Master 2024 internship topic

NAD+/NADH a biomarker of cerebral cellular energy metabolism: links between preoperative MRS and intraoperative optical approaches.

Context :

Neurosurgery for glioma and focal cortical dysplasia is strongly supported by pre- and intra-operative imaging. These approaches are often difficult to link in terms of the biomarkers measured, yet this is essential for surgical planning. Indeed, the contrast mechanisms underlying these biomarkers are similar, but often partially different. The main aim of this master's degree course is to develop the first experimental measurements to clarify the link between intra-operative optical biomarkers and pre-operative MRS magnetic resonance spectroscopy (MRS) of cellular energy metabolism in brain tissue.

Scientific Context :

In many neurological medical problems (glioblastoma and focal cortical dysplasia), the main therapy is surgery to remove the entire tumour. At present, the problem lies in the precise delineation of the edges of the lesion, especially as healthy tissue and tumor or epileptogenic tissue can have the same appearance during surgery.
The surgical procedure is aided by preoperative and intraoperative imaging approaches. The latter are preferred because of the problems of robustness of neuronavigation tools, particularly in relation to brain-shift. Intraoperative approaches are based on fluorescence microscopy. This has made it possible to increase the sensitivity of tumor zone detection. Fluorescence spectroscopy approaches have gone even further (Alston 2019). However, the specificity of tumor detection is still limited.
Preoperative approaches rely heavily on MRI. Magnetic resonance spectroscopy (MRS) work has also shown the value of this technique for surgical planning, particularly in its ability to quantify biomarkers involved in cellular energy metabolism (Laino 2020).
Intraoperative approaches using fluorescence spectroscopy can also be used to measure biomarkers of cellular energy metabolism (NADH, Flavin, Cytochrome c oxidase). Some work has shown the value of these approaches (Haidar 2015), but they remain difficult to interpret in the clinical context, due in particular to the difficulties of quantifying optical biomarkers and the origin of similar but not identical pre- and intra-operative contrasts.

Goals, scientific challenges and research programs:

The aim of this master's internship is to initiate experimental work to clarify the link between intra-operative optical and pre-operative SRM biomarkers of cellular energy metabolism in brain tissue. The work will focus on the NAD cycle (NAD+/NADH).
31P MRS is used to monitor this metabolite (Skupienski 2020, Bainbridge 2013). NAD has the advantage of also being tracked by 1H MRS (De Graaf 2014). Optical and fluorescence spectroscopy can also be used to track this metabolite (Schaefer 2019, Bale 2016).
Work will focus on setting up experimental phantom measurements on both modalities with associated treatments. The aim is to determine detection limits and implementation difficulties in both modalities, and to begin to understand the differences between optical and NMR measurements. Indeed, the origin of the contrast of the NAD cycle in MRS and optics is different. The reduced form NADH fluoresces, but the oxidized form NAD+ does not. However, NADH can bind to proteins, which strongly modifies its fluorescence lifetime.
This work is part of a feasibility study on pre- and per-operative measurements of biomarkers of cellular energy metabolism. It will enable us to explore this link in a clinical context. It could potentially lead to a PhD.

Candidate profile :

- Competence in MRI/MRS physics and/or biomedical optics,
- Signal processing and data analysis (Matlab, Python),
- Competence and interest in experimental measurements.

Supervision :

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Bibliography :

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