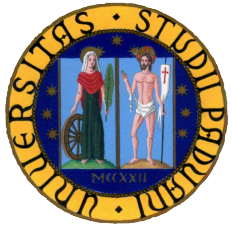
Stato e preventivi di spesa esperimenti gruppo 5



Gabriele Simi – Università di Padova e INFN

05.07.2024

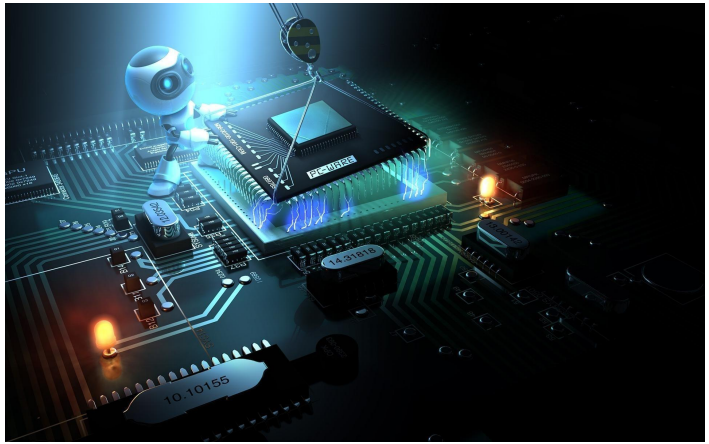
INFN
Istituto Nazionale
di Fisica Nucleare

Overview

- Tipologia esperimenti, presentazione proposte, missioni
- Storico Fondi e anagrafica
- Esperimenti già conclusi
- Esperimenti in continuazione
  - Computer science
  - Elettronica
  - Rivelatori
  - Fisica Interdisciplinare, Medicina

La Commissione 5

La CSN5 coordina le ricerche tecnologiche e lo sviluppo di applicazioni e promuove l'utilizzo, In altri settori, di strumenti, metodi e tecnologie della fisica fondamentale. L'INFN è un solido riferimento a livello nazionale e internazionale per lo sviluppo dei futuri prototipi e la realizzazione degli odierni acceleratori di particelle. Questi sono utilizzati, oltre che nelle ricerche di fisica fondamentale, in altri campi di ricerca e della vita economica e sociale.



- **Acceleratori di particelle**
- **Rivelatori di particelle**
- **Elettronica e software**
- **Applicazioni interdisciplinari della tecnologia INFN**

1. Applicazioni mediche
2. Energetica
3. Ambiente
4. Beni culturali

Tipologie di esperimenti
Presentazione proposte

Reminder

Tipologie di esperimenti

- Sigle Standard: progetti di 2-3 anni a budget medio-basso (≀ 50k€/y).
  - Incubatori di attività e idee promettenti e interessanti per l'Ente.
  - Supporto ad attività di più ampio respiro di altre commissioni.
  - Possono avere livelli di rischio elevati.
- Grant Giovani: Esperimenti (max 75k€/y) di 2 anni per giovani (PhD ≤ 6y). Viene finanziata l'attività sperimentale e l'AdR del PI.
  - Supporto per giovani ricercatori che presentino idee originali.
  - Supporto all'autonomia scientifica e alle capacità direzionali.
  - NOTA: riaperti i termini di presentazione delle domande (solo 7 domande per 6 grants)
- Call: Progetti ad alto budget e ampio network (≀1M€ max su 3y da bando).
  - Supporto alla formazione di network ampi per progetti di frontiera su argomenti strategici.
  - Finanziamento di Assegni di Ricerca.

Modalità Presentazione nuove proposte

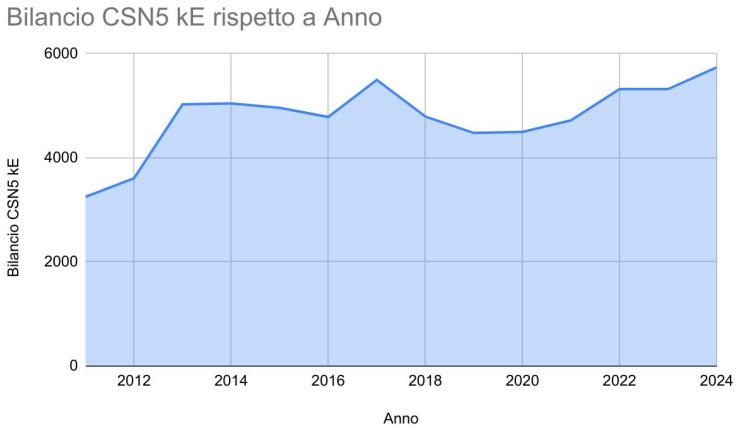
- Modalità di presentazione progetto
  - Template progetto disponibile su sito CSN5
  - presentazione progetto entro 14/7 tramite caricamento in database
- Criteri di valutazione proposte rivisti nel 2023
  - Valutazione nella riunione di luglio
  - Presentazione da parte del coordinatore di 5 slides (titolo e proponenti, introduzione, obiettivi, metodi, numeri - soldi e FTE)
  - Criteri di valutazione da parte della sottocommissione:
    - Impatto scientifico e sugli interessi dell'Ente
    - Chiarezza degli obiettivi e delle metodologie
    - Congruità economica e delle risorse
  - Punteggio
    - ogni voce 10pt, max 30.
  - Sufficienza
    - minimo 5pt per ogni voce, altrimenti cassato

Modalità Presentazione nuove proposte

- Referaggio a settembre
  - Due o tre referee di cui uno della commissione
  - Obbligatoria riunione con i referee prima della riunione della CSN5 per discutere criticità e rimodulazione finanziaria
  - Presentazione plenaria da parte dei proponenti con richieste finanziarie finali
- Criteri di valutazione referaggio
  - Stessi criteri/punteggio/sufficienza della slide precedente
  - Approvazione in base alla classifica/budget suddivisi per aree (Rivelatori, Acceleratori, Interdisciplinare)

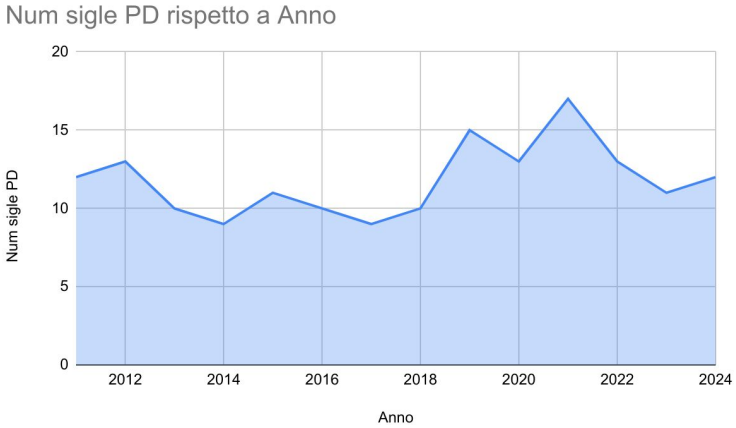
Storico Fondi e Anagrafica

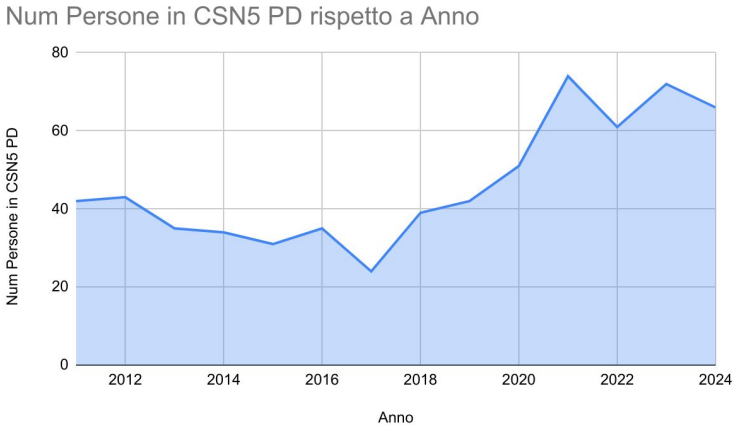
Storico Fondi CSN5 e Sigle a Padova



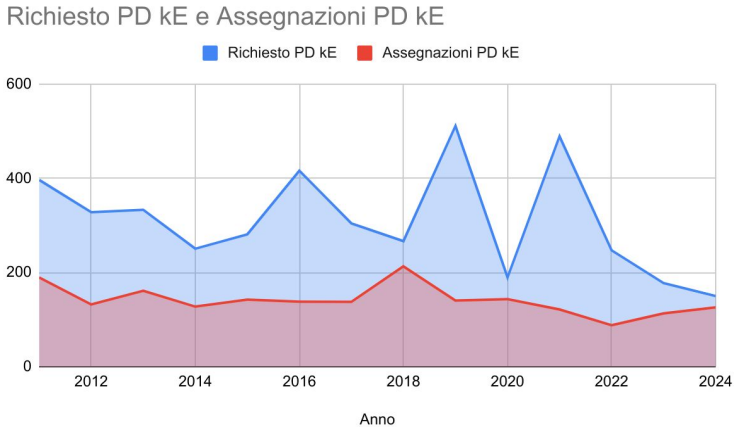
Negli ultimi 5 anni

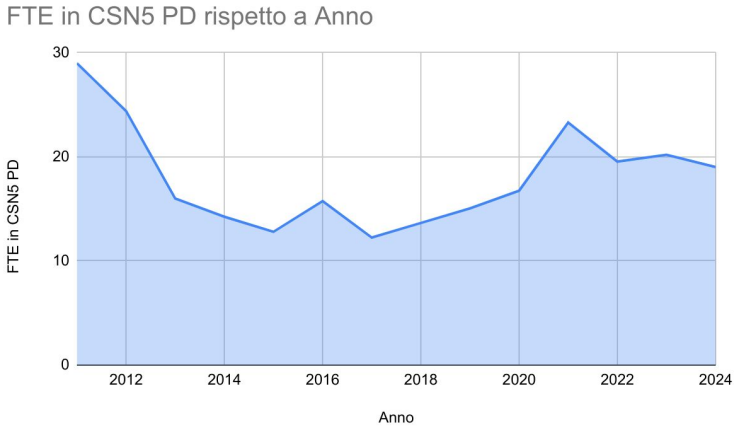
- Fondi CSN5: 5.1ME
- Numero sigle a PD: 13





Storico Fondi e Anagrafica CSN5 a Padova





Negli ultimi 5 anni

- 13 esperimenti/anno
- 19 FTE(66 Persone)/anno
- 120 kE/anno assegnati a PD
  - 6kE/FTE o 1.8kE/Persona

Nel 2024

- 83% FTE Università + altri enti, 17% Dipendenti INFN

Riassunto Sigle

In Chiusura	NEXT_AIM	Zucchetta	23,24	
	N3G	Recchia	22,23,24	
	PHYDES	Carugno	22,23,24	DEMIURGOS
	HISOL	Pepato	23,24,25	
In Continuazione	ADA_5D	Collazuol	23,24,25	ASAP
	ADMIRAL	Lunardon	23,24,25	ISOLPHARM_EIRA
	AI_INFN	M. Verlato	24,25,26	ML_INFN
	CUPRUM_TTD	L. De Nardo	23,24,25	REMIX
	FEROCE	Triossi	23,24,25	
Nuove Proposte	DOCET	Carugno		
	ASPIDES	Collazuol		
	MEDIPIX4.2	Collazuol		
	SPECO-PICO	Pisano		
	SQUEEZ	Zendri		
	HISOL_NEXT	Rebesan		

Computer science

AI_INFN progress report

27/6/2024

Marco Verlato

Obbiettivi del progetto AI_INFN (2024-2026)

Raccogliere **l'eredita` di ML_INFN** in termini di comunita`, hardware e software...

- ML_INFN nasce nel 2020 con l'obiettivo di sviluppare una visione di sistema dell'applicazione di tecniche di ML alla ricerca scientifica nei vari settori rilevanti per l'INFN

... per costruire un modello di calcolo in grado di soddisfare maggiore domanda e scalare agevolmente in vista di una piu` ampia disponibilita` ed **eterogeneita`** di risorse —> vedi ad es. Progetto PNRR Terabit

Potenziare il supporto ai molti eventi di livello base organizzati dall'INFN e dalle Universita`, concentrando la propria azione sullo sviluppo di **materiale audiovisivo (webinar)** ed eventi di aggiornamento di tipo Advanced **Hackaton**

Formare un nuovo **WP** dedicato allo studio di **futuri acceleratori** per le attivita` di ML, in particolare **FPGA** e processori quantistici

Quasi tutte le sezioni INFN coinvolte

Terabit – HPC Bubbles (in arrivo a Luglio)

Nodo CPU	Min 112 core fisici (max 192) RAM > 8GB/core DDR5 IB NDR 400G 20TBL + dischi di sistema
Nodo GPU	Come CPU + 4x NVIDIA H100 SXM5 con minimo 80GB e memoria HBM2e
Nodo FPGA	Min 32core RAM > 512GB DDR4 o DDR5 IB NDR 440G 4 x XILINX U55C o 4 x TerasicP0701
Nodo Storage (CEPH Bricks)	Min 48core fisici RAM >512GB DDR4 o DDR5 Almeno 360 TBL HDD + 12TBL SSD
Accessori	Switch IB, Switch ETH Cavi IB, Cavi ETH Transceiver vari Assistenza 3+2

In particolare, lato Infrastruttura

- Nel modello attuale della cloud le VM connesse a GPU sono assegnate in modo esclusivo a determinati progetti
  - ✔ E' Necessario superare questo limite

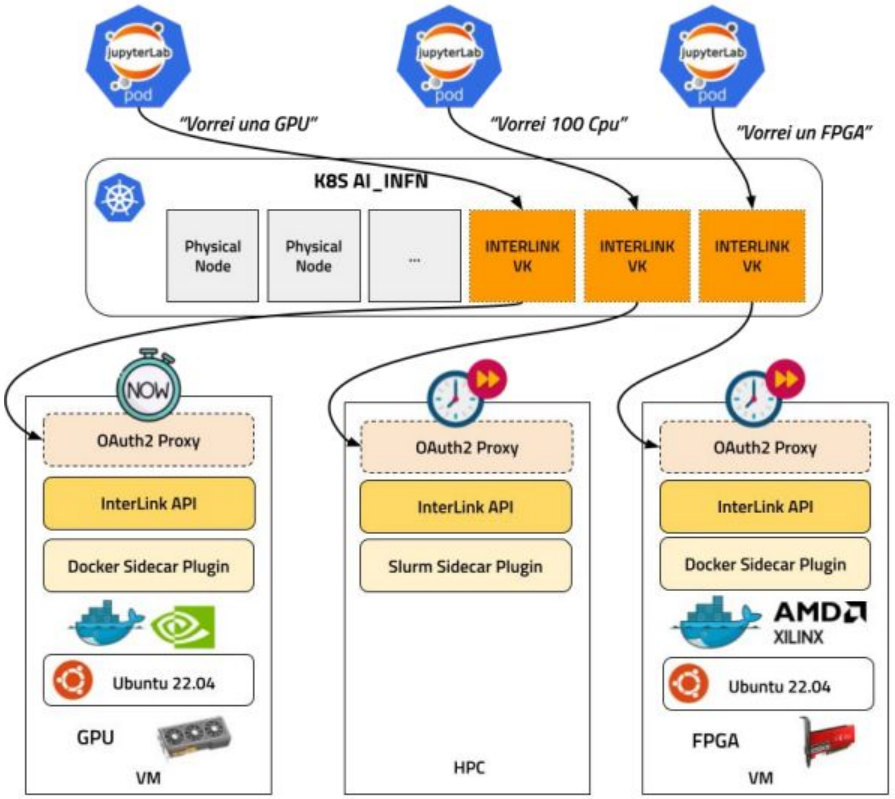
- Un nuovo modello basato sui container e` allo studio per:
  - ✔ abilitare il "resizing" delle risorse assegnate ad un progetto
  - ✔ riassegnare GPU altrimenti inutilizzate per lunghi periodi
  - ✔ abilitare un tuning piu` dinamico del n. di CPU core per GPU
  - ✔ abilitare l'uso opportunistico di risorse da parte di code batch
  - ✔ implementare soluzioni di autoscaling (dispiegamento automatico di VM)
  - ✔ ridurre il numero di utenti forzati ad amministrare la propria VM

Cos'è un Container?

- Un livello di virtualizzazione intermedio (semplificato) rispetto alla virtual machine
- L'Applicazione è eseguita in un ambiente isolato ma si appoggia cmq sul kernel del sistema operativo

Sinergie con attivita' R&D di INFN-DataCloud

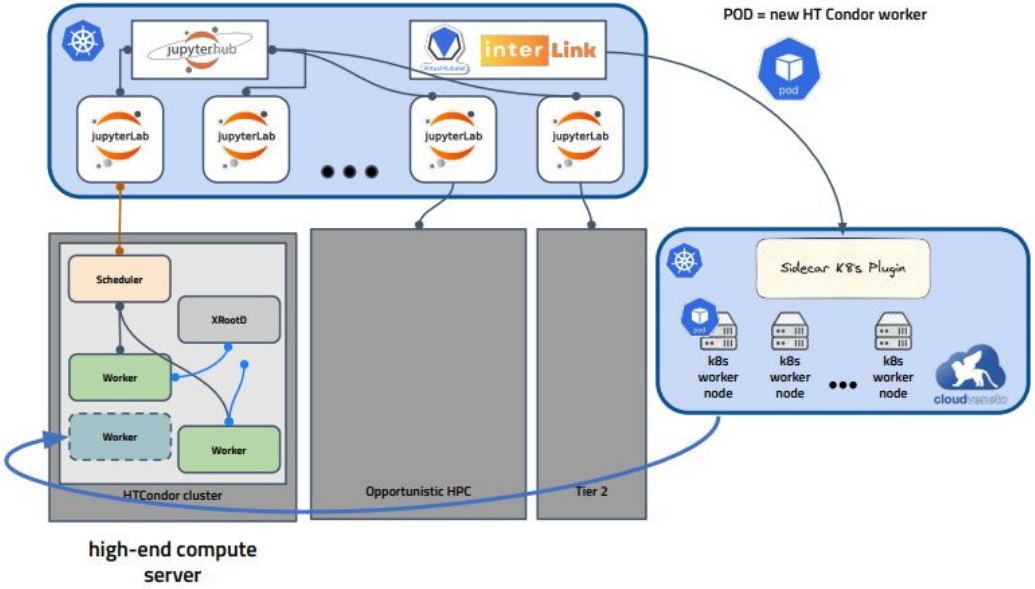
- Sinergia con INFN-DataCloud nello sviluppo di sistemi per testare ed eventualmente validare sia il modello che l'implementazione
- Rendere trasparente e agile l'uso di risorse disponibili con diversi backend
- La piattaforma AI_INFN offre uno use case complesso per InterLink
  - Svilppo di plugin Docker e Kueue



Integrazione col servizio CaaS di CloudVeneto

L'integrazione con il Cloud Veneto avviene attraverso plugins come JupiterNotebook

E' stato sviluppato il **plugin sidecar kubernetes**. Il POD sottomesso al VK del cluster k8s della Analysis Facility diventa un worker node che si aggiunge al pool centrale HT Condor sfruttando le risorse di un cluster K8s che utilizza risorse di CloudVeneto.



Stato

- **Workflow completamente funzionante.**
  - nel pool condor vengono aggiunti dei nodi CloudVeneto che possono essere utilizzati per mandare job condor
  - Molteplici VK coesistono nello stesso k8s di AF e fanno offloading su diversi provider:
    - VK dedicato al tier2 di Legnaro, Bari e Pisa (HTCondor sidecar)
    - VK dedicato al tier2 di Roma (ARC sidecar)
- **Sidecar plugin k8s**
  - Supporta provisioning di CVMFS

Stato dell'implementazione della piattaforma

Feature	Proof of concept	Beta-tested in hub.ai	Available for all users*	Ready for DataCloud
Interactive development (GPU)	2023-05-18	2023-12-13	2024-03-08	⏳
User-defined environments	2023-05-18	2024-04-22	2024-06-03	⏳
Interactive develop. (QC/FPGA)	*QC coming soon*	⏳	⏳	⏳
Monitoring & Accounting	2024-03-18	2024-04-22	2024-05-13	⏳
Group-specific resources	2024-04-22	2024-04-22	*upon review*	⏳
Batch job submission	2023-12-19	2024-04-18	*coming soon*	⏳
Offloading towards Kueue	2024-05-16	2024-05-27	⏳	⏳
Offloading to Docker (GPU)	*coming soon*	⏳	⏳	⏳

Documentazione in: https://ai-infn.baltig-pages.infn.it/wp-1/docs/

CSN5 Ricerca Tecnologica

1° AI_INFN User Forum 11-12 Giugno a Bologna

Welcome and introduction — *Lucio Anderlini*
Room BP-2B, Plesso Berti Pichat — 14:30 - 14:40

INFN-CNAF: status and perspectives — *Luca Dell'Agnello*
Room BP-2B, Plesso Berti Pichat — 14:40 - 15:00

Enhancing Nodule segmentation Utilizing Attention U-Net: Insights from LUNA-16 Dataset — *Arman Zafaranchi*
Room BP-2B, Plesso Berti Pichat — 15:00 - 15:25

Use of a UNet network for the identification of cavities inside mines — *Mr Andrea Paccagnella*
Room BP-2B, Plesso Berti Pichat — 15:25 - 15:50

Benchmarking image segmentation on AMD-Xilinx FPGAs — *Ms Valentina Sisini*
Room BP-2B, Plesso Berti Pichat — 15:50 - 16:15

Coffee break
Room BP-1A, Plesso Berti Pichat — 16:15 - 16:45

HERD data classification — *Luca Tabarroni*
Room BP-2B, Plesso Berti Pichat — 16:45 - 17:10

Virtual Painting recoloring using Vision Transformer on Deep Embedded X-Ray Fluoresce synthetic dataset
Alessandro Bombini

First Stages on Spectral Classification using Synthetic Datasets. — *Fernando Garcia-Avello Bofias*
Room BP-2B, Plesso Berti Pichat — 17:35 - 18:00

AI-based approach for provider selection in the INDIGO PaaS Orchestration System of INFN Cloud — *Luca Giommi*
Room BP-2B, Plesso Berti Pichat — 09:15 - 09:40

Leveraging RAG Architecture for Effective Email Response Automation: a CNAF Tier-1 User Support use case
Alberto Trashaj

10:00

Transformer-based models for scientific text classification — *Giovanni Zurlo*
Room BP-2B, Plesso Berti Pichat — 10:05 - 10:30

Coffee break
Room BP-1A, Plesso Berti Pichat — 10:30 - 11:00

11:00

Multi-scale cross attention transformer encoder for τ lepton pair invariant mass reconstruction — *Valentina Camagni*
Room BP-2B, Plesso Berti Pichat — 11:00 - 11:25

Hyperparameter Optimization for Deep Learning Models Using High Performance Computing — *Muhammad Numan Anwar*
Room BP-2B, Plesso Berti Pichat — 11:25 - 11:50

12:00

Quantum Machine learning frameworks for charged particle tracking — *Laura Cappelli*
Room BP-2B, Plesso Berti Pichat — 11:50 - 12:15

Final remarks and closing — *Elisabetta Ronchieri*
Room BP-2B, Plesso Berti Pichat — 12:15 - 12:30

https://agenda.infn.it/event/40489/overview

1° Advanced Hackaton a Padova in Novembre?

Day 1	Day 2	Day 3	Day 4
	Lectures: Introduction to Autoencoders	**Lectures**: Solving diff. eq. with ML	**Lectures**: ML in Medicine, QML in HEP, etc.
	Lectures: Introduction to Transformers	**Lectures**: Introduction to CNN and U-Net	**Lectures and closing**

Lunch Break

Lectures: Infrastructure and AI_INFN platform	Hackatons 1 & 2	Hackatons 3 & 4
Lectures/ Hands-on	Hackatons 1 & 2	Hackatons 3 & 4

Formato simile a quello di Pisa tenutosi nel
Novembre 2023:

https://agenda.infn.it/event/37650/overview

Elettronica per Rivelatori

INFN PADOVA
Istituto Nazionale di Fisica Nucleare
Sezione di Padova

INFN LNL
Istituto Nazionale di Fisica Nucleare
Laboratori Nazionali di Legnaro

FEROCE

Front-End Rdma Over Converged Ethernet

Area di ricerca: Rivelatori, Elettronica, Calcolo

Responsabile nazionale: Andrea Triossi (Unipd – INFN Padova)

Unita partecipanti: INFN sezione di Padova
Laboratori Nazionali di Legnaro

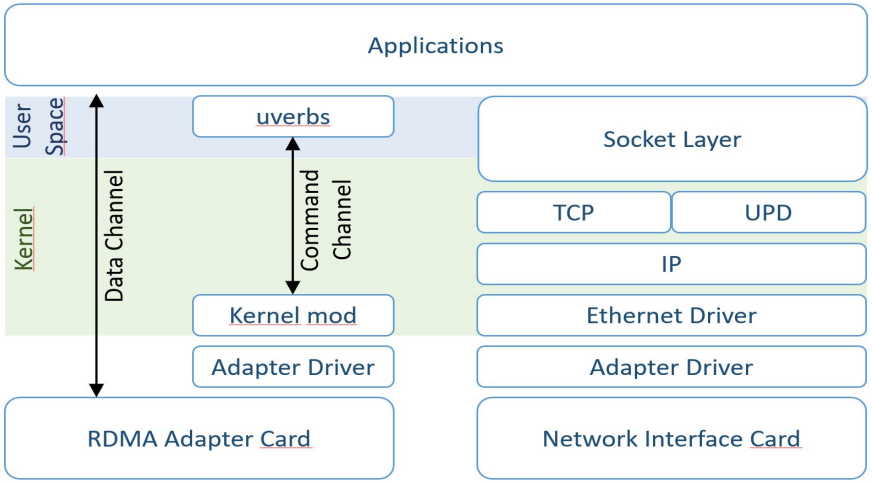
Objectives

Processing power is important as an efficient data movement

In a DAQ system a large **fraction of CPU** is engaged in networking

- Data manipulation (several copies)
- Latency increase and throughput reduction

Zero-copy is obtained by adding RDMA layer to the network stack



- **FEROCE wants to move the adoption of the network protocol to the data producer**
  - Front-end initiates the RDMA transfer
  - No point-to-point connection between front-end and back-end
  - Dynamical switching routing according to node availability

Methodology

Several network stacks implementing RDMA

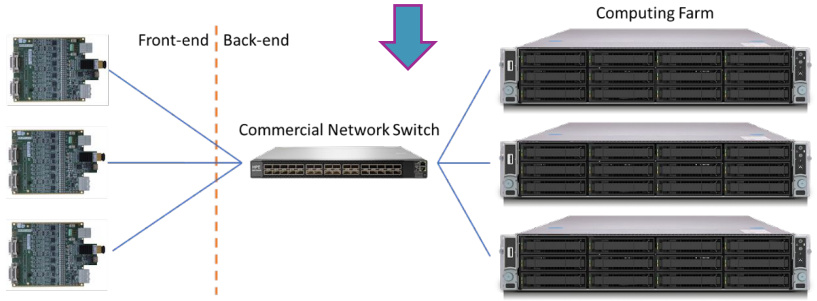
- InfiniBand, RoCE, iWARP…

RoCE (RDMA over Converged Ethernet)

- Based on Ethernet networks
- Industry-standard
- Multi-vendor ecosystem
- RoCE v2 packet switching (layer 2 and 3)

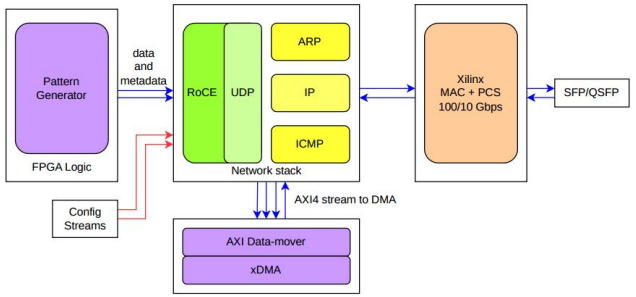
FPGA are already used for implementing network stacks

- Data center
- ATLAS



Attività

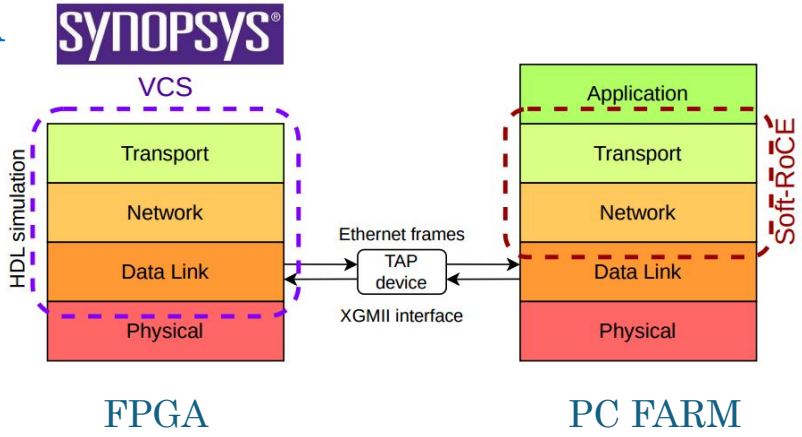
- Studio delle librerie esistenti
  - Librerie Opensource
    - ETH Zurich Network Stack
      - Scritto interamente in HLS
      - 10/100 Gbps via Xilinx 10G and 100G MAC IPs
      - xDMA, DDR4 memory and recently HBM support



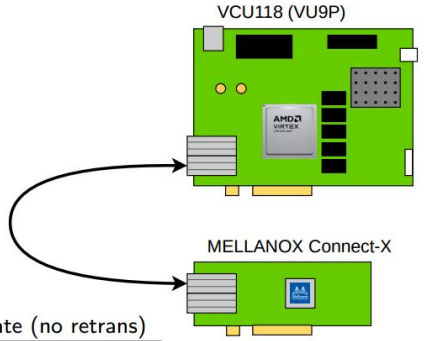
- Esempio di scrittura RMDA da FPGA
  - Generate the Queue Pair parameter from the receiver side and allocate memory
  - Send such parameter to FPGA on a sideband channel (e.g. ipbus/TCP-IP)
  - Pack the parameters in the configuration AXI streams ports
  - Stream data through the data AXI stream port
  - Notify somehow the receiver that the transfer is completed (Immediate message/sideband)
  - Dump the buffer

Simulazione e implementazione Hardware

- Test con simulazione SW della FPGA e del ricevitore (PC FARM)
  - RoCE firmware simulator sends data to Soft-RoCE end-point
  - RDMA WRITE tested successfully with a 10G MAC
  - Results presented at two international conferences TIPP and TWEPP: proceeding here

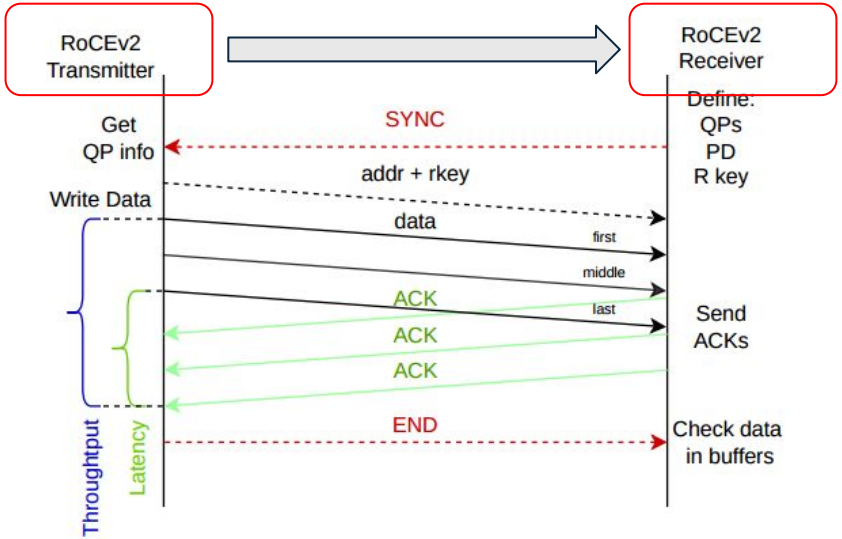


- Implementazione Hardware
  - UDP and TCP stacks deployment on VCU118
  - RoCE v2 stacks deployment on VCU118
  - Occupancy nella FPGA



RoCEv2 (no retrans)			TX only estimate (no retrans)		
LUT [k]	FF [k]	BRAM	LUT [k]	FF [k]	BRAM
38	49	93	~ 15	~ 15	~ 30

Misura della Latency and throughput



Transfer size	Throughput [Gbps]	Latency [μs]
8 kB	30.7	1.6
32 kB	62.8	2.3
64 kB	73.3	3.1
128 kB	80.5	3.3
512 kB	92.9	12.4
5.12 MB	95.8	12.4
51.2 MB	96.0	12.4
512 MB	96.0	12.4

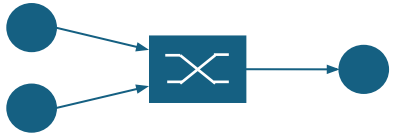
Altre attività legate al networking

- Scrittura con RDMA da una virtual machine a un'altra
- Stessa operazione tra due server reali
- Misura della velocità: 95Gps

Ongoing efforts

Congestion tests on a 10G network

- Two senders / one receiver link saturation
- Flow Control or RoceV2 congestion management throttle the sender without triggering retransmission



- Next steps
  - Repeat tests on a 100G network (Nvidia switch received)

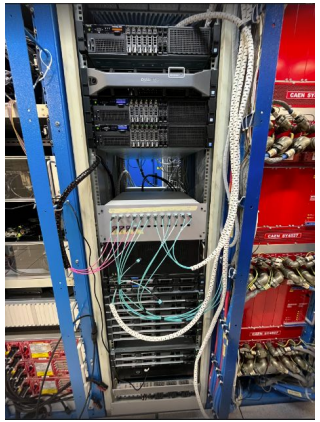
Rewrite RoCE TX module at RTL, only for RDMA WRITE (with immediate)

- Open-source network stack for low level layers (UDP, IP, ARP…)
- Tested in dynamic simulation towards soft-ROCE
- GitHub code
- Talk accepted at CHEP 2024
- Next steps
  - Add re-transmission module (depending on 100G congestion test)
  - Rewrite RoCE RX module at RTL, to decode ACK/NACK/CNP packets
  - Porting of the ROCE network stack on Microchip FPGA (evaluation board received)

Prospective applications

CMS (CSN1)

- L1T Scouting is a project aiming at acquiring the L1 primitives at the full bunch crossing rate
- It is meant for HL-LHC but a demonstrator based on commercial electronic is already deployed
- At present as DAQ link it adopts a light version of the TCP/IP protocol at 100G



Project organization

Two working package

- WP1 Front-end firmware core
- WP2 Application layer and emulation

Four milestones

DONE
- ~~31 Dec 2023~~ M1.1 Setting up of a global-oriented simulation environment for a small appliance of the RoCE stack (WP1)

DONE
- ~~31 Dec 2023~~ M1.2 Testing a RoCE network based on COTS products (WP2)

ON TRACK
- 31 Dec 2024 M2 Complete test of the scalable RoCE firmware stack for front-end (WP1+WP2)

- 31 Dec 2025 M3 Complete test of the developed firmware on a radiation tolerant front-end FPGA (WP1+WP2)

		2023			2024			2025		
		Q1	Q2	Q3	Q1	Q2	Q3	Q1	Q2	Q3
WP1	Front-end firmware core	Development light RoCE		Simulation light RoCE	Implementing different data paths		Test FE RoCE on network	Porting to flash technology		Test on flash FPGA
WP2	Application layer and emulation	Soft RoCE	Setting up RoCE	Test of RoCE network	Acquisition system		Test FE RoCE on network	GPUdirect	Test of GPUdirect	Test on flash FPGA

Research group

Padova

- Marco Bellato (0.1)
- Antonio Bergnoli (0.2)
- Gabriele Bortolato (0.3)
- Daniele Mengoni (0.15)
- Matteo Migliorini (0.3)
- Fabio Montecassiano (0.2)
- Jacopo Pazzini (0.15)
- Andrea Triossi (0.3)
- Marco Zanetti (0.1)

LNL

- Damiano Bortolato (0.15)

Total FTE: 1.95

Richieste

Anno	Missioni	Inventariabile	Consumo	Totale
2025	**1.5**	**10**		**11.5**

La parte di inventariabile è dettagliata come segue:

2025 1x GPU NVIDIA 10kE

Rivelatori

ADA_5D

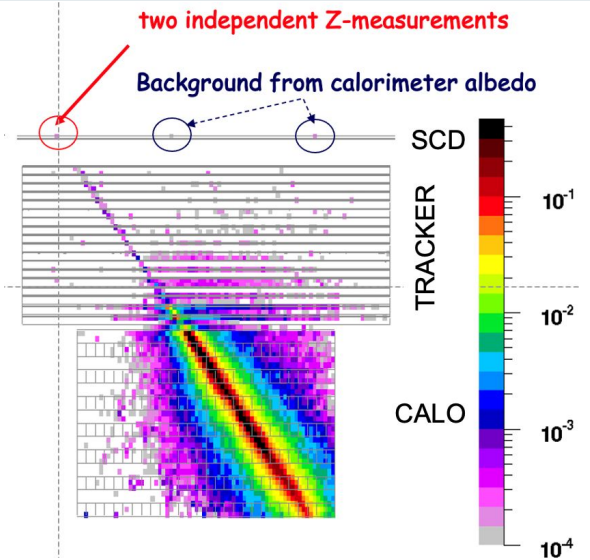
Charge & Timing **5D detector** (x,y,z, charge, time) based on **LGAD sensors** for the next generation of multi-TeV calorimetric experiments in space

CHARGE IDENTIFICATION of cosmic-ray ions with charge $1 \leq Z \leq 30$ via multiple dE/dx $\propto Z^2$ in a pixelated sub-ns **Charge-ToF detector** (SCD)

Backscattering (BSC) from calorimeter generates fake hits in SCD and tracker, degrading charge-ID as energy increases.

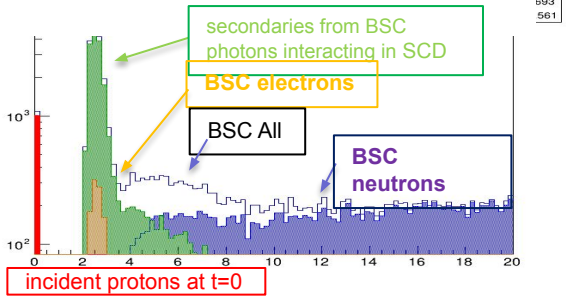
ADA_5D concept: BSC rejection with a high resolution ToF measurement

- large dynamic range > 1000 m.i.p
- 100 ps time resolution (e.g. for 20 cm flight path)
- large pixels (3mm x 3mm) to cover large O(m^2) sensitive area
- indipendent TRACKER for fine track resolution
- challenging power budget < 150 W/m^2
- modest Rad Hardness required in space < 10^{11} 1 MeV neq



simulation of 1 TeV incident carbon nucleus

Arrival time (ns) of BSC from calorimeter on SCD:
a GEANT4 simulation with 30cm flight path



Avalanche Diodes Array – ADA-5D

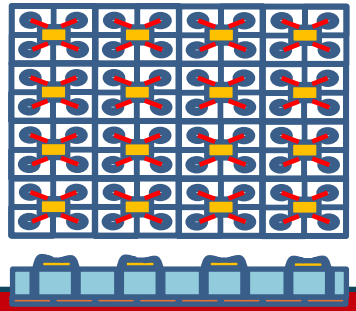
University of Pisa & INFN **Pisa** / University of **Siena** & INFN Pisa
University of Padova & INFN **Padova** / University of **Pavia** & INFN Pavia
University of **Trento** & **TIFPA** / Fondazione Bruno Kessler **FBK** (Trento)

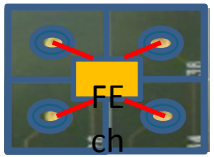
G.Collazuol
INFN Padova
CdS 2024/7/5

Development thick LGADs and related large dynamic range electronics

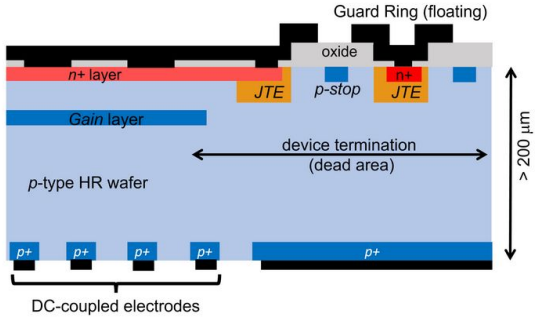
- large pixels (3mm x 3mm)
- sensor thickness 200-300 um

mini-TILE (2.4cm x 2.4 cm):
16 FE = 8 x 8 LGADs





Example of thick LGAD implementation

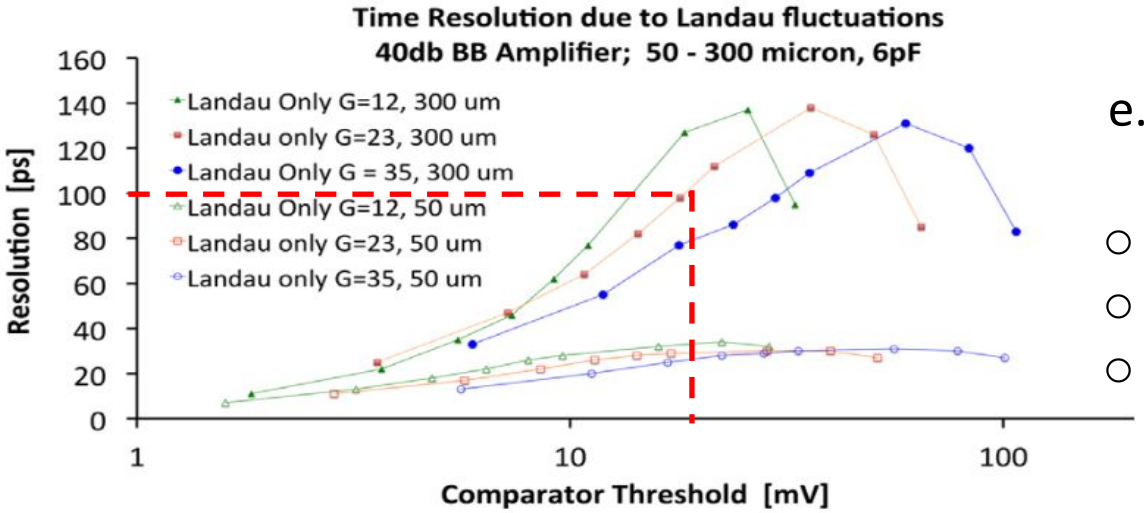


Each FE chip, connected to 4 LGADS, implements:
- double gain linear range to cover > 1000 m.i.p.
- internal ADC
- internal TAC + ADC conversion
- Track & Hold

Gain and Time resolution

with G ~ 10-20 dominant term in time resol. is the Landau tails jitter

~ 100ps feasible with a low threshold (ok as S/N>30 for 1 m.i.p)



e.g.: 100 ps resolution with:

- 300 um thickness
- G=23
- threshold ~ 20 – 30 mV

Nuclear Instruments and Methods in Physics Research A 845 (2017) 47–51

Activities in 2024

- **TIFPA** - caratterizzazione laser IR di campioni LGAD FBK con spessore 275um
- **Pisa** - ottimi risultati con CR muons tests con elettronica di r/o APIX/ASAP
- **Pavia** – completata produzione prima versione ASIC di FE (TAC, no ADC) => sotto test
- **FBK -** primo batch di LGAD per ADA_5 in consegna a Luglio 2024
- **Padova**
  - TIMEPIX3 silicon based tracker (only electronics)
  - Padova = 10GHz RF amplifier for single channels readout
- Test Beam @ SPS ions => November 2024

Activities in 2025

- **TIFPA** - caratterizzazione laser IR di campioni LGAD FBK con spessore 275um
- **Pavia** – nuova versione del ASIC con on-chip ADC e interfaccia digitale per R/O
- **FBK -** secondo batch di LGAD
- **Padova**
  - Digital readout fast digital readout board
  - Telescope tracker based on TimePix4
- Test Beam @ SPS ions => November 2025

Resources @ INFN Padova

FTE Padova 2024/7 => 50%

- G.Collazuol 10 %
- M.Feltre 30%
- M.Mattiazzi 30%

Preventivi 2025

- Consumo per circa 10kEuro
- Missioni (CERN) per circa 5kEuro

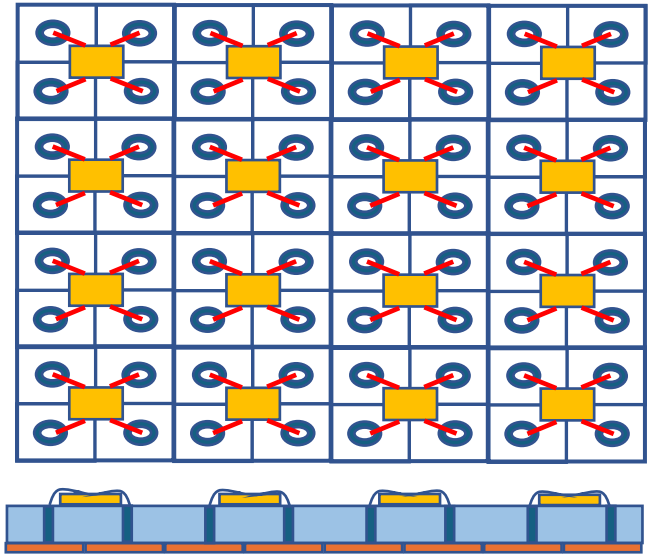
Richieste 2025 in Sezione PD

- Servizio Elettronica
  programmazione FPGA TimePix4+ SiPixels (collab. con INFN FE) ~ 3m.p.
- Servizi Tecnici ed Elettronici
  elettronica ancillare TimePix4 (collab. con INFN FE) ~ 1m.p.
- Servizio Progettazione Meccanica
  disegno setup telescopio (collaborazione con Stefano Levorato) ~ 1m.p.
- Servizio Officina Meccanica
  meccanica telescopio ~ 1m.p.

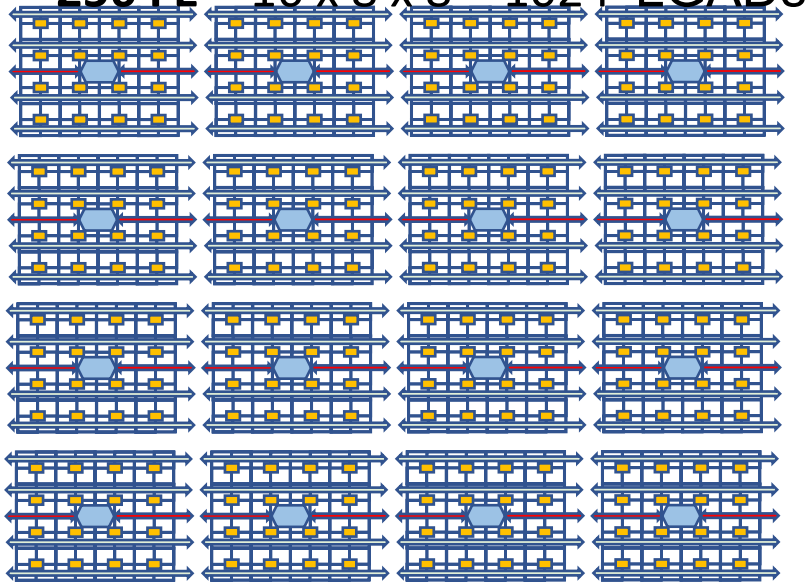
Additional material ADA-5D

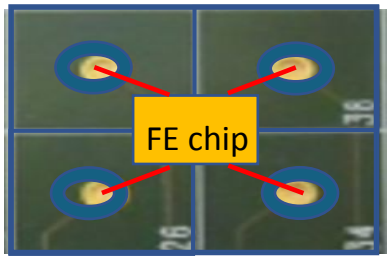
mini-TILE (2.4cm x 2.4 cm): TILE (9.6 cm x 9.6 cm): 16 mini-tiles

16 FE = 8 x 8 LGADs



= 256 FE = 16 x 8 x 8 = 1024 LGADs





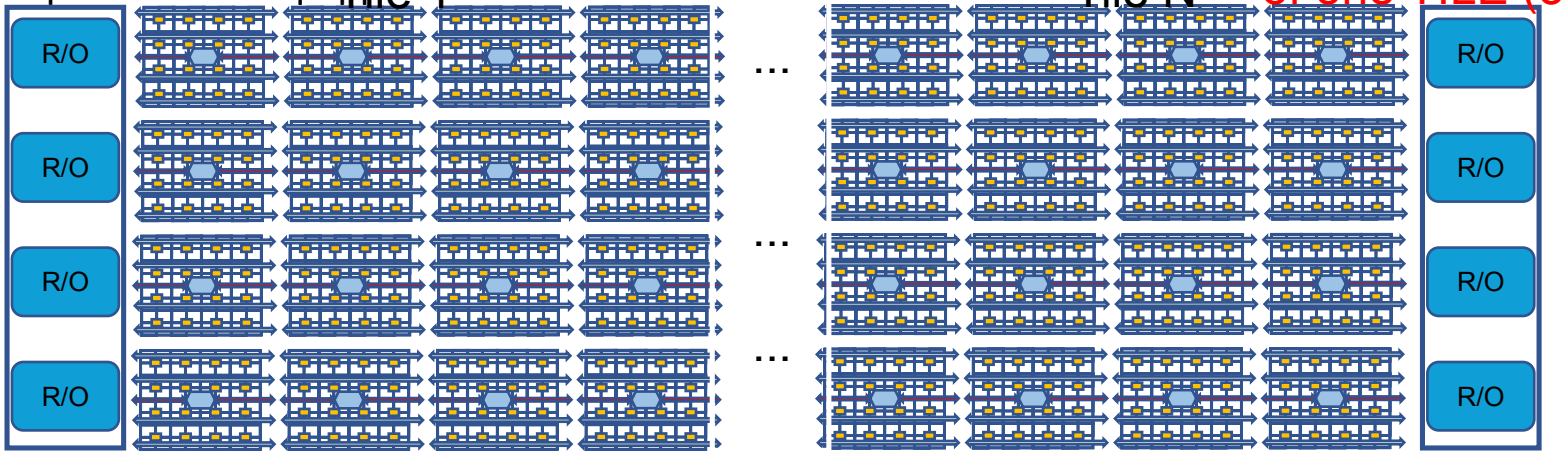
Each FE chip, connected to 4 LGADS, implements:

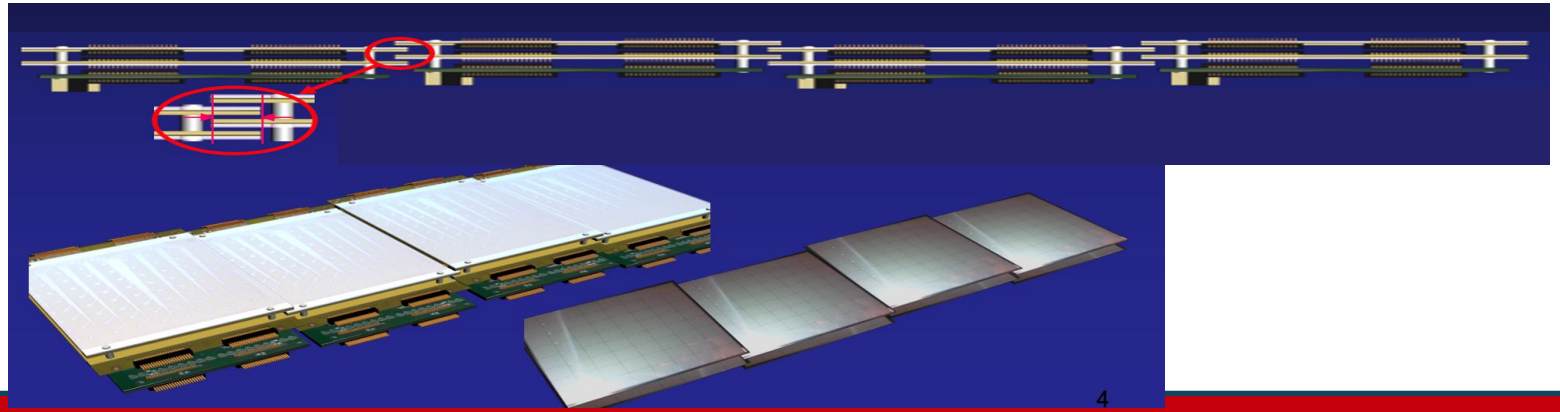
- double gain linear range to cover > 1000 m.i.p.
- internal ADC
- internal TAC + ADC conversion

LARGE AREA DETECTOR concept: N tiles per row x M rows

ADA-5D goal is limited to the development of one TILE (or mini-TILE)

Example of 1 row equipped with N tiles and readout on either side





overlapping staggered layers

Fisica interdisciplinare - Medicina

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.

CSN5 Ricerca Tecnologica

The ISOLPHARM collaboration

INFN 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

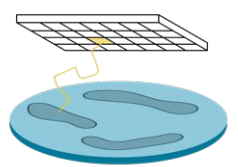
L.E.N.A.

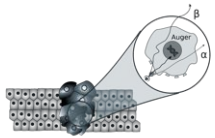
INFN PAVIA

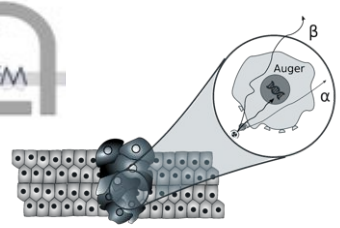
UNIVERSITÀ DEGLI STUDI DI BRESCIA

IBFM

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



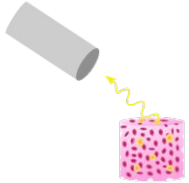




Radiopharmaceutical production

ADMIRAL ISOLPHARM

Radiobiological characterization



Development of a γ-imaging scintigraphic system

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

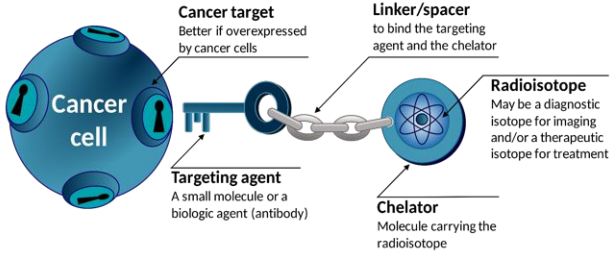
Interdisciplinary WPs: WP1 & WP4

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.

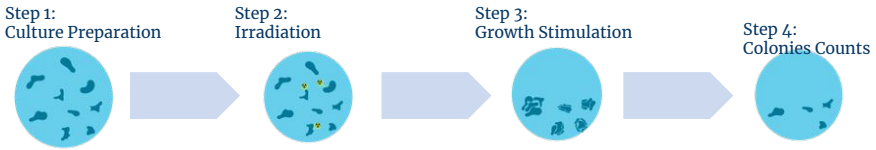


WP4

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**.



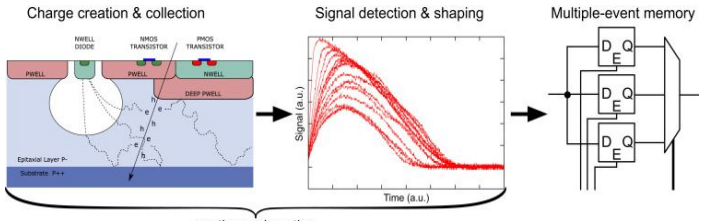
Detector development WPs: WP2 & WP3

WP2

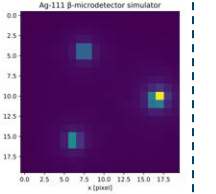
WP Leader: M. Lunardon (UNIPD)

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



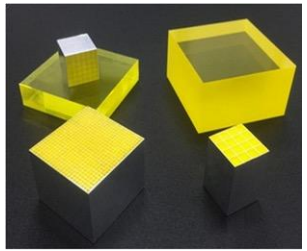
preliminary simulation of a cell distribution beta image

WP3

WP Leader: C. Sbarra (UNIBO)

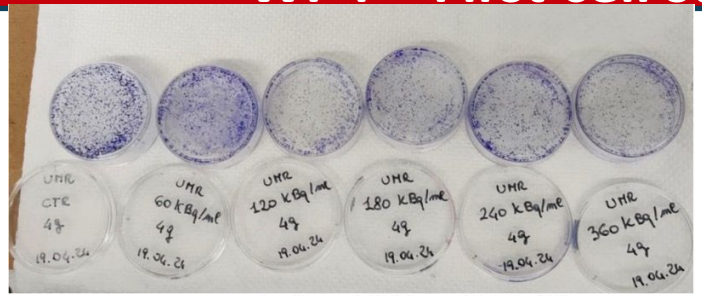
Work Package Aim

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**.

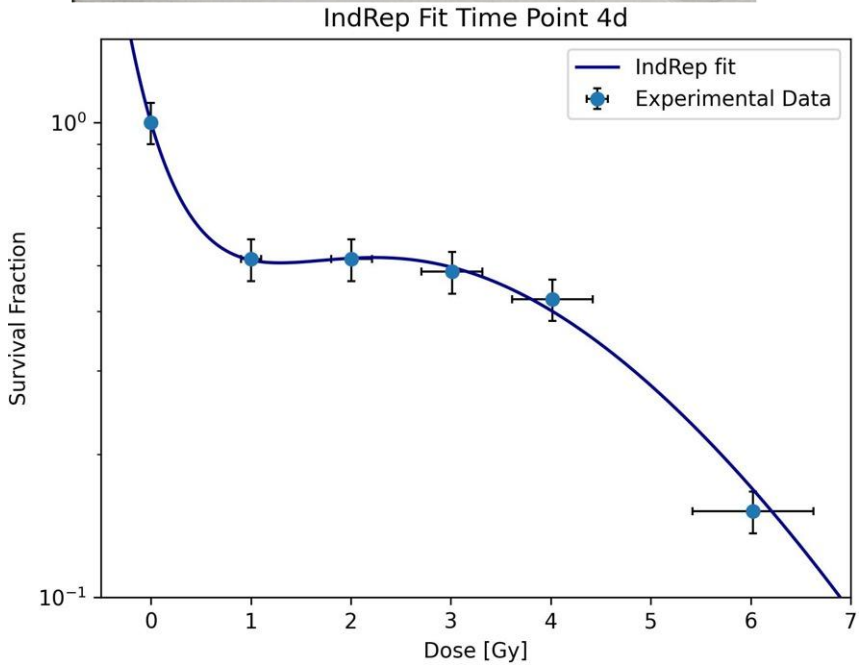


GAGG scintillators in slab and matrix produced by EPIC-Crystals

WP4 – First cell survival test with ^{111}Ag



$$S(D) = exp\left(-\alpha_r \cdot D \cdot \left(1 + \left(\frac{\alpha_s}{\alpha_r} - 1\right) e^{-\frac{D}{D_c}}\right) - \beta \cdot D^2\right)$$

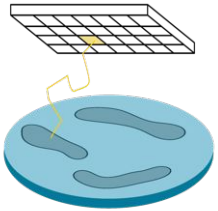


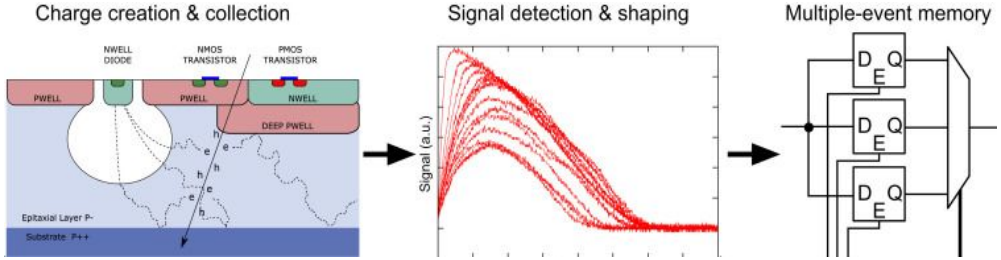
Fit parameters:

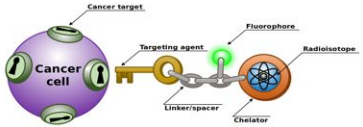
- $\alpha_r = 0.01 \pm 0.11\ ^{1}_{Gy}$
- $\alpha_s = 1.7 \pm 0.4\ ^{1}_{Gy}$
- $D_c = 1.0 \pm 0.3$ Gy
- $\beta = 0.05 \pm 0.02\ \frac{1}{Gy^2}$

the beta-imaging detector at PD: concetto

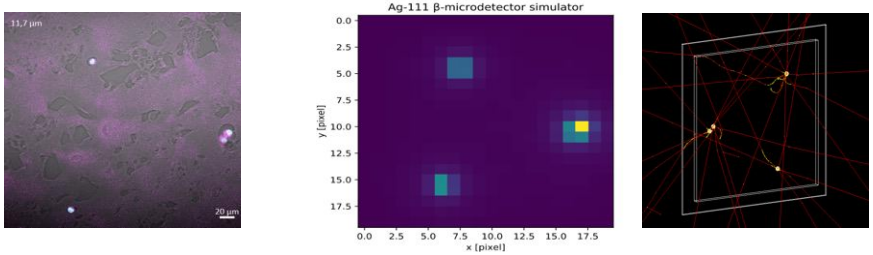
- **ALPIDE chips**: technology from HEP
- 15 mm x 30 mm active area with 512 x 1024 pixels (typical size about 25 um)
- **low-cost** readout electronics using commercial FPGA + custom PCB + dedicated Firmware
- **modular** system, scalable size, compact, easy to use. With 8 chips an active plate of **60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







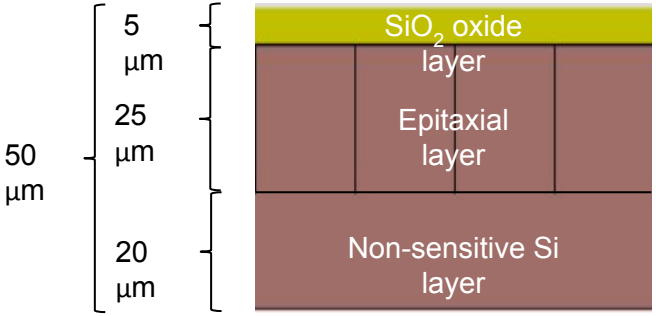
Schematic concept of a bivalent fluorescent radiopharmaceutical.

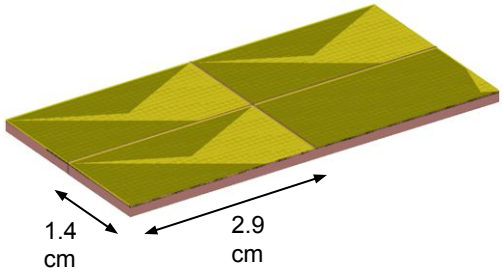


Cell culture in 3D scaffold slice administered with a pharmaceutical: fluorescence confocal microscopy (unlabeled) vs β-microdetector simulation using Geant4 (labeled with ^{111}Ag; pixel size 20 µm, noise 12%, 10^6 CCK2 receptors [26], detector distance 10 µm).

ALPIDE Modelling

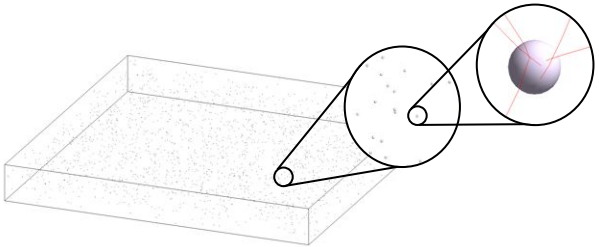
ALPIDE: silicon detector *developed for* ***particle tracking*** *in ALICE (CERN). It is made of 1024x512 sensitive pixels of size (28x28) μm².*

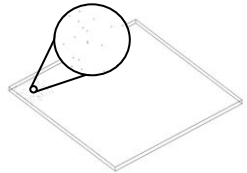


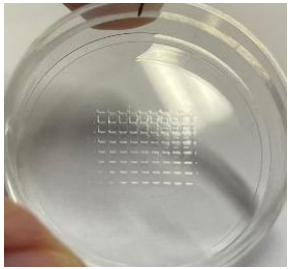


Source Modelling

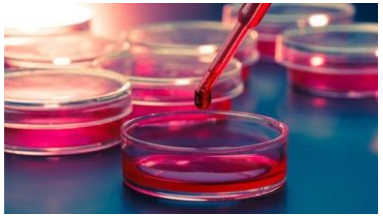
Radiation source: Scaffold → Aqueous spherical cells (10 μm *radius) dispersed in hydrogel matrix. Inside the cell volume,* ***^{111}Ag*** *undergoes β decay.*







→ **Scaffold**
- different geometries
- different substrates

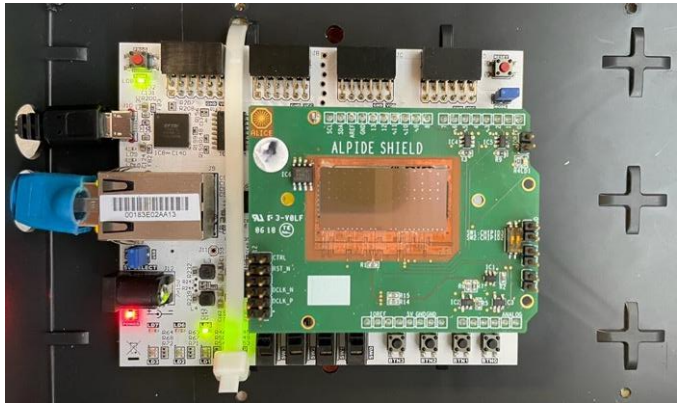


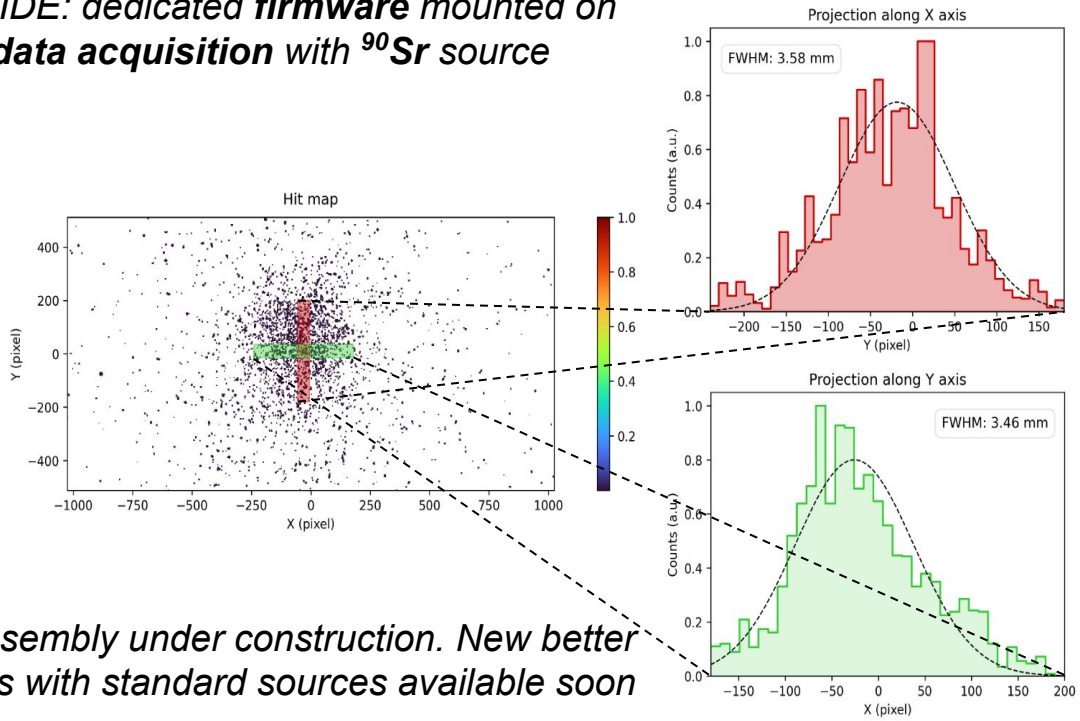
→ **Traditional cell culture**
- Petri dish
- Mylar (or other materials) substrate

first measurements with ALPIDE (2023)

Necessita
Migliore
Collimazione

*First measurements conducted with ALPIDE: dedicated **firmware** mounted on the detector and carried out preliminary **data acquisition** with ^{90}**Sr** source (roughly collimated).*

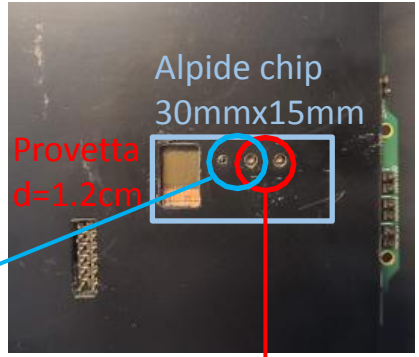


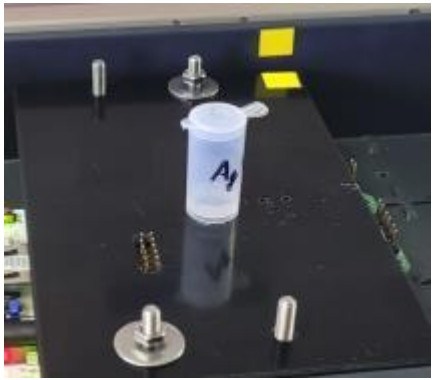


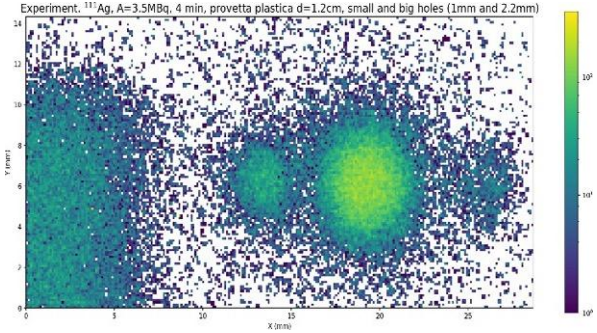
New more precise assembly under construction. New better images with standard sources available soon

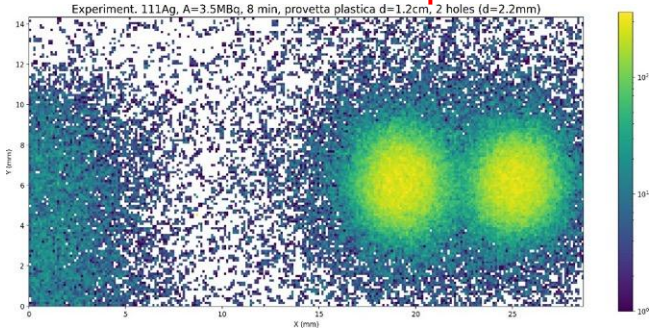
the beta-imaging detector at PD: misura con Ag

- Measurement performed with ^{111}Ag A=3.5 MBq, inside a plastic vial with d=1.2cm, and solvent solution 0.3ml.
- PVC was cut in order to have an idea of the spatial resolution of the detector:
  1. Two holes d=2.2mm
  2. Large slot 7.8mm x 12.2mm, almost half of the chip exposed
  3. Small and big holes, d=1mm and d=2.2mm



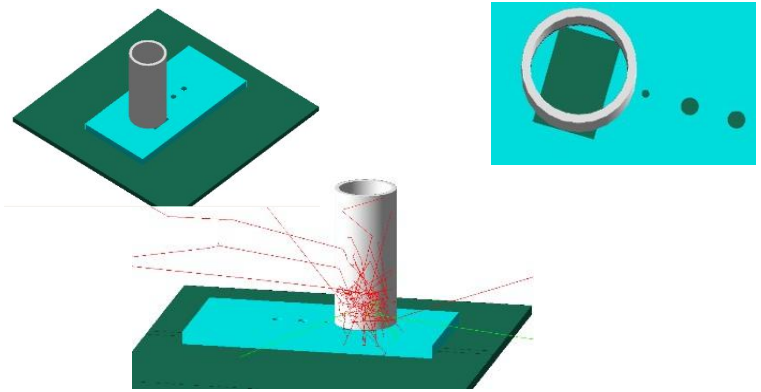




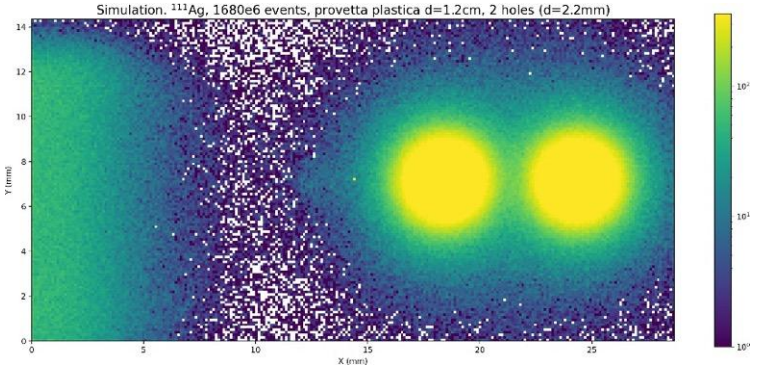


the beta-imaging detector at PD: simulazione Ag

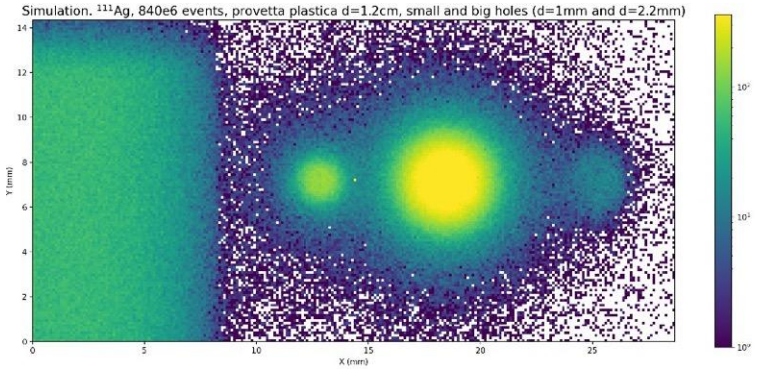
- Simulations on the same condition of the experimental measurements.
- Simulation of the beta spectrum emitted by the ^{111}Ag.
- Number of events simulated equivalent to the number of decays during the measurement



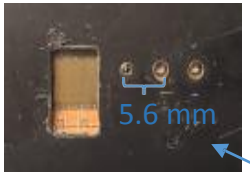
Two holes (d=2.2mm)



Small and big holes (d=1mm and d=2.2mm)

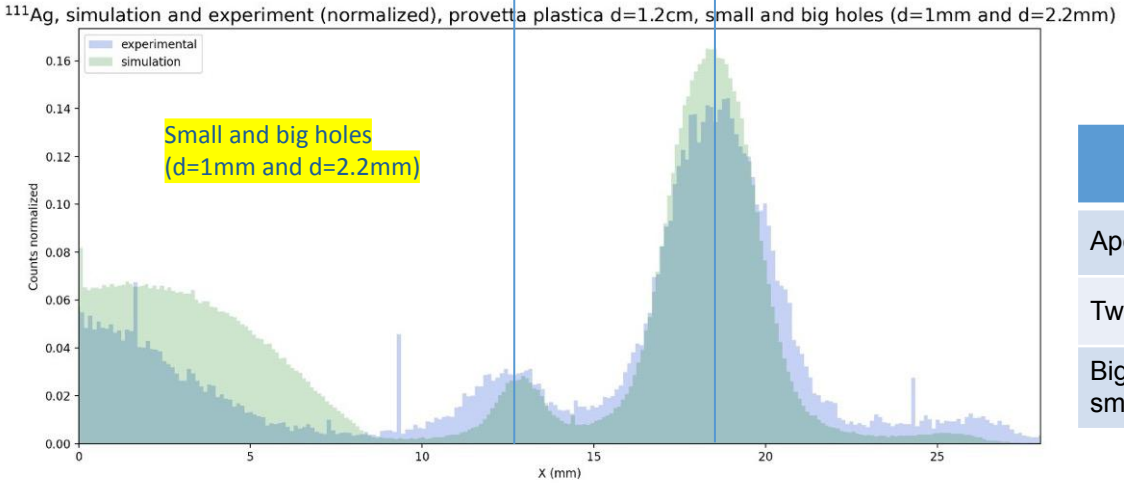


Exp. and Sim. comparison



Good agreement of the spatial distribution between the experimental and simulations results.

Δx≈6 mm



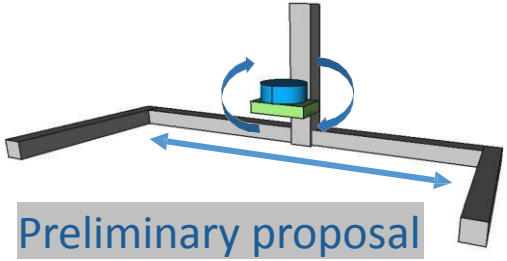
	Exp (counts)	Sim (counts)	Eff (%)
Aperture	6768623	39037992	17.33
Two holes	688339	1990557	34.58
Big and small holes	294995	842104	35.03

Higher rate

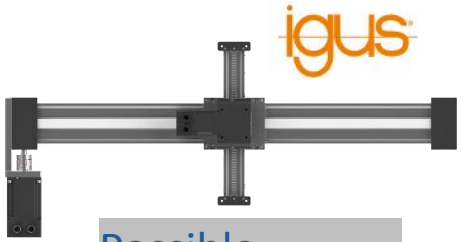
Lower rate

the beta-imaging detector at PD: meccanica

- Useful help from Roberto Michinelli, from the Mechanical Design Service at INFN Bologna.
- Some administrative difficulty for buying ready-to-use parts (mainly from China)
- Possible option: linear gantry two-dimensional movement, parameters can be customized by the user. Produced by IGUS and FESTO (German companies).
- Waiting for the budget proposal.



Preliminary proposal



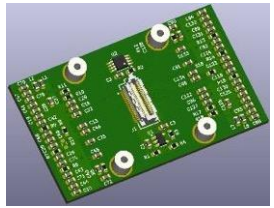
Possible Option

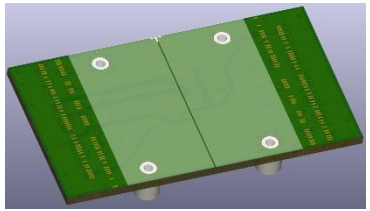
Possible Option

the beta-imaging detector at PD: elettronica

- Chip mounting PCB hosting two ALPIDE chips (basic module): design ready.
- Design of the mezzanine board still pending (to be defined next weeks).
- The bottom layer hosts the FPGA. A Raspberry Pi temporary option is also being evaluated

PCB design





PCB for chip mounting

mezzanine board

FPGA board

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

Raspberry Pi Pico

ADMIRAL – GANTT

ADMIRAL WP2

we are here

		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

Milestone MS2.1 : Elettronica e Meccanica

- work ongoing, design for electronic board and mechanics expected on time

Milestone MS2.2: Simulazione

- MC code already implemented and working. To be updated according with final E+M design

Milestone MS2.3 (2025): Caratterizzazione

- some first experimental test already done!

ADMIRAL
WP2

we are here

	WP2 - β-Imaging	Year 1				Year 2				Year 3				Notes
		M3	M6	M9	M12	M15	M18	M21	M24	M27	M30	M33	M36	Required for
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 2024:

- finalize the design of board and FW for a 2 chips module (30 mm x 30 mm) and start the realization. This module can be easily duplicated to allow for a 2 x N chip configuration
- finalize the design of the final mechanics and start the realization
- finalize the MC tool
- more experimental test with the currently working prototype

Activity proposed for 2025:

- complete the realization of the prototype detector and the mechanics
- test and characterization of the prototype

		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)

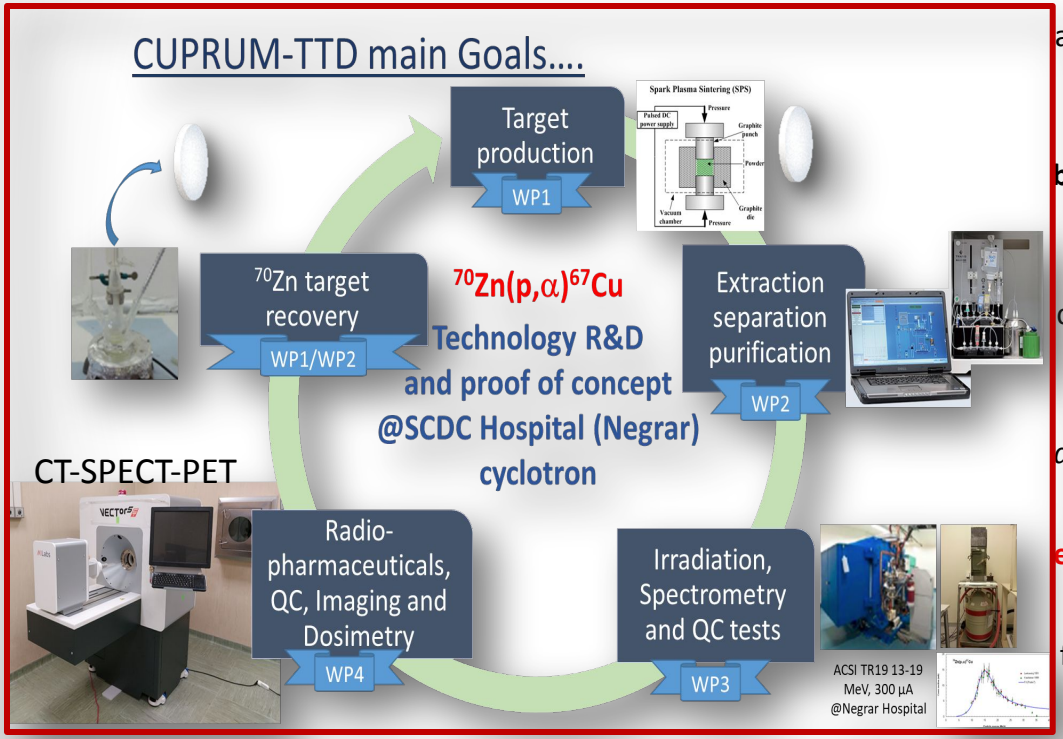
CUPRUM-TTD (2023-25)

Planned activities and Budget Requests 2025

$^{67/64}$**CU PR**oduction and **U**se in **M**edicine – **T**arget **T**echnology **D**evelopment

CUPRUM-TTD (2023-2025) main project goals

To develop a reliable technology aimed at **producing clinical-grade batches of ^{67}Cu-^{64}Cu by small medical cyclotrons on a routine basis.**



a) to acquire a **robust and reliable target manufacturing technology to produce ^{70}ZnO target**

b) **to manufacture targets** able to sustain **beam power levels from medical cyclotrons (i.e. 18-20 MeV, 2/3 kW max)**;

c) to develop/optimize the **radiochemistry separation/purification methods: Zn□Cu** to achieve a clinical-grade **^{67}Cu radionuclide**;

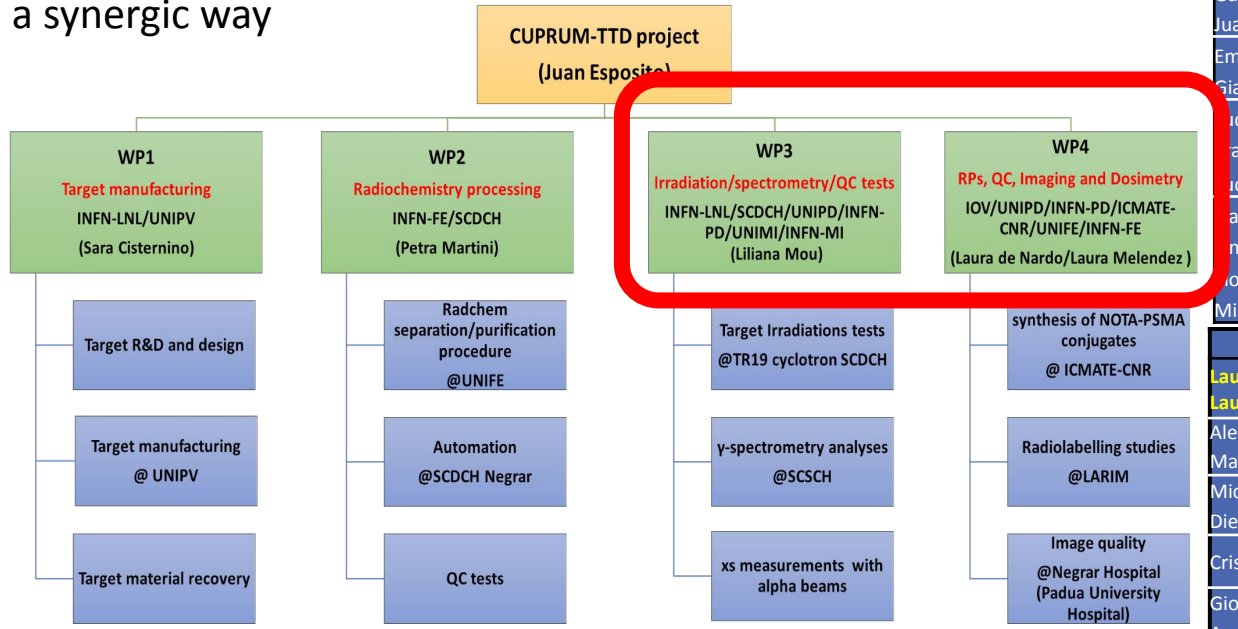
d) *in-vitro* cells studies with **^{67}Cu-labelleded RPs using NOTA derivate as chelating agent;**

e) **phantom imaging studies of produced ^{67}Cu with pre-clinical and clinical SPECT;**

f) to develop/optimize technology for the **costly ^{70}Zn-enriched target material recovery.**

CUPRUM-TTD project organization

CUPRUM-TTD project is organized in Work Packages (WP),interacting each-other in a synergic way

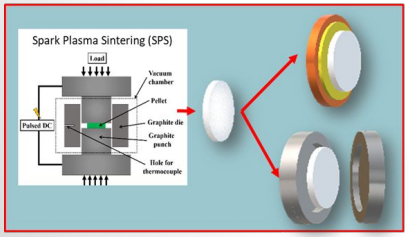


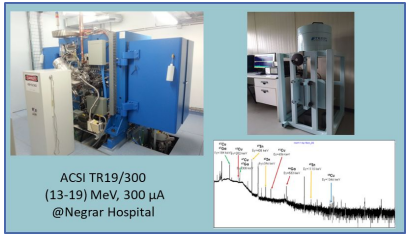
WP1	
Sara Cisternino	LNL
Juan Esposito	
Alisa Kotliarenko	
Giorgio Keppel	
Umberto A. Tamburini	UNIPV

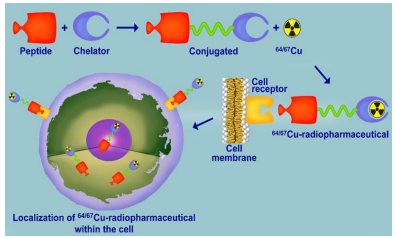
WP2	
Petra Martini	INFN-FE UNIFE
Alessandra Boschi	
Francesca Porto	
Teresa Ghirardi	
Licia Uccelli	
Lorenza Marvelli	
Emiliano Cazzola	HSCDC
Giancoarlo Gorgoni	

WP3	
Liliana Mou	LNL
Gaia Pupillo	
Juan Esposito	
Emiliano Cazzola	HSCDC
Giancarlo Gorgoni	
uciano Canton	UNIPD INFN-PD
rancesca Barbaro	
ucia De Dominicis	
avia Groppi	UNIMI INFN-MI
mone Manenti	
orella M. Cagnetta	
Michele Colucci	

WP4	
Laura De Nardo/ Laura Melendez-A.	INFN-PD IOV
Alessandra Zorz	IOV
Marta Paiusco	
Michele Bello	UNIPD INFN-PD
Diego Cecchin	
Cristina Bolzati	ICMATE CNR
Giov. Di Domenico	UNIFE INFN-Fe
Angelo Taibi	







Attività non a Padova

LNL, FE

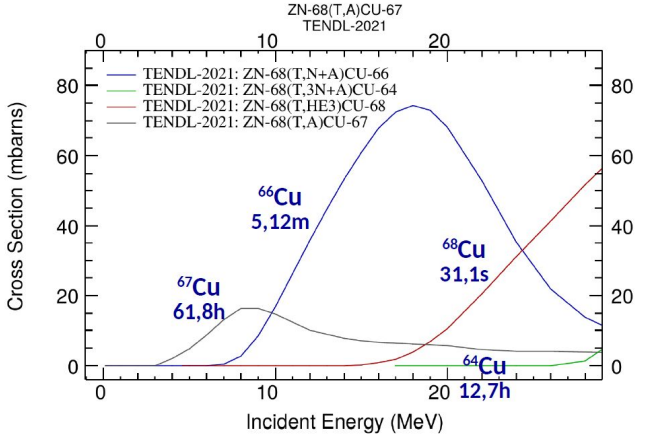
- WP1 fabbricazione target, caratterizzazione, recupero ^{70}Zn
  - Scelta materiale: ZnO
  - Target con Tecnica Magnetron Sputtering : sospesa, poco promettente
  - Target con Tecnica SPS: Sinterizzazione da polvere: ok
  - Bonding con substrato di Au o Nb: ok
  - Irraggiamento a Lena: fino a 1.2kW/cm^2
- WP2
  - Programma di recupero ^{70}Zn: in progress, recupero 98%
  - Investigate nuove strategie per separazione Zn/Cu

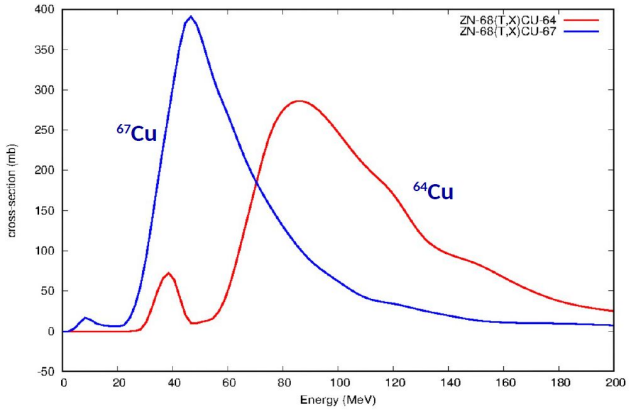
CUPRUM-TTD WP3 (PD): theoretical activities on alternative nuclear reaction routes to yield ^{67}Cu $^{68}Zn(t,\alpha)^{67}Cu$

UniPD/INFN-PD
F. Barbaro
L. Canton
Y. Lashko

- Started investigation of the triton production route: $^{68}Zn(t,\alpha)^{67}Cu$
- Comparison with the "standard" production routes: $^{68}Zn(p,2p)^{67}Cu$, $^{70}Zn(p,\alpha)^{67}Cu$
- Bibliography study and data search
- Started simulation analysis with Nuclear Reaction Codes Talys
- Supervision of a master thesis on this topic

Continuazione di REMIX





CUPRUM-TTD WP4 (PD-IOV-CNR-UNIFE): RP activities (Synthesis of new Cu conjugates)

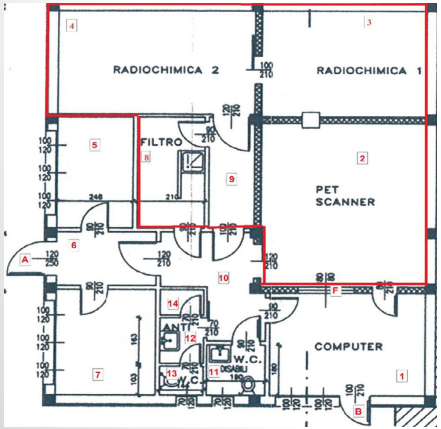
Feasibility of Radiopharmaceutical research studies within LNL LARIM (Padua Univ.)

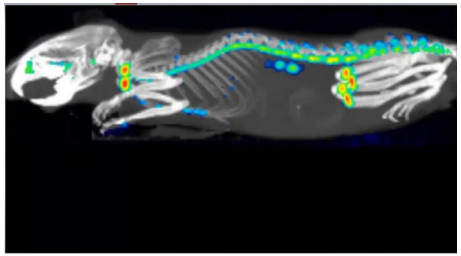
LARIM is located close to SPES building.
Now under renewal of HVAC/Electric/safety plants (Dec. '23 –July '24)
Expected to re-start first operations (new instr. included) on Sept/Oct '24

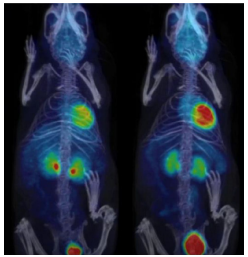
Last-generation small animal scanner: MILABS Vector 5 CT

Set of phantoms with different geometries

HPLC instrumentation in the radiochemistry lab

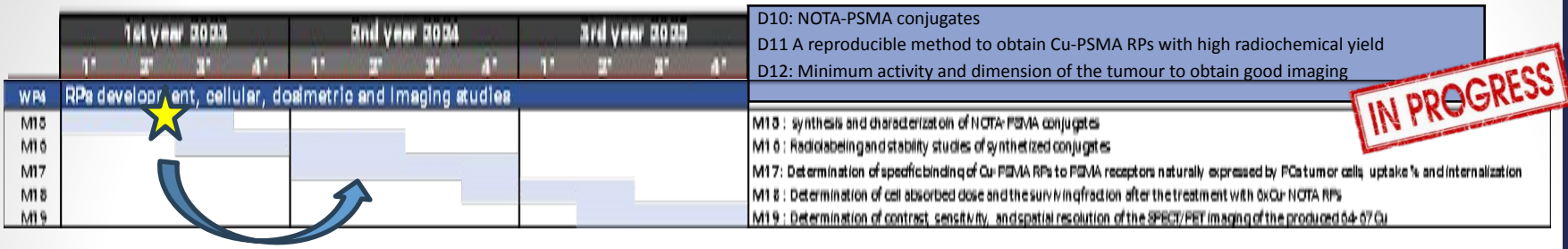




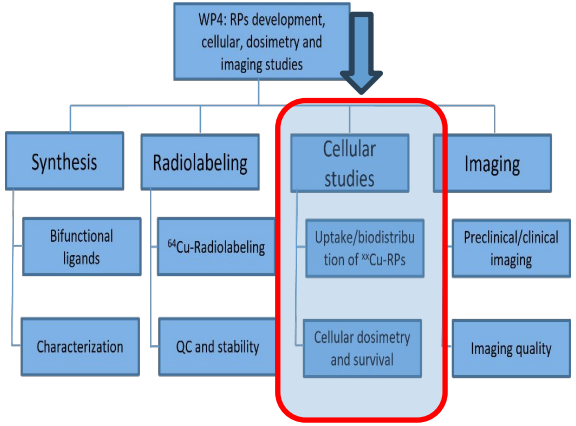


Radiochemical and Biological hoods

CUPRUM-TTD WP4: Cellular dosimetry calculations

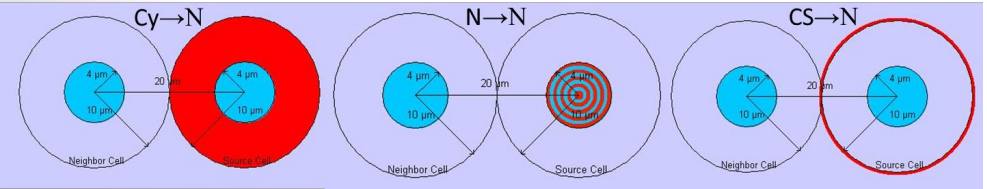


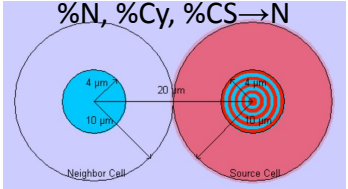
- Input data required: specific uptake and internalization in PSMA-positive and -negative PCa cells.
- MIRDCell calculations for ^{67}Cu and ^{64}Cu in spherical clusters of cells by assuming 100% subcellular distribution of radionuclides in Cytoplasm, Nucleus or Cell Surface provide preliminary information about dosimetric results to be obtained with a realistic distribution of RPs.

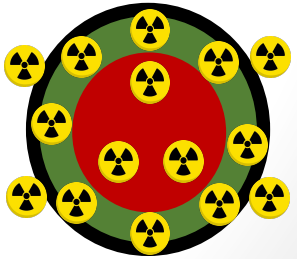


WP4	
Laura De Nardo/ Laura Melendez-A.	INFN-PD IOV
Alessandra Zorz Marta Paiusco	IOV
Diego Cecchin	UNIPD INFN-PD
Cristina Bolzati	ICMATE CNR
Giov. Di Domenico Angelo Taibi	UNIFE INFN-Fe

Source- Target configurations:







CUPRUM-TTD project 2025 FTE (subject to further refinement)

Personnel and FTE distribution expected among units taking part

LNL	FTE
Esposito J. (R.Naz.-Loc.)	0.50
Pupillo G.	0.25
Mou L.	0.20
Cisternino S.	0.70
De Dominicis L.	0.40
Melendez-Alafort L.**	1.00
Bello M.	0.80
Piteo G.	1.00
Anselmi-Tamburini U.	0.20
Cazzola E. #	1.00
Gorgoni G.#	1.00
Cecchin D. §	0.20
	7.25

INFN-Fe	FTE
Martini P. (R. Loc)	1.00
Taibi A.	0.10
Di Domenico G.	0.20
Boschi A.	1.00
Uccelli L.	1.00
Marvelli L.	1.00
Porto F.*	1.00
Speltri G.*	1.00
	6.30

INFN-Mi	FTE
Groppi F. (Res. Loc)	0.40
Manenti S.	0.25
Cagnetta F.M.	0.45
Colucci M.****	0.60
	1.70

TOTALE FTE 17.55

INFN-Pd	FTE
De Nardo L. (R. Loc)	0.80
Canton L.	0.20
Barbaro F.	0.60
Paiusco M. **	0.20
Zorz A. §	0.20
Bolzati C.***	0.20
Lashko Y.	0.10
	2.30

* studenti PhD associate INFN-Fe (da nov 2023)
** personale IOV associato LNL
*** personale CNR associato INFN-Pd
**** studente PhD associato INFN-MI
§ personale UNIPD associato INFN-LNL
# personale SCDCH associato INFN-LNL

Summary overall budget request CUPRUM-TTD FY2025

Sezioni / Lab	Missioni	Consumo/ Altri consumo	Trasporti	Manutenzione	Inventario	apparati	Sp- servizi	Tot. per sez/lab	FTE previsto
LNL	7,0	10,0	0,0	0,0	0,0???	0,0	0,0???	**17,0**	**7.25**
FE	4,0	15,0	2,0	0,0	17,0	0,0	0,0	**38,0**	**6.30**
PD	1,0	7,0	0,0	0,0	0,0	0,0	0,0	**8.0**	**2.30**
MI	8,5	8,0	8,5	4,0	0,0	0,0	0,0	**29,0**	**1.70**
TOTALE	**20.5**	**40.0**	**10.5**	**4.0**	**17.0**	**0.0**	**0.0**	**92.0**	**17.55**

*__Consumables__: Solvents for HPLC analysis, reagents for stability test, buffers and cell culture media, Sep-Pack cartridges for radiopharmaceutical purification, plastic and glassware (4Keuro).
64Cu to radiolabel the developed Radiopharmaceuticals (2x10mCi) (3keuro)

Further developments or applications

- **SPES-MED (Gr III, 2024-26)**
- **Nuclear cross section measurements**
- ^{68}Zn,^{70}Zn(p,x)**^{67}Cu,^{64}Cu** for proton beams with energy higher than 70 MeV, in collaboration with the i-Themba facility (LNL team, 1 and 2 year);
- ^{70}Zn(p,x)**^{67}Cu,^{64}Cu** in the energy range 25-50 MeV at SPES (LNL team, 3 year)
- **DECURTA** *DEvelopment of 67Cu-Radiopharmaceuticals for Theranostic of prostate cAncer* (Bando IOV Ricercatori Sanitari 2023) PI Laura Alafort Melendez

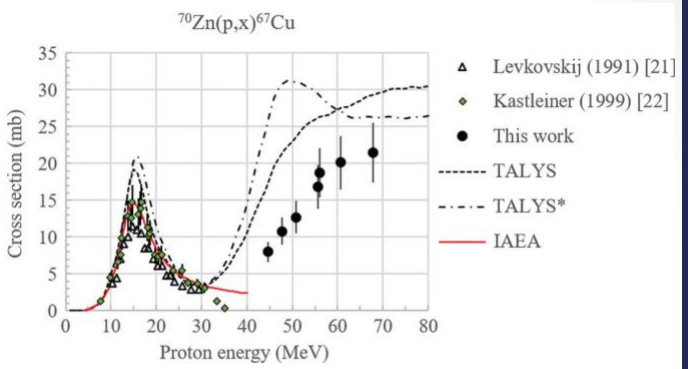


Figure 3: Results of the ^{70}Zn(p,x)^{67}Cu nuclear cross section.

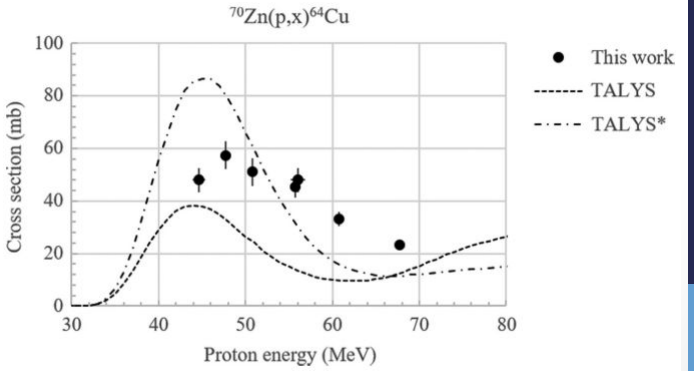


Figure 4: Results of the ^{70}Zn(p,x)^{64}Cu nuclear cross section.

[Pupillo, G. *et al. Radiochim. Acta* **108**, 593–602 (2020)]

Conclusioni

Riassunto Sigle

In Chiusura	NEXT_AIM	Zucchetta	23,24	
	N3G	Recchia	22,23,24	
	PHYDES	Carugno	22,23,24	DEMIURGOS
	HISOL	Pepato	23,24,25	
In Continuazione	ADA_5D	Collazuol	23,24,25	ASAP
	ADMIRAL	Lunardon	23,24,25	ISOLPHARM_EIRA
	AI_INFN	M. Verlato	24,25,26	ML_INFN
	CUPRUM_TTD	L. De Nardo	23,24,25	REMIX
	FEROCE	Triossi	23,24,25	
Nuove Proposte	DOCET	Carugno		
	ASPIDES	Collazuol		
	MEDIPIX4.2	Collazuol		
	SPECO-PICO	Pisano		
	SQUEEZ	Zendri		
	HISOL_NEXT	Rebesan		

Riassunto delle richieste ai servizi

Sigla	Prog. Meccanica	Off. Meccanica	Prog. Elettronica [Bellato]	Serv. Tecnici ed Elettronica [Nicoletto]
AI_INFN	-	-	-	-
ADA_5D	-	1 m.p. telescopio	3 m.p. FPGA	1 m.p. TIMEPIX4
FEROCE	-	-	-	-
ADMIRAL	-	-	-	3 m.p. scheda e bonding
CUPRUM_TTD	-	-	-	-
HISOL				
DOCET	1 m.u.	10 m.p.	2 m.u.	10 m.p.
ASPIDES	?	?	?	?
MEDIPIX4.2			vedi ada5g	
SPECO-PICO	-	-	-	-
SQUEEZ	-	1 m.p.	-	-
Tot	1 m.p.	12 m.p.	3 m.p.	

Riassunto delle percentuali nelle sigle

- Link alla tabella riassuntiva delle percentuali previste per il 2024

Considerazioni finali

- I grant giovani della CSN5 sono un'opportunità molto attraente per giovani ricercatori
  - Possibilità di essere assunti con un assegno di ricerca
  - Possibilità di fare esperienza diretta di gestione di un finanziamento
  - Permettono di sviluppare idee nuove che sono potenziali volani di ulteriori sviluppi

Esorto chi e' nelle condizioni di applicare di provarci

BACKUP

BACKUP