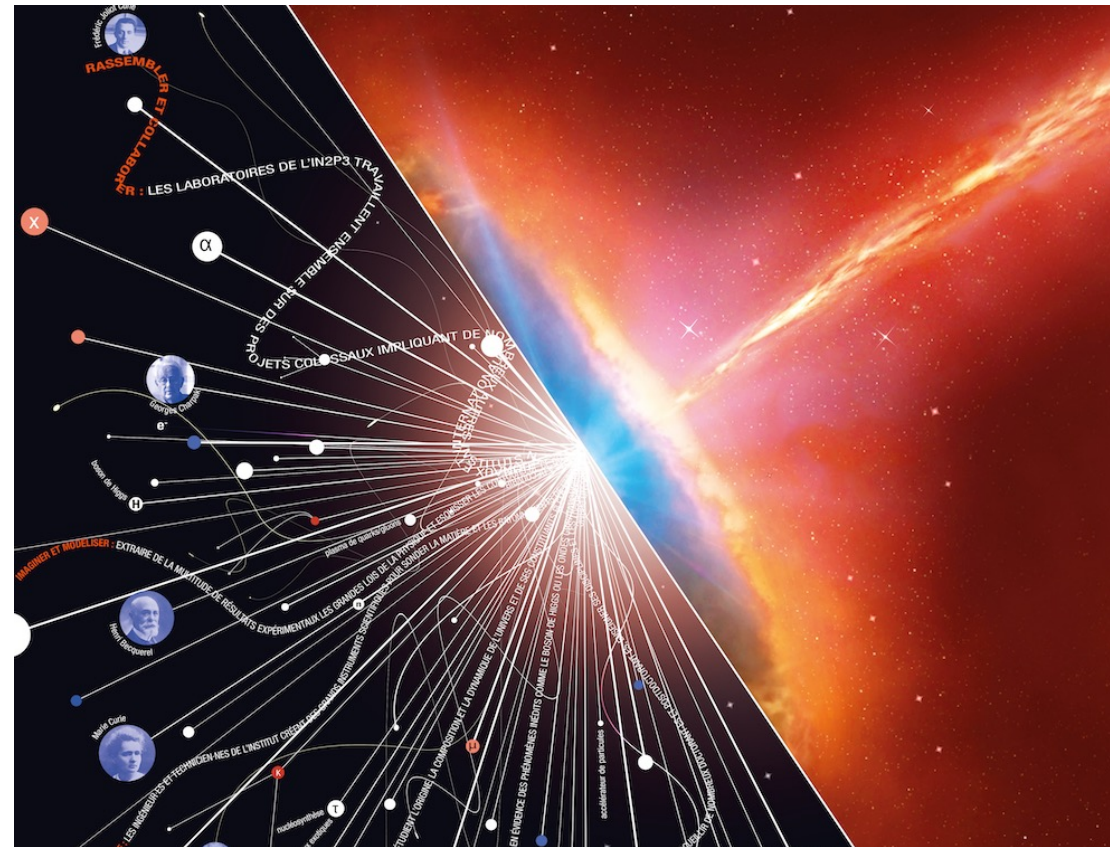




# National Institute of Nuclear and Particle Physics

[in2p3.cnrs.fr](http://in2p3.cnrs.fr)



## CNAO – IN2P3 Scientific strategy

Sébastien Incerti – scientific director for interdisciplinary research

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# « Nuclear physics for health » @ IN2P3

- At IN2P3, about **160 perm. researchers** (CNRS & faculties), **doctoral/postdoc fellows**, and **technicians & engineers** are involved in the interdisciplinary research program

## « nuclear physics for health »

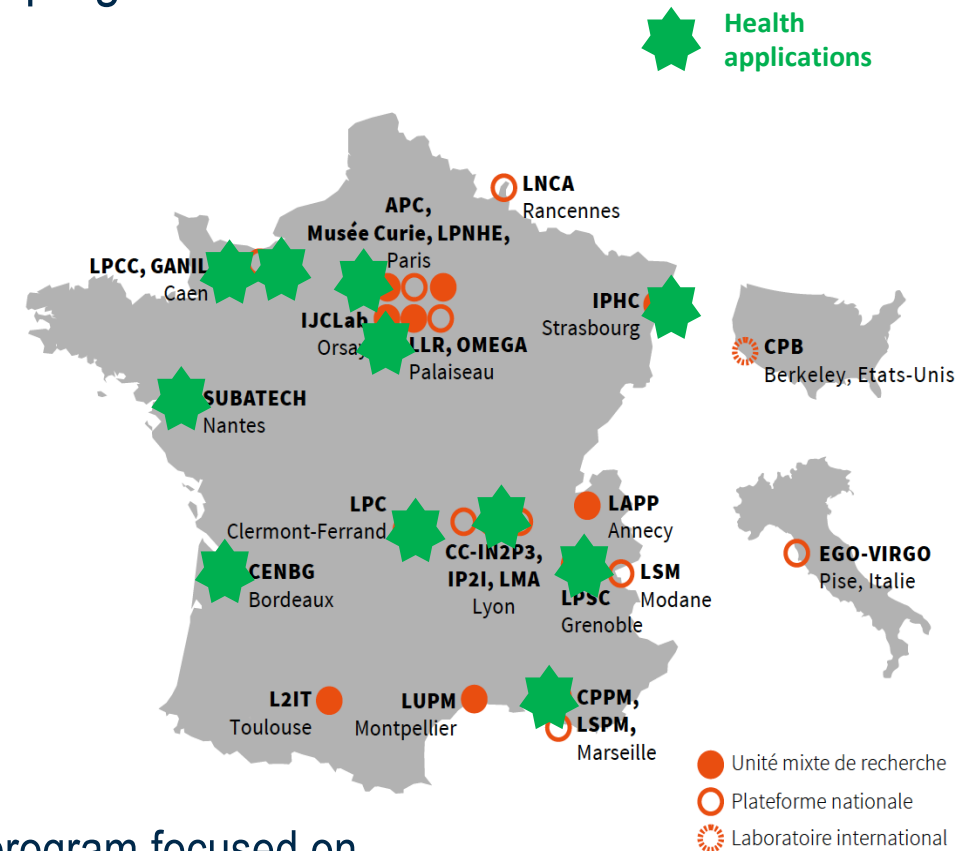
### – 4 priority topics

- Innovative **radiotherapies**, including **hadrontherapy**,
- Innovative medical **imaging**,
- **Radionuclides** for imaging and therapy,
- Multi-scale **radiobiology**

- 11 IN2P3 laboratories in France, including (often) s-o-a **irradiation PF** (see next)
- **Structured community** (IN2P3 & beyond) thanks to the « **GDR Mi2B : Nuclear tools and methods to fight cancer** » science animation tool, led by Denis Dauvergne

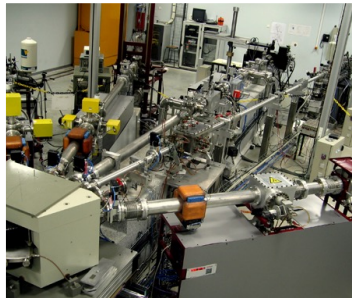
## • IN2P3 prospective exercise 2020-2030

- « **Improve the therapeutic efficiency of radiotherapy through innovative irradiation modalities** » identified as a « **Science Driver** »
- GDR Mi2B initiated in 2020 a brainstorming towards a national research program focused on hadrontherapy
  - Dedicated workshop (10/11/2020 – including CNAO) - <https://lpsc-indico.in2p3.fr/event/2534/overview>



# At the heart : IN2P3 ion beam irradiation platforms

Coming soon



**AIFIRA - Bordeaux**

p, d, alpha

3.5 MeV

Microbeam cellular irradiation  
in **single ion mode**

(<1.5  $\mu\text{m}$ , in vitro)

On-line videomicroscopy

« L2 » biology lab



**Cyrce - Strasbourg**

p, (alpha)

< 25 MeV

(in vitro, in vivo)

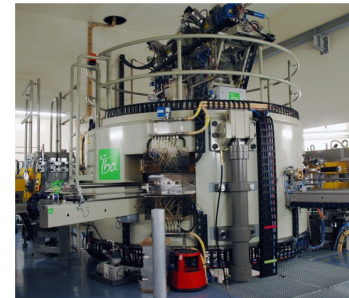
6 mm in water

Up to 26 mm field

Conventional  
(2 Gy/min)

to **Flash** (6 kGy/min),  
1  $\mu\text{s}$  pulses

L2, **small animal**  
(contention,  
anesthesia)



**ARRONAX - Nantes**

p (70 MeV),

d (35 MeV),

alpha (68 MeV)

(in vitro, in vivo)

Up to 3,8 cm in water  
(p)

Large field

Conventional  
to **Flash** (60 kGy/s),  
1  $\mu\text{s}$  pulses

Cells, Zebra, s. anim.



**GANIL - Caen**

from 95 MeV/A for  
light ions down to 24  
MeV/A for uranium

Cells irradiated with  
**C, O, Ne, Ar, Ni, Pb...**

IRABAT line

ARIA biology lab



**ALTO - Orsay**

H,  $^3\text{He}$ ,  $^4\text{He}$ , ...,  $^{14}\text{C}$ , ...  
up to  $^{127}\text{I}$

1 – 14.5 MV (HV)

Hadronbiology

NP-enhanced ther.

Organs-on-chips

FLASH...

- **No Carbon (& other ion) beams** in clinical conditions (120 – 400 MeV/A) : entrance up to Bragg peak
- Very limited beam time @ GANIL...
- Limited access to preclinical experiments or clinical trials
- Carbons **and** protons at the same facility



# Our ambition

- Highly motivated to **reinforce CNAO and IN2P3 scientific collaboration**
  - Priority : innovative projects involving carbon beams for hadrontherapy**
    - Goals** : more effective for radioresistant tumors, better sparing of healthy tissues, combined treatments (radio-, immuno-...)
    - Experiments from fundamental physics measurements to patient studies, including instrument dev. & simulations
    - Open to other **future** promising opportunities : **BNCT**, **alternative ions** for hadrontherapy (He, O, ...)
  - Historical links** between CNAO & IN2P3 teams
    - LPSC - Grenoble** : tests of the synchrotron dipoles, construction of the betatron magnet, design & construction of the low-level electronics of the accelerator cavity and beam dynamics studies
    - IPHC - Strasbourg** : charge identification of nuclear fragments with the FOOT TOF system (p, C, & O @ GSI)
- A stimulating **international context**
  - Heavy Ion Therapy Research Integration (HITRI+, <https://www.hitriplus.eu>) H2020 TNA : beam time @ CNAO
  - International Biophysics Collaboration initiative (IBC, <https://doi.org/10.3389/fphy.2020.00380>)

We proposed to organize a **brainstorming (« acculturation & ideation ») workshop** on 26/11/2021 @ CNAO

- 49 participants, including IN2P3, INSB, INS2I
- 4 sessions : **beam monitoring + online control + dosimetry**; **radiobiology**; **BNCT**; **simulations**

## Outcome

- Letter of intent**
- Basis of the IN2P3 – CNAO Collaboration framework agreement
  - Specific agreements**
  - Coordination committee** : **A. Facchetti & M. Pullia, M. Vanstalle & D. Dauvergne**

Welcome by CNAO	G. Vago et al.	08:00 - 08:10
Welcome by IN2P3	S. Incerti	08:10 - 08:20
CNAO accelerators and experimental room	M. Pullia	08:20 - 08:30
Clinical activities and clinical research at CNAO	E. Orlandi	08:30 - 08:40
3D sensors for microdosimetry with ions	C. Guardiola	08:40 - 08:50
Fast diamond beam monitors for online control of the treatment and application with TIARA project: prompt...	M.-L. Galin-Martel et al.	
Secondary neutron measurements	N. Arbor	09:00 - 09:10
PEPITES: a ultra-thin secondary-electron based beam monitor	M. Verderi	09:10 - 09:20
STRONG project: Si pixel sensors for particle tracking	J. Baudot	09:20 - 09:30
CNAO Neutron dosimetry and RP activities	M. Ferrarini	09:30 - 09:40
Prompt gamma camera developments at CNAO	C. Fiorini	09:40 - 09:50
Innovative detectors for beam monitoring in particle therapy	R. Sacchi	09:50 - 10:00
The CNAO dose delivery system and the DDS 4.0	M. Donetti	10:00 - 10:10
Discussion		10:10 - 10:40
Break		10:40 - 10:50
The PICTURE project	E. Testa	10:50 - 11:00
LPSC activities	D. Santos et al.	11:00 - 11:10
Some commissioning and dosimetry aspects of an AB-BNCT facility at CNAO-1	S. Aposteo	11:10 - 11:20
Some commissioning and dosimetry aspects of an AB-BNCT facility at CNAO-2	S. Alberti	11:20 - 11:30
Discussion		11:30 - 12:00
Lunch		
		12:00 - 13:15
LRCM activities	C. Rodriguez-Lafraisse	13:15 - 13:25
ISTCT activities	S. Valable	13:25 - 13:35
CNAO Radiobiology research	A. Facchetti	13:35 - 13:45
The radiobiological rationale for novel physics-based approaches in protontherapy	L. Mandl	13:45 - 13:55
Discussion		13:55 - 14:25
LURIS & IP2I activities	H. Ladjal	14:25 - 14:35
The GATE project	L. Maigne	14:35 - 14:45
IPHC & LPCC activities	Q. Raffy	14:45 - 14:55
Automatic procedures for setup optimization of an Eye Tracking System in ocular proton therapy	A. Pella et al.	14:55 - 15:05
Medical physics activities at CNAO and treatment planning developments	M. Ciocca	15:05 - 15:15

# Letter of intent : 6 research axes

Thanks to this « ideation » workshop, **six collaborative research topics** have been identified

- **short/mid term**, representatives for IN2P3 (+ other CNRS institutes) & CNAO

## 1. Innovative instrumental developments for beam monitoring and control of carbon therapy treatments

- M.-L. Gallin-Martel (LPSC- Grenoble) and/or E. Testa (IP2I-Lyon) + M. Donetti (CNAO-Italy)
- PEPITES in clinical C beam conditions, prompt gamma detection including timing detection (CLaRyS, TIARA)

## 2. Instrumentation and modeling challenges for BNCT

- N. Arbor (IPHC- Strasbourg) and R. Delorme (LPSC-Grenoble) + M. Ferrarini (CNAO-Italy)
- Neutron spectrometry, dosimetry, modelling of biological effects (eg. RBE) up to TPS : links to targeted alpha-therapy

## 3. Radiobiology with carbon ions and in BNCT

- C. Rodriguez-Lafrasse (IP2I-Lyon) and L. Sancey (IAB-Grenoble) + A. Facoetti (CNAO-Italy)
- Biological processes & endpoints (eg. cell survival), including combined therapies for different models : cell lines, bio-scaffolds, brain tumors, in ovo, small animals

## 4. New radiolysis measurements and simulation benchmarking in carbon therapy:

1. Radiolysis project, J. Vandenborre (Subatech-Nantes), M. Pullia for organization and access to beamtime (CNAO-Italy) :  
build reference data for radiolysis under several irradiation qualities (type of incident particle & energy, dose rates) – input & validation of mechanistic simulation codes
2. Benchmarking of Monte Carlo codes for treatment planning in carbon therapy project, L. Maigne (LPC-Clermont) + G. Magro (CNAO-Italy) :  
comparative evaluation of state-of-the-art codes (GATE-Nanox, FLUKA, UNIVERSE...) for carbon therapy treatment planning

## 5. Moving organs

- H. Ladjal (LIRIS-Lyon) and G. Baroni (Politecnico di Milano-Italy)
- Optimize irradiation of moving organs, using tumor tracking by external motion monitors and associated biophysical modelling

## 6. Accelerator studies

- M. Baylac (LPSC-Grenoble) and M. Pullia (CNAO-Italy).
- Open to proposals

# Towards the first two « specific agreements »

Identification of two collaborative projects : we are « ready to start »

- **Science** : « Multi-scale hadronbiology with Carbon ions »
  - Angelica Facchetti et al. (CNAO)
  - Claire Rodriguez-Lafrasse et al. (LP2i Lyon)
- **R&T** : « Beam monitoring @ CNAO with PEPITES » by Marie
  - Marco Donetti et al. (CNAO)
  - Marc Verderi et al. (LLR Palaiseau)

... paving the way to other innovative research & R&T projects :

« Collaboration topics between CNAO and IN2P3 partners » by Denis

**An ambitious workplan for the years to come ! Thank you**

# Backup

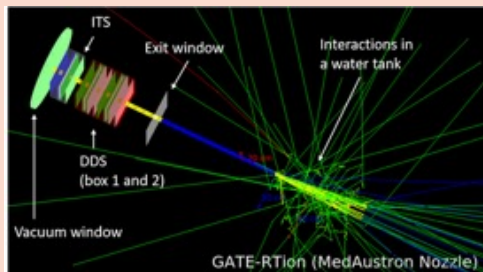


# Biomedical research activities

Coordinated by Denis Dauvergne (IN2P3) and Marie Dutreix (INSB)

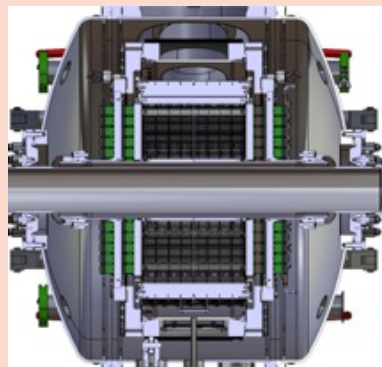
## Tools and methods for innovative radiotherapy

New modalities of **dose delivery**: various types of radiation (p, C...), spatial fractionation, flash therapy, radiosensitizers..., **dosimetry, instrumentation, modeling.**



## Methods and instruments for biomedical imaging

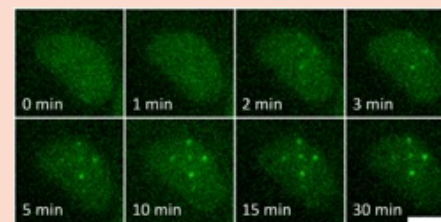
Nuclear and particle physics technical know-how to improve **molecular preclinical imaging techniques, treatment planning and monitoring**



XEMIS2 - Subatech

## Effects of ionising radiation on living organisms

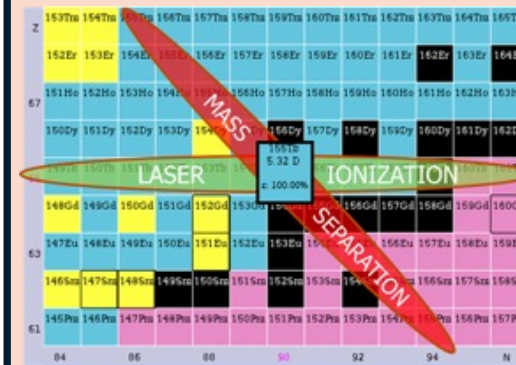
Structuring and implementation of **theoretical models and multi-scale simulations**, related tools and **technical platforms**, multidisciplinary collaborations (+physico-chemists, biologists, biophysicists) on **radiobiology**



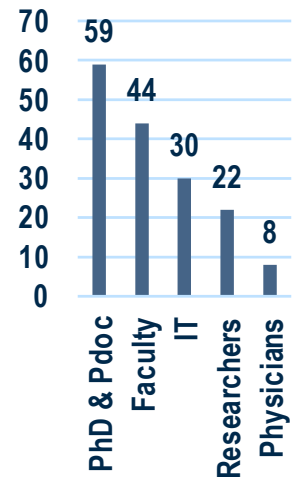
Cellular ion microbeam irradiation

## Radionuclides for imaging and therapy

Promiting research associated with innovative radionuclides: **theranostic** approach (imaging and therapy), availability of **radionuclides** of interest and **radiopharmaceuticals**



**160 Collaborators**



Slide by GDR & DD

Transverse topics: Clinical applications, Biology, Computing (simulation, data processing, modeling), Irradiation platforms (ResPlanDir network)