ISOLPHARM
SPES exotic beams for medicine

INFN
Istituto Nazionale di Fisica Nucleare
LABORATORI NAZIONALI DI LEGNARO

ADMIRAL

ISOLPHARM
SPES exotic beams for medicine

Advanced **D**osimetry **M**ethods and **I**n-vitro **R**adiobiology of **A**g-111 **L**abeled radiopharmaceuticals

- **Principal Investigator**
  Alberto Andrighetto, INFN-LNL.
- **INFN Research Units**
  LNL, Padova, TIFPA, LNS, Pavia, Bologna.
- **Research Fields**
  Medical Physics, Radiation Detectors, Radiobiology.
- **Duration**
  3 years.

The ISOLPHARM collaboration

ISOLPHARM
SPES exotic beams for medicine

Istituto Nazionale di Fisica Nucleare
LABORATORI NAZIONALI DI LEGNARO

Dipartimento di Fisica e Astronomia Galileo Galilei

INFN PADOVA
Istituto Nazionale di Fisica Nucleare
Sezione di Padova

UNIVERSITÀ DI SIENA 1240

INFN
Istituto Nazionale di Fisica Nucleare
LABORATORI NAZIONALI DI LEGNARO

UNIVERSITÀ DI PAVIA

dsf DISC

L.E.N.A.

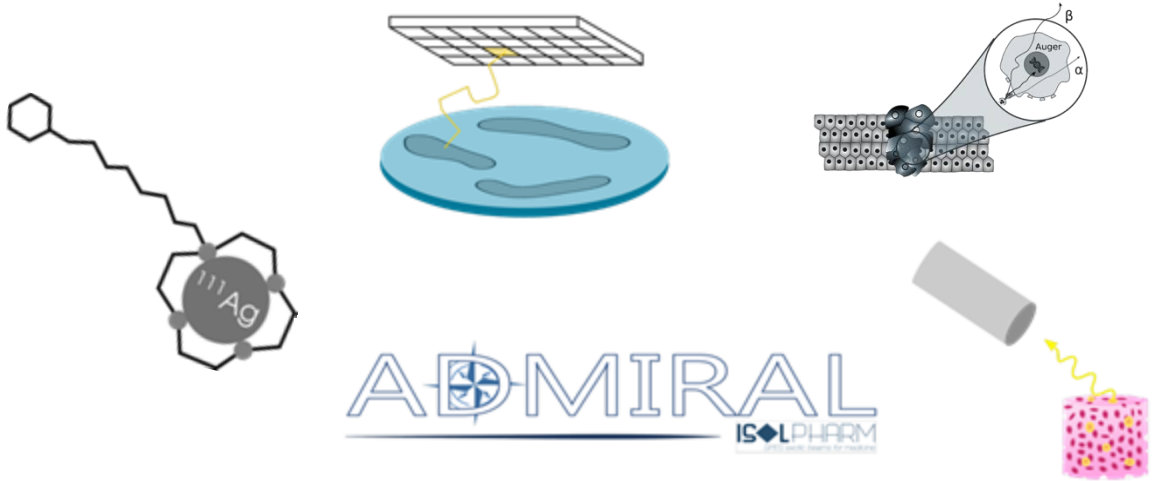
INFN PAVIA

UNIVERSITÀ DEGLI STUDI DI BRESCIA

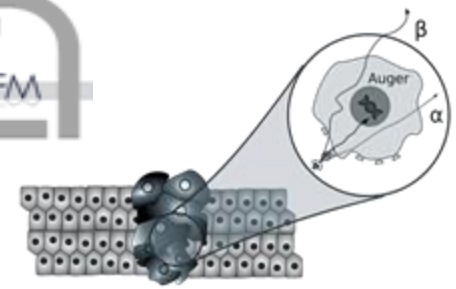
IBFM

Radiopharmaceutical production

Development of a β-imaging system based on solid-state detector



Development of a γ-imaging scintigraphic system



Radiobiological characterization

Fondazione Ri.MED

INFN LNS
Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali del Sud

UNIVERSITÀ DI TRENTO

CAPiR
Center for Advanced Preclinical in vivo Research

UNIVERSITÀ degli STUDI di CATANIA

TIFPA
Trento Institute for Fundamental Physics and Applications

CIBIO
Centre for Integrative Biology

ALMA MATER STUDIORUM UNIVERSITÀ DI BOLOGNA

INFN BOLOGNA
Istituto Nazionale di Fisica Nucleare
Sezione di Bologna

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Bologna
IRCCS Istituto di Ricovero e Cura a Carattere Scientifico

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale di Reggio Emilia
IRCCS Istituto in tecnologie avanzate e modelli assistenziali in oncologia

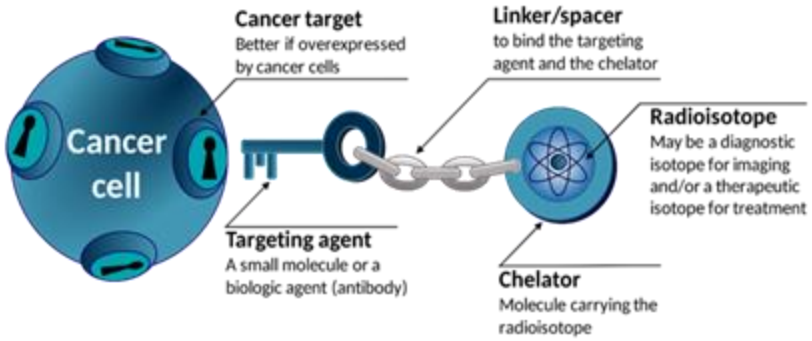
Interdisciplinary WPs: WP1 & WP4

WP1

WP Leader: V. Di Marco (UNIPD) and D. Meniglio (UNITN)

Work Package Aim

WP1 will sum up all the preexisting activities leading to the **development of the radiopharmaceutical itself**, with the addition of the **tissue-mimicking scaffold production** to generate **more realistic 3D cell cultures** to be employed in the other work packages.

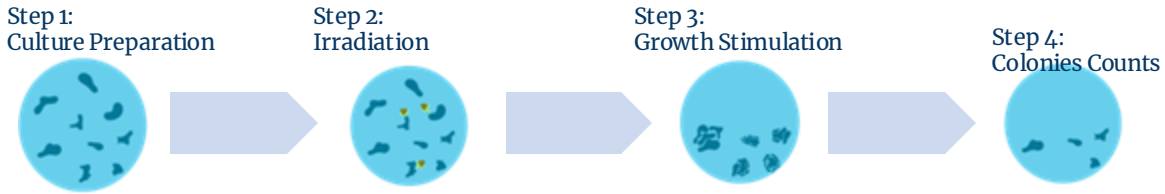


WP4

WP Leader: S. Bortolussi (UNIPV)

Work Package Aim

The whole set of experimental activities concerning **radiobiology**. In particular cell survival in 2D and 3D scaffolds will be evaluated. The acquired **radiobiological data** will be related to the absorbed **dose at cell** level, which will be calculated using Monte Carlo method, exploiting the available data about ^{111}**Ag uptake** *in vitro* and transporting the emitted radiation in simulated geometries that reproduce the monolayer or the **3D scaffold**.



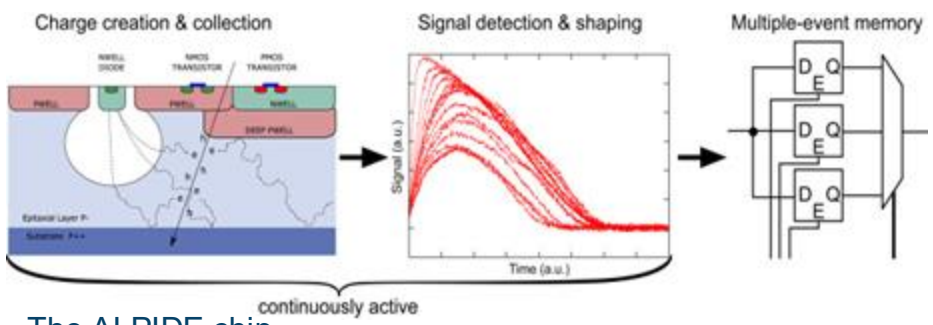
Detector development WPs: WP2 & WP3

WP2

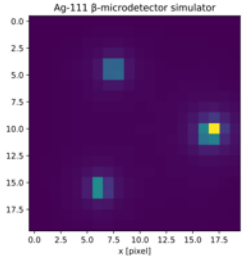
WP Leader: M. Lunardon (UNIPD)

Work Package Aim

This WP will be devoted to the **design**, **construction** and **characterization** of a new large-area detector for 2D β-imaging at high resolution. This new device will take advantage of the monolithic silicon pixel technology developed recently for the ALICE experiment, namely the **ALPIDE**, the Monolithic Active Pixel Sensor of the new Inner Tracking System (ITS).



The ALPIDE chip



preliminary simulation of a cell distribution beta image

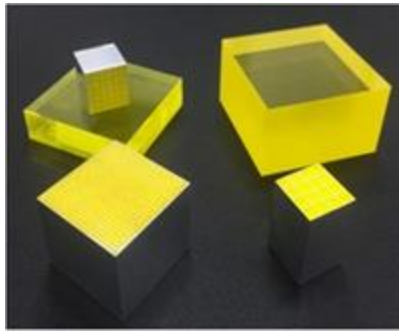
WP3

WP Leader: C. Sbarra (UNIBO)

Work Package Aim

This WP is aimed at the **design and development** of a planar scintigraphic system optimized for the incoming **γ emission** from the de-excitation of ^{111}Cd after the radioactive decay of **^{111}Ag**. The design and construction of the imaging device will begin considering **all its components**, from **detectors** to **data acquisition software**.

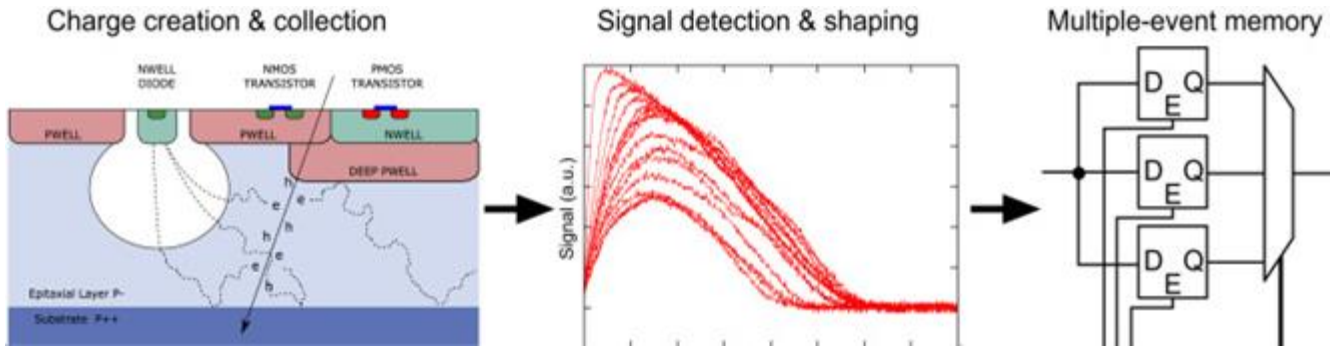
GAGG scintillators in slab and matrix produced by EPIC-Crystals

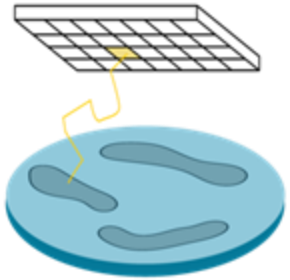


the beta-imaging detector at PD

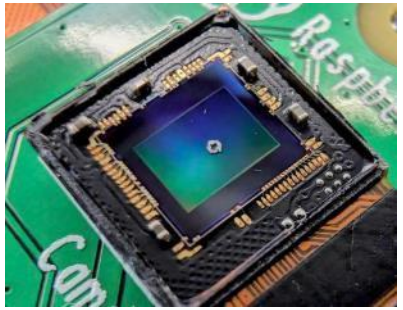
Proposal:

- **ALPIDE chips**: technology from HEP
- 15 mm x 30 mm active area with 512 x 1024 pixels (typical size about 25 um)
- low-cost readout electronics using commercial FPGA + custom PCB + dedicated Firmware
- modular system, scalable size, compact, easy to use. With 8 chips an active plate of **60 mm x 60 mm** can be easily assembled.

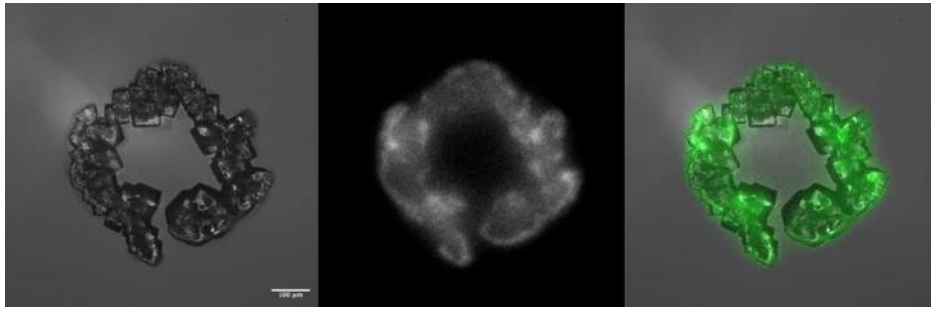




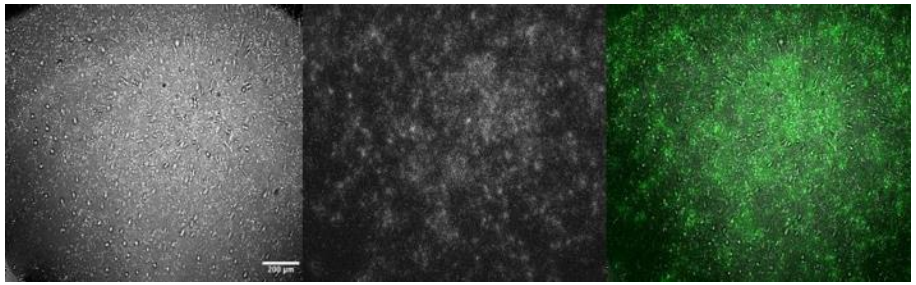
More low-cost beta-imaging detectors on the market



- Beta detector of INFN-Pisa



- Test with 18F-FDG



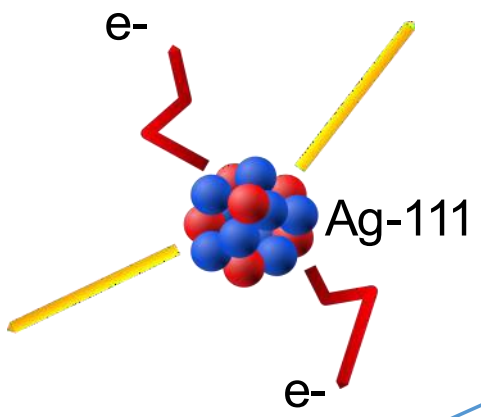
- Test with cells taking up 18F-FDG
- Test planned at CAPiR in June with cells uptaking Ag-111

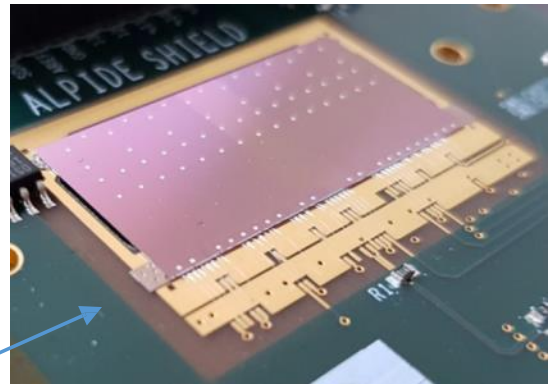
- **small active area** (3mm x 3 mm)
- micrometric spatial resolution with radioactive source in contact => **systematic contamination** of the chip and surrounding

the beta-imaging detector at PD

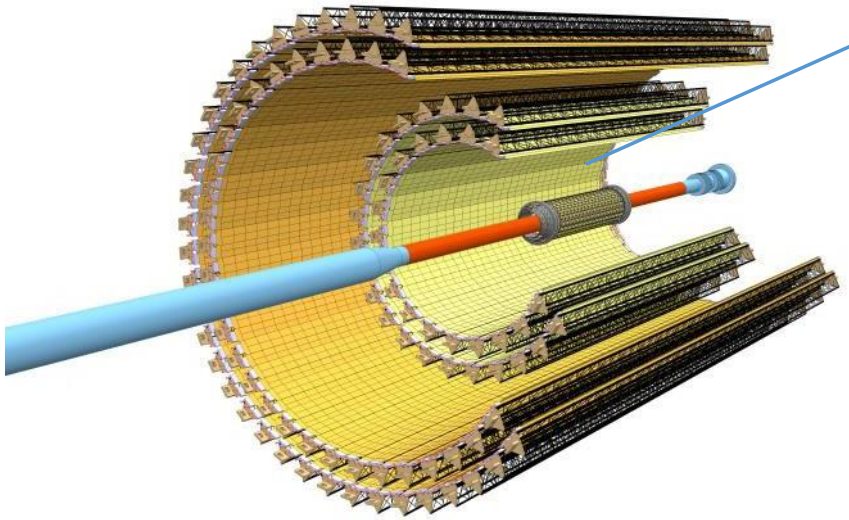
Realization: DUMBO

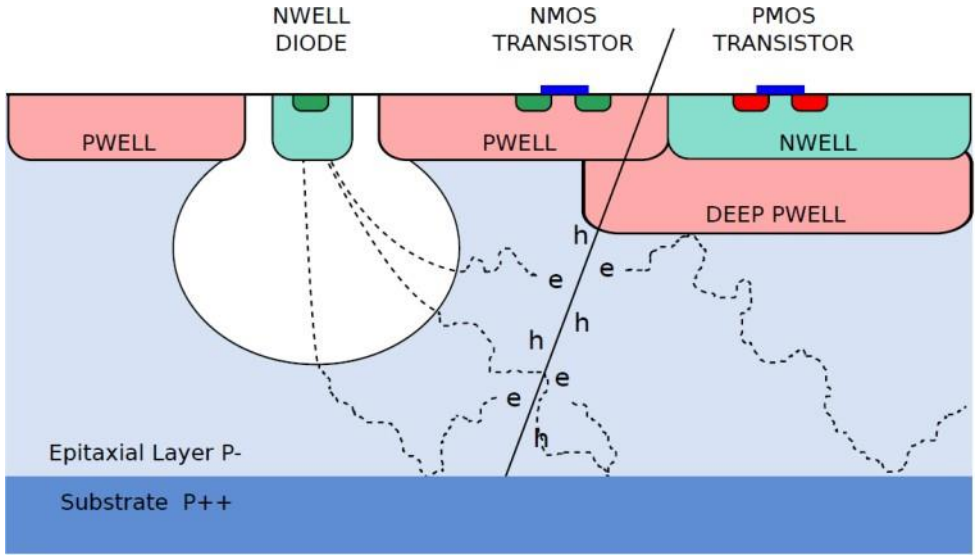
Detector
Using
Maps for
Beta-rays
Observation





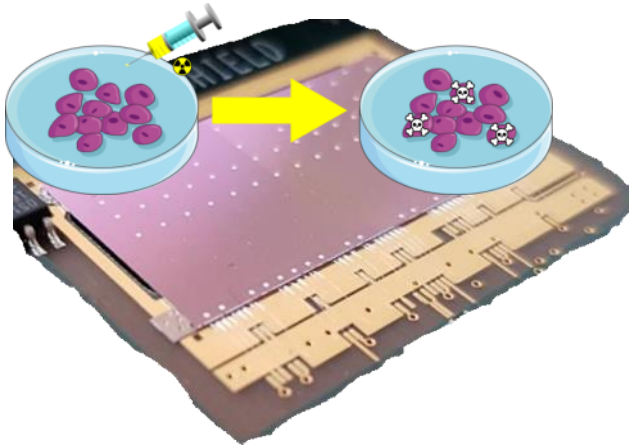
- MAPS -> ALPIDE
- ALice PIxel DEtector



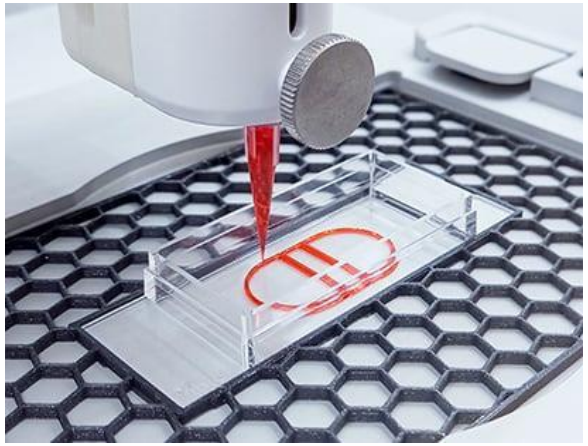


Why DUMBO

- **Features of DUMBO**
  - Sample isolated from the detector => no contamination
  - Spatial resolution of about 1 mm at 500 um distance
  - Large sensitive area (15x30 mm² / chip => 120 mm x 30 mm)
  - Scanner function using motors to increase FoV
  - Easy to use

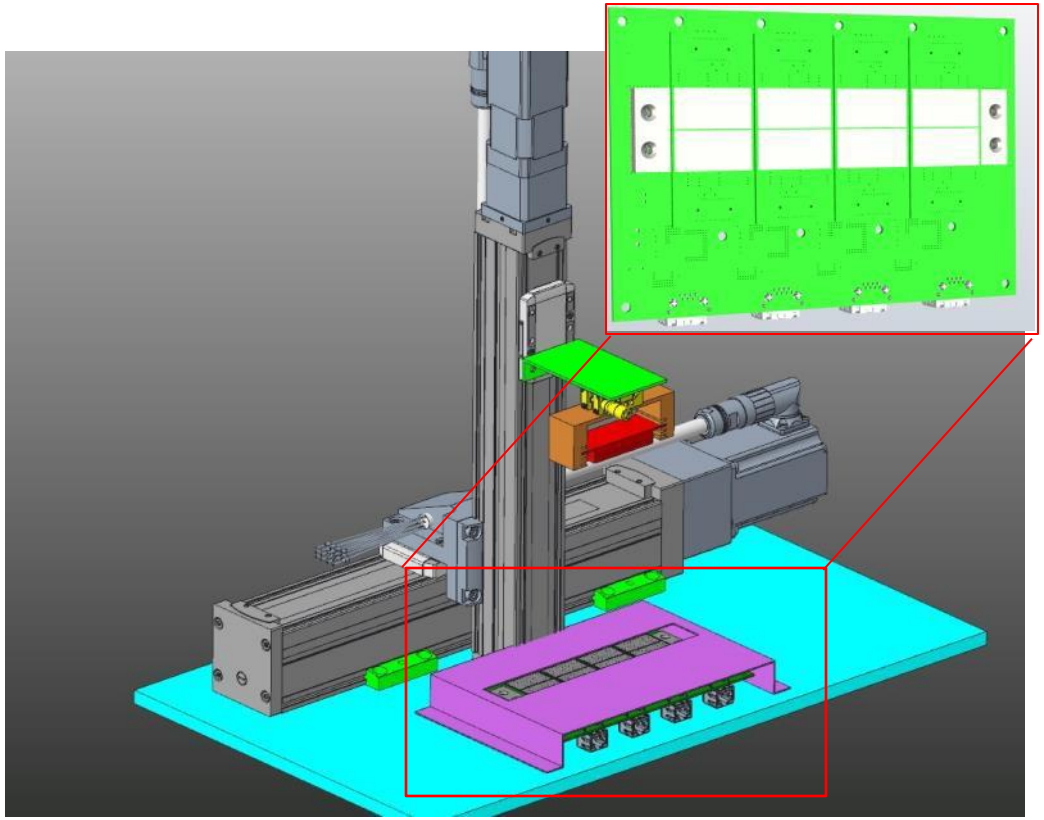


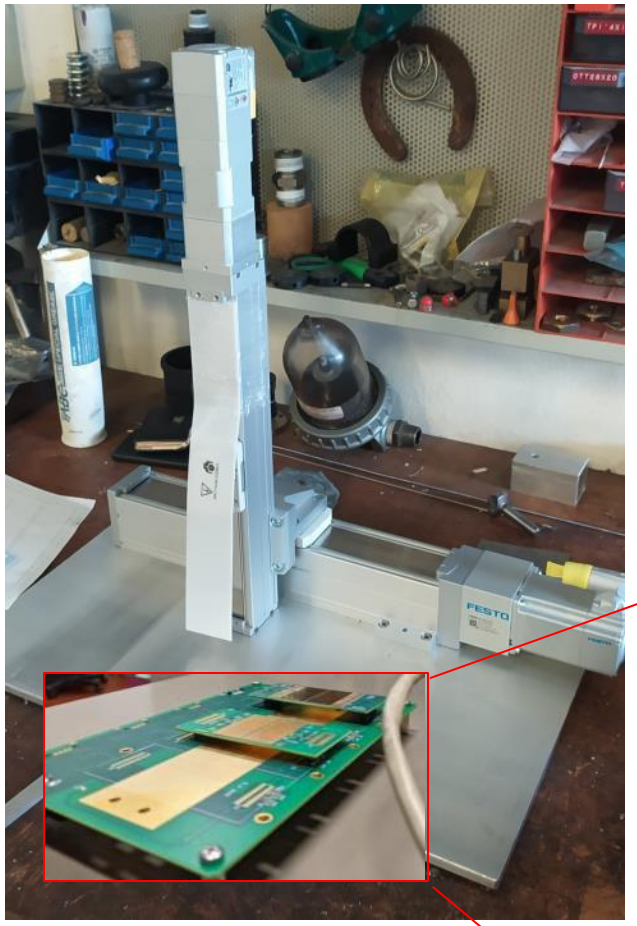
- **Applications**
  - Cell clusters imaging in-vitro for uptake
  - Imaging of 2.5D scaffolds



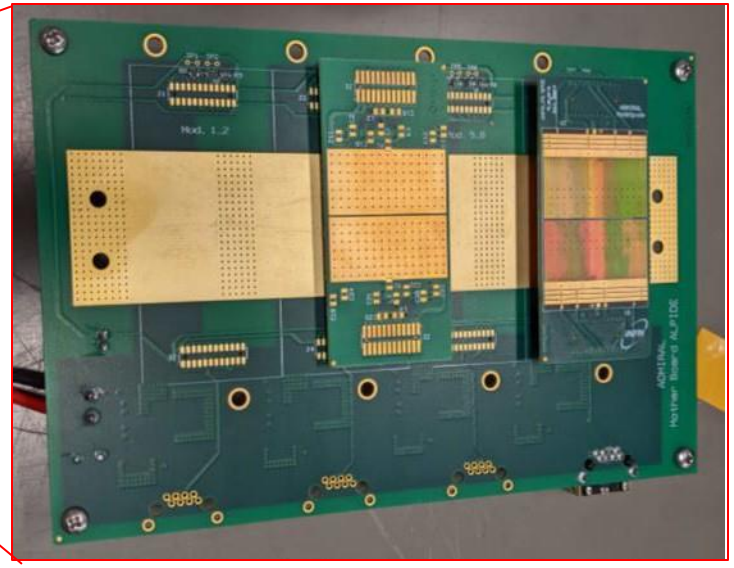
the beta-imaging detector at PD

Realization: DUMBO





- 8 ALPIDE chips are the sensitive elements
- Mechanics system to place the sample
  - x-y movement



WP2 active people

Staff:

- Marcello Lunardon -> WP leader
- Piero Giubilato -> Resources
- Sandra Moretto -> Resources
- Devis Pantano -> ALPIDE electronics
- Lorenzo Castellani -> ALPIDE electronics
- Roberto Michinelli (BO) -> mechanics designer

PhD students:

- Aurora Leso -> Geant4 simulation
- Davide Serafini -> experimental setup

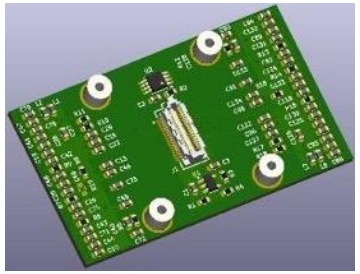
Bachelor students:

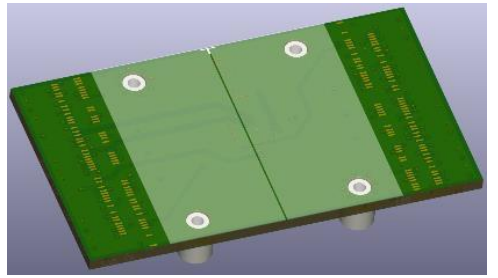
- Sofia Busatto -> Geant4 simulation
- Tommaso Coppelli -> movement tests and phantoms
- Edoardo Cervi Gambaro -> ALPIDE tests

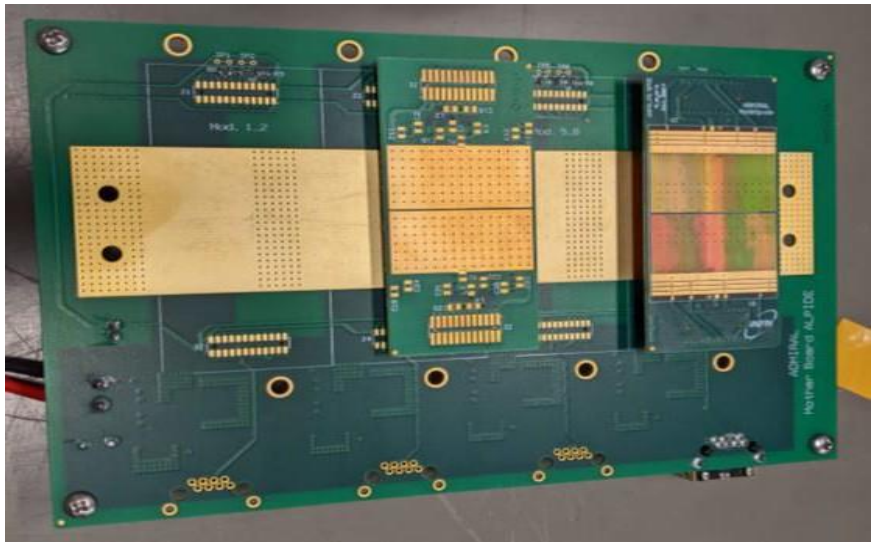
Design and realization of the PCB for the chips

- Chip mounting PCB hosting two ALPIDE chips (basic module): design complete and boards printed
- Mezzanine and FPGA board designed and printed.

PCB design







PCB for chip mounting

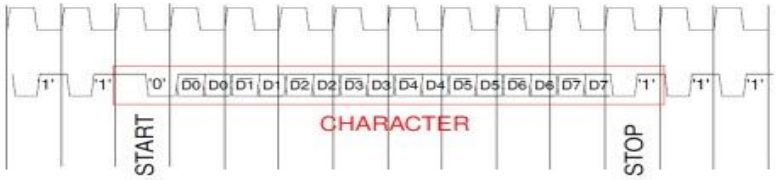
mezzanine board

FPGA board

connection from commercial FPGA (standard connectors) to custom PCB with ALPIDE chips

Thanks to support of PD Electronic Shop (Lorenzo Castellani)

ALPIDE communication and DAQ software



- Communication with the ALPIDE
- Bachelor thesis of Edoardo Cervi Gambaro

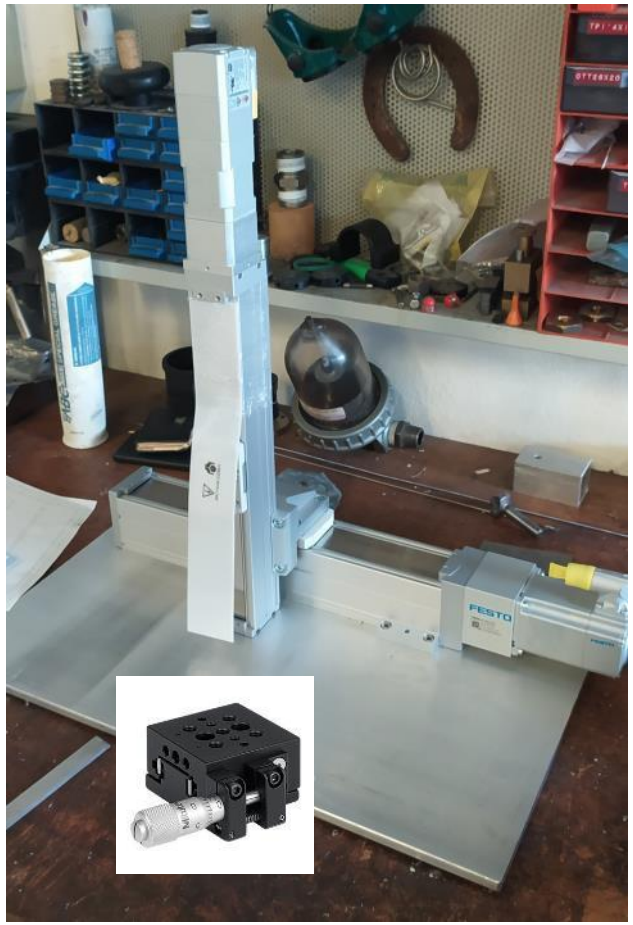
ALPIDE Operations Manual

ALICE ITS ALPIDE development team

July 25, 2016
Version: 0.3
Status: DRAFT

python

Step-motor control software



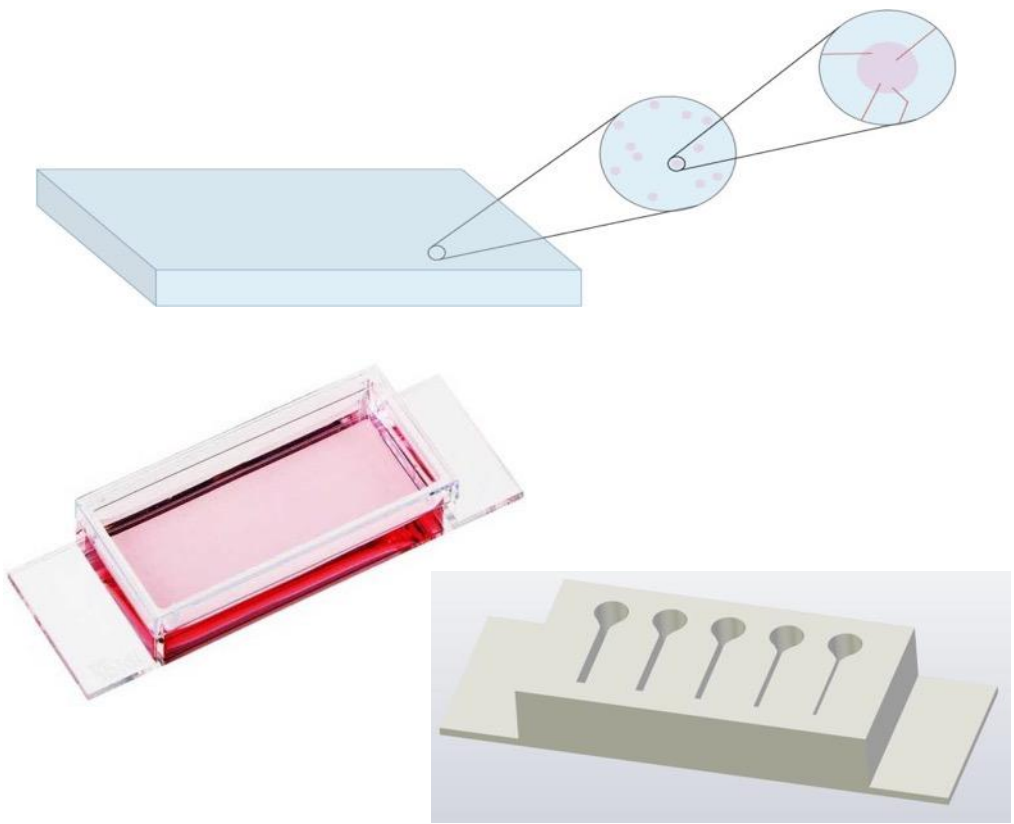
- Two motors for two axes
- One micrometric manual traslator on the 3rd axis

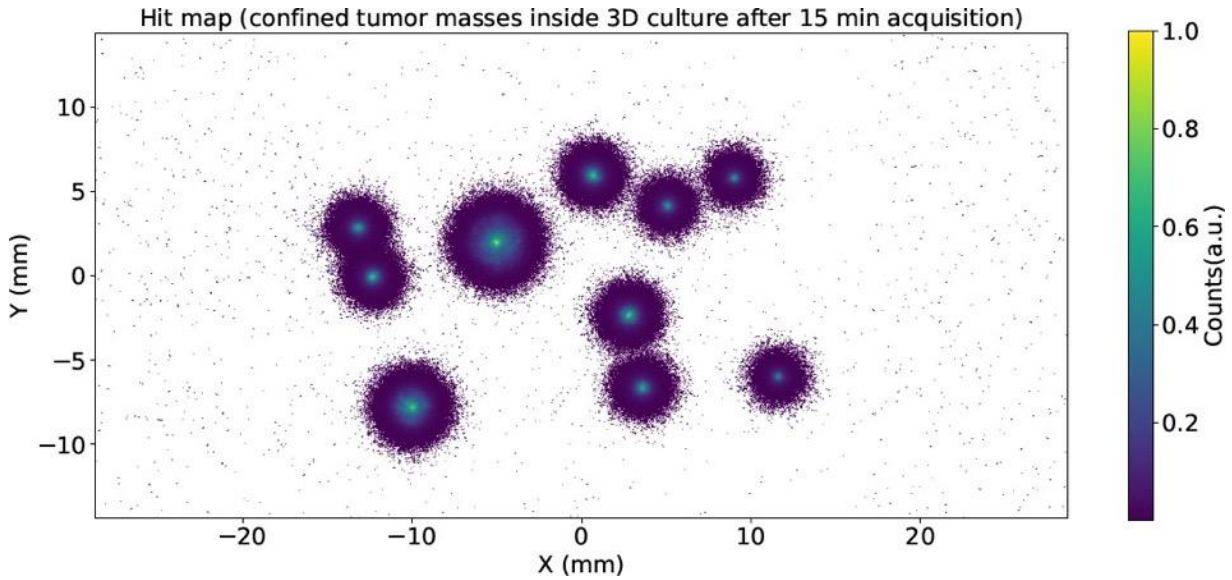
- Festo automation suite can be be used for manual and automatic control
- Festo-edcon python library for modbus communication with the motors
- Python scripts with several target positions
  - Integration with ALPIDE communication python script
- Bachelor thesis of Tommaso Coppelli

the beta-imaging detector at PD

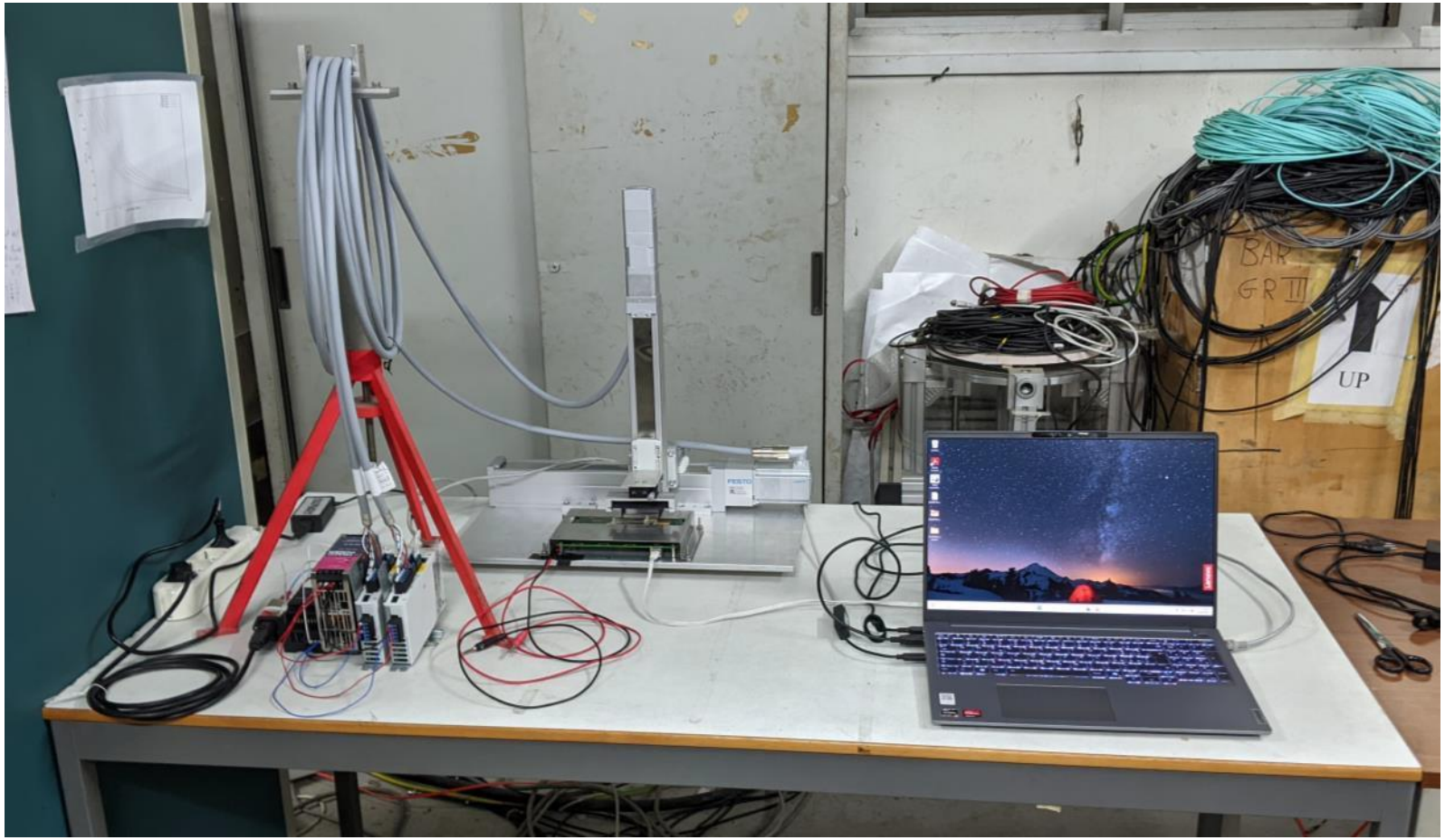
Simulations

- Simulation framework developed by previous students
- Different experimental conditions can be simulated
- Thesis of Sofia Busatto





Development setup

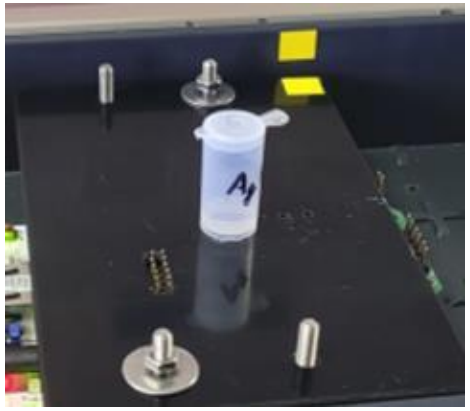


One python script:

- Motors movement
- Chip communication

the beta-imaging detector at PD

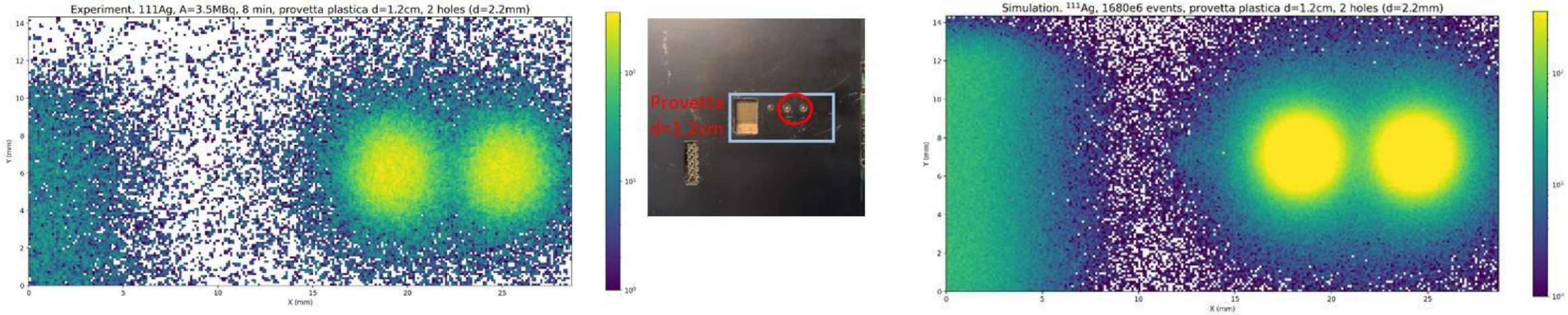
Last experiment in 2024



Beta detector tests at LENA:

- Characterized the ALPIDE sensor
  - No mechanics
- Validated the Geant4 simulations
- Ag-111 solution in big vials (diameter 12.5 mm)
  - With collimator

Due fori di d=2.2 mm



the beta-imaging detector at PD

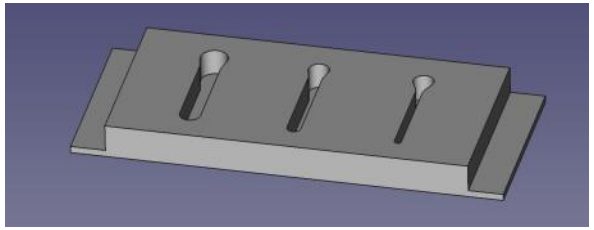
Next experiment in July 2025

DUMBO tests at LENA:

- Characterize the whole device
  - ALPIDE chip (still temporary)
  - Movement system

Preliminary tests

- Study of diffusion of Ag-111 ions
  - In GelMA scaffolds prepared ad the radiolab of Pavia in collaboration with the BIOtech of Trento



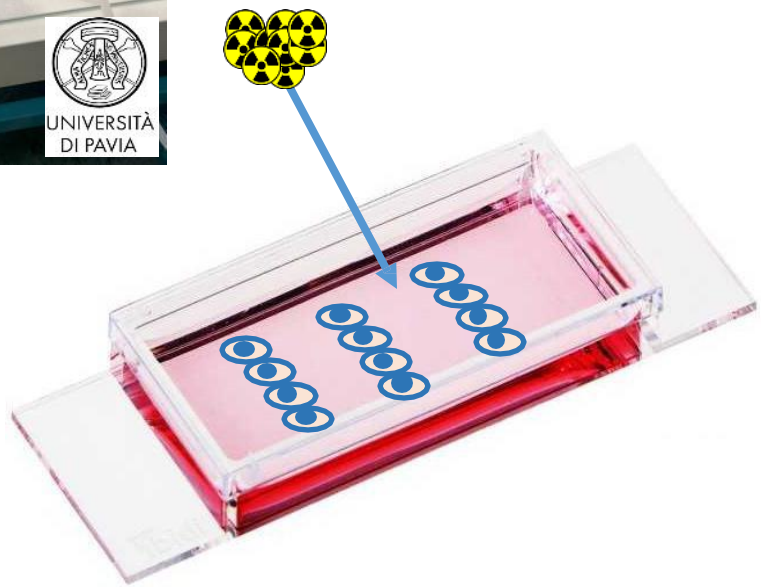
Designed by Tommaso Coppelli

- Evaluation of the spatial resolution
  - In plastic phantoms

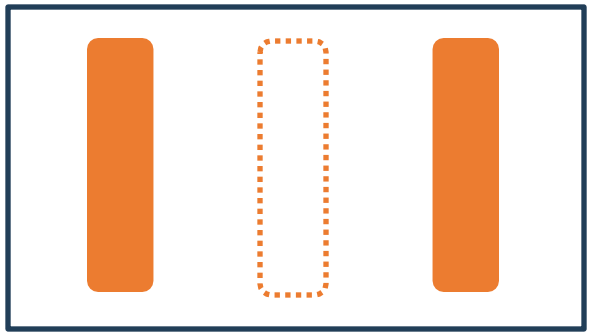
Last ADMIRAL experiments

Experiments with cell cultures:

- Estimate uptake of different cell lines in the same culture
  - Uptake of Ag-111 ions
  - Uptake of Ag-111 radiopharmaceutical



DUMBO imaging



ADMIRAL – GANTT

we are here

ADMIRAL WP2

		Year 1				Year 2				Year 3				Notes
		M3	M6	M9	M12	M15	M18	M21	M24	M27	M30	M33	M36	Required for
	WP2 - β-Imaging													
MS2.0	Development of the detector control firmware prototype	→			●									MS2.3
MS2.1	Electronics and mechanics design	→			○		○		●					MS2.3
MS2.2	Preliminary Monte Carlo simulations for mechanics and detector design	→		○					●					MS2.3
MS2.3	Detector characterization and test with fluorescence							→	○				●	MS4.4

Activity planned for second semester 2025:

- complete the assembly of the electronic board with O(4) chips
- finalize the communication and DAQ software
- finalize the step-motor control software and image-reconstruction software
- more experimental test with cell cultures in slides and scaffods and fluorescence imaging comparison

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LABORATORI NAZIONALI DI LEGNARO

Thank you for your attention!

BACKUP

INFN-PD – budget for 3nd year

		Requested [k€]	Granted [k€]
Consumables	**Mechanics**	1	-
	Electronics	4	-
Shipping	Shipping of detectors from PD to test sites in Italy	2	-
Travels	Travels for experimental activity	4	-
TOTAL INFN-PD		**16**	-

Anagrafica 2024: M. Lunardon **0.6**, S. Moretto **0.1** , P.Lotti **0.3**, L. Zangrando **0.2**, Chiara Bonini (PhD) **0.5,** Daiyuan Chen (PhD) **1.0**, Jessica Delgado Alvarez (Assegno) **1.0**

TOT = 3.7 FTE

Anagrafica 2025: M. Lunardon **0.5** (0.2 in SPES_MED), S. Moretto **0.1** (0.5 in SPES_MED) , Jessica Delgado Alvarez (Assegno) **1.0 +** possibile percentuale parziale di dottorando elettronica nel corso del 2025

TOT = 1.6 FTE

Collaborano inoltre: Piero Giubilato, Michele Giorato

Richieste servizi: 2/3 M.U. officina elettronica per realizzazione scheda, chip bonding e altre operazioni (TBD next con Marino)