

## Interventional imaging in neurosurgery of gliomas: use of several fluorescence emission spectra of 5-ALA induced protoporphyrin IX to guide neurosurgeons

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Gliomas are infiltrative tumors of the central nervous system that account for more than 50 % of primitive brain tumors [1]. Their current treatment is based on surgery when possible but a tradeoff needs to be found by neurosurgeons between removing the maximum amount of tumor cells and preserving functionality of the brain. To help removing the maximum amount of tumor cells, a clear definition of tumor margins is required and yet the identification of infiltrative parts is still a challenge [2]. To assist neurosurgeons, fluorescence techniques provide high expectations since aminolevulinic acid (5-ALA) induced protoporphyrin IX (PpIX) accumulates in tumor cells and emits a reddish fluorescence when excited with UV/blue light. Intraoperative fluorescence microscopy enables therefore neurosurgeons to visualize some tumor cells [3] but its sensitivity is limited, particularly in tumor margins or in low grade gliomas. Moreover, this is a qualitative technic. In parallel, the relevance of 5-ALA induced PpIX fluorescence spectroscopy to increase the sensitivity has been shown [4,5] and allows quantification of PpIX concentration. Previous studies on human beings concentrated on the fluorescence emission spectrum of PpIX with a main peak at 634 nm. However, we demonstrated the presence of second fluorescence emission spectrum of PpIX with a main peak at 620 nm. We showed that the use of the two spectra of fluorescence enables to discriminate solid part of the tumor against tumor margins ex-vivo [6]. We now want to see how the two spectra can help discriminate tumor margins against healthy tissue during neurosurgery.

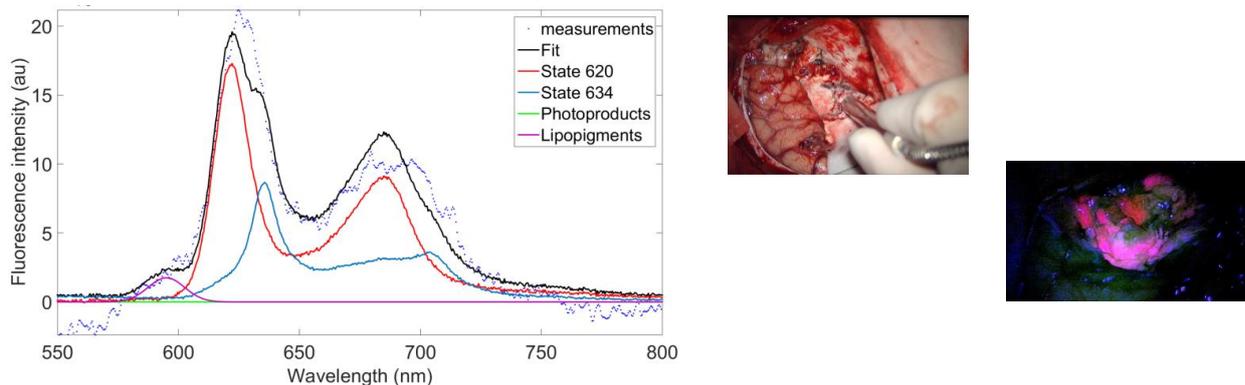


Figure : fit of intraoperative measurements in tumor margins with reference spectra (left). Intraoperative use of the probe (upper right). Visible fluorescence in a high grade glioma (bottom right)

To reach our goal, we developed a portable spectroscopic device ending with a probe that neurosurgeons put on the brain during surgery. Excitation light is lead to the tissue through the probe and emitted fluorescence is collected through the same probe and sent to a spectrophotometer. Fluorescence measurements are then fitted with a linear combination of characteristic spectra. Results of the fit are then compared with anatomopathological results. We present the development and use of our intraoperative device and preliminary results comparing fluorescence measurements and anatomopathological results.

[1] Wrench et al, Neuro Oncol., 2002,278-299 [2] Dhermain et al, Lancet Neurol, 9, 906–20,2010 [3] W. Stummer et al., Acta Neurochir. (Wien), 140 (10), p. 995-1000, 1998. [4] Valdes et al. Journal of Neurosurgery, 123 (3), 771–780, 2015 [5] Abi Haidar et al. Biomed. Opt. Express, 6 (4), 12–19, 2015 [6] B. Montcel et al., Biomed. Opt. Express, 4 (4), 548–558, 2013

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