Instrumental and numerical developments for health-related activites at IN2P3

E. Testa (IP2I) on behalf of the community

IN2P3 scientific committee, July 8, 2025

Particles/nuclear physics and “physics for health”: Same tools and methods

Instrumentation

- Particle Detection: Detectors + Electronics and acquisition systems + Data analysis
- Beam lines: Beam physics and diagnostics (irradiation platforms)

Numerical developments

- Monte Carlo simulations of particle transport
  - Detection system design and interpretation of the experimental data
  - Modeling the impact of radiation on living organisms
- Statistical physics approach to predict the effect of radiations (eg. cell survival)

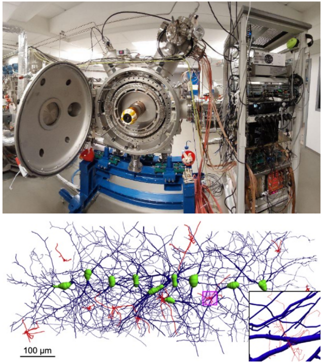


Fig. 1: Top: XEMIS2 camera at the Nantes University Hospital. Bottom: Geant4-DNA simulations of ion tracks and radiolysis within a neural network.

Medical applications of Particle Physics: The "pillars"

@CERN

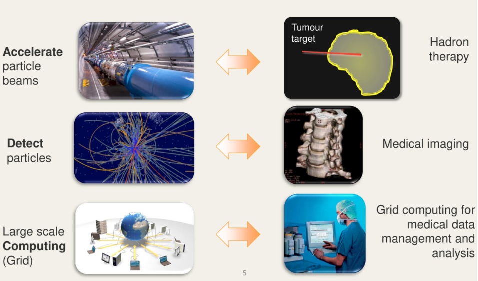


Fig. 2: The 3 "pillars" according CERN (from Sparsh Navin 2014, CERN – Knowledge Transfer Life Sciences Section)

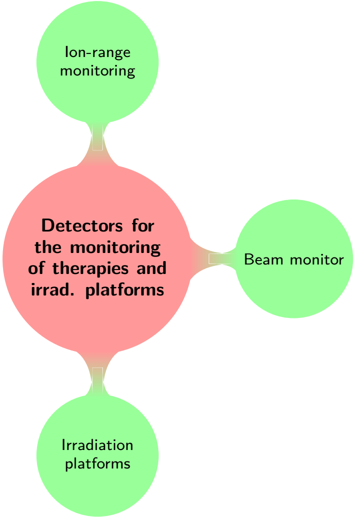
@IN2P3

- Same considerations although topics are slighlty different
- NB: Arrows in both directions. Examples of transfer from medical to fundamental physics in IN2P3
  - "TOF-PET" ASIC → CMS ECAL timing layer electronics
  - Liquid Xenon for PET @ LPSC (early 2000's) → Dark matter detection @ SUBATECH

Requirements of medical applications

- Need for close interdisciplinary connections with biologists, chemists, physicians. . .
- Need to go beyond the HE technology
  - Technical challenges (10 ps challenge for TOF-PET, FLASH dosi. . .)
  - Harsch conditions (implanted detectors, FLASH dosi. . .)
  - Clinical constraints (hadronth., theranostics. . .)

1st type of dev.: "Detectors for the monitoring of therapies and irrad. platforms"



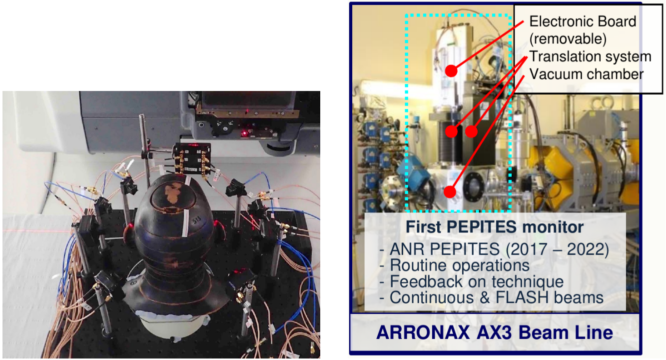
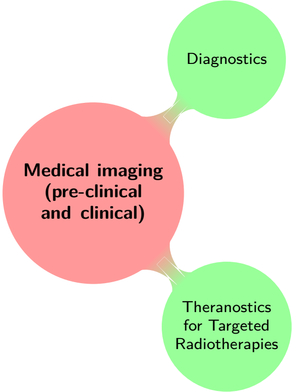


Fig. 3: Left: TIARA prototype for ion-range monitoring . Right: PEPITES as beam monitor at ARRONAX.

2nd type of dev.: "Imaging for diagnostics and theranostics"



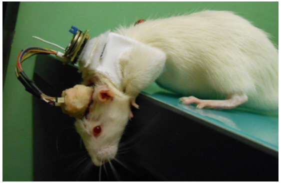
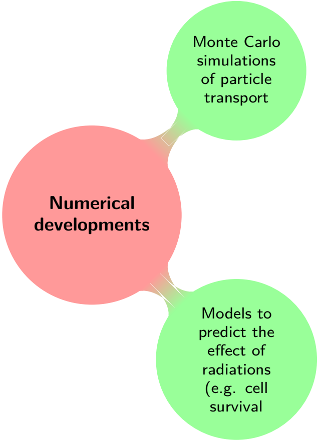


Fig. 4: Left: PIXSIC probe dedicated to small animal imaging. Right: Mobile gamma-camera for estimation of absorbed dose in targeted radiotherapy.

3rd type of dev.: "Numerical developments "



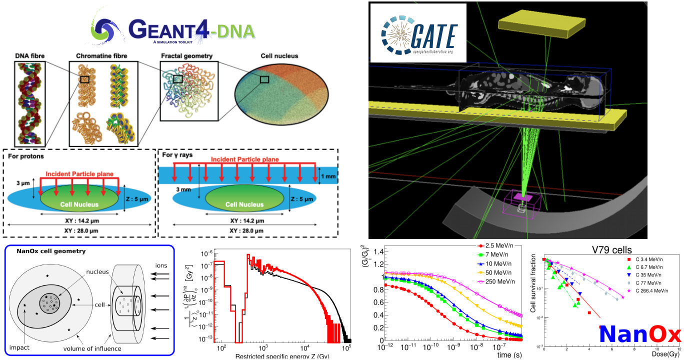


Fig. 5: Top: Monte Carlo simulations with Geant4-DNA (from physics to biology) and GATE (Imaging and Therapy based on Geant4). Bottom: The NanOx model of cell survival predictions.

Plan

Beam hodoscope

Applications

- Therapies : Hadrontherapy (including FLASH) but also X-ray micro-beam radiotherapy (MRT)
- Irradiation beam lines including low-energy and high LET ions (radiobiology) and FLASH
- Main specifications: low budget material, radiation hardness and (for "PG Fast-timing") timing resolution

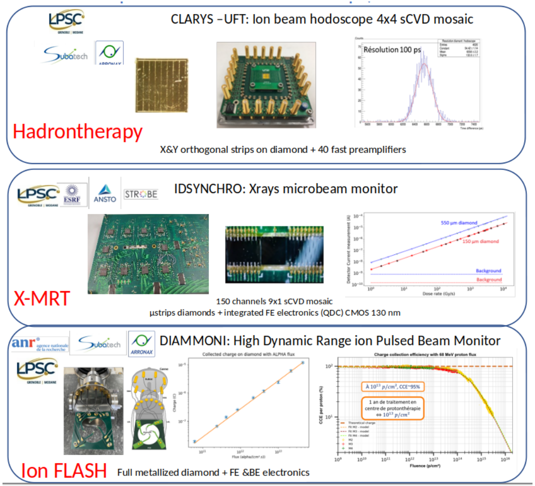
Technologies investigated in IN2P3

- Secondary Electron Emission (PEPITES project)
- Semi-conductors: Diamond (DIAMOND project) and GaN (MATRIX project)

	Bandgap (eV)	**Breakdown field (MV/cm)**	**Electron mob. (cm^2/Vs)**	**Thermal cond. (W/mK)**	**Radiation hardness**	**Large area (industry)**	**Cost**
SiC	2.36–3.23	3.5	900	320	+	+	+
GaN	3.4	3.4	1500	1300	+	+	+
Si	1.1	10	3000	230	−	+	+
Diamond	5.47	0.3	1500	2130	++	−	−

Table 1: Comparison of semiconductor materials for particle detectors.

Master Projet “DIAMOND”: Technology and Status



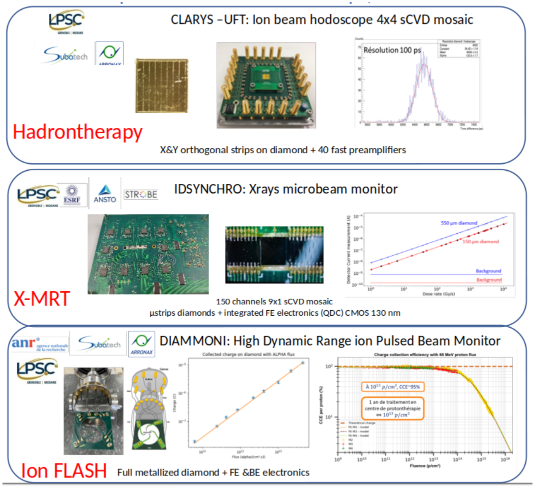
Detectors

- Single and polycrystalline diamond detectors (sCVD and pCVD)
- Metallization with thin (100 nm) Al layer by laser lithography
- PCB with various arrangements (single, 4x4 mosaic or 9x1) or thin membrane (few µm)

Electronics

- FE electronic developments: e.g. fast preamps, DFC, QDC, . . . discrete and integrated electronics
- BE electronic developments: e.g TDC (40 on a single Cyclone 10 FPGA - STD 25 ps / CMOS 130 nm STD 12 ps)

Master Projet "DIAMOND": Technology and Status



Status

- Hadrontherapy: CTR of 130 ps and prototype of 4x4 single crystals in progress (1x1 cm^2)
- X-MRT: Linear response at the clinical dose rate with a prototype of 9x1 single crystals
- Ion FLASH: Linear response up to a few 10^{13} alpha/(cm^2.s) and radio-resistance up to 10^{13} p/(cm^2)
- High LET ion beams ("beam halo detector") (e.g BioALTO) : operational
- Ion micro beam (e.g. AIFIRA) (active beam line window): operational at 8 µm, objective: 1 µm

Human resources: $\sim$ 6 IN2P3 FTE + external collaboration: Néel, ASNR (IRSN), ESRF, ALTO, Japan (Tsukuba)

Master Projet "DIAMOND": Characterization techniques and Perspectives

New diamond characterization techniques: Application of various "Beam Induced Current" techniques

- ToF eBIC ("pulsed" SEM - Institut Néel) & XBIC (BM05 - ESRF)
- IBIC (Ion Beam Induced Current – AIFIRA)

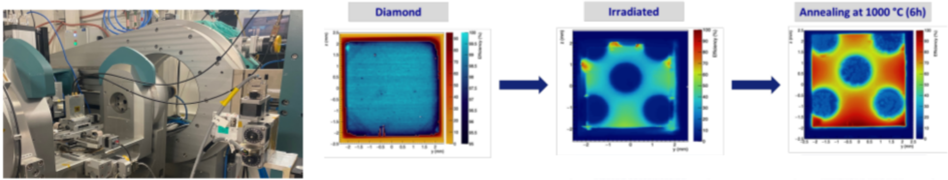
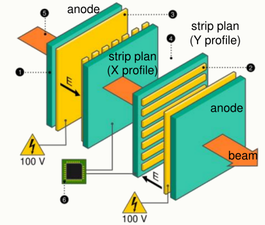


Fig. 6: XBIC chracterization system (BM05-ESRF): Creation of vacancies with alpha irradiations (identification with Raman spectro.) + Annealing [F. Lafont, 2023]

Main perspectives

- Short-term: single and polycristalline CVD diamond beam monitors (hadrontherapy, X-MRT)
- Long-term: development of "full scale" sensors with integrated electronics

PEPITES : Principle and Advantages



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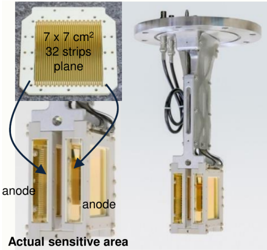


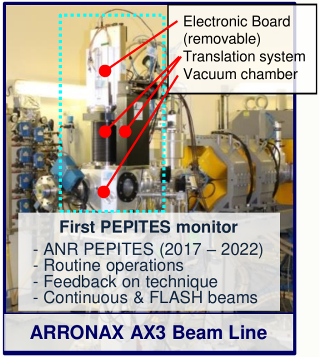
Principle

- 50 nm thick gold strips on thin substrate
- Beam passage ejects secondary electrons from strips (collected by anode) $\Rightarrow$ Signal of monitor
- Operates in vacuum

Advantages

- Very thin ($\lesssim$ 10 µm WET)
- Can be adapted to beam
- Very linear $\Rightarrow$ FLASH

Human resources (IN2P3): $\sim$ 12 persons (IN2P3) + 3 outside IN2P3



PEPITES: Status and Perspectives

PEPITES @ CNAO: monitoring 6.5 m upstream from patient (CNRS – CNAO specific agreement)

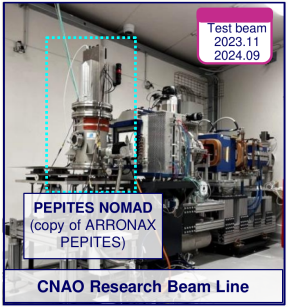
1. 1st phase: Adaptation of the current prototype
   - Functioning with carbon ions verified
   - Reduced WET 10 → 5 μm option, with off axis anodes, validated
2. 2nd phase: 3 - 4 years: Production a dedicated monitor
   - Phase starting now. Revision of the readout considered

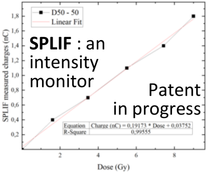
FLASH (X/IPP premat' for continuous and FLASH beam portable monitors)

- SPLIF (2023 – 2024), SPLASH (2025) : Portable PEPITES

ULTRA-FLASH: laser-plasma beams

- SEE with ∼ 10 fs beams ? MITI 2 years 2023 – 2024 with LOA
  - Strong signal, attenuation observed!
- Next: Physics understanding and Monitor feasibility?





Ion-range monitoring by means of Prompt Gamma detection (PG)

Pionneering work at IN2P3

- Collimated and Compton cameras coupled with beam hodoscope (TOF) (ANR Gamhadron 2009-2013)
- Prompt Gamma Peak Integration (compact device): PG counting with TOF detectors (PCSI Project "GammaDosi")
- Conclusion : millimetric precision on large beam spots (10^8 protons)

Main objectives of the current projects (compact devices)

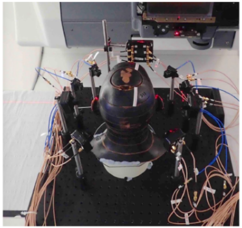
- PG Time Imaging: Improvement of the precision on ion-range control by means of fast-timing detection at low beam intensity
- PG Energy integration (PGEI): PG detection for pulsed beams (synchro-cyclotron)

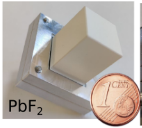
		synchrotron		cyclotron (IBA, Varian)	synchro-cyclotron (S2C2, IBA)
		Carbon	Protons		
Typical intensity (ions/s)		10^7	10^9	10^{10}	$\sim 10^{10}$
Macrostructure	Period (s)	$1-10$		$\varnothing$	10^{-3}
Microstructure	Bunch width (ns)	$20-50$		$0.5-2$	8
	Period (ns)	$100-200$		10	16 (variable)
	Ions/bunch	$2-5$		200	4000

Fig. 7: Typical beam time structure of hadrontherapy accelerators. Beam currents of the order of nA in cyclotron and μA in synchro-cyclotron (current peak)

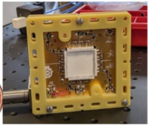
PG Time Imaging: Principles and developments

WP1. Detector development

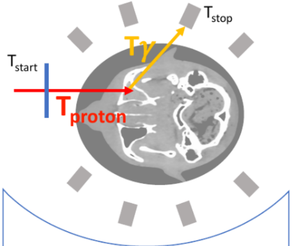




Gamma module based on Cherenkov radiators

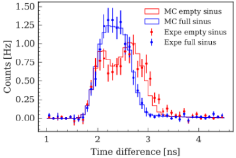


Fast beam monitor



WP.3 Test in clinical environment

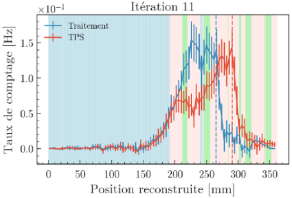
Measurement of TOF distributions



WP2. Data reconstruction

From TOF measurement to PG vertex distributions

$$TOF = t_{stop} - t_{start} = T_{proton}(\mathbf{r}_v, \mathbf{v}_p) + T_\gamma(\mathbf{r}_v, \mathbf{r}_d)$$



Detection of anatomical variations and particle range measurement

Human ressources (IN2P3): $\sim$ 12 FTE

TIARA project, 2020-2023

Funded by the European Union

European Research Council
Established by the European Commission

PGTI project, 2022-2027

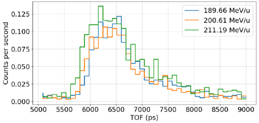
PG Time Imaging: Main achievements and next goals

Main achievements

- Detector R&D completed (8-channel prototype), validated with:
  - protons from cyclotrons, synchrotron and synchro-cyclotron at low intensity
  - carbon ions (CNAO) at clinical intensity
- No saturation with protons at high intensity (prelim. results)

Next goals (2-3 years)

- WP1: 30-channels full-scale prototype
  - DAQ system under development + Mechanics design
- WP2: AI-based data reconstruction
  - To improve the accuracy of PG vertex profiles (1D)
  - To obtain 3D images (synthetic-CT and dose maps)
- WP3: Tests of prototypes and customization
  - Range monitoring at clinical intensities + Detection of anatomical modifications at low intensities and proton tomography configuration



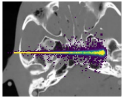
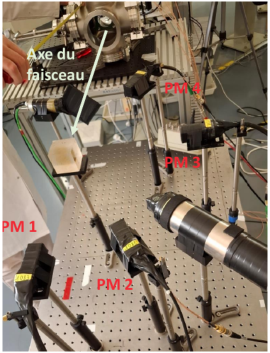


Fig. 8: Top: PG TOF profile obtained from ^{12}C at CNAO. Range accuracy is 2.4 mm sigma for 3000 PG events. Bottom : PG emission map (left) and mechanics design of the 30-channel prototype (right)

PG Energy Integration: Principles, Status and Perspectives

MITI
Mission pour les Initiatives Transverses et Interdisciplinaires



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Thèse MITI 2023-2026

Principle

- Detectors around the patient in integration mode to cope with high beam intensity during beam pulses of synchro-cyclotrons (S2C2) (1 μA)

Status

- Feasibility study with Monte Carlo simulations
- Systematic detector characterization and calibration ($2.5 \times 2.5 \times 5$ cm^3 PbWO4 + fast PMT): ESRF, ARRONAX and CAL-Nice

Perspectives

- Short term: Test on the S2C2 accelerator at CAL-Nice
- Mid term: Joint development with PGTI?

Human ressources (IN2P3): $\sim$ 3 FTE

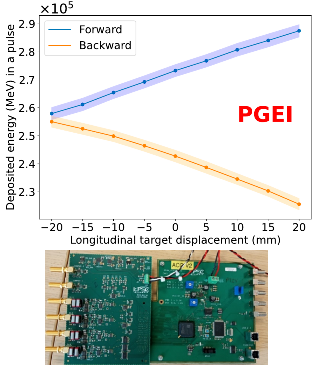


Fig. 9: Top: Energy measured in forward and backward detectors as a function of longitudinal target displacement. Bottom: 4-channel acquisition board.

Plan

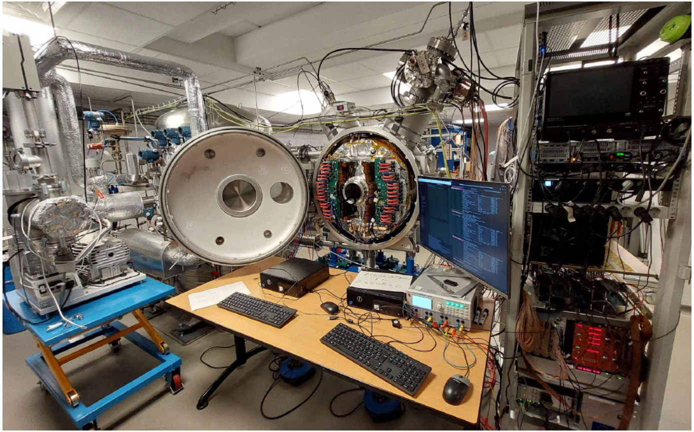
XEMIS: Compton Camera for medical imaging

Context and objectives

- Small animal imaging with LXe based Compton camera
- Following the developments for dark matter detection in Subatech

Status

- Camera installed in CHU Nantes
  $\Rightarrow$ Access to:
  - Mice store
  - Nuclear medicine department (radiopharmaceuticals, mice CT images)
- First data in Sep 2025
  - Following 10 years of dev. with $10-12$ FTE



XEMIS: Compton Camera for medical imaging

Principle

- Monolithic Time Projection Chamber of Liquid Xenon
- Detection of HE γ: (HE $>$ 400 keV)

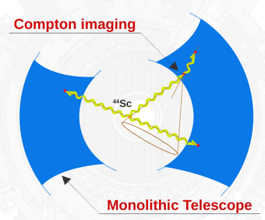


Fig. 10: Schematic representation of 3-γ detection with ^{44}Sc

Main characteristics

- First of its kind worldwide
  - Pioneering techonologies
  - First application: reduced activity demonstration
- Multi-HE γ radio-isotopes
  - 1 γ
  - 2 γ (PET or multi radio-isotopes)
  - 3 γ (e.g. ^{44}Sc)
- Image reconstruction
  - Open distributed data

Operations

- Up to 2040 @ Nantes Univ. Hospital
- Exploitation: 2027 -2031 : Under discussion

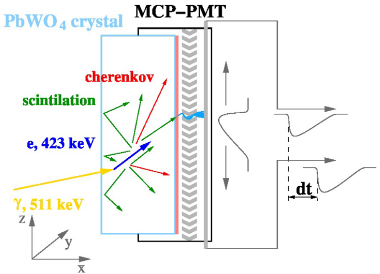
Milestones

- Short-term: Image assessment with reduced activity
- Mid-term $(5-6$ years)
  - Fast photo-detection upgrade and image assessment with reduced exposure time
  - Monitoring studies on hadrontherapy and targeted internal therapies
- Long-term: Total body imaging design and construction

ClearMind: Towards sub-100 ps CTR for PET using "scintronic" detector concept

Context and objectives

- Pushing toward a coincidence time resolution (CTR) of 10 ps $\Rightarrow$ no need for image reconstruction with improvement of image quality
- Objective: develoment of "scintronic" detectors with $PbWO_4$ monolithic scintillator optically coupled to a $5{\times}5\,\mathrm{cm}^2$ MCP-PMT (encapulsation) (ANR ClearMind, 2020-2025)



Material and methods

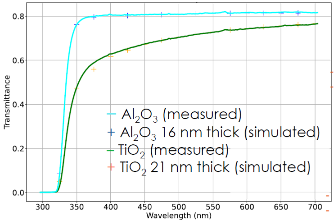
- Detection of scintillation (energy) and Cherenkov photons (time) emitted in $PbWO_4$
- Direct deposition of a photocathode ($n \sim 2{,}7$) on the crystal surface ($n \sim 2{,}3$) and passivated by a thin optical coating
- Experimental work at CPPM using the tomXgam mechanical test bench for experimentation in tomography

Human resources (IN2P3): $\sim$ 3 FTE

ClearMind: Results and Perspectives

Results

- Expected CTR ~ 20 ps FWHM (excluding MCP-MT) (MC simulation results)
- Modeling of light transmission through surfaces with thin film optical coating in Geant4
  - Update of Geant4 version 11.1 to model optical coating



Perspectives

- Development and characterization of "scintronic" detection modules within AAIMME: Machine Learning for molecular imaging and future medicine (CEA-DM2S, CEA-IRFU, CEA-BioMaps, INRIA, CPPM, ANR 2025-2029)
- Contribute to the development and characterization of new fluoride crystals with cross-luminescence and index of refraction within the Chronos EIC Pathfinder project (submitted in May 2025)
- Contribute to model multilayer optical coating and crystal anisotropy for Geant4 and to extend the SiPM model developed for GATE to SiPM arrays within the submitted Master Projet ModOp

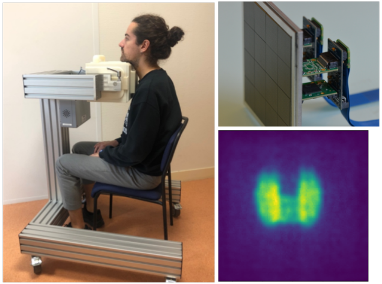
THIDOS project: Theranostics for iodine treatment of thyroid diseases

Motivation and objective

- Accurate, personalized dosimetry essential for optimizing treatment
- Objectives: new instrumental (gamma camera) and methodological (dose uncertainties) approaches aimed at improving control of the dose

Results

- Clinical prototype of a mobile gamma camera (10×10 cm^2 field of view) operational (^{131}I, 365 keV)
- Evaluation of the accuracy and robustness of the quantification protocol using 3D phantoms (calibration of the camera response, segmentation of the source image, partial volume effect and scattering corrections)



Human ressources (IN2P3): $\sim$ 13.6 FTE

PCSI Project 2019-2023

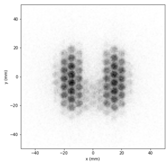
Short-term perspectives

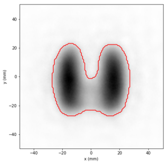
- First clinical evaluation of the mobile camera completed in March 2025 (IUCTO). Results under analysis.
- Comparison of quantification performances with conventional clinical systems (Fall 2025, Baclesse, Cochin).
- Adaptation of a Bayesian network developed by IRSN for the estimation of dosimetric uncertainties (2025-2026, IRSN)

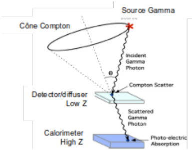
THIDOS project: Mid/long term perspectives & AIDER project

Mid/long-term perpectives (2025-2027)

- Extended clinical protocol of the mobile gamma camera for the treatment of thyroid diseases
- Open up the use of the mobile camera to clinical applications using medium-energy gamma-emitters (200-400 keV, ^{177}Lu or ^{225}Ac)
- Adaptation of the camera for dose-based treatment planning of thyroid diseases using ^{123}I (160 keV, Cochin)







Long-term perpectives (2026-...)

- Development of a Compton camera dedicated to dosimetric monitoring with high-energy gamma rays (> 400 keV) for targeted alpha therapy with ^{149}Tb, ^{211}At ^{213}Bi, ^{225}Ac or ^{212}Pb (South Korea collaboration)

AIDER project

- European project (HORIZON-EURATOM): Development of a CC for vectorized internal radiotherapy (2025-2029)
- @Lyon (CREATIS-IP2I) : Camera optimization using MC simulations + image reconstruction

MAPSSIC: a radiosensitive telemetric probe for behavioral imaging

Context and objectives

- Behavioral neuroimaging: limitation for preclinical PET imaging due to the required anesthesia.
- Alternative: Development of β^+ microprobes for freely moving small animal + image analysis methods + validation
- Development of pharmacokinetic models to associate with radiotracers

Material and methods

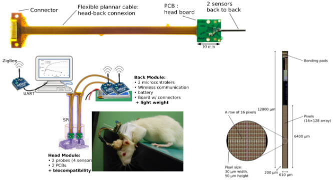
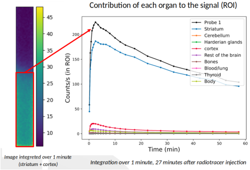


Fig. 11: 1st prototype with PIXSIC detectors

- MC simulations for physical validation

Results and status

- First prototype operational



- $\Rightarrow$ Improvement with MAPSSIC detectors (electronics on going)

21 IN2P3 persons involved

MAPSSIC: 2-year Perspectives

Short term

- Physical validation (radioactive phantom)
- Biological validation (anesthetized/awake) and comparison with microPET (imaging gold standard)

Middle term

- Pharmaco-behavioral analysis
- Comparative studies with freely moving adapted systems (RatCap, Motion Tracking)

Long term

- Industrial transfer
- Optical/isotopic duality

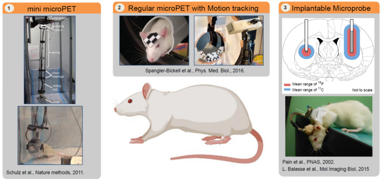
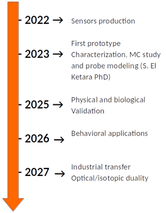


Fig. 12: Planned comparative neuropharmacological study PET systems dedicated to behavioral neuroimaging



Plan

Irradiation platforms: The ResPlaNDIR network

Ions		
Centers	Ions	Energy (MeV/n)
CPO (Orsay)	p	76–201
CAL (Nice)	p	65
GANIL (Caen)	C, O	up to 95
Arronax (Nantes)	p, d, α	70
CYRCé (Strasbourg)	p	25
AIFIRA (Bordeaux)	p, α	3
BioAlto (Orsay)*	p $\rightarrow$ O	8–25
SILab (Lyon)*	α	~ 3

X-rays and e^{-}
Centers
ICO (Nantes)
CERVO (Lyon)
PARMIVA (Clermont)
RadeXp (Orsay)
IRCM (Fontenay aux roses)
Cyceron (Caen)
CGFL (Dijon)
CREFRE (Toulouse)
Gustave Roussy, (Villejuif)
CRAN (Nancy)
IRCM (Montpellier)
ESRF (Grenoble)

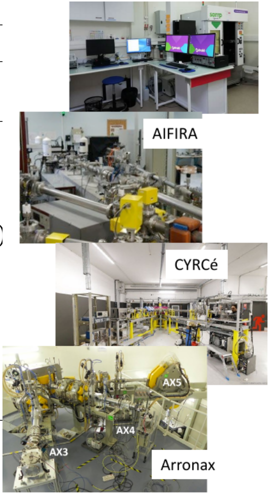


Table 2: *: Platform currently under development. All ion irradiation platforms are accelerator-based, except for SILab, which uses a radioactive Americium-241 source and affiliated to IN2P3 except CPO and CAL (clinical centers).

Irradiation platforms: Focus on the ion beam facilities

Center	Ions	Energy (MeV)	Range (mm)	FLASH	Access
CPO (Orsay)	p	76–201	46 – 260	Yes	Paid beam
CAL (Nice)	p	65	31	In progress	PAC
GANIL (Caen)	C, O	$\rightarrow$ 95 MeV/n	17 (C)	Yes†	iPAC
Arronax (Nantes)	p, (d), α	70	40 (p), 3 (α)	Yes	Platform
CYRCé (Strasbourg)	p	25	6	Considered	Platform
AIFIRA (Bordeaux)**	p, α	3	0.150 (p), 0.018 (α)	No	Collab.
BioAlto (Orsay)*	p	4–25	0.16 – 6.19	Considered	PAC
	α	14-43	0.13 – 1.29		
	C	87.5	0.17		
	O	128	0.14		
SILab (Lyon)*	α	~ 3	~ 0.018	No	

Table 3: PAC: Program Advisory Committee. GANIL : 120 – 240h/year for radiobiology (between 60 and 100% of the beam time allocated by the interdisciplinary PAC). CAL: 24h/year (3 year CNRS-CAL agreement). Platform: internal scheduling of the experiments. Collaboration : Collaboration with the group in charge of the beam line is required to obtain beam time and to prepare the experiment. (*) are currently under development. (**) microbeam facility. † FLASH irradiation are in particular available at very low energy on IRSSUD (< 1 MeV/n) + D1

Irradiation platforms: Focus on the ion beam facilities

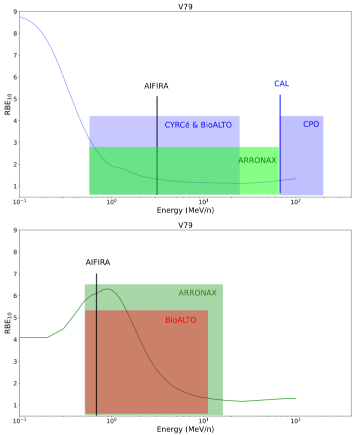
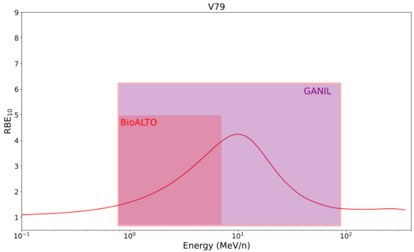


Fig. 13: RBE for the V79 cell line (preditions of the NanOx model): top: p, bottom: α, right: ^{12}C



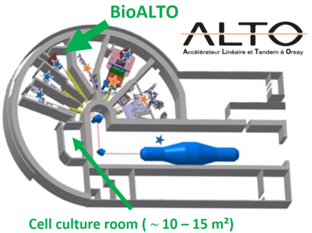
"Radiobiological relevance" of the various beams

- Considering the RBE as the biological endpoint for the sake of simplifity
- Specificity of ion irradiation at relatively low energy (high RBE): $\sim$ 10 MeV/n (C), $\sim$ 1 MeV/n (α), $\sim$ 0.1 MeV/n (p)
- Low energy limits in the figure correspond to ion ranges of 10 µm (typical cell dimension)

"BioALTO" Master Projet: "Hadron biology" Platform @ ALTO

Objective

- Development of a platform dedicated to radiobiological research for therapies involving ions (hadrontherapy, Target Alpha Therapy, Boron Neutron Capture Therapy)
- BioALTO beamline based on Radiograaff device (previously at the IP2I 4 MV accelerator in Lyon)



Characteristics of ALTO

- 14.5 MV Tandem "Van de Graaff" accelerator
- Wide range of intense (up to μA) ions beams ($^{1}H \rightarrow {}^{79}Au$)
- Continuous beam
- Additional pulsed beam possible (100 ns to 100 μs)

Part.	Energies [MeV] (MeV/u)	Irradiation depth [μm WET]*
^{1}H	4 – 25 (4 – 25)	160 – 6190
^{4}He	15 – 43 (3.8 – 10.8)	130 – 1290
^{7}Li	50 (7.1)	480
^{12}C	87.5 (7.29)	170
^{16}O	128 (8)	140

*(at 5 cm air)

"BioALTO" Master Projet: "hadron biology" Platform @ ALTO

Main tasks

- Upgrade the Radiograaff device to exploit the wide range of ions
- Development of new beam diagnostics and dosimetry tools
  - Diamond counter
  - Scintillating fibre counter
  - Microdosimeter based on Si microdetectors
  - Beam monitoring profiler based on air fluorescence
- Modeling of the line (analytical model and digital twin)
- Equipment of a cell culture room nearby
- Access to external users → platform in 2027

Human resources (IN2P3): ∼ 4 FTE

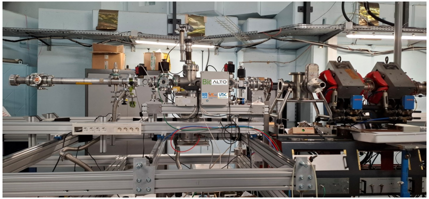


Fig. 14: BioALTO beamline under installation

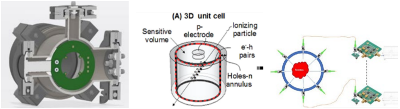


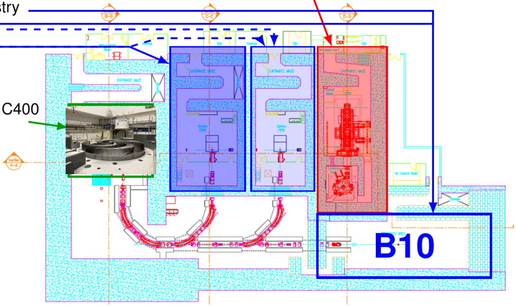
Fig. 15: From left to right: Diamond counter, Si micro-dosimeter, beam profiler based on air fluorescence

CEREINHAd: Project of irradiation platform in CYCLHAD (C400)

CEREINHAd : "CEntre de REcherches INternational en Hadronthérapie"

- Hadrontherapy center :
  - Protontherapy treatments (from july 2018)
    Proteus One (S2C2)
    Protons at 250 MeV
  - Research in particle-therapy
    - Physics & radio-chemistry
    - Biology
    - Clinical room
- Supraconducting Cyclotron C400
  ^{12}C at 400 MeV/u
  Protons at 250 MeV
  All light nuclei with A/Z=2
  p, ^{4}He, ^{12}C at start
  first beam mid 2026

NHa NORMANDY HADRONTHERAPY



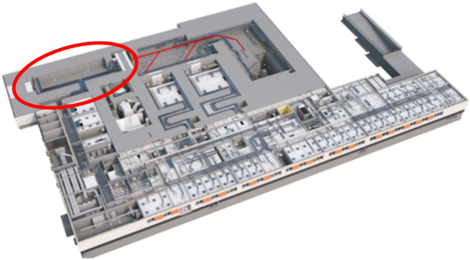
Motivations

- Clinical quality beams (p, α, C) without the clinical constraints in the B10 room
- $\Rightarrow$ Radiobiol. (in vitro/in vivo)
- $\Rightarrow$ Radiochemistry
- $\Rightarrow$ Physics and detector testing

CEREINHAd: Project of irradiation platform in CYCLHAD (C400)

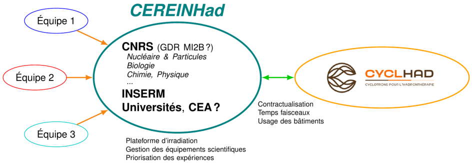
Development of the (passive) beam line

- Beam shaping systems
- Energy degraders
- Ridge Filter (Conformal flash (in vivo))
- Microbeam systems
- Restraint systems
- Dosimetry and metrology equipment



5-year plan

- Contracts with CYCLHAD
- Light hadron irradiation platform in 2028-2030
- Committee to prioritize experiments
- Other beams ($A/Z = 2$ from ^{4}He to ^{20}Ne)?



Plan

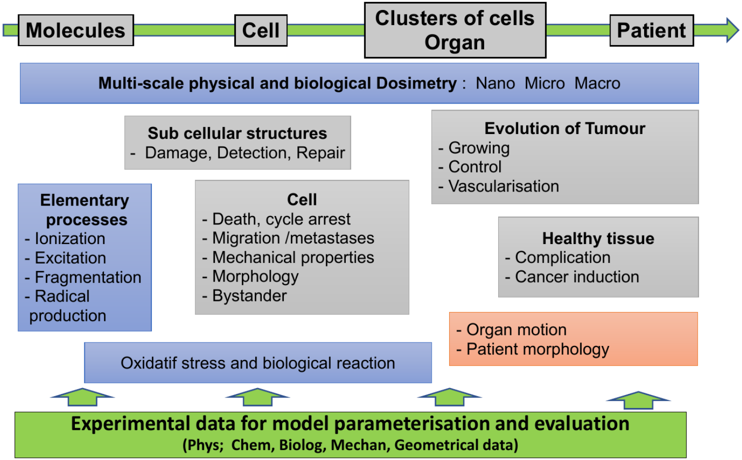
MyLife: National Efforts in Multi-Scale Modeling for Innovative Radiotherapies

Context

- Modeling the biological effects of ionizing radiation = complex multidisciplinary and multi-scale challenge
- Multiscale: From atomic interactions to whole-body effects
- Multidisciplinary: physics, chemistry, biology + clinical insights

Objective

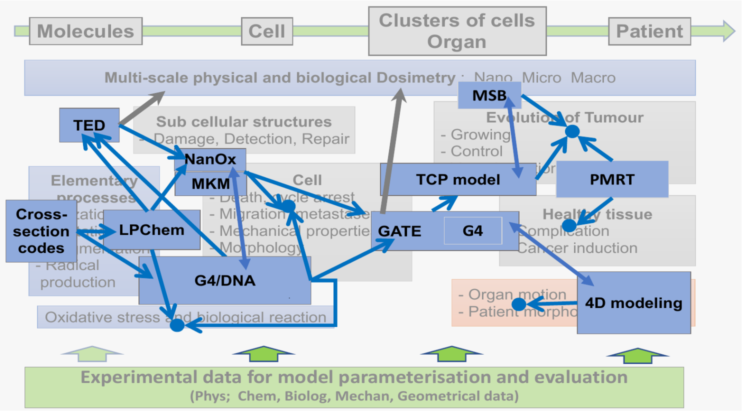
- Creation of a national/international reasearch program



MyLife: Multiscale multidisciplinarY modeLing of Irradiation efFects on lifE

MyLife: National Efforts in Multi-Scale Modeling for Innovative Radiotherapies

- TED: Transfered energy Distribution (IP2I)
- LPChem: MC Track-Structure code (Physics+Chemistry) (IP2I et al.)
- NanOx, MKM: Models of Cell Survival predictions (IP2I, LPSC, LPCA)
- TCP: Tumor Control Probability (IP2I et al.)
- MSB: Modélisation des Systèmes Biologiques (IJCLab)
- PMRT: Plateforme de Modélisation en RadioThérapie (LPCC)



Geant4-DNA: Objectives and Status

https://geant4-dna.org

Context and objectives

- Major challenge in current radiobiology: Mechanistic understanding of the biological effects of ionizing (radiotherapy, radioprotection)
- Objective of G4-DNA: Track-structure code from phys. interact. (water + other materials) and chemical stage (radiolysis) to damage at (sub)cellular scale. Specificity: The only open-access platform in this field (full component of G4)
- Activity of the "Geant4" IN2P3 Master Project (RN : Marc Verderi, LLR ; DS Calcul & données), presented at IN2P3 CSI on 06/2022

Collaboration

- 17 countries (62 collaborators, including non-permanents)
- IN2P3 : 9 IN2P3 permanent collaborators (current FTE < 3)
  - Coordination of the project (S. Incerti, LP2I, spokesman since 2008, current mandate until 2026) + technical coordinator (H. Tran, Research engineer)
- Strong impact: 152 peer-reviewed papers since 2006 (involving IN2P3)
- Geant4-DNA international tutorials & Geant4 at the Physics-Medicine-Biology Frontier" series of conferences

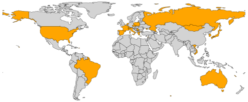


Fig. 16: Geant4-DNA world map of collaborators in 2023-2026

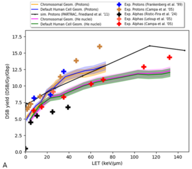


Fig. 17: Example of recent achievement: Quantification of Double-Strand Break yields for several Geant4-DNA human cell models (Chatzipapas et al. 2024)

Geant4-DNA: Perspectives at IN2P3

Core development of Geant4-DNA

- Physics: Improvements of track-structure models and implementation of new models (e.g., electrons up to 10 MeV in liquid water, electrons in GNP, low energy models for Li and C ions, etc.)
- Chemistry: Extension of radiolysis modeling for ultra high dose rate irradiation + experimental validation
- Geometries of biological targets: completion of multi-scale library of biological models (plasmids, bacteria, cells, 3D multi-cellular assemblies, DNA packing. . .) + experimental validation of damage prediction
- Computing: possibly GPU porting & AI R&D (both within the workplan of the Geant4 collaboration)

Geant4-DNA applications

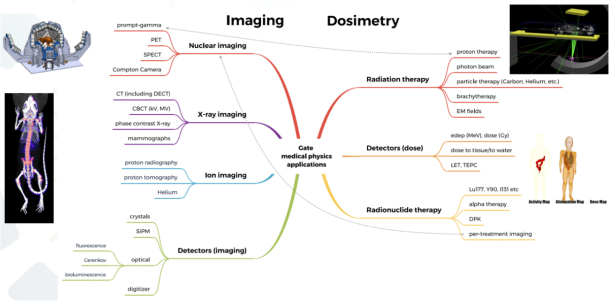
- Development of new example applications, including:
  - Innovative radiotherapy approaches (e.g. hadrontherapy with a variety of ions, Flash irradiation, VHEE, TRT. . .)
  - Radiation protection in space (e.g. multi-scale mechanistic simulation down to the cell scale)
  - Environmental applications (e.g. track-structure simulations in the atmosphere)

GATE: Objectives and Status

https://github.com/OpenGATE/opengate

Objective

- Need for easy-to-learn macro mechanism to configurate simple or highly sophisticated experimental settings
- ⇒ GATE: open source interface to run Geant4 simulations (imaging, dosimetry)



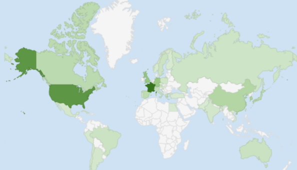


Fig. 18: GATE world map of users in 2025 (2000 registered users)

Status

- Release of GATE 10 in Fall 2024 (after 4 years of development) ⇒ Python library
- Successful! (smoother installation, consistent integration within "python workflow")

GATE: Collaboration and Perspectives

Collaboration

- Creation in 2002 with a strong contribution of IN2P3
- Strong impact in the field: $\sim$ 1000 citations since its creation
- 23 laboratories, companies and clinical centers (Total FTE = 20)
  - Technical coordinator: D. Sarrut (CREATIS)
- IN2P3 (LPCA, LPSC, IP2I, IPHC, CPPM, IJCLab) : 4 FTE
  - Spokesperson: L. Maigne (LPCA) + Research engineer (from Fall 2025)
- Strong policy of trainings on the GATE simulation platform in LPCA: for researchers + compagnies (partnership with "CNRS Formation Entreprises") + medical physicists and physicians (collaboration with "UNICANCER")

Perspectives

- Construction of "digital twins" for instrumentation developments + creation of learning data bases fo AI (e.g. improvement of image reconstruction)
- Special effort on FLASH irradiation modeling (Master Projet "FLASH")
- Stronger link with the Geant4 collaboration (python interface in G4?)

NanOx model: “Nanodosimetry and Oxidative Stress”

NanOx

Main assumptions

- Sensitive volume: cell nucleus + 2 types of biological events:

	Local lethal events (LLE)	Global events (GE)
Event	Inactivation of nanometric targets	Oxidative stress in the sensitive volume
Scale	Nanometric	Micrometric
Evaluation	Specific energy*	Production of chemical species*

  - *: evaluated from Monte Carlo simulation (e.g. Geant4-DNA)
- Cell survival for the configuration c_K (ion impacts, target positions, track structures): ${}^{c_K}S = {}^{c_K}S_{LLE} \times {}^{c_K}S_{GE}$

Full modeling of radiation stochastic effects

- Average cell surviving fraction: $\overline{S(D)} = \sum_{K=0}^{\infty} P(K,D) \cdot \langle {}^{c_K}S \rangle$
  - $P(K,D)$: probability to have K impacts with a dose D
  - $\langle {}^{c_K}S \rangle_{c_K}$: mean survival over all configurations c_K

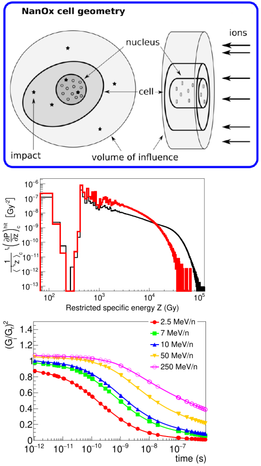


Fig. 19: Cell geometry, specific energy spectra and OH$^{\bullet}$ prod.

NanOx model: Main parameters / input data & Results

NanOx

Main parameters	Cell nucleus diameter	Effective lethal function of nanometric targets
Main input data	Cell microscopy	$\sim$ 3 cell survival curves 1 RX + 2 ions (intermediate and high LET ions)

Results (“for hadrontherapy”)

- “NanOx predictions for three cell lines irradiated by monoenergetic ions were more often more accurate than the ones issued from 5 other biophysical models (MKM, LEM I–IV)” [Monini 2019]

Perspectives

- Extension of the model to TAT and BNCT $\Rightarrow$ Consistent modeling for all therapies involving ions
- Towards “fast” and open NanOx

Human resources (IN2P3): $\sim$ 3

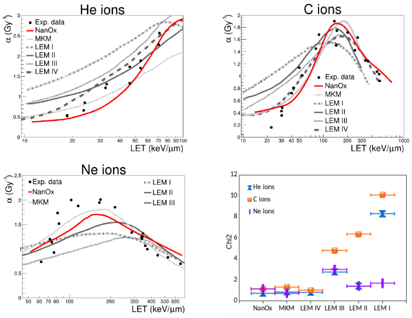


Fig. 20: NanOx predictions of α coefficients for HSG cell [Monini 2019]

Conclusion

General conclusion

- Instrumental and numerical developments in health-related IN2P3 projects fall entirely within the core expertise of the institute ⇒ They clearly belong within the scope of IN2P3
- The developments are built on strong, long-standing collaborations between our laboratories and clinical or biological centers - sometimes even within the same lab - ensuring their relevance and applicability
- Strong potential to deliver technological breakthroughs at the interface between cutting-edge particle physics and critical medical applications
- ⇒ Projects based on technological opportunities and/or opportunities of collaborations with stakeholders in the clinical field

Instrumentation

- Main developments in beam monitors for therapies and irradiation platform & gamma detection (hadrontherapy monitoring and nuclear imaging for diagnostics and theranostics)

Conclusion

Irradiation platforms

- Scientifically relevant and complementary for both detector characterization and biological measurements.
- Dosimetric intercomparison under progress
- Ongoing development of platforms to better meet the need for biological data using relatively low-energy ions: BioALTO (@IJCLab) and SILab (ion sources@IP2I)

Numerical developments

- Strong IN2P3 contribution to high impact numerical platforms (Geant4-DNA, GATE)
- "MyLife": Nat. research program for Multiscale multidisciplinarY modeLing of Irradiation efFects on lifE
  - From atomic physics and chemistry (Geant4-DNA) to biology at cell scale (NanOx) and tumor responses (modeling at IJCLab).
  - Example of results: Tumor Control Probability in Targeted Alpha Therapy

Perspectives

Instrumentation

- Possible research axis gathering competences in various labs: Compton camera (CC) for targeted radiotherapy monitoring
  - Targeted radiotherapies in full expansion with crucial need for monitoring
  - IN2P3 expertise: CC (IJCLab/Astroparticules, SUBATECH, CPPM, IP2I) and γ camera for theranostics (IJCLab/Health) (instrumentation, MC simulations, image reconstruction)

Irradiation platforms

- CEREINHAd@CYCLHAD $\Rightarrow$ Need for agreement between academical research (CNRS, CEA...) and CYCLHAD
- GANIL: Irradiation platform@SME (13.6 MeV/n ^{12}C) and SOBP (Spread-out Bragg peak)@D1?

Numerical platforms

- 2 recent research engineering positions to support both Geant4-DNA and GATE. Future spokespersons?
- Many scientific perspectives to model the new modalities of radiotherapies: Temporal and spatial dose fractionation (microbeams, FLASH) and targeted therapies (TAT and BNCT)

Thank you for your attention

Physics and Medicine: Closely Intertwined

"Medical imaging and cancer treatments have benefited from developments in particle physics over the years, and the innovations continue today..." (from CERN news, February 2024)

Medical imaging

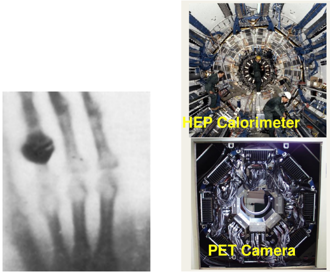


Fig. 21: From Röntgen 1885 to PET imaging (from Sparsh Navin, CERN – Knowledge Transfer Life Sciences Section)

Cancer treatments

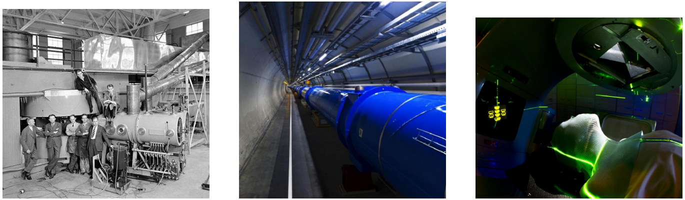


Fig. 22: From the first patient treatment by proton therapy in Berkeley (1954) to modern hadron-therapy center with gantry (from Sparsh Navin 2014, CERN – Knowledge Transfer Life Sciences Section)

Strategies of developments: Combination of . . .

"Health needs", e.g.:

- Ion-range monitoring in hadrontherapy
- Theranostics

"New technologies", e.g.:

- CMOS detectors and hybrid pixels originally developed for charged particle trajectography at the LHC ⇒ What could the benefit of such detectors in medical imaging?
  - MAPSSIC: in vivo positron imaging with CMOS pixels
  - Photon-counting CT : Small animal X-ray imaging with hybrid pixels
- Large Liquid Xenon detector for dark matter detection ⇒ What could the benefit of such detectors in medical imaging with 3-γ detection?
  - First application: low activity diagnosis imaging
  - Then: Hadrontherapy and Targeted Therapy monitoring?

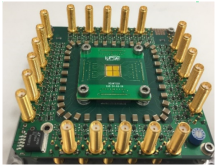


Fig. 23: Diamond beam hodoscope for hadrontherapy.

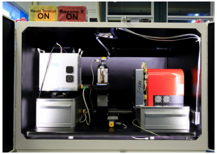
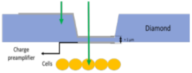


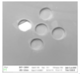
Fig. 24: PIXSCAN-FLI Photon-Counting CT prototype

Master Projet “DIAMOND”: Applications

DéFi DiaMs

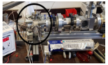


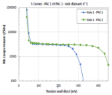
Diamond membrane



Ion Micro Beams

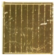
4-diamond counter & dedicated electronic

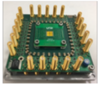


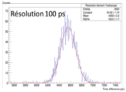


High LET ion Beams

CLARYS –UFT: Ion beam hodoscope 4x4 sCVD mosaic



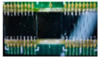


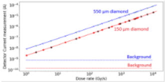


Hadrontherapy

X&Y orthogonal strips on diamond + 40 fast preamplifiers

IDSYNCHRO: Xrays microbeam monitor



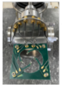


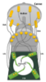
X-MRT

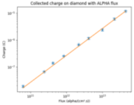
150 channels 9x1 sCVD mosaic

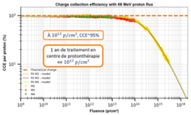
µstrips diamonds + integrated FE electronics (QDC) CMOS 130 nm

DIAMMONI: High Dynamic Range ion Pulsed Beam Monitor





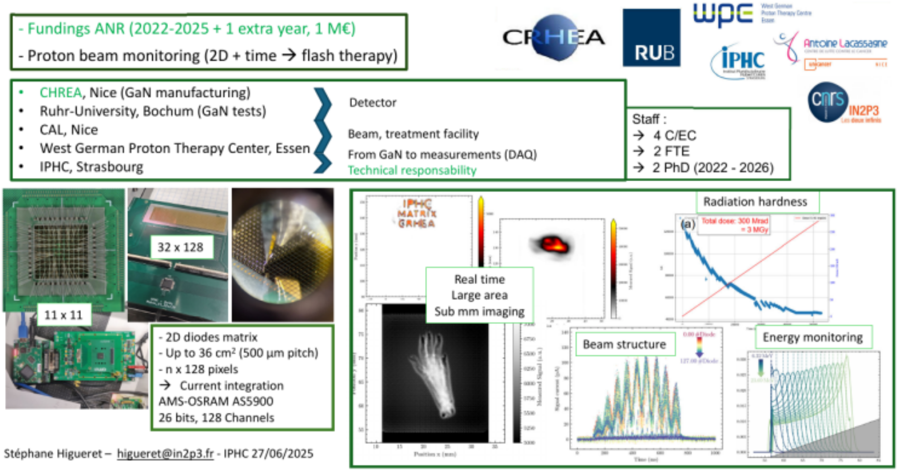




Ion FLASH

Full metallized diamond + FE &BE electronics

MATRIX project: a GaN proton beam monitoring



MATRIX project: Prospectives

Time line

2021 — 2023 — 2025 — 2027

NECTAR → >100 % completion

(PCSI Cancer – INSERM)

CHREA + CAL

GaN research (led technology)

MATRIX → 90 % completion (06/25)

GaN diode structure

PIN vs Schottky

From single

to linear

to 2D diode array

DAQ (

Staff (ANR) :
→ 4 C/EC
→ 2 FTE
→ 2 PhD
→ Up to 2025
→ Up to 2026

MATRIX∞ In2p3

K x 128 compact stand alone daq system

COTS components

→ Hadrontherapy beam monitoring, CNAO

→ Radiobiology beam current monitoring

→ Industrial irradiation beam line monitoring

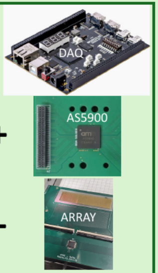
→ Flash therapy beam structure

→ Real time imaging (treatment plan, sub mm)

Staff (CHREA + IPHC)
→ 3 C/EC
→ 2 FTE 150 – 200 k€
→ 1 PhD ? (2025 -)
→ 1 Post-Doc ? (2025 -)

2025 - 2026
→ DAQ testing + fine tuning
→ Array improvement
→ AMS/Analog device testing
→ In depth detector simulation

2026 -
→ Facility testing



+ +

= > 8 fp/s
Compact DAQ
beam monitoring

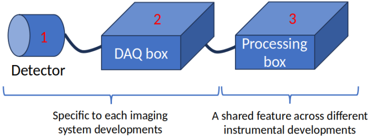
N x (128 channels) x integration time (< 1ms)

Stéphane Higueret – higueret@in2p3.fr - IPHC 27/06/2025

IPHC: Team IMR (Molecular Imaging and Radiobiology) (1/2)

Global strategy

- Towards a modular and ≪ portable ≫ approaches
- Development of the full acquisition chain to achieve optimal performances

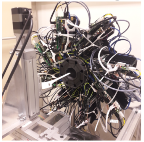


Implementation example

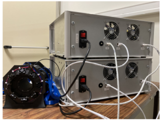
The digiPET project

- Fundings region Grand-Est / Eurométropôle

Former PET design



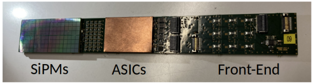
Ongoing valorization of th current design



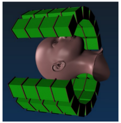
- 17664 Physical channels (LYSO crystals)
- 2048 Photodetector channels (SiPM)
- 512 Electonic channels (custom Front-End)

2 ongoing PET projects

- Preclinical PET Insert (2026-2027)

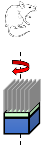


- Dedicated Brain PET (2030)

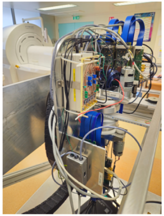


IPHC: Team IMR (Molecular Imaging and Radiobiology) (2/2)

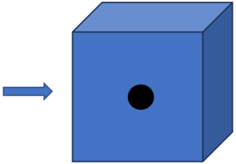
The WRC project (Use of a Rotating Slat Collimation)



- Improvement in efficiency by up to 1%
- Preservation of the detection FoV size
- Required data processing from 1D to 2D, and ultimately to 3D



Curent SPECT design



Ongoing valorization of the projected « boxed » design

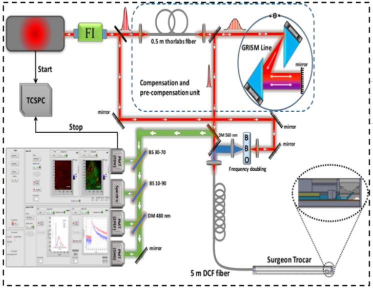
- Dual-head imaging system
- 72 x 20 x 0.1 mm3 tungsten slats
- 512 PMT channels & CeBr3 monolithic crystals
- 512 Electronic channels (custom Front-End)
- Modularity
  - 2 or more detection heads
  - Possible extended axial FoV
  - Fast acquisition protocol (depending on collimation characteristics)
- Portability
  - Small footprint
  - Increased portability
  - Facilitate collaborative research

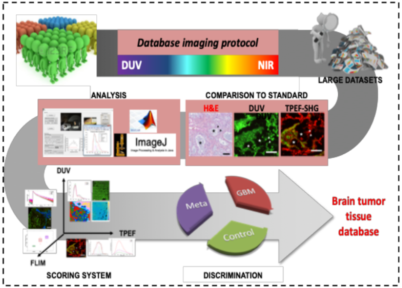
OPALIS project: Endomicroscopy for real-time diagnosis and biopsy

Context and objectives

- Context: The precise definition of the excision limits is a major challenge in neurosurgical oncol. operation
- Objectives: Enhance the quality of surgical procedures using rapid, sub-cellular-resolution optical methods

Material and Methods





Human resources: 3.3 FTE

OPALIS project: Endomicroscopy for real-time diagnosis and biopsy

Results

- Development of a miniature scanning system
- Creation of a multimodal, multiscale tissue database (from the deep ultraviolet to the near infrared) discriminating against tissue carcinogenesis

Fig. 25: Miniature scanning system

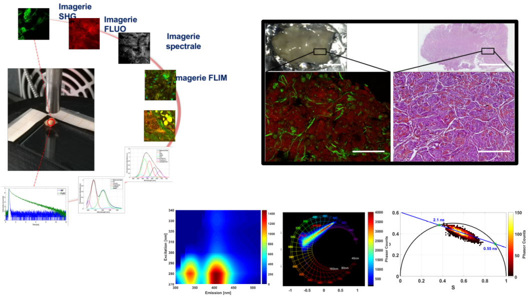
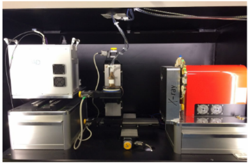
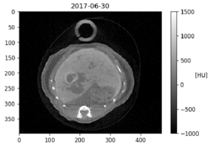


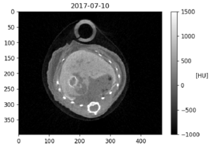
Fig. 26: Multimodal, multiscale tissue database

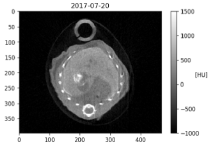
Photon Counting-CT



PIXSCAN-FLI PC-CT prototype





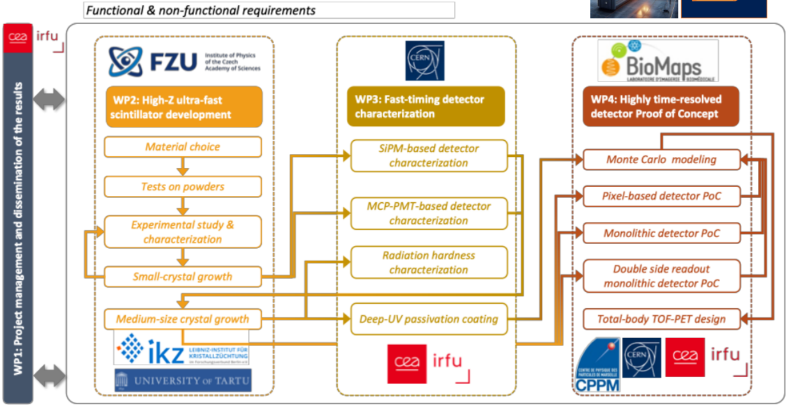


- Suivi de la croissance de tumeurs du foie et de leur réponse au traitement chez la souris
  - Thèse **Loriane Portal** (BDO CNRS/Région, 2018) -> IDL
  - F. Cassol, L. Portal *et al.* iScience 21 (2019) 68
  - Thèse **Floriane Cannet** (MITI, 2024) -> CERIMED
- Décomposition en matériaux de base par des méthodes proximales à métrique variable
  - Thèse **Souhil Tairi** (BDO CNRS/Région, 2019) –> Institut Fresnel
  - S. Tairi *et al.* IEEE TRMPS 5 (2021) 548
- SELF PorTrait (CRCM, CPPM, I2M), Fondation arc (2024-2026)
  - Recherche des vulnérabilités aux stades précoces et avances pour cibler des cellules cancéreuses et immunitaires dans des modèles de cancer du foie
- FLAP*VAP (C2VN, CERIMED, ICR, CRCM, CPPM, iDEAL), AMIDEX interdisciplinaire (2024-2026)
  - [^{18}F]F-fluorinated apelin for PET vasculomonitoring of APJ expression

Chronography

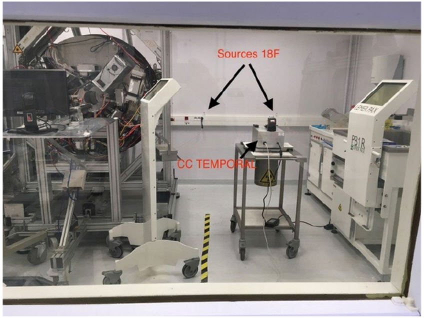
Cherenkov and cross-luminescence timing for highly time resolved ionizing radiation detectors for physics and society

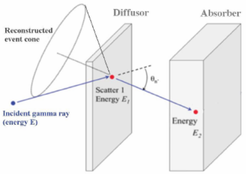
EIC Pathfinder Open 2024 – rated: 3.95/5.00 – resubmission in 2025

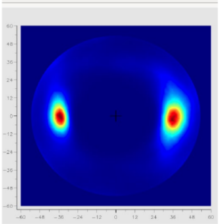



Characterization of the Temporal Compton camera using Philips dSiPM

- Angular resolution (ARM): (21.3 ± 0,4)°
- Intrinsic efficiency: ~8‰ (measured), 11.2‰ (simulated)
- Thèse **Brahim Mehadji** (AMU, 2021) -> Associate Prof. UC Davis

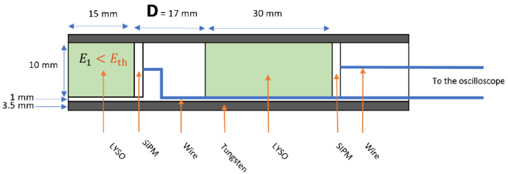




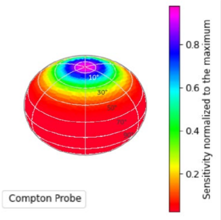


Source 1 : –30 cm — source 0 : 30 cm
Source-camera distance_ : 60 cm

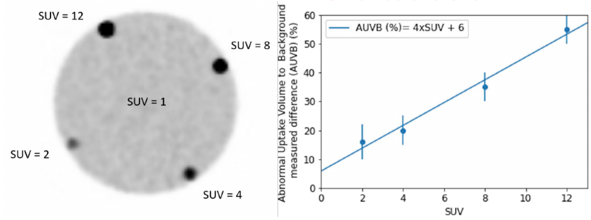
CCP: Compton Collimated Probe



$$\theta_{max} = \mathrm{acos}\left(1 - \frac{E_{th}}{E}\frac{m_e c^2}{E - E_{th}}\right)$$



B. Mehadji, *et al.* JINST 19 (2024) T08002
B. Mehadji, M. Dupont *et al.* PCT/EP2024/075264
CNRS Déclic 2023-2024



ResPlaNDIR: Motivations and Projects

Creation

- Informal network of physicists and biologists working in the field of X-ray and Hadron radiobiology
- ResPlaNDIR: Network of National Platforms for Dosimetry, Instrumentation and Radiobiology
- Creation within the GDR MI2B in 2013
- Steering Committee: P. Annalisa (CPO-Orsay), E. Bayart (Radiotransnet), F. Chevalier (CIMAP-Caen), C. Koumeir (Arronax-Nantes), A. Leite (IJCLAB-Orsay), C. Mirjolet (CGFL-Dijon), M. Rousseau (LPCC-Caen), M. Vidal (CAL-NICE

Main objective : Bringing users and developers together

- Definition of requirements for the development of hadronic platforms (Biologists $\Rightarrow$ Physicists)
- Assistance with dosimetry and good practice for commercial X-ray irradiators (Physicists $\Rightarrow$ Biologists)
- Dosimetric intercomparison (under progress)
- Regular meetings: 8 since 2013 (between 30 and 60 participants/meeting)
- ...

ResPlaNDIR: Current study and project

Current study

- Dosimetric inter-comparison (dose monitoring with Alanine + LET measurement in irradiation fields from the hadron platforms)

Projects

- Development of common control instruments
- Creation of a master bank of cells and common biological protocols enabling biological inter-comparison (Dedicated budget needed)
- Creation of a dedicated webpage to help access equipment

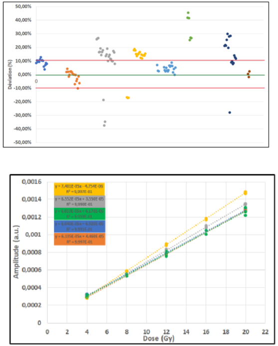
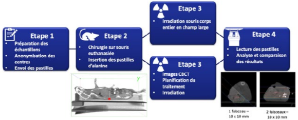
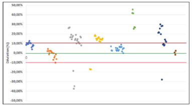


Fig. 27: Preliminary results of the dosimetric inter-comparison performed by M. Dos Santos (ASNR).

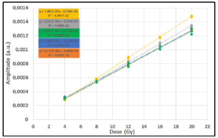
Resplandir: Intercomparison of irradiation platforms using alanine dosimetry

- Etude réalisée par M. Dos Santos (ASNR)
- Plateformes X:





- Plateformes hadrons:



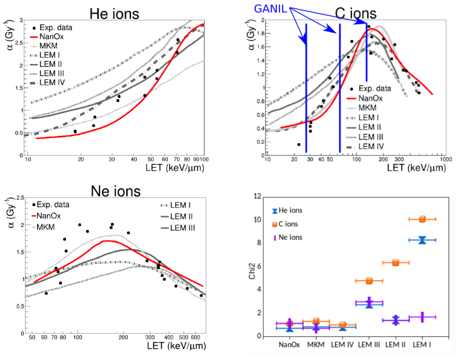
Alanine dosimetry

- Internationally recognized technique
- Based on the irradiation of the amino acid alanine, which produces free radicals in proportion to the absorbed dose.
- These radicals are reliably quantified using electron paramagnetic resonance (EPR) spectroscopy.

Importance of GANIL for cell irradiations and positioning in Europe/France

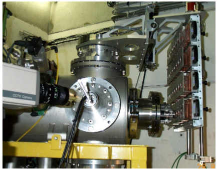
Room	Ion	Energy (MeV/u)	LET $\left(\frac{keV}{\mu m}\right)$	Range in H_2O (mm)
GANIL	^{12}C	95 (D1)	28	$\gg 1$
		35 (D1)	63	
	^{13}C	13.6 (SME)	134	0.8
ALTO	p	$\rightarrow 15$	3	2.5
	α	$\rightarrow 10.75$	17	1.5
	^{7}Li	$\rightarrow 12.5$	55	0.5
ARRONAX	p	$\rightarrow 65$	1	$\gg 1$
	α	$\rightarrow 16$	10	

α coefficients for HSG cell [Monini 2019]



- GANIL's carbon ion energies $\Rightarrow$ Sampling of the energy range of interest (with the increase of biological efficiency)
- Unique facility in France and few similar facilities in Europe for cell irradiations with carbon ion beams

Current status and perspectives in GANIL (cell irradiation beam lines)



Current status

- Cell irradiation with IRRABAT (mono-energetic carbon ion beams in D1)
- Energy: $\sim$ 35 MeV/u (with degrader) $\rightarrow$ 95 MeV/u

Possible additional facilities and measurements

- Mono-energetic "low-energy" carbon ion beams @ SME (13.6 MeV/u)
- SOBP @ D1: SOBP of $\sim$ 1 cm with a distal position at 25 mm

Outcomes

- Cell response + cell survival
- Physico-chemical measurements such as radiolytic yields (model constraints + dosimetry)

Methodology

- 1st meeting in September 2022: directions of GANIL, LARIA, CIMAP, GDR MI2B + M. Beuve (IP2I)
- Consultation of the community
- [$\Rightarrow$] Estimate of the beam time request (Go/No-go for a premilinary project)

Platforms: CAL and ARRONAX

CAL Nice

- CAL: protontherapy center ⇒ No IN2P3 staff
- Current CNRS-CAL agreement: beam time of 24h/year for research

	Année	1		2		3		
Porte-parole	**Intitulé de l'expérience**	**COMEX1 Mai2021**	**COMEX2 Dec2021**	**COMEX3 Juillet2022**	**COMEX4 Nov2022**	**COMEX5 Juin2023**	**COMEX6 Oct2023**	**TOTAL**
MARCATILI	TIARA		12	8	10	10	12	52
PANGAUD	Tests ASIC		4		8	16		28
BALDACCHINO	Mesures de rendements radiolytiques	12		8				20
DAUVERGNE	PGPI-PGEI			8			12	20
ARBOR	Mesures de rayonnements secondaires Endommagements de molécules	8	**12**					8
RODRIGUEZ-LAFRASSE	Radiobio « phénotype et réponse immun. »						5	5
GUARDIOLA	Microdosimètre 3D	4						4
	TOTAL	52		42		55		137
							Prévues	144

ARRONAX

- IN2P3: 8 persons (not only an IN2P3 platform)
- Max: 50% of beam time for commercial activities (44% in 2024)

Platforms: CYRCé

- FTE: 6.2 (IN2P3) et 1 (CDD Université de Strasbourg
- Activities: 90% research and 10% for valorization
- Research projects: CYRCé has around 15 users from outside IN2P3 + 5-6 IN2P3 users (mainly IPHC groups)
- Beam time:
  - Total: 900 hours/year
  - Radiobiology: 300 h
  - Sensor, detector and dosimetry testing: 400 h
  - Radiolysis: 100 h
  - Isotope production (Zr89, Cu64, Cu67): 100 h
- Fundings
  - 15k€ per year from IN2P3
  - 15k€ annually from the University of Strasbourg
  - in-kind support and services (“prestations”) valued at around 20k€ to 30k€ per year
  - funding provided by France Life Imaging for the imaging-related components of the project

Platforms: AIFIRA

- FTE
  - Research: 1.7 FTE IN2P3 + 0.05 FTE Bordeaux University
  - Valorization: 1 FTE Bordeaux University
- Activity: 70% research and 30% valorization
- Research projects: 10 users for 13 different research projects - 6 projects led by laboratories outside of IN2P3
- Fundings
  - 15k€ from IN2P3 (shared between 3 technical platforms in the laboratory, including AIFIRA).
  - 50k€ allocated to AIFIRA from valorization activities.

Platforms: GANIL

- Interdisciplininary research platform@GANIL: CIMAP (INP). D1@GANIL: INP staff. Beam delivering@GANIL: IRFU/IN2P3
- Valorization: service of GANIL
- Beam time for radiobiology: between 120h and 240h corresponding to 60% to 100% of the beam time allocated with the "interdisciplinary" PAC (iPAC = 10% of the total beam time in GANIL)
- Number of experiment proposals/year: btw 5 and 10 (20-25 people in total)
- Funding: GANIL is a TGIR (Très Grande Infrastructure de Recherche) or IR; beam time is free of charge for fundamental research experiments and academic users