Symbolic Monte-Carlo Method with Fluorescence for Biomarker Quantification in Neurosurgery

The use of medical imaging in the diagnosis and management of patients is becoming increasingly important. In particular, intraoperative imaging (**in the surgical operating room**) is developing strongly. However, many scientific, technical and experimental problems remain to be solved in this multidisciplinary field of research at the borders of Physics and Medicine. In particular, we are developing **intraoperative optical and fluorescence imaging** methods to assist the surgical gesture during **brain tumor neurosurgeries**.

MEDICAL CONTEXT

Multiform glioblastoma is a serious tumor in terms of malignancy and progression. It is the most common and aggressive primary brain tumor. The main therapy is complete tumor resection surgery. Currently, the problem lies in the precision in terms of delineation of the lesion margins, especially because the healthy tissue and the tumor margin may have the same appearance during the surgery. The 5-ALA-induced protoporphyrin IX (PpIX) fluorescence microscopy technique is currently the most effective clinical standard but it still suffers from a lack of sensitivity.

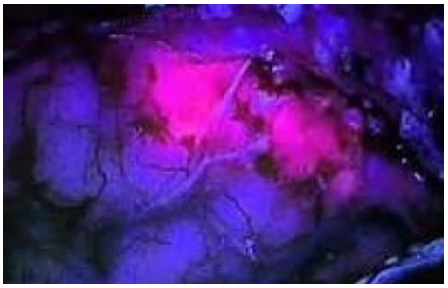

Figure 1 - 5-ALA induced PpIX fluorescence inside a high-grade glioma

SCIENTIFIC CONTEXT

We have demonstrated (Montcel, et al., *Biomedical Optics Express, 4(4)*, 2013 ; Alston et al. *Journal of Biomedical Optics, 23 (9)*, 2018) that the spectral complexity of intraoperative PpIX fluorescence emission is relevant for identifying tumor tissue and particularly the infiltrated component. An initial clinical trial including 10 patients demonstrated the relevance of the new biomarkers to identify the tumor margin and its border with healthy tissue (Alston et al. *Biomedical Optics Express 10(5)*, 2019). However, to quantify these new biomarkers, it is necessary to model and simulate the propagation of light and the phenomenon of fluorescence in the brain. The brain is composed of gray matter and fluorophores agglomerated in tumor cells only and is therefore a complex heterogeneous environment.

To simulate the propagation of photons in this type of complex media, Monte-Carlo methods are used as reference tools. Today, the realization of these quantifications requires the use of Look Up Table or simplistic optical models that induce errors impacting the sensitivity of the quantification. Also, a need to accurately describe the propagation of light and fluorescence is crucial. However, the quantification of biomarkers from measurements on the brain surface is an inverse problem that requires as many simulations as possible physical configurations and makes the use of Monte Carlo simulations cumbersome or impossible. To address this limitation, Symbolic Monte Carlo methods (Maanane, et al. *J. Quant. Spectrosc. Radiat. Transfer, 249(107019)*) represent a promising tool. By keeping in symbolic form some parameters, these methods allow to express the measured fluxes as simple functions (polynomials) of these parameters. In other words, a single simulation - comparable in computation time to a classical Monte-Carlo - allows, without bias, to express an observable on a whole parameter space. Thus, it becomes possible to quickly simulate the propagation of radiation in the brain for a wide variety of configurations.

The objective of this internship is to use Symbolic Monte-Carlo methods with fluorescence in this context of quantification of biomarkers of the glioma tumor margin. Experimental acquisitions on optical phantoms simulating brain properties will be performed to validate the simulation results. The impact of variations in the radiative properties of the brain related to wavelength and fluorophore concentrations will be studied in an exploratory and innovative methodological framework.

The internship will be carried out in two laboratories: the CREATIS laboratory (for the experimental acquisitions) and the CETHIL laboratory (for the simulations) at the campus of La Doua in Villeurbanne.

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