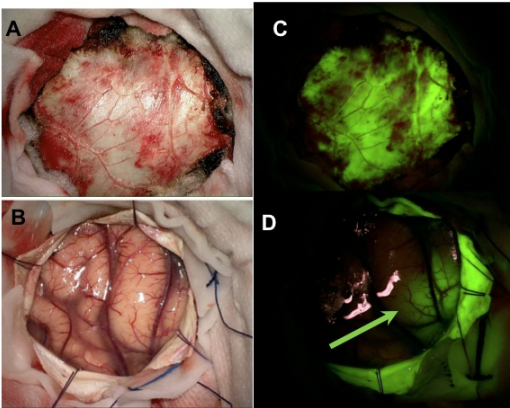


Introduction

Sodium fluorescein capability to accumulate in cerebral areas with blood-brain barrier damage makes it an ideal dye for intraoperative visualization of high-grade gliomas (HGG) (Figure 1). A fluorescein-guided technique for HGG removal with a dedicated filter on the surgical microscope is presented (FLUOGLIO trial).

Figure 1



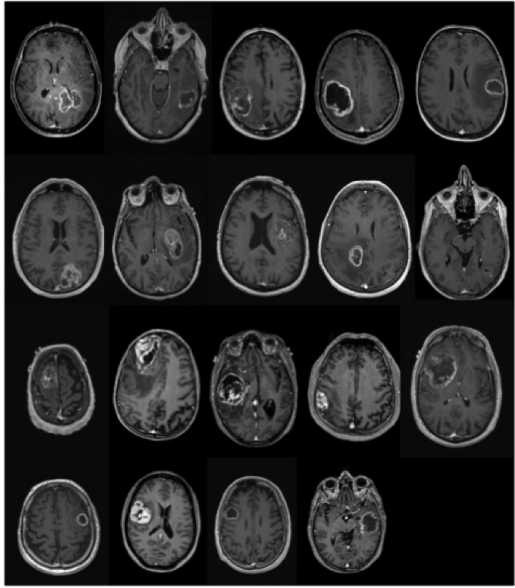
Inraoperative view of a left frontal GBM with white light (A and B) and with dedicated fluorescein filter (Yellow560) activated (C and D). The dura shows intense fluorescence (C). Note how the tumor appears fluorescent and recognizable with filter activated (D, green arrow) compared to white light (B).

Methods

The FLUOGLIO study is a prospective phase II-trial to evaluate safety and obtain indications about efficacy of fluorescein-guided surgery for HGG. Until January 2015, 36 patients (mean age 62, range 40-74) were enrolled.

Methods continued. Fluorescein was intravenous injected after intubation (5-10 mg/Kg). Tumor was removed with microsurgical technique and fluorescence visualization by BLU400 or YELLOW560 filters on the Pentero microscope (Carl Zeiss, Germany). Degree of tumor resection was calculated on an early (within 72 hours of surgery) postoperative MRI. In 13 patients, biopsies were performed at the tumor margin to evaluate sensitivity and specificity of fluorescein in tumor tissue identification. Some examples of tumor included in the study are shown in Figure 2.

Figure 2

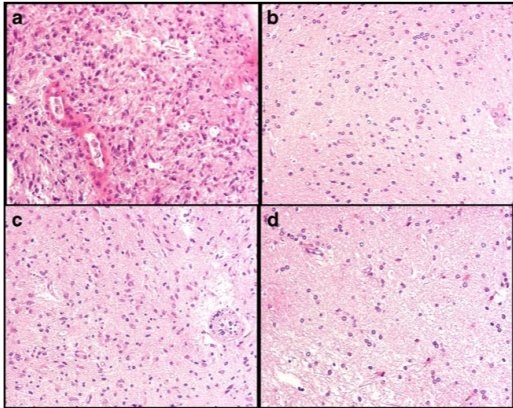


Results

Median pre-operative tumor volume was 29.68 cm3 (1.3-87.8 cm3). No adverse reaction related to the administration of fluorescein was registered.

Results continued. Contrast-enhanced tumor was completely removed in 86% of the patients on early postoperative MRI (31/36). The remaining patients had a mean tumor resection of 92.1%. With a median follow-up of 12 months (mean follow-up 13,71 months), the 6 months PFS rate was 55.5% and median survival was 12 months (mean survival 13,71 months). Estimation of sensitivity and specificity of fluorescein in identifying tumor tissue was 81% and 79% respectively (Figure 3).

Figure 3

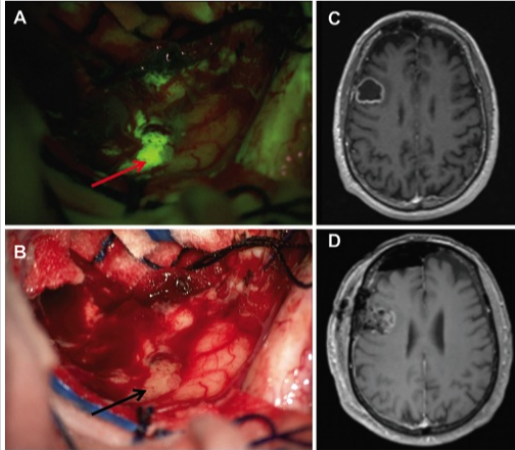


Histological pictures (hematoxylin-eosin) of biopsies at the tumor margin. a and c were obtained from fluorescent tissue and showed a sample of true GBM (a) and nervous tissue widely infiltrated by HGG cells (c) (true positive for estimation of sensitivity). b and d were obtained from non-fluorescent tissue and showed normal nervous tissue (b) or some gliosis (d) (true negative for estimation of specificity)

Conclusions

Fluorescein-guided technique with a dedicated filter on the surgical microscope is safe and allows a high-rate of complete resection of HGG at the early post-operative MRI (Figure 4).

Figure 4



A and B: Intraoperative view of a right frontal GBM. With the YELLOW 560 filter activated (A) it is possible to visualize tumor tissue still to be removed (red arrow); the same picture with white light illumination (B), with the tumor indicated by a black arrow. C: Preop axial T1-weighted MR with contrast showing a right frontal GBM (volume 8.93 cm3). D: Early post axial T1-weighted MR with contrast showing a complete tumor resection.

References

- Acerbi F, Broggi M, et al. Fluorescein- guided surgery for grade IV gliomas with a dedicated filter on the surgical microscope: preliminary results in 12 cases. Acta Neurochir (Wien). 2013 Jul;155(7):1277-1286.
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