



Nuclear Physics Applications in Medicine (ISOLPHARM) and Civil Security

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Alberto Andrichetto (INFN), **Felix Pino** (UniPD) and
more...



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Main Research Area

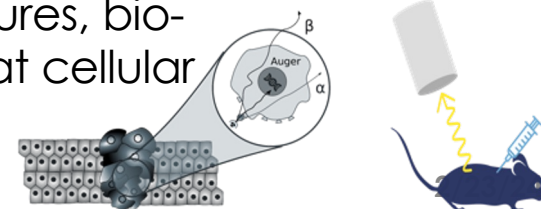
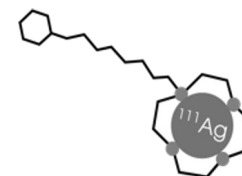
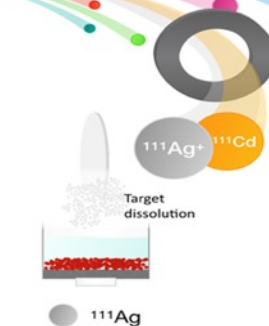


- Development of new Radiopharmaceuticals for Targeted Radionuclide Therapy and Diagnostic

Experimental Activities



- Study of the **production of new radioisotopes of medical interest** at SPES (LNL) using the ISOL technology, including **MonteCarlo simulations** (GEANT4, PHITS, FLUKA...), development of target, source ionization and **radiation detection systems** for production characterization and diagnostic
- Synthesis and test of new macro-molecules to carry the interesting radioisotopes, including chelation and linking to the targeting agents
- Testing of the new macro-molecules in **pre-clinical in-vitro and in-vivo experiments**, including radiobiology tests on cell cultures, bio-distribution experiments and **dose/damage calculations** at cellular level.



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Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali di

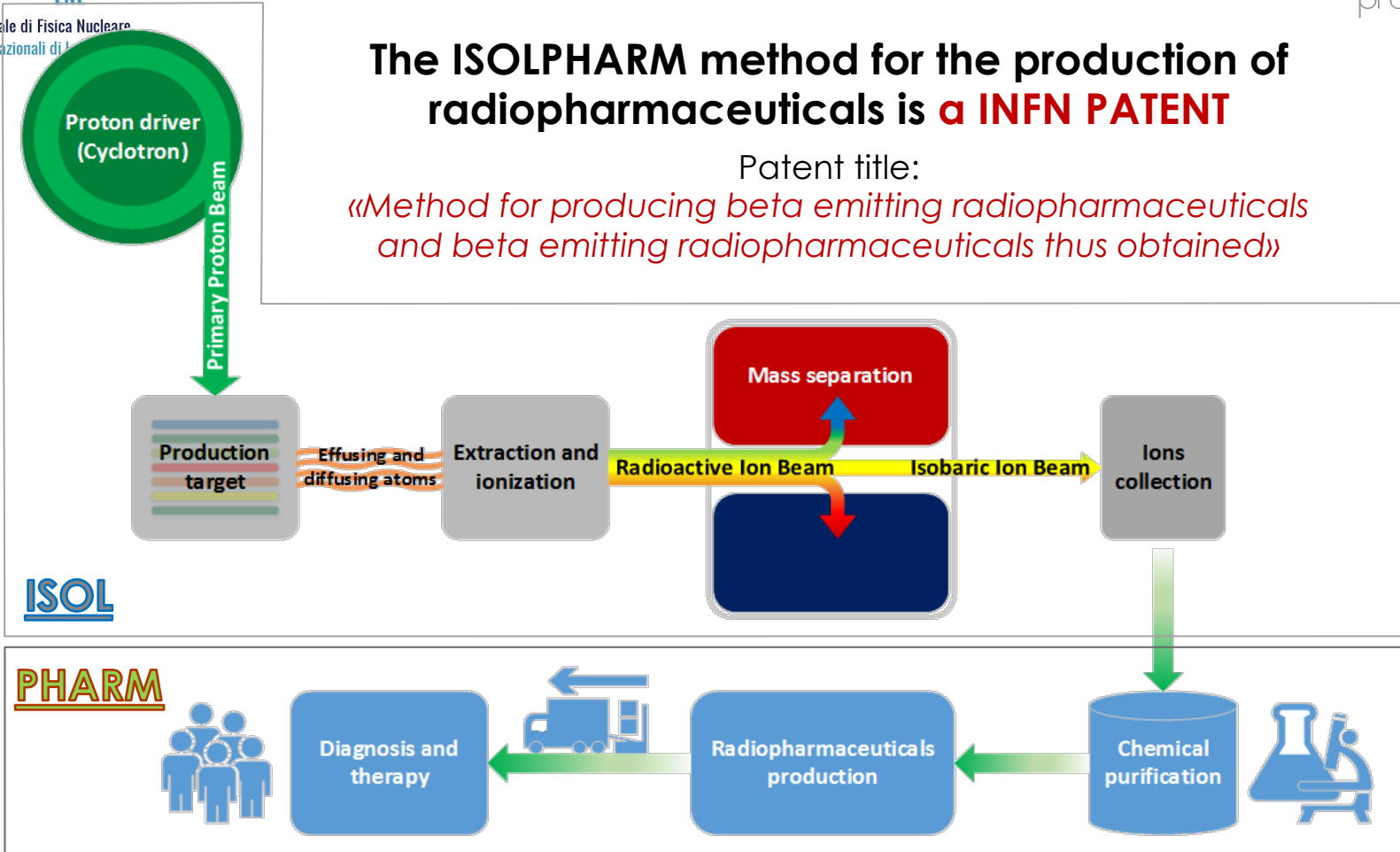
the ISOLPHARM scheme



The ISOLPHARM method for the production of radiopharmaceuticals is **a INFN PATENT**

Patent title:

«Method for producing beta emitting radiopharmaceuticals and beta emitting radiopharmaceuticals thus obtained»

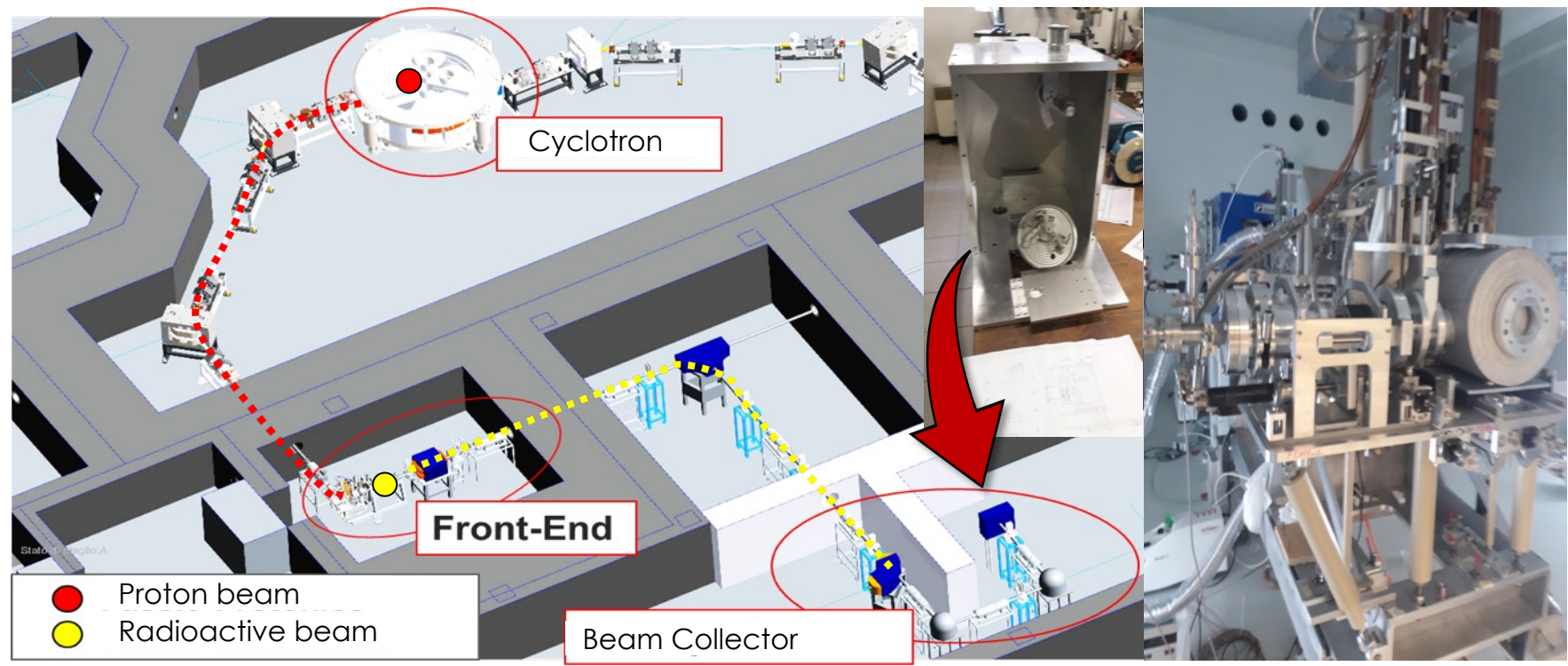


Flexible production, high specific activity & radionuclidic purity

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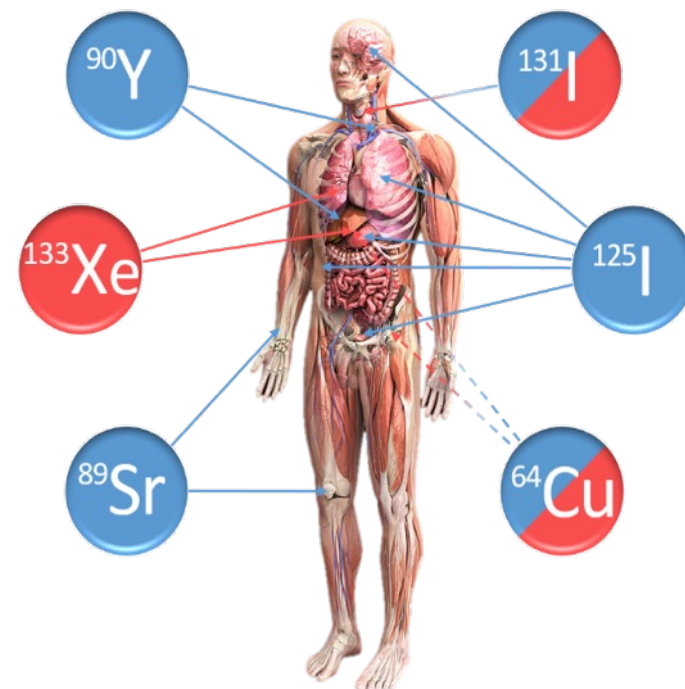
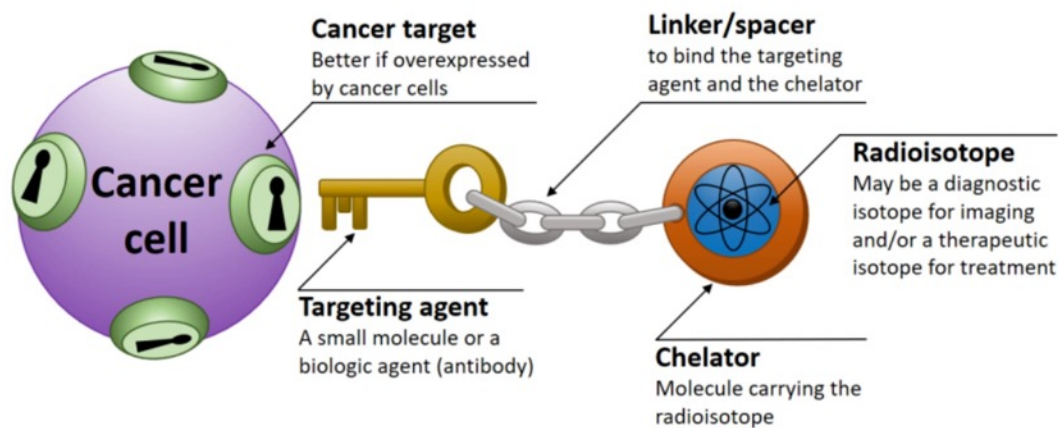
ISOLPHARM @ SPES (LNL)



<https://isolpharm.pd.infn.it/>

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Radiopharmaceuticals for cancer therapy and diagnostic

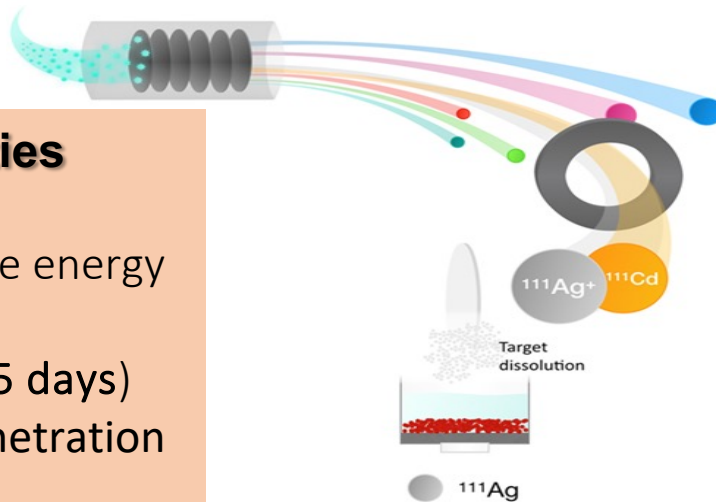


● Diagnosis
 ● Therapy
 ● Theragnostic

F. Borgna et al., *Appl. Rad. Iso.*, 2017

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An interesting new candidate: the beta-emitter Ag-111



¹¹¹Ag properties

- β^- emitter (average energy 360 keV)
- Good half-life (7.45 days)
- Average tissue penetration (1.8 mm)
- Medium energy γ rays (342 keV) -> SPECT

- In the market **No radiopharmaceuticals Silver-based!**
- Ag-111 can be produced @ SPES with high purity & also with high production rate.**
- No Isobaric radioactive contamination** in the secondary target (also with LASER off)!

111 Isobaric chain	$t_{1/2}$	Decay	Target Yield
¹¹¹ Cadmium	Stable		Low yield production
¹¹¹ Silver	7.45 days	β^-	Good yield production
¹¹¹ Palladium	23.4 min	β^-	Bad release, short $T_{1/2}$
¹¹¹ Rhodium	11 sec.	β^-	No release, very short $T_{1/2}$



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ISOLPHARM: a wide interdisciplinary Collaboration

ISOLPHARM started as a **scientific gathering** of local **competences**, now coordinated by **INFN-LNL**



Trento Institute for Fundamental Physics and Applications



UNIVERSITÀ
DI TRENTO

BIOTech
BIOtec
Biomedical Technologies

CIBIO
Centre for Integrative Biology

Development of cell-lines, *in-vitro* and *in-vivo* studies, imaging



UNIVERSITÀ
DEGLI STUDI
DI PADOVA



UNIVERSITÀ
degli STUDI
di CATANIA

ACAPiR
Center for Advanced Preclinical *in vivo* Research

Development and synthesis of small molecules for cancer treatment



UNIVERSITÀ
DEGLI STUDI
DI PADOVA



SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA

Azienda Unità Sanitaria Locale di Reggio Emilia
Azienda Ospedaliera di Reggio Emilia
Arcispedale S. Maria Nuova
Istituto in tecnologie avanzate e modelli assistenziali in oncologia
Istituto di ricerca e cura a carattere scientifico

Other possible field of collaboration?



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DI BRESCIA



Unconventional radionuclide (e.g. ^{111}Ag) production with an innovative method



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DI PADOVA



Dipartimento
di Fisica
e Astronomia
Galileo Galilei



Study and development of tumor targeting agents for specific targets (e.g. CCK2R)



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DI PAVIA

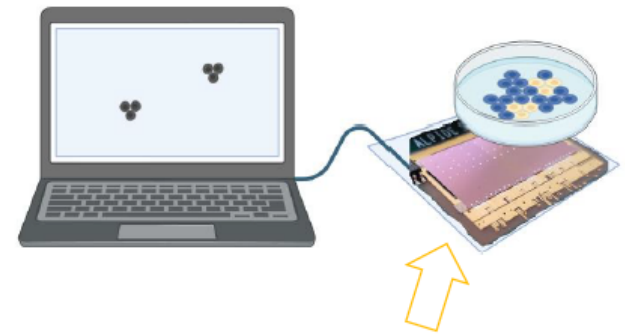
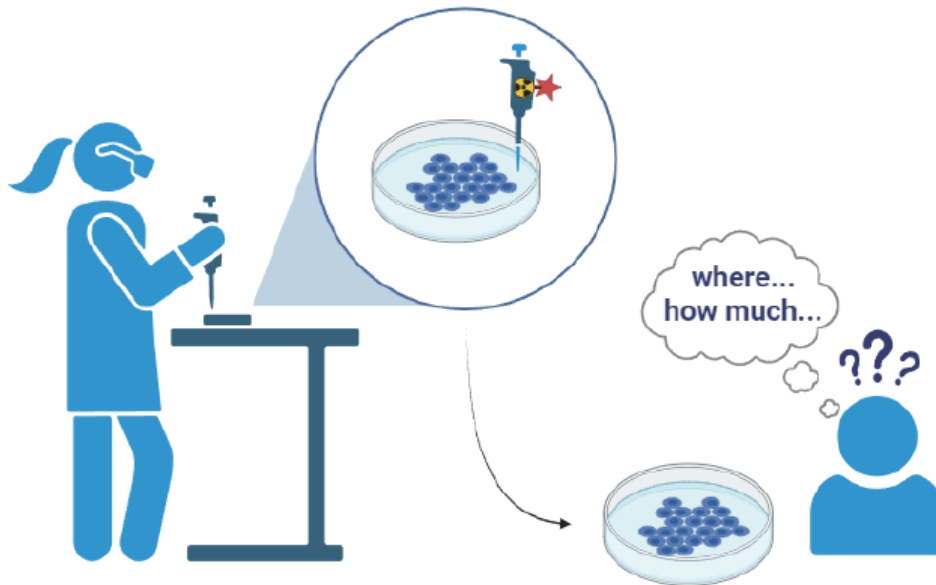


Development of chemical purification procedures and innovative chelators

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A beta-imaging detector for Ag-111 studies

Beta activity assessment in pre-clinical experiments



β imaging detector

Requirements:

- 0.1 – 1 mm spatial resolution
- Activity quantification

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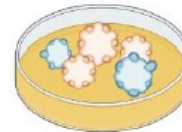
A beta-imaging detector for Ag-111 studies

Detailed MonteCarlo simulations using the GEANT4 toolkit

Cell geometry:

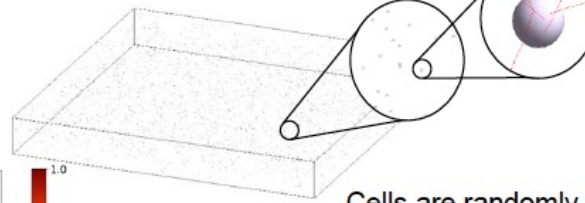
- Aqueous spherical cells (10 μm radius)
- Inside the cell volume, ^{111}Ag undergoes β decay

Source geometry:



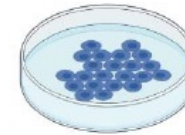
3D hydrogel culture

Created in BioRender.com kb2

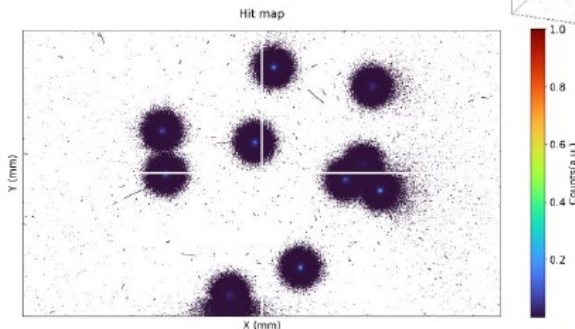


Cells are randomly dispersed in hydrogel matrix.

10 cells dispersed in hydrogel matrix



2D Planar culture

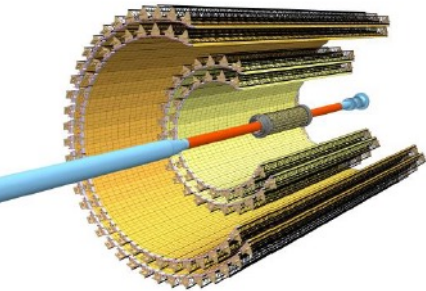


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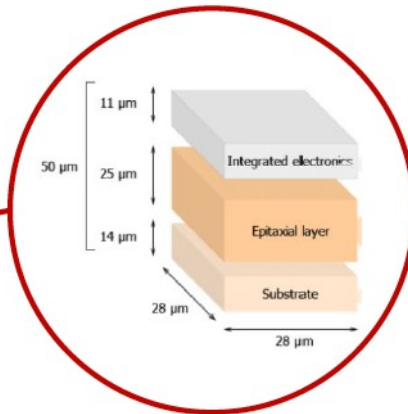
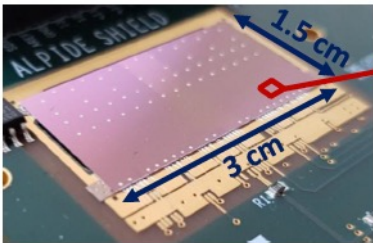
A beta-imaging detector for Ag-111 studies

The beta-imaging detector will take advantage of the MAPS technology developed at CERN for the LHC experiments

- It will consist of 4 or 8 **ALPIDE chips** arranged in a flat geometry
- ALPIDE is a monolithic active pixel sensor (**MAPS**) originally developed for the Inner Tracking System of the **ALICE** experiment at CERN

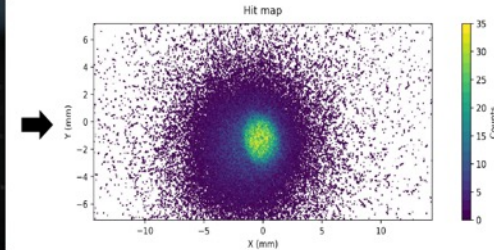


- 1.5 cm × 3 cm × 50 μm
- 1024 × 512 sensitive pixels
- 28 μm × 28 μm × 50 μm



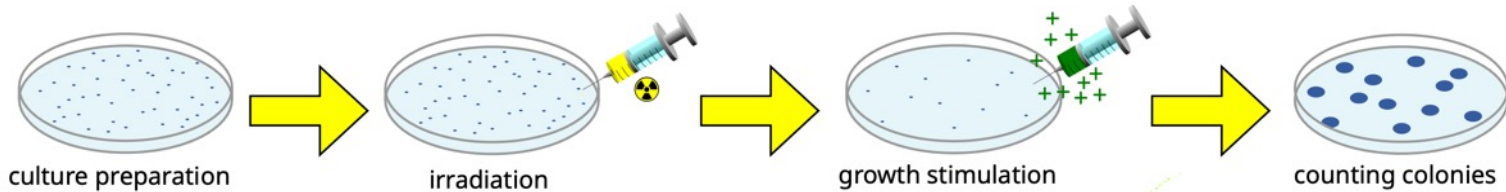
First measurements conducted with ALPIDE:

- Dedicated **firmware** mounted on the detector
- Preliminary **data acquisition** with ⁹⁰Sr source

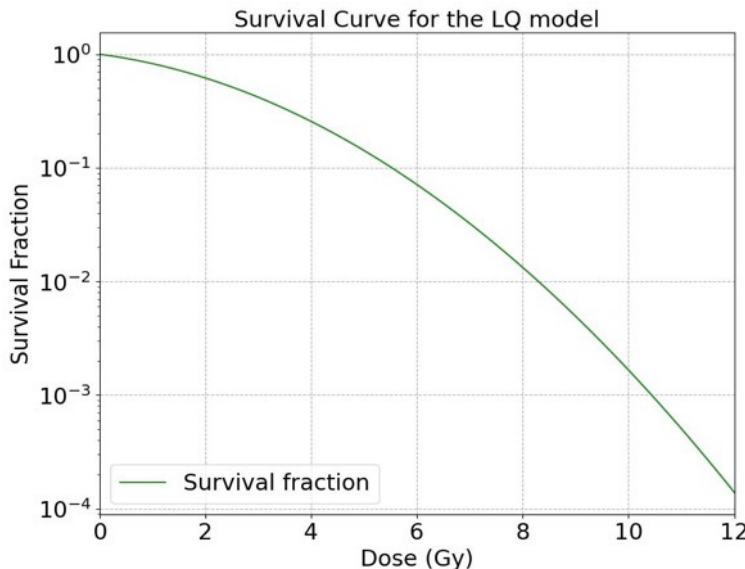


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Radiation Biophysics: cell survival



Clonogenic assay of an irradiated 2D cell culture.

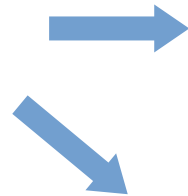


The effectiveness of a **radionuclide therapy** can be studied in terms of the **surviving fraction** of cancer cells as a function of the **absorbed dose**.

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Radiation Biophysics: cell uptake and dosimetry

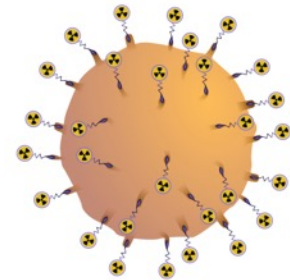
The radiopharmaceutical **uptake** can be measured with a **radiation detector** to...



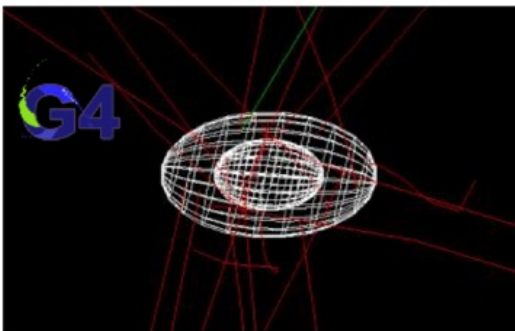
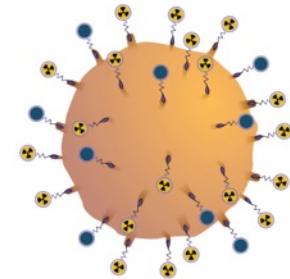
...assess the **targeting efficiency** of the molecule

...compute the **cell dosimetry** with **Monte Carlo** methods

High Targeting of desired species



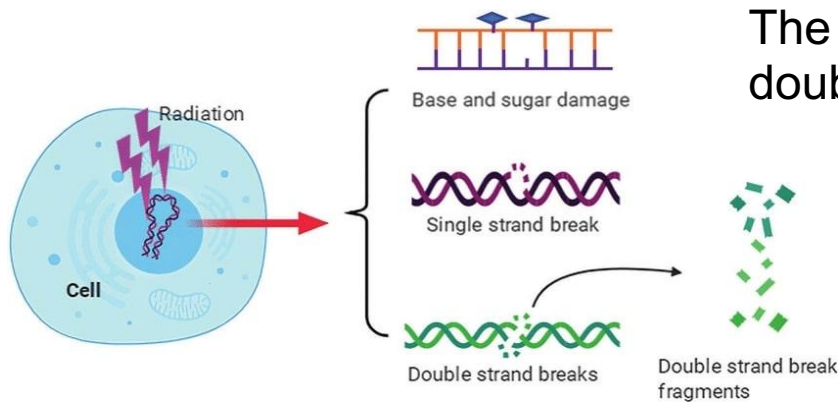
Poor targeting of desired species



GEANT4 Monte Carlo simulation of the absorbed dose in the cellular compartments.

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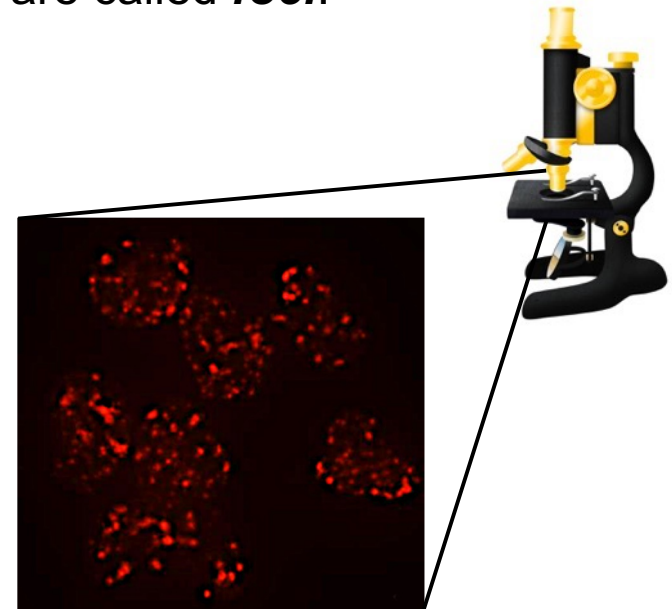
Radiation Biophysics: *foci* assay



The break points of the irradiated DNA double helix are called ***foci***.

The phosphorylation of certain *foci* proteins can be used to relate the **DNA damage** to a **fluorescent signal**.

Detailed simulations and predictions on DNA damages can be realized using **GEANT4-DNA**



Confocal microscopy imaging of a γ -H2AX foci assay.

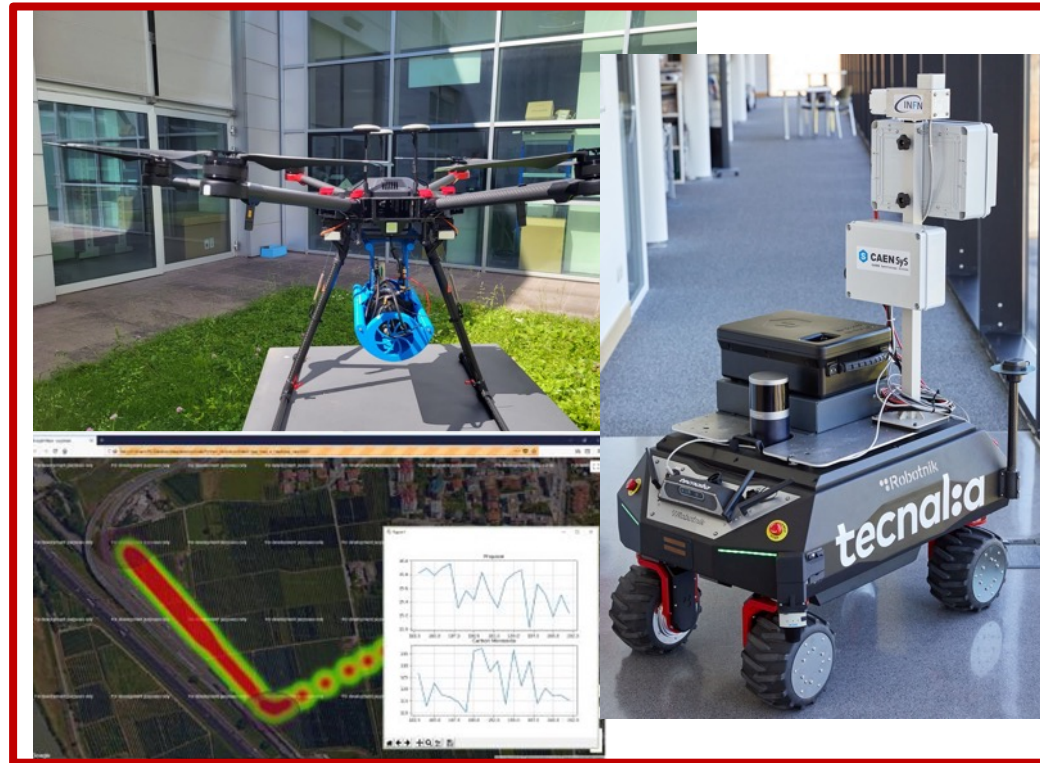
Applied Nuclear Physics in Civil Security

Main Research Area

- Applied Nuclear Physics in security, in nuclear decommissioning, environmental monitor, nuclear security, homeland security...

Experimental Activities

- Novel neutron detectors characterization
- Detector characterization & prototype development
- MonteCarlo Simulation (GEANT4)
- Laboratory, Accelerator and field "real" tests



Examples of UAV and UGV with new detectors and new autonomous prototypes for dangerous situations

Graduate School on Medical Physics

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Graduate School on Medical Physics at UNIPD

- Possible study continuation after LM in the context of public health, with the goal to be employed as Medical Physicist on hospitals and other health facilities
- 3 years path with fellowship with a smaller part of “theoretical” formation at DFA and associate sites, and a larger part of internship at different health facilities
- Access by competition, usually in November (submission deadline just after the October Master Degree session). Having a Master Thesis in Medical Physics is a plus!
- For more information:
 - prof. Silvia Monica Lenzi (silviamonica.lenzi@unipd.it)
 - dott. Raffaella Cesaro (Raffaella.cesaro@unipd.it)

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