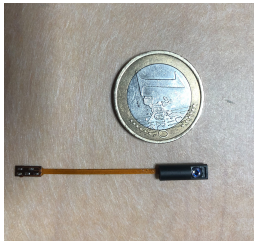
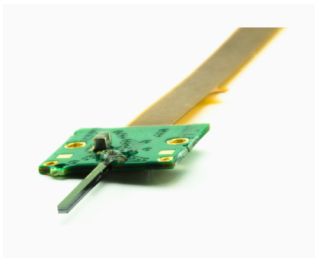
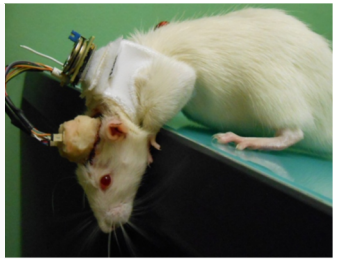
Sondes optique et isotopique pour la caractérisation physiologique et pathologique des tissus cérébraux



darine.abihaidar@ijclab.in2p3.fr





Axes scientifiques

Approches instrumentales multimodales basées sur la miniaturisation des systèmes dédiées à la caractérisation tissulaire

- Isotopique
- Optique

- Conditions d'exploitations extrêmes
- Systèmes d'imagerie intégré

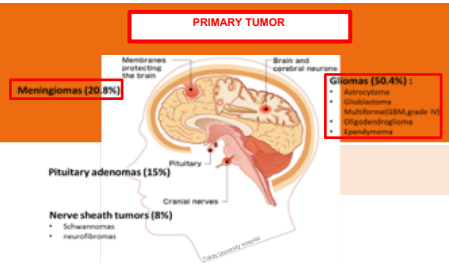
Projet IMOP : Imagerie fibrée multimodale et analyse clinique des tumeurs cérébraux

Projet MAPSIC : sonde intracérébrale pour l'imagerie comportementale chez le petit animal

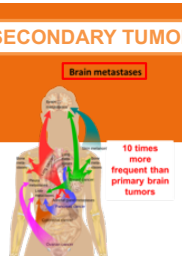
caractérisation tissulaire

- Physiologique
- Pharmacologique
- Pathologique

Projet IMOP : Enjeux



Même traitement pour tous les types de tumeurs cérébrales

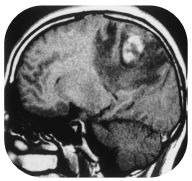


Patient with symptoms

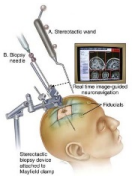


Headache, seizure, moodiness, ….

Diagnosis



MRI, CT-scan, …



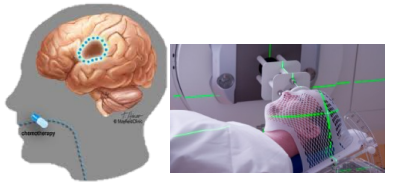
Frameless biopsy

Surgery 2



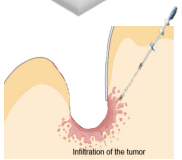
Critical point in brain tumor management

Long-term treatment



Radiotherapy, chemiotherapy

Surgery 1

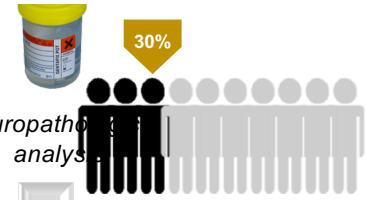




Neuropathological analysis



5-year survival rate : **brain tumors**



Neuropathological analysis

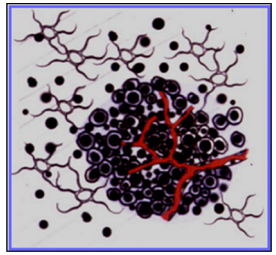
National Cancer Institute
American Cancer Society's
Cancer Facts & Figures 2018

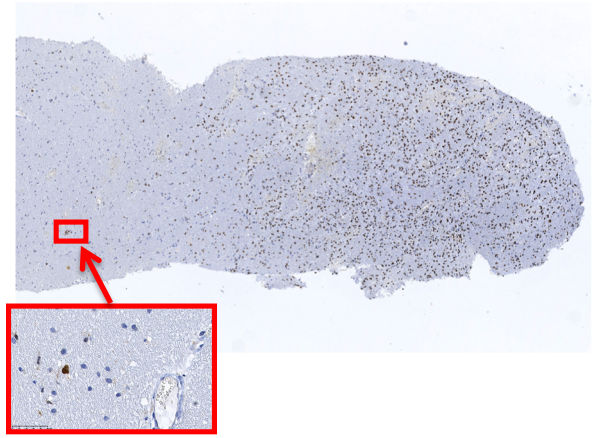
Response @ 2 weeks ago.



Enjeux thérapeutiques: Exérèse complète

– Tumeurs **infiltrantes**





– Délimitation difficile des berges → tissus sains et infiltrés ≃ apparence visuelle
– Techniques proposées *per-opératoire* → manque de résolution et de précision y compris examen extemporané.
– Histologie: Réponse quelques jours après l'opération

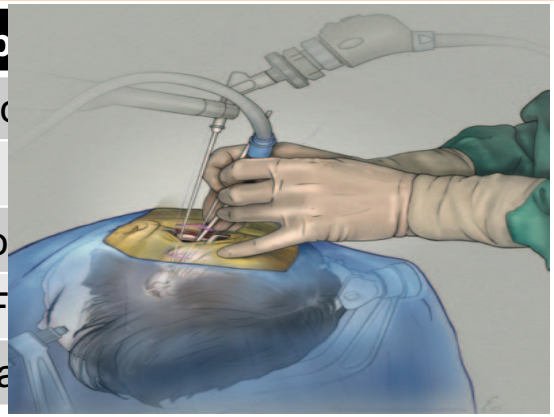


Human judgment

Solution proposée

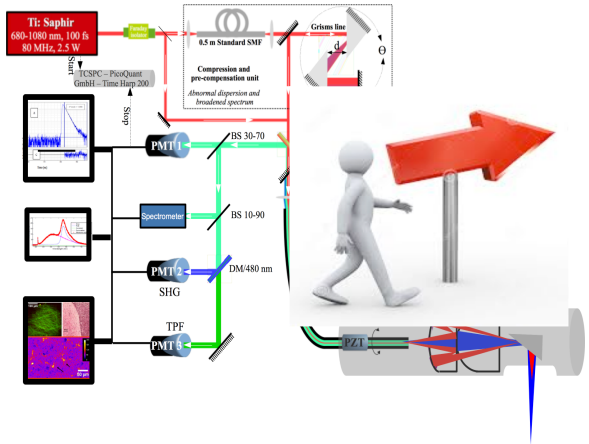
Needs	
In vivo Imagin	omic
High reso	ical
Miniaturiz	tro
Multimoc	G,F
Wide field	foca

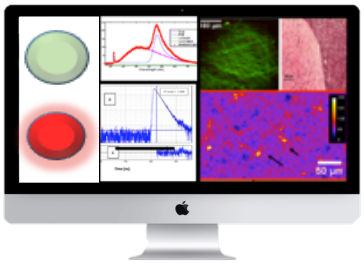




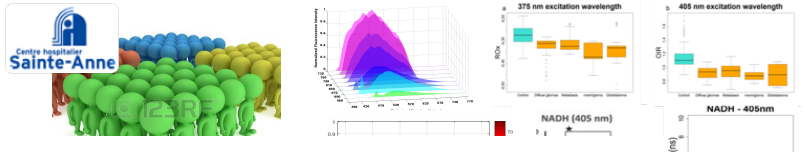
Solution
Multimodal Nonlinear Endomicroscope

Instrumental development (OGINS)

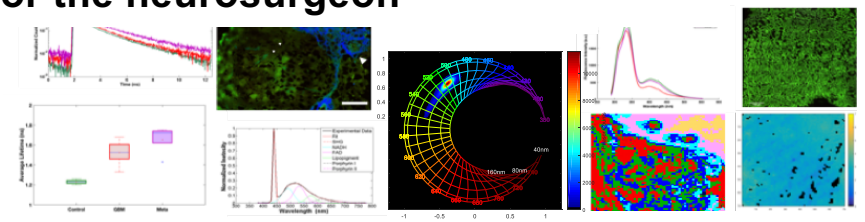




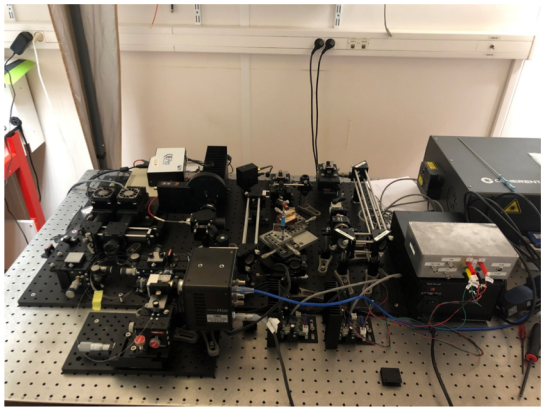
Large Database & in depth analysis (DATAbase)



Discriminative, fast and reliable tool for the neurosurgeon

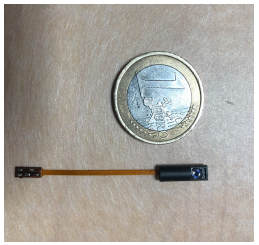


Développement instrumental

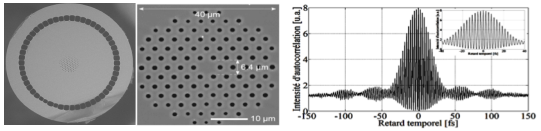


Divers verrous scientifiques à lever :

- Système de balayage miniature, innovant et biocompatible
- Optique Varifocale
- Multimodalité de détection
- Compatibilité utilisation clinique par des praticiens
- Maintenir un confinement temporel et spatial de l'impulsion après 5 m de fibre optique

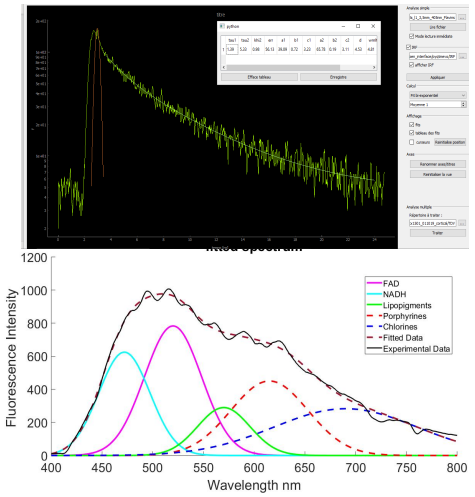






Premier prototype





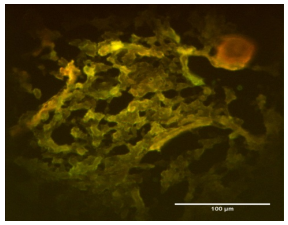
Base de données tissulaires: de l'UV à l'IR



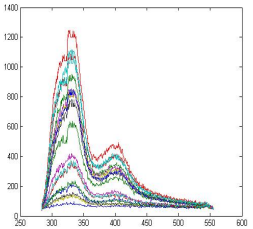
A

SOLEIL SYNCHROTRON — DISCO — 250-350 nm

Wide Field Microscopy



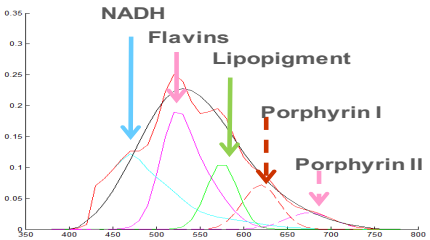
Spectroscopy



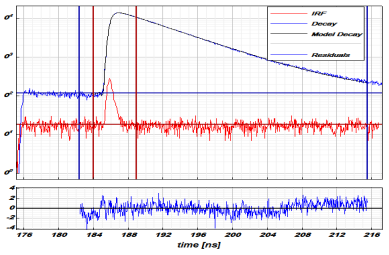
B

Centre hospitalier Sainte-Anne — 375-405 nm

Spectral analysis



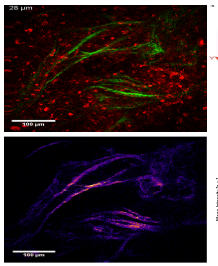
Lifetime analysis



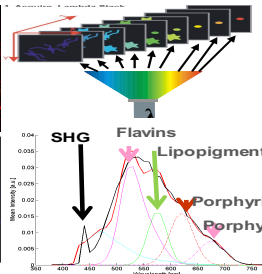
C

PIMPA — 690-1040 nm — Cerveau et Cognition — Imagerie et modélisation en neurobiologie et cancérologie

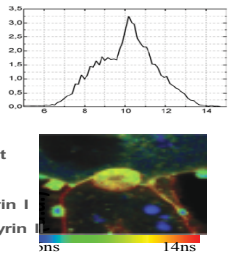
Fluorescence and SHG imaging



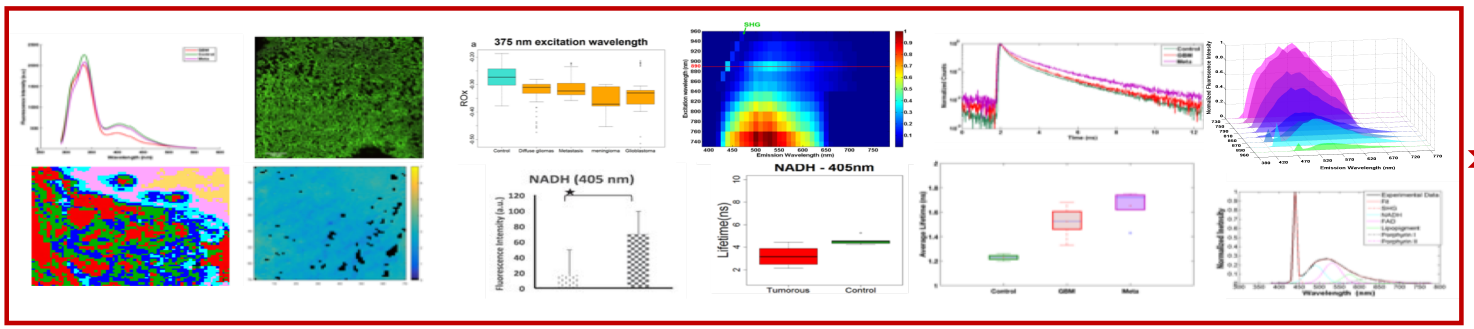
Spectral imaging



FLIM

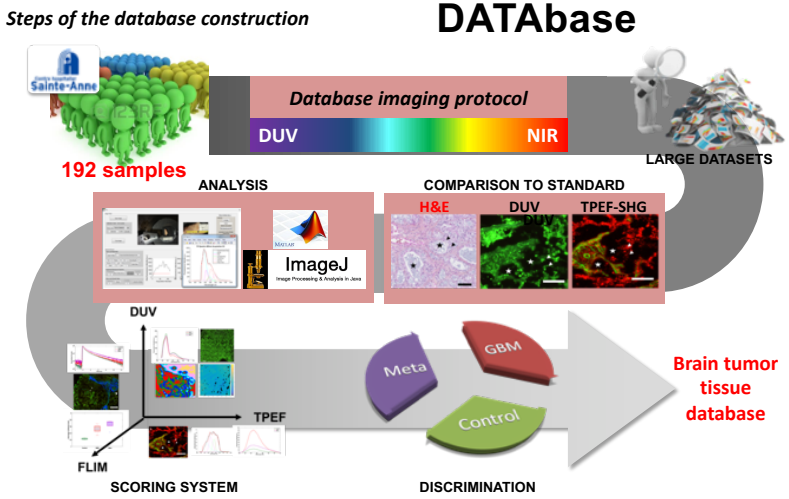


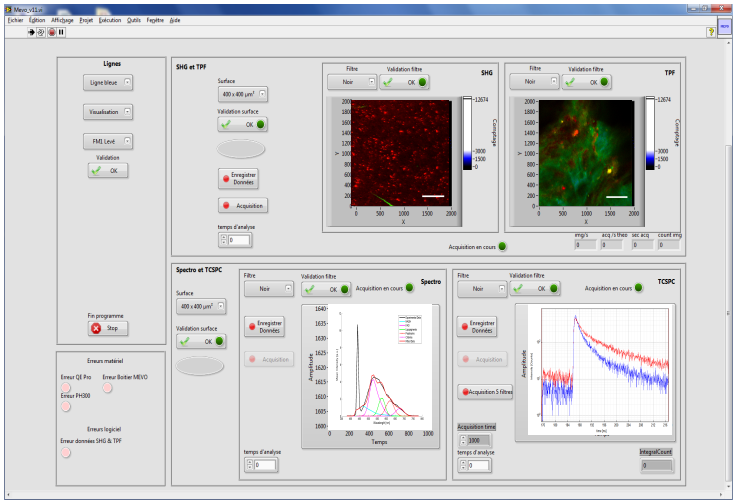
Advanced data analysis





Base de données / Interface homme-machine

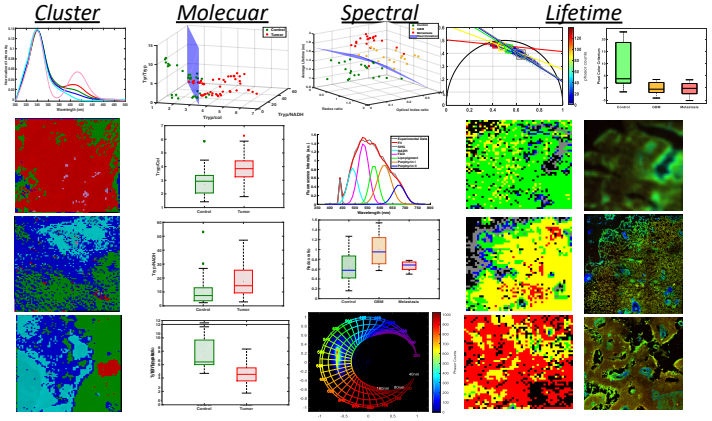




Intelligence artificielle **DATAuse**



Deep-UV analysis **NIR analysis**

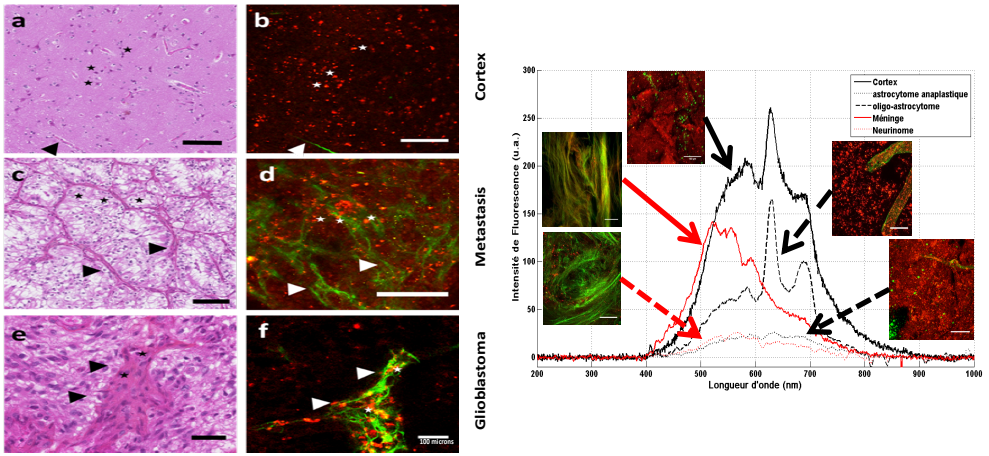


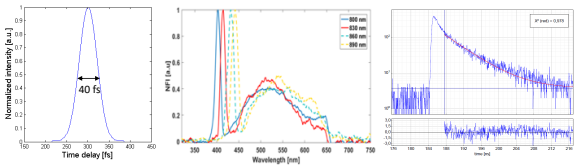
Valorisation/financement

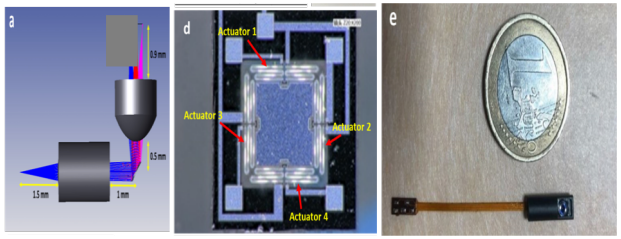
Valorisation :

- 25 Revues Internationales ISIS ou SCOPUS
- 27 proceedings
- 2 chapitres de livre
- 10 conférences invitées
- 3 présidences de session dans des conférences internationales
- 1 vidéo grand public
- 1PI

https://www.synchrotron-soleil.fr/fr/videos/lumiere-sur-les-cellules-tumorales





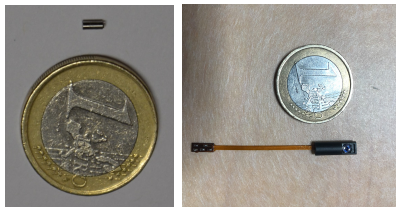


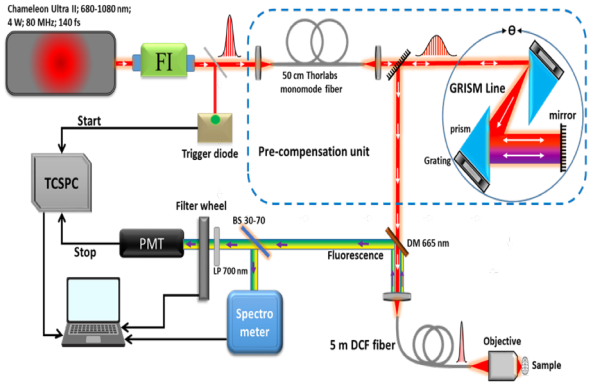
Financements obtenus :

- AP Plan Cancer (projets MEMBO, MEVO, IMOP): 640 keuros
- Mission pour l'interdisciplinarité "l'instrumentation aux limites"- CNRS: 63 keuros
- Cancéropôle Île de France 65 keuros
- AP in2p3: 20 keuros
- WP3- FLI "Imagerie Interventionnelle": 48 keuros
- Contrat de prestation de service –Société NANOBACTERIE: 30 Keuros
- Labex P2IO - Physique des 2 infinis et des origines de l'université Paris Saclay

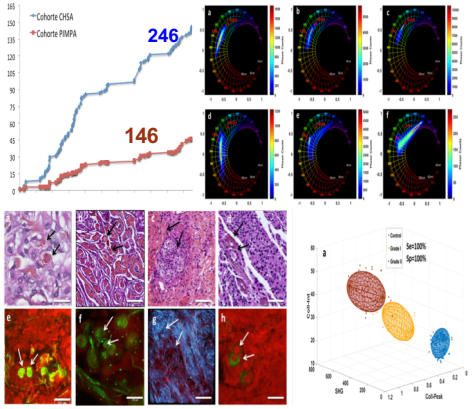
Perspectives

Instrumentation





Banque de donnée





OPTIPen



De l'étude pilote vers l'étude clinique

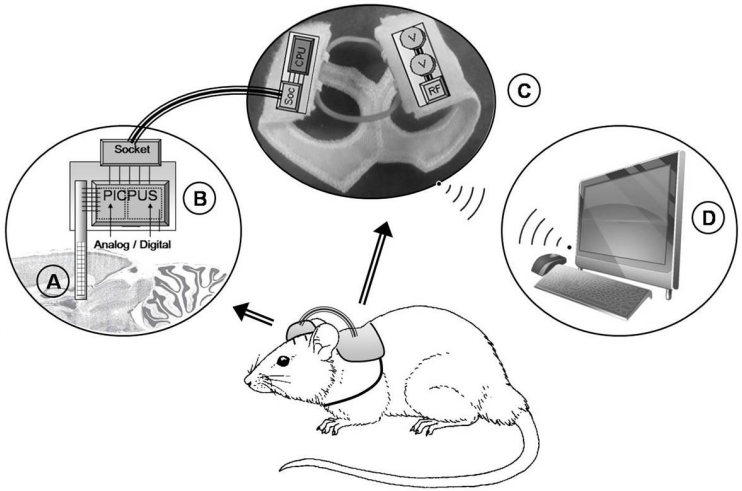
valorisation

PI
&
SATT
&
prematuration
CNRS

Projet MAPSIC

Développement d'une sonde intracérébrale télémétrique MAPSIC pour la mesure cinétique de radiotraceurs PET chez l'animal éveillé et libre de ses mouvements

IJC Lab

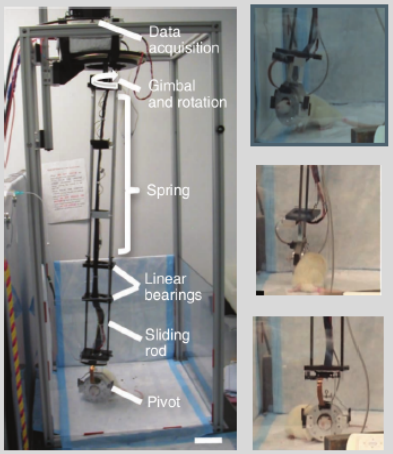


MAPSIC: Contexte

imagerie moléculaire cérébrale dédiée à l'animal éveillé:
limitation pour l'imagerie préclinique car nécessite l'anesthésie ou la contention de l'animal

Emergence d'outils pour la neuroimagerie comportementale

RatCAP



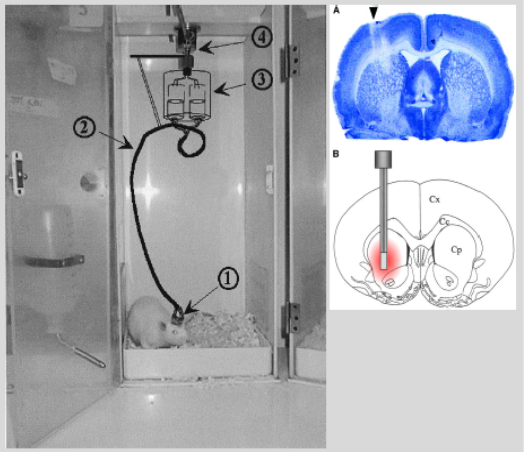
Schulz et al., Nature Methods, 2011.

Motion tracking



Spangler-Bickell et al., Phys. Med. Biol., 2016.

Beta Microprobe



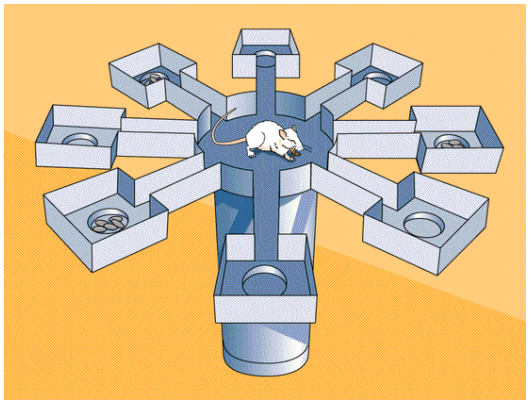
Pain et al., PNAS, 2002.

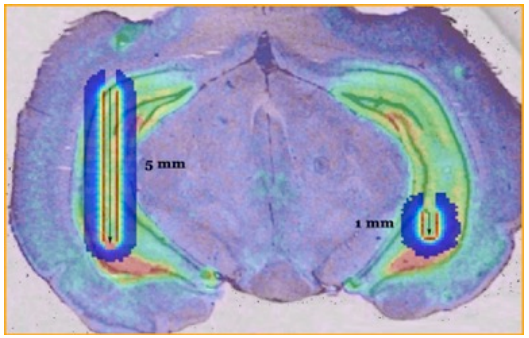
Objectifs du projet MAPSIC

Préserver une totale autonomie pour l'animal

Développer une sonde intracérébrale pixelisée compatible avec la detection β+

Limiter la sensibilité au rayonnement γ et la lumière visible





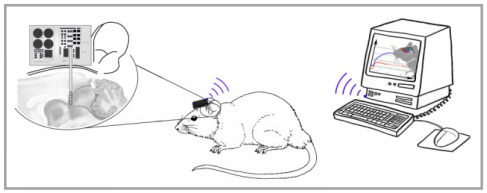
Structuration du projet MAPSIC

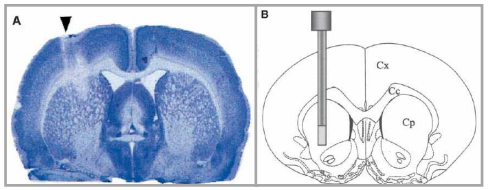
Workpackages et taches

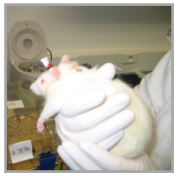
- Task 1: Développement d'un préprototype pixelisée CMOS (basse et haute tension) et caractérisation électronique et physique
- Task 2: Développement et intégration de la sonde (format sonde, sac à dos, acquisition)

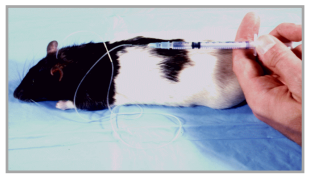
- Task 3: Détermination de l'impact des sondes implantées sur le long terme (physiologie et sensibilité) et étude échauffement
- Task 4: Modélisation du détecteur et de son exploitation biologique

- Task 5: Validation pharmacologique de la sonde et comparaison avec PIXSIC, microPET et éveillé/anesthésié
- Task 6: Validation physiologique et comportementale de la sonde







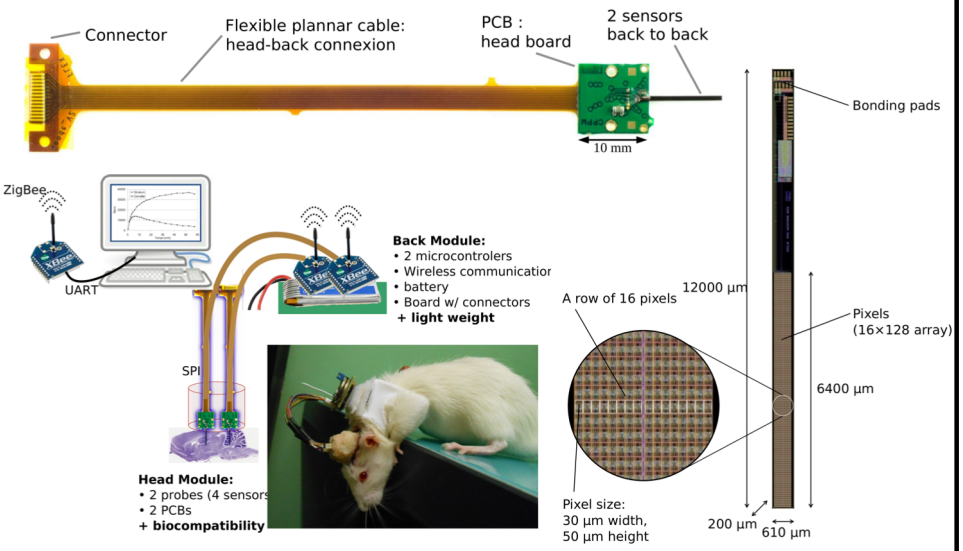






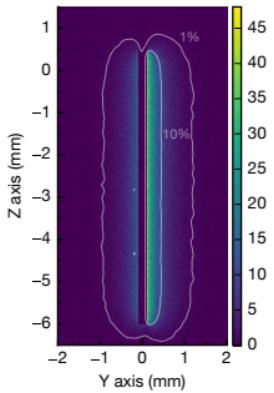
MAPSIC: premiers résultats

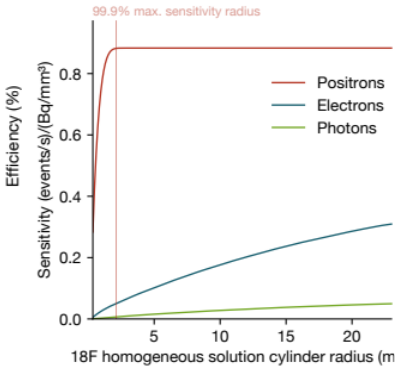
MATERIALS & METHODS

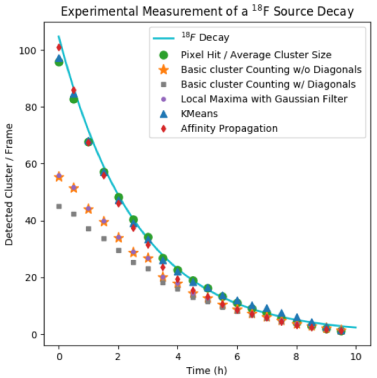


- First probe prototype : 2 dedicated MAPS sensors on a single PCB
- MC simulation for physics validation in brain geometry and water phantoms

RESULTS





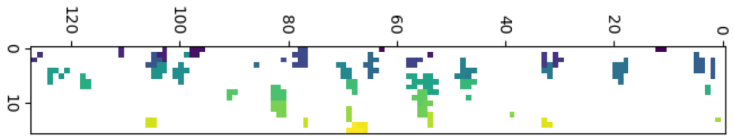


Short range of β^+ allows measurement of local concentration of radiotracer (simulation)

High sensitivity to β^+ (simulation)

Count rate linearity correction

Events counting from clusters in CMOS images



FINANCIAL SUPPORT

- Mission interdisciplinaire Défi instrumentation aux limites – CNRS (2015 et 2017)
- WP3- FLI Imagerie Interventionnelle (2017-2019)
- AP IN2P3 (2015-2018)

PUBLICATIONS

J. Heymes, et al. NIM A, 911, 2018

L. Ammour, et al. IEEE TRMPS, 2019

L. Balasse, et al. Mol Imaging Biol, 17(2):163-167 (2015)

J. Märk, et al. Phys Med Biol, 58: 4483-4500 (2013)

Perspectives

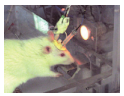
MAPSIC: un outil robuste pour l'imagerie in vivo



Neuroscience

Validation inter-modalité
Protocole original de neuroimagerie comportementale

Pré-Test





Cocaïne

Salin
e



Conditionnement



Test



Test de préférence de place conditionnée

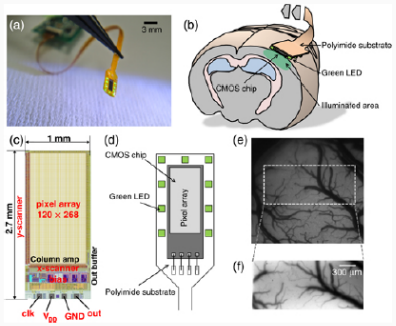
Instrumentation

Adaptation vers imagerie per-op



Capteurs à pixels actifs pour l'imagerie médicale

Capteur Cmos pour sonde optique cérébrale



Vers plus de multimodalité

valorisation

Brevet européen: Dispositif de détection de la désintégration de radioisotopes dans un tissu biologique

