



Frédéric Pouzoulet

Responsable de plateforme – BIP

Site d'Orsay – Plateforme de Radiothérapie Expérimentale



Thématiques : Radiobiologie, Radiothérapie, Hadronthérapie, Lymphome primitif du cerveau, Physique Médicale, Expérimentation animale, Codes

- **Plateforme:**
 - Gestion et administration de la plateforme de radiothérapie expérimentale (6 équipements, 6 personnels)
 - Support scientifique et technique aux équipes de recherche et médicales
- **Scientifiques:**
 - Lymphome primitif du cerveau
 - Stratégies innovantes de radiothérapie:
 - Minifaisceaux
 - Activation de molécules par les rayonnements ionisants
 - Développements de nouveaux modèles expérimentaux
- **Mandats:**
 - Représentant du personnel (Centre de Recherche, Institut Curie)
 - Administrateur de la Société Française de Biologie des Radiations
 - Membre du « bureau » de Resplandir

Experimental Radiotherapy Facility

Frédéric POUZOULET

Translational Research Department

Introduction



Experimental Radiotherapy

Aim: therapeutic window increase

Biology

- Targeted therapy
- Immuno therapy

Physics

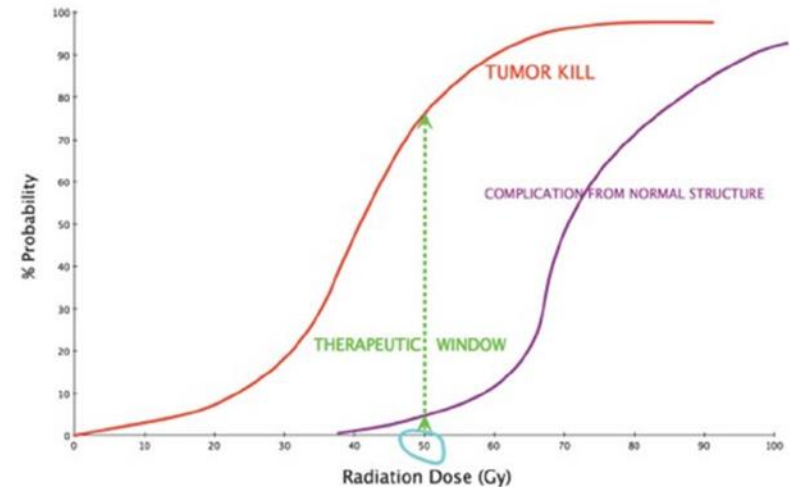
- Spatial-temporal dose splitting
- Ionizing particles (carbon ions, protons,...)

Chemistry

- Free radicals scavenger
- Water radiolysis modulation

Interdisciplinary field

Needs to gather together scientific and technical expertise ranging from medical physic to preclinical research

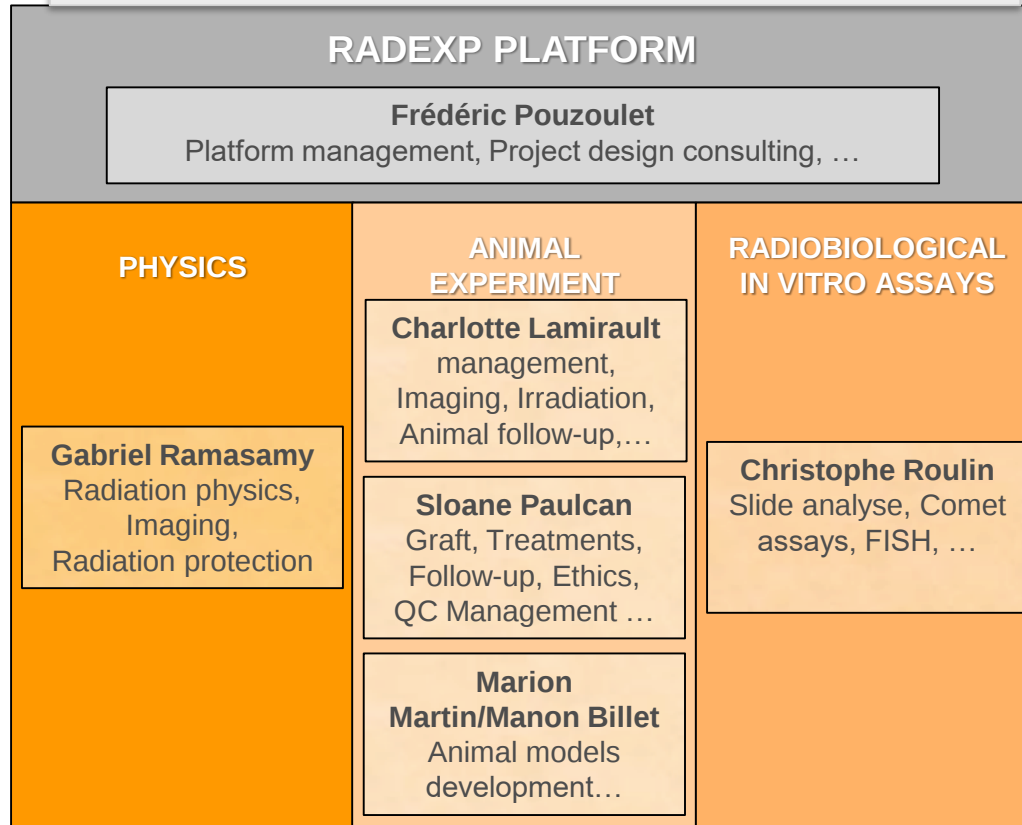


Experimental Radiotherapy Facility

- **Project initiated in 2011 by the Translational Research Department**
- **Objectives of the facility :**
 - ☐ Gathering together scientific and technical expertise ranging from medical physic to clinical and preclinical research providing support and guidance to community
 - ☐ Managing access to a large panel of irradiation devices
 - ☐ User training

RadeXp Facility supports projects in the field of experimental radiation therapy

Multi-skilled team to encompass the main areas of radiation biology



Operating Modalities

- Irradiator autonomous use
- Partially outsourced projects
- Completely outsourced projects

Ionizing Radiation Sources available on



X-Rays generators

- **Source:** 320 kV X-rays generator

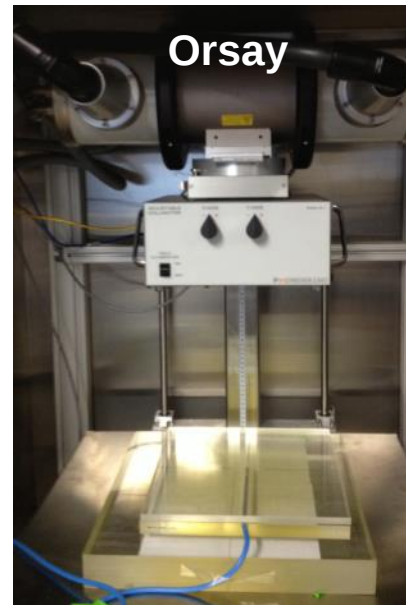
- **Mean energy:** from 30 to 160 keV

$HVL_{320kV} = 3,3 \text{ mm Cu}$

$HVL_{200kV} = 1 \text{ mm Cu}$

$HVL_{50kV} = 2 \text{ mm Al}$

- **Dose rate:** from 0.05 to 4 Gy/min



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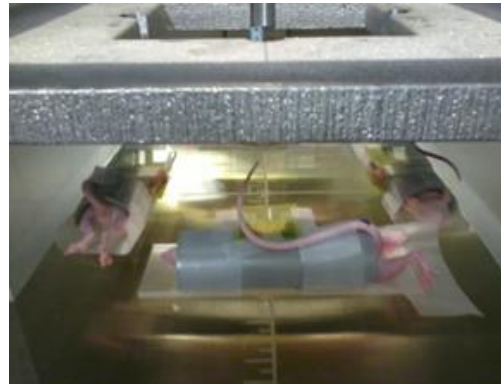
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- **Applications:**

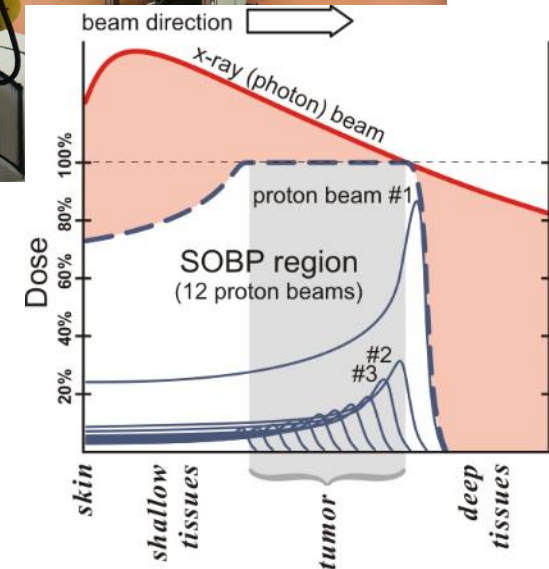
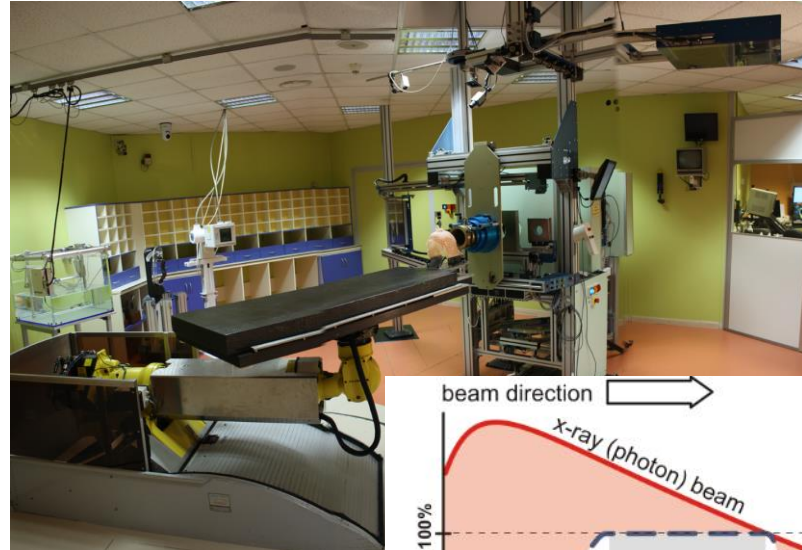
- Cells irradiations

- Mice irradiations (total body, localized)



Access to proton medical beams of Protontherapy Center of Orsay

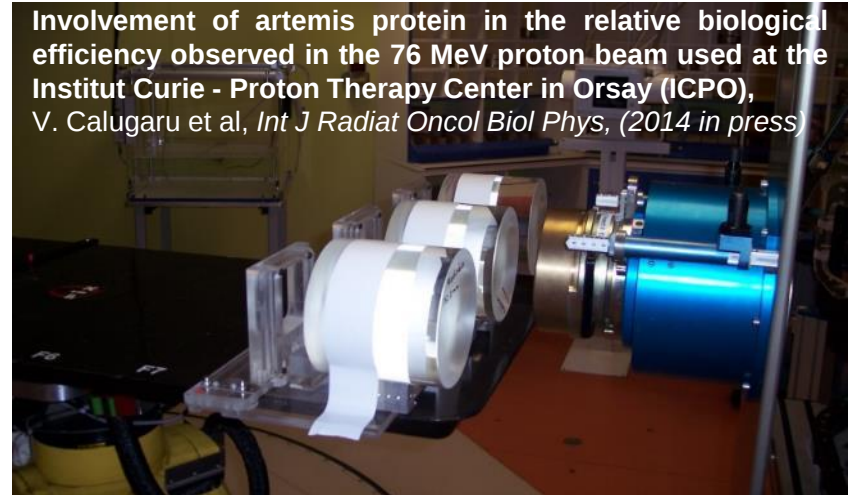
- **Source:** *Cyclotron (IBA)*
- **Energy:** *76-201 MeV*
- **Raw or Spread Out Bragg Peak**
- **Dose rate:** *0.1 to 20 Gy/min*



Access to proton medical beams of Protontherapy Center of Orsay

- **Source:** *Cyclotron (IBA)*
 - **Energy:** *76-201 MeV*
 - **Raw or Spread Out Bragg Peak**
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 - **Applications:**
 - *Cells irradiations*
 - *Mice/rat irradiations*
- (total body, localized: leg, head, chest)*

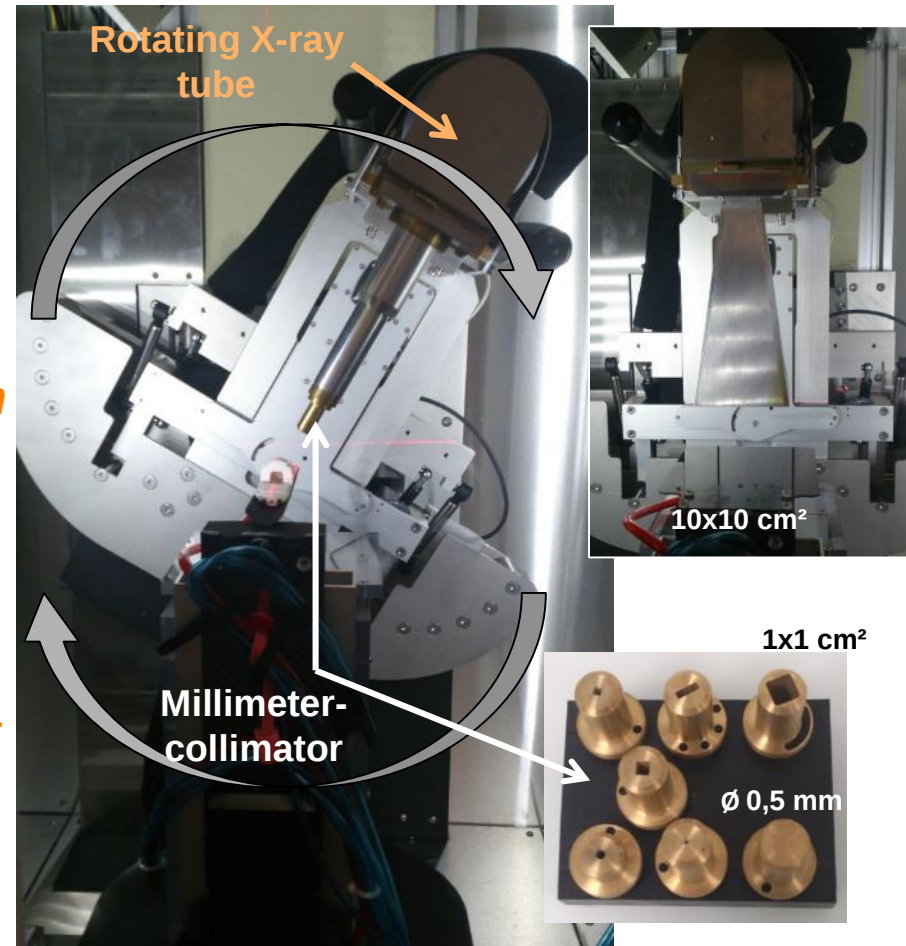
Involvement of artemis protein in the relative biological efficiency observed in the 76 MeV proton beam used at the Institut Curie - Proton Therapy Center in Orsay (ICPO),
V. Calugaru et al, *Int J Radiat Oncol Biol Phys*, (2014 in press)



Improving the performance of protontherapy using nanoparticles Y. Prezado (IMNC, Paris XI university)

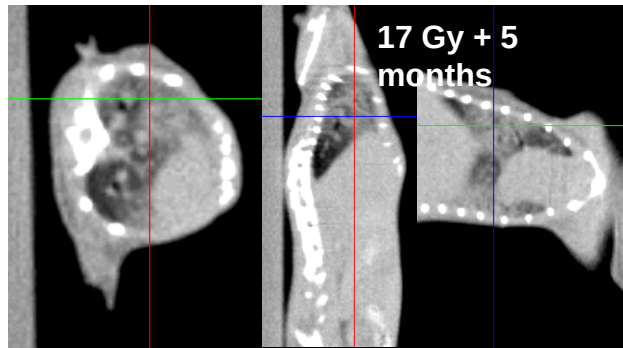
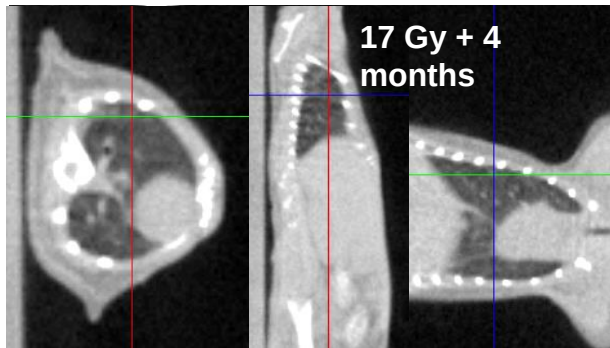
SARRP: Image-guided micro-irradiation System

- **Source:** 225 kV X-rays generator
- **Mean Energy:** 30-70 keV
- **Dose rate:** 0.1 to 4 Gy/min
- **Features:**
 - Combined system of CT imaging and **multi-incidence X-ray μ -irradiation**
 - Dose calculation and treatment planning software
- **Applications:**
 - **Mimicry of real radiotherapy patient set-up techniques**
 - Orthotopic tumor image-guided treatments

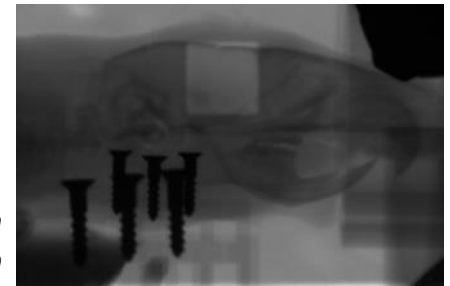


SARRP Applications

✓ Pulmonary fibrosis follow-up (CT imaging)



*Radio-induced fibrosis study:
V. Favaudon, C. Fouillade*

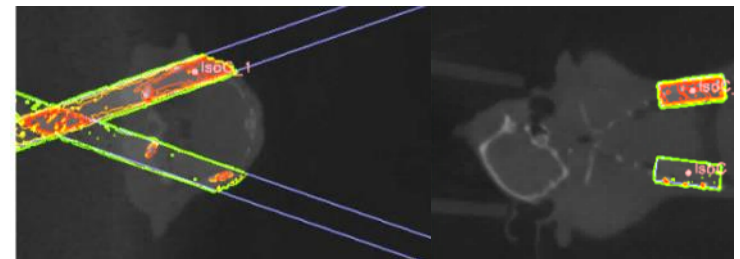


*Non-isocenter rat brain
irradiation: Y. Prezado*

✓ Brain irradiation on rats and mice

✓ Localized lung irradiation:

- heart avoidance
- dealing with lung movement: respiratory gating system to be implemented



Healthy lungs irradiation: V. Monceau

✓ Orthotopic grafts treatments

ImPLY target localization → Requires the development of multi-modal imaging



Activities

Platform staff involvement

- **Preparatory Phase:**
 - Project design consulting (experimental protocols, funding application, ethics committee application)
 - Personalized irradiation set-up
 - Animal models development
 - Characterization of tumor models radiosensitivity
 - Drugs synthesis and quality control (collaboration with Chemolibrary staff)

Platform staff involvement

- **Experimental Phase:**
 - Tumor inoculation
 - Tumor growth follow-up
 - Treatments
 - Irradiation
 - Imaging (BLI)
 - Behaviour studies
 - Tissue sampling
 - Histological analysis (collaboration with Pathex and Sophie Le Boucher Dodier)
 - Results analysis



In the future

Specific room for radioactive animals (activation, imaging, treatment)

- **Planned to open beginning 2023:**
 - Biosafety level: A1/A2
 - Capacity: 100 cages
 - Species: rats/mice
- **Preclinical MicroPET / MicroCT**
- **Perhaps Preclinical ultrasound imaging**



How to turn user into
collaborator?

Main projects

- **Primary Central Nervous System Lymphoma (Carole Soussain, MD/PhD, Hematologist)**
 - **MiniBeam Radiotherapy (Yolanda Prezado, DR Cnrs, Physicist)**
 - **Ionizing Radiation-Triggered Theranostic Treatment (Guillaume Bort, CR Cnrs, Chemist)**
 - **Treatment of retinopathy induced by ionizing radiation (Alexandre Matet, MD/PhD, Denis Malaise MD, Ophtalmologist)**
 - **Combination PARPi + Protontherapy (Carine Laurent, Archade Scientist, Radiation Biologist, Dinu Stefan, MD, Radiation Oncologist)**
 - **Protontherapy/Radiotherapy: Ludovic De Marzi, Rémi Dendale, Annalisa Patriarca, Samuel Meyronneinc, Pierre Verrelle, Valentin Calugaru, Hamid Mammar,...**
-

Profile

- **At the beginning user profile:**
 - Lack of time to manage project
 - Lack of access to manpower (without staff or team,...)
 - Lack of access to devices (Protontherapy, animal house,...)
 - Lack of expertise (Radiation Biology, Animal experiment, Biology, Physics, Chemistry, administrative process, Medical Doctor...)
 - **Evolutionary factors**
 - Complete outsourced project
 - Grant hunting (targeting call, writing support,...)
 - Staff skills
 - Access to Medical Doctor/scientific community
 - Network
 - Non scientific or non technical support (IC knowledge, national network,...)
 - Long term support
-

Results

- **Long term collaboration/projects**
- **Publications**
- **Patent**
- **Academic/Industrial contracts**
- **Institut Curie Attractiveness (Yolanda Prezado and Guillaume Bort hired at IC)**

Thanks

Steven Le Gouill
Alain Fourquet
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Stephane Thépault
Eric Brot
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Jonas Assuli
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Olivier Madar
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Jeremy Lachet
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Regis Ferrand
Claire Alapetite
Nathalie Cassoux

Denis Malaise
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Pierre Loap
Roman Rouzier
Pierre Bey
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Marc Bollet
Alejandro Mazal
Michel Auger
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Annick Gandhar
Vincent Bailly
Sebastien Brocoletti

Laurence Roy
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Morgane Dos Santos
Philippe Voisin
Hélène Elleaume
Nicolas Foray
Adeline Granzotto
Clément Devic
Jean-Louis Habrand
Jean Bourhis
Anna Chauvain
André Bridier
Dominique Violot

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Franck Assayag
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Sergio Marco
Fabrice Cordelière

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ENSEMBLE HOSPITALIER

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EXTERNES

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