

Animal experimentation on radiation beamlines

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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

Extended set of radiation devices to address all aspects of experimental radiotherapy

RADEXP PLATFORM

Frédéric Pouzoulet

Platform management, Project design consulting, ...

PHYSICS

ANIMAL EXPERIMENT

RADIOBIOLOGICAL IN VITRO ASSAYS

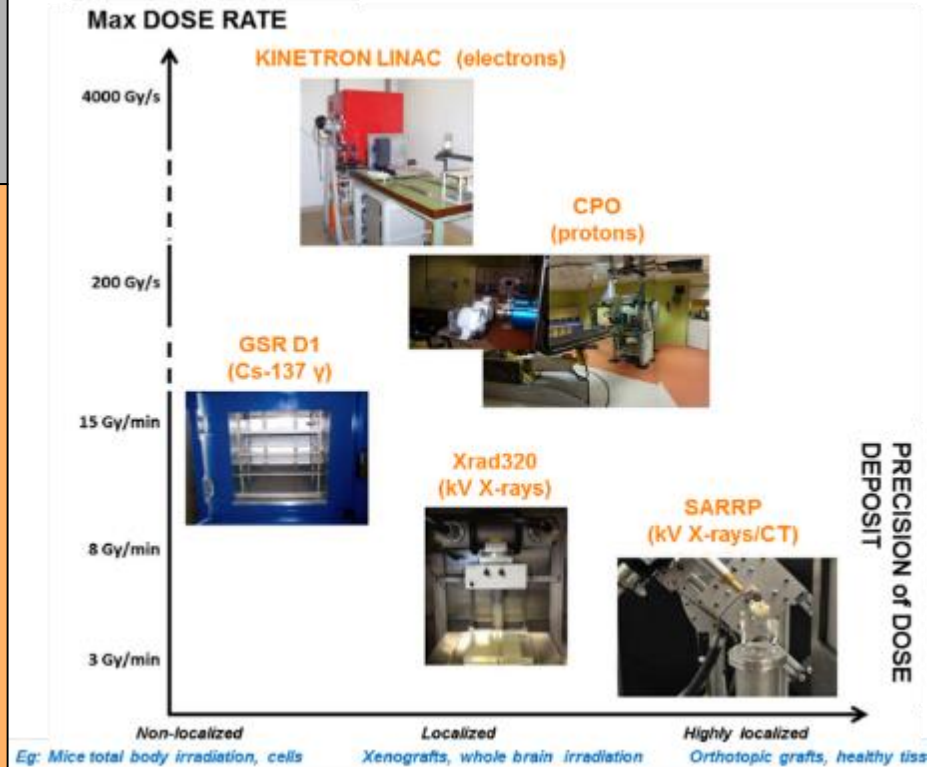
Sophie Heinrich
Radiation physics,
Imaging,
Radiation protection

Dalila Labiod
Graft, Treatments,
Follow-up,
Sampling, Ethics, ...

Gaëlle Mitton
Imaging, Irradiation,
Animal follow-up,...

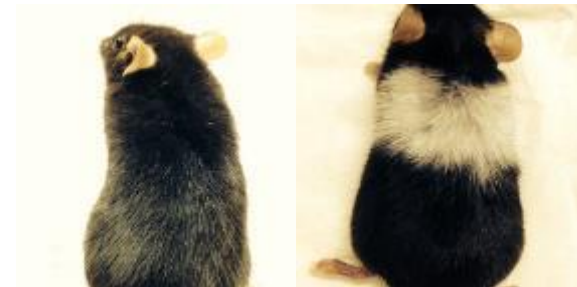
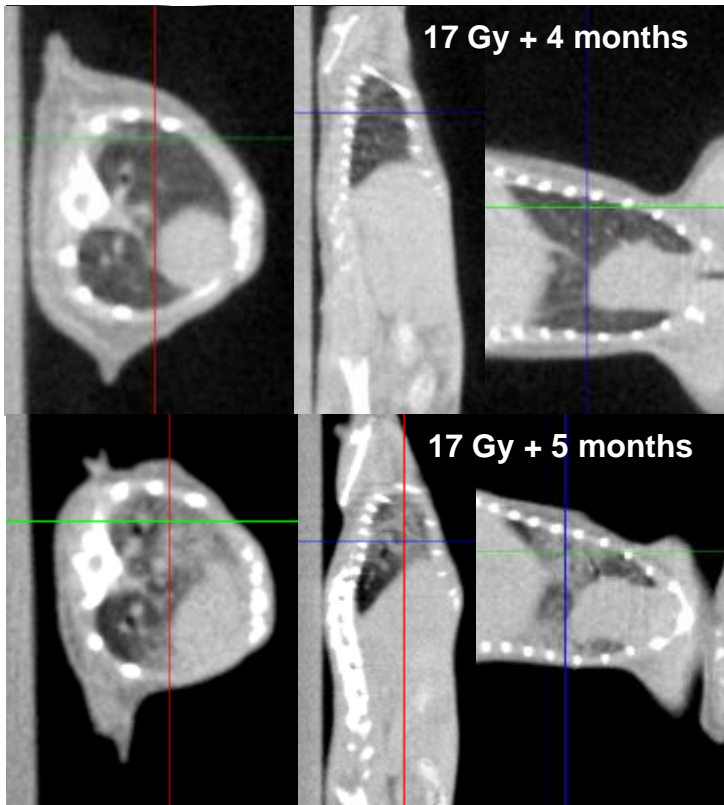
Franck Assayag
Animal models
development, Graft,
Follow-up,...

Christophe Roulin
Slide analyse,
Comet assays,
FISH, ...



Animal models

Healthy tissues irradiation:
Wild type or transgenic animals



Applications:

- Early or late healthy tissue toxicity of treatments assessment
- Biomarkers identifications

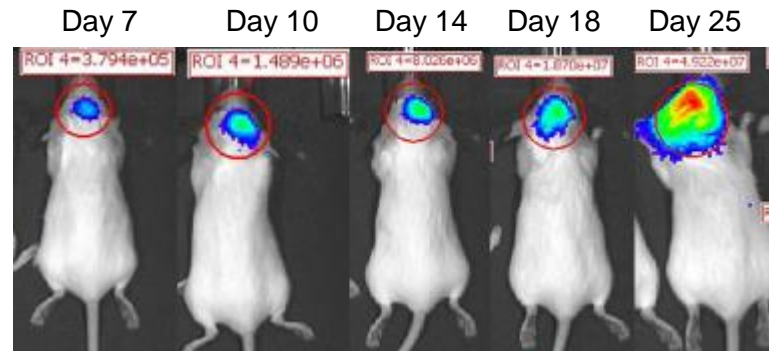
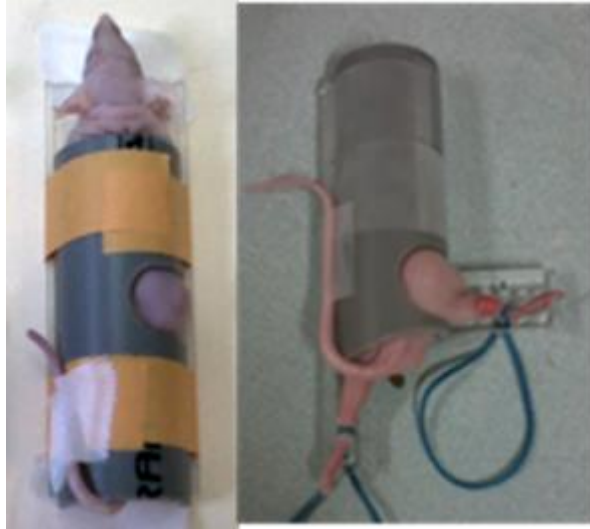
Required:

- Long term follow-up (up to 12 months)
- Access to imaging device (CBCT, MRI, ultrasound imaging)
- Histological analysis

Animal models

Tumor irradiation:

Xenograft implanted subcutaneously or orthotopically



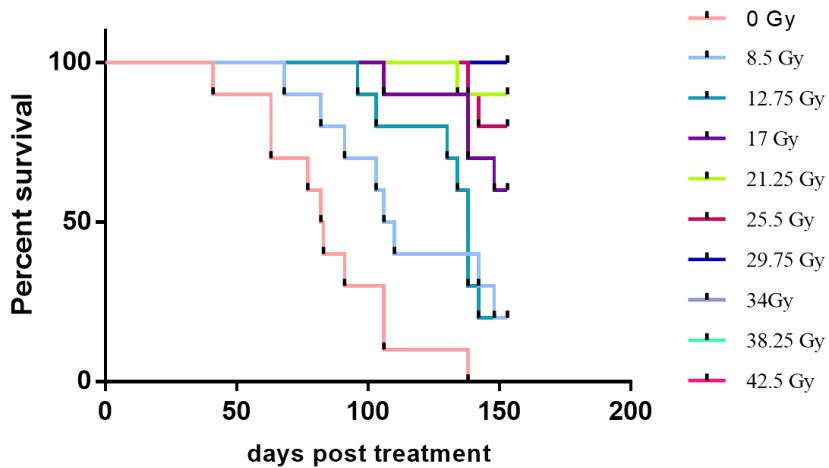
Bioluminescence follow-up of primary central nervous system lymphoma

Applications:

- Tumoral model characterisation
- Treatment efficacy
- Biomarker identification
- Metastatic dissemination

Animal models

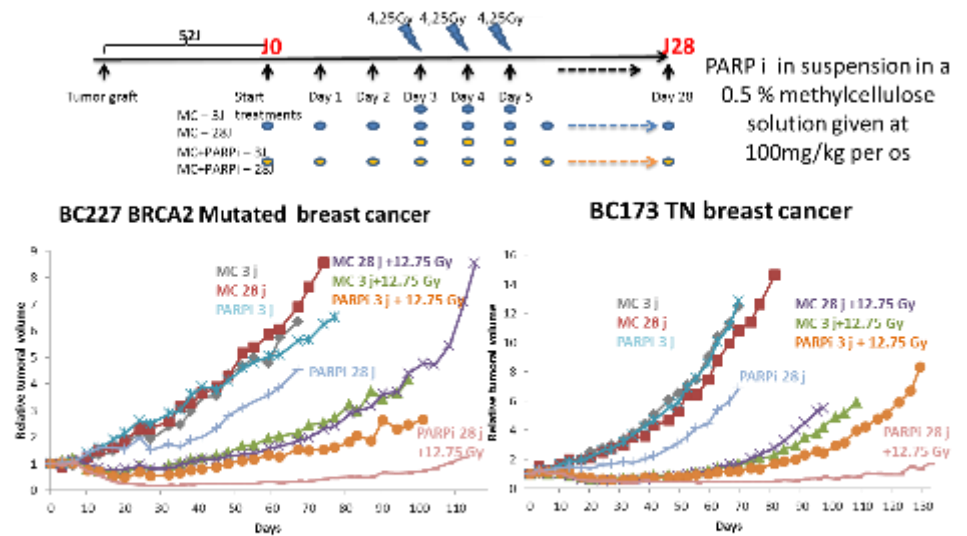
Survival curves of HCx-12A tumors



Required:

- Long term follow-up (up to 12 months)
- Access to imaging device (MRI, ultrasound imaging, ...)
- Histological analysis

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



PARP inhibition radiosensitises both BC227 and BC173 breast xenografts

Collaborative project U612, Radiation platform, LIPs and RT Dept

Animal experiment project authorisation

- **Project autorisation submission to an ethical comittee required if pain equivalent to a needle sting is induced to animals**
- **Need of project autorisation dependent of the ethical comittee**
- **Project autorisation linked to a place**
- **Often two project authorisations required: one for the user one for the beam provider**

Sanitary Health Status

- **List of bacteria, viruses and parasites harboured by animals**
 - **Three levels of containment**
 - Specific Opportunistic Pathogen Free (SOPF)
 - Animal house dedicated mice/rat breeding
 - Use of animal products forbidden
 - Specific Pathogen Free (SPF)
 - Animal house dedicated to animal experiment
 - Animal experiment room
 - Quarantine (zoonosis free)
 - Terminal animal house (imaging facilities)
 - **Beam lines**
 - If animals are free in air considered as animal experiment rooms with a level of containment
 - Referent animal house defines the level of containment
 - Could limit animal transfert from an animal house to another
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Sanitary Health Status

Experimental Beam Line



- **Concerns**
 - Avoid contamination of animals by wild animals
 - Sealed restrains
 - Avoid contamination of animal house
 - Quarantine animal house

Sanitary Health Status

Medical Beam Line



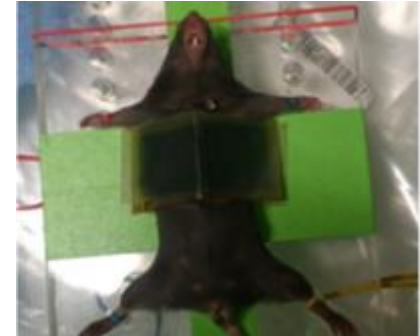
- **Concerns**
 - Avoid to cross patient pathway
 - Experimentation after ends of treatments
 - Avoid contamination of patients by animals
 - Hydrogen peroxy decontamination

Radiation protection

- Depending on particles used and their energy:
 - Specific studies depending on the compounds to be irradiated
 - Gamma spectrometry of samples before experiments to determine the type of radionuclides produced (short or long half-life)
 - Allowed exit for the samples dose rate = 2 X building background (between 1 to 3 hours)
 - Authorization of nuclear safety agency could limit the use of the beam (medical versus research authorization)
 - Access limited to classified investigators for radiation protection
 - If investigators from other companies prevention plan requested
- **Simpliest to manage if irradiations performed by a dedicated internal staff**
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Animal positioning

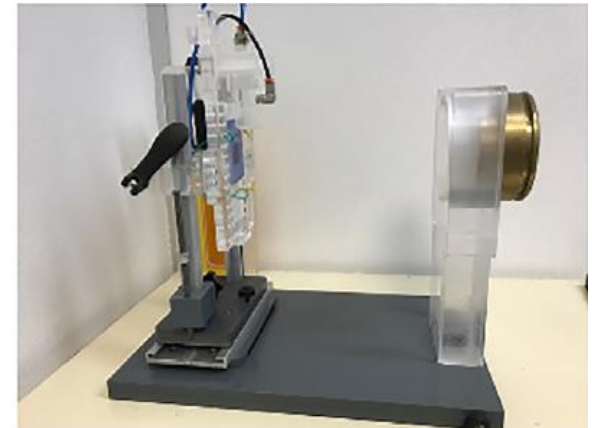
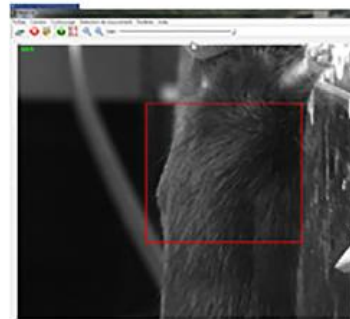
- **Animal restrains:**



- Needed to limit target movement
- Used without or with anesthesia
 - Gaseous anesthesia
 - Needs anesthetic device, oxygen and meters of pipe
 - Close to treatment room
 - Anesthesia by injection
 - Induce hypoxia

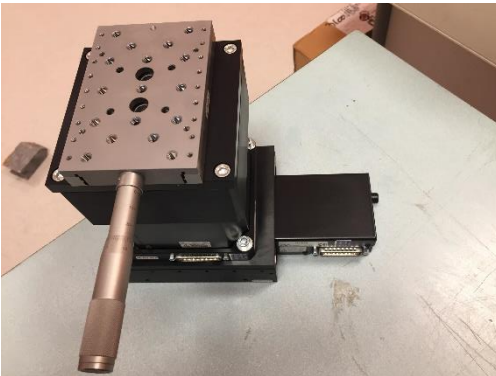
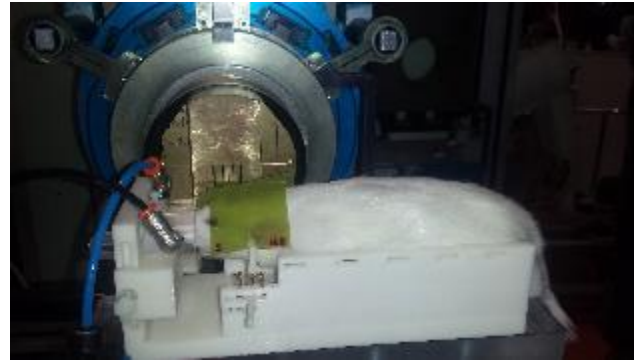
Animal positionning

- **Animal positionning:**
 - External marker (subcutaneous xenograft)
 - Laser
 - Bright field
 - Camera (Patriarca et al 2018)



Animal positionning

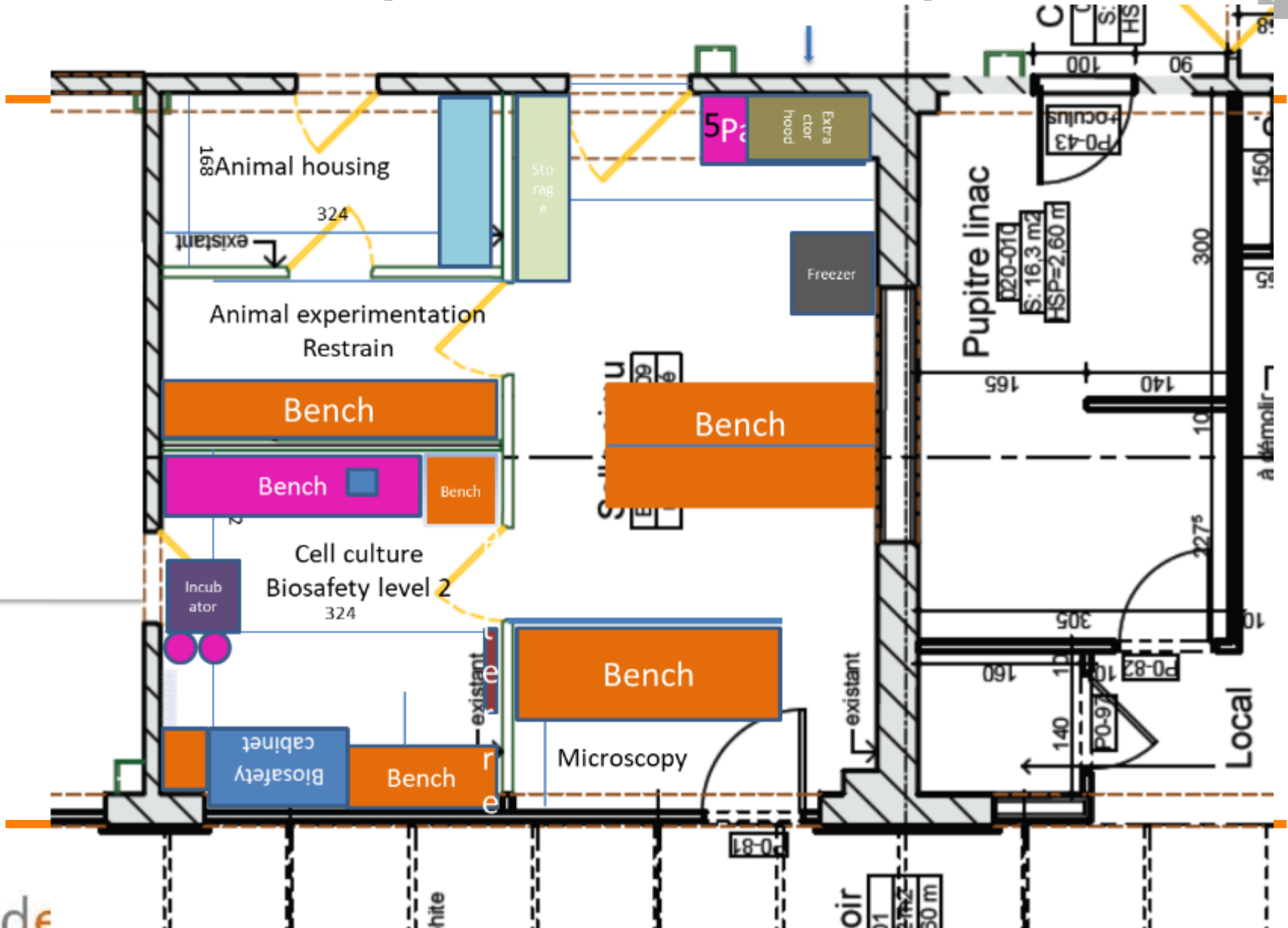
- **Animal positionning:**
 - Anatomical marker (bone)
 - X-rays imaging
 - Position correction:
 - Patient robot
 - 3 axis motorised mechanical stage



Other concerns

- **Chemical risk:** Hazardous chemicals (chemiotherapy, formalin, isopentane,...) used to treat animals/fix tissues:
 - Need of equipment to manipulate these chemicals (extractor hood)
 - Process for chemical waste management
 - **Secondary radiations (neutrons):** Failure of equipments stored in the bunker (computer, electronic card, ...)
 - **Animal housing:** animals staying more than 24 hours need to have a local animal house with a specific agreement
 - **Fractionnated irradiations:** often access to beam line is limited (medical beam, shift allowed). Then it will not be possible to plan fractionnated experiment.
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Preparation room example



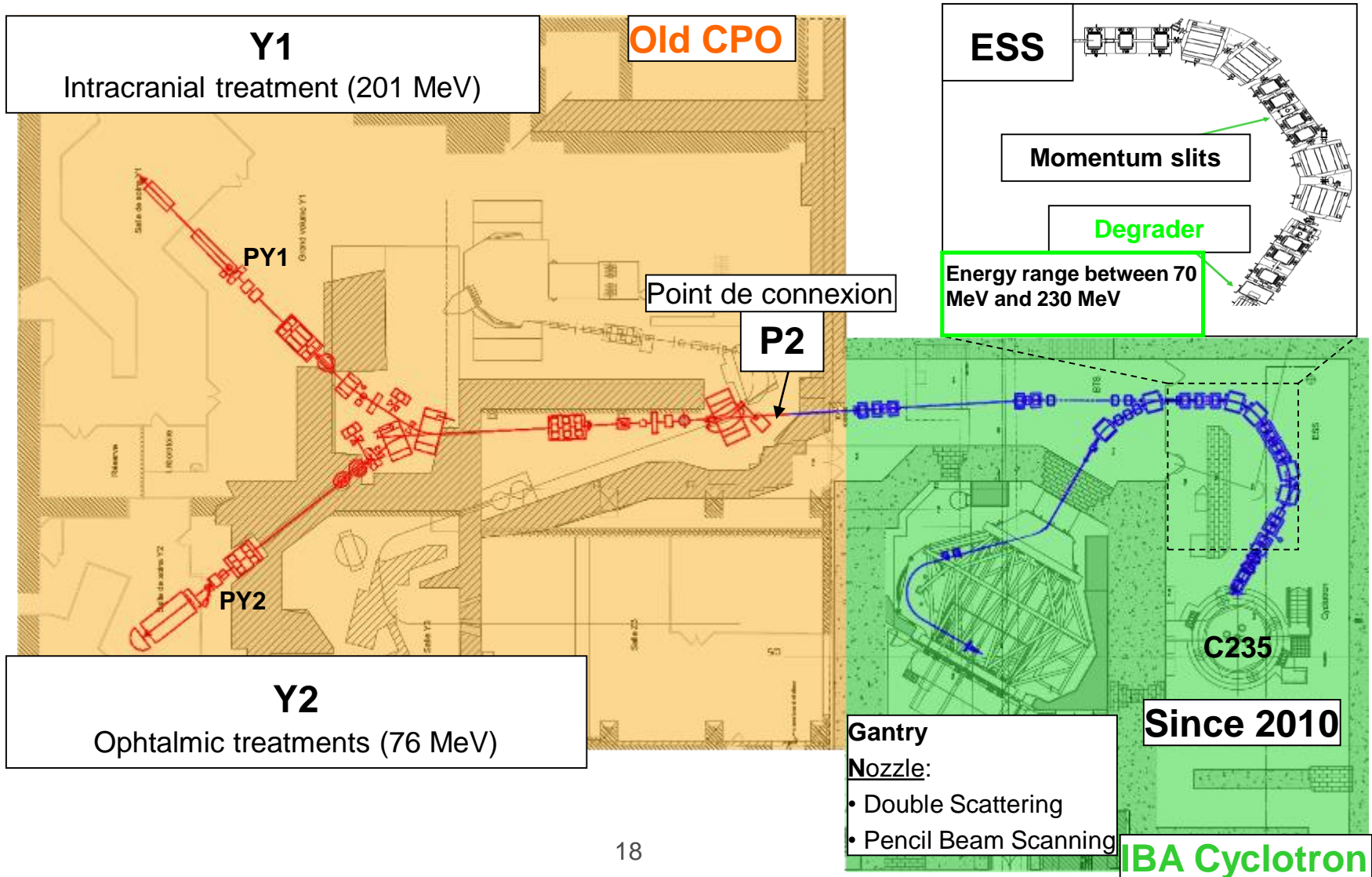
Support

- Medical physicist/physicist:
 - Beam characterization, dosimetry, irradiation, imaging, consulting
 - Engineers and technicians:
 - Beam providers, irradiation set-up development, manufacture of accessories, imaging, consulting
 - Biologist/Animal experiment expert:
 - Samples irradiations, irradiation set-up development, in vivo/in vitro experiment, project autorisation, Consulting
 - Radiation Oncologists:
 - Consulting
-

Thank you for your attention



Orsay Protontherapy Center (CPO)



Orsay Protontherapy Center: Fixed beamlines

Room Y1: Intracranial tumors



- ✓ $E = 201 \text{ MeV}$
- ✓ $(\text{Dose rate})_{\text{mean}} = 2 \text{ Gy/min}$
- ✓ $(\text{Dose rate})_{\text{max}} = 20 \text{ Gy/min}$

Room Y2: Eye tumors



- ✓ $E = 76 \text{ (and } 201) \text{ MeV}$
- ✓ $(\text{Dose rate})_{\text{mean}} = 18 \text{ Gy/min}$
- ✓ $(\text{Dose rate})_{\text{max}} = 40 \text{ Gy/min}$

Orsay Protontherapy center: Gantry



- ✓ Different localisations
- ✓ $E = 100 \text{ à } 230 \text{ MeV}$
- ✓ $(\text{Dose rate})_{\text{mean}} = 2 \text{ Gy/min}$
- ✓ $(\text{Dose rate})_{\text{max}} = 5 \text{ Gy/s (PBS)}$

Accessibility/Availability

- **Accessibility:**
 - ✓ Academics and industrials (comex.cpo@curie.fr)
 - ✓ Feasibility study
 - ✓ Beam characteristics at CPO:
 - Energy : 20 à 200 MeV
 - Fluence (min-max) : 10^5 - 10^8 p/s/cm²
 - Field size: de 2 à 12 cm diameter and 40 X 40 cm²
 - Samples: Cells/Mice/Rats
- **Availability:**
 - ✓ After the treatments and saturday
 - ✓ Around 140h/year available