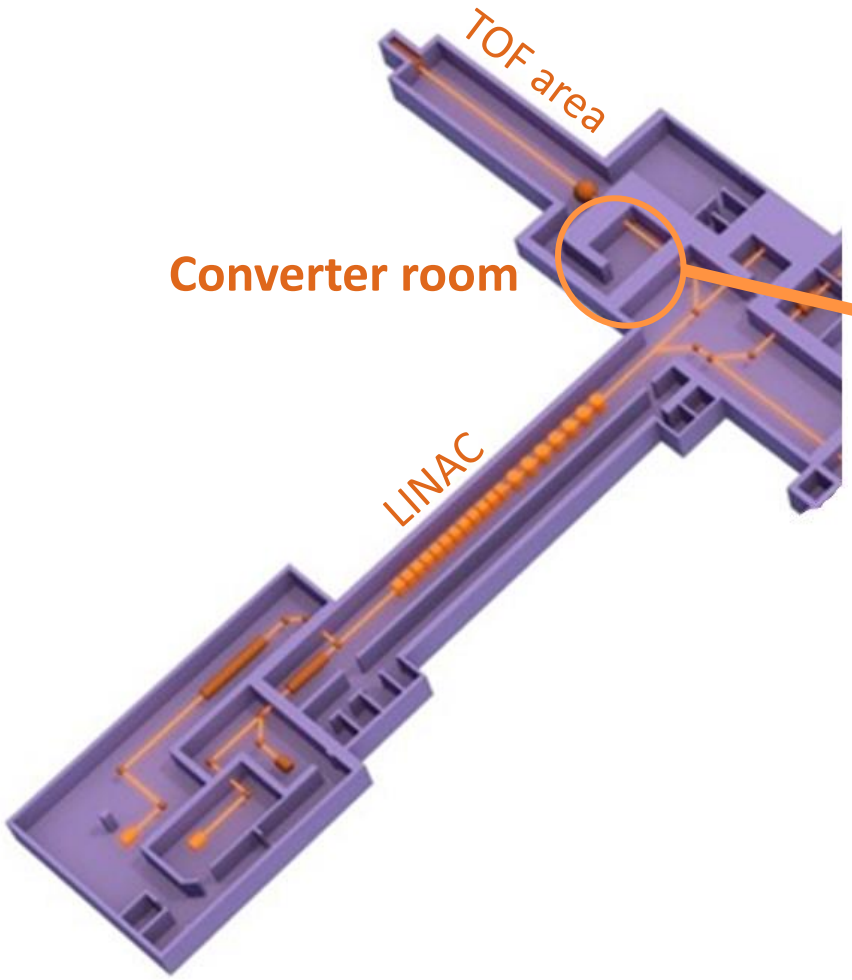
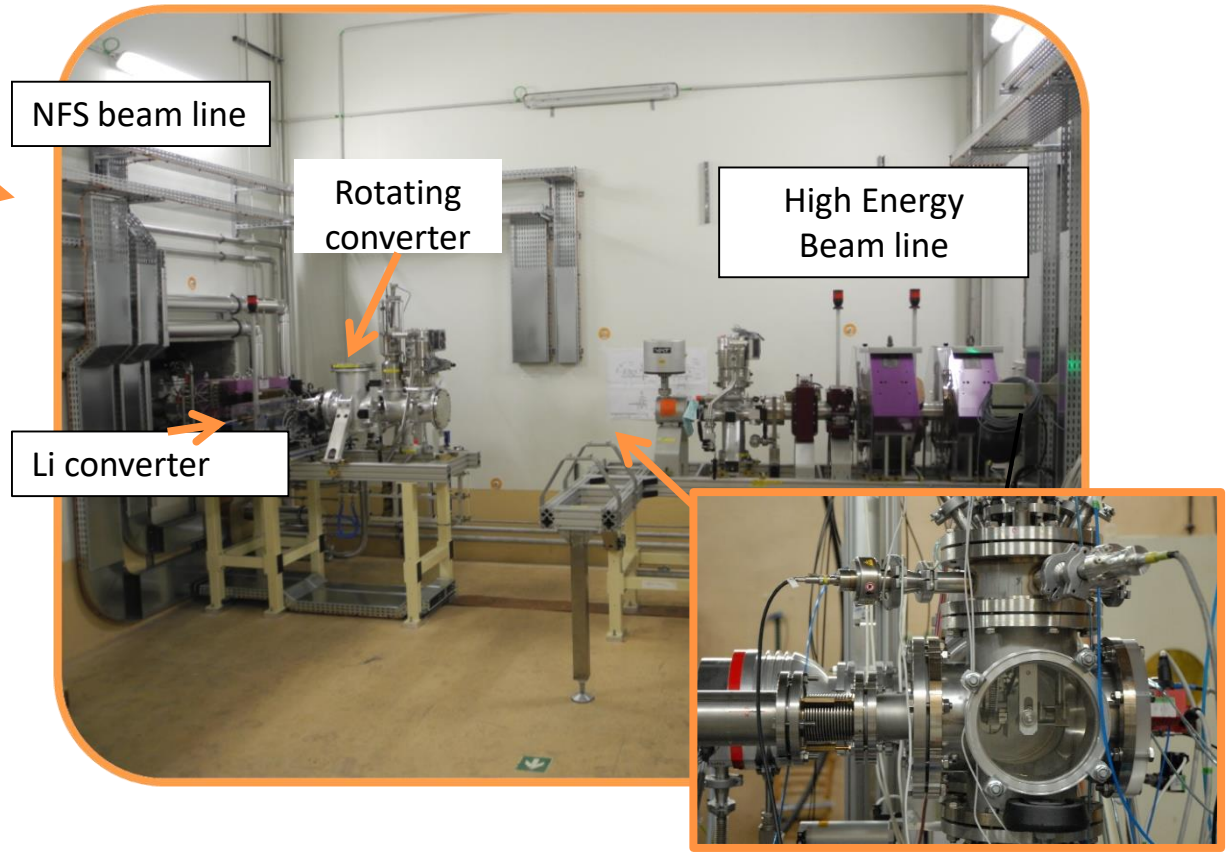
Physics at NFS using charged particles

Anne-Marie Frelin

NFS Converter room



GANIL-SPIRAL 2 Layout

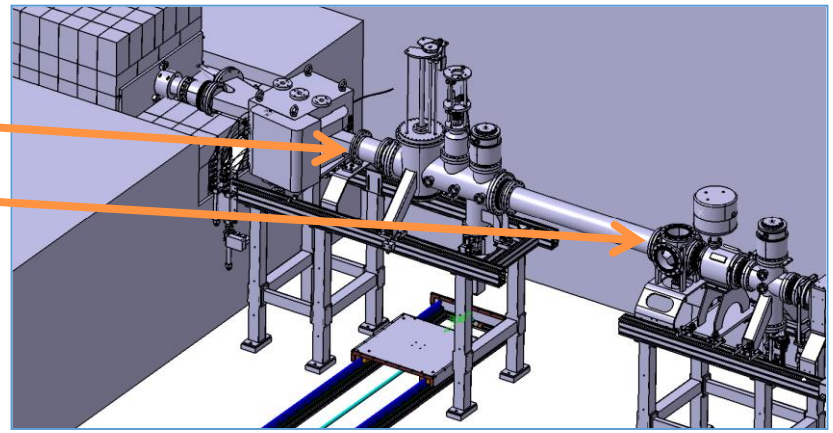


Irradiation station

Measurement by activation technique

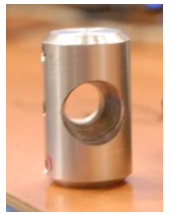
1- Irradiation of a sample in the converter room :

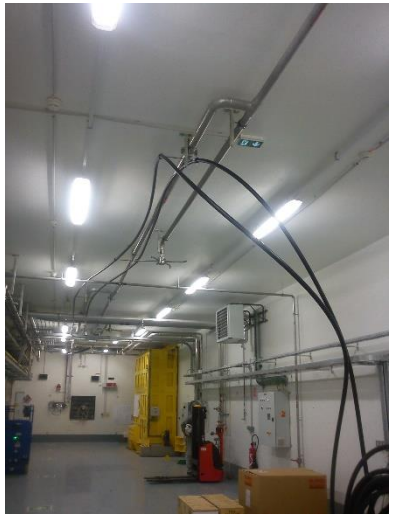
- with neutrons (in air)
- with ions (in the irradiation station)

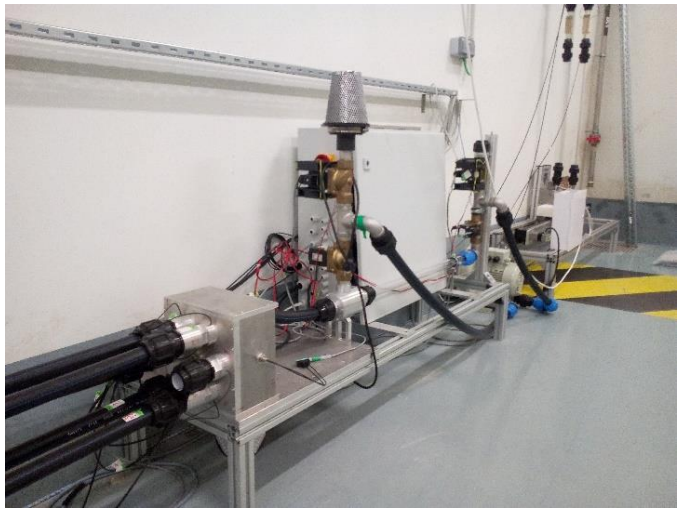


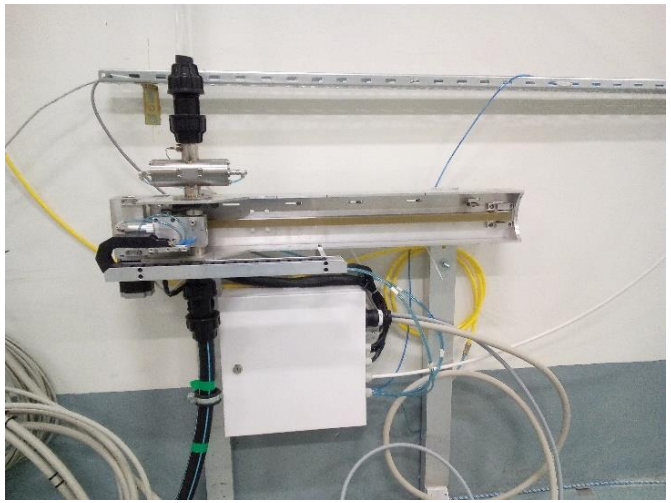
2- Transfer of the sample to the TOF room for activity measurement

- Fast ($\rightarrow$ short half-lives)
- Limited access to change sample/energy







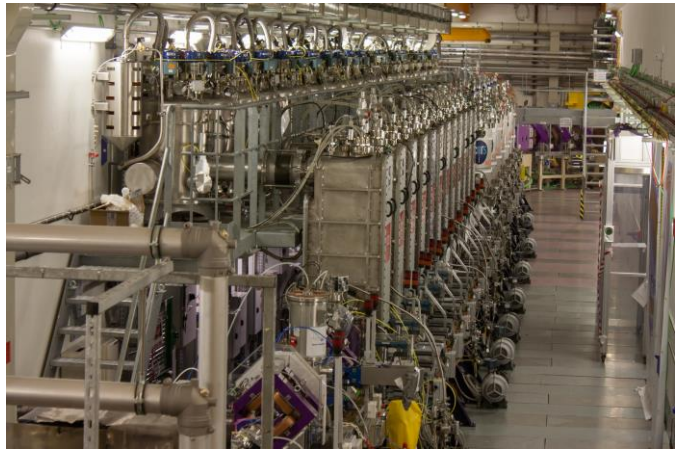


Pneumatic transfer system

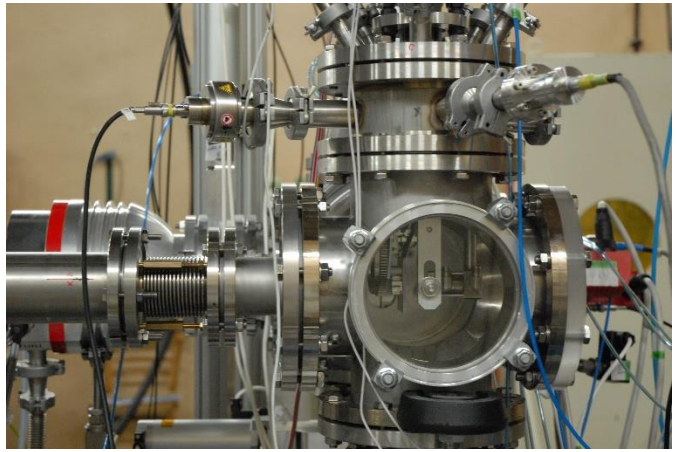
Ion induced reactions

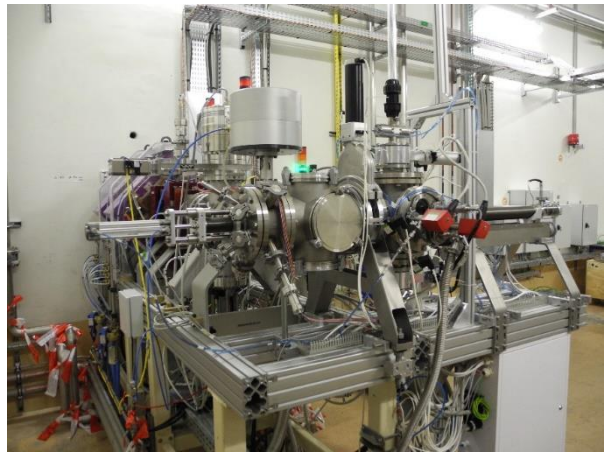
- All ions accelerated by the LINAC can be used at NFS
- In the converter room only
- Experiment type:
  - Activation technique
  - Vacuum chamber + detector
- Energy domain
- Imax :
  - P< 2 kW in any case (thermal constrains only)
  - P> 2 kW to be studied case by case (thermal and radiological constrains)

	Protons H^+	deutons $^2H^{1+}$ alpha He^{2+}	Heavy ions	
	q/A=1	q/A=1/2	q/A≥1/3	q/A≥1/6
E_{min} (MeV/A)	2	2	2	2
E_{max} (MeV/A)	33	20	15	9



The SPIRAL 2 Linac

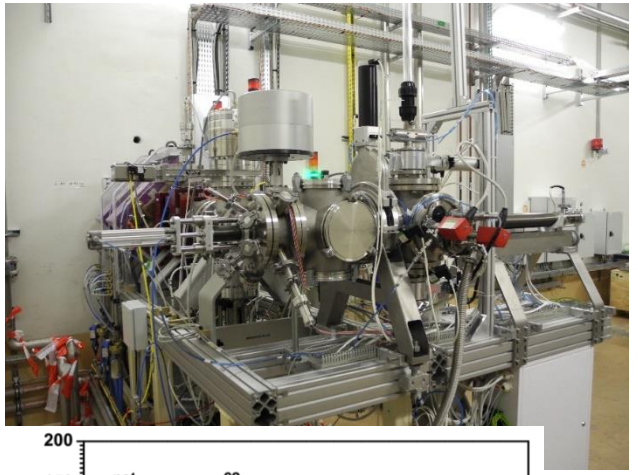




Irradiation station connected to the pneumatic transfer system

E799: Excitation functions of short-lived isotopes in proton-induced reactions on ^{nat}Fe

Spokesperson : E. Simeckova, NPI, Rez



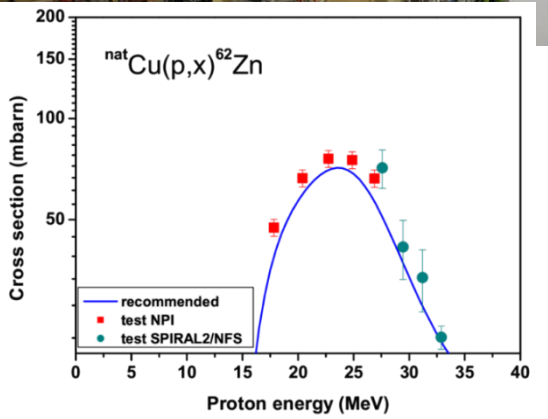
Measurement of reaction cross-sections by activation technique :

- data for IFMIF facility design
- improvement of reaction model

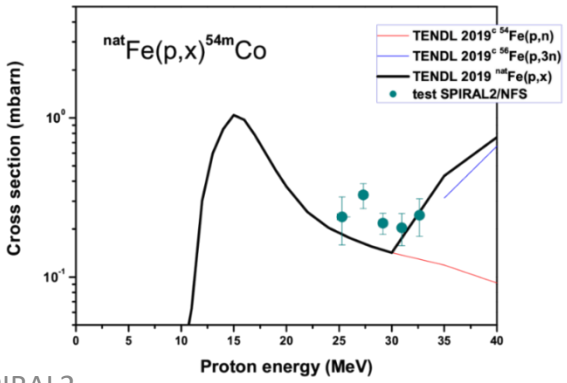
Goal: measure the ^{58m}Co and ^{58g}Co alimentation

Commissioning : Irradiation station tested in December 2019

- **33 MeV proton** beam
- **80 nA** beam intensity
- **Fe and Cu samples** irradiated



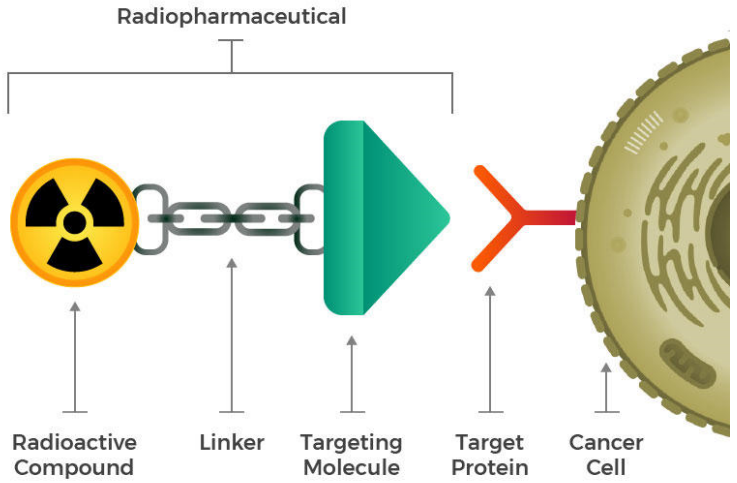
- Good agreement between production cross section of ^{62}Zn and recommended values → **proves the validity of the method**



- **^{nat}Fe(p,x) ^{54m}Co measure for the first time** the production cross section of the **short-lived isomeric state of ^{54}Co**

Radio-isotopes for medical use
Motivations and opportunities

- **Societal issue:**
  Aging population ⇨ Cancer = leading cause of death in many countries
  (157 400 deaths in France in 2018)
- Local/solid tumor → External beam radiotherapy
- Diffuse/small tumor cancer → **Targeted Radionuclide Therapy**
  - Target receptors present at the surface of the tumor cells or in the microenvironment
  - Less toxicity
  - Various particles (α, β, Auger electrons)
  - Theranostic approach (imaging + therapy)



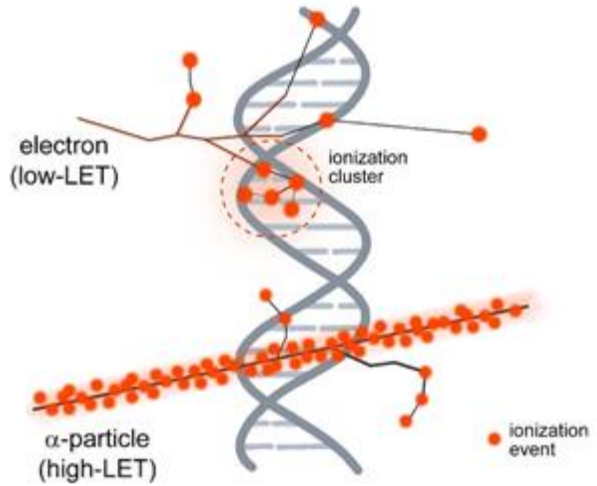
Radio-isotopes for medical use
Motivations and opportunities

- **Societal issue:**
  Aging population ⇨ Cancer = leading cause of death in many countries
  (157 400 deaths in France in 2018)
- Local/solid tumor → External beam radiotherapy
- Diffuse/small tumor cancer → **Targeted Radionuclide Therapy**
  - Target receptors present at the surface of the tumor cells or in the microenvironment
  - Less toxicity
  - Various particles (α, β, Auger electrons)
  - Theranostic approach (imaging + therapy)

- **Alpha particles**
  → Short range (< 100 µm)

  → High LET (~100 keV/µm)
  ⇨ DNA double-strand breaks ++

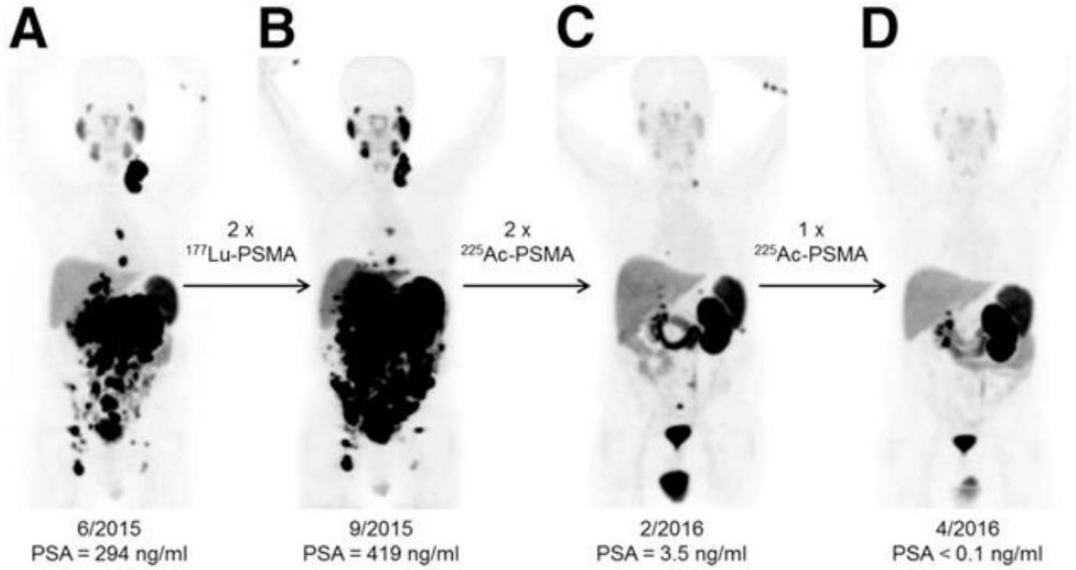
  → Less sensitive to low cell oxygenation state (hypoxia) and radio-resistance



Schematic distribution of ionizations generates in DNA by electrons of low LET or high LET alpha particles. Source: (Iliakis, Mladenov & Mladenova 2019)

Radio-isotopes for medical use
Motivations and opportunities

- Promises of Targeted Alpha Therapy



From *C. Kratochwil et al., Journal of Nuclear Medicine December 2016*

- ^{223}Ra: only α-emitter radiopharmaceutical (Xofigo©)
  - cannot be stably linked to a vector
  - "Metabolic treatment" based on ^{223}Ra natural concentration in Bones

➡ Other α-emitters needed to target other types of cancer
  - Candidates with high potential interest: Astatine, Lead, Terbium, Bismuth…

Radio-isotopes for medical use
Motivations and opportunities

- New possibilities at NFS to address this strong societal issues
  - Very intense beams (Imax=5mA for 40 MeV d)
  - Variable energy ($\rightarrow$ reduced uncertainties compared to stack method) and new beams compared to existing production facility machines
- Isotopes and contaminants production cross sections
- Low availability of isotopes for research in radiochemistry, biology…

- Radio-isotopes studies at GANIL
  - R&D on the production of innovative radioelements for nuclear medicine research
  - Collaboration: Nuclear physics, radiobiology, medicine…

Radio-isotopes for medical use
Motivations and opportunities

- New possibilities at NFS to address this strong societal issues
  - Very intense beams (Imax=5mA for 40 MeV d – 1 mA ~10^{15} pps)
  - Variable energy ($\rightarrow$ reduced uncertainties compared to stack method) and new beams compared to existing production facility machines
- Strong interest for medical isotopes and contaminants production
- Low availability of isotopes for research in radiochemistry, biology…

Production cross sections of Terbium :
^{155}Gd(p,x)Tb

in particular:

^{155}Gd(p,n)^{155}Tb $\rightarrow$ SPECT imaging
^{155}Gd(p,n)^{156}Tb $\rightarrow$ contaminant

Current isotopes of interest

^{211}At (ARRONAX et al, ANR REPARE $\rightarrow$ target design + measurements)

^{212}Pb , **^{223}Ra** (ISTC et al, ISOTOP 2020 $\rightarrow$ dosimetry)

Current limitations for ^{211}At
$^{209}Bi(\alpha,2n)^{211}At$

- Maximum alpha **beam intensity** available at accelerator centres (ARRONAX 70 eµA max).
- Energy loss of alpha particles in the bismuth target (90 µm to absorb 8.3 MeV alphas from 29 MeV to 20.7 MeV, production threshold) => **melting of bismuth**.
- Production of **^{210}At** decaying to **^{210}Po** which concentrates in bones (for patients) and high energy gamma-rays in the **decay of ^{210}At** (radioprotection issue for the personnel).
- Uncertainty on **allowable ^{210}At/^{211}At** and **production cross-sections** of contaminants (Po, At)
- The **half-life** of 7.2 h, which limits the delivery zone.

REP At RE + 27 EU PRISMAP Medical Radionuclides

***R**esearch and d**E**velopments for the **P**roduction of innov**A**tive **R**adio**E**lements*

The REPARE Project

Research and d**E**velopements for the **P**roduction of innov**A**tive **R**adio**E**lements

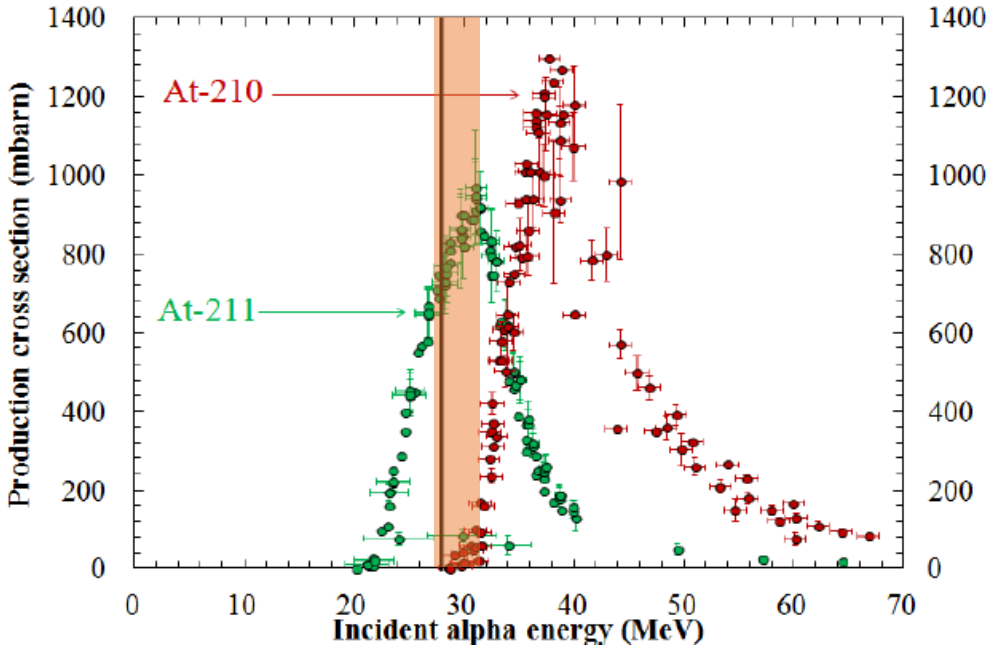
- ^{211}At ($T_{1/2}$ = 7.2h): promising α-emitter for **Targeted α Therapy**

- WP1: Inventory calculations and cross section measurements (α, Li induced reactions)
- WP2: High power solid target
- WP3: High power liquid target
- WP4: ^{211}Rn (14h half-life) / ^{211}At generator

- GANIL objectives are:
  - To study ways to increase ^{211}At production through the **^{209}Bi(α,2n)** reaction (WP1)
  - To take advantage of the characteristics of **SPIRAL 2 beam** (up to 80MeV and **mAe of α**) (WP3)

WP1: Cross section measurements
$^{209}Bi(\alpha,2n)^{210\text{-}211}At$

Finding a compromise between ^{211}At and ^{210}At production



$^{209}Bi(\alpha,2n)^{211}At$, 20.7 MeV — therapeutic use

$^{209}Bi(\alpha,3n)^{210}At$, 28.6 MeV $\rightarrow$ ^{210}Po — toxic contaminant

Little data around this energy

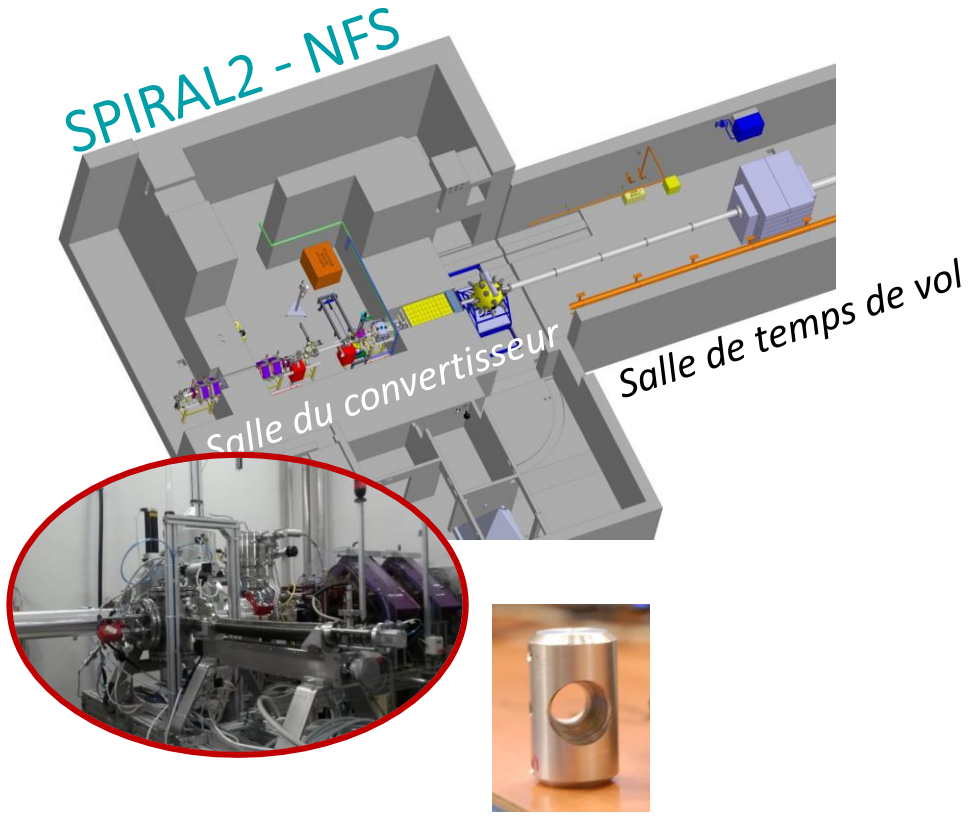
Better knowledge needed

- Consolidated data
- Production optimization

- Accurate measurement of the relevant production cross-sections
- SPIRAL2 alpha beams between 28 and 31 MeV

WP1: Cross section measurements
$^{209}Bi(\alpha,2n)^{210\text{-}211}At$

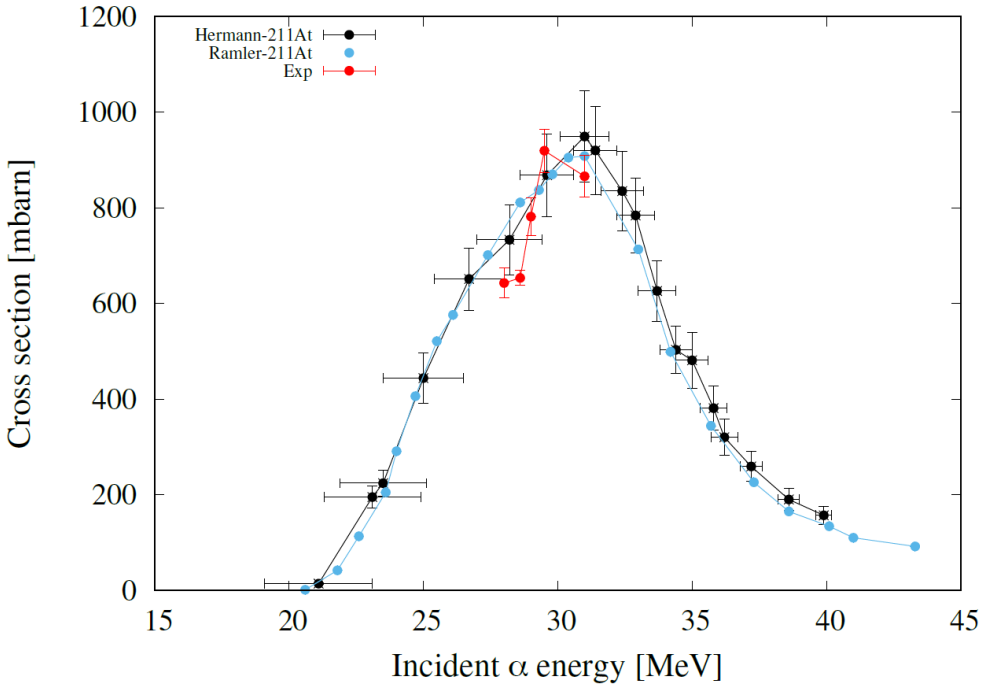
- Manip Sep. 2022 @NFS
  Collaboration ARRONAX, NPI Rez



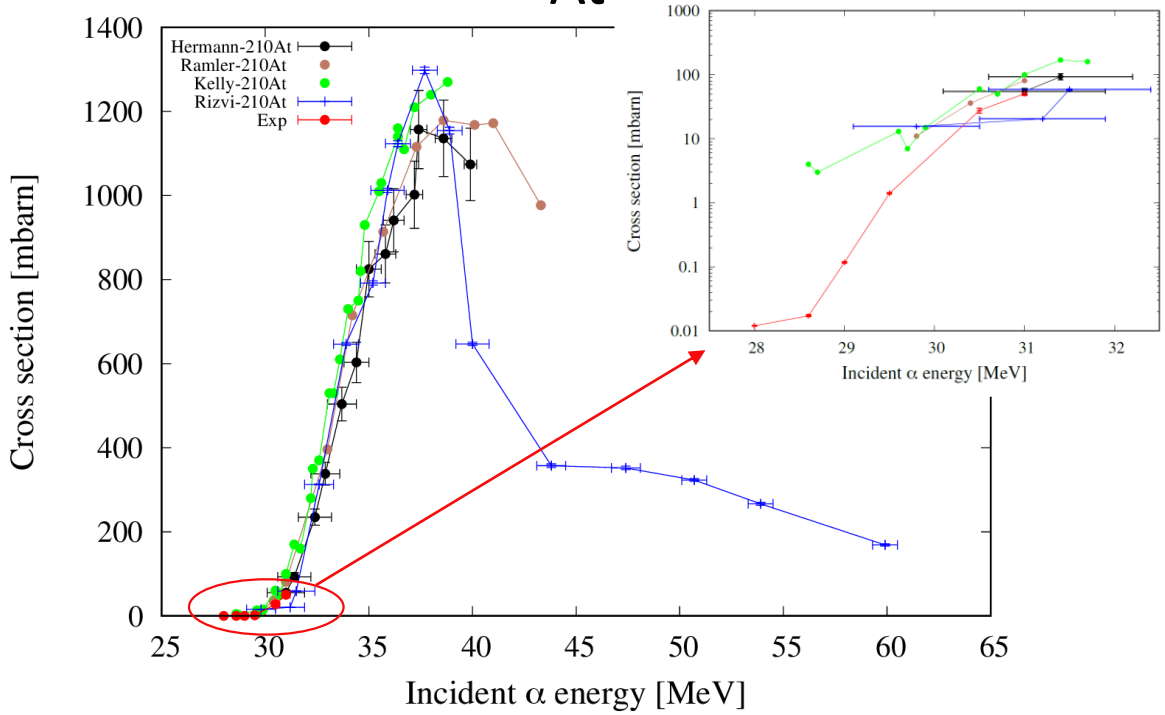
- Irradiation station + pneumatic transfer system
- Bi (and Cu) targets
- 7 energies between 28 and 31 MeV
- Gamma spectrometry
  - HPGe detect in TOF hall
    ← pneumatic transfer system
  - Remote Exogam detectors

WP1: Cross section measurements

$^{209}Bi(\alpha,2n)^{210\text{-}211}At$



^{210}At



Preliminary

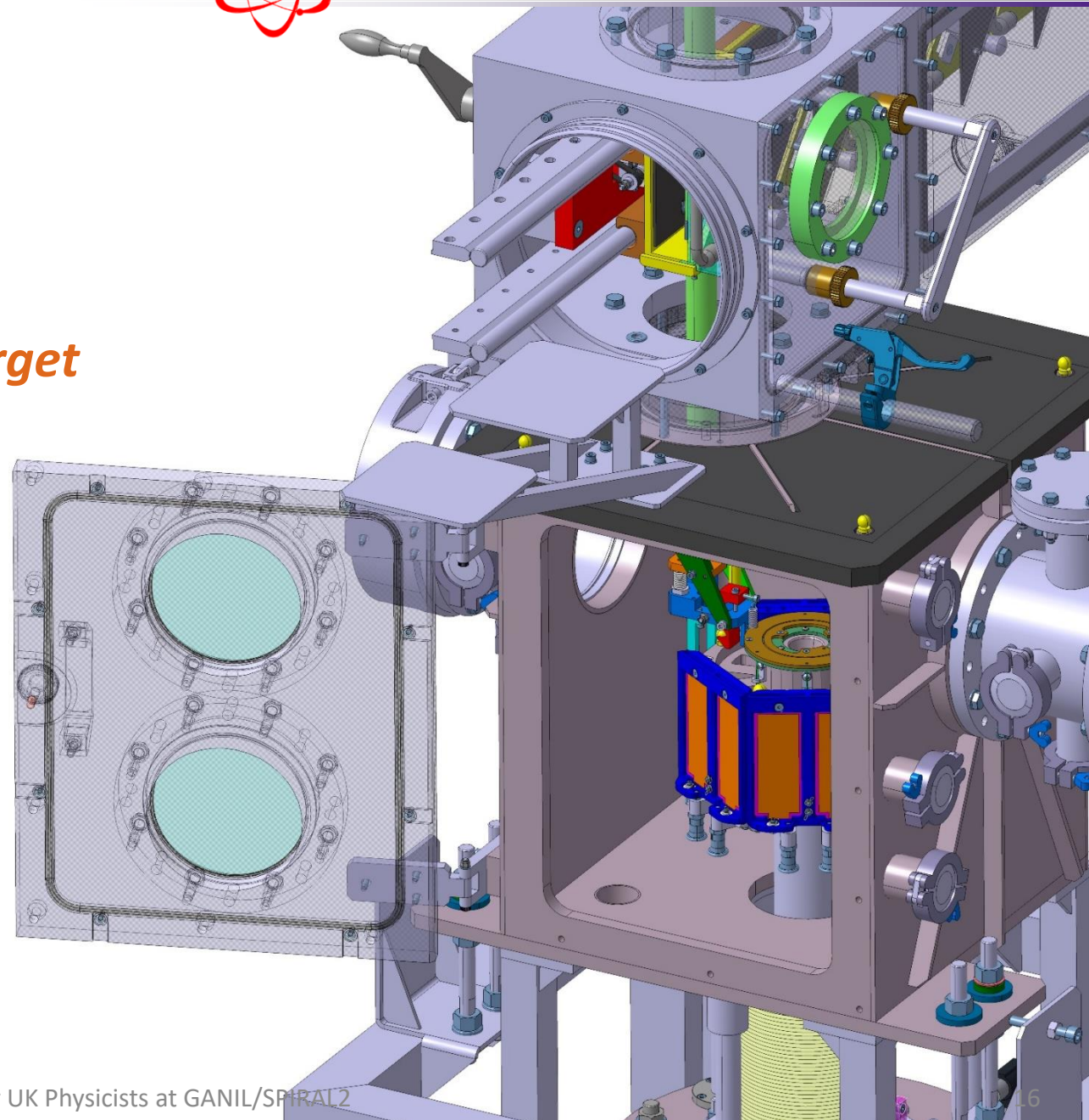
Saba Ansari Chauveau

WP2: Solid Bi target

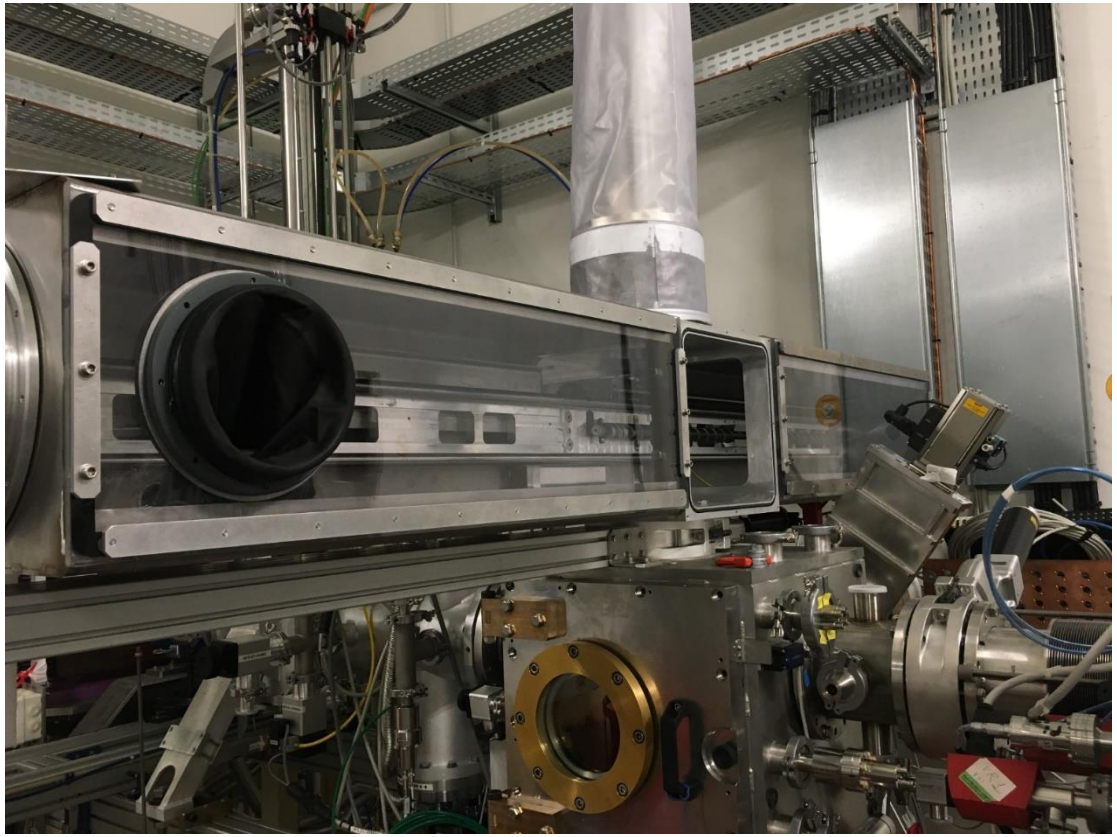
- *Take full advantage of the beam intensity*
- *Maximizing activity production*

- *Low melting point of Bismuth (271°C)*
- ***Development of a high power rotating target***

- *Rotating wheel synchronized to beam frequency*
- *6 rackets – 2 targets/racket*
- *Target cooling ← water cooling + rotation*
- *Monitoring: beam setting, current measurement*
- *Radioprotection/safety*



WP2: Solid Bi target



Tests:

- July: **cyclo**, ^{20}Ne, 4.5 MeV/A → Hardware, software, handling…
- Sept 3-4: α, 7MeV/A, low power (**10 W**) → Contamination, production yield…
- Sept 10-11: α, 7MeV/A, high power (**10 kW**) → Activity production at high intensity
  (→ Arronax for extraction of ^{211}At)

WP2: Solid Bi target

- Results:
  - **Cyclo**:
    - Mechanics, cooling, current readings, vacuum, beam synchronization with wheel rotation, hard/soft of automatic system handling REPARE,…
  - **10 W**:
    - no contamination (sputtering): validation of hypothesis of the safety file
    - no trace of ^{210}At: good energy
    - ^{211}At activity (~16 MBq) scaling well with beam current
    - no activity on collimator: beam synchro confirmed

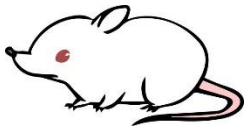
  - **10 kW**:
    - **Wrong beam structure** (3ms/s) → **target damage** during target scanning for precise adjustment of synchro (w/o rotation)
    - **Loss of communication** with automatic system (with human machine interface); **failure of card** handling rotation of the wheel → beam stop. Too large neutron flux?

- Full analysis ongoing
- Cure/Improvements identified

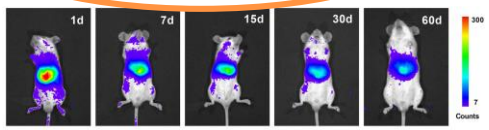
Beyond the production of radio-isotopes

The full chain of research for nuclear medicine

Preclinical studies

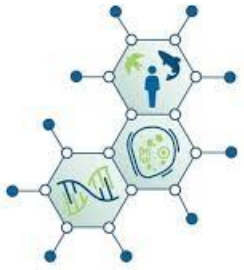


Dosimetry
Biodistribution



Clinical trials

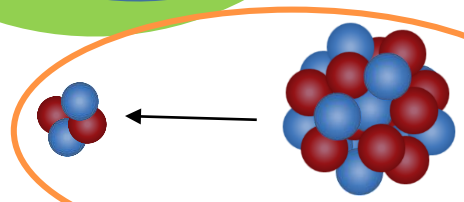
Toxicology



Targeted
Alpha
Therapy

Drug design/chelation

Synthesis/
Physicochemistry

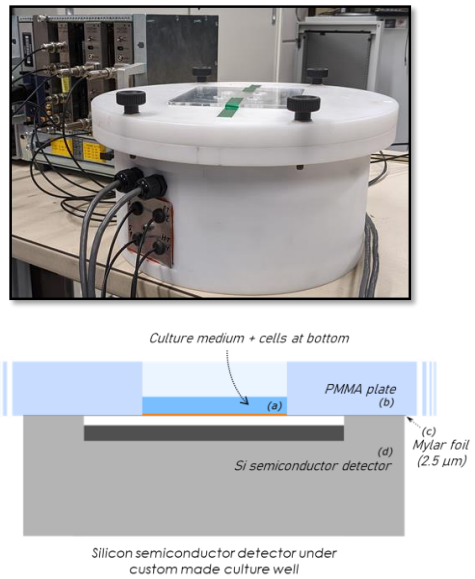


- **Isotopes** necessary to any developments
- **Interdisciplinary** collaborations essential in this field
- Other levels concerned by collaborations with physics (characterizations, **dosimetry**…)

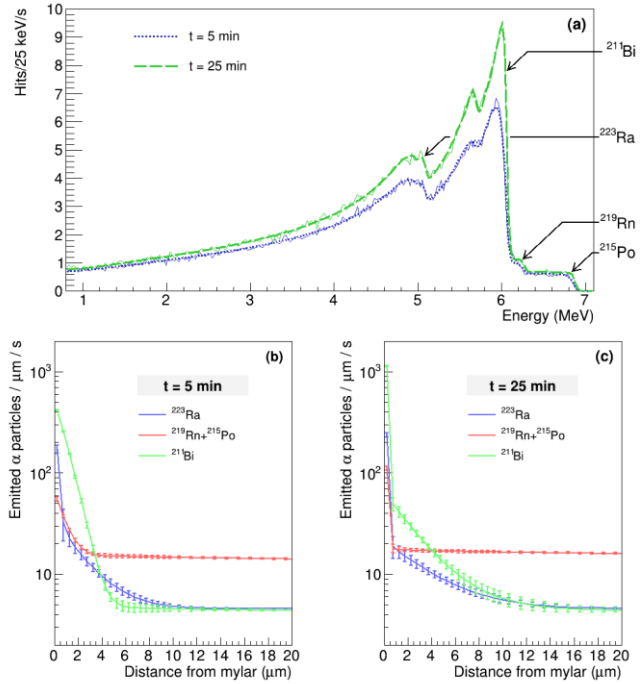
In vitro, *in vivo* dosimetry

Ce projet est financé par CNRS/MITI

- ^{212}Pb and ^{223}Ra *in vitro* irradiations
- *Dose – biological effect (DNA DSB here) relation ?*
- *Injected activity not relevant and α particles dosimetry difficult*
- Development a new dosimetry system for *in vitro* experiments

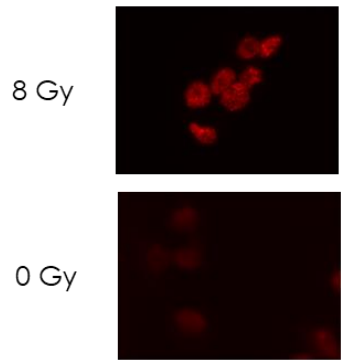


^{223}Ra



Absorbed dose
(or other metrics)

DNA DSBs



MDA-MB (Br) cells seeded on a custom culture plate (2.5 µm mylar foil)

Conclusion

- NFS converter room
  - High intensity charged particle beams
  - Variable energy
  - Irradiation station
  - Fast pneumatic transfer system
- Activation experiments
  - Nuclear data – short-lived isomeric states
  - Radio-isotopes for nuclear medicine
    - R&D production
    - Provide isotopes to interdisciplinary collaborations
    - Local project to implement a full research chain from production to clinical research