Experimental Radiotherapy Facility

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Translational Research Department

Introduction

RadeXp+
Plateforme de radiothérapie expérimentale

Experimental Radiotherapy

Aim: therapeutic window increase

Biology

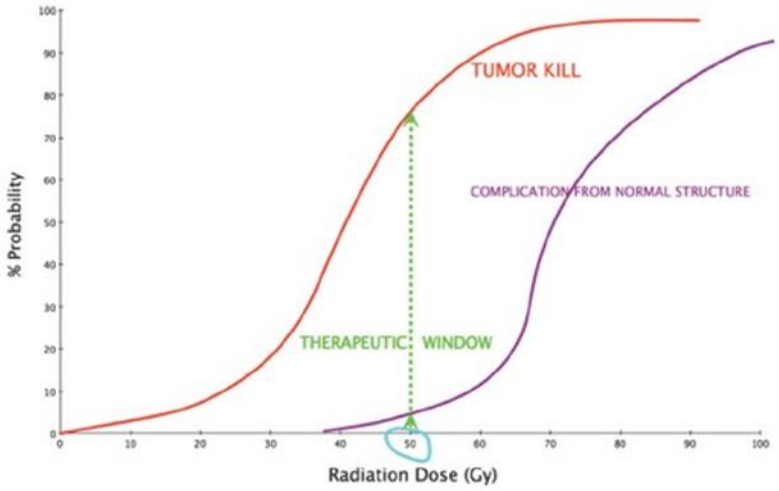
- **Targeted therapy**
- **Immuno therapy**

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 Translationnal 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

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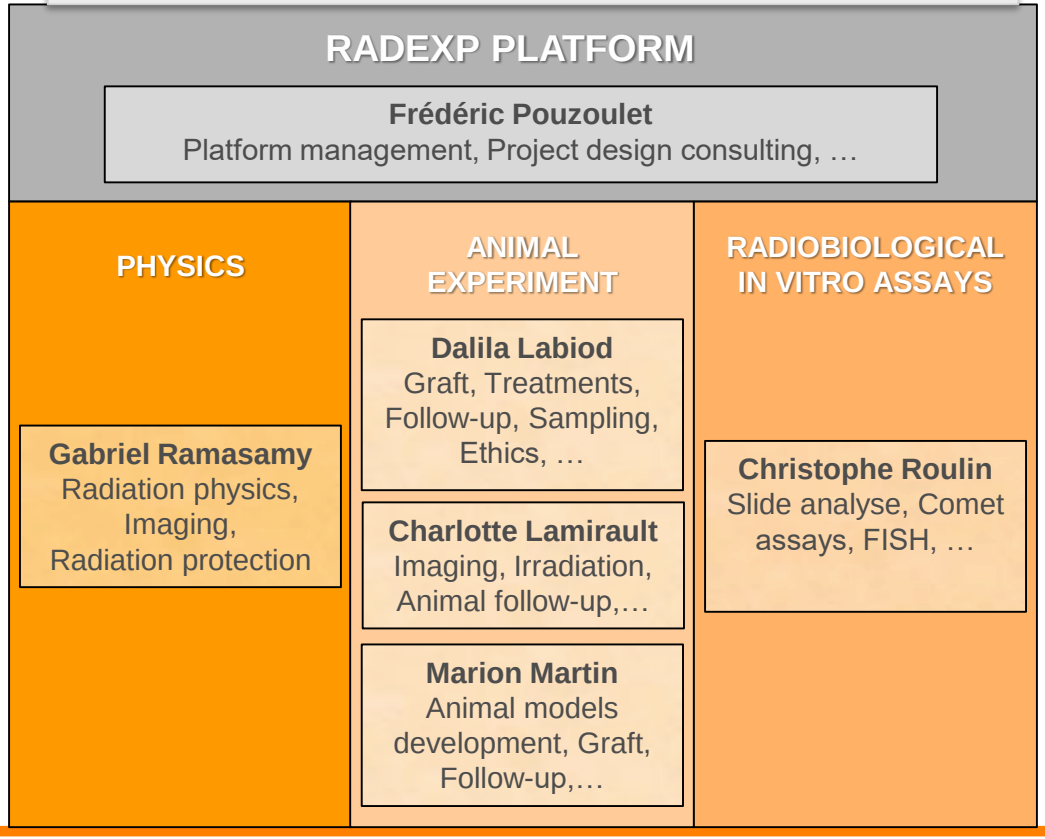
RadeXp Facility supports projects in the field of experimental radiation therapy

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



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Operating Modalities

- **Irradiator autonomous use**

- **Partially outsourced projects**

- **Completely outsourced projects**

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Ionizing Radiation Sources available on

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IBL637 / GSR D1

- **Source**: *Cesium 137*
- **Energy**: *662 keV photons*
- **Dose rate:** *1 Gy/min to 15 Gy/min*
- **Applications:**

- Cells irradiations

- Mice irradiations (total body)

X-Rays generators

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

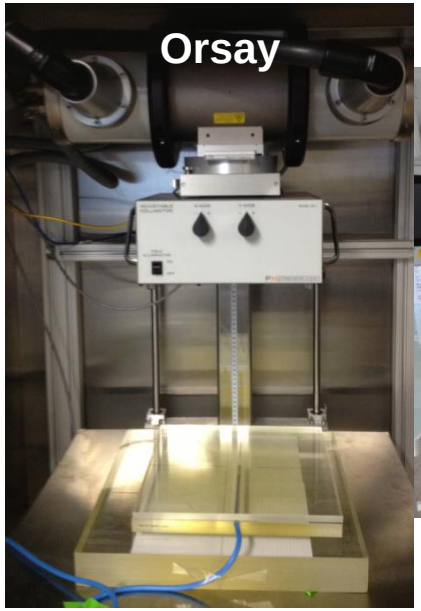
- **Mean energy:** *from 30 to 160 keV*

HVL_{320kV} = 3,3 mm Cu

HVL_{200kV} = 1 mm Cu

HVL_{50kV} = 2 mm Al

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



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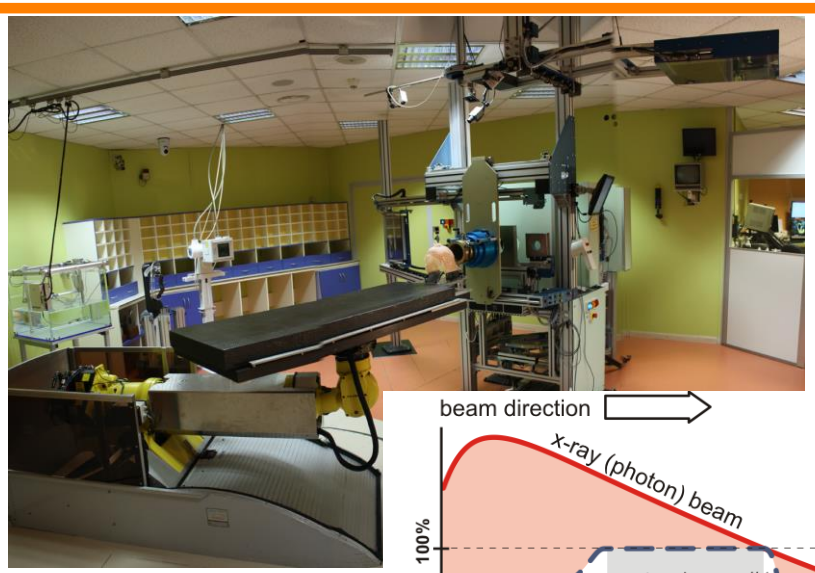
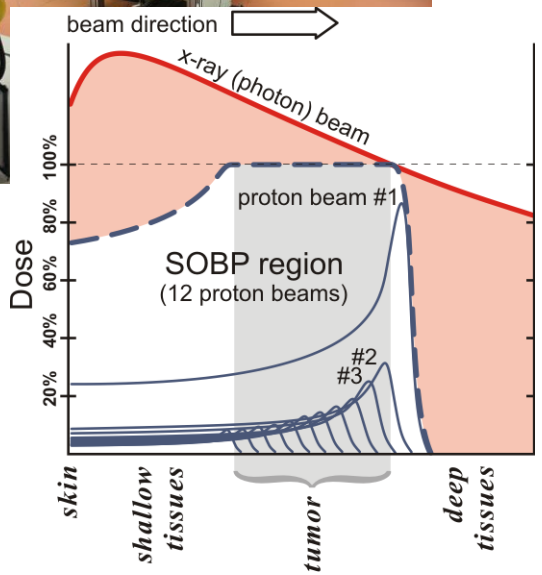
- Mice irradiations (total body, localized)

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*





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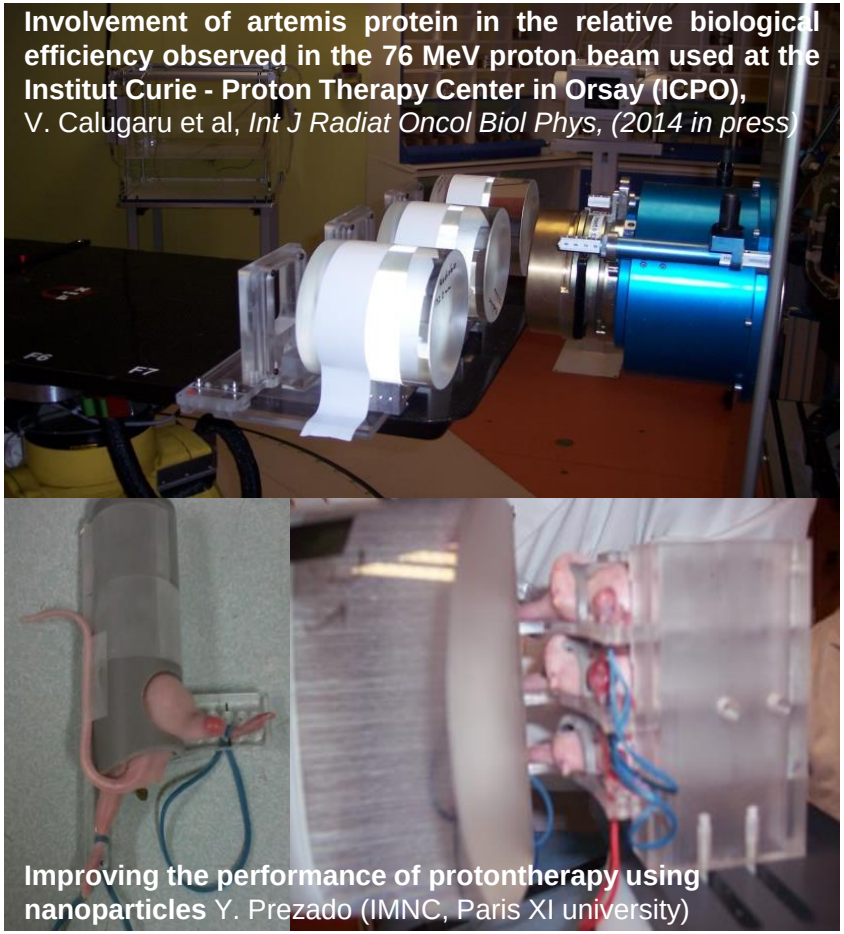
- **Energy:** *76-201 MeV*
- **Raw or Spread Out Bragg Peak**
- **Dose rate:** *0.1 to 20 Gy/min*
- **Applications:**

- 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:**

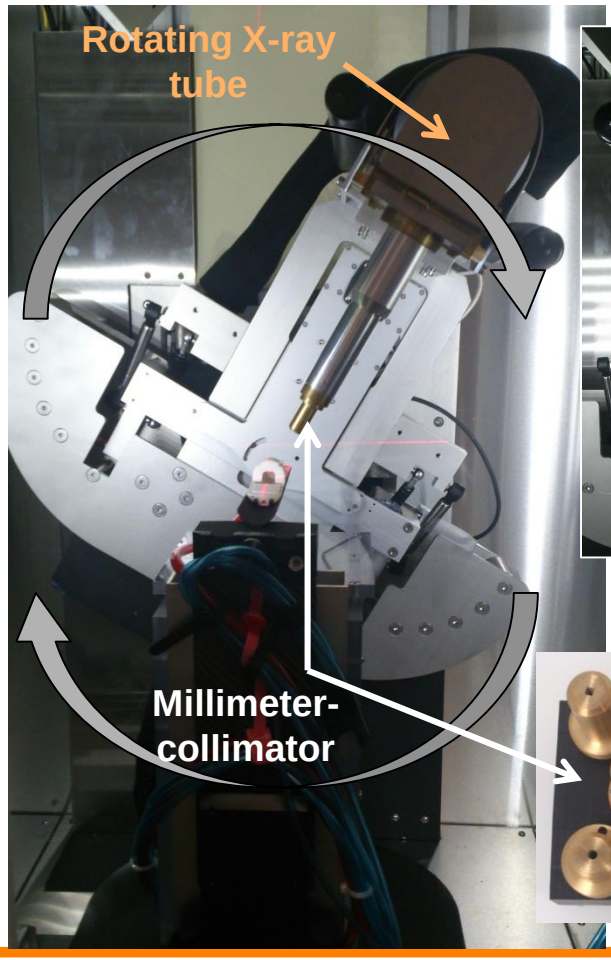
- Combined system of CT imaging and ***multi-incidence X-ray µ-irradiation***

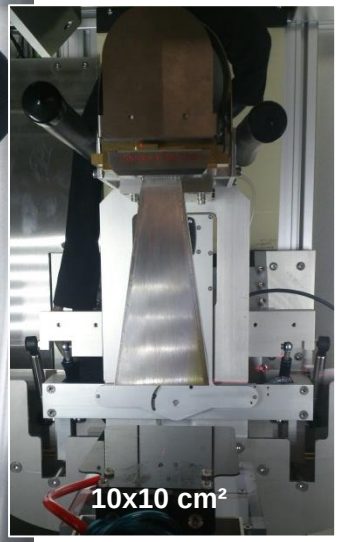
- Dose calculation and treatment planning software

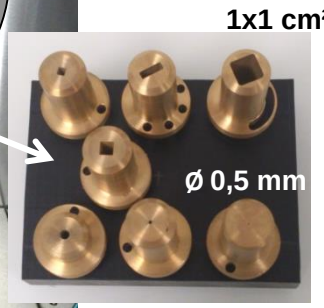
- **Applications:**

- ***Mimicry of real radiotherapy patient set-up techniques***

- Orthotopic tumor image-guided treatments

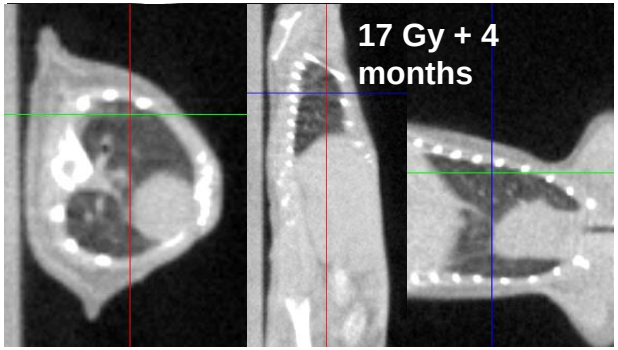


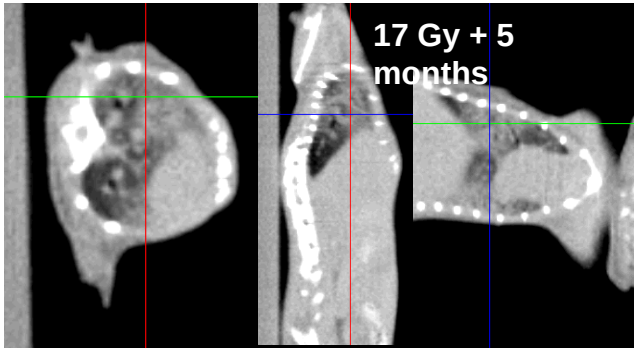




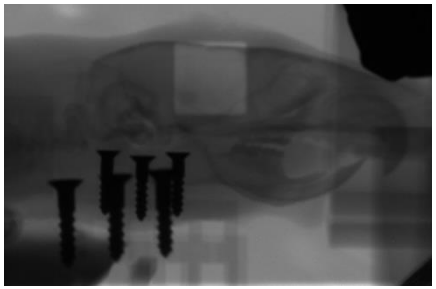
SARRP Applications

✓ **Pulmonary fibrosis follow-up (CT imaging)**





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

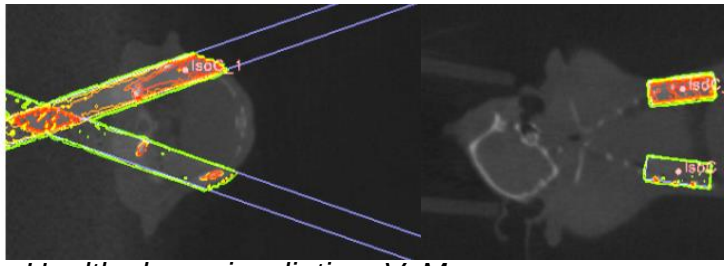


Non-isocenter rat brain irradiation: Y. Prezado

✓ **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

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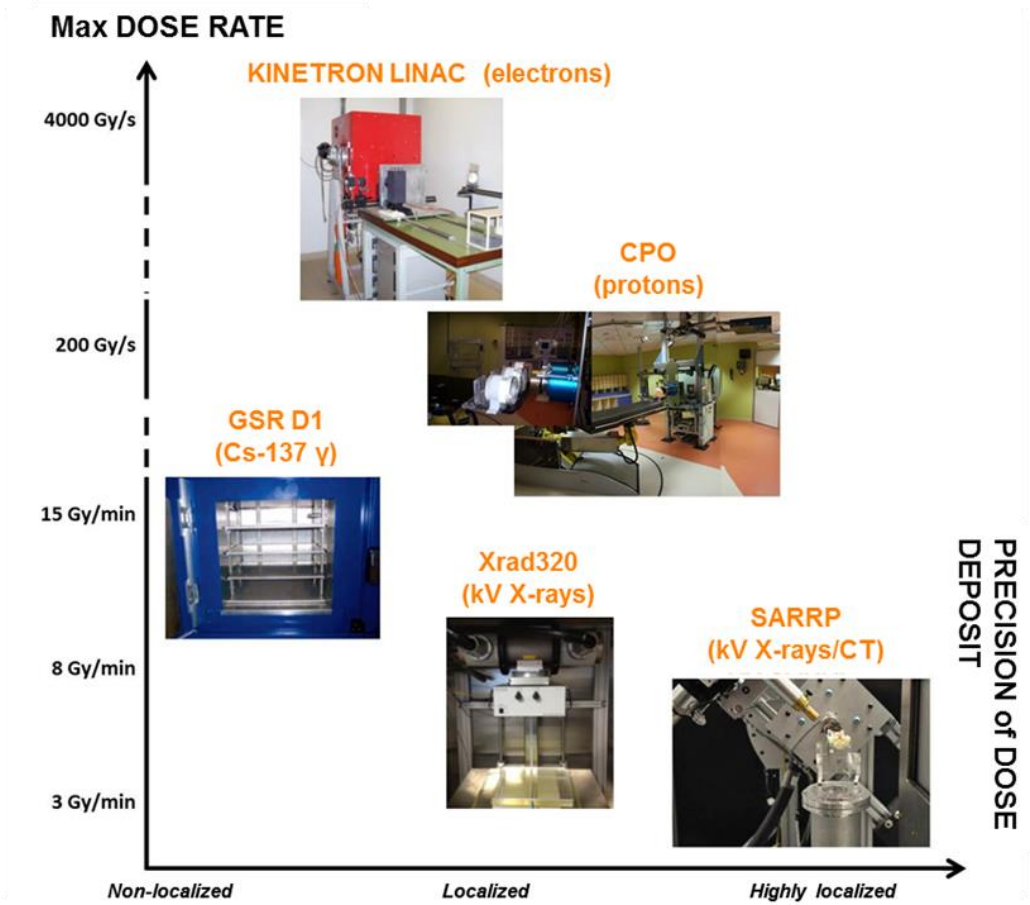
Summary of available radiation sources



Main Selection criterion	Recommended device
Many specimens at once	Cesium sources
Low dose/dose rate	X-ray sources
High dose / High dose rate / short irradiation	Cesium sources
Ultra High dose rate	Linear accelerator / proton beam
Pin-point precision	SARRP
Xenografts	Xrad320 / SARRP
Orthotopic grafts	SARRP
Radiotherapy treatment mimicry	SARRP
Radiotherapy RBE mimicry	Cesium sources
Bone marrow suppression	Cesium / 320kV X-ray sources
…	

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Activities

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Platform staff involvement

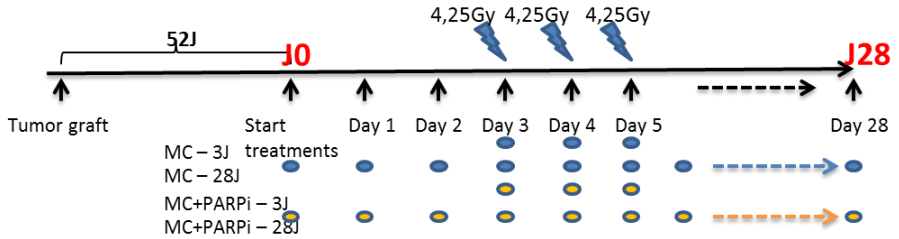
- **Preparatory Phase:**
  - **Project design consulting (experimental protocols, funding application, ethics committee application)**
  - **Personalized irradiation set-up**
  - **Animal models development**
  - **Characterization of tumor models radiosensitivity**
  - **Drugs synthesis and quality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

Platform staff involvement

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

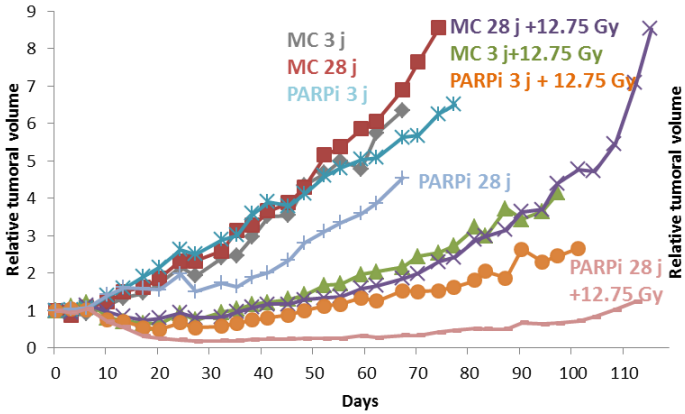
Project Example - Modulators of radiation susceptibility and innovative therapeutics.

Combined effects of AZD-2281 (PARPi) and X-rays on breast xenograft growth

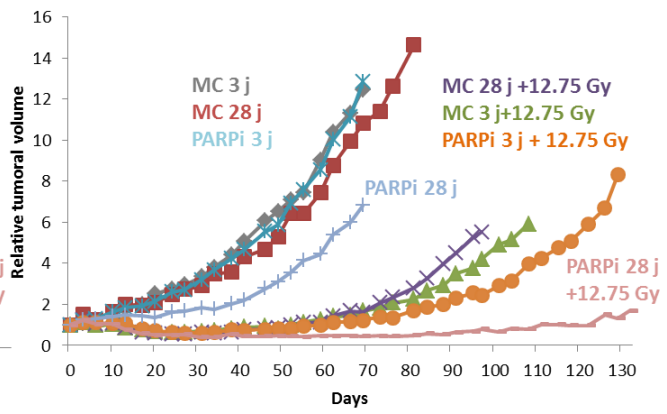


PARP i in suspension in a 0.5 % methylcellulose solution given at 100mg/kg per os

BC227 BRCA2 Mutated breast cancer



BC173 TN breast cancer



PARP inhibition radiosensitises both BC227 and BC173 breast xenografts

Collaborative project U612, Radiation platform, LIPs and RT Dept

Main projects

- **Primary Central Nervous System Lymphoma (Carole Soussain)**
- **Mini Beam Radiotherapy (Yolanda Prezado)**
- **Ionizing Radiation-Triggered Theranostic Treatment (Guillaume Bort)**
- **Treatment of retinopathy induced by ionizing radiation (Alexandre Matet, Denis Malaise)**

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In the future

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

- **Planned to open mid 2022:**
  - Biosafety level: A1/A2
  - Capacity: 100 cages
  - Species: rats/mice

- **Preclinical PET/CT**

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Thank you for your attention

Contact: radexp@curie.fr

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