INTERVENTIONAL IMAGING FOR NEUROSURGERY OF GLIOMAS BASED ON FLUORESCENCE AND OPTICAL SPECTROSCOPY.

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1. INTRODUCTION

Gliomas are infiltrative tumors of the central nervous system that account for more than 50% of malignant primitives brain tumors. The WHO classify them into 4 groups [1] and glioblastomas are considered as the strongest ones, highly infiltrative, with a survival rate not much higher than 14 months [2]. Studies showed that the survival rate was linked with the extent of resection [3, 4, 5] but a tradeoff between the resection of a maximum amount of tumor cells and the preservation of functional areas needs to be found during neurosurgery. Thus, interventional imaging is clearly relevant to help neurosurgeon intraoperatively.

The fluorescence of protoporphyrin IX (PpIX) is widely used to guide tumor resection through a surgical microscope since PpIX accumulates in tumor cells and emits reddish fluorescence under violet/blue excitation [6] (see fig. 1) but the sensitivity of this technic is limited when it comes to tumor margins. If fluorescence spectroscopy of PpIX is currently studied [7, 8], those studies only consider PpIX with a spectrum peaking at 634 nm. We demonstrated *in vitro* and *ex vivo* the presence of a second peak around 620 nm, attributed to a second state of PpIX and we showed that the use of the two states can help discriminate strong high-grade gliomas towards their isolated cells and towards low grade gliomas[9]. We now want to apply this *in vivo* to get new parameters to discriminate the different kinds of gliomas among themselves and against healthy tissue.

In parallel, to identify functional areas, one can either study the electrical response of neuronal cells or the haemodynamic response of the brain [10]. Indeed, we assume that brain activity leads to haemodynamic variations which latter yield small color variations however visible in processed color images, thus allowing identification.

For now, the two aspects are developed in parallel, with two different protocols that both need to be performed in the operating room.

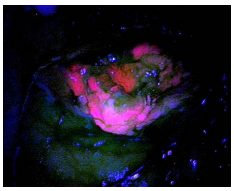

Fig. 1. Qualitative fluorescence of protoporphyrin IX

2. MATERIALS AND METHODS

For the identification of the tumor margins, a portable device has been designed, developed and characterized and is now used in the operating room. During surgical gesture, the neurosurgeon puts an optical probe on the tissue to be analyzed and light is transmitted and collected through the optical fibers. We thus measure the emitted fluorescence which is assumed to be the sum of known base fluorescence spectra corresponding to PpIX and other fluorescing products, whose relative proportions are fitted during post-processing as presented in [9].

For the identification of functional areas, a camera is used to acquire videos of the exposed brain while intentional or non intentional stimuli of the subject is made to induce cerebral activation. A preliminary step of image registration is required to get rid of small motions of the brain while being real time. Then, we apply a conversion matrix to convert colorimetric information to haemodynamic variations. The conversion matrix is based a model of light propagation in the brain and on the spectroscopic charateristics of the camera as done in [11]

3. RESULTS

For the identification of tumor margins, nine patients out of ten have been tested and we demonstrated *in vivo* the presence of the two states of PpIX. We can confirm that the state peaking at 634 nm is predominant in solid parts of grade IV glioblastoma and we can identify the presence of the state peaking at 620 nm in tumor margins. Moreover, in vitro results show that the two states have different quantum yields and excitation/emission spectra, which helps us caracterise them [12]

Before identifying functionnal areas on videos, our model for image registration enables us to get rid of repetitive motion of the brain while being real time and robust to the intrusion of a surgical tool [13]. The conversion matrix is not yet full implemented but preliminary work with a matrix from literature is promising

4. CONCLUSION-DISCUSSION

Interventional imaging devices are relevant to help neurosurgeons answer two major issues during brain surgery : the identification of tumor margins and the identification of functionnal areas. This project aims at answering those issues by the development of new tools that are promising. Fluorescence spectroscopy is more sensitive than the currently used fluorescence microscopy and gives more information. If the presence of a peak at 620 nm *in vivo* is obvious in this study, some post precessing is required to identify its relevance. Thus, we are comparing and discussing the response of solid tumor, tumor margins and healthy tissue and the help of the two states to discriminate the different tissues. Moreover, some theoretical work is required to discuss if the state peaking at 620 found *in vivo* still some form of PpIX or if it is Uro- or coproporphyrin. In parallel, the model we developed for video registration enables us to get rid of the brain's movement, while being real time but we now need to be sure we kept oxymetry information. To do so, a rigorous identification of functional area is still an ongoing issue so that we can compare the computed functional area to the theoretical one.

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