filter designed for surgical microscopes [13]. Observations on postoperative MRI indicated a GTR of nearly 85%. This result was better than the 30% observed by the authors in a control group where surgery was performed without fluorescein. However, no statistically significant difference in survival could be found between these groups. These findings were consistent with the present study.

Similar results were reported by Koc K et al., who described the results of a prospective analysis on two non randomised groups. One group operated with the assistance of fluorescein (20 mL/kg at the time of dural opening) without a specific filter on the microscope (group 1), and the other group without fluorescein administration (group 2) [14]. In groups 1 and 2, the percentage of GTR based on MRI following surgery was 83% and 55%, respectively. Kuroiwa T et al., were the first to explain an approach in which a fluorescence filter was incorporated into the microscope (Zeiss OPMI) [26]. Ten patients were included in this study, where in eight cases, tumour removal was complete. The same group studied a larger number of 30 patients using a similar technique and compared the intraoperative findings with histological analysis in five cases [27].

Areas that were fluorescein-negative displayed minimal tumour cell invasion and no vessel abnormality, while fluorescein-positive areas showed abnormal tumour vasculature and numerous tumour cells. The study outcomes were correlated with this study. A study that utilised a yellow 560 filter for the excision of MG surgery was published. Among the 30 cases treated by fluorescein-aided surgery, cases of wide infiltration in the basal ganglia or brainstem tumours were not included. In the remaining 25 cases, fluorescent regions were completely resected, and enhanced regions disappeared on postoperative CT and MRI. No instances of aggravation were found with this treatment [27].

In a study by Schebesch KM et al., the authors found that 26 patients had gliomas (1 WHO grade I, 3 WHO grade II, 5 WHO grade III, 17 WHO grade IV), five patients had cerebral metastases, two had non malignant astrogliosis, and two had post-radiation necrosis. The fluorescence signal was detected in all patients immediately after the FL administration. The FL application was classified as 'helpful' in 28 patients, implying improved visualisation of the tumour margins. The intensity of the fluorescence signal seemed to be correlated with the histology and was strongly dependent on the pretreatment status. No allergic reactions or other adverse effects were recorded [20].

A study conducted by Ott C et al., on paediatric posterior fossa lesions using sodium fluorescein between 2018-2022 included 19 cases. Originally intended to perform a total resection in 14 patients, one gross complete resection (78.6%) was possible in 11 of these patients. Most instances (58.8%) had staining that was deemed severe. Throughout the surveillance period, no outwardly FL-related side-effects other than yellow-coloured urine were discovered [28].

A retrospective study of 33 paediatric cases with supratentorial lesions, conducted by Falco J et al., revealed that fluorescence was rated as intense in 17 out of 33 (51.5%) patients, moderate in 14 out of 33 (42.4%), and slight in two out of 33 (6.1%) procedures. Intraoperative fluorescence was consistent with preoperative contrast enhancement as reported by MRI. SF was deemed helpful in 28 out of 33 (84.8%) surgeries, partially helpful in two out of 33 (6.1%), and not necessary in three out of 33 (9.1%) procedures since the lesion were already identifiable. No negative impact of SF administration was noted [29]. These findings correlate with this study. Similar studies from the literature have been tabulated in [Table/Fig-7] [13,14,16,17,20,26,28-30].

S. No.	Author's name	Publication year	Place of study	Sample size	Groups compared	Parameters assessed	Conclusion
1	Shinoda J et al., [13]	2003	Gifu, Japan	32	FS and Non FS	GTR	Observations on postoperative MRI showed GTR to be nearly 85%. They were better than the result of 30% observed by the authors in a control group.
2	Koc K et al., [14]	2008	Kocaeli, Turkey	80	FS and Non FS	GTR	Use of fluorescein injection is a simple procedure, which allows a significant increase in the number of patients having GTR (83 vs. 55%).
3	Kuroiwa T et al., [26]	1998	Takatsuki, Japan	30	FS only	Intensity of fluorescence and histo-pathological findings	In conclusion, this fluorescein surgical microscope appears to be an apparatus that contributes grealy to cytoreductive surgery for malignant glioma.
4	Schebesch KM et al., [20]	2013	Regensburg, Germany	35	FS and Non FS	EOR	Use of FL for the resection of brain tumours is safe and feasible.
5	Ott C et al., [28]	2023	Regensburg, Germany	19	FS only	Intensity of fluorescence	In combination with a specific filter, FL is a reliable, safe, and feasible tool in posterior fossa surgery in children.
6	Falco J et al., [29]	2023	Milan, Italy	33	FS only	Intensity of fluorescence	FS deemed helpful and no negative impact on FS administration.
7	Kerschbaume J et al., [30]	2023	Innsbruk, Austria	79	FS and Non FS	GTR, Overall Survival (OS)	FS use significantly reduced the post op residual tumour.
8	Cheng X et al., [16]	2023	Chongquing, China	52	FS and Non FS	EOR	Use of FS was promising.
9	Zhang N et al., [17]	2017	Qingdao, China	35	FS only	EOR	Use of FS is better.
10	Present study	2024	SDM, Dharwad India	30	FS and Non FS	MSR, GTR and EOR	Use of FS is better and safe.

[Table/Fig-7]: Similar studies from the literature.
FS: Fluorescein sodium; GTR: Gross total resection; MRI: Magnetic resonance imaging; EOR: Extent of resection; MSR: Maximal safe resection

Limitation(s)

The study had limitations, including a small sample size, a retrospective study design, and a short follow-up duration.

CONCLUSION(S)

The application and use of fluorescein have been explored in present study. Recent data suggest that a safe, effective, and easy technique for achieving higher rates of GTR, MSR, and EOR is through FGS. The recurrence rate at six months was significantly better in the FS group than in the non FS group. Prolonging the life of the patient by six months or more in HGG is good enough evidence. However, further studies are needed to validate the long-term results.

REFERENCES

[1] Acerbi F, Cavallo C, Broggi M, Cordella R, Anghileri E, Eoli M, et al. Fluorescein-guided surgery for malignant gliomas: A review. Neurosurg Rev. 2014;37(4):547-57.
[2] Tonn JC, Stummer W. Fluorescence-guided resection of malignant gliomas using 5-aminolevulinic acid: Practical use, risks, and pitfalls. Clin Neurosurg. 2008;55:20-26.
[3] Restelli F, Bonomo G, Monti E, Broggi G, Acerbi F, Broggi M. Safeness of sodium fluorescein administration in neurosurgery: Case-report of an erroneous very high-dose administration and review of the literature. Brain Spine. 2022;2(101703):101703.
[4] Stummer W, Pichlmeier U, Meinel T. Fluorescence guided surgery with 5-aminolevulinic acid for resection of malignant glioma: A randomised controlled multicentre phase III trial. Lancet Oncol. 2006;7(5):392-401.
[5] Valle D, Solis T, Gastearena I, De Eulate G, Echávarri D, Mendiroz A. Surgery guided by 5- amino-levulinic fluorescence in glioblastoma: Volumetric analysis of the extent of resection in a single-centre experience. J Neurooncol. 2011;102(1):105-13.
[6] Stummer W, Novotny A, Stepp H, Goetz C, Bise K, Reulen HJ. Fluorescence-guided resection of glioblastoma multiforme by using 5-aminolevulinic acid-induced porphyrins: A prospective study in 52 consecutive patients. J Neurosurg. 2000;93(6):1003-13.
[7] Stummer W, Stocker S, Novotny A, Heimann A, Sauer O, Kempski O, et al. In vitro and in vivo porphyrin accumulation by C6 glioma cells after exposure to 5-aminolevulinic acid. J Photochem Photobiol B. 1998;45(2–3):160-69.
[8] Stummer W, Stocker S, Wagner S, Stepp H, Fritsch C, Goetz C, et al. Intraoperative detection of malignant gliomas by 5-aminolevulinic acid-induced porphyrin fluorescence. Neurosurgery. 1998;42(3):518-25; discussion 525-26.
[9] Kwan ASL, Barry C, McAllister IL, Constable I. Fluorescein angiography and adverse drug reactions revisited: The Lions Eye experience. Clin Experiment Ophthalmol. 2006;34(1):33-38.
[10] Kwiterovich KA, Maguire MG, Murphy RP, Schachat AP, Bressler NM, Bressler SB, et al. Frequency of adverse systemic reactions after fluorescein angiography. Results of a prospective study. Ophthalmology. 1991;98(7):1139-42.
[11] Novtny HR, Alvis DL. A method of photographing fluorescence in circulating blood in the human retina. Circulation. 1961;24:82-88.
[12] Yannuzzi LA, Rohrer KT, Tindel LJ, Sobel RS, Costanza MA, Shields W, et al. Fluorescein angiography complication survey. Ophthalmology. 1986;93(5):611-17.
[13] Shinoda J, Yano H, Yoshimura SI, Okumura A, Kaku Y, Iwama T, et al. Fluorescence-guided resection of glioblastoma multiforme by using high-dose fluorescein sodium. Technical note: Technical note. J Neurosurg. 2003;99(3):597-603.
[14] Koc K, Anik I, Cabuk B, Ceylan S. Fluorescein sodium guided surgery in glioblastoma multiforme: A prospective evaluation. Br J Neurosurg. 2008;22(1):99-103.
[15] Schupper AJ, Rao M, Mohammadi N, Baron R, Lee JYK, Acerbi F, et al. Fluorescence-guided surgery: A review on timing and use in brain tumour surgery. Front Neurol. 2021;12:682151.
[16] Cheng X, Chen J, Tang R, Ruan J, Mao D, Yang H. Sodium fluorescein-guided surgery for resection of brain metastases from lung cancer: A consecutive case series study and literature review. Cancers (Basel). 2023;15(3):882.
[17] Zhang N, Tian H, Huang D, Meng X, Guo W, Wang C, et al. Sodium fluorescein-guided resection under the YELLOW 560 nm surgical microscope filter in malignant gliomas: Our first 38 cases experience. Biomed Res Int. 2017;2017:01-10.
[18] Laws ER, Parney IF, Huang W, Anderson FA, Morris AM, Asher AL, et al. Survival following surgery and prognostic factors for recently diagnosed malignant glioma: data from the Glioma Outcomes Project. J Neurosurg. 2003;99(3):467-73.
[19] Acerbi F, Broggi M, Schebesch KM, Höhne J, Cavallo C, De Laurentis C, et al. Supplementary data from fluorescein-guided surgery for resection of high-grade gliomas: A multicentric prospective phase II study (FLUOGLIO). Clin Cancer Res. 2018;24(1):52-61.
[20] Schebesch KM, Proescholdt M, Höhne J. Sodium fluorescein-guided resection under the YELLOW 560 nm surgical microscope filter in malignant braintumour surgery-A feasibility study. Acta Neurochir (Wien). 2013;155(4):693-99.
[21] Rey-Dios R, Cohen-Gadol AA. Intraoperative fluorescence for resection of hemangioblastomas. Acta Neurochir (Wien). 2013;155(7):1287-92.
[22] Höhne J, Hohenberger C, Proescholdt M, Riemenschneider MJ, Wendl C, Brawanski A, et al. Fluorescein sodium-guided resection of cerebral metastases-an update. Acta Neurochir (Wien). 2017;159(2):363-67.
[23] Acerbi F, Cavallo C, Schebesch KM, Akçakaya MO, de Laurentis C, Hamamcioglu MK, et al. Fluorescein-guided resection of intramedullary spinal cord tumours: Results from a preliminary, multicentric, retrospective study. World Neurosurg. 2017;108:603-09.
[24] Höhne J, Acerbi F, Falco J. Lighting up the tumour fluorescein-guided resection of gangliogliomas. J Clin Med. 2020;9(8):2405.
[25] Okuda T, Kataoka K, Yabuuchi T, Yugami H, Kato A. Fluorescence-guided surgery of metastatic brain tumours using fluorescein sodium. J Clin Neurosci. 2010;17(1):118-21.
[26] Kuroiwa T, Kajimoto Y, Ohta T. Development of a fluorescein operative microscope for use during malignant glioma surgery: A technical note and preliminary report. Surg Neurol. 1998;50(1):41-48; discussion 48-49.
[27] Kuroiwa T, Kajimoto Y, Ohta T. Comparison between operative findings on malignant glioma by a fluorescein surgical microscopy and histological findings. Neurol Res. 1999;21(1):130-34.
[28] Ott C, Proescholdt M, Friedrich M, Hoehne J, Rosengarth K, Schmidt NO, et al. The use of the sodium fluorescein and YELLOW 560 nm filter for the resection of pediatric posterior fossa lesions. Childs Nerv Syst. 2023;39:1495-500.
[29] Falco J, Broggi M, Schiariti M, Vetrano IG, Esposito S, Ferroli P, et al. The role of sodium fluorescein in pediatric supratentorial intra-axial tumour resection: New insights from a monocentric series of 33 consecutive patients. Childs Nerv Syst. 2023;39:1463-71.
[30] Kerschbaumer J, Demetz M, Krigers A, Pinggera D, Spinello A, Thomé C, et al. Mind the gap- The use of sodium fluoresceine for resection of brain metastases to improve the resection rate. Acta Neurochir. 2023;165:225-30.

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- iThenticate Software: May 11, 2024 (9%)

ETYMOLOGY: Author Origin

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