



## Fluorescence-guided surgery of brain abscesses



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### ABSTRACT

**Objectives:** Fluorescein Sodium (FL) enhances areas in the brain with a disrupted blood brain barrier (BBB). Solitary brain abscesses (BA) are characterized by the pathognomonic finding of BBB disruption. Consequently, FL may have the potential to improve the intra-operative visualization of BA. Here, we report a series of patients with BA that were treated surgically after application of FL in combination with a dedicated light filter integrated in the surgical microscope.

**Methods:** 7 patients (4 female, 3 male; mean age 53.8 years) with BA were included, all of them gave written informed consent. 5 mg/kg bodyweight of FL was administered via the central venous line at induction of anesthesia, approximately 30–45 min prior to surgery. We screened the surgical reports for any statement concerning the intensity of fluorescent staining.

**Results:** Fluorescent staining was bright in all patients. Surgical removal of all parts of the BA, aspiration of pus and dissection of the capsule, were performed in the fluorescence-mode under the filtered light. We encountered no adverse events.

**Conclusion:** The accumulation of FL resulted in brilliant visualization of the infected area under the YELLOW 560 nm filter. This small clinical study adds to the rapidly emerging clinical experiences of the use of fluorescein in neurosurgery, even for non-neoplastic lesions. However, prospective and randomized clinical trials are still necessary to establish the beneficial use of FL.

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### 1. Objectives

Commonly, surgical removal of space-occupying brain abscesses (BA), followed by specific or calculated antibiotic treatment is considered the treatment of choice [3–5]. Complete resection of pus and capsule should always be aimed for, in order to avoid local chronic inflammation of the brain. However, in complex cases, when the BA involves eloquent areas, and/or is multi-focal, at least aspiration of pus is recommended while the capsule can be left undisturbed. In any case, identification of the BA, especially when small infectious spots are located deeply in the brain, and, for improved differentiation between unaffected brain tissue and the abscess capsule, fluorescence-guidance may enhance *in situ* visualization.

Fluorescein Sodium (FL), when administered intravenously 30–45 min prior to skin incision, has the potential to cause areas with damaged blood brain barrier (BBB) to enhance [1]. Nowadays, FL in combination with the dedicated YELLOW 560 nm surgical microscope filter (PENTERO 900 surgical microscope, Carl

Zeiss Meditec, Germany), has become a promising tool in neuro-oncologic surgery [2,8,9,12,16]. As FL is a marker of pathologically increased vascular leakage rather than a specific tumor marker, strongly accumulating in areas with BBB breakdown, some authors advocated that the uptake of the original vascular dye Gadolinium, generally used for contrast-enhanced magnetic resonance imaging (MRI), is similar to the intensity of fluorescent staining after FL injection, irrespective of the histopathological origin of the lesion [8,12]. Consequently, FL may have the potential to be beneficially applied in BA for improved depiction of inflammatory tissue, as disruption of the BBB is pathognomonic in the perifocal area of the BA.

To the best of our knowledge, this is the first report of the use of FL in combination with the dedicated light filter in a series of patients with solitary BA.

### 2. Methods

The observed study period was January 2016 to November 2016. Seven patients (4 female, 3 male; mean age 53.8 years) with supratentorial BA were included in this retrospective analysis. As per our institutional standard, all patients received FL in the dosage 5 mg/kg bodyweight, administered via the central venous line at

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**Table 1**  
Baseline data.

| Pat.nr. | Sex | Age | Location of BA  | Specimen     | Navigation | Indication | Fluorescence |
|---------|-----|-----|-----------------|--------------|------------|------------|--------------|
| 1       | m   | 40  | right temporal  | no           | yes        | Tumor      | bright       |
| 2       | m   | 45  | right parietal  | No           | yes        | BA         | bright       |
| 3       | f   | 53  | right temporal  | Staph aur    | yes        | BA         | bright       |
| 4       | f   | 53  | right frontal   | Staph aur    | yes        | BA         | bright       |
| 5       | f   | 50  | left frontal    | No           | yes        | BA         | bright       |
| 6       | f   | 55  | right occipital | Staph aur    | no         | Tumor      | bright       |
| 7       | m   | 61  | right frontal   | Strept inter | no         | BA         | bright       |

m = male, f = female; Staph aur = Staphylococcus aureus, Strept inter = Streptococcus intermedius.

induction of anesthesia, approximately 30–45 min prior to skin incision. In two patients, neoplastic lesions (high grade glioma in pat#1 and cerebral metastasis in pat#6) were assumed initially but histological and microbiological evaluation revealed a BA. The remaining five patients initially presented with signs of central nervous system infection and preoperative MRI showed a lesion strongly suspicious for BA (strongly hyperintense diffusion weighted images).

Microbiological specimen isolation from the BA was successful in four patients (Streptococcus intermedius (n = 1), Staphylococcus aureus (n = 3)). In three patients, no microbiological specimen could be isolated. All patients either received empirical or specific antibiotic treatment primarily intravenously and secondarily orally.

All the seven patients underwent craniotomy and microsurgical resection of the BA, strictly conducted under fluorescence-guidance with Fluorescein Sodium (FL, 10%, ALKON, Germany) and the YELLOW 560 nm filter in the PENTERO 900 surgical microscope (Carl Zeiss Meditec AG, Oberkochen, Germany).

All patients were informed about the off-label use of FL and gave written informed consent. The study was approved by the local ethics committee of the University of Regensburg (12-101-0215). Exclusion criteria were: age below 18 years, hepatic or renal failure, and any known or suspected allergic reaction to FL.

The illustrated case of one patient (pat#2) has been published before [10].

We evaluated the surgical reports for the grade of fluorescent staining (bright versus unremarkable) and for any reported consequence of the fluorescence-guidance. Accordingly, we evaluated the medical records for any adverse reaction due to FL administration, including allergy or anaphylaxis.

### 3. Results

The baseline data are presented in Table 1.

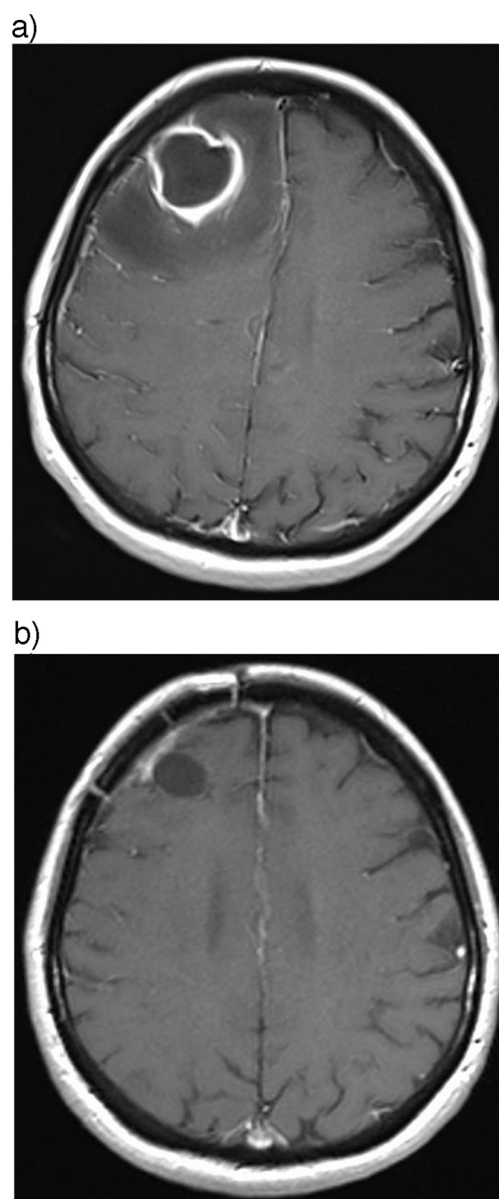
In all patients, intense fluorescent staining of the BA capsule was documented, see Fig. 3a. In all cases, the dissection and removal of the capsule was conducted under the YE 560 nm filter.

The pre and postoperative contrast-enhanced T1-weighted sequences of patients 4 and 6 were chosen for illustration, see Figs. 1 and 2. Intraoperative photographs of patient 2 were chosen for illustration of the grade of fluorescent staining (Fig. 3).

The morbidity and mortality was 0%. We encountered no adverse event or anaphylactic reaction due to FL use.

### 4. Conclusion

As a proof-of-principle, FL strongly accumulated in the capsule and in the adherent infectious brain tissue which similarly stored Gadolinium in the preoperative contrast-enhanced T1-weighted sequences. The accumulation of FL resulted in bright visualization of the infected area under the YELLOW 560 nm filter, without exception. Recently, Neira et al. showed that the intensity of Gadolinium uptake in the preoperative MRI was equivalent to objective intraoperative FL intensity in patients with high grade



**Fig. 1.** Superficial BA right frontally (pat#4).  
(a) preop. MRI (T1, contrast-enhanced)  
(b) postop. MRI (T1, contrast-enhanced)

gliomas [12]. Furthermore, some authors evaluated, and consecutively advocated, the use of FL in non-malignant [6,7,11,13] and non-glioma [14,15] lesions because of its simple and safe usage. Taken together, this suggests that FL may have the potential to strongly accumulate even in non-neoplastic lesions like BA.

According to our opinion, the benefit of improved visualization of BA with FL and the dedicated light filter is two-fold: The capsule

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