

Intraoperative optical imaging for neurosurgery guidance

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Intraoperative optical imaging for neurosurgery guidance

Context

- Cerebral tumor resection operation
- Neurosurgery with awake patients or patients under general anesthesia

Identification of functional brain areas

- Guide the surgical gesture
- Optimize tumor resection operation
- Avoid any cognitive impairments

Glioma resection

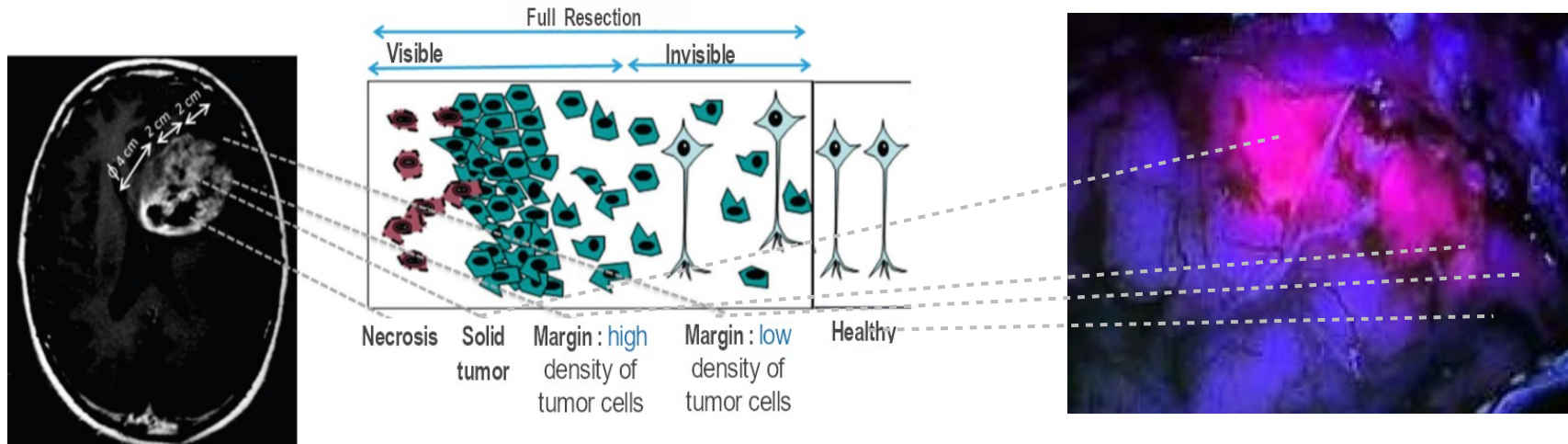
- Resection as complete as possible
- Distinguish low density tumor margin from healthy tissue



*Neurosurgical operation at Hospices
Civils de Lyon*

5-ALA induced PpIX fluorescence guided surgery of gliomas

Glioma identification during neurosurgery



Schematic of infiltration in high grade gliomas (HGG) [1]

Fluorescence of PpIX induced by 5-ALA in high grade glioma [2]

50 % primitive tumors of Central Nervous System; High-grade glioma mean survival rate: 14 months

Distinguish low density tumour margin from healthy tissue for a resection as complete as possible

Clinical drawbacks

Gold standard : fluorescence microscopy (5-ALA induced PPIX) is limited in sensitivity.

[1] L. Alston, et al., SPIE Proc. 10411, 2017

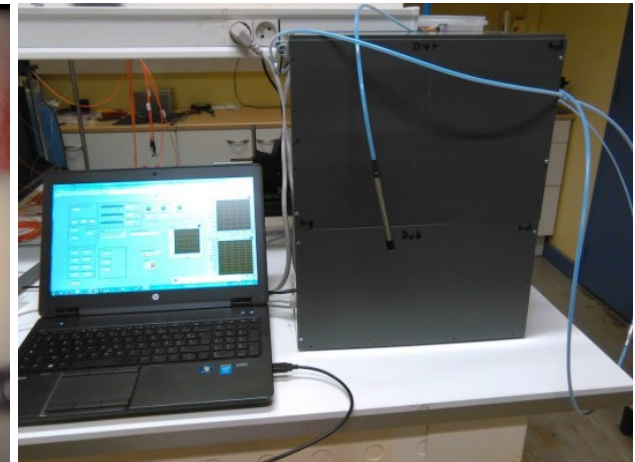
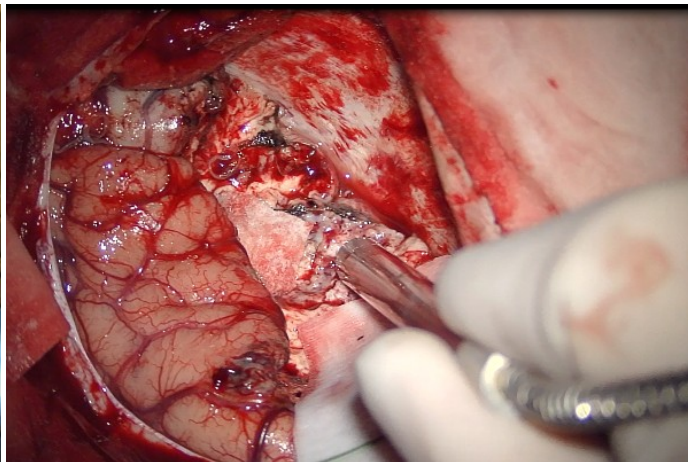
[2] W. Stummer *et al.* Acta Neurochir., 140(10):995–1000, 1998.

Glioma identification during neurosurgery

Intraoperative fluorescence spectroscopy set up

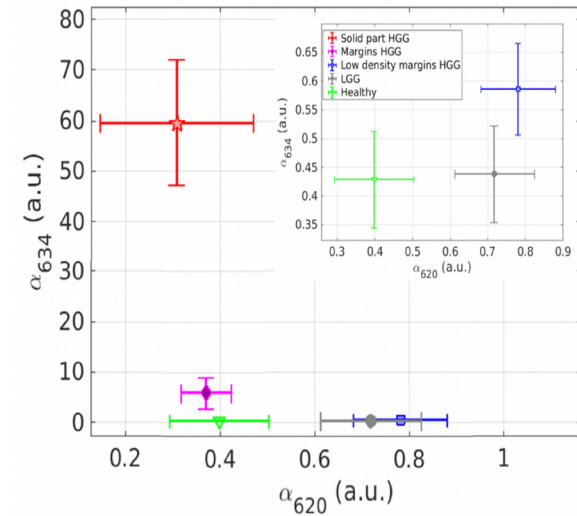
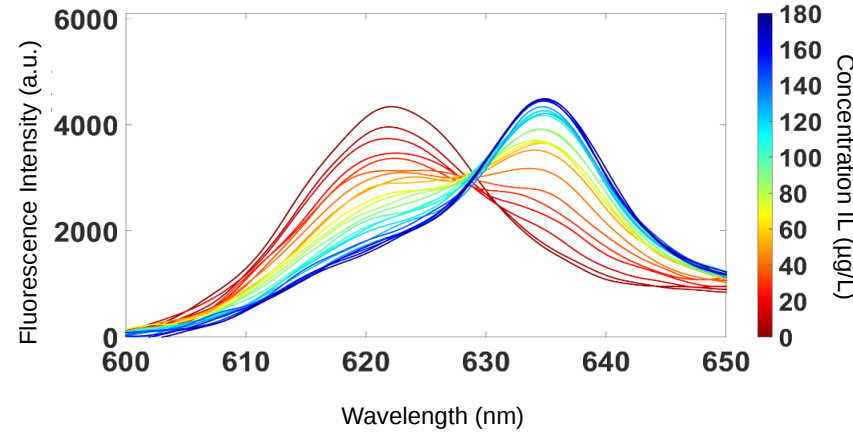
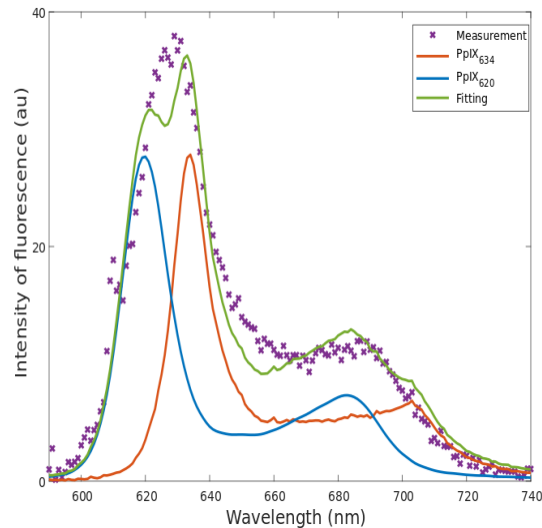
in vivo clinical study using 5-ALA induced Protoporphyrin IX fluorescence

- Clinical protocol approved by the ANSM and by ethical committee .
- Inclusion of 10 patients : 6 high grade glioma (HGG) and 4 low grade glioma (LGG)



Glioma identification during neurosurgery

Fluorescence Spectral Shape Analysis - « Blue shifted » PpIX spectrum in margins



Two fluorescing states of PpIX [2]

Fluorescent spectra of PpIX depends on micro-environment [3]

Improves group separability [4]

Expert model

$$S(\lambda) - \text{Autofluorescence} = \alpha_{620} [\text{PpIX}_{620}] S_{620}(\lambda) + \alpha_{634} [\text{PpIX}_{634}] S_{634}(\lambda)$$

- [2] Montcel et al. Biomed. Opt. Express, 4(4):548–558, Apr 2013
[3] L. Alston, et al., *Journal of Biomedical Optics*, 23(9), 097002, 2018
[4] L. Alston et al. Biomed. Opt. Express, 10(5):2478–2492, May 2019.

Glioma identification during neurosurgery

Data driven biomarker model - Machine Learning of PpIX spectra

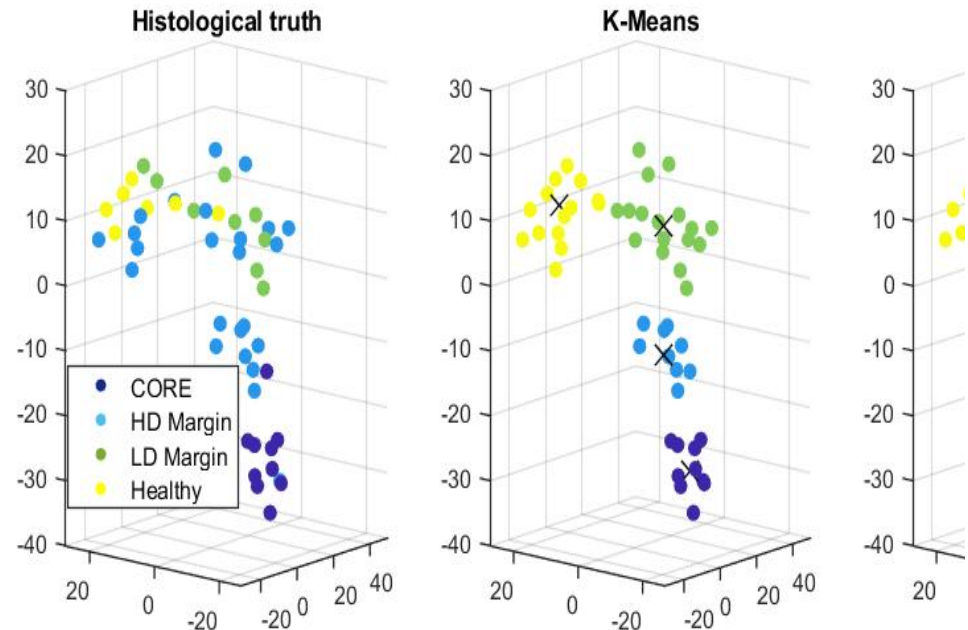


Dimension reduction : T-SNE

Unsupervised classification : k-Means

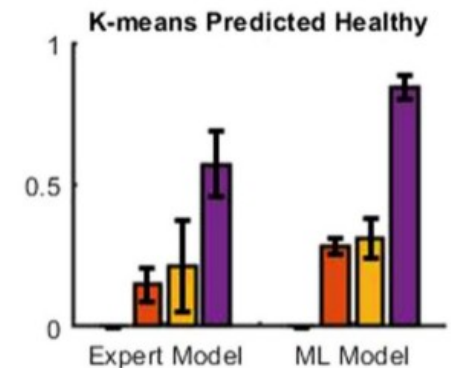
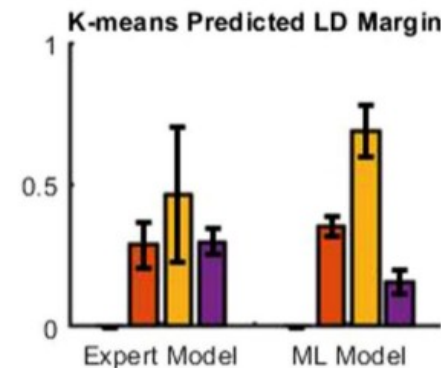
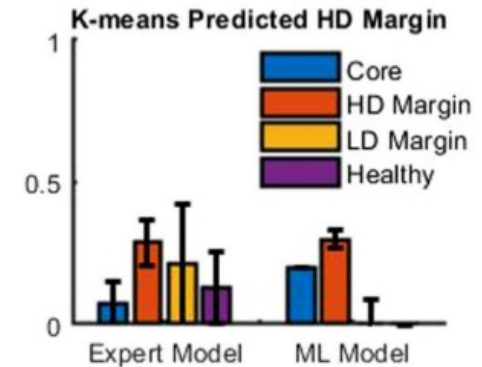
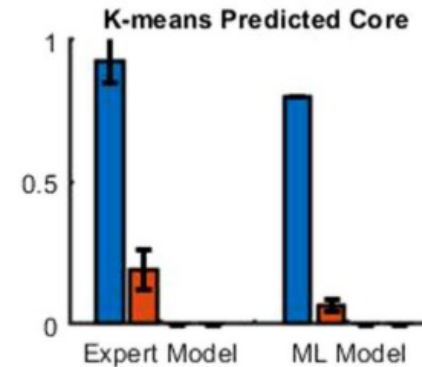
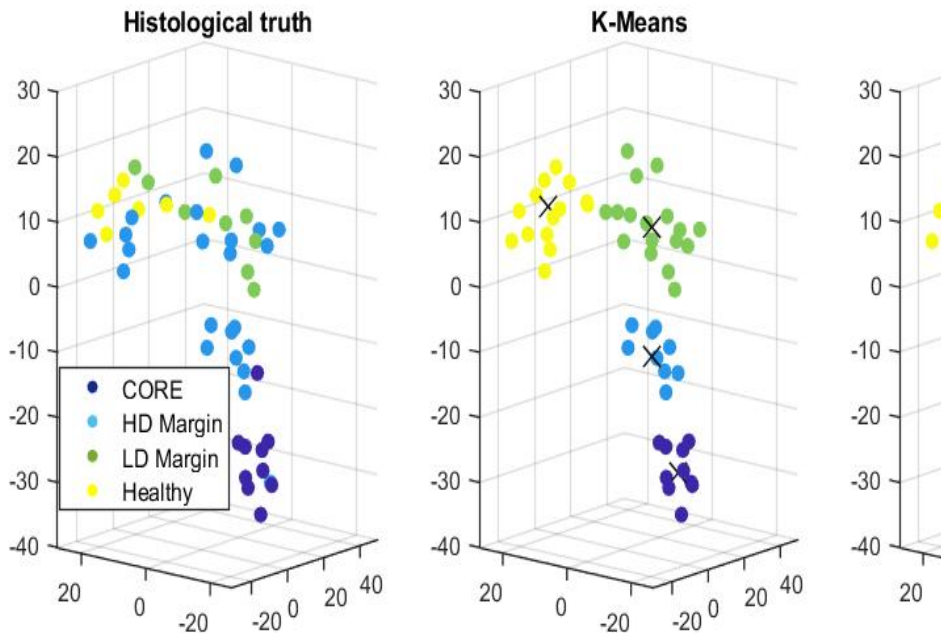
Results :

- Data driven model confirms expert based biomarker :
 - Predominance of PpIX 634 peak
 - Autofluorescence
 - Diagnostic relevance of blue shift
- Clusters aligned along with the ordinal severity of gliomas



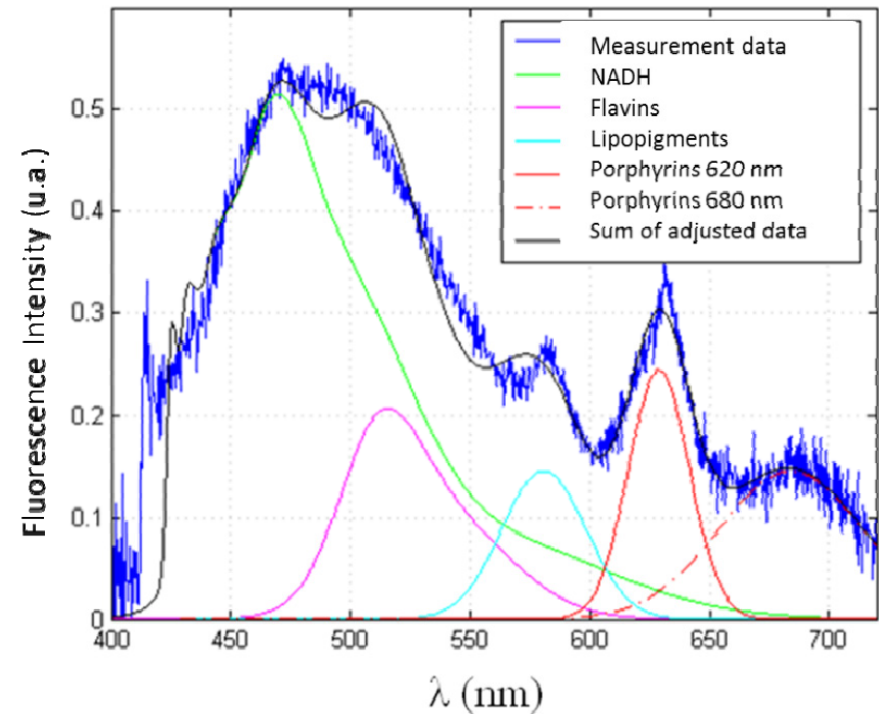
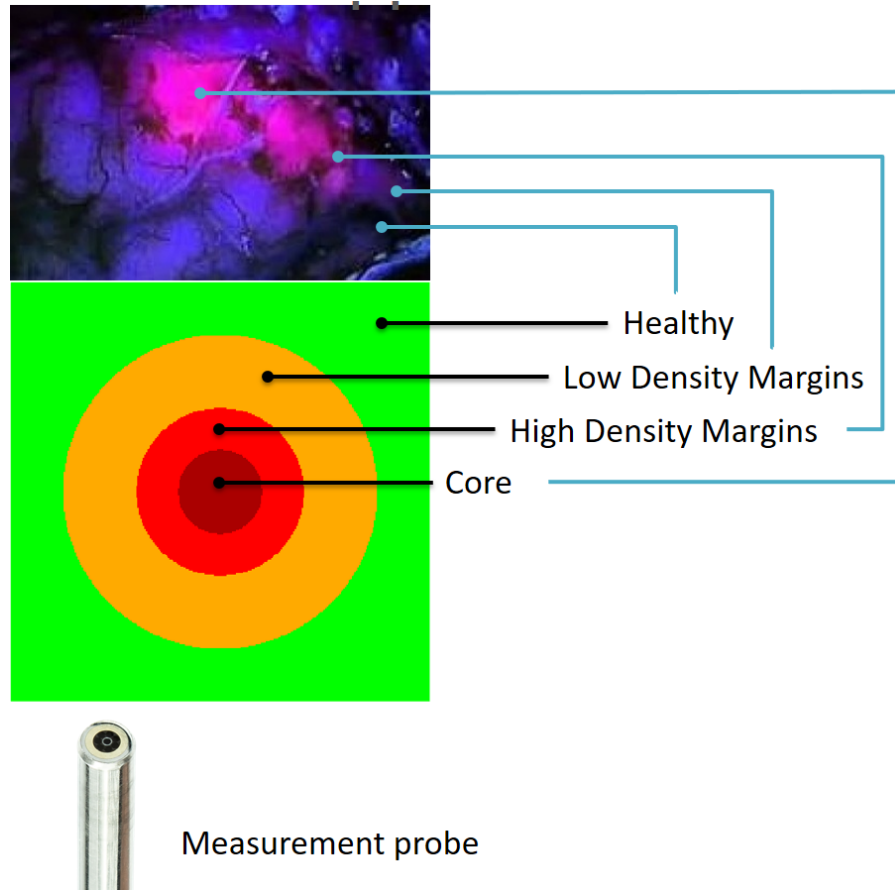
Glioma identification during neurosurgery

Data driven biomarker model - Machine Learning of PpIX spectra



Glioma identification during neurosurgery

Estimation of 5-ALA-induced PpIX using multiple excitations wavelength – A phantom study

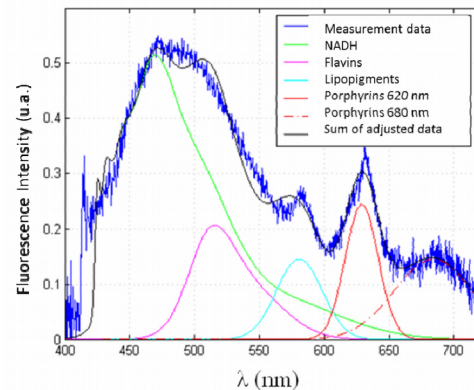
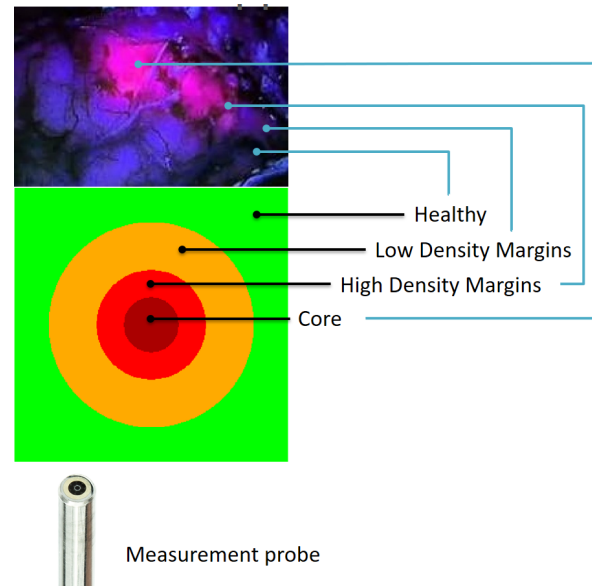


Fluorescent spectrum acquired at 405 nm and five fluorophores [5]

Evaluate the effect of auto-fluorescence crosstalks on PpIX fluorescence estimation

Glioma identification during neurosurgery

Estimation of 5-ALA-induced PpIX using multiple excitations wavelength – A phantom study



Fluorescent spectrum acquired at 405 nm and five fluorophores [5]

		Specificity
Classified	GT	0,84
	BF ₁	0,00
	GB ₁	0,01
	BF ₂	0,00
	GB ₂	0,00
EB ₂		0,81
Outside		
No Crosstalk		
Inside		
Crosstalk		

Without auto-fluorescence crosstalks:

- State of the art models: Good estimation of PpIX 620 and 634
- EB model: Good estimation of PpIX 620 and 634

With auto-fluorescence crosstalks:

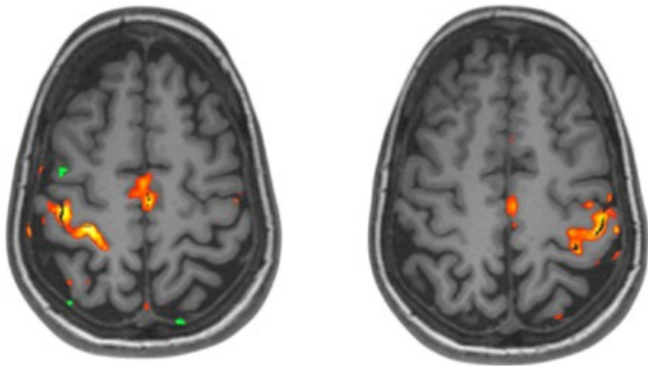
- State of the art models: Loss of specificity (bad estimation of PpIX 620 and 634 in healthy tissues)
- EB model: Good estimation of PpIX 620 and 634

Intraoperative functional neuroimaging

Intraoperative functional neuroimaging

Gold standard

Functional Magnetic Resonance
Imaging (fMRI) [1]

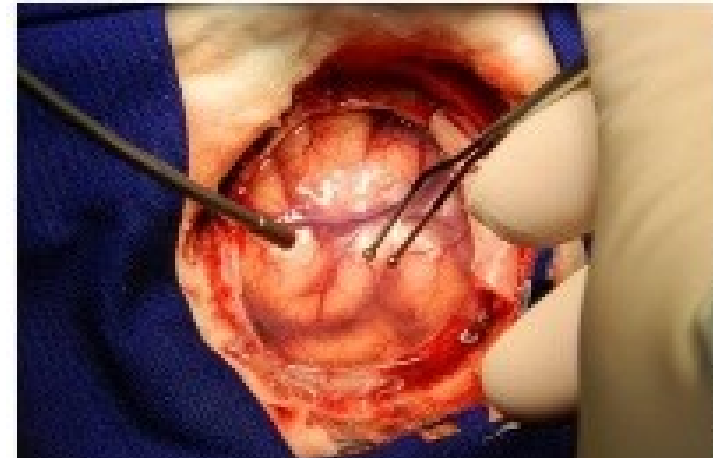


Control hand motricity [2]

Preoperative gold standard

Rarely used during neurosurgery: Brain shift [3]

Direct electrical brain stimulation [4]



Electrical stimulation of motor cortex (hand) [5]

Intraoperative gold standard

Punctual detection, epilepsy seizures

**Need for an optical imaging technique to identify patient's
functional brain areas during neurosurgery**

[1] S. Ogawa et al. (1992) Proc of the National Academy of Sciences 89(13)

[2] T. A. Yousry et al. (1997) Brain 120, 141–157.

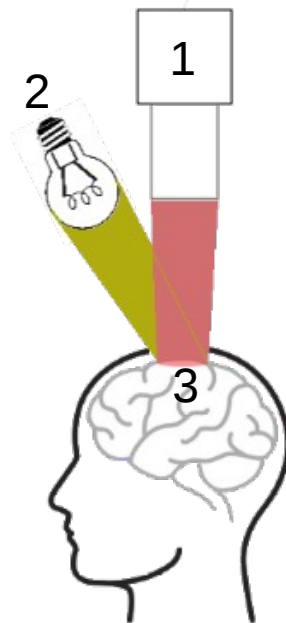
[3] I. Gerard et al. (2017) Medical Image Analysis 35, 403–420.

[4] W. Penfield et al. (1937) Brain 60(4)

[5] W. S. Palva (2012) Neuro. Dis. Treat. 8 197-201

Intraoperative functional neuroimaging

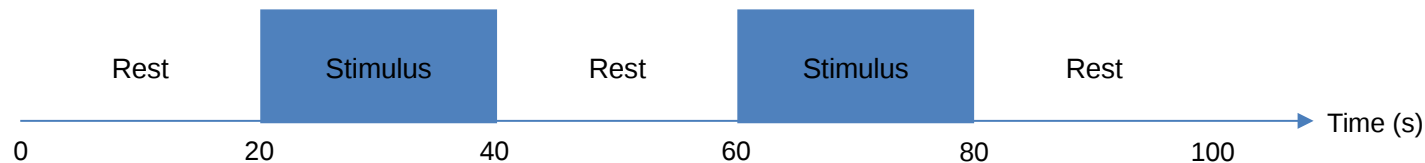
Experimental setup



- 1 - RGB camera
- 2 - Light source
- 3 - Exposed patient's brain



Task-based procedure



Resting state procedure



Intraoperative functional neuroimaging

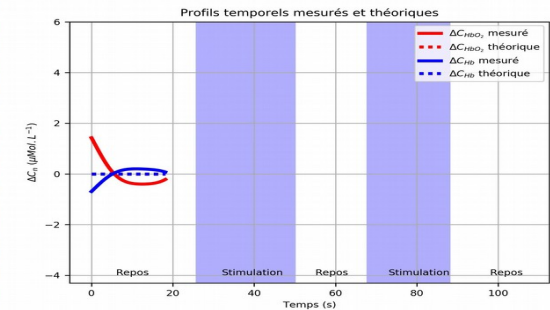
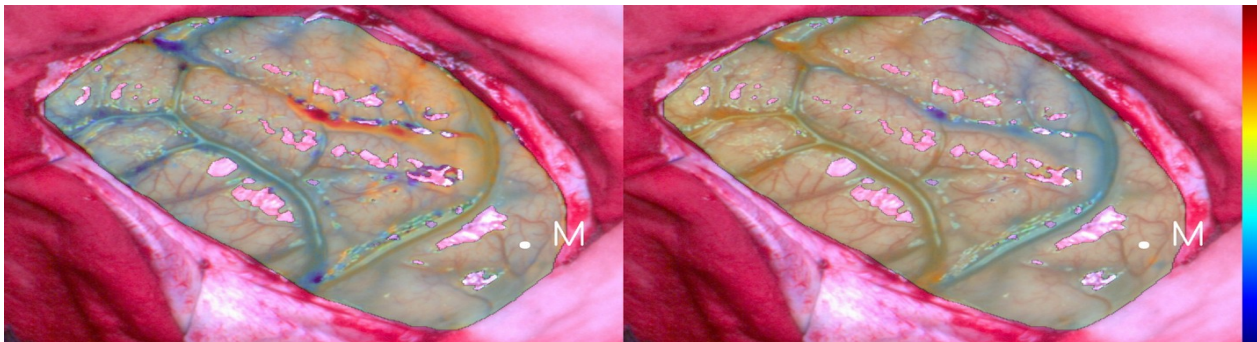
Hemodynamic monitoring during a task-based procedure

$$\Delta C_{HbO_2}$$

$$\Delta C_{Hb}$$

5 $\mu\text{Mol/L}$

*Hemodynamic time courses
measured at point M*



M : Motor area (hand) identified by electrical brain stimulation

-5 $\mu\text{Mol/L}$

Model of brain hemodynamics

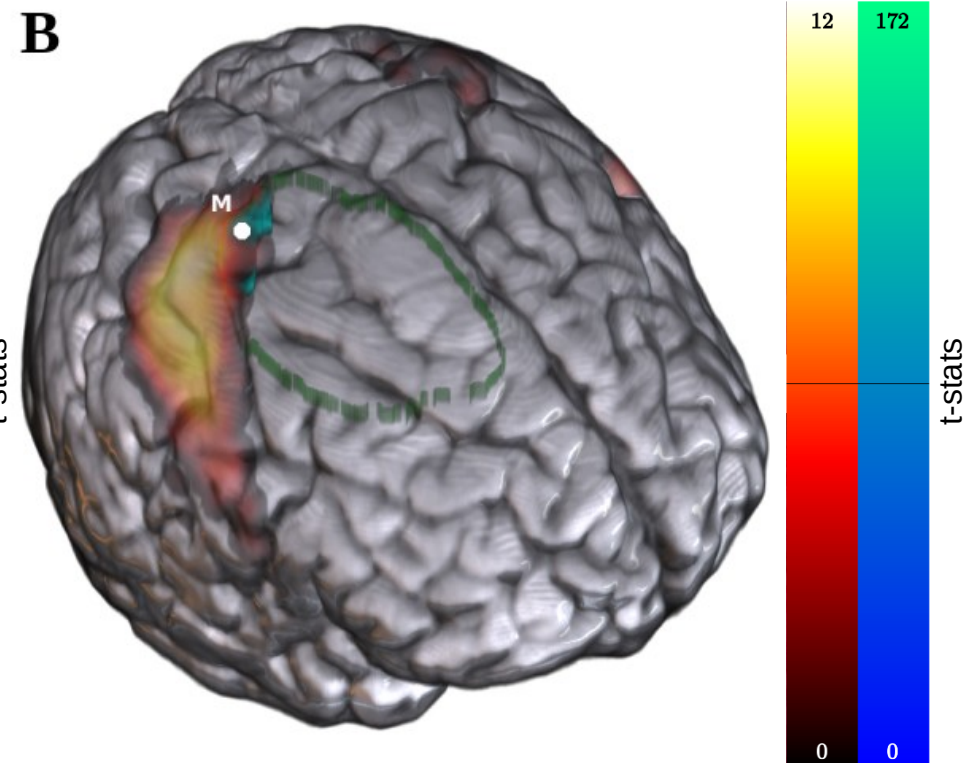
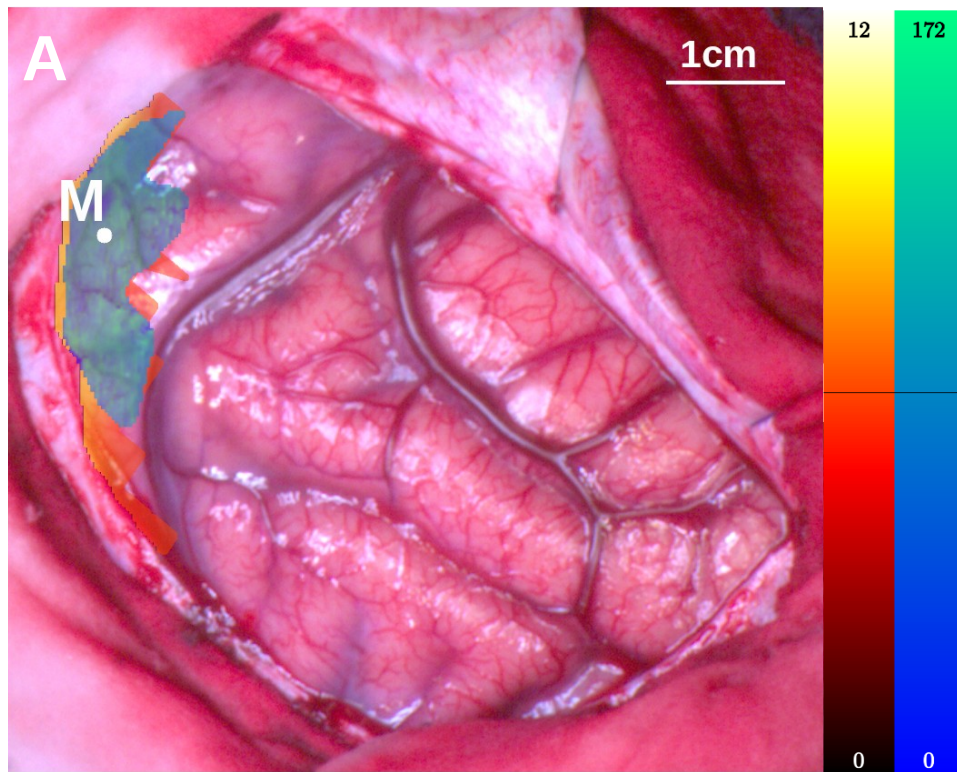
Need to define an operational tool for identifying
the functional brain areas during neurosurgery

Intraoperative functional neuroimaging

Identification of functional brain areas during a task-based procedure

Task-based functional brain mapping using
intraoperative optical imaging and preoperative fMRI

Preoperative task-based functional brain
mapping using fMRI



M : Motor area identified by electrical stimulation

Intraoperative functional neuroimaging

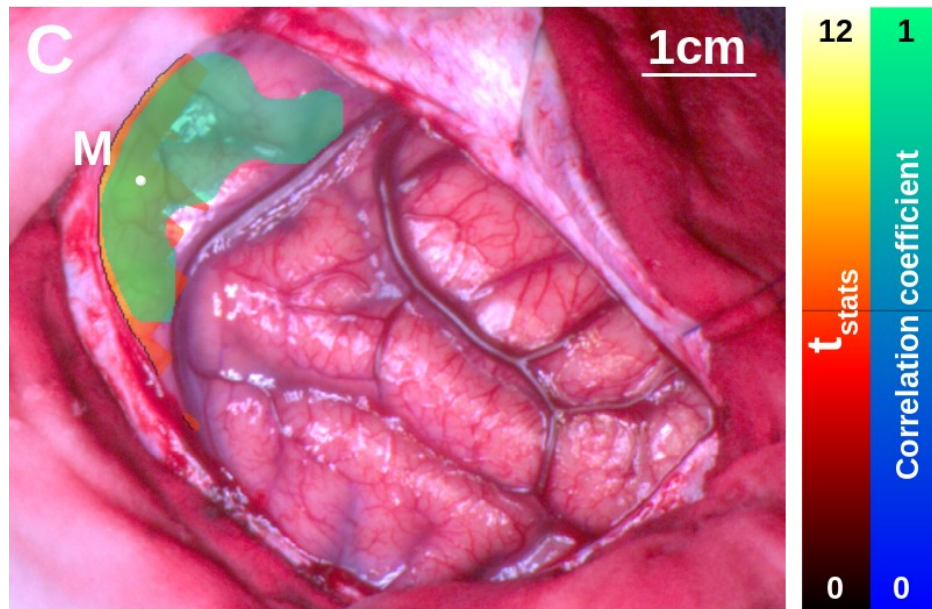
Resting-state: Analysis of the slow hemodynamic fluctuations ($<0.1\text{Hz}$)

Advantages vs task-based procedures: Data acquisition is shorter, less complex, and less demanding for the patients, especially for those unable to perform the tasks

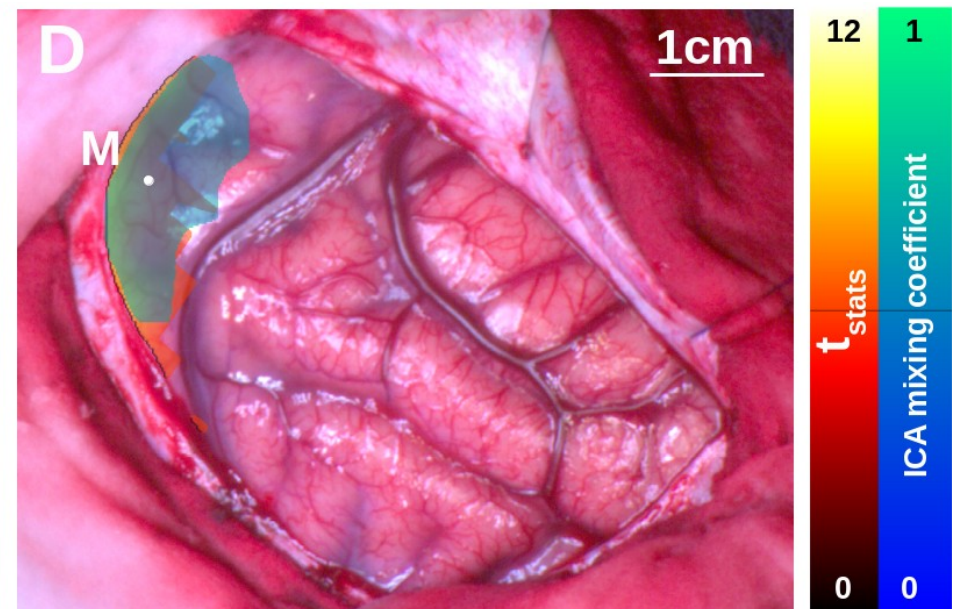
Applications of resting state fMRI techniques with intraoperative optical imaging
Seed correlation [6], Independent component analysis [7,8]

Intraoperative resting-state functional brain mapping using **optical imaging** and **preoperative task-based fMRI**

Seed correlation



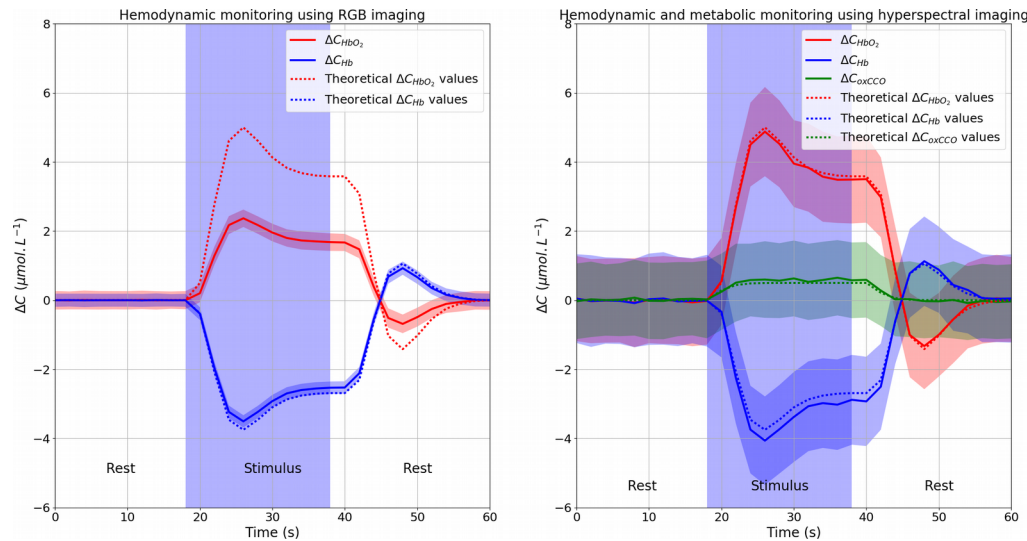
Independent Component Analysis



M : Motor area identified by electrical stimulation

Hemodynamic and metabolic brain mapping

Numeric brain phantom : Evaluate the quantification performance of RGB and hyperspectral imaging



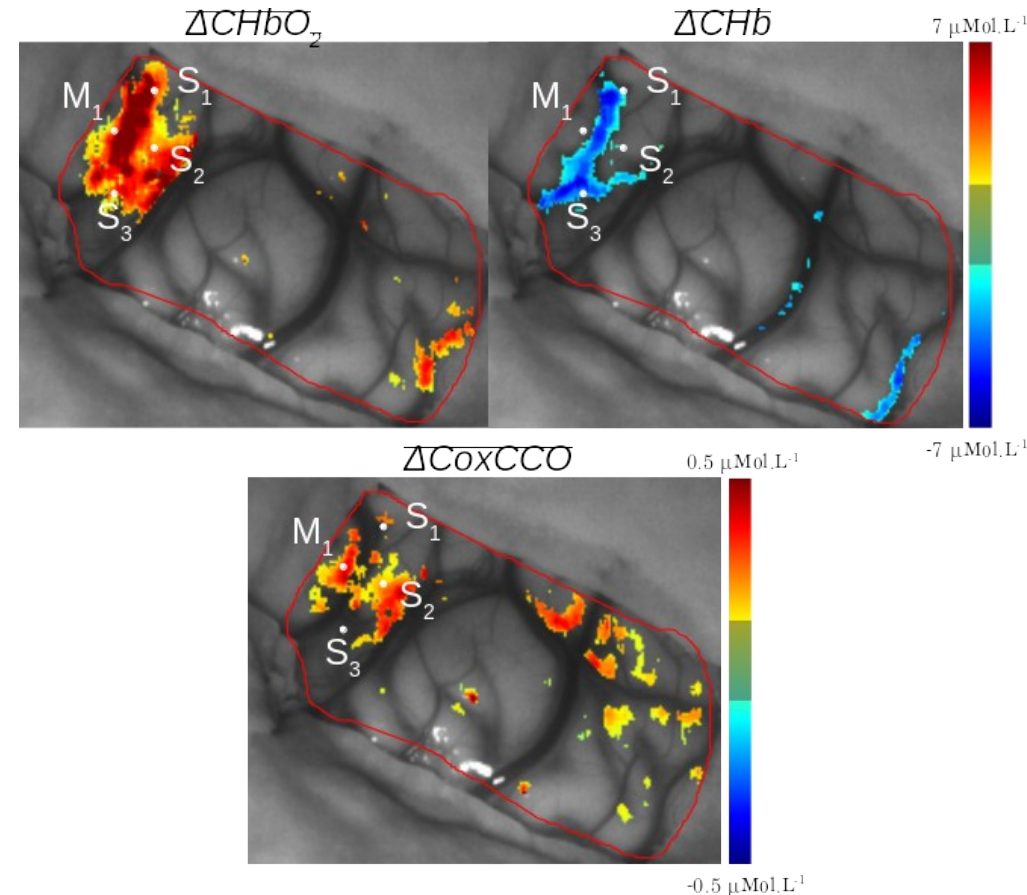
RGB imaging

- Adapted for hemodynamic monitoring
- High accuracy to quantify deoxy-hemoglobin (4% errors)

Hyperspectral imaging

- Adapted for hemodynamic and metabolic monitoring
- Specificity for oxCCO estimation (700 to 900nm)

Quantitative hemodynamic and metabolic brain mapping



Intraoperative optical imaging for neurosurgery guidance

CREATIS

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David Meyronet



Hôpitaux de Lyon

CHU Saint Etienne

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Lab. LARIS

David Rousseau



Fundings



European project HyperProbe

Intraoperative quantitative monitoring of brain activity
and functions using hyperspectral imaging

Post-doc and phd positions open in october 2022

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