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# Fluorescein sodium-guided surgery in cerebral lymphoma

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ABSTRACT

*Objectives:* Growth and progress of primary central nervous lymphoma (PCNSL) severely disrupt the blood brain barrier (BBB). Such disruptions can be intraoperatively visualized by injecting fluorescein sodium (FL) and applying a YELLOW 560 nm surgical microscope filter. Here, we report a small cohort of patients with PCNSL that mimicked high grade gliomas (HGG) or cerebral metastases (CM), who had been operated on with the use of FL.
*Patients and methods:* Retrospectively, seven patients with PCNSL were identified, who had been operated on by means of microsurgery after intravenous FL injection. The surgical reports were screened for statements on the grade of fluorescent staining in the tumor area. One representative case was chosen to show the staining under white light as well as under filtered light at different distances to the tumor area.
*Results:* All patients had shown bright and homogenous fluorescent staining of the tumor ($n = 7$. 100%). No adverse effects had been observed.
*Conclusion:* Similar to patients with HGG or CM, patients with PCNSL may benefit from use of FL and the dedicated YELLOW 560 nm filter in open surgery.



## 1. Introduction

Primary central nervous system lymphoma (PCNSL) is an extranodal non-Hodgkin lymphoma accounting for less than 5% of primary brain tumors [14,15,19]. Standard treatment consists of chemotherapy regimen containing high dose methotrexate sometimes combined with cytarabine or targeted anti-CD20 treatment using rituximab [19,20]. Histological confirmation of PCNSL is mandatory before initiating any further adjuvant treatment [15]. Generally, a stereotactic biopsy is taken, but an open approach – in terms of craniotomy and microsurgical dissection – may be necessary because of the possibly complicated anatomical location of the lesion for instance, close to or surrounded by principal veins and arteries. If the PCNSL causes a mass lesion with acute compression of the brain stem, a surgical resection may be indicated to reduce intracranial pressure and generate a time window for adjuvant treatment. In fact, a recent study from the German PCNSL research group analyzing 551 patients has demonstrated an improved progression free and overall survival in PCNSL patients receiving subtotal or complete resection compared to biopsy only [18]. In open surgery, even neuronavigation or intraoperative ultrasound can be misleading [5,9] in the case of small or tiny lesions deeply located inside the brain, so that intraoperative fluorescence may help identify the target.

Our groups have already described a fluorescein-guided technique for removal of high-grade gliomas (HGG) [1,2,17] and cerebral metastases (CM) [16] by the use of a dedicated surgical microscope filter 'YELLOW 560 nm' (Carl Zeiss Meditec, Germany). The retrospective analysis of our databases with regard to patients with brain tumors suspicious for HGG or CM, who had undergone surgery with FL and the YELLOW filter, identified seven patients with the histological diagnosis of PCNSL. Based on our surgical expertise with FL [16,17], we have applied FL-guided surgery almost exclusively in lesions suspicious for HGG or CM since 2012.

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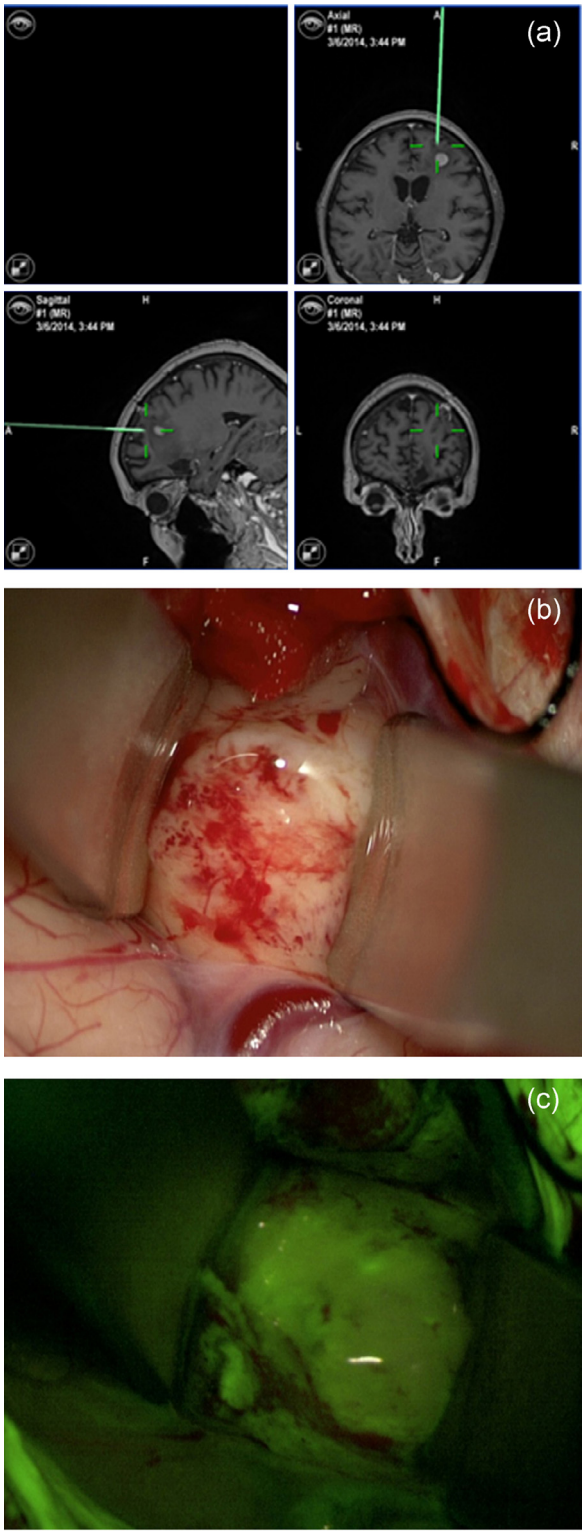


**Fig. 1.** Case illustration (patient 1). (a) Intraoperative neuro-navigation shows a distance of approximately 10 mm to the target. (b) Intraoperative view under white light at the exact location of (a). (c) Intraoperative view through the YELLOW filter at the exact location of (a).

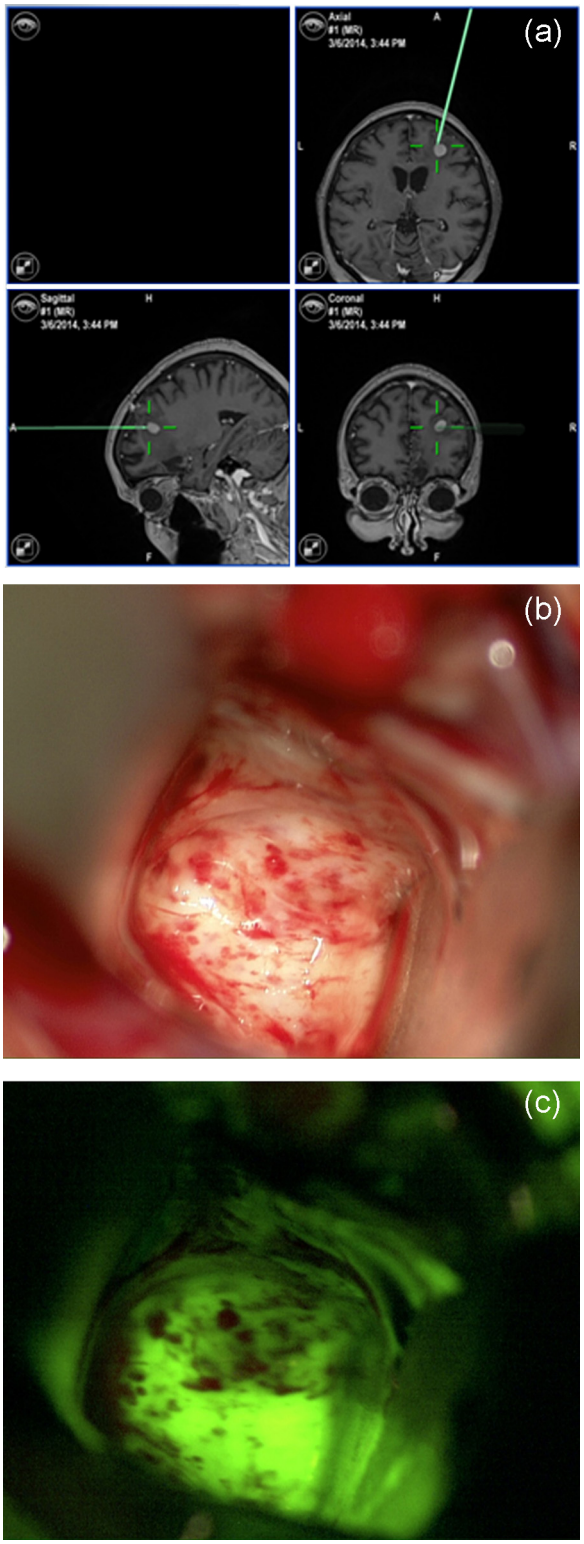


**Fig. 2.** Case illustration (patient 1). (a) Intraoperative neuro-navigation shows a close approach to the target. (b) Intraoperative view under white light at the exact location of (a). (c) Intraoperative view through the YELLOW filter at the exact location of (a).

Here, we present our first experiences with this innovative technique of FL in patients with PCNSL.

## 2. Methods

The neuropathological databases at Regensburg University Hospital and Fondazione IRCCS Istituto Neurologico Besta were retrospectively analyzed with regard to patients with brain tumors suspicious for HGG or CM who had presented between December 2011 and May 2015. Seven patients (four women, three men; mean age of 66.3 years) with the final diagnosis of PCNSL were identified, who had undergone open neurosurgery guided by FL and the dedicated YELLOW 560 nm filter. The regimen of FL administration