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Letter to Editor: Fluorescence-guided surgery for high-grade gliomas

Dear Editor,

Recently, our group gladly read the article published by Cossu et al. (2024) regarding the significance of fluorophores in assisting neuro-oncology and neuro-vascular surgical approaches. We share the opinion that the use of fluorescence-guided surgery (FGS), namely for high-grade glioma (HGG) surgery, revolutionized the oncological outcomes by maximizing the extent of resection and empowering the surgical teams with biological information to optimize the onco-functional balance.

As stated by the Cossu et al. since the early 2000s, FGS has improved the capacity of neurosurgeons to visualize pathological tissue enhancing surgical accuracy with the assistance of fluorophores such as fluorescein sodium (FNa), 5-aminolevulinic acid (5-ALA) and indocyanine green (ICG) (Ahrens et al., 2022). Altogether, they allow for a clearer identification of tumoral tissue and intraoperative delineation of the vasculature in and around the tumor.

Our group performs regular HGG resections using FGS with 5-ALA-guided resections (Baig Mirza et al., 2021). Despite the multiple benefits highlighted in this comprehensive review, we also faced some limitations related with appropriate tissue illumination. This is particularly relevant when working through limited surgical corridors (as for example during minimal invasive parafascicular approaches using tubular retractors to access deep-seated lesions) while resecting HGG where microscope-based blue light source for tumour excitation may not reach the tissue of interest due to loss of co-axial corridor-light source orientation.

To overcome this obstacle, we have been recently using the Nico Myriad Spectra System™ hand-held device. This illumination system allows to switch between white and blue 405 nm light with a foot pedal and bring the light source closer to the surgical field, overcoming the issues of the angle of incidence of the microscope light.

The use of *in situ* illumination increases the degree of fluorescence observed, as depicted in one of our illustrative cases in Fig. 1, resulting in maximized resection rates. Through optimization of lighting at the depth of the surgical field and the edges of the cavity, it allows for maximal resections that correlate with the histologic findings of the neuropathological analysis by decreasing the rate of false negatives related not with the 5-ALA fluorescence technique but with poor illumination.

Another useful feature of the Nico Myriad Spectra System™ is the possibility of integration with intraoperative neuromonitoring, which makes the surgical removal of the tumour safer while obviating the need to have multiple devices obliterating at the surgical field at once (Gallagher et al., 2022). Again, this integration is particularly relevant in the above-described situation where narrow corridors require

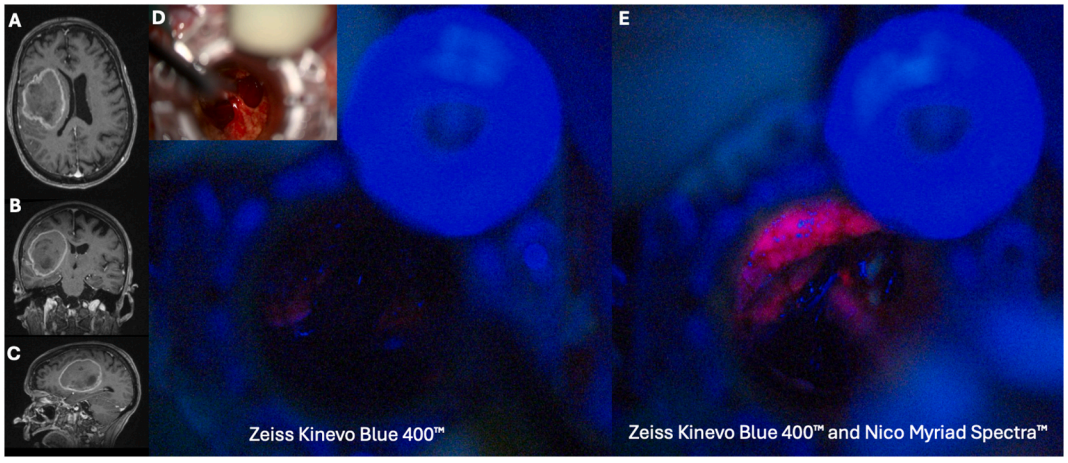

Fig. 1. ***In situ*** **light source enhanced fluorescence-guided resection** - T1 gadolineum-enhanced (A) axial, (B) coronal and (C) sagittal sequences right-sided fronto-insular glioblastoma in a patient with a progressive-onset left-sided hemiparesis. (D) Intraoperative Zeiss Kinevo Blue 400™ view of the removal of the tumour through a BrainPath® tubular retractor, with a minimized image depicting the Kinevo standard white light illumination on the left and upper part figure. (E) *In situ* light source system - Nico Myriad Spectra™ - enhanced fluorescence (in conjunction with Zeiss Kinevo Blue 400™) showing optimized lighting at the depth of the surgical field and the edges of the cavity, overcoming false negatives related with poor tissue excitation and illumination misalignment. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

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minimization of instrumentation through surgical channels to preserve the degrees-of-freedom necessary for tumour resection and visualization.

In summary, the development and advances made on FGS in the recent years enhance intraoperative decision making, potentially improving the extent of resection regarding HGG surgery and ultimately improving patient outcomes. *In situ* light source delivery systems focusing on 5-ALA show potential to maximize the intraoperative use of 5-ALA-driven information overcoming false negatives related with poor tissue excitation and illumination misalignment. In our center, the Nico Myriad Spectra System™ is being useful to improve the extent of resection in tubular-assisted resections and chasing gross-total/supra-maximal resections. These results would benefit from further validation with multicenter data.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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