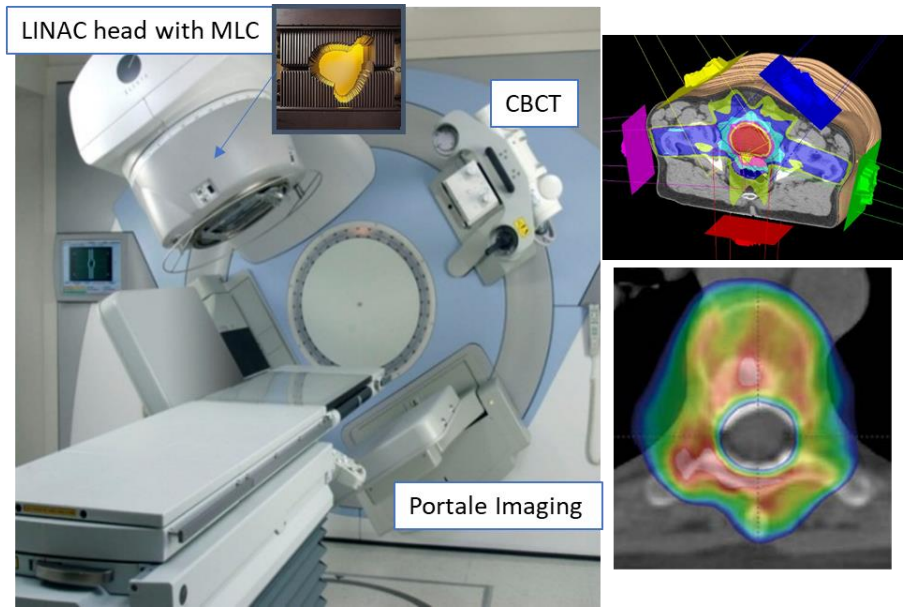
NUCLÉAIRE & PARTICULES

New Approaches in Radiation Therapy

Rachel DELORME on behalf of the community

« Conventional » external beam radiotherapy (EBRT)

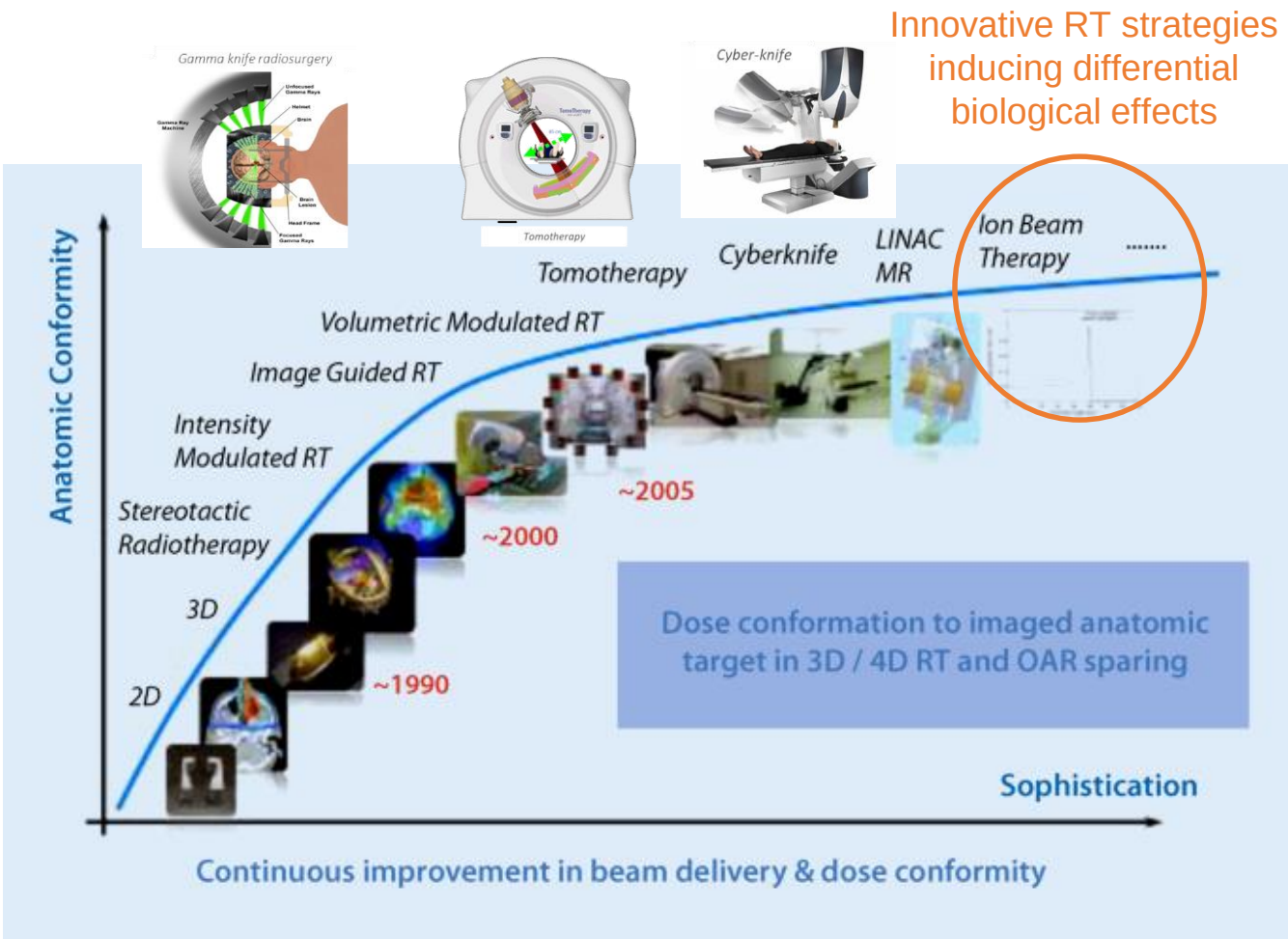
- **The technological evolution of X-rays EBRT improved the dose conformation to the tumor through advanced techniques of radiation intensity modulation (IMRT, VMAT..) and image guidance (IGRT)**:



Standard clinical accelerator (IMRT, VMAT) with embedded imaging systems

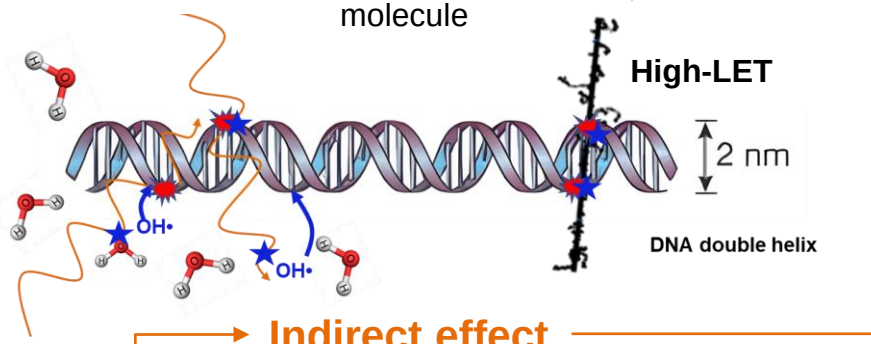
Typical treatment characteristics:
Particles: X-rays 6-25 MV (all tumors), electrons 3-25 MeV (surface)
Time fractionation: 2 Gy/session, 5 session/week
Dose: 40-70 Gy
Dose rate: 30-70 mGy/s (2 Gy/min)
Field sizes: 2 - 40 cm² (homogeneous dose coverage)

Innovative RT strategies inducing differential biological effects



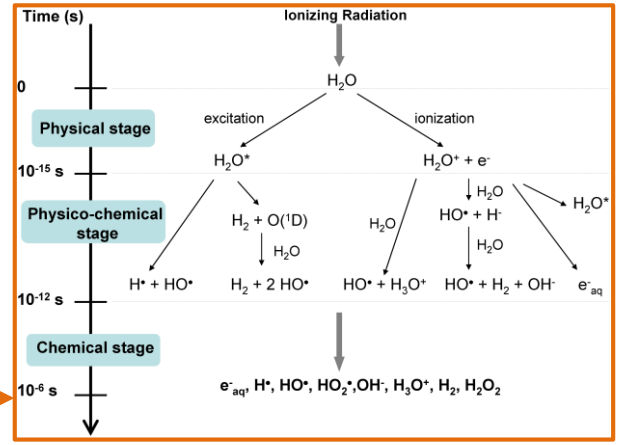
Basic of radiobiology: from physical to biological effects

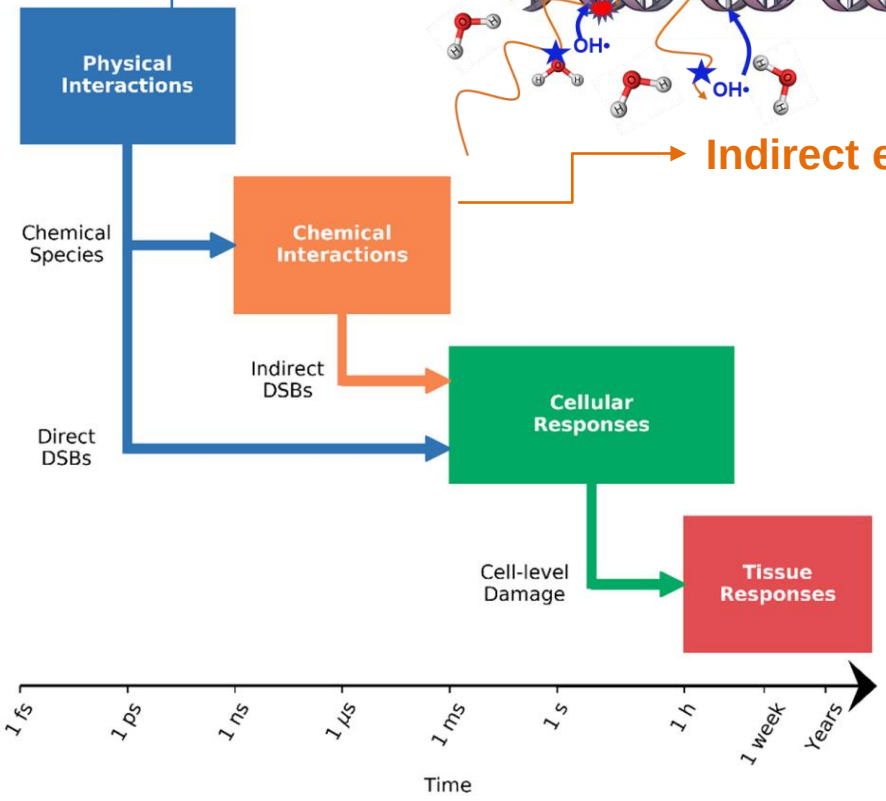
Direct effect
direct ionization of the molecule



Indirect effect

Water radiolysis: creation of reactive chemical species ($OH^•$, H_2O_2, e^-_{aq}…) that will interact with organic molecules

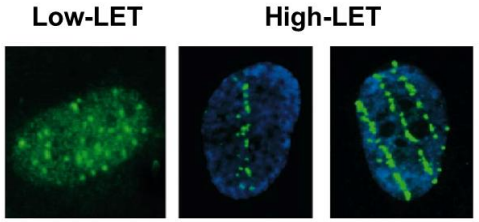




+ tumor microenvironnement, immune response…

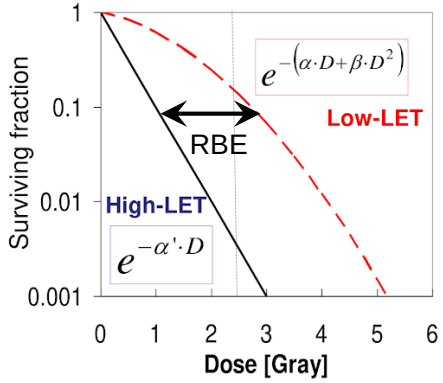
Biological damage

at molecular scale
(e.g. DSB)

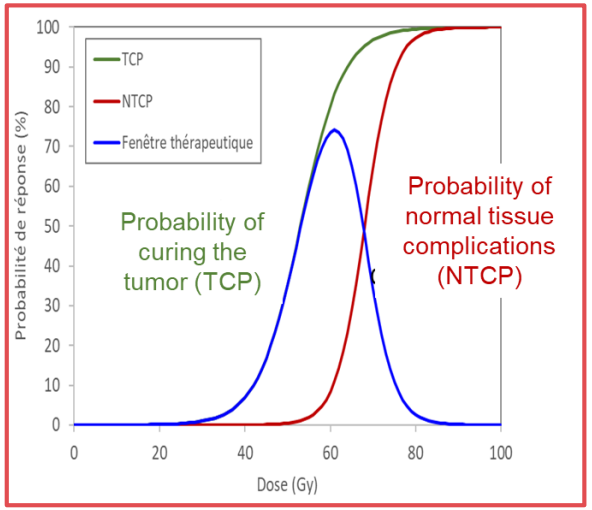


Question of other sub-cellular damage (membrane, mitochondria…)

at cellular scale



Tissue Response

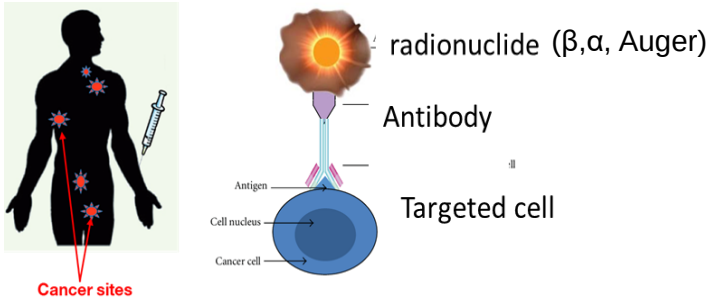


Limitations and other therapeutic strategies

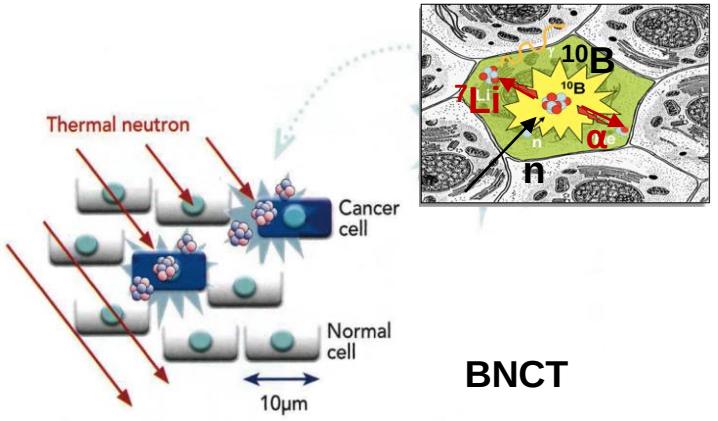
- The **toxicity to healthy tissue** still limits the dose delivered and the curative use of RT :
  - In particular for very **radioresistant, bulky** and **diffuse cancers** (e.g. glioblastoma…), and for **non-localized tumors** (multiple metastasis)

	α-TRT	BNCT	NP
Radionuclide/particle	^{223}Ra, ^{225}Ac, $^{212/213}$Bi, ^{211}At, ^{212}Pb…	^{10}B/^{11*}B	e- (PE, Auger)
Energies α (et ^{7}Li) or e-	5-9 MeV	0.8-1.7 MeV	0-100 keV
Range α (and ^{7}Li) or e-	40 –100 µm *(few cells)*	5 –9 µm *(<cell)*	0-100 µm
LET *(keV/µm)*	60 – 100	≥ 200	0.5-20

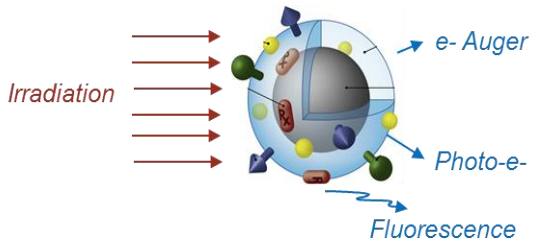
- **How to improve the treatment?**
  - Induce a more efficient tumoral irradiation
    - **High-LET particles**: hadrontherapy (p, α, ^{12}C, ions)
    - **Targeted radiotherapies** (using molecular targeting or sensitizers)**+high-LET**: radionuclide therapy (**TRT**), **BNCT**, **nanoparticles**…



Targeted Radionuclide Therapy (TRT)



BNCT



Nanoparticle-enhanced RT
(radiosensitizers)

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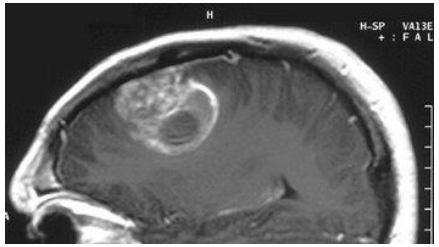

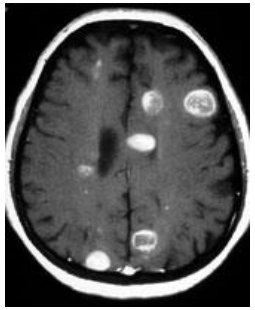

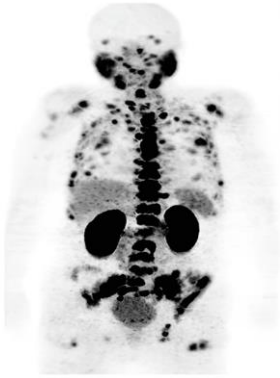

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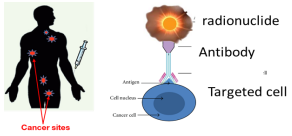
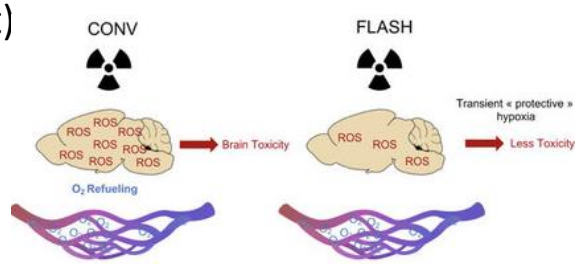
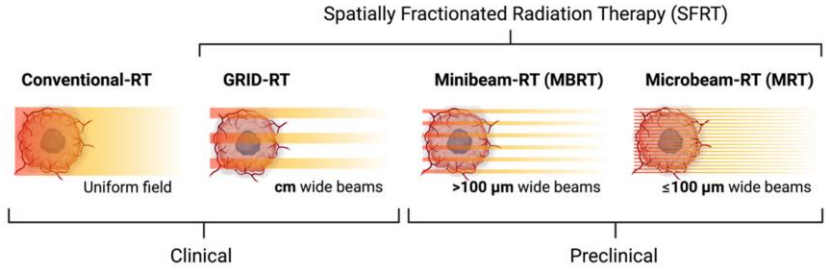


  - Preserve the healthy tissues:
    - **Improve ballistics** with different particle/energy/molecular targeting: hadrontherapy, VHEE, **TRT (α /Auger)**
    - **Dose delivery mode**: spatial fractionation of dose (**SFRT**) (beam size < mm), Ultra-high dose-rate (UHDR, "**FLASH**" effect)





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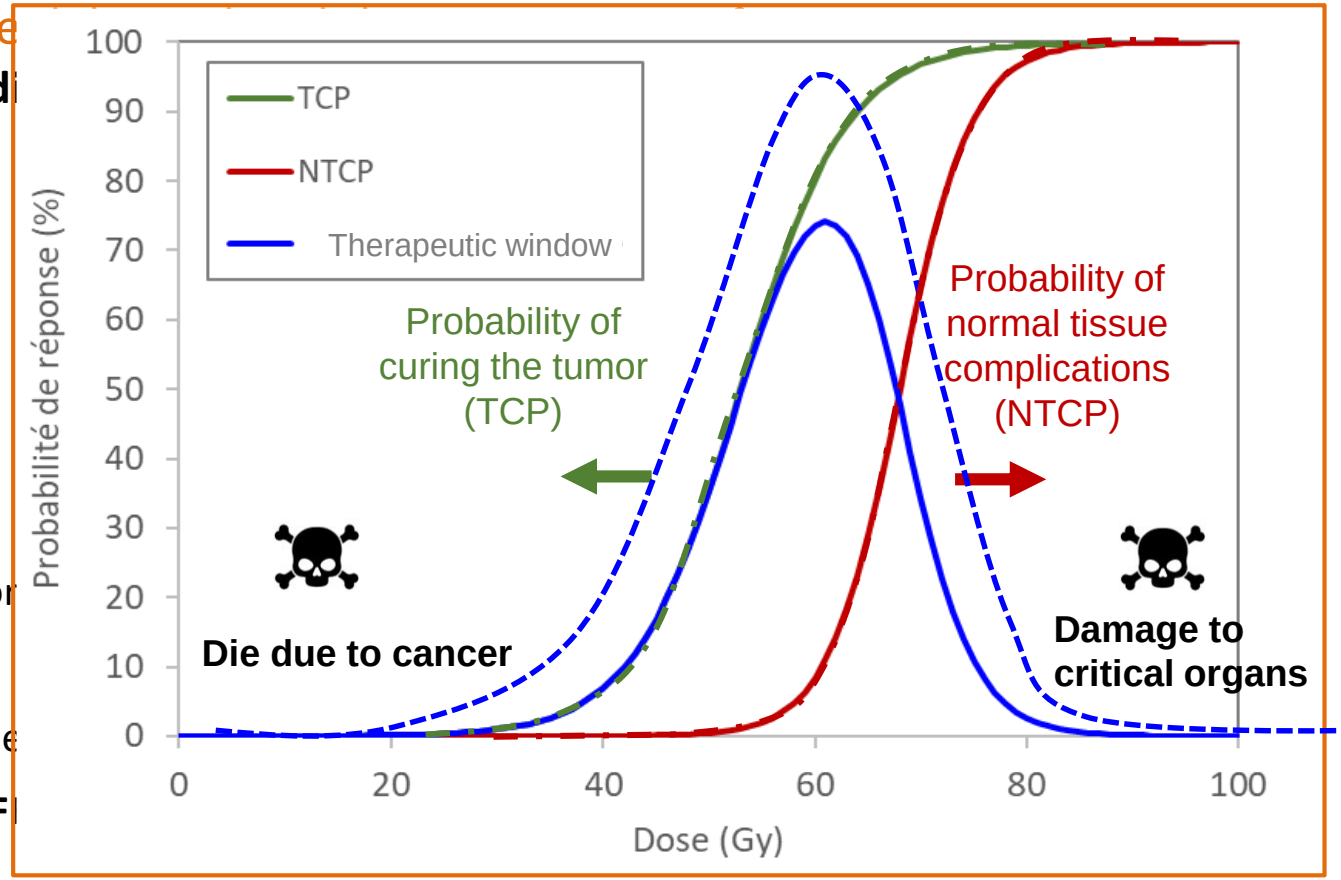

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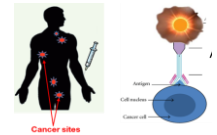
  - Preserve the healthy tissues:
    - **Improve ballistics** with different particle/energy/mole
    - **Dose delivery mode**: spatial fractionation of dose (**SF** Ultra-high dose-rate (UHDR, "**FLASH**" effect)

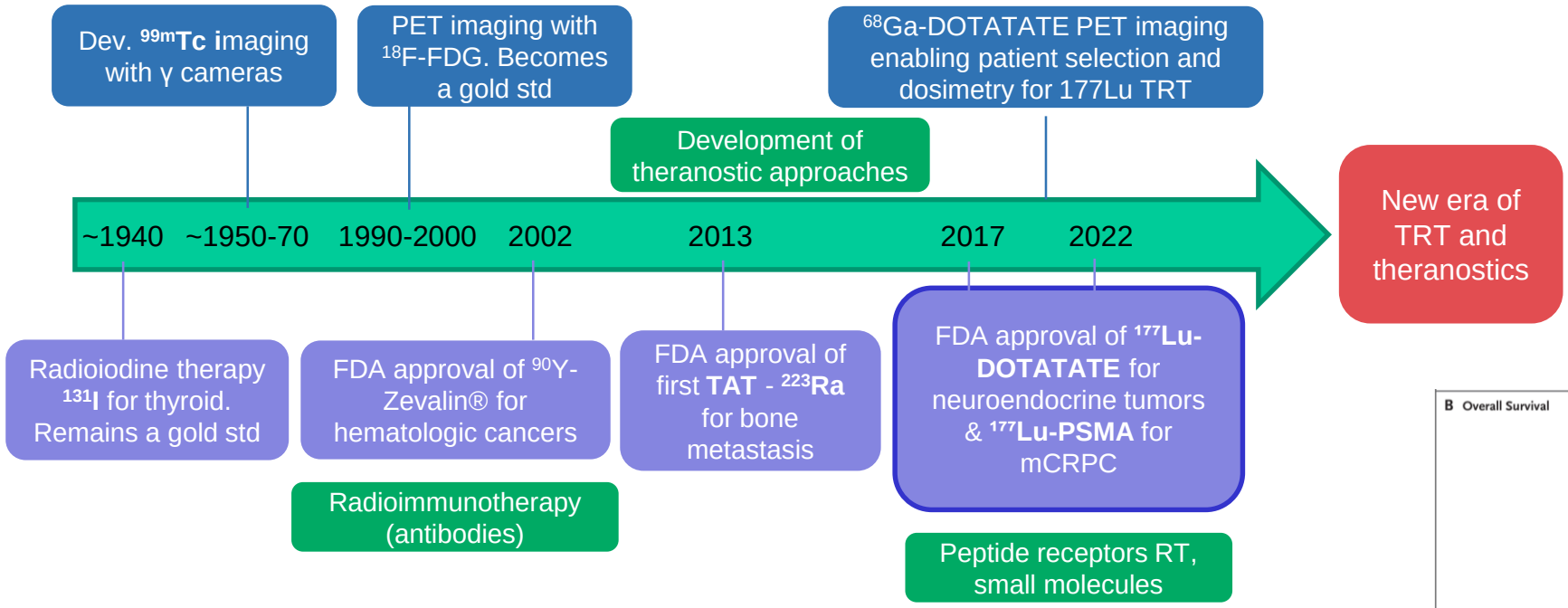
→ Play on physical parameters to induce a different biological effect

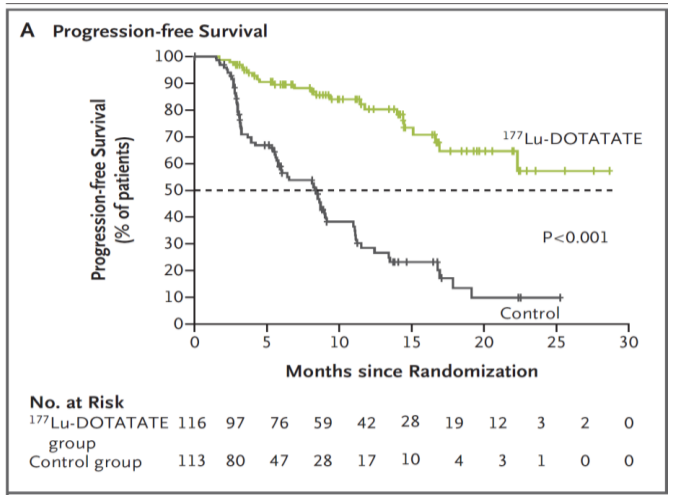
Targeted Radionuclide Therapy (TRT)



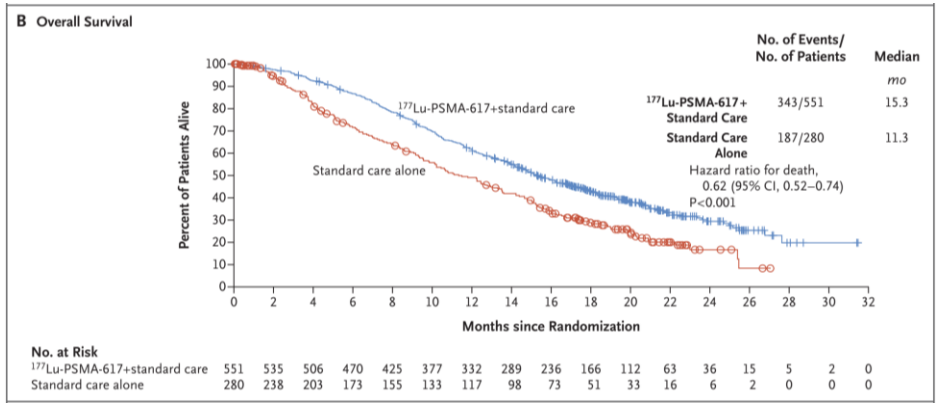
➢ TRT uses unsealed sources for selectively target cancer cells thanks to radiopharmaceuticals (RP).

Rapid evolution of diagnostics and TRT over the past 20 years :





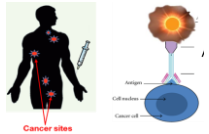
Strosberg et al. Phase 3 Trial of 177Lu-Dotatate for midgut Neuroendocrine tumors, N. Engl. J. Med. 376;2, 2017



Sartor et al.,, 177Lu-PSMA-617 for metastatic castration resistant prostate cancer, N. Engl. J. Med. 385; 12, 2021

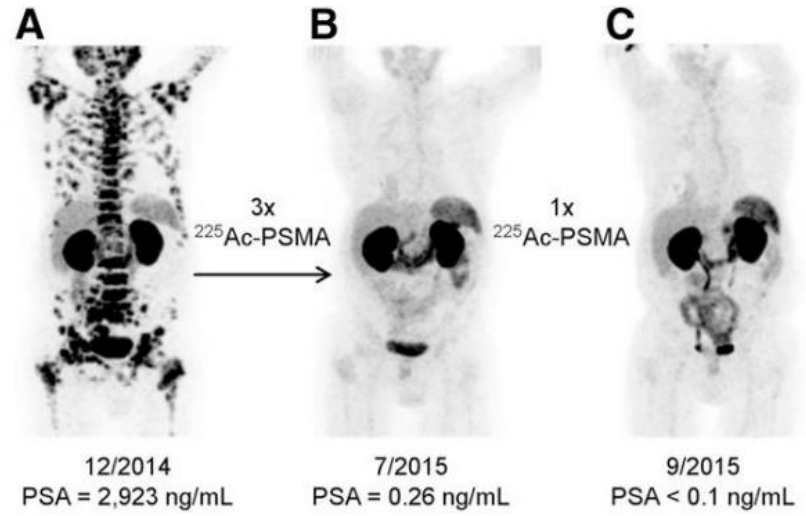
*PET: Positron Emission Tomography ; FDA: Food and Drug Administration
PSMA: Prostate-Specific Membrane Antigen ; mCRPC: metastatic castration-resistant prostate cancer

Targeted Radionuclide Therapy (TRT)

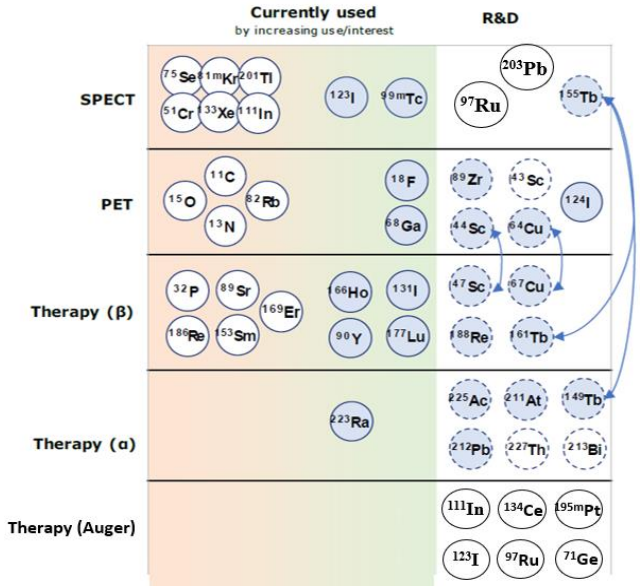


- **Interest in Targeted Alpha Therapy (TAT)** with various emitters *(^{225}Ac, ^{211}At, ^{213}Bi, ^{212}Pb…)* and ligands. ~30 clinical trials ongoing
- **Novel targets & ligand development** to expand TRT applications with theranostic pairs
- **Expension of TRT to earlier treatment indications**, and proposition of combined β/α/Auger TRT

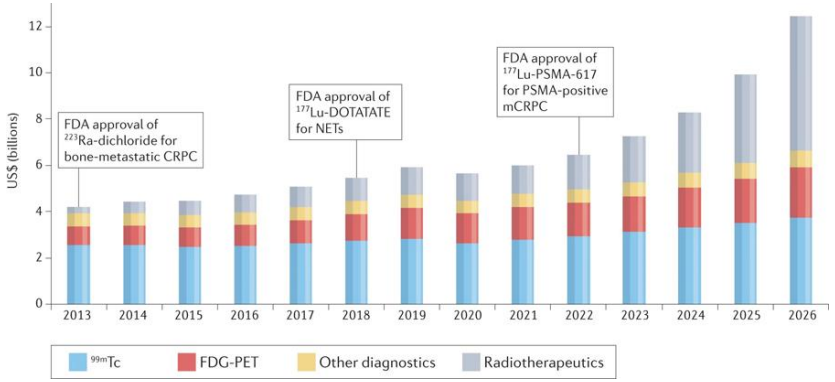
➔ Increasing demand for new isotopes with reliable production routes



Spectacular response of Metastatic Castration-Resistant Prostate Cancer patient using ^{225}Ac-PSMA-617 TAT, Imaging performed with ^{68}Ga-PSMA. From Kratochwill J. Nucl Med, 57(12), 2016



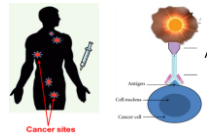
Adapted from Co-ordinated Approach to the Development and Supply of Radionuclides in the EU - N°ENER/D3/2019-231 - Final Report



The predicted global nuclear medicine market 2013–2026, from Bodei L, et al... Nat Rev Clin Oncol. 2022 Aug;19(8):534-550.

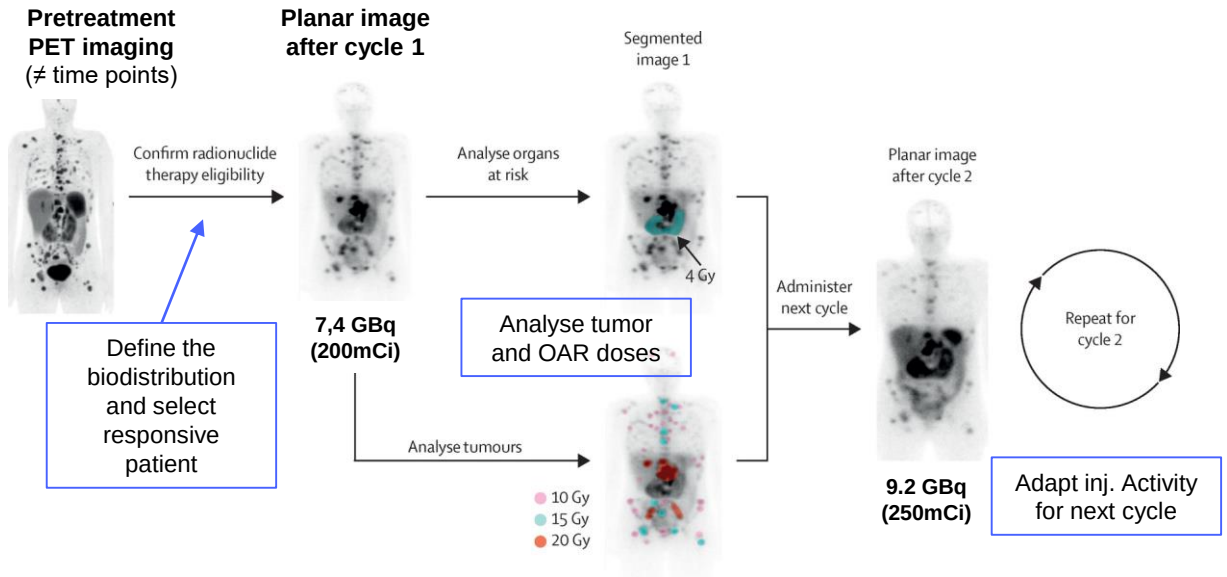
Financial interest, most pharmaceutical companies launched nuclear medicine programs

TRT: Theranostic and Dosimetry



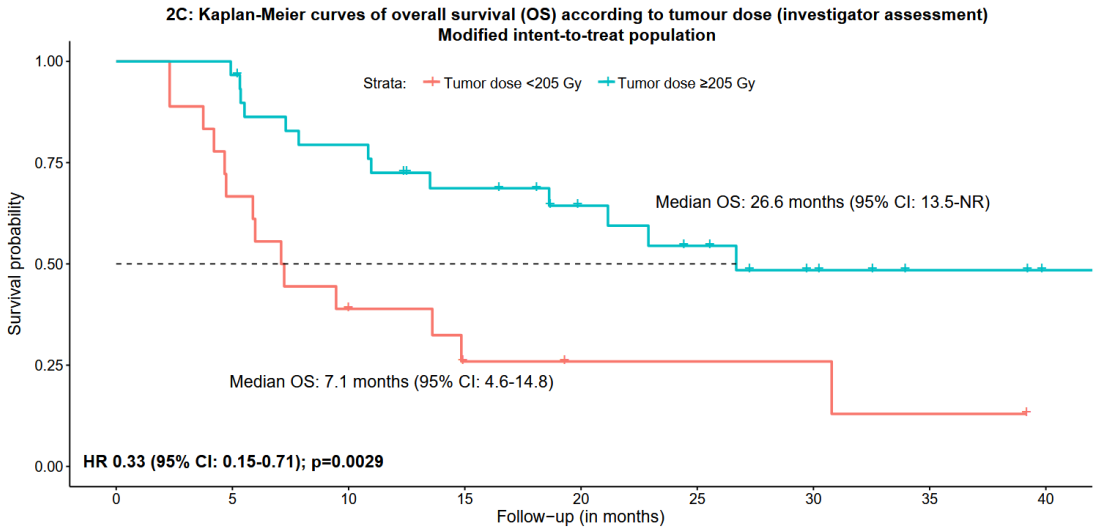
➢ Despite effective palliation of tumor growth, current fixed activity is applied, sub-optimal for curative treatment:

- **Dosimetry may guide personalization** to achieve durable complete response by adapting activity / cycle



Dosimetry in radionuclide therapy: the clinical role of measuring radiation dose. Lawhn-Heath C, et al. Lancet Oncol. 2022; 23:e75-e87.

- **Demonstration of personalize dosimetry benefit**

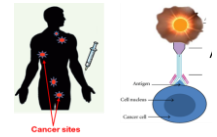


Garin et al., SIRT using personalised dosimetry for locally advanced hepatocellular carcinoma (HCC) patients: multicenter randomised phase 2 study (DOSISPHERE-01 trial). Lancet, 6(1),2021

- **TRT is not systematically performed in clinics** due to heavy protocol, additional cost and patient's discomfort

➢ Need to simplify dosimetric protocols with the improvement of imaging systems and reconstruction algorithm (e.g. AI-based)

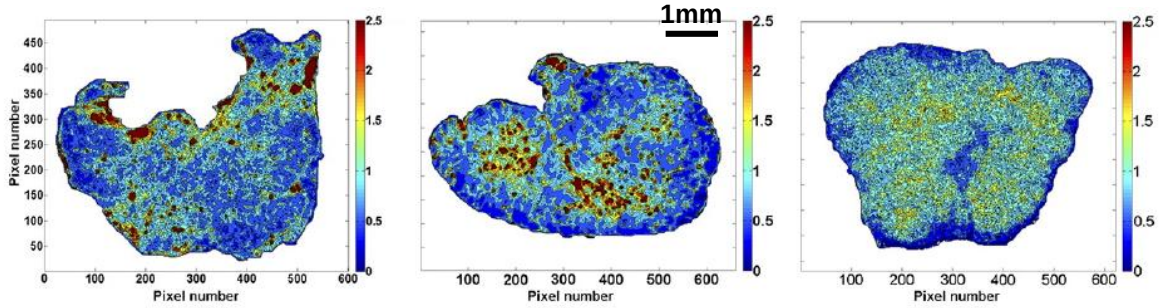
TRT: Theranostic and Dosimetry in TAT



➢ Additional difficulties with alpha emitters or high-LET/short range emitters:

Difficulty to observe clear "dose-effect relationship".

- **High heterogeneity** at micro/tissue scale (range < 100 µm), often unknown
  → *homogeneous hypothesis may lead to errors*
- **High** (and variable) **RBE**
- **Complex direct** *(role of sub-cellular target damage)*, **bystander and systemic biological response**.

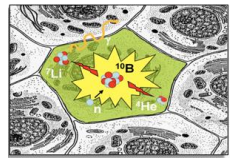


Example of heterogeneous activity distribution in tumor after 7min, 7h, and 21h after injection, via alpha-camera method. From Bäck T & Jacobsson L. J Nucl Med. 2010;51(10):1616-23.

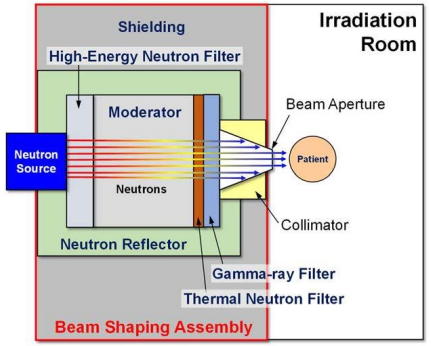
➢ TAT personalize (bio)dosimetry requires:

- **Theranostic radionuclide pairs** with alpha emitters
- **Gamma camera adapted to high-energy** (> 300 keV)
- **Multiscale modeling tools** to account for heterogeneities in bio-dose prediction and quantify uncertainties
- **Dedicated controlled radiobiological experiments** *(in vitro / in vivo)* to characterize complex TAT biological effects
- Identify the relevant metrics to characterize TAT efficacy (beyond absorbed dose)

BNCT: combined therapy



- BNCT Principle: combine external **epithermal neutron irradiation** with injected **^{10}B-based compound to maximize neutron capture cross section at tumor location → lead** to local emission of very high LET-ions (α, $^{7}Li^{3+}$)

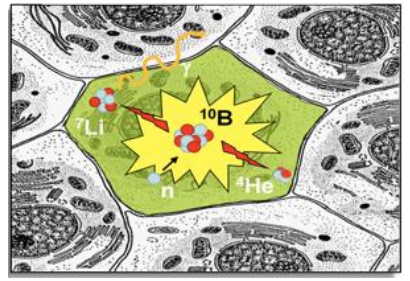


Enriched boron isotope, delivered in cancerous cells (BPA or BSH)

$^{10}B + n_{th}(0{,}025\ eV) \rightarrow [^{11}B]^*$

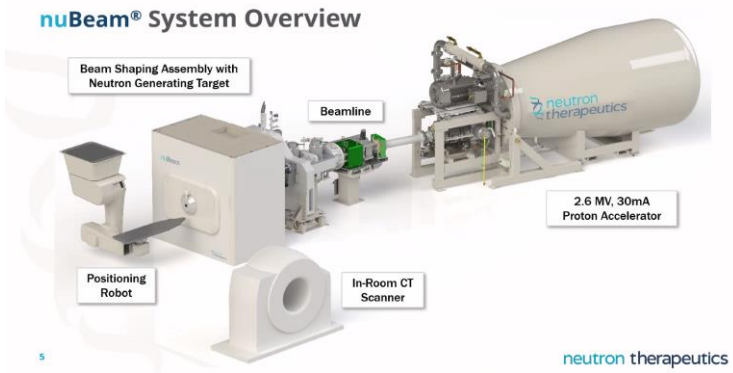
- 6 % → ^{4}He (1,77 MeV) + ^{7}Li (1,01 MeV)
- 94 % → ^{4}He (1,47 MeV) + ^{7}Li (0,84 MeV) + γ(0,48 MeV)

Max range ~5-9µm; LET > 200 keV/µm



- Several clinical trials *(Barth et al. 2012; Shen S et al. 2024*: promising results for **high-grade glioblastoma** and recurrent **Head & Neck cancers.** Historically delivered on nuclear facilities...

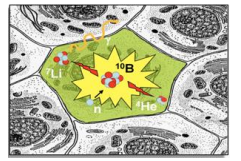
- **Accelerator-based BNCT:** new era for clinical trials as compact accel neutron sources (CANS) allow **performing BNCT in hospital**.
  - About **26 new AB-BNCT** facilities world-while, 9 in Japan *(IAEA*)*. Clinical trial started **in Finland** 2025, **BNCT accepted in clinical routine** for **recurrent H&N cancers** in **Japan.**
  - Compagnies proposing integrated systems *(e.g. neutron therapeutics, TAE life science…)*



NuBeam® system (ex. installed in Finland, Japan, UK…)

**IAEA report 2023 "advances in boron neutron capture therapy"; https://nucleus.iaea.org/sites/accelerators/Pages/default.aspx*

Accelerator-based BNCT

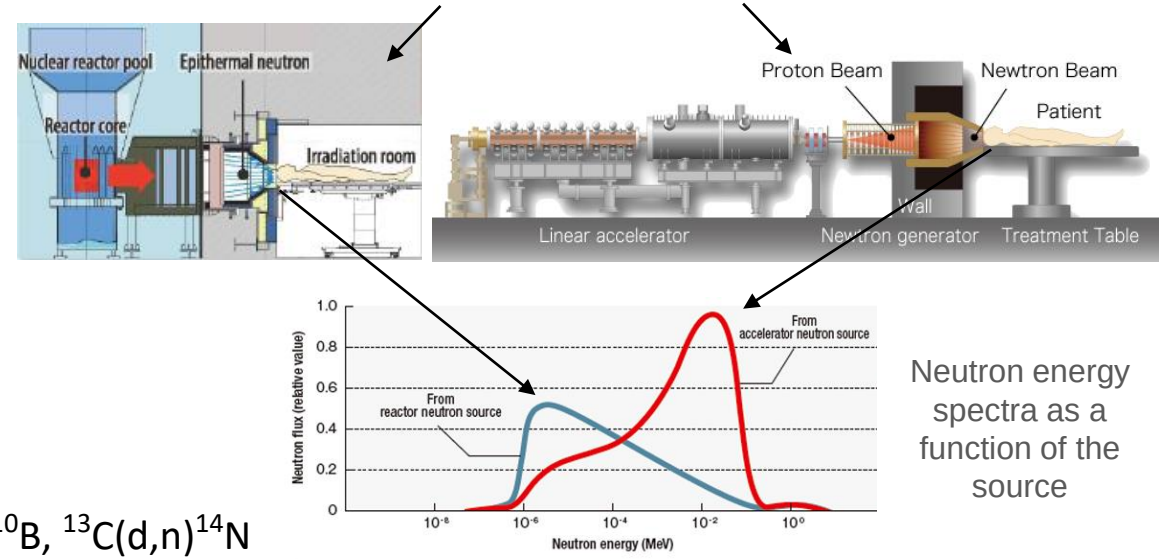


- AB-BNCT: improved patient care and beam spectra for treating deeper tumors.

- IAEA recommandations for neutron beam quality:

	Epithermal Flux Φ_{epi} 0.5eV<E_n<10keV (n/cm²/s)	Fast Neutron Contamination $D\Phi_f/\Phi_{epi}$ (Gy/cm²/n)	Thermal Neutron Contamination $\Phi_{thermal}/\Phi_{epi}$	Gamma Contamination D_γ/Φ_{epi} (Gy/cm²/n)	Beam Collimation J/Φ
IAEA Reference Value	≥ 1 x 10^9	≤ 7 x 10^{-13}	≤ 5%	≤ 2 x 10^{-13}	≥ 0.7

Produced in **reactors** or **accelerators** :



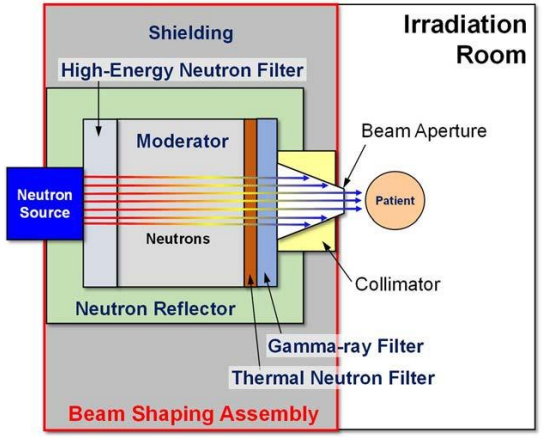
Neutron energy spectra as a function of the source

- Some Challenges:
  - **Production targets**: possible reactions $^{7}Li(p,n)^{7}Be$, $^{9}Be(p,n)^{9}B$, $^{9}Be(d,n)^{10}B$, $^{13}C(d,n)^{14}N$

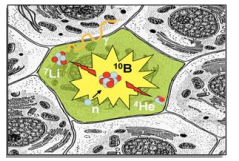
    High power (30-75 kW) degrades targets. Residual radioactivity with ^{7}Li, needs frequent change.
    → **Design optimal targets.**
  - **Online monitoring**: need for real time monitoring : target aging (neutron flux ↘) and delivered dose
    → **Develop n & γ** (480 keV) **detectors.**
  - **Beam shaping assembly**:

    → **Find optimal moderation to maximize penetration in tissue** with high-enough intensity.
  - **Lack of standardization** : complexify treatment comparisons.

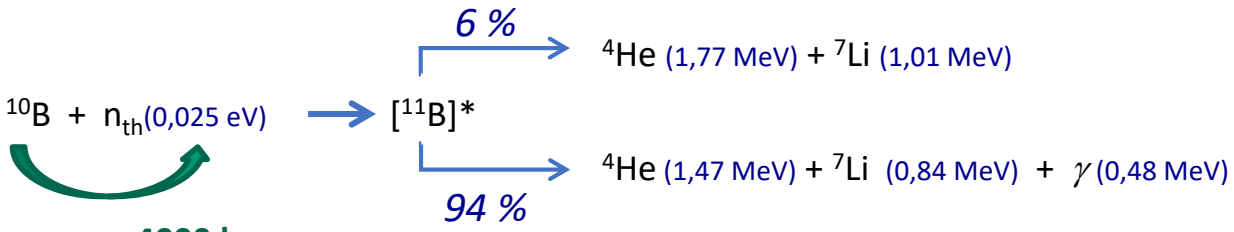
    → **Neutron field spectral and fluence characterization** with adapted detectors.



BNCT dosimetry

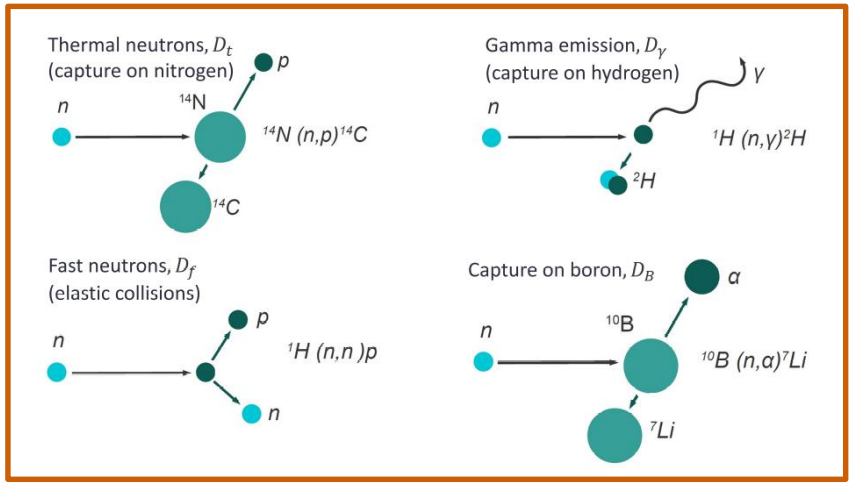


- BNCT dosimetry: complex cumulation of several components due to **neutron thermalization**, **neutron capture in normal tissue** and **gamma component** (from source and capture) in addition to the **desire boron dose** → MC based TPS



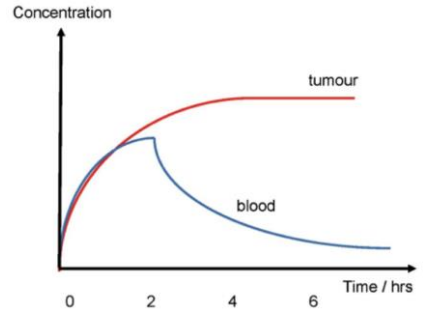
$\sigma_{B\text{-capt}}$ ≈ 4000 barns
(vs $\sigma_{H\text{-capt}}$ ≈ 0,3 b & $\sigma_{N\text{-capt}}$ ≈ 1,7 b)

Main neutron interaction of interest in BNCT:



- Biological dose: based on boron concentration measurement and cumulation of **weighted** components by **fix RBE** (or CBE) factors.

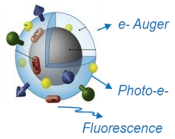
$$D_W = w_f D_f + w_t D_t + w_\gamma D_\gamma + w_B D_B$$



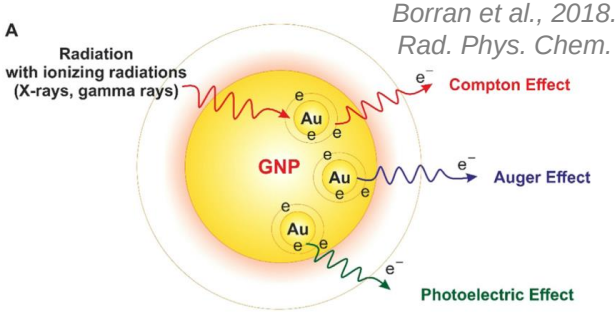
Minimum required tumor/tissue uptake ratio = 3.5

Insuffiscient: high variation in RBE according to cell line, neutron spectra, particle type and dose, in addition to **high dose heterogeneity** due to compound biodistribution and very low-range/high RBE of He/Li ions.

Nanoparticle-enhanced therapy



- Metallic / Oxide NP can enhance radiosensitization of RT: local dose boost due to Auger/PE electron emission cascades.
  - **First showed by Hainfeld *et al.*** in 2004: Gold NP + RX
  - **Confirmed in numerous studies** with different NP/beams
  - **2 clinical trials** in France: AGuIX® (Gd), NBTXR3® (Hf oxide)



Borran et al., 2018. Rad. Phys. Chem.

Clinical Trial > Radiother Oncol. 2021 Jul:160:159-165. doi: 10.1016/j.radonc.2021.04.021. Epub 2021 May 5.

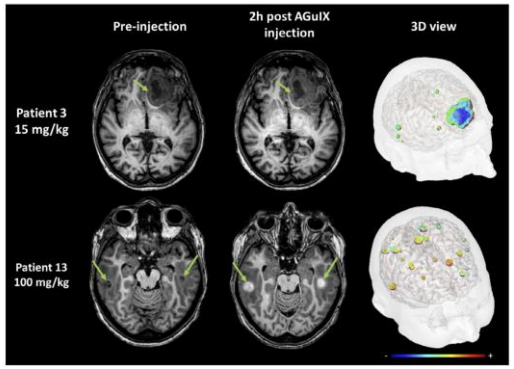
Theranostic AGuIX nanoparticles as radiosensitizer: A phase I, dose-escalation study in patients with multiple brain metastases (NANO-RAD trial)

Camille Verry [1], Sandrine Dufort [2], Julie Villa [3], Marylaure Gavard [4], Carole Iriart [3], Sylvie Grand [5], Julie Charles [6], Benoit Chovelon [7], Jean-Luc Cracowski [8], Jean-Louis Quesada [8], Christophe Mendoza [8], Lucie Sancey [9], Audrey Lehmann [10], Florence Jover [3], Jean-Yves Giraud [3], François Lux [9], Yannick Crémillieux [11], Stephen McMahon [12], Petrus J Pauwels [13], Daniel Cagney [14], Ross Berbeco [14], Ayal Aizer [14], Eric Deutsch [15], Markus Loeffler [2], Géraldine Le Duc [2], Olivier Tillement [9], Jacques Balosso [3]

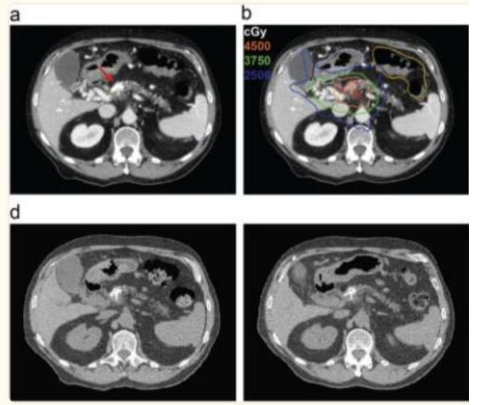
Affiliations + expand

PMID: 33961915 DOI: 10.1016/j.radonc.2021.04.021

Free article



Verry C. et al., R&O, 2021



Bagley F.B. et al., Clin Transl Radiat Oncol, 2021 Pancreatic adenocarcinoma

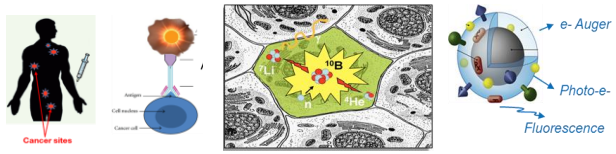
Clinical Trial > Lancet Oncol. 2019 Aug;20(8):1148-1159. doi: 10.1016/S1470-2045(19)30326-2. Epub 2019 Jul 8.

NBTXR3, a first-in-class radioenhancer hafnium oxide nanoparticle, plus radiotherapy versus radiotherapy alone in patients with locally advanced soft-tissue sarcoma (Act.In.Sarc): a multicentre, phase 2-3, randomised, controlled trial

Sylvie Bonvalot [1], Piotr L Rutkowski [2], Juliette Thariat [3], Sébastien Carrère [4], Anne Ducassou [5], Marie-Pierre Sunyach [6], Peter Agoston [7], Angela Hong [8], Augustin Mervoyer [9], Marco Rastrelli [10], Victor Moreno [11], Rubi K Li [12], Béatrice Tiangco [13], Antonio Casado Herraez [14], Alessandro Gronchi [15], László Mangel [16], Teresa Sy-Ortin [17], Peter Hohenberger [18], Thierry de Baère [19], Axel Le Cesne [20], Sylvie Helfre [21], Esma Saada-Bouzid [22], Aneta Borkowska [23], Rodica Anghel [24], Ann Co [25], Michael Gebhart [26], Guy Kantor [27], Angel Montero [28], Herbert H Loong [29], Ramona Vergés [30], Lore Lapeire [31], Sorin Dema [32], Gabriel Kacso [33], Lyn Austen [34], Laurence Moureau-Zabotto [35], Vincent Servois [36], Eva Wardelmann [37], Philippe Terrier [38], Alexander J Lazar [39], Judith V M G Bovée [40], Cécile Le Péchoux [41], Zsusanna Papai [42]

- High complexity to optimize NP-based treatments
  - **Radiosensitization is cell-line and NP-type dependent**: standardization
  - **Treatment efficacy may depend on tumor targeting and cell-uptake**
  - **Macroscopic dose-enhancement** cannot explain alone observed biological effects

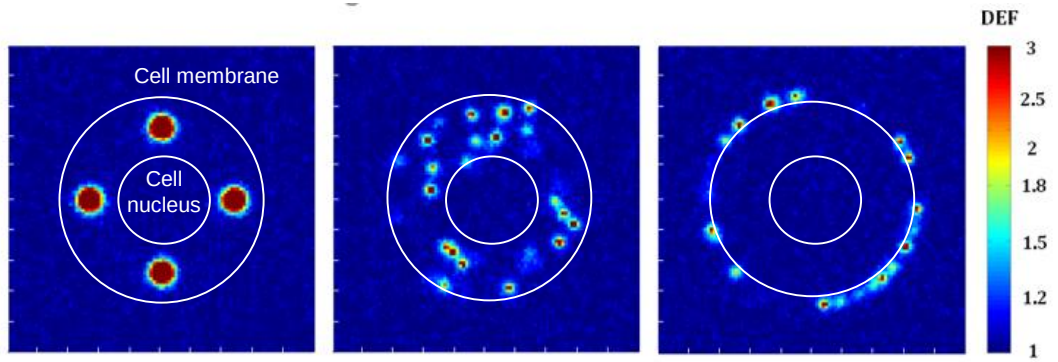
Targeted therapies: dosimetric issues



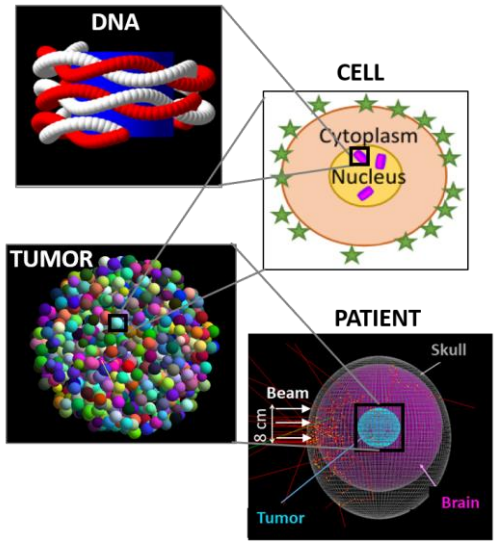
➢ Common difficulties in dose calculations and biological response prediction:

- « **Local** » (cell scale, larger? lower?) **dose** due to **low-range particles of potential high-LET** (Auger e-, α, ions)
- **Heterogeneity ++ of energy deposition at nano / micro /tumor scale**
- **Question of the relevant sensitive target at cell scale** to consider biological damage

DNA, Cell nucleus, Cytoplasm, Membrane, tumor…? How?



*Exemple of heterogeneous dose deposition at cellular scale according to **internalization case of Gd-NP** (Delorme et al. (2017), Med. Phys. 44 (11):5949)*

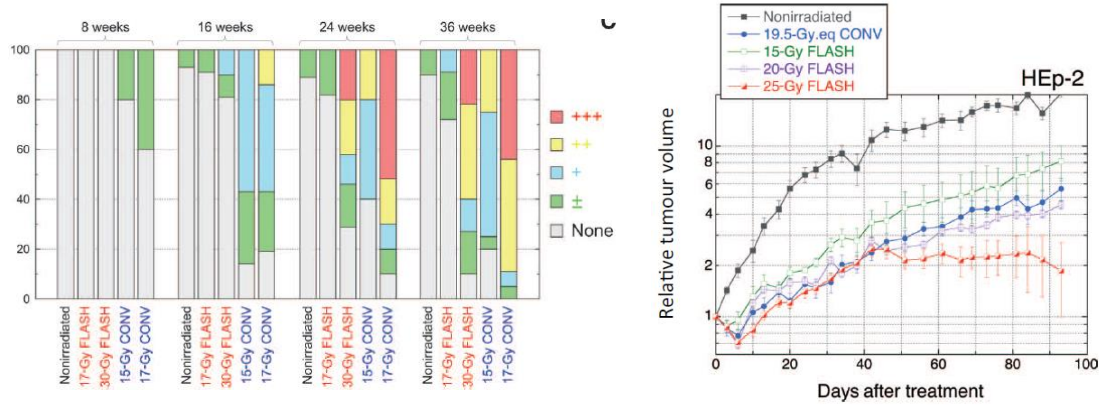


- P**hysical, chemical** and **biological mechanisms** involved in **NP-radiosensitization ?**
- **Lack of precise biological/clinical data of such heterogeneities**:
  → But can be simulated to quantify the impact of such « unknown » heterogeneous distributions.

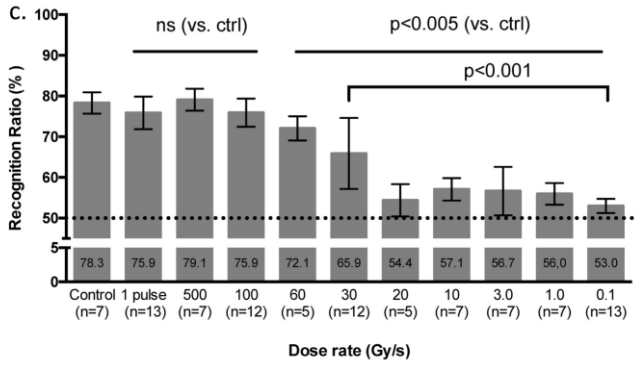
Multiscale modeling tools

UHDR irradiation: « FLASH » therapy

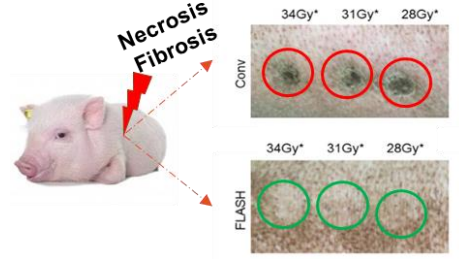
- Very-high dose rates (> 40 Gy/s) protect normal tissues:
  - Pioneer work of Favaudon *et al.* 2014: observed **lower normal tissue toxicity** (lung fibrosis) using **high-dose rate e- beam (> 40 Gy/s,** E~6 MeV**)** with **similar tumor control** to conv. (~0.03 Gy/s)



First demonstration of **lung fibrosis reduction** (**twice more dose**) on mice treated with FLASH compared to CONV irradiation, with comparable tumor response *(Favaudon et al. 2014)*.

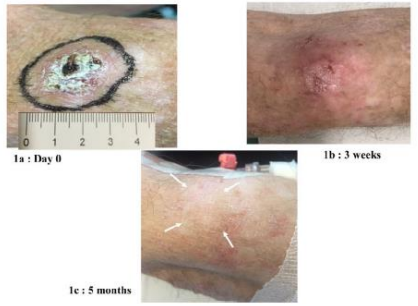


Memory sparing in mice after **whole brain irradiation for dose rates > 100 Gy.s^{-1}** (Montay-Gruel et al. 2017)



Vozenin et al. 2018
Rohrer-Bley et al. 2022

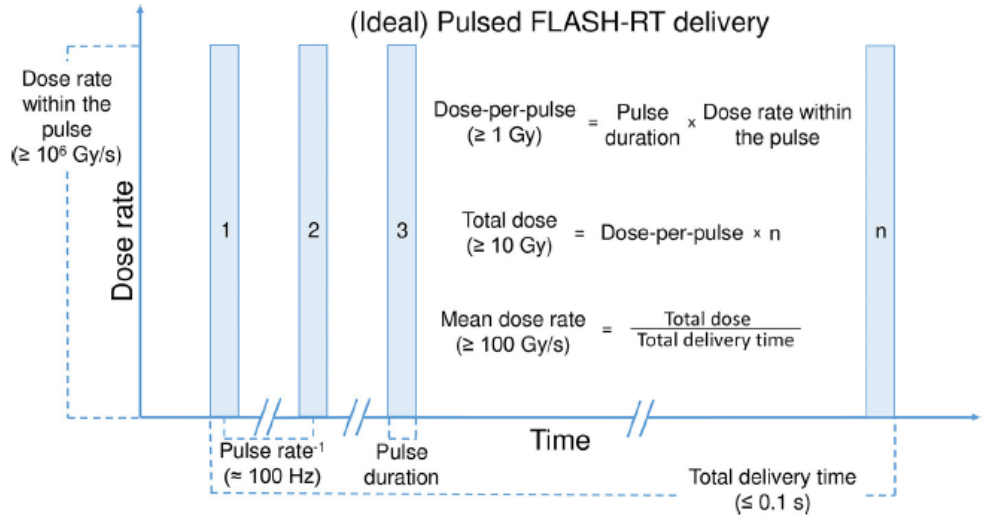
  - FLASH-effect confirmed with **e-/γ/p beams** in several *in vivo* experiments.
    Recently demonstrated with **scattered and PBS proton beam** *(Diffenderfer et al. 2019)*.
  - **First patient treated** in Lausanne *(Bourhis et al. 2019)*.
  - **Several clinical trials planned/started** (on electron beam UHDR facilities, < 10 MeV)



High and fast enthousiasm with FLASH therapy… Sometimes forgeting the basic rules of protection in RT
➔ Some negative results in veterinary trials on cats (Vozenin et al.) or dogs (*Børresen B. et al., Front Onc 2023) with osteonecrosis*

UHDR irradiation: « FLASH » therapy

➢ What physical parameters are needed to have a "Flash" effect ?



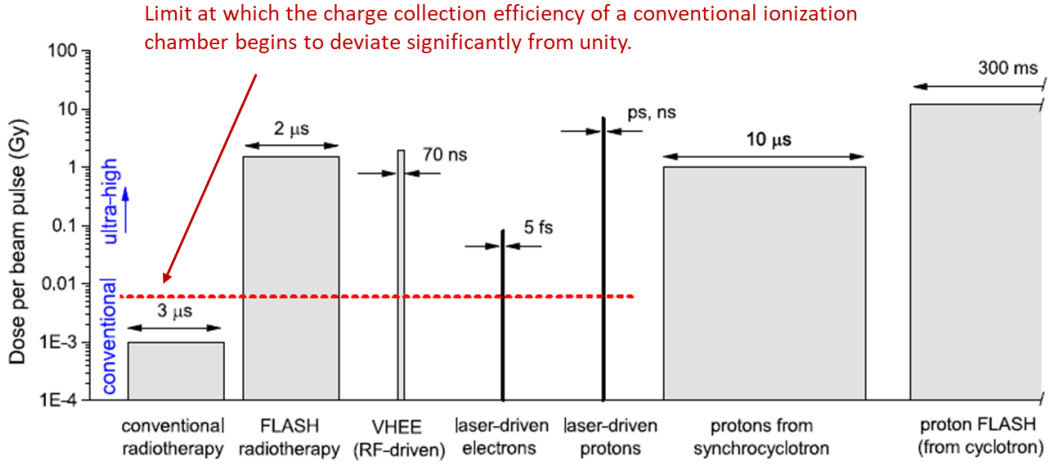
From Wilson et al. (2020), Frontiers in Oncology, volume 9:1563.
https://doi.org/10.3389/fonc.2019.01563

	FLASH	CONV
• **Mean dose rate ($\dot{D}$)**	≥ 100 Gy/s	~ 0,03 Gy/s
• **Total irradiation time (t)**	≤ 100 ms	> min
• **Dose per pulse (DPP)**	≥ 1 Gy	~ 1 mGy
• **Pulse dose rate ($\dot{D}_p$)**	≥ 10^6 Gy/s	≥ 10^3 Gy/s
• **Pulse duration (t_p)**	?	~1 µs

➢ Challenges/Questions:

- **Limits of physical parameter's impact on FLASH biology**: pulse duration/intensity, mean or instantaneous dose-rate, beam size, total dose…
- **Chemical and biological mechanisms** of FLASH-effect ?
  Is it observable in vitro ? → **need for FLASH-compatible irradiation platforms & multidisciplinary teams**
- **Need for Adapted dosimetry solutions** for very-high dose rates needed

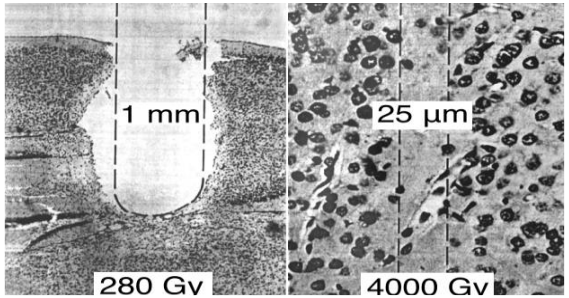
➢ Which beams: different time-structures



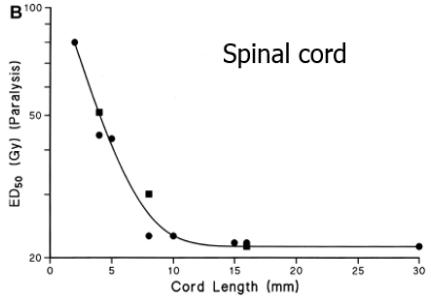
From Schuller et al. (2020), Physica Medica 80 (2020) 134–150.
https://doi.org/10.1016/j.ejmp.2020.09.020

Spatially Fractionated RT

- SFRT can (also) protect normal tissue, with equivalent tumor control efficiency.
  - Combines **submillimetric beam sizes** with **spatial fractionation of the dose**

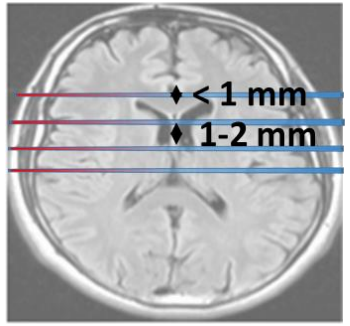


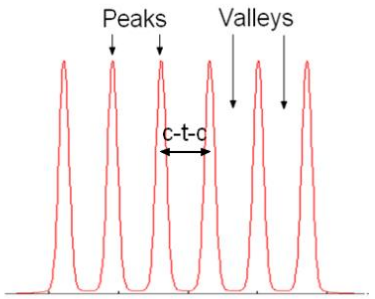
Dose-Volume effect (Zeman et al. 1959)



Hopewell et al., Radioth. Oncol. (2000)

+





Heterogeneous dose profiles

→ Dose-volume effect = the smaller the beam size, the higher the tolerance dose in healthy tissues.

- **MRT**: Beam < 200 µm (synchrotron) ;
  MBRT: 400-700 µm (accessible compact sources)
  Grid (or Latice): ~0.5-1 cm (used clinically)

- Challenge/questions:
  - Explore the terra incognita of influence parameters
  - Biological processes induced in normal and cancerous cells/tissues ?
  - **Reliable dosimetry protocols for very small beam size**

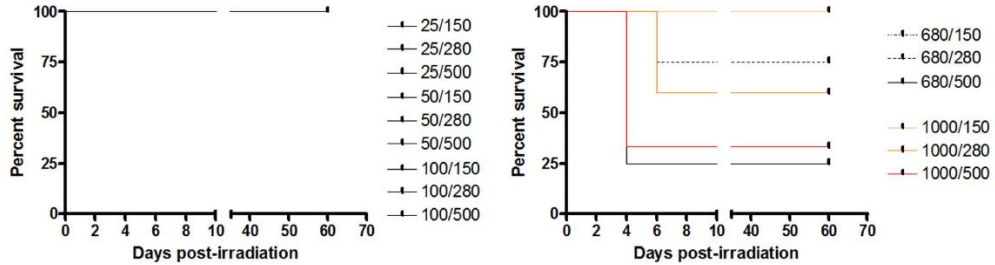
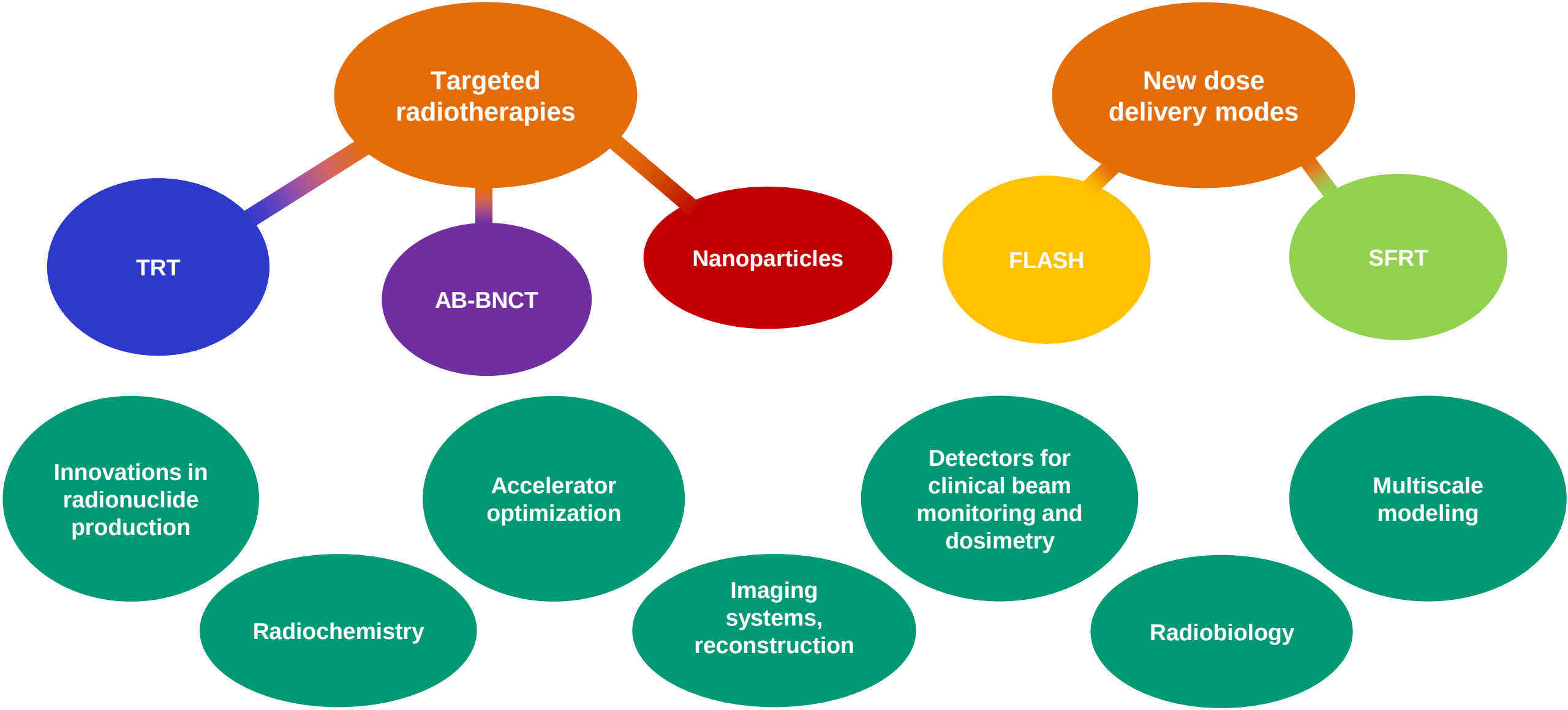


Figure 2. Survival curves of normal rats as a function of the configurations for irradiation. The first number in the legend denotes the width (µm) of the beamlets, the second, the dose (Gy), for instance: 25 µm/150 Gy. All surviving rats were culled at day 60 after exposure.
doi:10.1371/journal.pone.0088244.g002

IN2P3 contributions for innovative radiotherapies (RT)



IN2P3 contributions in TRT – Radionuclides

Innovations in radionuclide production

Optimal production routes for **high-LET** and **theranostic pairs**

EUROPA | REPARE | PRALINE

Targetry: explore projectiles/materials, high power…

REPARE

Nuclear data cross section

Clinical
almost all are for clinical application… mid/long term

Bio-conjugation methods for diverse vectors (antibody, peptides…)

PRALINE

Improve radiolabeling and vectorization

Advance separation chemistry, ligands

Develop **selective, fast and robust chemical processes**

SMILES

PRALINE

Explore **novel ligands, radiolysis impact**

PRALINE

Multimodal & multi-isotope imaging systems

PET/SPECT | XEMIS | CLEARMIND | THIDOS

Preclinical and clinical imaging evaluation

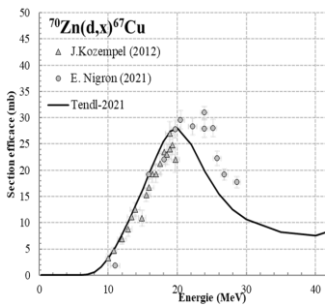
Preclinical evaluation of radiopharmaceuticals

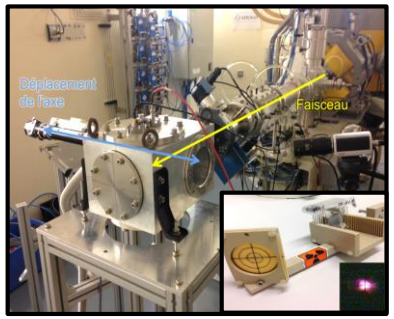
Radionuclide production @ Subatech - PRISMA

Permanent IN2P3
FTE ~11

2020 – 2025 highlights: develop non-conventional methods for producing radionuclide with high purity

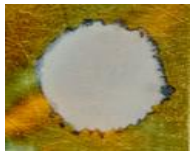
- **Numerous cross-section meas**. (~20y exp), especially based on **d** (and α) **beams:** **^{211}At**(α), **^{64}Cu**(γ)**/^{67}Cu**(β), ^{117m}Sn(CE), ^{186}Re(β), **^{161}Tb**(β)…
- Used for **nuclear code constraints**.





^{67}Cu production σ meas. ; Stacked foils for reaction monitoring

- **Develop innovative targets** resistant to **high current** (~150 µA): enriched vs natural. E.g. **co-deposition** methods of Gd on Ni

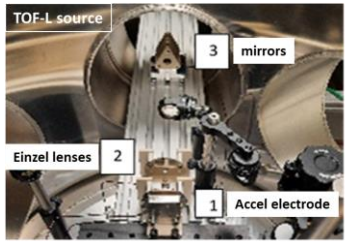


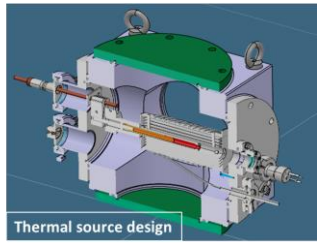
Ni-Gd Co-deposition

- **Advance separation: SMILES project** *(2023-*)*:

Mass separation devices using electrostatic or magnetic fields coupled to laser ionization. 3 phases:

1. **Charged particle optics simulations** (SIMIONS): achieved setup optimization.
2. **Analytical mass separator development**: construction of a TOF system coupled with Laser/thermal ionization sources *(1st exp 2025)*
3. **Magnetic mass separation**: completion ~2028





TOF-L desorption-ionization source ; Thermal source design

- **Understanding chemical speciation:** radiolysis study on astatine *(Ghalei et al. 2022)*

5-year prospects:

- **Collecting new nuclear data** (5y): monitor reactions (^{61}Cu, …), contaminants (^{177m}Lu, …), alpha route..
- **Optimizing production** (5y): focus on Auger emitters (^{197m}Hg with d, ^{71}Ge with p, d and α …)
- **Developing new targets :** molecular plating (2y), molten salts techniques (5y). Pelletizing (2y)
- **Collecting fundamental chemistry data** (5y): speciation studies on Pa, Ru and Rh
- **Explore alternative method** for purification and acceleration of particles: launched of **SMILES** facility (2y) and operations (5y), **Laser Plasma Acceleration** (5y) → **EUROPA** (European call) project launched in 2025 to demonstrate feasibility of RI production for medicine.

Collaborations

- **Local**: CRCI^{2}NA, LS^{2}N, CHU Nantes, ICO, radiochemistry subatech
- **IN2P3**: IPHC, IJCLab, GANIL
- **International**: INFN Milano, INFN Legnaro, Univ. Granada, Oslo university, VUB, LARISSA (DE)
- **Industry**: AI4R, ORANO

Main articles

Cross section	Nigron E. et al (2023), ARI, vol. 200, 110927
Targetry	Bigourdan T. et al (2023), doi:10.1051
Theranostics	Sounalet T. et al (2024), ARI, Vol. 205, 111190
Mass separation	Formento R et al (2020), NIM B, 463: 468-471
Speciation studies	Ghalei M. et al (2022) , Rad.Phy.Che 198 110224

REPARE@ GANIL

Permanent IN2P3
FTE ~1
(15 persons in collab)

2020 – 2025 highlights: REPARE ANR (2019-2024): R&D for Production of innovAtive RadioElements

Project focused on the **production of ^{211}At**, as a pilot study. Aims to develop innovative technologies, later being adapted to industrial production.

- **Innovative targets:** main achievements:
  1. Conception of a **high-power target based on solid Bismuth**.
     → Built and **tested (2023/2024)** at the Neutron for Science (NFS) facility at GANIL.
     →**Two Bi targets** of **~1 GBq**, irradiated with $^{4}He^{2+}$ beams of 28 MeV, **shipped to ARRONAX**.
  2. Investigation of **liquid bismuth target**: no go for prototype.

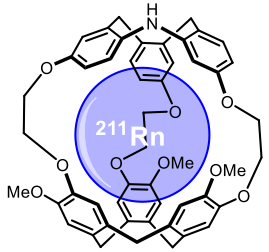
- **Cross-section measurements of ^{210,211}At:**

Measurement of the **^{211}At production** cross section, and this of **^{210}At** in the alpha+^{209}Bi reaction at threshold energies, a contaminant for ^{211}At production that is important to characterize.

The REPARE target station installed in the converter room of the NFS facility at GANIL

5-year prospects:

- **Conception of a ^{211}Rn/^{211}At generator** with regional partners (GANIL, CERMN, IMOGERE). Work on **Rn cage molecules:**



^{211}Rn@Cryptophazane

- **Repeated production of ^{211}At:** 1 or 2 irradiations per month on SPIRAL2 beam (within PRISMAP+ network)
- **Investigation of new alpha and Auger emitter production.**
- **SIMS station** pre-project install @GANIL

Collaborations

- **IN2P3**: GANIL, Subatech, ARRONAX
- **Local**: CYCERON, CERMN, IMOGERE
- **International**: CERN

Funds

anr agence nationale de la recherche

PRISMAP Medical Radionuclides

Main article

Ansari-Chaveau et al. 2025, Optimizing 211At production cross section by studying the rise of 210At cross section: First measurement using Linac SPIRAL2, submitted

PRALINE : Production de Radionucléides et Ligands pour la dosimétrie et l'Imagerie NucléairE

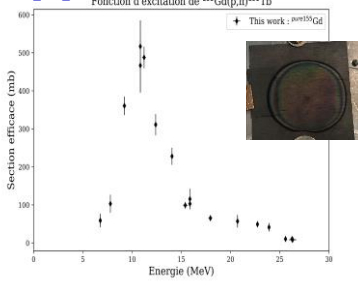
Permanent IN2P3
FTE ~5
(~9 persons in collab)

2020 – 2025 highlights: new methodology for theranostic pair radioisotope developments

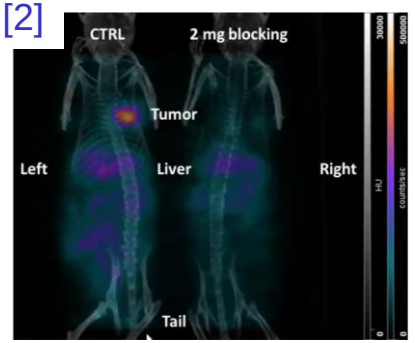
ANR TTRIP (2021-2025): Tools for Tb RadioIsotope Production for nuclear medicine :

- **Target production:**
  - **co-electrodeposition technique** for **Gd target**
  - **pure ^{155}Gd (> 99.9%) target production** by implantation on SIDONIE electromagnetic separator of IJCLab.
- **Cross section measurements:**
  - pure **^{155}Gd(p,n)^{155}Tb** (Auger + SPECT) and **Tb contaminants** [1]
- **Complexation studies, radiolabeling :**
  - **new chelator** compatible with **Tb** and **antibody**;
  - **^{161}Tb** (β^-, Auger) **biolabeling with antibody** [2]
- **Preclinical & clinical imaging evaluation:**
  - Impact study of **^{156}Tb pollution** on **^{155}Tb SPECT image** quality [3]
  - **Clinical validation of THIDOS** camera (^{131}I therapy, 365 keV) [4]

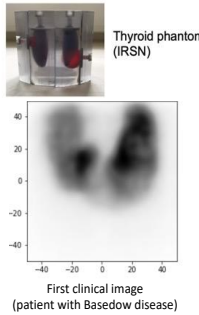
[1]



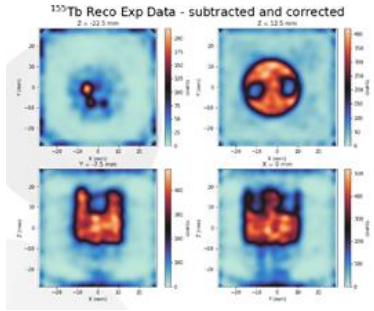
[2]



[4]



[3]



3-year prospects:

New production/chelation solutions for use of **theranostic Sc** (43-PET, 47-β^-) **and Tb pairs**:

- Exploration of other **Tb isotope production** (^{149}Tb (α) and ^{152}Tb (PET)).
- **Production of ^{43}Sc** (minimizing ^{44}Sc contaminant). Sc(III) complexation

Imaging :

- Study **3γ imaging** possibilities with **^{44}Sc**
- **γ camera** (THIDOS evolution) for imaging isotopes **(Eg ≲ 250 keV)**

Main articles

- Wang et al. ARI, 2022, 186, pp.1102
- Wang et al., ARI, 2023, 201, pp.110996
- Bouteculet et al., ARI, 2024, 213, pp.111485
- Bossis et al., IEEE TRPMS, 2024, vol. 8, no. 5, pp. 556-570
- Bossis, et al., NIM A 2023, 1048 : 167907.

3 PhD: M.Bouteculet & S.Lam (defense: fall 2025), M.Hussein (2nd year).

Collaborations

- **IN2P3**: IJCLab, Subatech, ARRONAX, GANIL
- **National**: ICMub (Dijon), IC-UNISTRA (Strasbourg), ASNR, ICR (Toulouse)
- **Clinique**: ICR (Toulouse), CHU Lausanne, Bordeaux
- **International**: NPI-CAS (Czek republic), Catholic Uni. KAERIS (south korea)

Funds

CNRS NUCLÉAIRE & PARTICULES
IJCLab Irène Joliot-Curie Laboratoire de Physique des 2 Infinis
anr agence nationale de la recherche

Instruments and methods for preclinical theranostic @ IPHC Institut Pluridisciplinaire Hubert Curien STRASBOURG IMR

Permanent IN2P3
FTE ~ 8

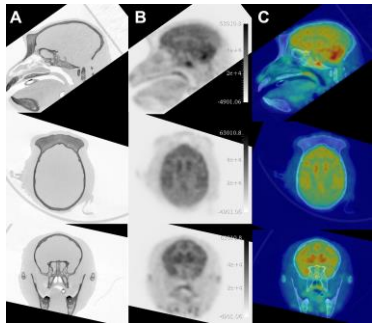
2020 – 2025 highlights:

Instrumental development for preclinical imaging:

Past decade: several **design of PET and SPECT imaging systems,** especially in collab with Inviscan company (FPGA dev, PET design…).
→ *evaluate possible transfer with SATT & CNRS innov.*

- **Primate imaging, pharmacokinetics:** Performance evaluation of the IRIS XL-220 PET/CT new camera dedicated to non-human primates. *(Boisson et al. 2022).* [1]

[1]



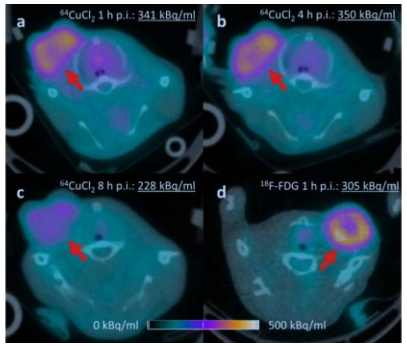
Preclinical imaging studies :

investigate **tumor characterization at both molecular and functional levels**.

- **Macroscopic radiobiology rpPET INCA project**: Comparison of the [18F]-FDG and [18F]-FLT PET tracers in the evaluation of the preclinical proton therapy response in hepatocellular carcinoma. *(Brasse et al. 21)* [2]
- **Radiomarker for breast cancer**: $^{64}CuCl_2$ PET imaging of 4T1-related allograft of triple-negative breast cancer in mice. *(Latgé et al. 2023)* [3]

The $^{64}CuCl_2$ is produced at Cyrcé.

[3]



[2]

5-year prospects:

Université de Strasbourg

Instrumental & methods developments:

1. **Dose delivery optimization** (hypofractionation, flash) with protons → TEL & dose rate biol impact
2. **Dedicated preclinical instrumentation**: Whole-body &Brain mouse PET, High-efficiency SPECT
3. **Dedicated reconstruction and quantification algorithms** (AI based)

Innovative combination therapies and companion trials *(glioblastoma, pancreatic cancer)*

1. **Proton beam irradiation + activation molecules**: chemotherapy (1y), or nanoparticles (3y)
2. **TRT + activation molecules** (chimio, nanoparticles): first with ^{67}Cu (β) (1y), then with theranostic pairs (Cu, Tb) (3-5y)

Collaborations

- **IN2P3:** IPHC (DSA, DEPE, Cyrcé), LPC Caen, Arronax
- **Industry**: Inviscan SA
- **National**: CINAM, LATIM
- **Clinical**: CLCC Paul Strauss, ITI Institut du Médicament de Strasbourg

Funds

Université de Strasbourg IMS
CNRS CPER

Main articles

- Latgé, A., et al. (2023). $^{64}CuCl_2$ PET imaging of 4T1-related allograft of triple-negative breast cancer in mice. *Molecules 2022, 27, 4869.*
- Brasse, D. et al. (2021) *Molecular Imaging and Biology*. 2021 Oct;23(5):724-732
- Boisson et al. (2022), *EJNMMI Physics* 9, 10.

Imaging systems

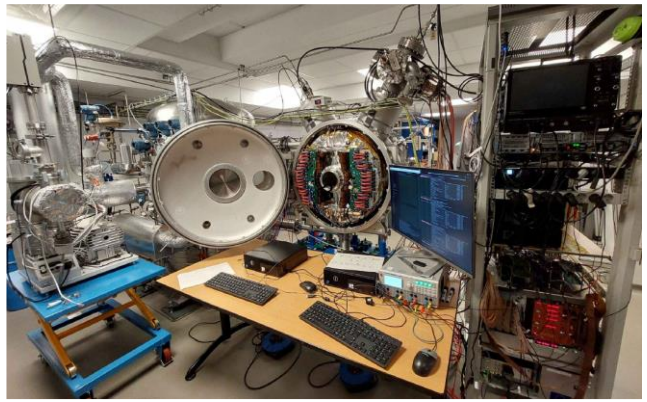
→ See Etienne Testa talk for details

2020 – 2025 highlights: several imaging systems for theranostic applications developed in IN2P3 labs, that can have an important role in the development of personalized dosimetry in TRT

XEMIS:

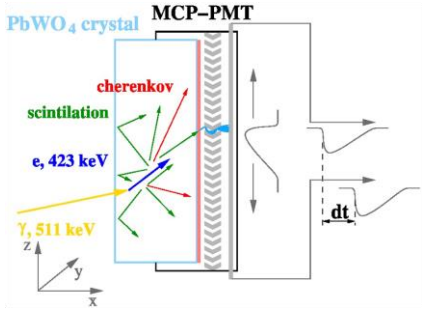
Compton camera based on liquid Xe detection material → fast and sensitive, allowing very low injected activity imaging,
+ possible meas. of 3 γ emissions (↗resolution).

→ **1st Preclinical prototype installed at the Nantes University Hospital**, for diag**.**

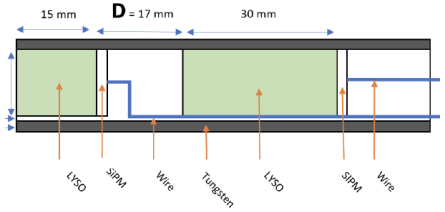


CLEARMIND:

"scintronic" detector concept with TOF <100ps to improve PET imaging sensitivity and resolution (to ~1 mm).

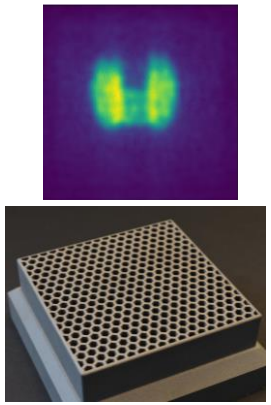


CCP: Compton collimated probe **intraoperative probe for radio-guided surgery**.
Valo "Déclic" ongoing
Livrable: Preclinically testable probe prototype (pork)



THIDOS:

New portable **gamma camera** to control the dose delivered during radioactive iodine treatment for thyroid diseases.
Adaptation to high-energy emitters to apply TAT dosi



IN2P3 contributions in « Targeted RT » (MP)

Clinical

Accelerator optimization & field characterization in BNCT (BSA, target, design, meas…)

Innovative production targets

Neutron beam characterization

Optimal moderation (?)

Experimental microdosimetry

Modeling at sub-cell, cell and multicell (2D/3D) scales

Preclinical (in vivo) and clinical (patient) modeling/dosimetry

Multiscale modeling of physical dose and biological response

Monitoring of dose delivery

For in vitro/in vivo radiobiological studies

BIOALTO

THIDOS

XEMIS

AIDER

For clinical dose monitoring (TRT, BNCT)

Sub-cell (nucleus, mitochondria, membrane…), cell and multicell (immunogenicity…) biological responses

Vector (or NP)/irradiation combination

Understanding the biological mechanisms

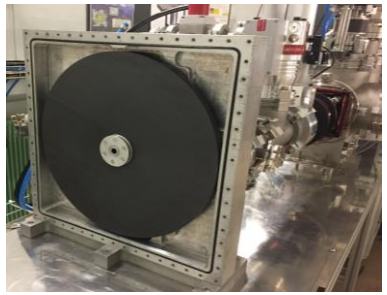
Accelerator Based-BNCT @ LPSC GRENOBLE | MODANE

Permanent IN2P3
FTE ~1.6
(~9 persons in collab)

2020 – 2025 highlights: Master projet AB-nCT (2024-2027)

Project aims at proposing an optimal set of accelerator-based BNCT systems, including:

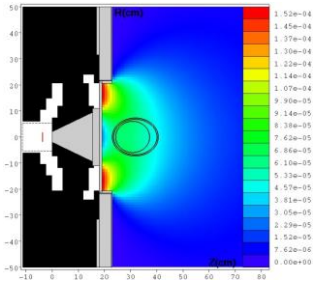
1. **Innovative targets for intense epithermal neutron:**
   - **Develop** a **rotating target on a graphite wheel** + ^{9}Be (or ^{13}C) deposit [1]
   - **Design** of a recycling **liquid ^{7}Li-based target** *(patent ghetta 2020)*
   - Development of an **e- thermal test beamline** (3 kW/cm²)
     → graphite whell held up to 500°C



[1]

2. **Neutron field detection**: develop **2 detector types.**
   - NFM[2] : Gas detector (Ar/CO2) with ^{10}B-coated foil for field monitoring
   - MIMAC-FastN[3]: used as **neutron spectrometer in epithermal and fast ranges** or as **microdosimeter,** meas. 3D ion tracks after ^{10}B capture in tissue-equivalent gaz.

3. **Design of optimal moderator (BSA)** [4]:
   inverse topological optimization algorithm.
   Optimal BSA design for BNCT, reach treatment depth up to ~10cm (std ref ~7.6cm).



[4]

[3]

[2]

3-year prospects:

All dev aims at proposing an **optimal AB-BNCT facility** based on Argentina Deuteron accel design *(reflexion in the frame of BNCT-GLOBAL)*

1. **Targets:** demonstrator of the ^{13}C target deposited on the graphite wheel by sputtering method. (with Argentina collab)
2. **Detectors:** neutron angular distrution + NFM neutron meas. @ GANIL + TANDAR
3. **Microdosimetry:** validate µdosi meas. With tissue-eq. Gaz + compare Geant4 ionization
4. **Moderator:** design and construct the moderator for the metrological epithermal neutron beamline at LMDN. + TANDAR

Main article/patents

N. Sauzet, D. Santos et al., NIMA 2020, arXiv: 1906.03878
M. Hervé et al. Phys. Medica 88 (2021) 148–15
S. Chabod et al., Phys. Med. Biol 67(2022) 105009 .
C. Beaufort et al., 2024 *JINST* 19 P05052.
S. Chabod et al., Phys Med Biol. 2025 70(3).
Patents "Fast neutron detector and spectrometer", Santos et al.. 2021, FR GB DE 36525633 ; "Liquid target for the production of nuclear particles" Ghetta et al. FR 1906353

Collaborations

- **IN2P3**: IP2I
- **National**: LMDN-ASNR, IAB
- **International**: TANDAR (CNEA, Argentina), BNCT-GLOBAL (Germany)

Funds

cnrs NUCLÉAIRE & PARTICULES

MITI-CHEMINS

cnrs ASNR

Multiscale modeling in TAT and BNCT

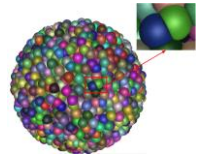
Permanent IN2P3
FTE ~2-3
(+10 persons in collab)

***see E. Testa presentation**

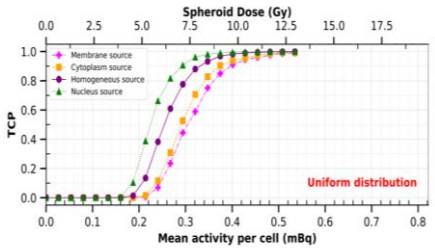
2020 – 2025 highlights: PICTURE PCSI (2021-25) + MP BioALTO (2024-2027) + MITI AlphaBioDose

Project aims at **developing flexible multi-scale models** , based on Geant4-based MC codes and NanOx*, for biological dose prediction in TAT & BNCT considering source heterogeneity, RBE and cell geometry.

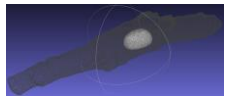
1. **TAT**: - **CPOP-Geant4-NanOx** calculation chain in spheroid geometries evaluate impact of **intra-cell** and **intra-tumor source heterogeneities** on **cell Survival** and **TCP**. [1]
   - Analysis and CPOP code on **github** (CPOP will be in GATE soon).

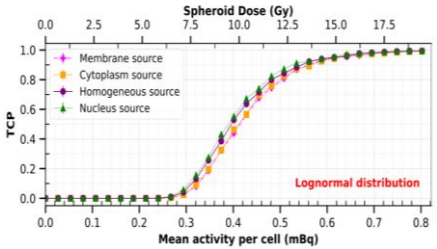

[1]

2. **BNCT**: - preliminar TCP calculation showing **huge impact of boron internalization** (factor 5-6 on $D_{TCP=0,5}$)
   - Collab with **Univ.of Granada** to compare on ILL experiments.



3. **Experiments**:
   - instrumentation of the **BioALTO* beamline** (MP) for low-energy ion radiobiology - **LPSC diamond monitor**.
   - **MITI collab** (GANIL, ISTCT, LITO) to perform **in vitro dose-controlled** cell survival with α-emitters + alpha@Silab.
   - with LIRIS: **3D cell microscopy images** →





Objective to **characterize and quantify cellular lethal mechanisms** (DNA and other cytoplasm or membrane targets…) to constraint models.

5-year prospects:

TAT:

- Benchmark TAT **cell survival** + study impact of **cell geometry** + scale-up to ***in vivo*** **biological-dose maps**.
- Include in **NanOx extra-nuclear cell damage**. *Fit on BioALTO + α emitters experiments. (+µbeams?)*
- **Create digital database** of various cell lines

BNCT:

- **Confirm heterogeneity impact** on TCP.
  Extend **multi-scale approach** including full BNCT dose components. IAB collab to **constraint BNCT model** and study **cell-biological mechanisms**
- **Collab Univ. Granada** → BNCT dose formalism comparison & inclusion in TPS.

Availabiliy in open-source codes G4-DNA/GATE:
TAT/BNCT BioDose actor in GATE, BioALTO digital twin

Extend modeling to tumor response models

Collaborations

- **IN2P3**: IP2I , LPCA, GANIL, IJCLab
- **National**: LIRIS, ISTCT, LITO, IAB, Baclesse
- **International**: Univ. Granada, AMA/NASA, Argentina

Funds

Main articles

1. Levrague et al., 2025, Med. Phys., in proof
2. Alcocer-avila et al., 2024, Med. Phys. 51(12):9358-9371.
3. Levrague et al. 2024, ⟨hal-04775893⟩ ⟨hal-04775900⟩

Github: https://github.com/lpc-umr6533/cpop.git ;
https://github.com/VictorLevrague/py_nanox_package.git

Dose control in radiobiology

Permanent IN2P3
FTE ~1
(~4 in2p3 persons)

2020 – 2025 highlights: complementary solutions for dose-control in biology exp

TAT dosimetry:

Started 2018

4-Si detector [1] develop for TAT dosimetry, to qualify the **dose delivered** in **2D in vitro** irradiation experiments with dedicated cell supports [2]. Part of a program that studies multiscale biological effects for the treatment of brain metastasis.

New deconvolution method developed for alpha energy spectra reconstruction *(Doudard et al.)*

From 2024: collab with LPSC/IP2I and LITO *(MITI AlphaBioDose)* to **provide exp. Data constraining the models**.
+ **preclinical in vivo dosimetry** with multimodal-imaging data to evaluate treatment efficiency and toxicity.

Microscintillator for TRT:

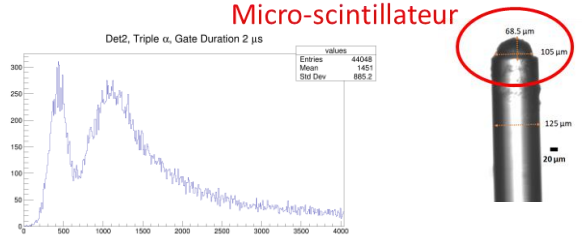
Objective:

Preclinical liquid source microdosimetry from isotope production to biodistribution studies:
- meas. activity at a **micrometer scale**
- Detecting **low activity levels**
- Implantation **near** (in vitro) or **within** structures of interest (in vivo)

Results:

Efficacy and energy measurement with sealed α-sources.

Micro-scintillateur



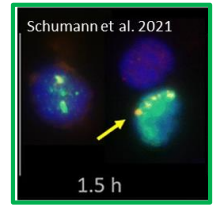
5-year prospects:

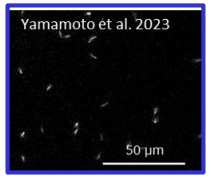
TAT Dosemeter @ GANIL objectives:

- **Short-term: - Dose-effect relationships in TAT** *(survival and DNA break)* on metastatic breast cancer cells irradiated with ^{223}Ra (or available α emitters)

- Benchmark biological effect models (collab LPSC/LITO)

- **Medium/long-term :** In vitro dosimetry at the cellular level. Joint measurements of **α particle interactions**…
  →**Microscopy + Scintillator**…
  and the **rate of DSB** at the cellular level





µscintillator @ LPC:

- **Short-term**: test various organic scintillators. Control reproducibility of detector sizes and shapes. Study response as function of β/α
- **Delivrable 3-4 y**: functional and dose-calibrated detector

Collaborations

- **IN2P3**: LPSC, IP2I, IPHC
- **National**: ISTCT, LITO, Baclesse, CINAM

Funds

Main articles

A. Doudard* et al.. Med. Phys. 2023; https://doi.org/10.1002/mp.16279
A. Corroyer-Dulmont et al. Front. Oncol. 2021; https://doi.org/10.3389/fonc.2021.714514
Frelin-Labalme A-M et al. Med. Phys. 2019; https://doi.org/10.1002/mp.13969
Corroyer-Dulmont A et al.. Neuro-Oncology 2019; https://doi.org/10.1093/neuonc/noz169

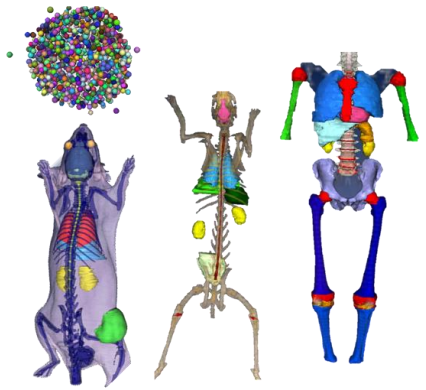
Preclinical and clinical dosimetry of TRT

Permanent IN2P3
FTE ~1.6
(~9 persons in collab)

2020 – 2025 highlights: Over 15 years of partnership IMOST- Jean Perrin cancer center

Several projects, **studying the dosimetric and microdosimetric impact of innovative targeted radionuclide radiotherapy treatments** or radiopharmaceuticals dedicated to SPECT or PET imaging using the GATE simulation platform.

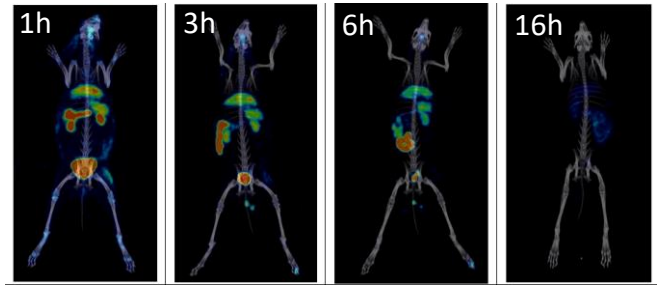
Demand from medical centers & INSERM lab to perform the dosimetry to accompagny Radiopharmaceutical developement and clinical transfert.



3D reconstruction (spheroid, mouse, rabbit and human) from microscopic or CT imaging. Definition of ROIs

Clinical transfert phase
I MELRIV - CARSPECT

- ^{131}I-ICF01012 Melanoma
- ^{177}Lu-Tz ^{177}Lu-PSMA Breast cancer
- ^{99m}Tc-NTP-15-5 ^{68}Ga/^{64}Cu/^{67}Cu Cartilage (arthrosis)
- ^{90}Y Hydrogel de chitosane Glioblastome



Biodistribution study of radiopharmaceuticals by SPECT, PET imaging and dosimetric calculation

5-year prospects:

General:

- LPCA will continue dosimetry studies for preclinical and clinical treatments to **support the market introduction of innovative radiopharmaceuticals**.
- Development & validation of **GATE 10 simulation** platform and **Geant4-DNA**.

ANR IRHydroBRAIN (2025-2028) :

- Strategy for intraoperative TRT in glioblastome with radiolabeled hydrogel with ^{90}Y or ^{177}Lu.

Apply to TAT : FANTαSTIC
Development and testing
of new biophysical models
for biological dose predictions.

^{225}Ac, ^{212}Pb, ^{211}At

Collaborations

- **Local**: IMOST, CLCC Jean Perrin
- **National**: CRAN
- **International**: OpenGate Collab
- **Industry**: NanoH

Funds

anr agence nationale de la recherche

Main articles

1. Thivat E et al. *BMC Cancer*. 2022;22(1):417. doi:10.1186/s12885-022-09495-3
2. Jouberton E et al.. *Med Phys*. Published online 2018. doi:10.1002/mp.13165
3. Chanchou M et al. *Méd. Nucl. - IFM*. 2021;45(4):175. doi:10.1016/j.mednuc.2021.06.008
4. Fois GR et al. *Med Phys*. 2020. doi:10.1002/mp.14603
5. Thivat E et al. *Front Med*. 2022;9:993151. doi:10.3389/fmed.2022.993151

Clinical dose control systems

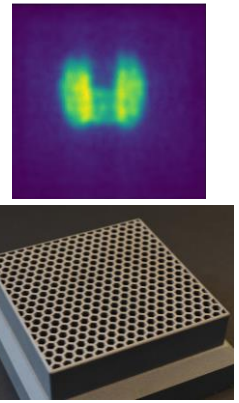
→ see E. Testa presentation

Permanent IN2P3
FTE ~10
(++ persons in collab)

2020 – 2025 highlights:

THIDOS:

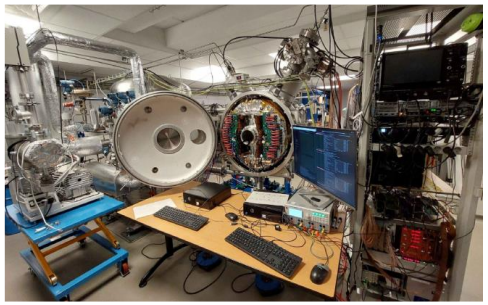
New **portable γ camera** of 10x10cm field of view, to control the **dose delivered** during ^{131}**I** (β 364 keV) treatment for thyroid diseases.
Evaluate accuracy and robustness of the quantification protocol.



5-year prospects:

XEMIS:

→ **Medium** (4-5y) : apply for **TRT dosimetry planification** for preclinical appy



→ **Long** (>5y): patient-scale prototype.

Complementary Compton camera solutions to guide TRT dosimetry:

THIDOS → 2025: test in 3 clinical centers: IUCTO, Baclesse, Cochin for thyroid.

→ 2025-27: adapt to ^{123}I (160 keV) for plan dose + exploit possible applications for ^{177}Lu (

→ >2026… Develop a DL-enhanced **Compton camera** to allow dosimetric monitoring of **TAT** (Eg ≳ 400 keV). ^{149}Tb, ^{213}Bi, ^{225}Ac or ^{212}Pb

AIDER

European-horizon 25-29: develop Compton cameras for radiopharmaceutical dose control.
→ In charge of optimizing the CC prototype by MC simulation and image reconstruction

Collaborations

- **IN2P3**: IJCLab, Subatech, IP2I
- **Clinical/national**: IUCTO, Baclesse, Cochin, CREATIS
- **International**: Korea (thidos) + European (AIDER)

Funds

Main articles

- Bossis et al., IEEE TRPMS, 2024, vol. 8, no. 5, pp. 556-570
- Bossis, et al., NIM A 2023, 1048 : 167907.
- Lequertier, V. et al.. PMB, 70:045001.
- Lainé et al.. Sensors, 2024, 24 (17), pp.5826.

Nanoparticles and radiosensitization

Permanent IN2P3
FTE ~2.7

2020 – 2025 highlights: explores radiobiology with an emphasis on radiosensitization (NP)

5-year prospects:

Development of mitochondria-targeted gold NP

The team develop since several years innovative NP specifically targeting the cell mitochondria.

→ Despite effective targeting, **no significant radiosensitizing effect** was observed on prostate tumor cells. →abandon

Investigate radioprotective effect :

Key molecular pathways highlighted in **mitochondria DNA mechanisms** involved in radioprotective effect in hibernation thanks to advanced instrumentation & analysis developments.

Other NP studies @ in2p3:

- NP radiobio: **IP2I** C. Rodriguez's team have 15 y experience in NP research, especially with **AGuIX® NP** and radiosensitization mechanisms implying **extra-nuclear cell organelles.**
  LP2IB – IRIBIO: radiosensitization quantification studies performed on metallic/oxide NP with AIFIRA µbeam & analysis tools
- NP modeling: **IP2I** Beuve's team (F. Poignant PhD) + R. Delorme:

Innovative approaches and metabolism impact

1. Dose enhancement using nanoparticles

- 2025-2028 : **Mitochondrial / metabolism** impact of dose enhancement of well characterized **metal nanoparticles.**
- Complementary analyses from IP2I partner

2. Hibernation: a bio-inspired approach to radiosensitize human cells

- 2025-2027: Deciphering specific mechanisms involved in radiosentization
- 2026-2028: Characterization of bear serum specific compounds

3. Follow-up of irradiation impact on cells

- Dev of prototype of an **epifluorescence microscope coupled with** a **mini-irradiator** (X-rays)
- Development of related dosimetry

Collaborations

- **IN2P3**: IPHC, IP2I
- **National**: UNH, LNHB, CRCI2NA
- **International**:

Funds

LABEX PRIMES UNIVERSITÉ DE LYON — 80 | PRIME

Main articles

Debar L et al.(2023). Mitochondrion., 71:93-103.
Martucci M et al. (2023). Methods Mol Biol., 2615:121-137.
Martucci M et al. (2024). Nucleic Acids Res., 52(10):5912-5927.
Mehmedović M et al. (2022). Biochim Biophys Acta Mol Basis Dis.,1868(10):166467.

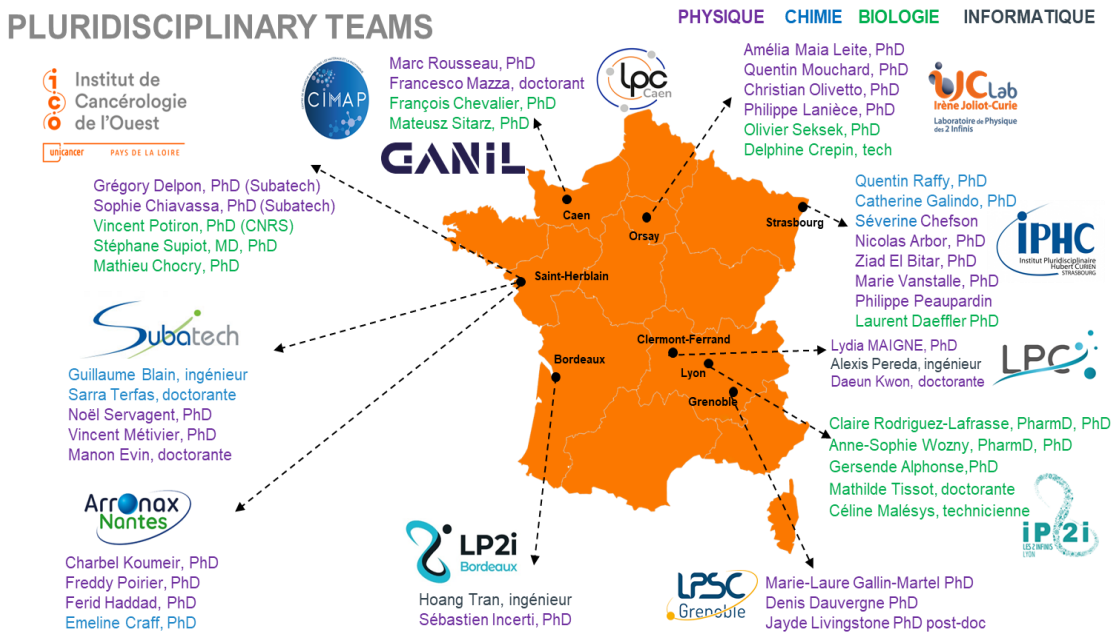
IN2P3 contributions in « FLASH therapy » (MP)

ARRONAX, Nantes

BioALTO, IJCLab Saclay

GANIL…

CYRCé, IPHC Strasbourg



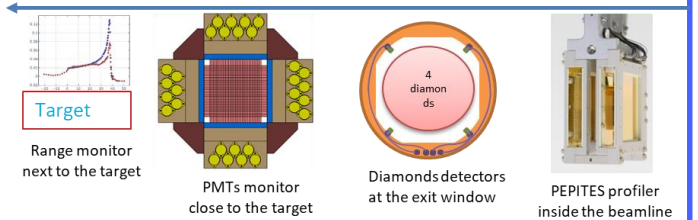
Understanding mechanisms of FLASH therapy

Permanent IN2P3
FTE ~10

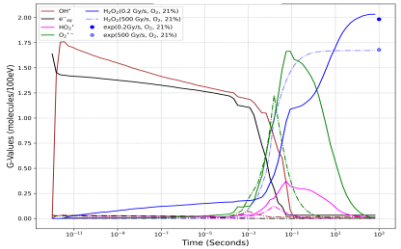
2020 – 2025 highlights: FLASHMOD & beyond…

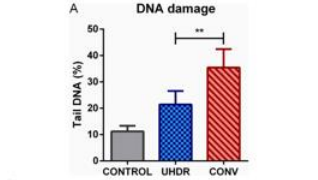
FLASHMOD aimed to develop a comprehensive environment around the **ARRONAX** proton beam to study the **FLASH effect** [0,1 Gy/s – 300 kGy/s].

1. **Arronax FLASH beamline adaptation:** developed pulsed irradiation modes allowing $\dot{D}$ = **1 mGy/s to 1 MGy/s** + innovative beam monitoring instrumentation:
2. **Beamline modeling with GATE*** (digital twin) and dosi validation.
3. **Radiochemistry studies:** Measurements of production yields of several ROS in CONV and UHDR, including H2O2 and e^-_{aq}

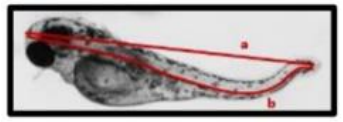


$$H_2O \rightarrow H_2O^* \qquad e^-_{aq} + H_2O \rightarrow OH^- + H^\bullet \qquad OH^\bullet + OH^\bullet \rightarrow H_2O_2$$
$$H_2O \rightarrow H_2O^+ + e^- \qquad H_2O^+ \rightarrow H^+ + OH^\bullet \qquad R^\bullet + O_2 \rightarrow R_2^\bullet$$





4. **Modeling of radiolysis in GATE*, validate Geant4-DNA** models against experiments.
5. **Biological zebrafish embryos** and endothelial cells experiments. New small animal holder.



Bogaerts *et al*, Radiother Oncol 2024

5-year prospects:

*see E. Testa presentation

Fruitful & interdisciplinary collab within IN2P3 (LPCA, Subatech, Arronax, LP2IB) → **being continue within next "FLASH MP" + AAP**:

- Measurement of **ROS in cellular environments** (until now pure water).
- **LPCA** will continue **validation of G4-DNA** + implementation in GATE* (Chemistry Actor)
- **Subatech** investigate exp. chemistry of FLASH, targeting LET influence, time structure effect and superoxide species.
- **FLASHDANZE** project submitted to PIANOFORTE call (with ASNR)

Collaborations

- **IN2P3**: Subatech, LPCA, LP2I, soon IPHC
- **National**: CLCC, ICO Nantes, INSERM US2B, CIMAP/GANIL
- **International**: Dredse Flash team (Germany)

Funds

PCSI FLASHMOD

Main articles

Fois GR, et al. *Med Phys*. Published online 2024. doi:10.1002/MP.17281
Evin M et al. (2024), Physica Medica, 120, 103332
Ghannam Y et al. Radiother Oncol. 2023 Oct;187:109820.
Terfas et al. (2025) J.of Physical Chemistry A, DOI: 10.1021/acs.jpca.5c00629

Radiolysis of Biomolecules for FLASH irradiation

Permanent IN2P3
FTE ~1.5

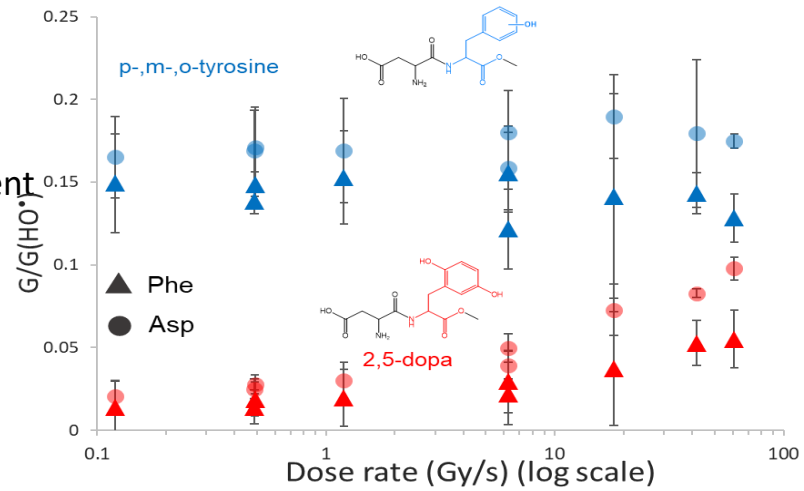
2020 – 2025 highlights:

This project aims at developing a **systematic study**, at the **molecular scale**, of the **radiolysis of protein biomolecules by accelerated ions** studying LET, Ph and the **dose-rate effect** on radiolytic yields.

Other Objective: to deliver robust experimental data for simulation codes Geant4-DNA).

1. **Results: - In water:** radiolytic yields of ·**OH and e^-_{aq} remain unaffected by dose rate under** 24 MeV proton from dose rates (0.1 Gy/s) up to 200 Gy/s (300ns), but **decreased above several kGy/s**.

- **In biomolecules**: **2,5-DOPA** and **aspartame analog** yields increased clearly with D.



2. **Another applied project:**

Dev of **thin dosimetry films for skin dose** measurement during treatment →**CNRS Prématuration, Q. Raffy, 2023–2025** → continues with SATT.

5-year prospects:

- **Study dose-rate effects on radiolysis** of **water and biomolecules** under **electron and X-ray** (Aerial-CRT), **UHDR µpulses H+** @ ARRONAX and at HIMAC (Japan).
- Study of the impact of **O2 concentration on dose-rate effects** in **biomolecule** radiolysis.
- Study **more complex peptides** to identify **potential intramolecular radical–radical transfer** processes that may occur in proteins.
- Investigation of the **evolution of radicals** formed **in proteins** under irradiation, using low-temperature (26 K) irradiation conditions.

Collaborations

- **IN2P3**: Subatech, Arronax
- **National**: Icube, the platform Acacia, G4-DNA collab , G. Baldacchino.
- **International**: NIRS-QST (Japan) and CNAO (Italy), ICANS, Aerial-CRT (Illkirch) platform

Funds

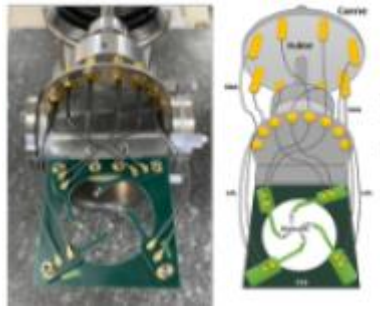
2 PCSI plan cancer projects
PHC Sakura Project (2021-23)

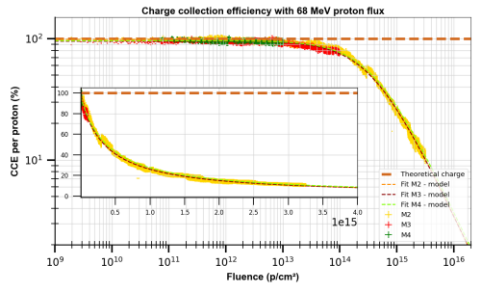
Dose monitoring for FLASH &microbeams

Permanent IN2P3
FTE ~2.6

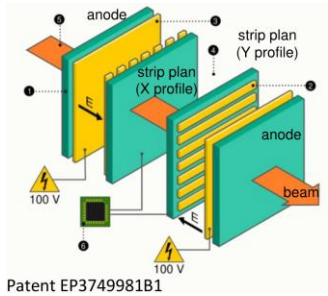
2020 – 2025 highlights: Find solutions to monitor ion beams at **UHDR** [1-1MGy/s] … and **SFRT**

DIAMONI:





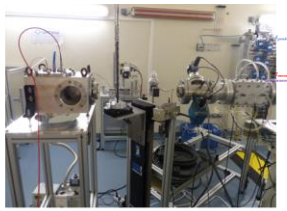
PEPITES:

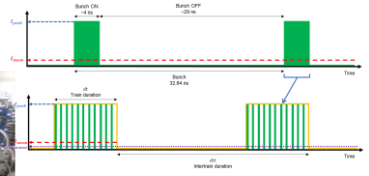


Patent EP3749981B1

***see E. Testa presentation**

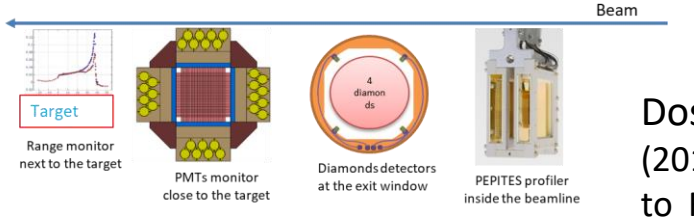
Irradiation platforms





CYRCé

BioALTO



ARRONAX

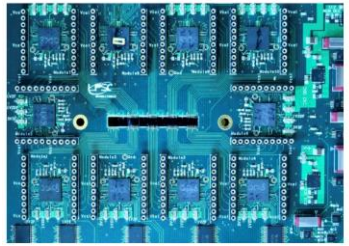
Dose monitoring for FLASH beam is a hot topic: UHDPulse (2019-2023) European project from metrological labs dedicated to FLASH detector development to support the FLASH clinical transfer challenge

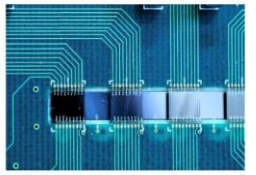
EMPIR EURAMET
The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

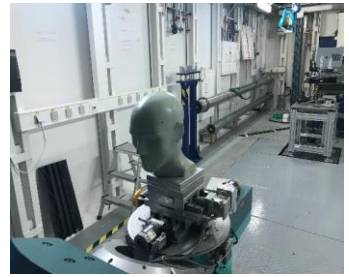
Diamond detector for MRT

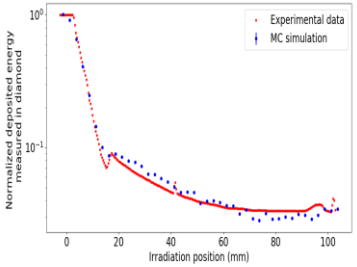
LPSC GRENOBLE | MODANE

MRT is progressing toward clinical application. At **ESRF synchrotron**, a veterinary trial has started, very promising for resistant/diffuse tumors.
→ LPSC developed a stripped diamond detector to monitor the irradiation.









→Transfer on Australian synchrotron and other compact sources.

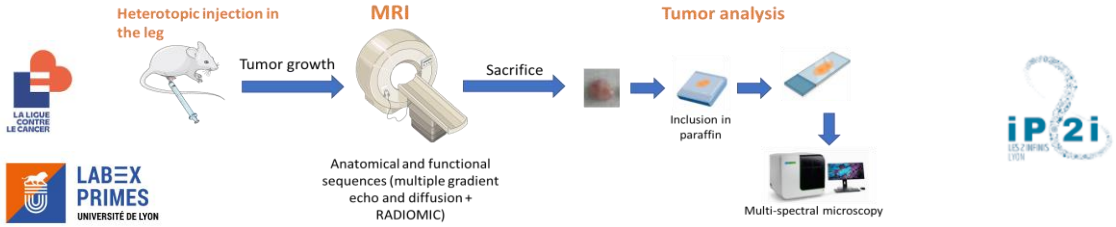
Radiobiology & Patient based models

Permanent IN2P3
FTE ~

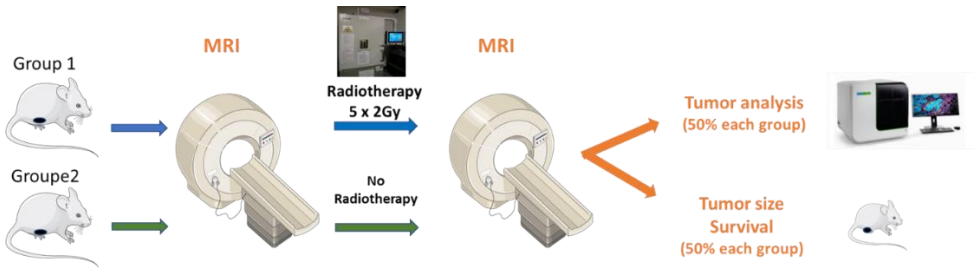
2020 – 2025 highlights:

Correlation of RADiomic and RADiobiological parameters to predict tumor response of oral cavity and oropharyngeal cancers to RADiotherapy

Validation of the mouse model, calibration of MRI images and tumor sections

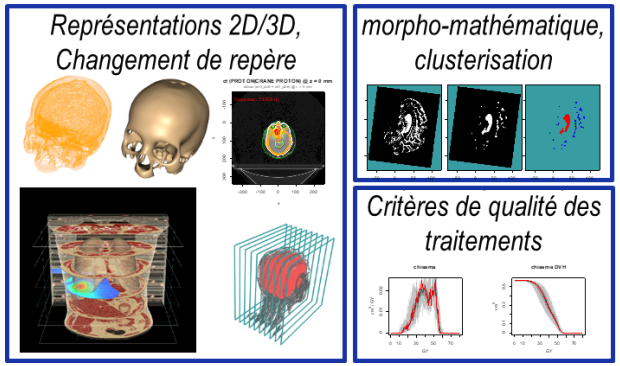


Correlation of radiobiological datas and radiomics parameters

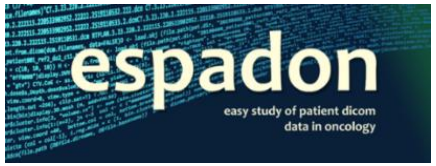


	2025	2026	2027	2028	2029
Pré-clinical model: Mouse model and acquisition of biological datas and radiomics					
Correlation of biological and MRI datas					
Validation of pre-clinical parameters on human tumoral samples					
Clinical validation of the parameters					

Numerical tool developments for patient-based modeling (PMRT program), analysis and treatment choice

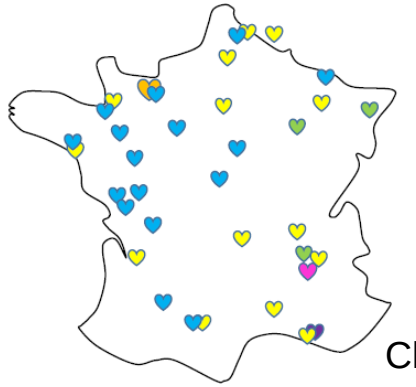


librairie logicielle R



https://CRAN.R-project.org/package=espadon
Information sur https://espadon.cnrs.fr
~350 ⬇/mois en 2024

Spécification du Parcours Médical (SPaM)



Study of comparative toxicity with Xrays or proton treatments at CLCC Baclesse

Clinical collaborations

Summary – FLASH MP perspective (in construction)

WP1 - Contrôle qualité et dosimétrie des lignes faisceaux UHDR H^+, He^{2+} , C, e^-, RX (Resp: Charbel Koumeir, Ziad El Bitar)

- TASK 1 – Contrôle de la structure temporelle du faisceau
- TASK 2 - Développement instrumental spécifique UHDR
- TASK 3 - Protocole dosimétrique ions et validation
- TASK 4 – Protocole dosimétrique électrons et validation

WP2 – Effet du débit de dose sur la radiolyse de l'eau expérimentale (Resp: Quentin Raffy, Guillaume Blain)

- TASK 1 – Effet du débit de dose en fonction du TEL
- TASK 2 – Effet de la structure temporelle des faisceaux
- TASK 3 – Influence du pH et de O_2
- TASK 4 – Radiolyse de biomolécules

WP3 - Irradiations de populations cellulaires (Resp: François Chevalier, Claire Rodriguez-Lafrasse)

- TASK 1 – Effet du débit de dose en fonction du TEL
- TASK 2 – Effet de la structure temporelle des faisceaux
- TASK 3 – Influence du pH et de l'O_2

WP4 – Jumeaux numériques multi-échelles (Resp: Lydia Maigne, Nicolas Arbor)

- TASK 1 – Simulations des lignes/faisceaux d'irradiation avec GATE 10
- TASK 2 – Simulations de la chimie de la radiolyse avec Geant4-DNA
- TASK 3 – Simulations des dommages biologiques (modèles biophysiques)
- TASK 4 – Création d'une base de données ouverte

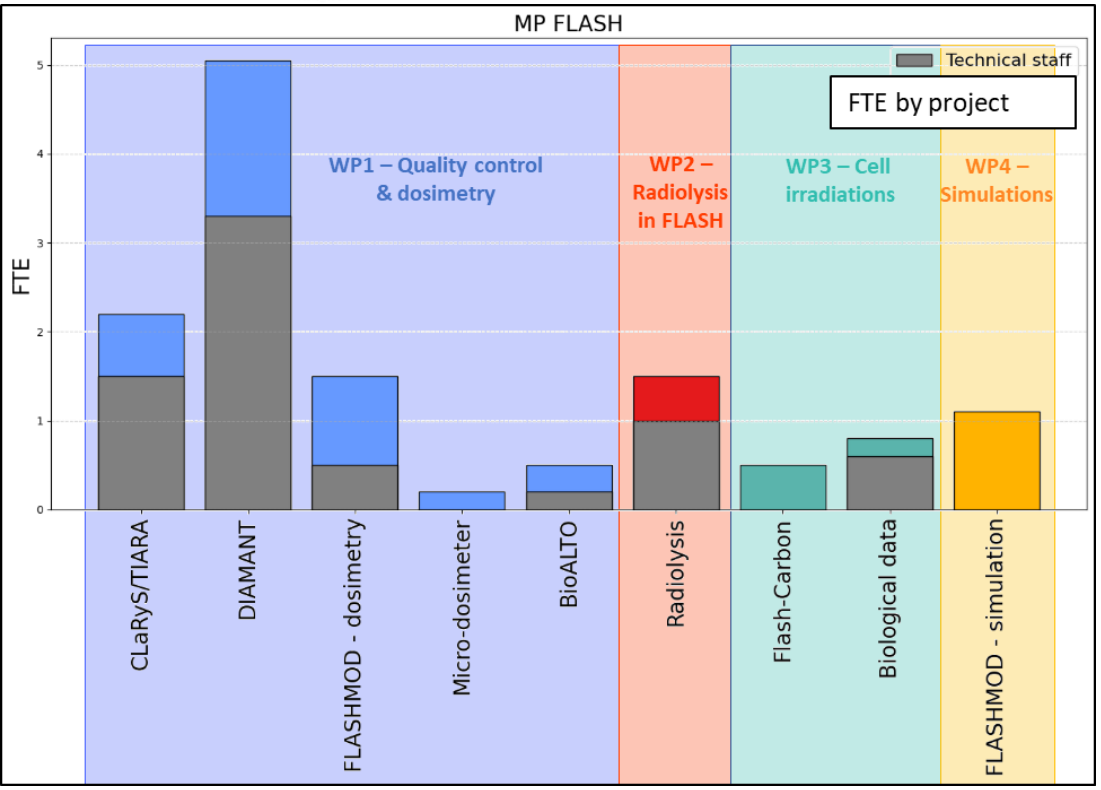
Summary – FLASH MP perspective (in construction)

WP1 – Quality control & dosimetry

WP2 – Radiolysis in FLASH

WP2 – Cell irradiations

WP3 – Simulations



Total FTE – in2p3:
- 6.25 researchers,
- 7.2 technical staff
- 10 PhD defended
  7 PhD ongoing
- 5 CDD researchers
- 1,5 CDD techn. staff

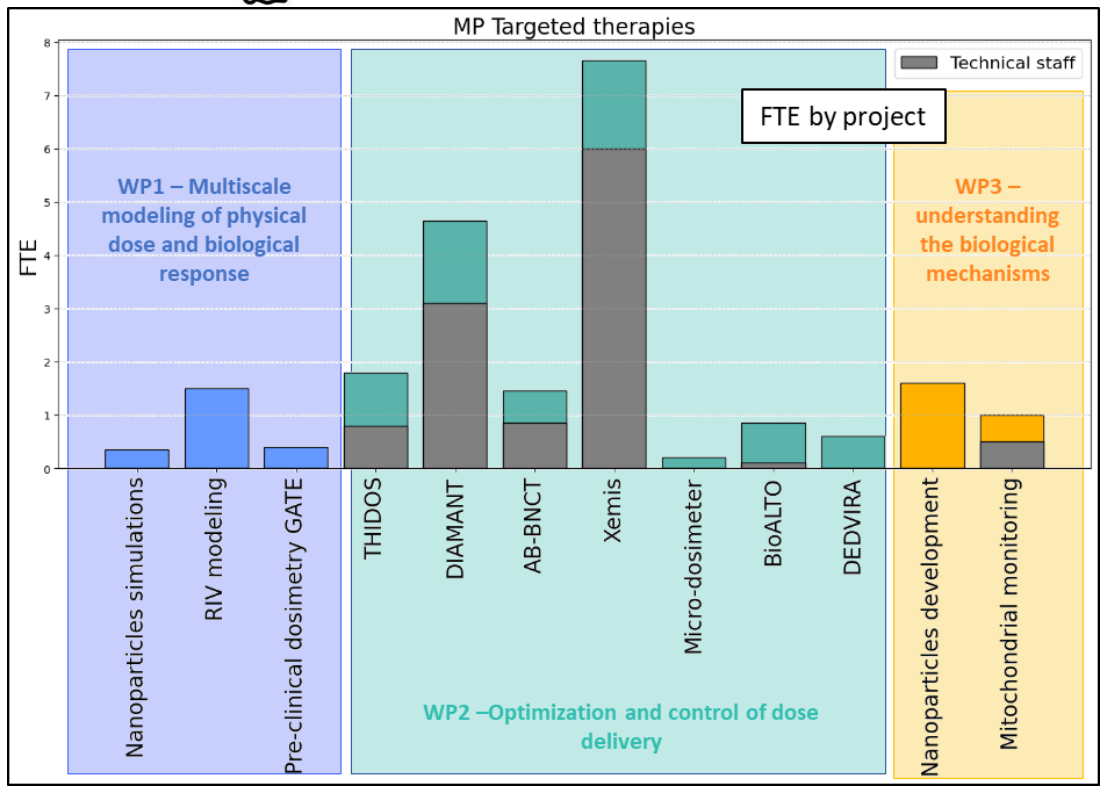
Total articles: 40

Total funds:
- 185 K€ in2p3,
- 818 K€ non-in2p3

Scientific Objectives of the MP :

Better understand the fundamental mechanisms in FLASH by studying the FLASH phenomenon
- on different types of beams (ions and e-)
- Combine UHDR and TEL / pH / biological model
  → **Multidisciplinary approach**
- Dosimetry and implementation of UHDR ion beams
- Understanding chemical mechanisms
- Understanding biological mechanisms
- Developing innovative predictive digital twins

Summary – Targeted RT MP perspective (in construction)



WP1 – Multiscale modeling of physical dose and biological response

Task 1.1: Modeling at the subcellular, cellular, and multicellular scales *(2D and 3D)*

Task 1.2: Preclinical and clinical modeling *(in vivo, patient)*

WP2 – Optimization and control of dose delivery

Task 2.1: Optimization and characterization of neutron fields in BNCT
Task 2.2: Dose delivery control in in vitro and preclinical radiobiology
Task 2.3: Clinical dose delivery control in internal radiotherapy *(personalized dosimetry)*

WP3 – understanding the biological mechanisms

Task 3.1: Studies of subcellular *(nucleus, mitochondria, membrane…)*, cellular, and multicellular *(immunogenic…)* responses

Task 3.2: Vector (or NP) /irradiation combination studies

Total FTE – in2p3:
- **10.3** researchers,
- **11.4** technical staff
- **12** PhD defended
- **4** PhD ongoing
- **6** CDD

Total articles: 25

Total funds:
- **162 k€** in2p3,
- **1.44 M€** non-in2p3

Scientific Objectives of the MP :

Optimize therapeutic efficacy, improve personalized dosimetry

1. Optimize dose delivery and radiation control
2. Determine the physical dose delivered and predict a biological response to treatment.
3. Understand the mechanisms involved in therapeutic efficacy and how to quantify them

Necessary multidisciplinary collaborations (physical, biological, chemical and clinical)

Summary – Radionuclide MP perspective (in construction)

WP1 – High-LET particles

Optimizing the therapeutic use of alpha and Auger emitters.

WP2 – Theranostic approaches

Designing effective theranostic pairs. →Lanthanides, transition metals, biological and chemical compatibility

WP3 – Innovative radionuclide production

Exploring laser-plasma acceleration and mass separation

WP4 – Separation and formulation chemistry

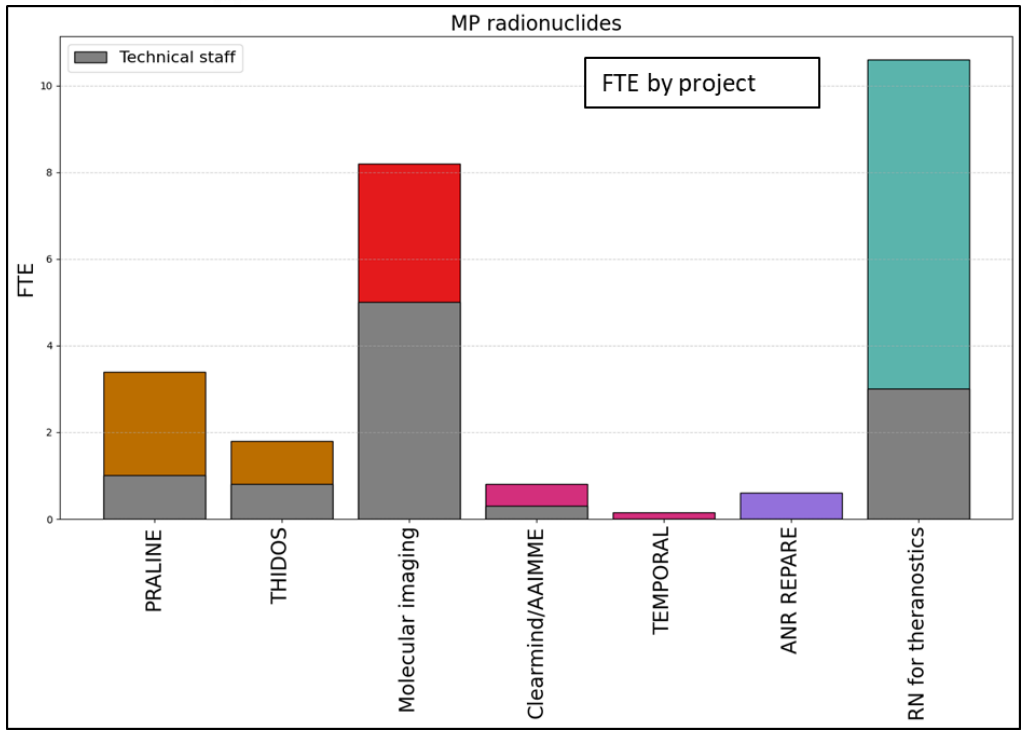
Developing rapid and selective chemical processes

WP5 – Vectorization, radiolabeling

Efficiently coupling radionuclides and biological vectors

WP6 – Imaging & Dosimetry

Evaluating the spatiotemporal distribution of radiopharmaceuticals



Total FTE – in2p3:

- **15.5** researchers,
- **10.1** technical staff
- **13** PhD defended
  +**11** PhD ongoing
- **5.2** CDD

Total articles: 69

Total funds:

- 152 kEuros in2p3,
- 1.3 MEuros non-in2p3

Scientific Objectives of the MP Project:

1. Innovate in the production of radionuclides
2. Master chemical and biological transformation
3. Evaluate, visualize, and optimize clinical efficacy

Conclusion

GDR Groupement de recherche MI2B Outils et méthodes nucléaires pour la lutte contre le cancer

- Highly dynamic activity in the very interdisciplinary field of “innovative therapies” :
  - Some **fundamental researches** : understanding/modeling biological or chemical effects, technological breakthrough in instrumentation, cross section measurements…
  - Others **pushed up to clinics / valorization** → importance of large variety of profiles and projects. Offer flexibility

- Significant number of peer-reviewed publications and successful calls for proposals attest to the relevance of the research conducted.

- Structuration:
  - **Strong local collab** with numerous INSERM/clinical and other academic partners (Labex…)
  - **National** with consolidated intra-in2p3 and inter-institute (INSERM, ASNR, CNRS, CEA…) collab, notably thanks to the **MI2B GdR**, MITI programs, “IN2P3” platform activities, scientific networks (FLI, PRISMA…) and **project call opportunities**.
  - **International** through important scientific and technical collabs (e.g. Radionuclide PRISMAP, BNCT, CNAO, major role within the GATE and Geant4DNA collaborations…)

- Next 4 (?) in2p3 MP construction to come in fall 2025…

NUCLÉAIRE & PARTICULES

Thank you

Rachel DELORME on behalf of the community

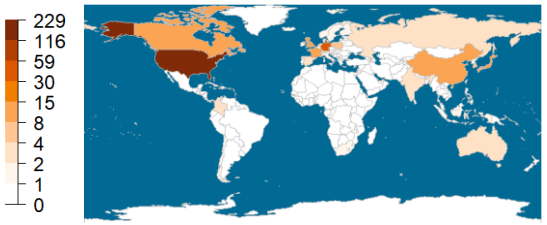
Appendix

C. & J.M. Fontbonne

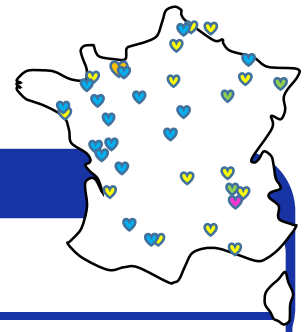
LPC CAEN

espadon
easy study of patient dicom data in oncology

https://CRAN.R-project.org/package=espadon
Information sur https://espadon.cnrs.fr



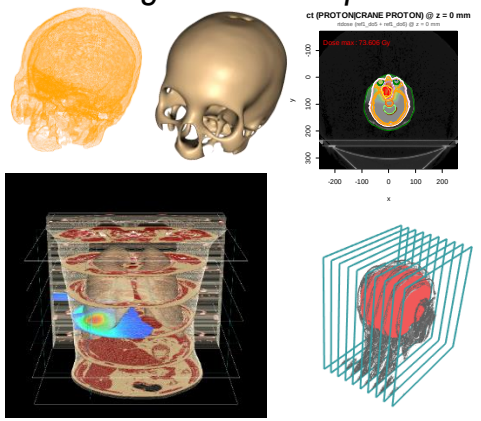
~350 ⭳/mois en 2024



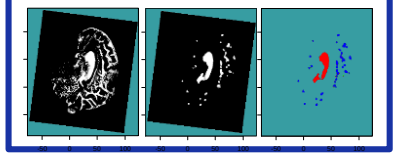
librairie logicielle R

- lecture fichiers DICOM
- pseudonymisation
- contrôle qualité : représentation 2D-3D, lien entre les données
- calcul de métriques usuelles + nouvelles
- automatisation des analyses et des études cliniques
- exploration

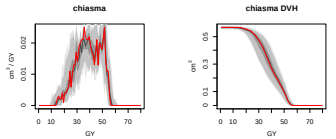
Représentations 2D/3D, Changement de repère



morpho-mathématique, clusterisation



Critères de qualité des traitements



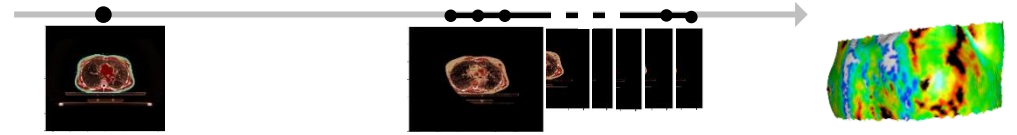
Collaborations

Centre François Baclesse — CHU Caen Normandie — unicancer Normandie-Caen

Thèse de Nathan Azémar

ICANS — GHMF — utt Université de Technologie Troyes

Etude des corrélations dose / dermites radiques & œdèmes.

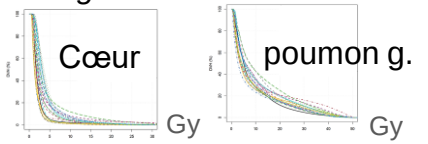


scanner initial *scanners de repositionnement….*

ARPHYCO — Institut de Cancérologie de l'Ouest — unicancer Pays de la Loire

Comparaison multicentrique d'un traitement du cancer du sein

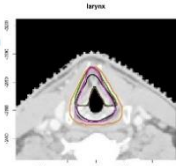
Histogrammes dose - volume



GORTEC — Groupe d'Oncologie Radiothérapie Tête et Cou

Comparaison des délinéations automatiques des OAR TPS / délinéations manuelles de référence.

SIEMENS Healthineers — RayStation — RAD formation — MVISION — THERAPANACEA — Limbus AI



Institut du Cancer Sainte Catherine Avignon-Provence

Comparaison des CT et synthetic CT (←IRM), + conséquence sur la dosimétrie.

GHMF Groupe Hospitalier Mutualiste de Grenoble

Développement d'outils pour le calcul de la dosimétrie en cas de ré-irradiations (cancer secondaire).

Spécification du Parcours Médical (SPaM)

J.Hommet, D.Cussol

- **Formalisme permettant la spécification des pratiques médicales et la description des parcours médicaux.**
- Implantation en langage ADA
- **Utilisations de SpaM**
  - Etude des toxicités **comparées de traitements avec des RX et des protons** au CLCC Baclesse
    - ***PREFERANCE*** (J.Balosso) : Irradation des tumeurs de l'encéphale
    - ***PIOTOX*** (J.Thariat, J.M.Fontbonne, N.Azémar) : toxicités oculaires
    - ***MOPROS*** (C.Laurent, A.Corroyer-Dulmont) : toxicités cutanées
  - Utilisation d'**ESPADON** (C.Fontbonne, J.M.Fontbonne, N.Azémar) pour la lecture et la manipulation des images

➔ **Présentation Thao PHAM à 11h30**

Exemple de spécification d'un parcours médical

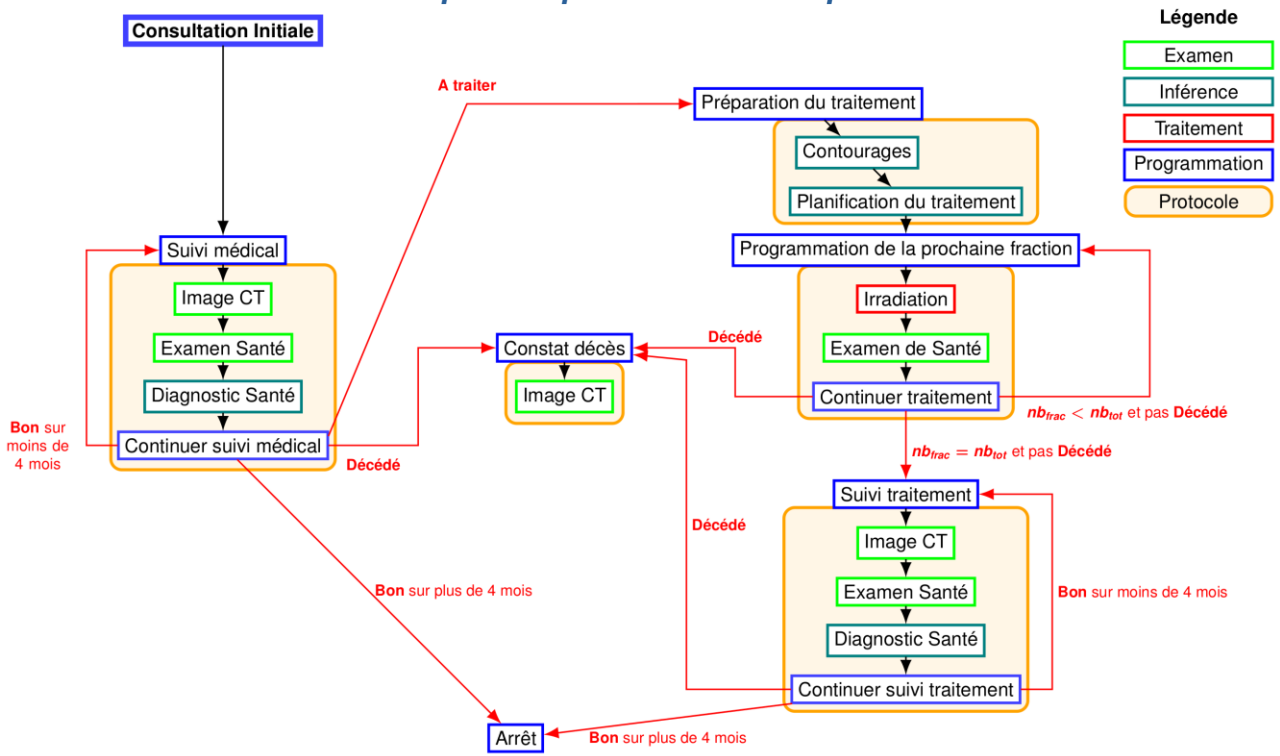
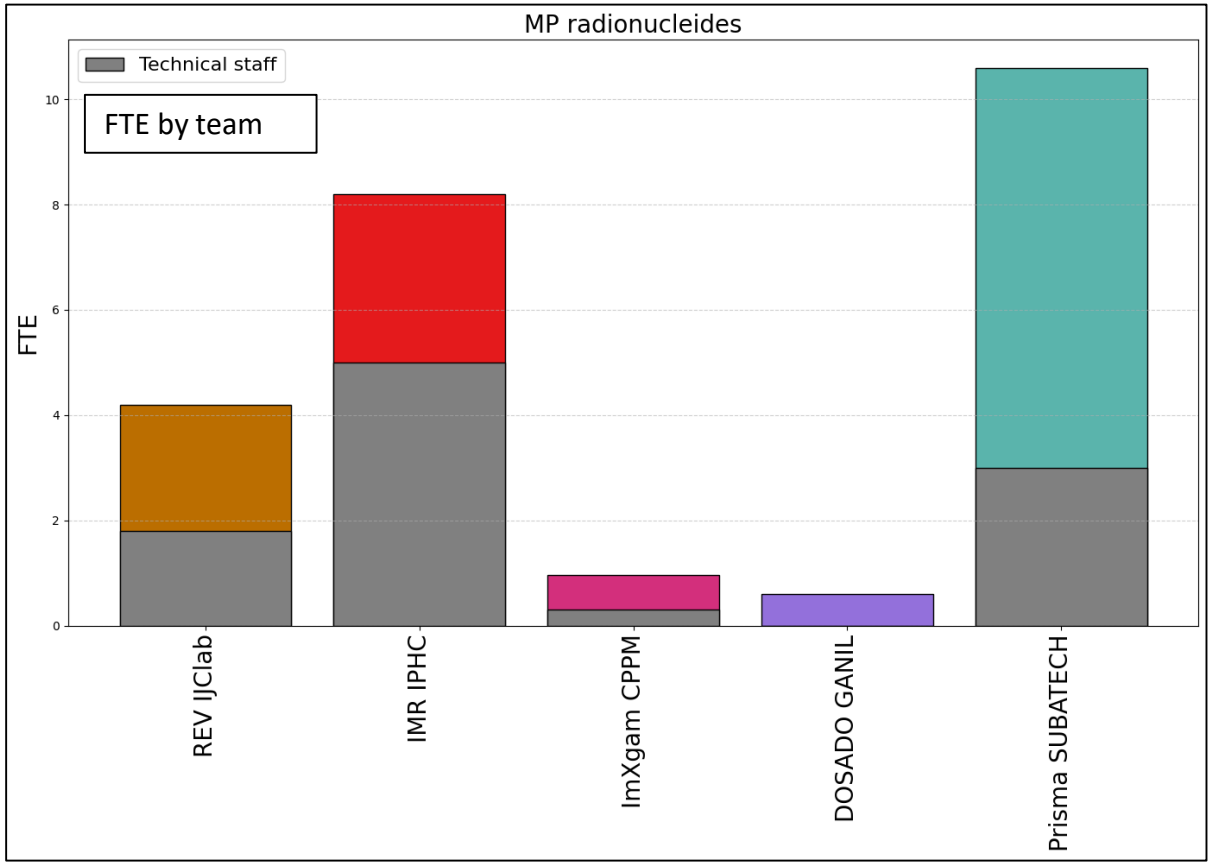


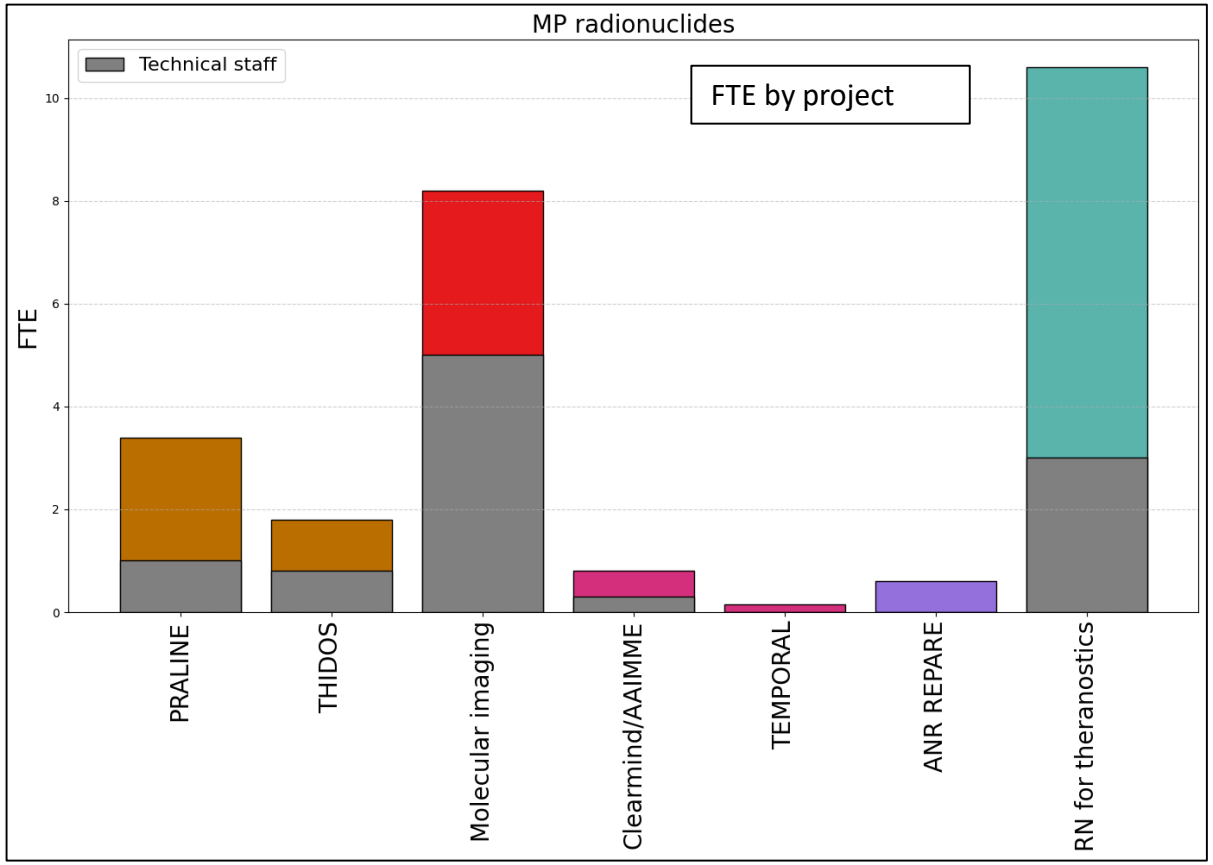
Tableau Comparatif des NTCPs

ROI/NTCP	RX Dosimetry	Proton Dosimetry
Brain		
Mental Disorder	0.01 % (1.09643E-04)	0.02 % (2.35200E-04)
Mental Trouble	23.43 % (2.34299E-01)	37.17 % (3.71662E-01)
Necrosis/Infarction	0.00 % (1.19209E-07)	0.00 % (1.78814E-07)
Chiasma		
Altered view	35.55 % (3.55547E-01)	60.20 % (6.02040E-01)
Blindness	0.71 % (7.05943E-03)	2.18 % (2.17566E-02)
Eye L		
Altered view	1.71 % (1.71446E-02)	0.55 % (5.48735E-03)
Blindness	0.10 % (1.01840E-03)	0.04 % (3.62009E-04)
Dryness	65.56 % (6.55623E-01)	35.65 % (3.56519E-01)
Eye R		
Altered view	1.81 % (1.81056E-02)	0.45 % (4.53568E-03)
Blindness	0.11 % (1.07208E-03)	0.03 % (3.06368E-04)
Dryness	67.02 % (6.70154E-01)	31.34 % (3.13374E-01)
Lens L		
Cataract requiring intervention	45.98 % (4.59847E-01)	0.68 % (6.77693E-03)
Lens R		
Cataract requiring intervention	56.35 % (5.63454E-01)	1.54 % (1.53589E-02)
Optic Nerve L		
Altered view	9.00 % (9.00496E-02)	3.28 % (3.27869E-02)
Blindness	0.09 % (8.86589E-04)	0.03 % (2.57760E-04)
Pain	62.45 % (6.24523E-01)	37.20 % (3.71984E-01)
Optic Nerve R		
Altered view	18.37 % (1.83733E-01)	11.93 % (1.19270E-01)
Blindness	0.24 % (2.38827E-03)	0.13 % (1.29005E-03)
Pain	81.11 % (8.11137E-01)	70.04 % (7.00353E-01)

Radionuclides

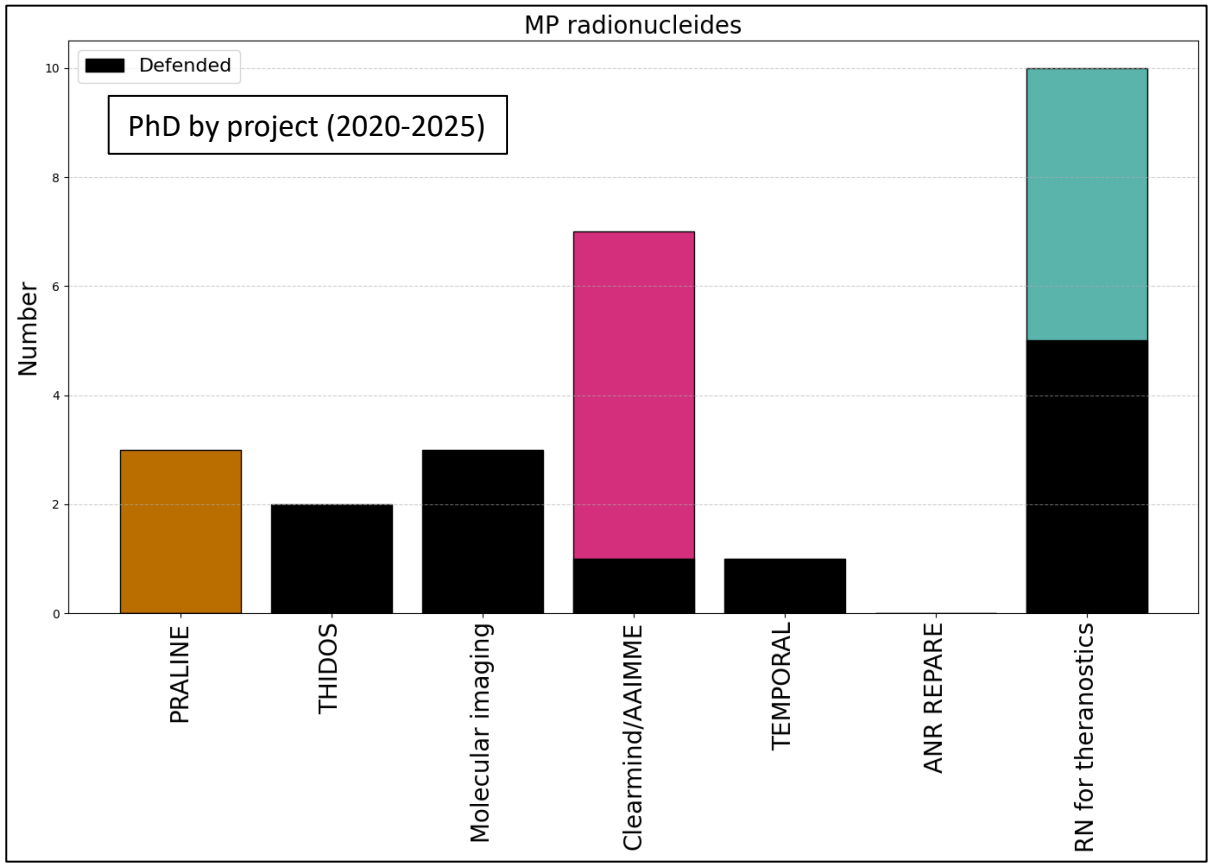
FTE in the radionucleides Master-project of **in2p3**



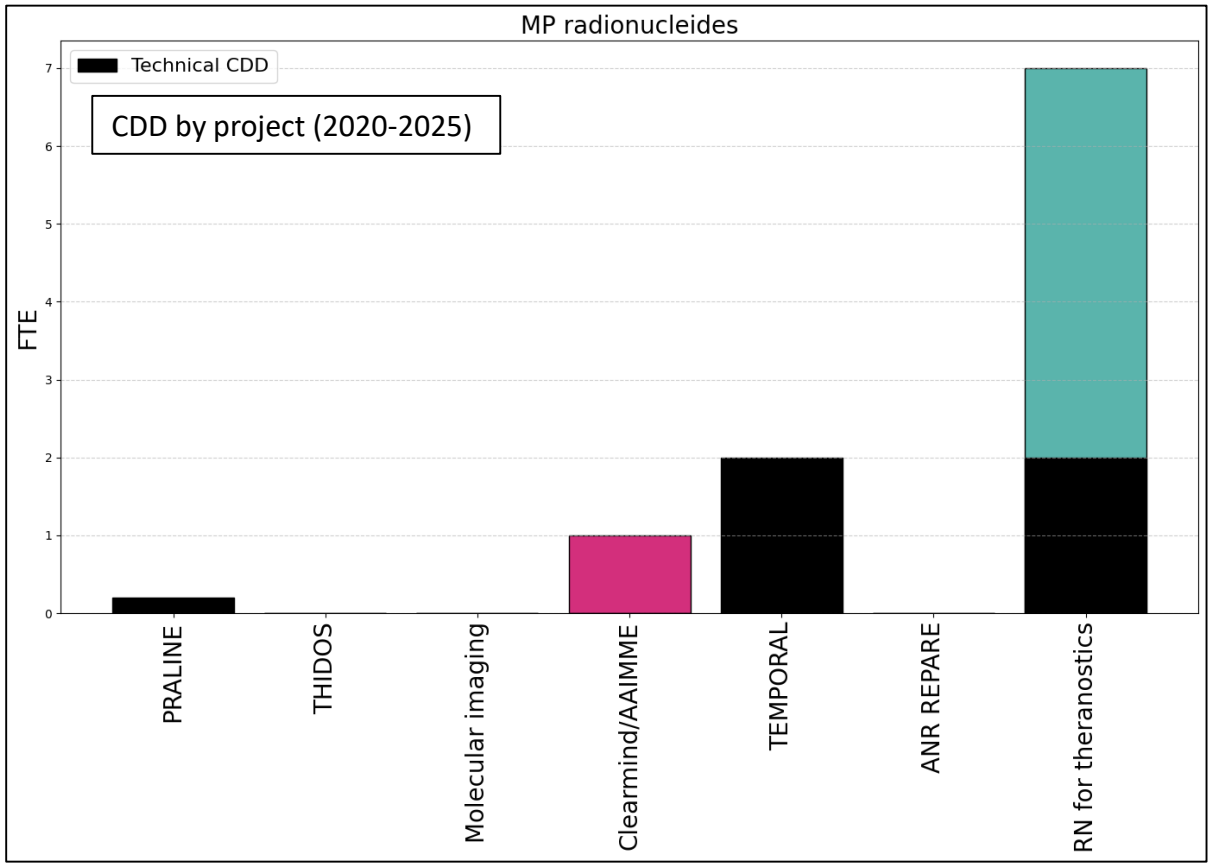


Total FTE in radionucleides MP: 15.46 researchers, 10.10 technical staff

FTE in the radionucleides Master-project of **in2p3**

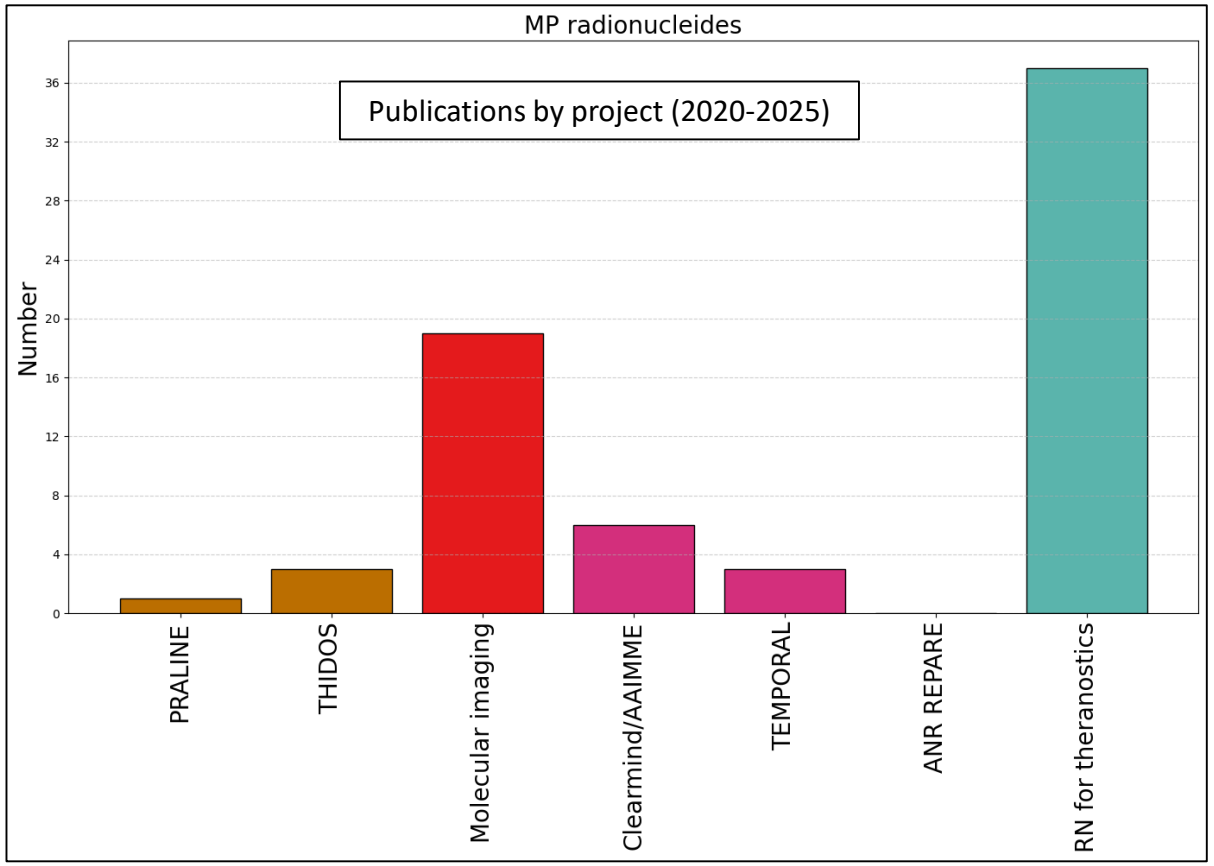


Total PhD in RN MP: 13 defended, 11 on-going

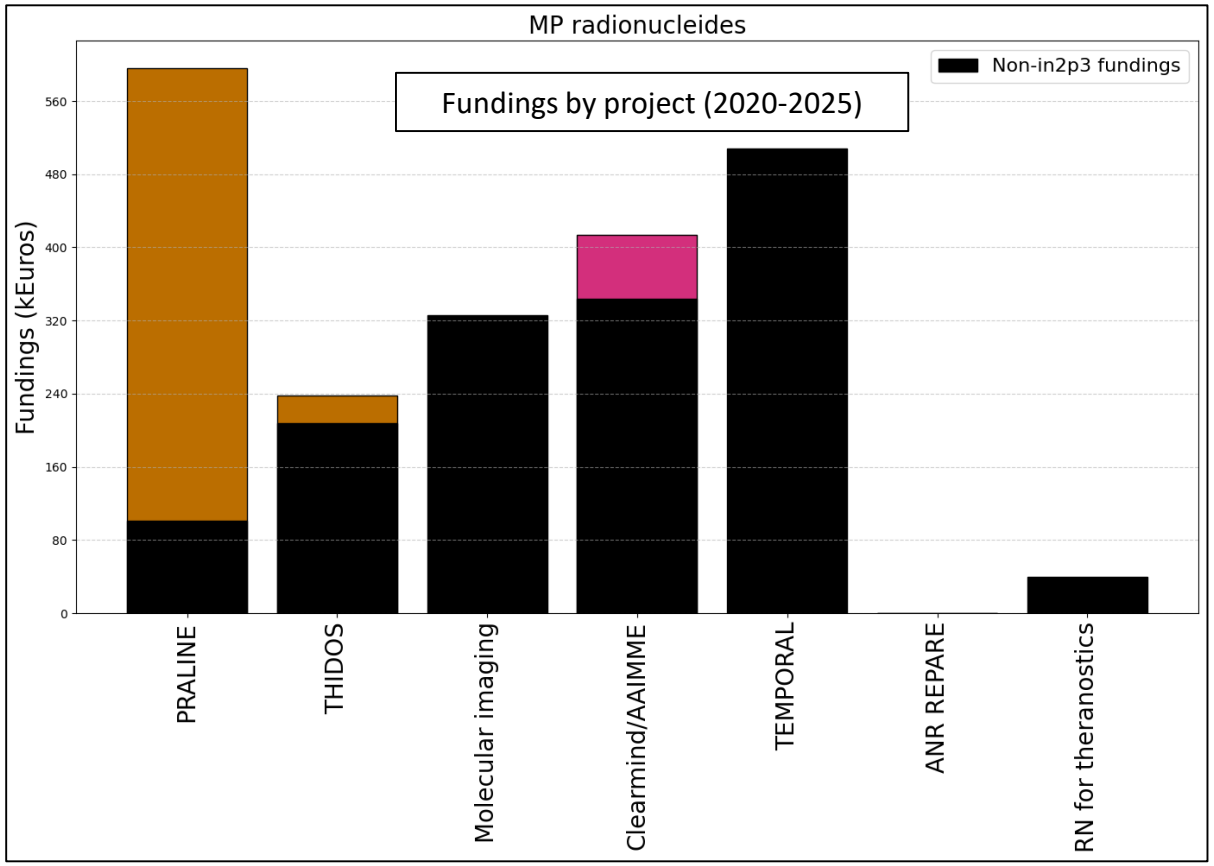


Total CDD in RN MP: 3 FTE researchers, 2.2 FTE technical staff

Publications & fundings in the radionucleides Master-project of **in2p3**

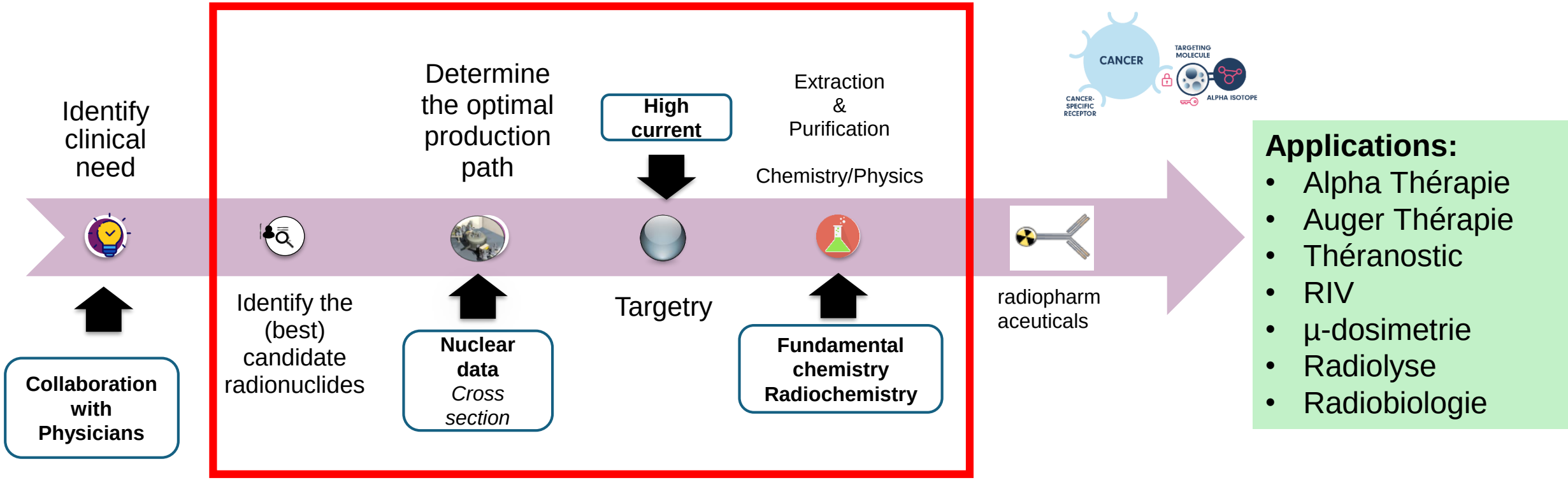


Total publications in FLASH MP: 69



Total fundings in FLASH MP: 152 kEuros in2p3, 1267 kEuros non-in2p3

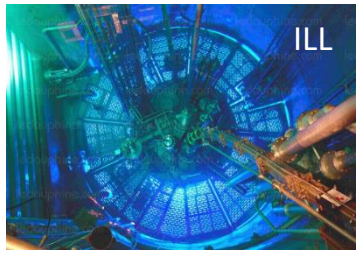
Les radionucléides sont au Cœur des activités de Médecine Nucléaire

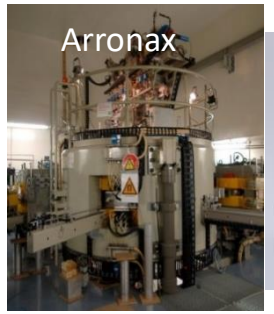


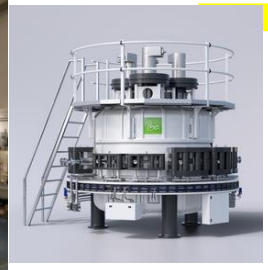
Contour de Master Projet "Radionuclides"

Radionuclide production scheme

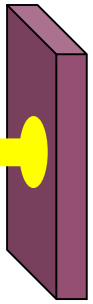
Nuclear reactor

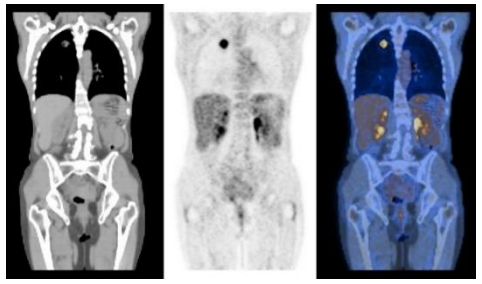






Particle accelerator





radiopharmaceutical

Extraction/
Purification

Radiolabeling

production

- Identification and evaluation of production routes
- Production cross section measurements for radionuclide of interest and contaminants
- Target preparation (thin and thick targets, enriched targets)
- High power targetry (10kW or more)

- Fundamental chemistry on radionuclides
- Dry and wet extraction and purification methods
- Impact of radiolysis on the chemistry (speciation)
- Automation

- Impact of radiolysis on radiolabelling
- Impact of radiolysis on the stability of radiolabelled molecules

For the next 5 years

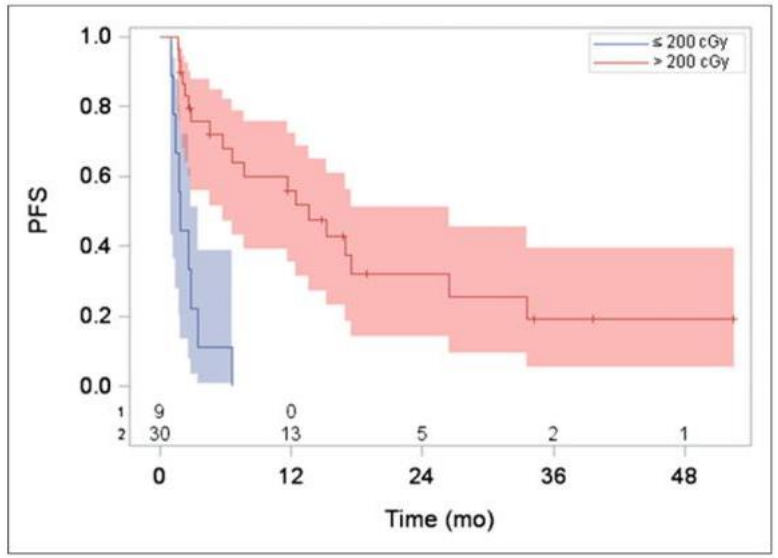
- Production routes and cross section measurements for
  - radionuclide production using deutrons and alpha particles
  - Auger emitters (^{97}Ru, ^{197m}Hg, ^{71}Ge …), lanthanides (^{155}Tb, ^{152}Tb, ^{134}La, ^{134}Ce …),
  - Theranostic imaging radionuclides (^{203}Pb, …)
- Better understanding of ^{211}At production using high power targetry
  - Internal target at Arronax
  - 10 kW targetry at GANIL
- Studies of generators
  - Development of a ^{44}Ti/^{44}Sc for PET and 3 photons imaging
  - ^{103}Ru/^{103m}Rh
  - ^{230}U/^{226}Th
- Study of radiolysis effect on radionuclides
  - Speciation of Ruthenium and Rhodium
  - Stability of ^{211}At in different solution

Dosimetry

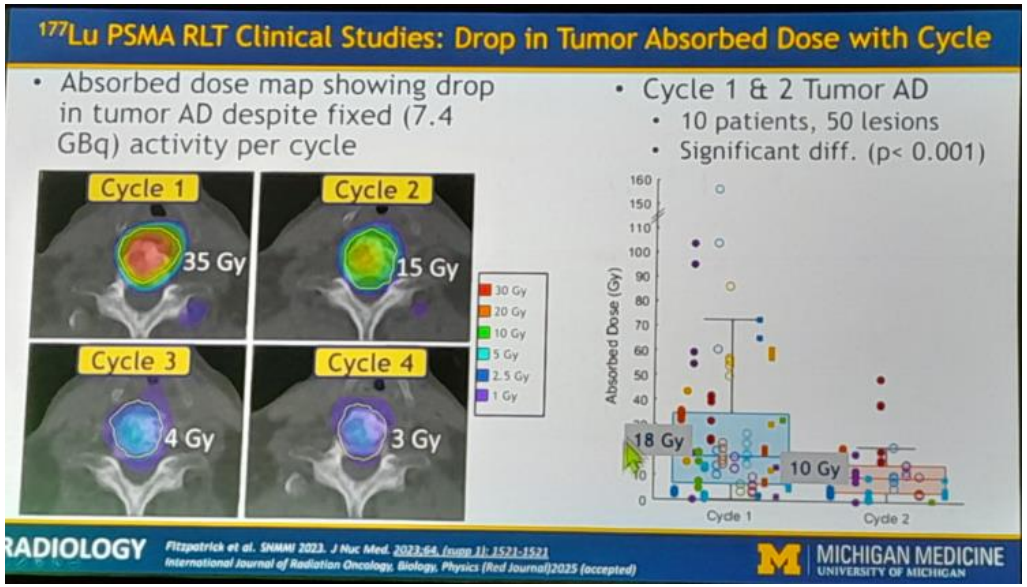
Current procedure in targeted therapies:

Despite effective palliation of tumour growth, current fixed activity is not curative

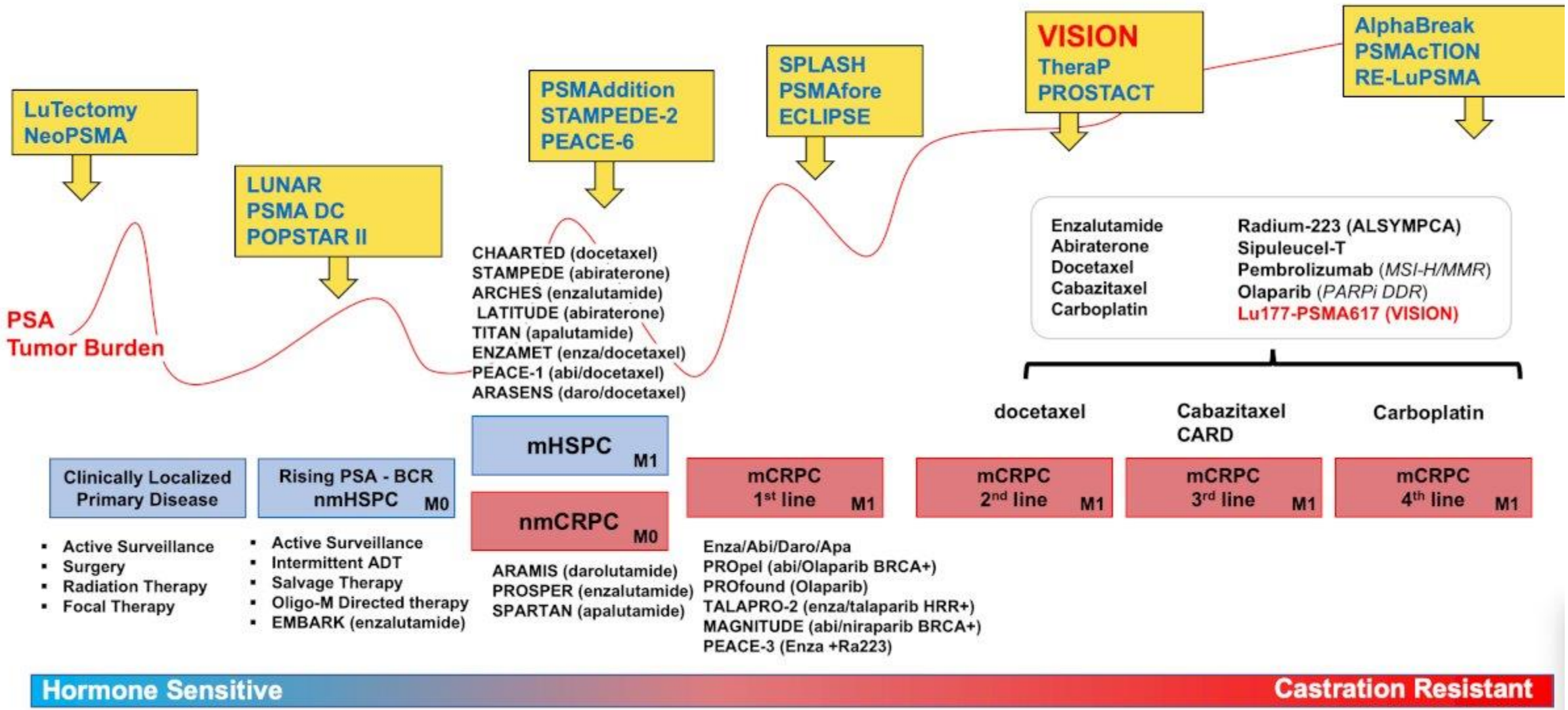
Dosimetry may guide personalization to achieve durable complete response
Dosimetry may allow to adapt activity/cycles to enhance efficacy while ensuring safety



^{131}I therapy for NHS
(Dewaraja et al, J.Nuc. MED. 2014)



Dose to the tumour is different among cycles
Dewaraja et al, SNMMI 2025

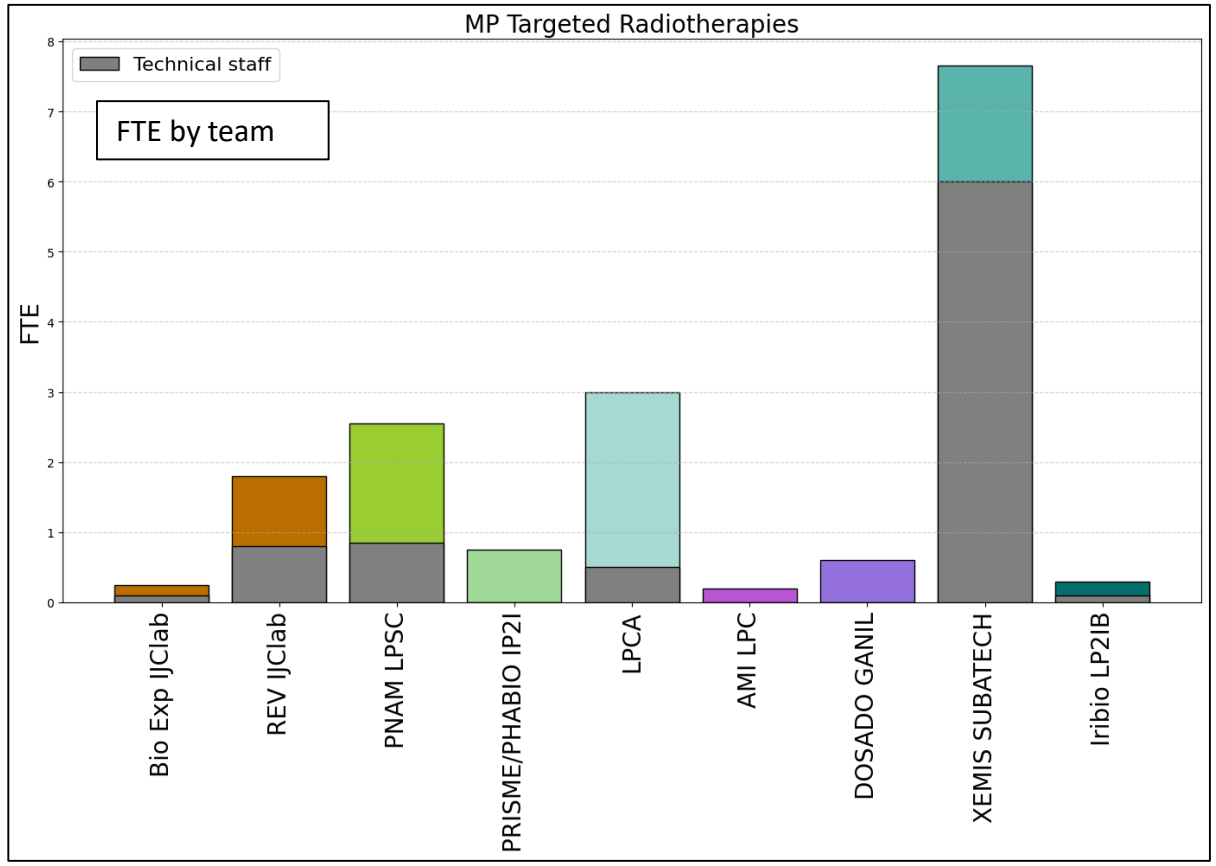

LuTectomy
NeoPSMA
LUNAR
PSMA DC
POPSTAR II
PSMAddition
STAMPEDE-2
PEACE-6
SPLASH
PSMAfore
ECLIPSE
VISION
TheraP
PROSTACT
AlphaBreak
PSMAcTION
RE-LuPSMA
PSA
Tumor Burden
CHAARTED (docetaxel)
STAMPEDE (abiraterone)
ARCHES (enzalutamide)
LATITUDE (abiraterone)
TITAN (apalutamide)
ENZAMET (enza/docetaxel)
PEACE-1 (abi/docetaxel)
ARASENS (daro/docetaxel)
Enzalutamide
Abiraterone
Docetaxel
Cabazitaxel
Carboplatin
Radium-223 (ALSYMPCA)
Sipuleucel-T
Pembrolizumab (MSI-H/MMR)
Olaparib (PARPi DDR)
Lu177-PSMA617 (VISION)
docetaxel
Cabazitaxel
CARD
Carboplatin
Clinically Localized
Primary Disease
Rising PSA - BCR
nmHSPC M0
mHSPC M1
nmCRPC M0
mCRPC
1st line M1
mCRPC
2nd line M1
mCRPC
3rd line M1
mCRPC
4th line M1
Active Surveillance
Surgery
Radiation Therapy
Focal Therapy
Active Surveillance
Intermittent ADT
Salvage Therapy
Oligo-M Directed therapy
EMBARK (enzalutamide)
ARAMIS (darolutamide)
PROSPER (enzalutamide)
SPARTAN (apalutamide)
Enza/Abi/Daro/Apa
PROpel (abi/Olaparib BRCA+)
PROfound (Olaparib)
TALAPRO-2 (enza/talaparib HRR+)
MAGNITUDE (abi/niraparib BRCA+)
PEACE-3 (Enza +Ra223)
Hormone Sensitive
Castration Resistant

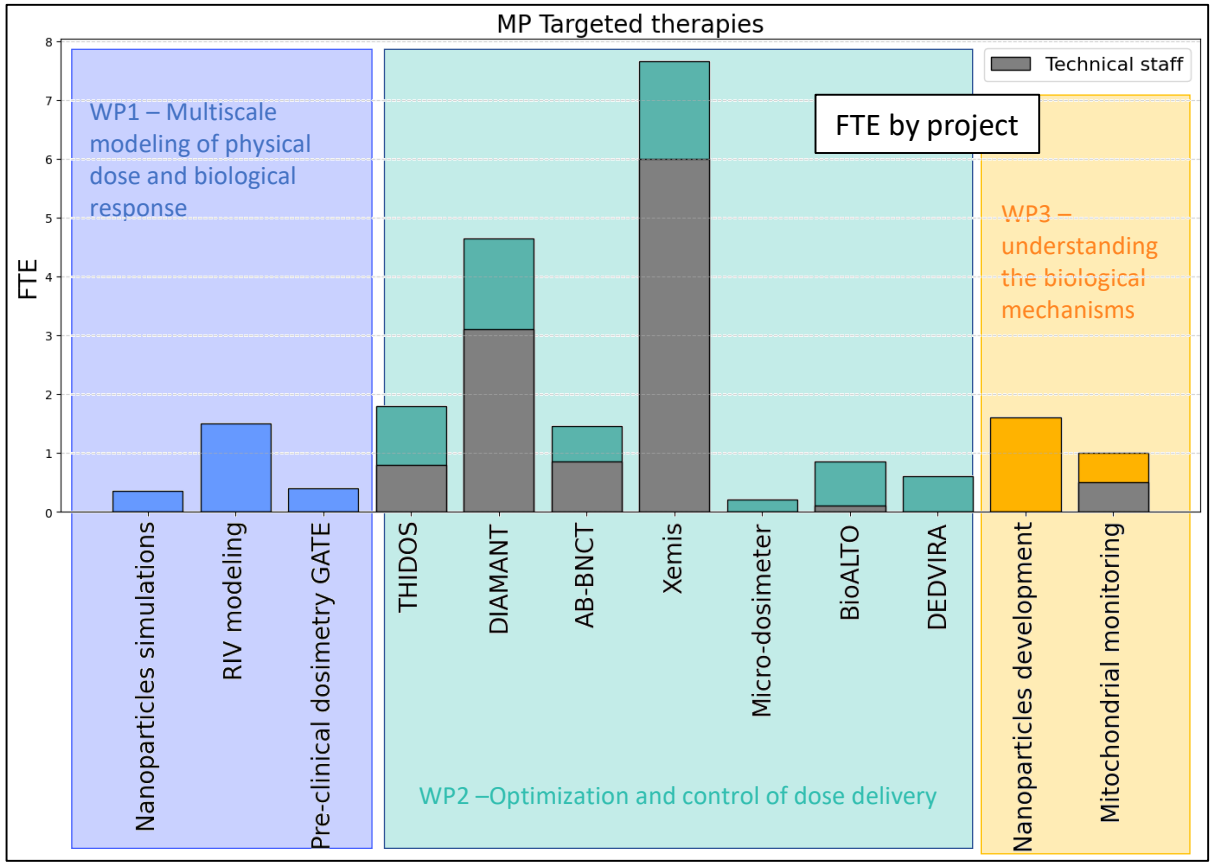
Targeted RT

TRT: main challenges in2p3 can adress

- **Innovate in the production of RN and radiopharmaceuticals(RP) to expand TRT applications:**
  - Identify and produce high-LET emitters of interest *(alpha: ^{225}Ac, ^{211}At, ^{212}Pb…, Auger: ^{111}In, ^{123}I, ^{97}Ce…)* and theranostic pairs *(e.g. $^{64}Cu/^{67}Cu$, $^{44}Sc/^{47}Sc$, $^{155}Tb/^{149}Tb(\alpha)/^{161}Tb(\beta)$…) with* optimal and alternative production routes.
  - Scale-up production addressing high-power target issues
  - Contribute in nuclear metrology (cross section measurements, model validations…)
  - Advanced extraction, separation and characterization techniques for off trace-level radionuclides
- **Understanding and optimizing vector biodistribution:**
  - Bio-chemistry: develop innovative ligands with enhanced stability and kinetics, radiolabeling strategies and radiolysis impact on it, site-specific bioconjugation
  - Dedicated in vitro and preclinical studies to characterize microscopic biodistribution of RPh
- **Developing advance imaging (PET/SPECT) to track RP and gamma cameras for personalized patient dosimetry**
- **Understand and model radiobiological mechanisms specific to TRT (especially α, Auger):**
  - Instrumental development to control/measure the delivered dose in radiobiological experiments with unsealed sources
  - Produce quantified biological data to evaluate the role of sub-cellular or multicellular structures
  - Develop multiscale methodology and modeling to evaluate TAT biological dose distribution in vivo.

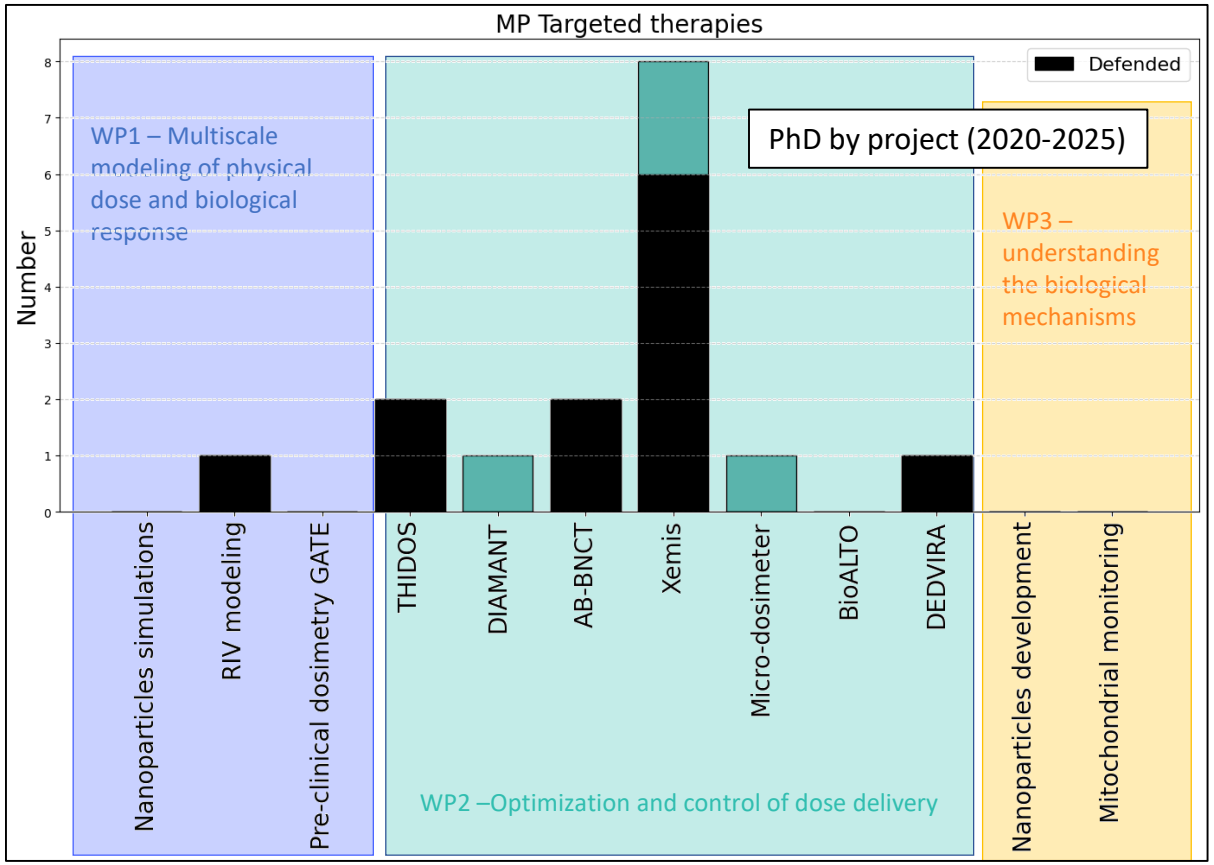
FTE in the targeted radiotherapies Master-project of **in2p3**



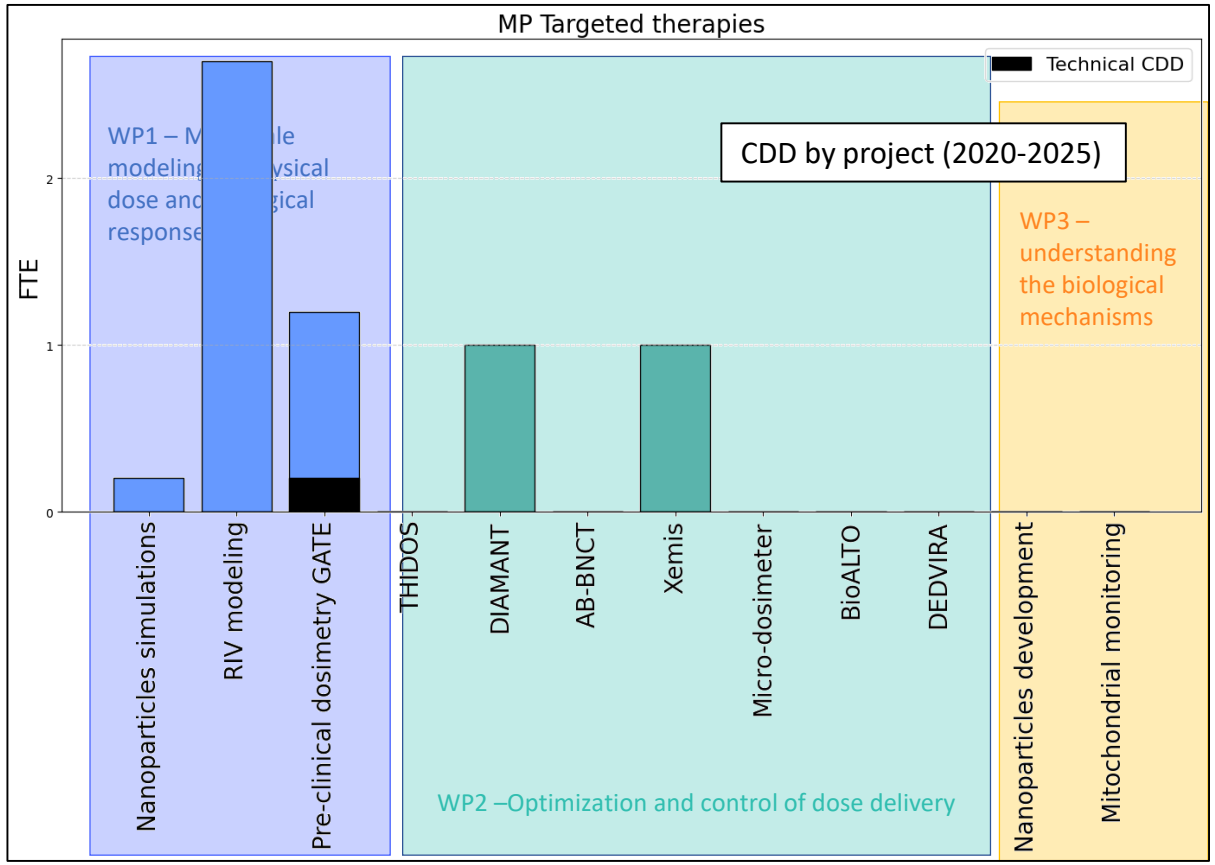


Total FTE in targeted radiotherapies MP: 10.3 researchers, 11.35 technical staff

FTE in the targeted radiotherapies Master-project of **in2p3**

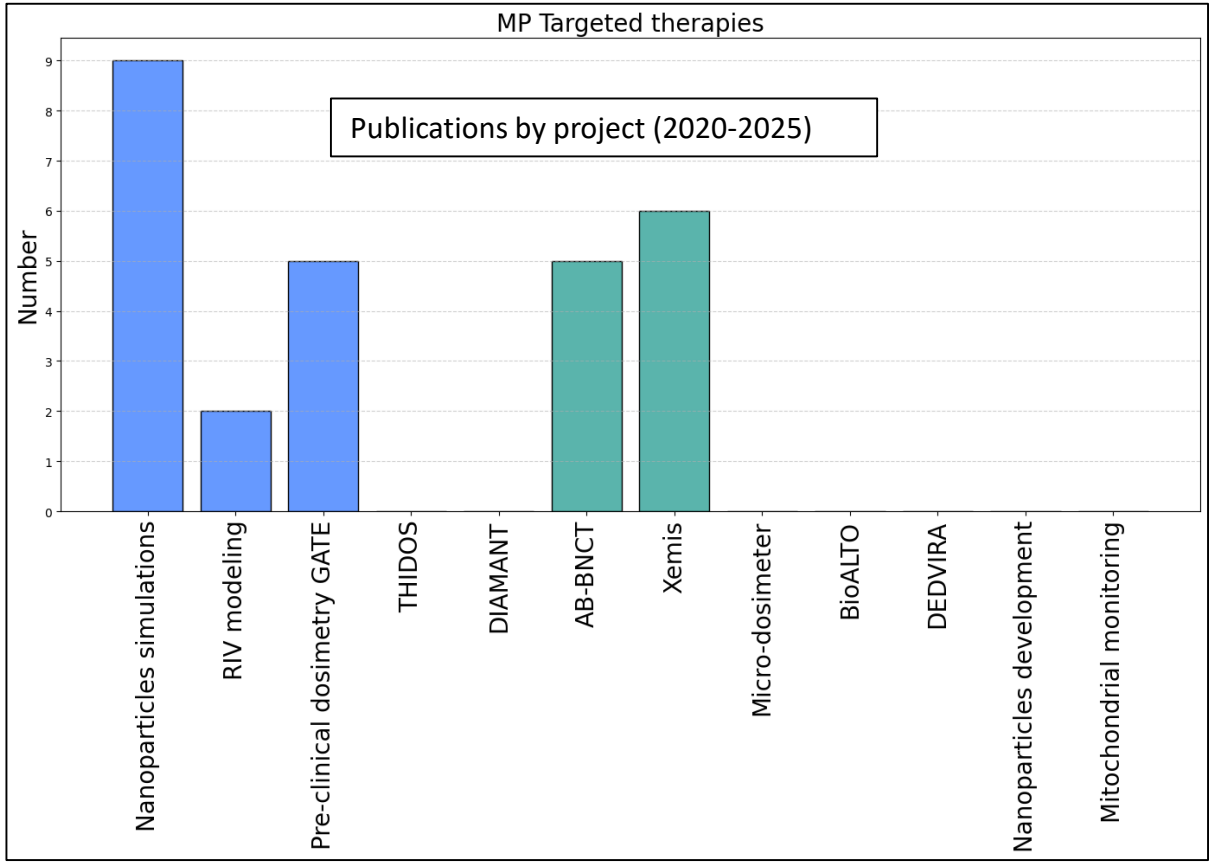


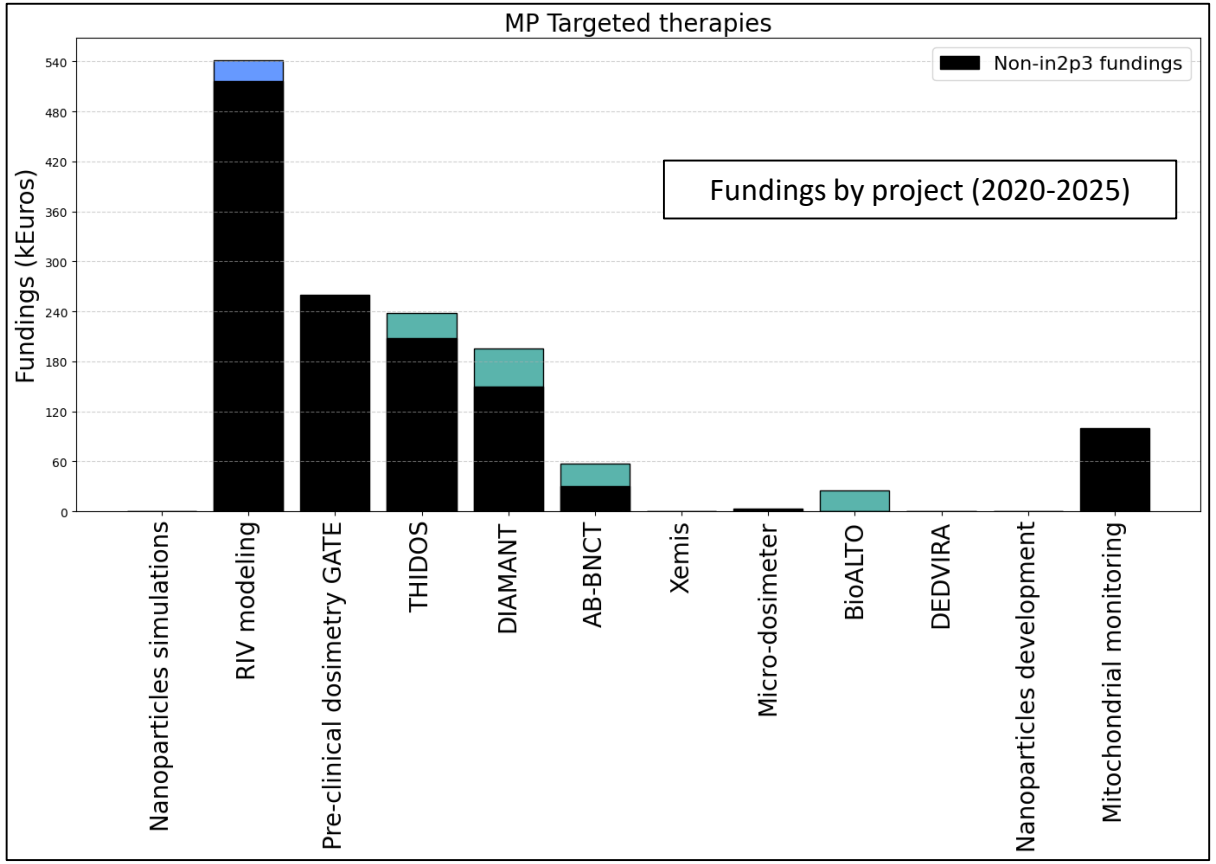
Total PhD in Targeted radiotherapies MP: 12 defended, 4 on-going



Total CDD in Targeted radiotherapies MP: 5.7 FTE researchers, 0.2 FTE technical staff

Publications & fundings in the targeted radiotherapies
Master-project of **in2p3**



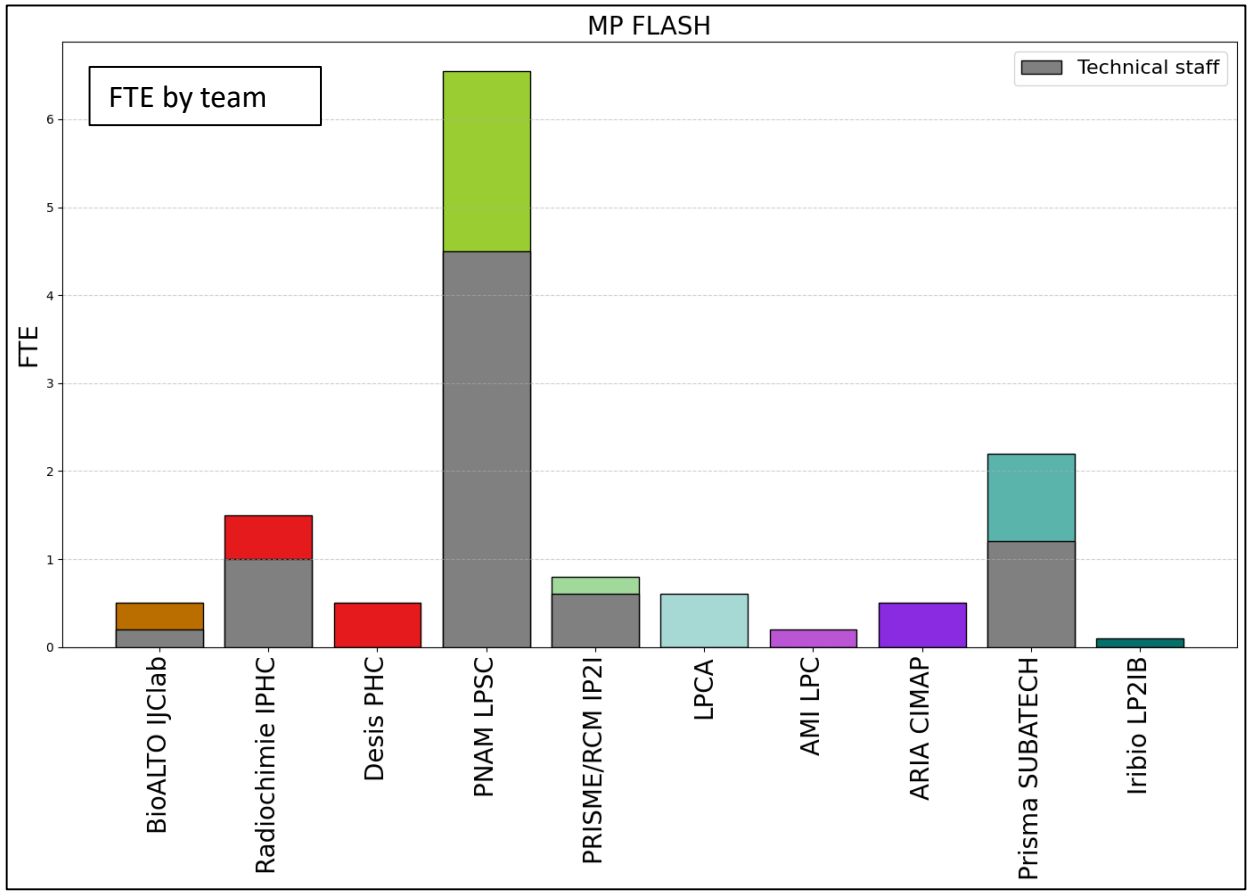


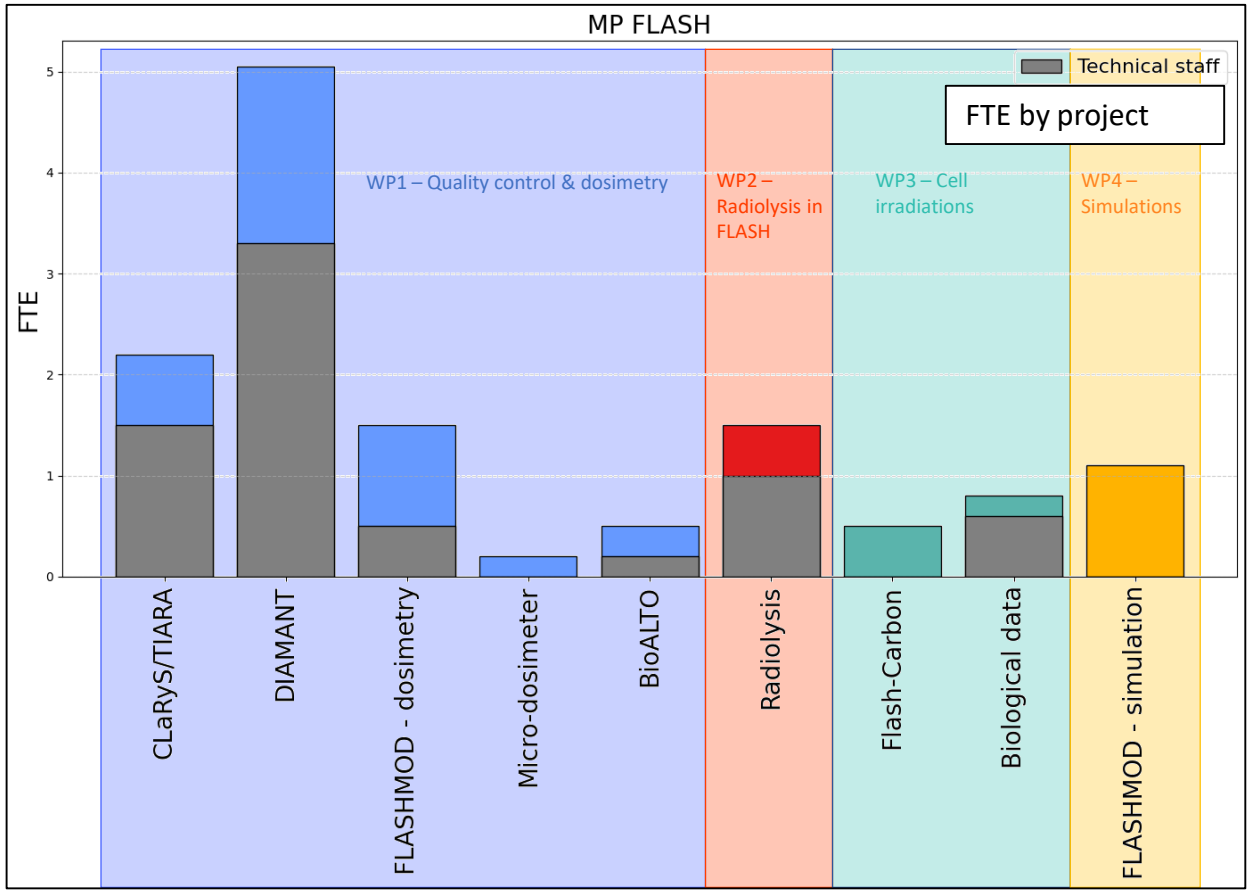
Total publications in FLASH MP: 25

Total fundings in FLASH MP: 152 kEuros in2p3, 1267 kEuros non-in2p3

FLASH/SFRT

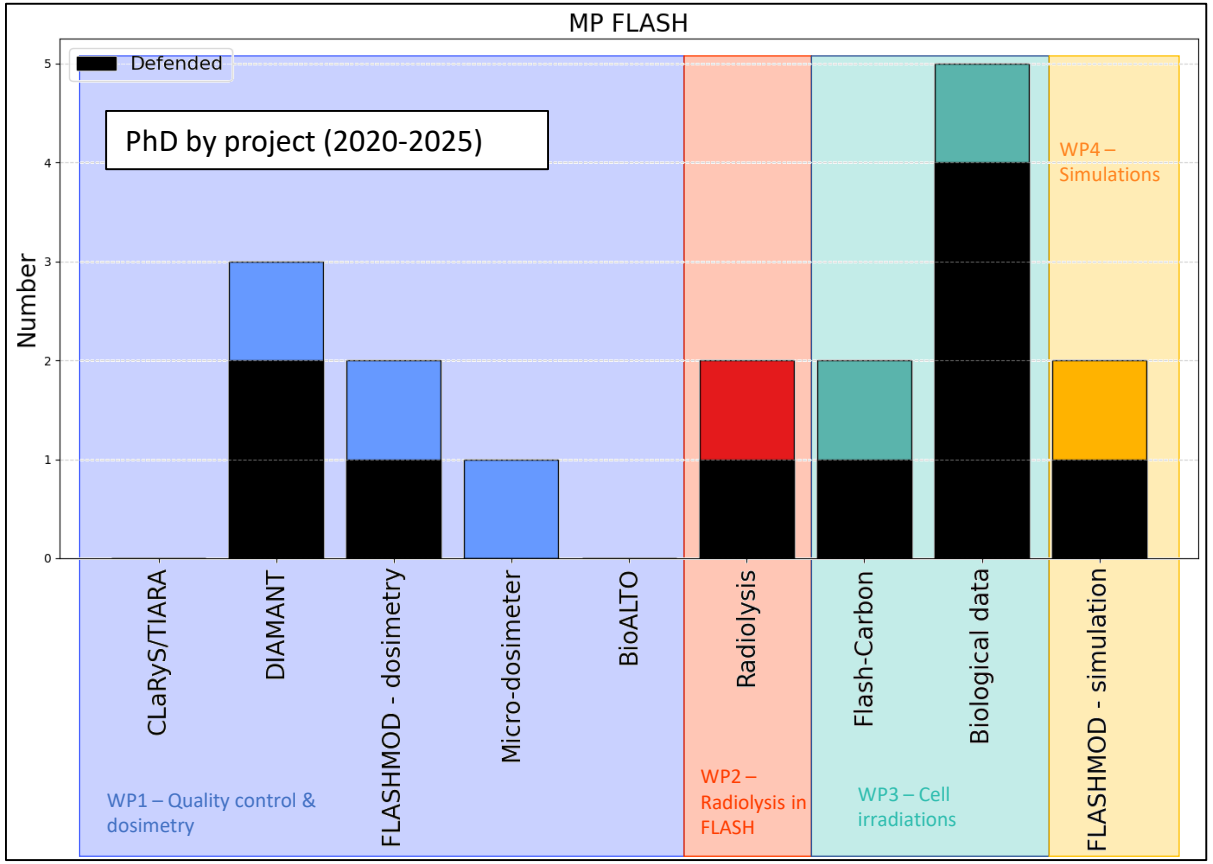
FTE in the FLASH Master-project of **in2p3**



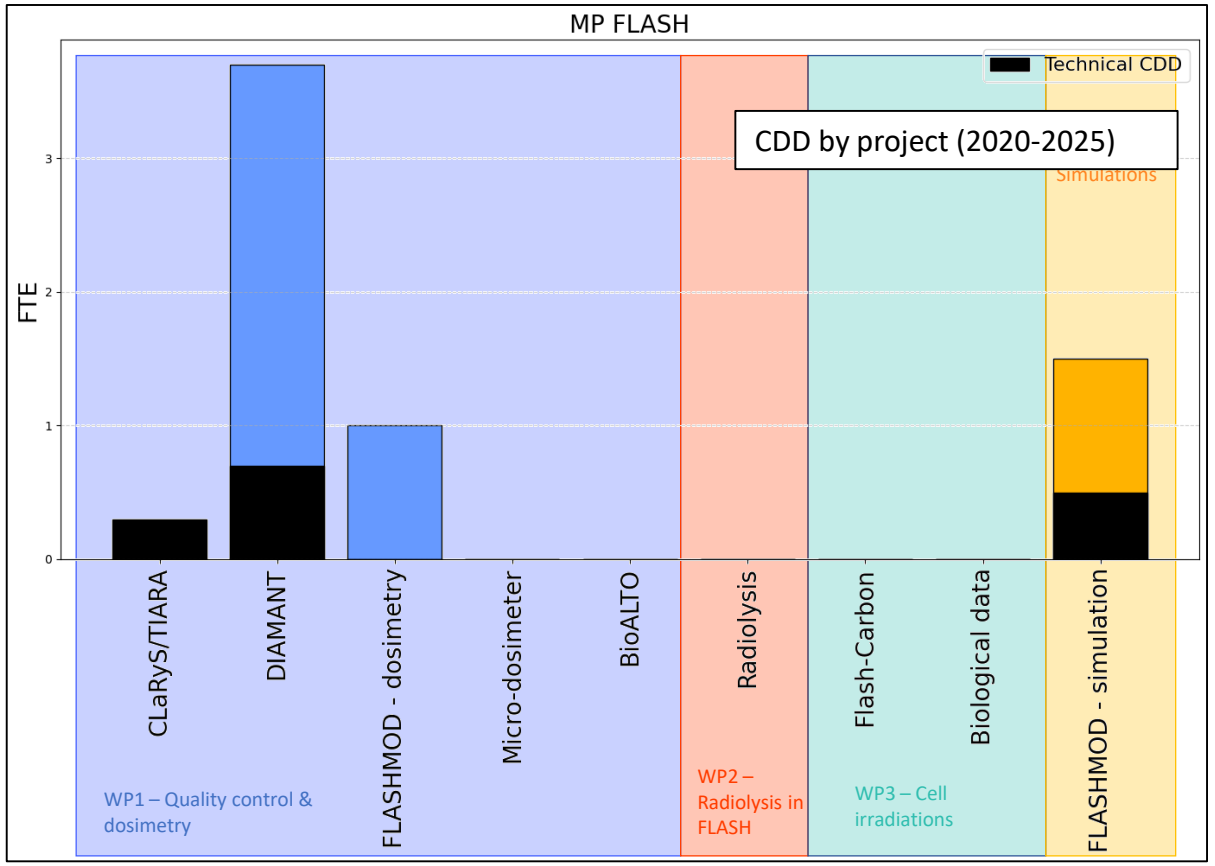


Total FTE in FLASH MP: 14.13 researchers, 19.70 technical staff

FTE in the FLASH Master-project of **in2p3**

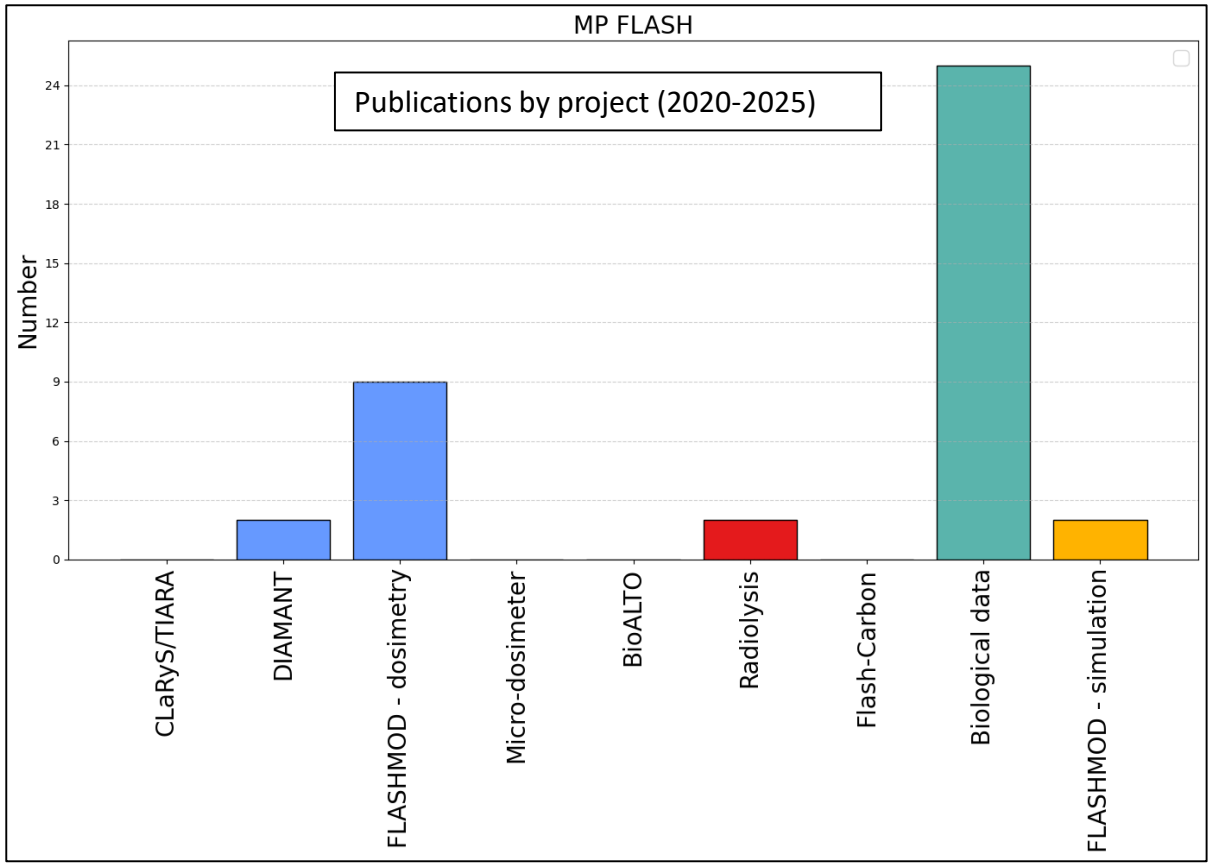


Total PhD in FLASH MP: 6 defended, 6 on-going

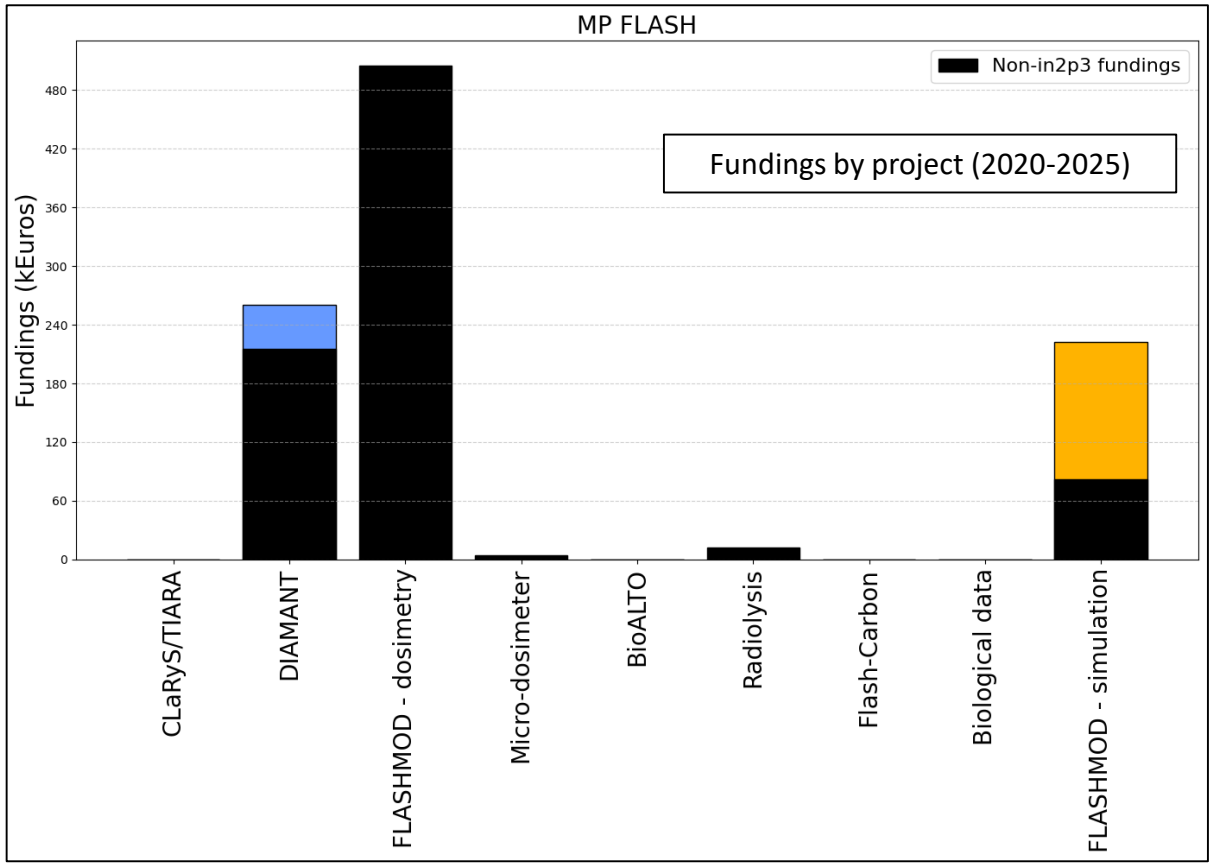


Total CDD in FLASH MP: 5 FTE researchers, 1.5 FTE technical staff

Publications & fundings in the FLASH Master-project of **in2p3**



Total publications in FLASH MP: 40



Total fundings in FLASH MP: 185 kEuros in2p3, 818 kEuros non-in2p3

General

Biological effects – quantification at cell scale

➢ **Cell survival:** To compare irradiation protocols and RT approaches, we can use **clonogenic cell survival** which quantify biological effects at cell level *(elementary constituent of living matter)*

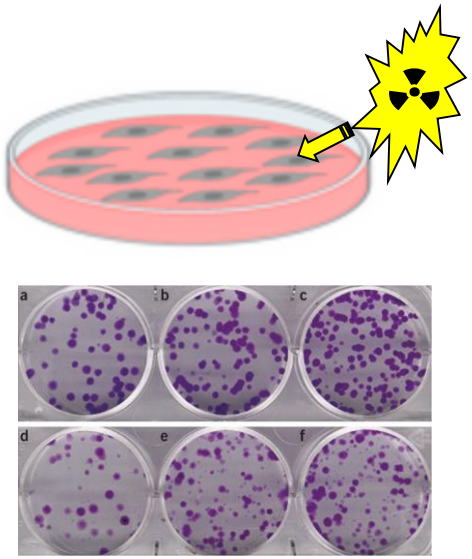
Curve linking **dose** to **cell survival: Linear Quadratic Model**

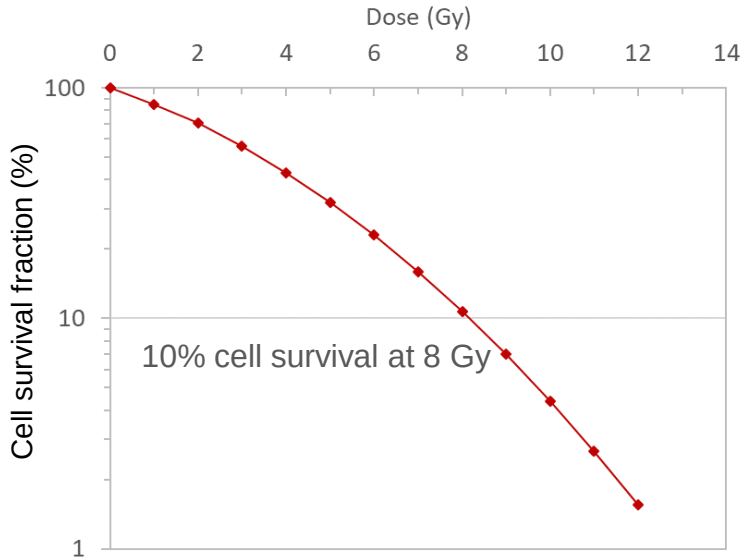
« Macroscopic" description using **mathematical models**

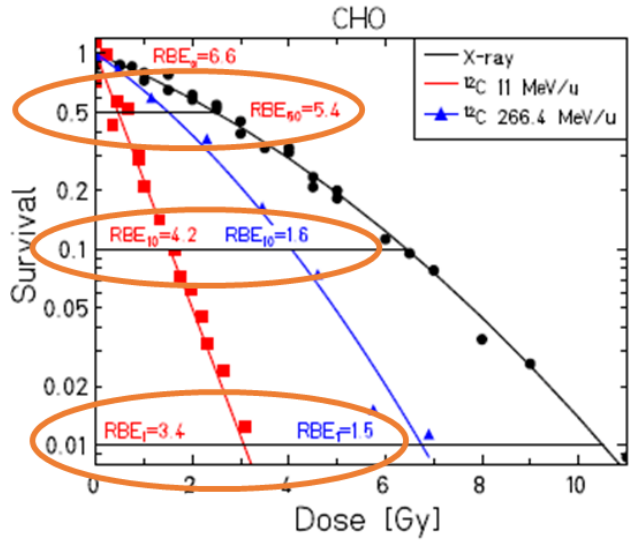
$$S(D) = e^{-(\alpha D + \beta D^2)}$$

Linear (lethal) component — Quadratic (sublethal) component

Radiobiological parameters:
α (Gy^{-1})
β (Gy^{-2})







M. Krämer, NIM-B. Vol.267 I.6 (2009)

RBE depend on many parameters (cell line, oxygenation, % survival considered…)

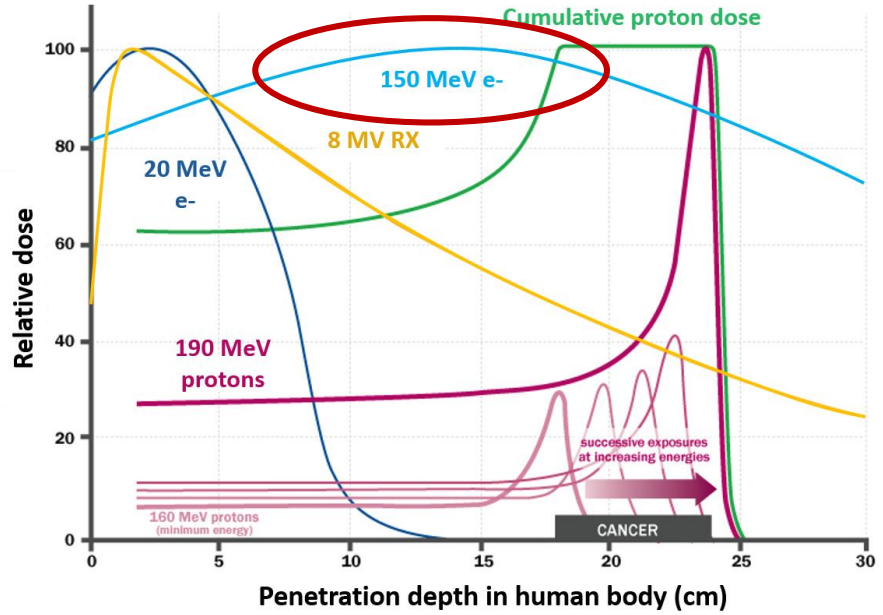
Different particles: VHEE (50-250 MeV)

➢Advantages vs MV photons

- Flatter depth dose profile: deep tumors
- Relative insensitivity to heterogeneities
- Magnetic collimation
- “Flash” dose rate accessible

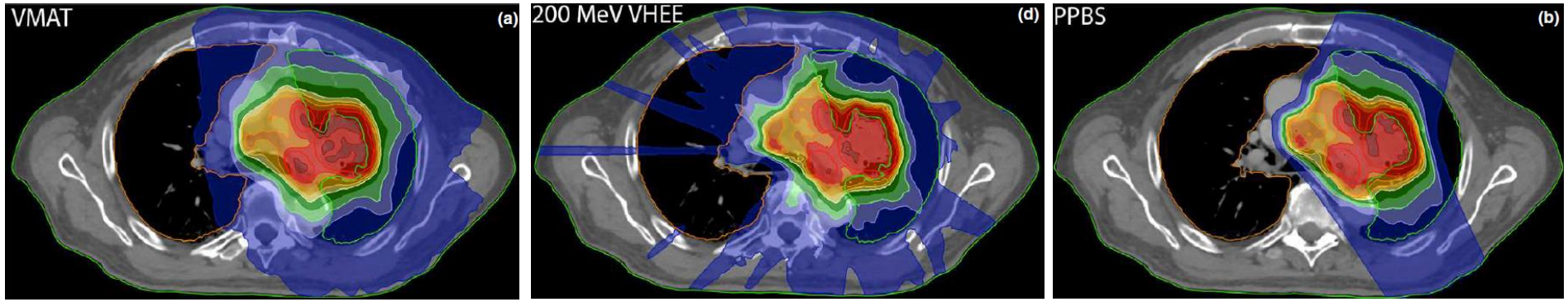
➢Advantages vs protons

- Potential reduced cost, compactness and beam shaping



➢Current challenges:

- Radiobiology of VHEE and pulsed-regime unknown
- Reliable VHEE dosimetry protocols (potential ultra-short pulses, high-dose rates)



Clinical case VHEE compared to VMAT → Better protection of OAR (prostate, Lung, brain, H&N…)
Schuler et al. 2017