

Pros and cons of FLUORESCHEIN-guided neurosurgery

- Clinical cases and experience sharing



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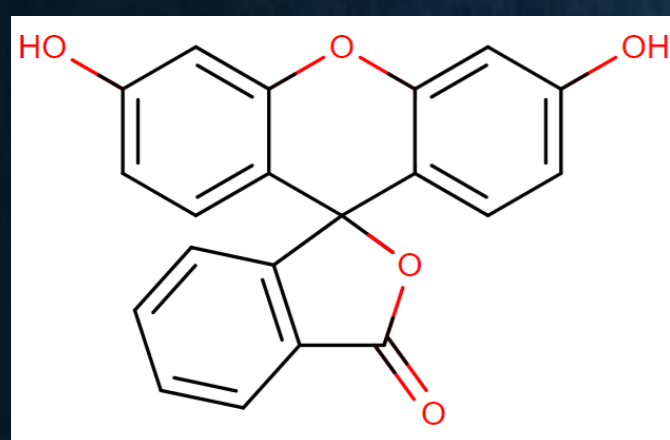
Introduction

Fluorescein sodium has been used as a surgical adjunct in neurosurgery. Our centre has recently started to use it in aiding our brain tumour excision and brain biopsy surgeries. We would like to introduce the chemical properties and the pros and cons of fluorescein as well as share the surgical experience in using fluorescein in our centre.

What is fluorescein?

Fluorescein is a green fluorescent synthetic organic compound that can exist as water-soluble dye in form of fluorescein sodium. It has a major green emission peak in the region of 540 to 690 nm. The first study on the use of fluorescence in neurosurgery was conducted in 1948. Nevertheless, it is first commonly used in the field of ophthalmology as a diagnostic tool. In neurosurgery, it has been reported to be useful to improve the discrimination between tumour tissue and peritumoral brain parenchyma in order to achieve a gross total resection (GTR) of brain tumours.

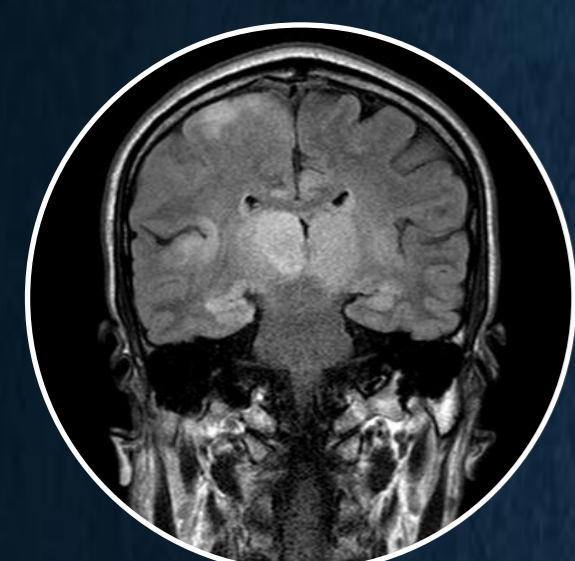
The mechanism of action of fluorescein is when brain tissue is under conditions of damage or disturbance of the blood-brain barrier (BBB), fluorescein can penetrate from the blood vessel into extravascular space. Hence, the presence of glioma causing mechanical interference to the BBB and increased blood vessel formation can lead to the accumulation of fluorescein and visualization of the tumour



Our experience and cases illustration

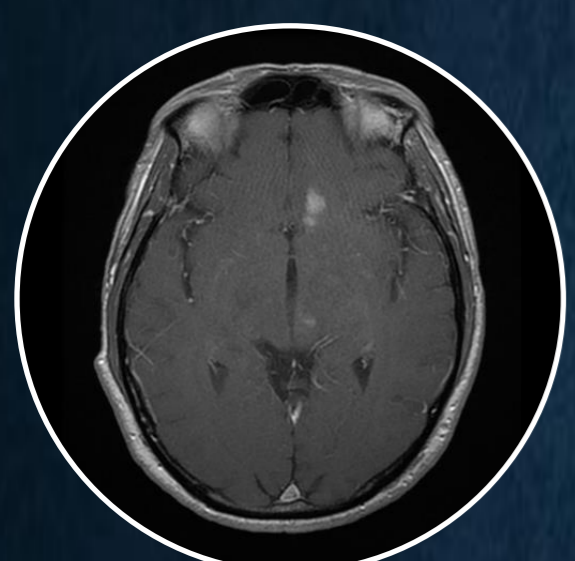
In 2021, we have performed fluorescein-guided surgeries for tumour excision or biopsy on 5 different patients in our centre. Fluorescein can help to visualise brain tumour tissue and guide tumour resection and biopsy in all 5 cases. We would like to share our clinical experience in using fluorescein and the associated pros and cons.

Scan the QR code on the photos to check the videos of the surgeries!



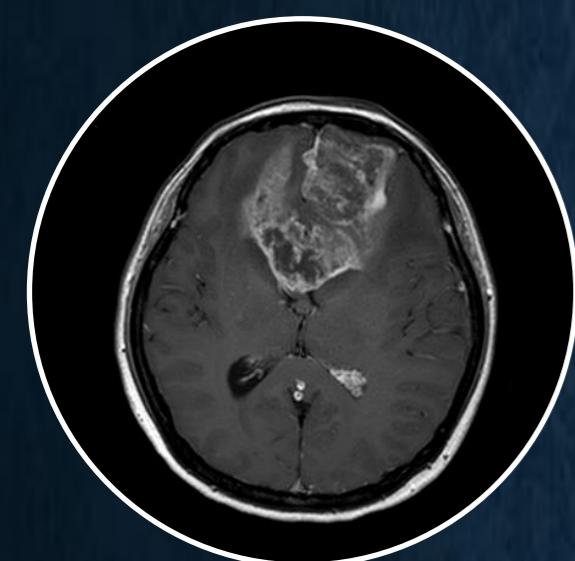
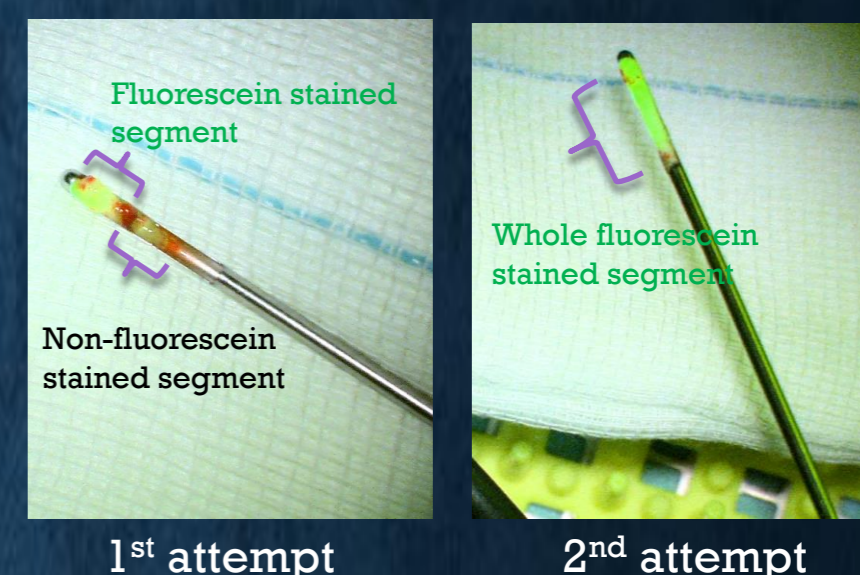
72/M
Multiple brain lesions
Stereotactic biopsy of right parietal tumour
Histopathology: diffuse astrocytoma WHO grade II

What's best visualization setting of fluorescein-guided biopsy?
Clockwise from top: Over metal kidney dish, over blue kidney dish, over biopsy needle with blue drape background, over glove piece, over black background
From our experience, a fluorescein-guided biopsy is best seen over the biopsy needle



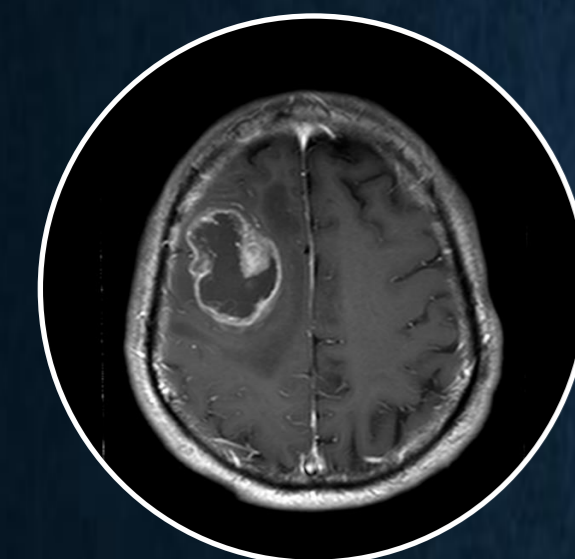
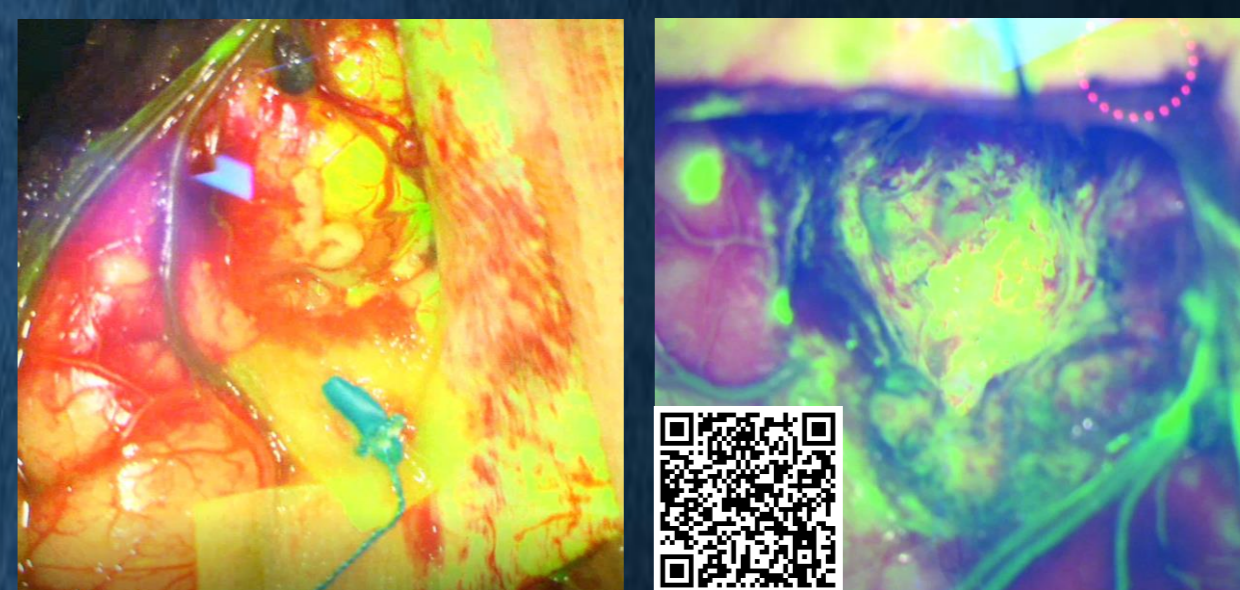
66/M
Left frontal lobe, left cerebellum and left brain stem
Stereotactic burr hole biopsy of left frontal lobe tumour
Histopathology: diffuse large b-cell lymphoma

Fluorescein can help to guide the adequacy of biopsy
First attempt: only a short segment of fluorescein
Second attempt with deeper biopsy: a whole segment of fluorescein
→ Yield more tumour tissue for histological investigation



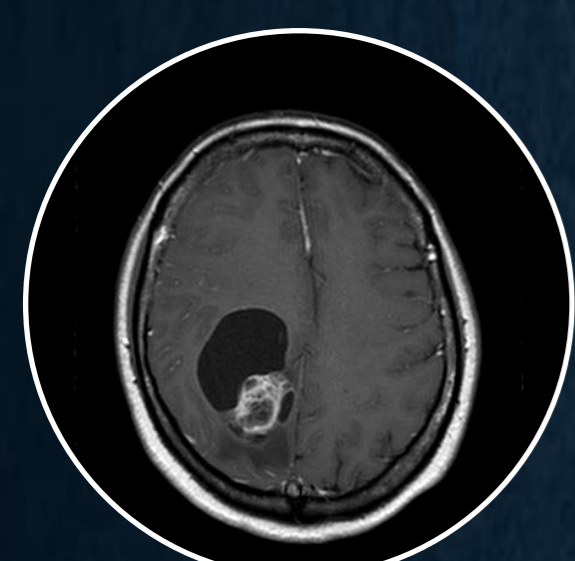
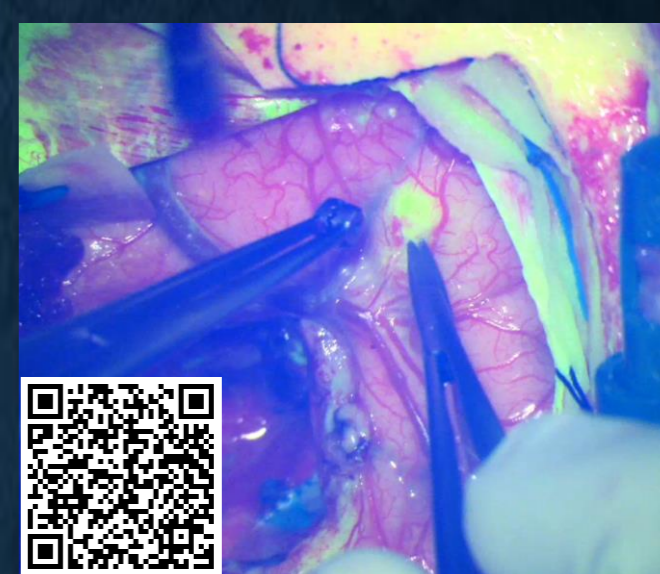
45/F
Bifrontal butterfly tumour
Craniotomy for excision of tumour
Histopathology: Glioblastoma

Is fluorescein good for glioma resection?
Fluorescein stains the surrounding normal brain tissue, so it may not give a good visualization for guiding tumour resection in glioblastoma



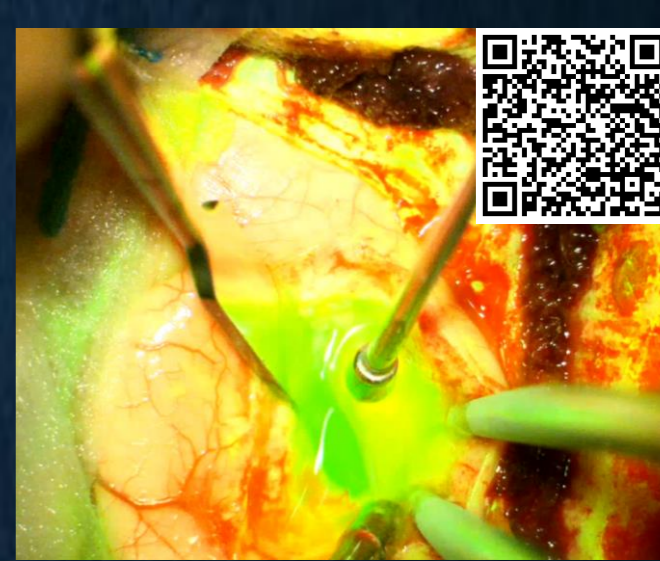
66/M
Right frontal lobe tumour
Craniotomy for tumour excision
Histopathology: Glioblastoma

Is all fluorescein stained tissue tumour? NO!
A patch of fluorescein noted over a non-MRI enhancing area
Histology: gliosis, no definite tumour involvement



54/M
Right parieto-occipital tumour with peritumour cyst
Craniotomy for excision of brain tumour
Histopathology: poorly differentiated malignant tumour

Tumour cystic fluid can also be stained
Fluorescein stain appeared in the cystic fluid of the tumour

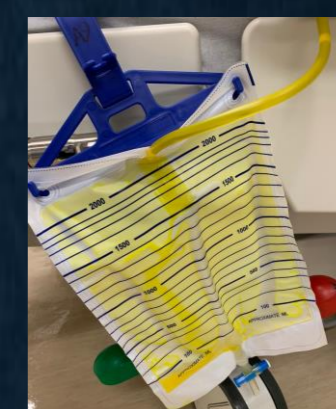


Adverse drug reaction: Transient yellowish staining of urine which disappeared in about 24 h

*****Contraindication:** Patients with known hypersensitivity to fluorescein

Other possible adverse reactions include skin discoloration, nausea, vomiting, headache, hypersensitivity reactions and cardiopulmonary reactions

No justifiable evidence for withholding metformin before using fluorescein



Comparison between fluorescein and 5-ALA

Fluorescein and 5-aminolevulinic acid (5-ALA) are two commonly used intraoperative fluorescence in neurosurgery, the following table is demonstrating the comparison between the two dyes in different aspects.

	Fluorescein	5-ALA
Physical property	Visualized using microscope with a yellow 560nm light filter, tumour tissue glows green	Visualized using microscope with blue-violet light filter (wavelength of 375–440nm), tumour tissue glows red
Mechanism	Staining tumour tissue via damaged or disturbed blood-brain barrier	Metabolized to the heme precursor protoporphyrin IX (PpIX) which has a much higher affinity to high-grade tumours than normal brain tissue
Route & dosage	IV, 5mg per kg	Oral, 20mg per kg
Efficiency (for high grade glioma)	GTR rate 68.4% to 84%	GTR rate 56.3% to 92.6%
Adverse effect	Urine and skin discoloration, GI upset, headache, hypersensitivity and cardiopulmonary reactions	Skin reaction (photosensitivity)
Limitation	Relatively low specificity, both tumour and surrounding edema can be stained	Limited use in low grade brain tumour
Cost	HKD \$165/ 5ML (10%)	HKD \$25,250 /50ML (30mg/ml)

Conclusion

Although fluorescein is not a perfect fluorescence without limitation, it is a sensitive, safe and cheap intra-operative dye for visualization of brain tumour tissue as well as improving tumour resection.

Reference

1. Falco J, Cavallo C, Vetrano IG, de Laurentis C, Siozos I, Schiariti M, Broggi M, Ferroli P, Acerbi F. Fluorescein Application in Cranial and Spinal Tumors Enhancing at Preoperative MRI and Operated With a Dedicated Filter on the Surgical Microscope: Preliminary Results in 279 Patients Enrolled in the FLUOCERTUM Prospective Study. *Front Surg.* 2019 Aug 13;6:49. doi: 10.3389/fsurg.2019.00049. PMID: 31475153; PMCID: PMC6705221.
2. Mazurek M, Kulesza B, Stoma F, Osuchowski J, Mańdziuk S, Rola R. Characteristics of Fluorescent Intraoperative Dyes Helpful in Gross Total Resection of High-Grade Gliomas-A Systematic Review. *Diagnostics (Basel).* 2020 Dec 16;10(12):1100. doi: 10.3390/diagnostics10121100. PMID: 33339439; PMCID: PMC7766001.