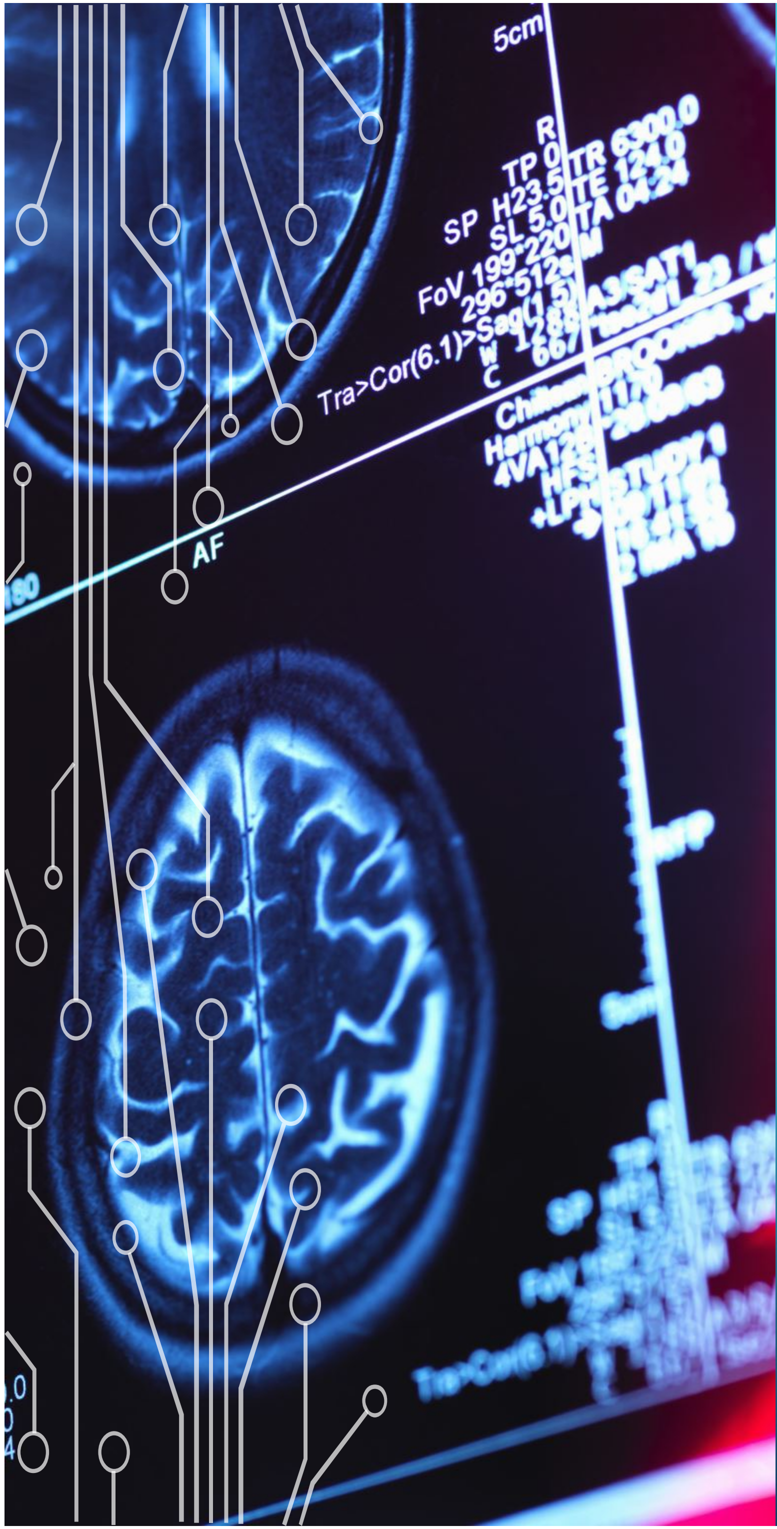
PROGETTI INFN NEL SETTORE LIFE SCIENCE NELLA REGIONE PUGLIA

PROF. SABINA SONIA TANGARO

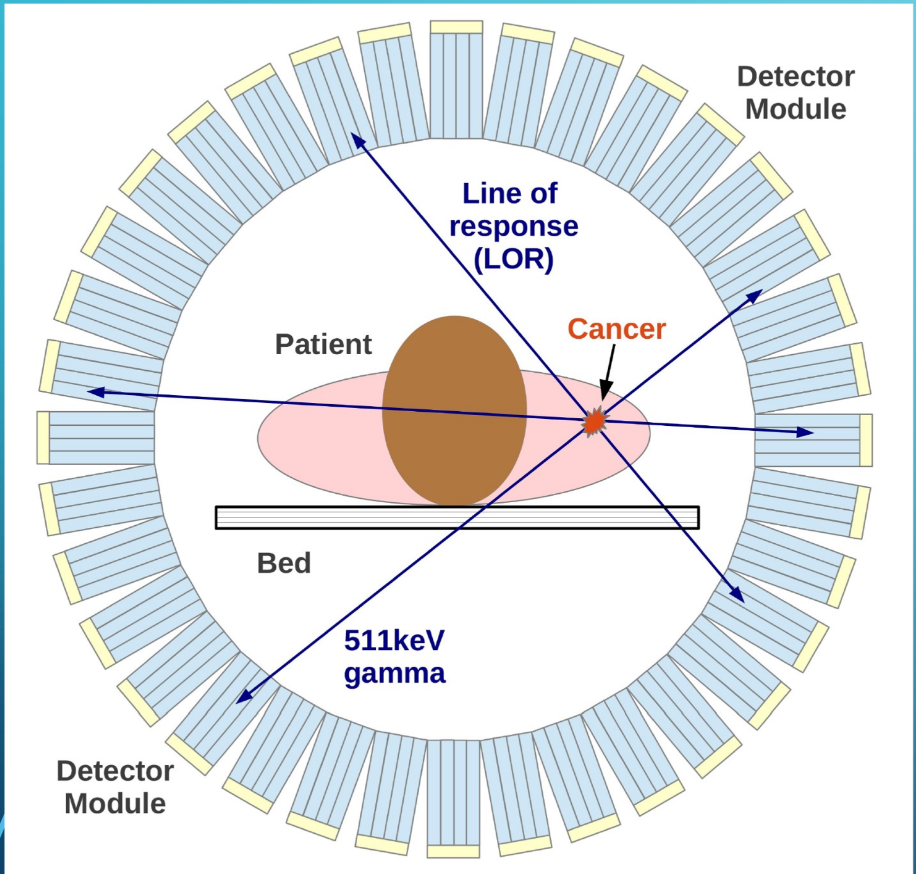
UNIBA &INFN-BA



SUMMARY

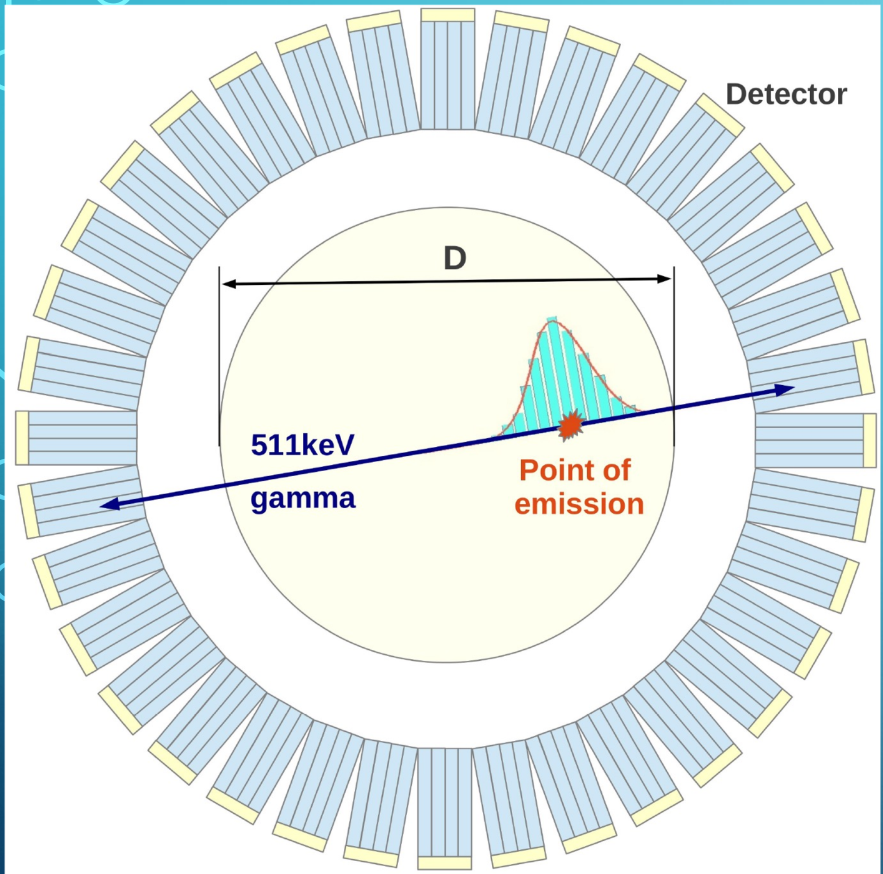
- Detectors
  - Diagnostics
  - Dosimetry
- Interdisciplinary
  - Reconstruction algorithm
  - Computing
  - AI for health
  - Environment

DIAGNOSTICS:
POSITRON EMISSION TOMOGRAPHY

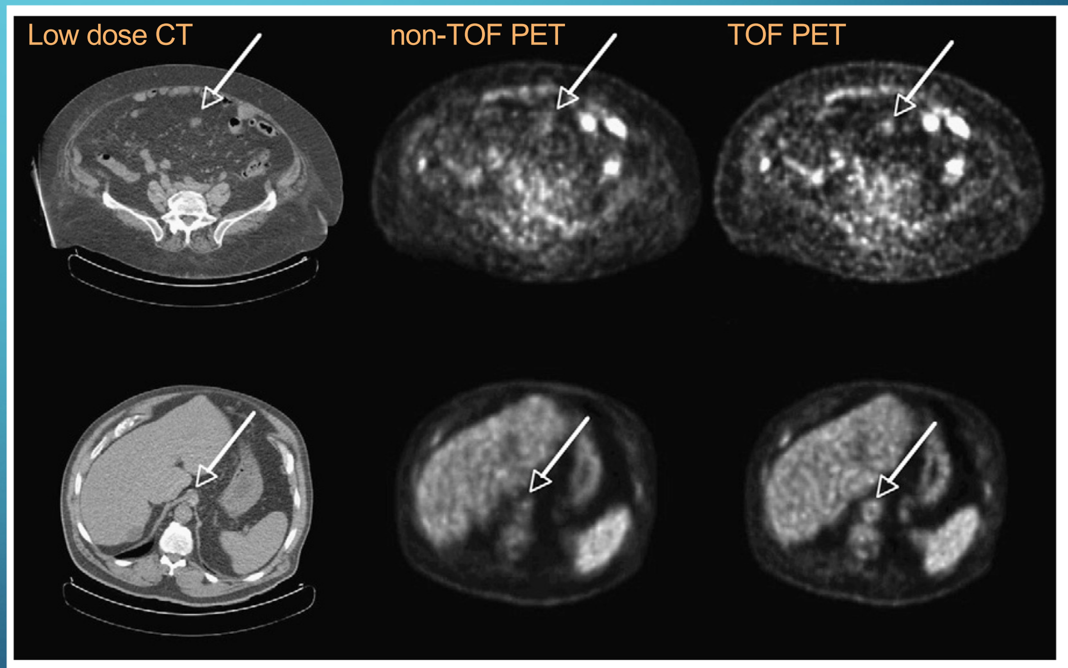


- Distribution of biomarkers labelled with a radioactive isotope which undergoes β^+-decay
- Emitted e^+ annihilates in the tissue producing two collinear 511 keV gammas ($e^+ e^- \rightarrow 2\gamma$)
- Detect such energetic photons in coincidence via scintillating crystals:
  - high gamma attenuation, light yield, probability of photoelectric effects and fast decay time
  - LYSO (Lutetium Oxyorthosilicate) shows the best compromise

TIME OF FLIGHT PET

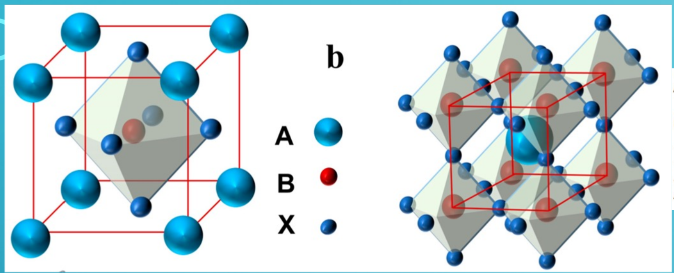


The image quality (SNR) can be drastically improved by using time of flight (TOF) information to estimate the emission position.

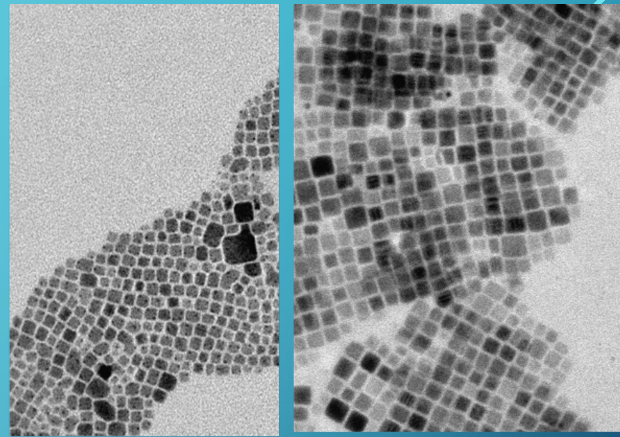


FAST TIME SCINTILLATING NANOCRYSTALS

Typical perovskite chemical formula ABX_3

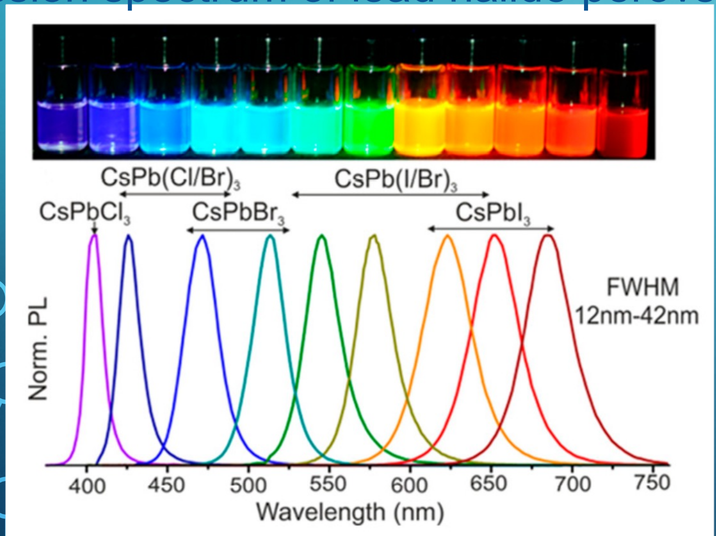


A: cation, organic (i.e. $CH_3NH_3^+$, $CH(NH_2)_2^+$) or inorganic (i.e. Cs^+, Rb^+)
B: metal cation (i.e. Pb^{2+}, Sn^{2+}, Ge^{2+})
X: halogen anion (i.e. F^-, Cl^-, Br^-, I^-)



Fanizza et al. Nano Research 2019, 12(5): 1155–1166

Emission spectrum of lead halide perovskites



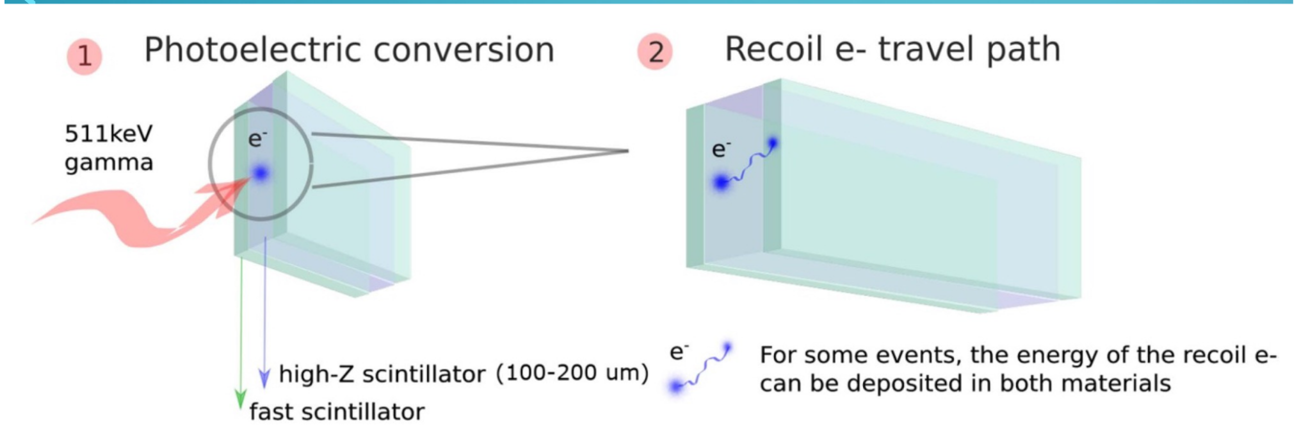
- Perovskite Material ABX_3: large stopping power; high mobility lifetime product; fast response (~ns); large bulk resistance, low cost.
- High photoluminescence quantum yields ;
- Tunable band-gap with composition
- Possibility to synthesize 3D nano-dots, nano-wire and nano-plates
- Their nano-scale sizes impose several limitations in terms of energy deposition per platelet.

HETEROSTRUCTURED SCINTILLATORS FOR FAST TIMING

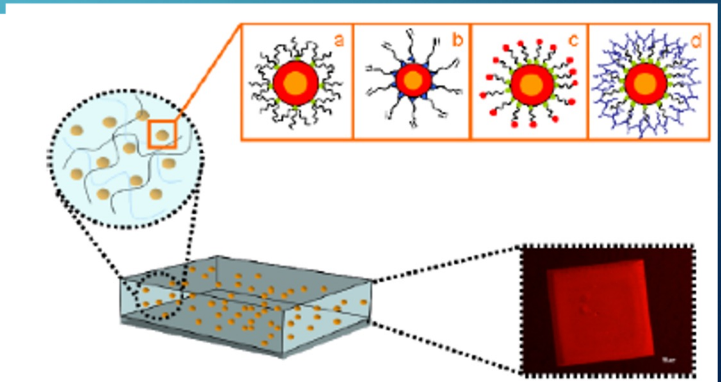
Hybrid structures in which high-Z inorganic scintillator is combined with scintillating nano-crystals (NC) for time tagging.

Alternating layers of a high-Z and a fast NC

Perovskite-polymer 3D composite

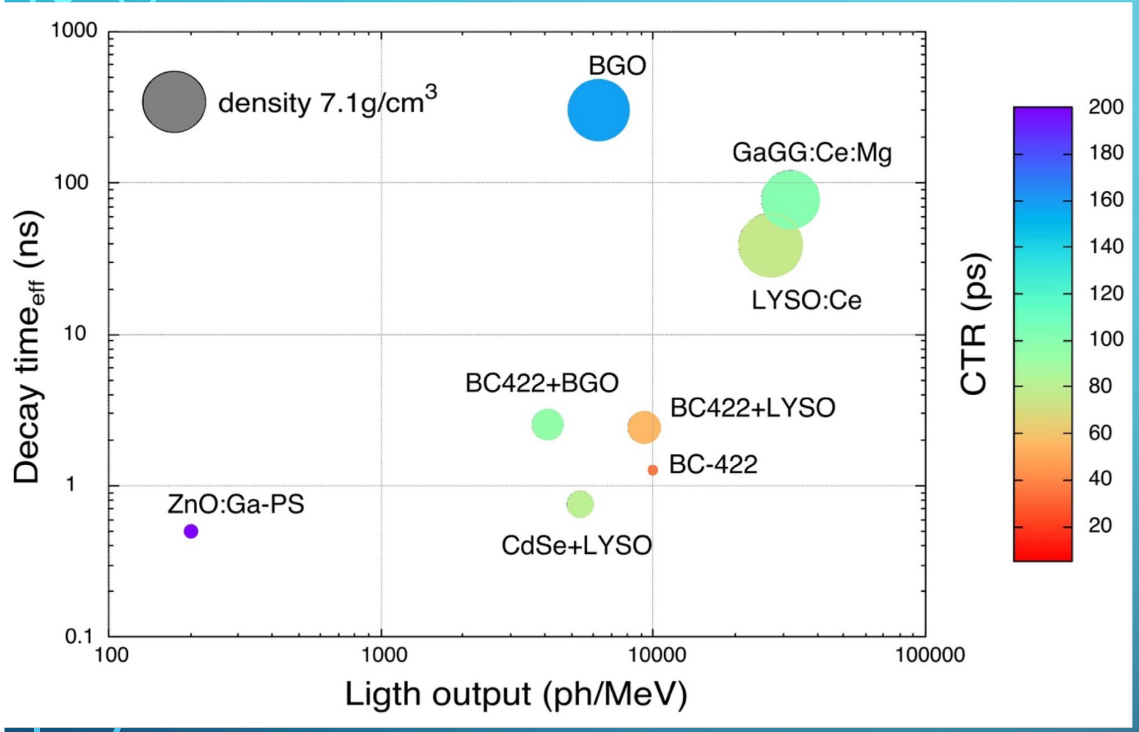


P. Lecoq et al 2020 Phys. Med. Biol. 65 21RM01



Striccoli et al Materials **2010**, 3, 1316-1352

STATE OF THE ART



ONGOING R&D

- ultra-fast scintillators for medical applications and HEP (Crystal Clear Collaboration)
- doped plastic scintillators (AidaInnova)

Despite the low light output, the timing obtained is at the level of state-of-the-art inorganic scintillators, leaving a **rather large room for optimization.**

P. Lecoq et al 2020 Phys. Med. Biol. 65 21RM01

PEROVSKITES NCS SYNTHESIS AND DEPOSITION

Possible collaboration with CNR-IPCF

Synthesis and Characterization

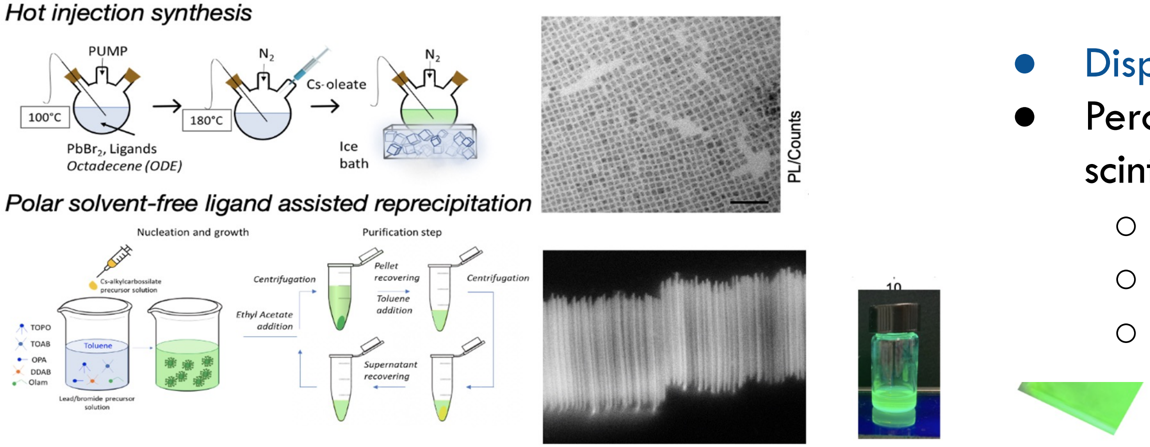


Fig. 2: Scheme of the synthetic approaches for the preparation of colloidal perovskite NCs with tuneable size and shape. TEM (scalebar 50 nm) and SEM-FEG characterization of the perovskites. Time decay recombination of nanocomposites with PMMA and PS host matrices and structure of the PVK NCs. Picture under UV light of colloidal NC solution and film.

Heterostructures Fabrication

- Dispersion into polymeric host matrix
- Perovskite NCs solid-state films depositions for scintillator device fabrications:
  - Drop-casting (CNR)
  - Spin coating (CNR)
  - Laser Ablation (INFN-Le and UniLe)

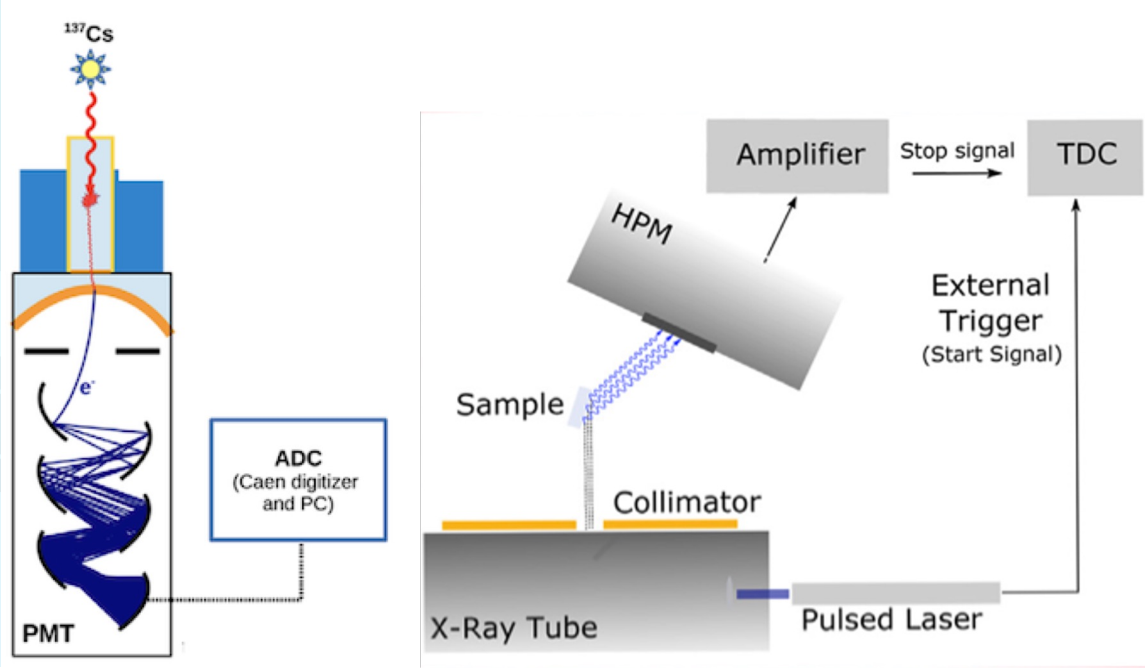
Courtesy of A. Panniello

Consiglio Nazionale delle Ricerche

IPCF Istituto per i Processi Chimico-Fisici

DETECTOR CHARACTERISATION FOR TIMING PERFORMANCE

LY measurement setup CTR measurement setup



S. Gundacker et al 2016 Phys. Med. Biol. 61 2802
https://cds.cern.ch/record/2840754/files/document.pdf

Facilities and Synergies:

- Dedicated facilities at Bari Phys. Dep.
- Synergies:
  - HEP group (expertise on radiation detection, DAQ and data analysis)
  - solid state physics (fabrication, thin layer deposition)
  - External collaborations (CNR) for material synthesis

Setup for timing detector characterization aiming at measuring:

- Steady-state light yield
- Coincidence Time Response
- Time-resolved light yield
- Emission spectrum

FUNDED PROJECTS / INFN-COLLABORATIONS

QUASIMODO

- Our department has been granted funds for the project "**Quantum Sensing and Modeling for One Health (QuaSiModO)**".
- Collaboration: CNR-Bari (perovskites synthesis and deposition).
- Facilities dedicated to these activities are foreseen within this project. We are building the setup to characterize the time performance of the scintillator using pulsed X-rays.
- 5-years starting from 2023. Funded about 200k euro for instrumentation and consumables

PRIN-PNRR

- Our group has been granted funds for the project "**Development of Ultra-fast Perovskites ScinTillAtoR for TOF-PET** (UPSTART)" Collaboration: CNR-Bari (perovskites synthesis and deposition), INFN-Lecce (deposition using laser ablation)
- 2-years starting from Nov 2023. Funded a 2-years post-doc contract and about 20k of instrumentation/consumables

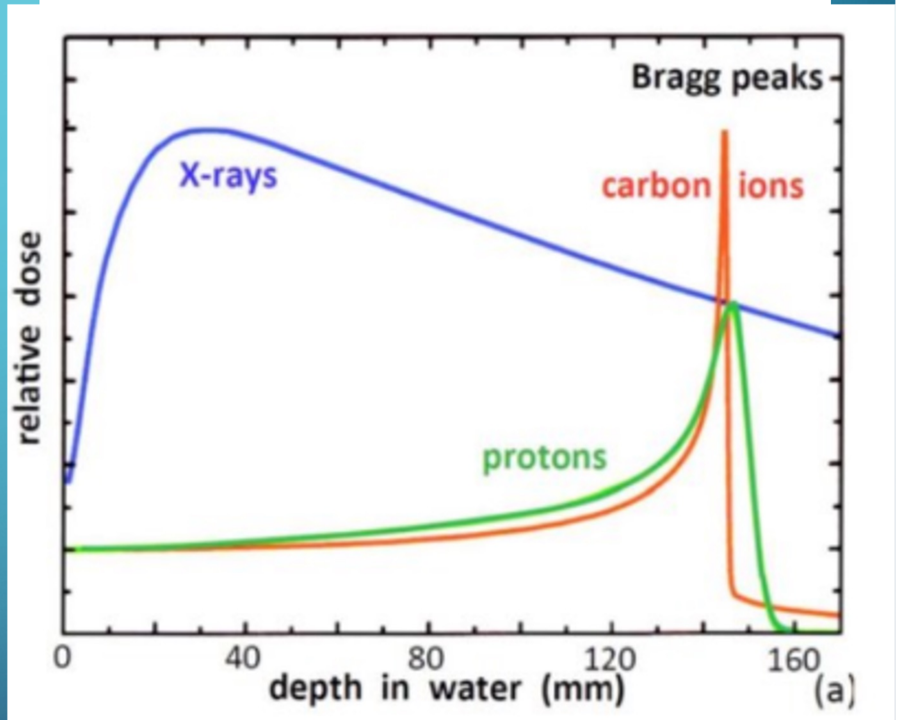
SHINE

- Existing INFN-project "**Plastic Scintillators Phantom via additive manufacturing techniques**" (Responsible Anna Paola Caricato INFN-Lecce)
- Perovskite-polymer nanocomposite and polysiloxanes-based resin for 3D-printable scintillators.
- Collaboration: INFN-Lecce, LNFN-LNS, TIFPA
- 3-years starting from 2023. INFN-Bari involved in SHINE this year (2024). Funded 3k for SiPM and other consumables.

THE PROTON THERAPY (DOSIMETRY)

- Radiotherapy: **use of ionizing radiation to damage cancer cells preserving as much as possible healthy tissues**
- Dose: energy absorbed per unit target mass [Gy]
- Charged particles deposit dose in a narrow region, named “Bragg peak”.
- Range uncertainties are important.

Depth-dose distribution for X-rays, protons and carbon ions



BEAM QUALITY ASSURANCE (QA) IN PBT

Each proton therapy centre has a rich program of Quality Assurance (QA) controls necessary to ensure a safe treatment to the patient.

QA checks are:

- Daily
- Monthly
- Annually

Daily checks include the measurement of beam parameters such as the proton beam range, spot size, spot position and dose.

➡

Daily beam QA checks are time-consuming operations (~44 min/day/treatment room).

BEAM DAILY QA STATUS OF ART

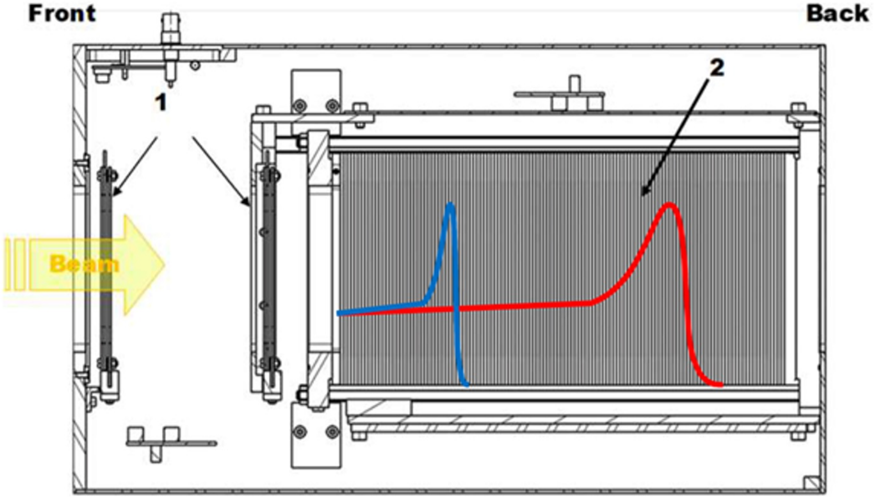
Commercially available devices are:

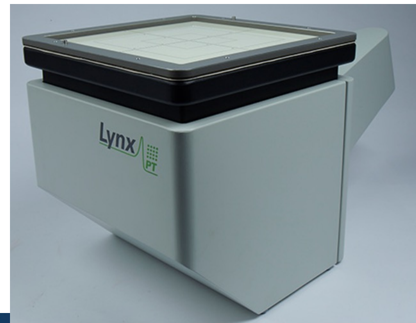
- IBA Giraffe detector for the Bragg peak measurement in a one single proton beam shot. It suitable for pencil beams.
- IBA Lynx detector for beam spot characterization

(Main) Disadvantages:

Fast acquisition time but long setup time

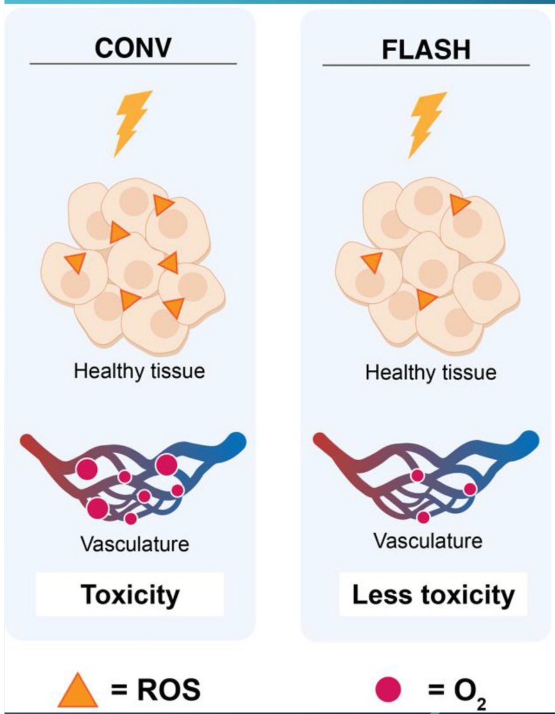
No device exists to make simultaneous measurements of different beam parameters





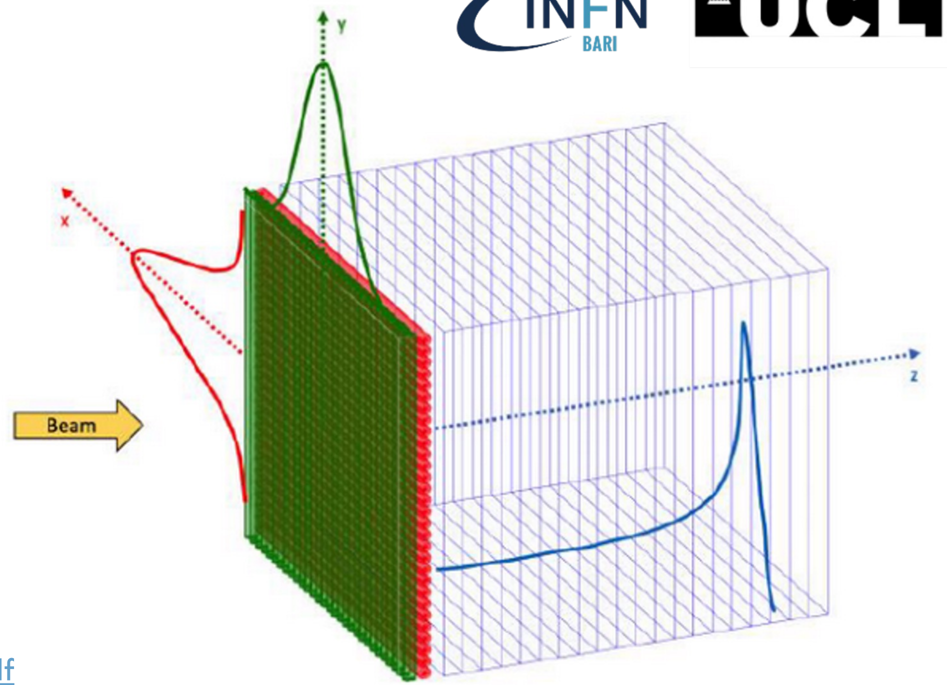
FAST DOSE DELIVERY: THE FLASH RADIOTHERAPY

- FLASH radiotherapy: new radiation delivery technique at ultra-high dose rate (>40 Gy/s) using short-duration pulses.
- FLASH effect: **reduces the trauma to normal tissue around the tumour**, whilst equalling the anti-tumour effect of conventional dose rate radiotherapy.
- Commercial Dosimetric Detectors:
  - Radiochromic films and Alanine (passive detectors, no online measurements)
  - Scintillators (dose rate independent)
  - Ionization Chambers (dose rate dependent)
- No Dosimetric protocol available for FLASH
- None of the existing QA device is scalable at FLASH rate.



A NOVEL INTEGRATED DETECTOR FOR PROTON BEAM QA

- **Development of an integrated system for FLASH proton beam QA**
  - Scintillating fibers beam monitoring to measure the beam spot size and position
  - Integration with a range module made of a stack of plastic scintillator sheets to measure the depth-dose profile [1] (collaboration with University College London)



[1] https://iopscience.iop.org/article/10.1088/1361-6560/ab9415/pdf

FUNDED PROJECTS / INFN-COLLABORATIONS

FLASH Radiotherapy with hIgh Dose-rate particle beAms

FUTURE PLANS

- Main challenges will be mechanical and DAQ integration of range module and beam tracker.
- Test the integrated system with clinical and FLASH beams.

SPOC - SPect for Online boron dose verification in bnCt (Boron Neutron Capture Therapy)

G. Pugliese (RL), G. Bruno, G. Iaselli, D. Ramos Lopez, N. Ferrara
on behalf of SPOC collaboration

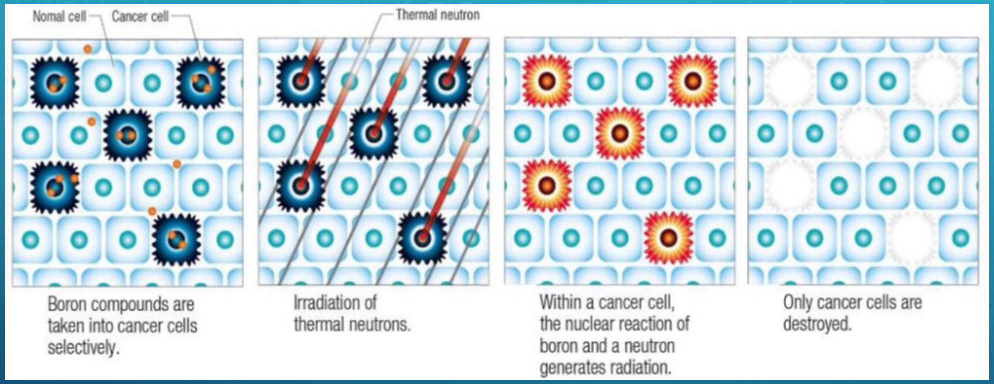
Sezione INFN e Politecnico di Bari

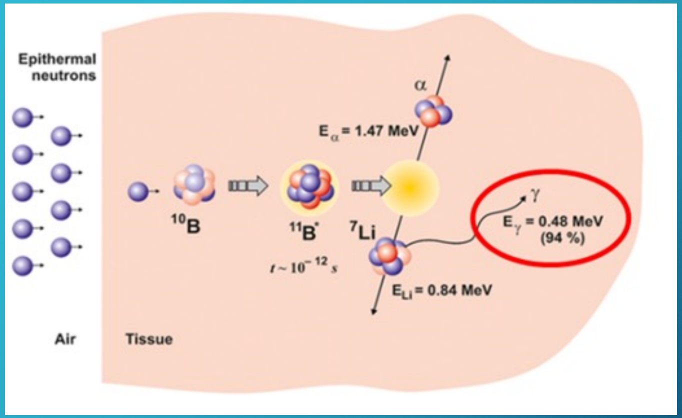
Email: gabriella.pugliese@ba.infn.it

Working Principle and Worldwide Diffusion of Boron Neutron Capture Therapy (BNCT)

BNCT is a targeted hadrontherapy technique:

- Tumor cells are loaded with ^{10}B-enriched molecules and then irradiated with thermal neutrons
- Neutron undergo to capture reaction with boron-10: $^{10}B(n,alpha)^{7}Li$
- Energetic charged particles released by reaction produce damage to the tumour cells.





- In recent years BNCT has re-gained significant attention and investments thanks to the development of accelerator-based BNCT (AB-BNCT) facilities [1].

Italian projects:

- CNAO
- Anthem @ Caserta

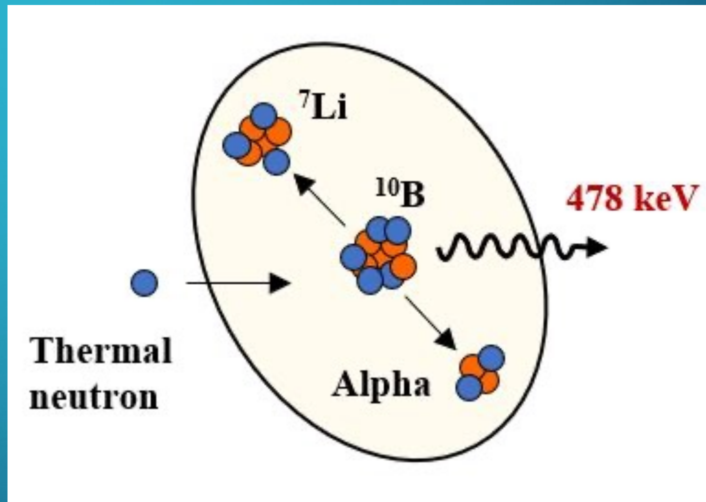
[1] Advances in Boron Neutron Capture Therapy. in Non-serial Publications. Vienna: INTERNATIONAL ATOMIC ENERGY AGENCY, 2023. [Online]. Available: https://www.iaea.org/publications/15339/advances-in-boron-neutron-capture-therapy

The Dosimetry Issue in
Boron Neutron Capture Therapy (BNCT)

Delivered dose is currently estimated <u>offline</u> using:

- Direct/indirect measurements of Boron concentration in tissues (ICPS, PET)
- Neutron flux in treatment room
- Monte Carlo calculations

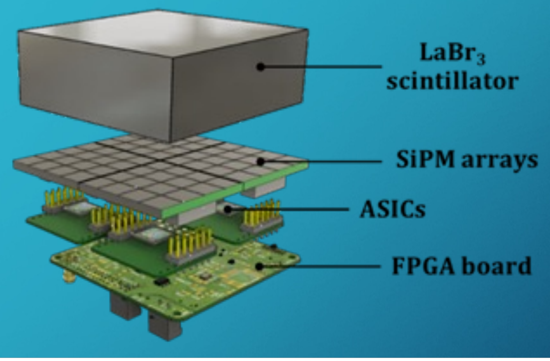
Possible alternative method: online SPECT imaging of 478-keV gamma rays emitted by ^{7}Li produced in capture reaction (personalized dosimetry).



SPECT main specifications:

- Good efficiency and energy resolution at 478keV (to separate it from 511keV annihilation photons)
- Spatial resolution: 5-10mm (limited by the collimator)
- Possibly, extended efficiency up to 2.2MeV (H-capture) for neutron flux estimation

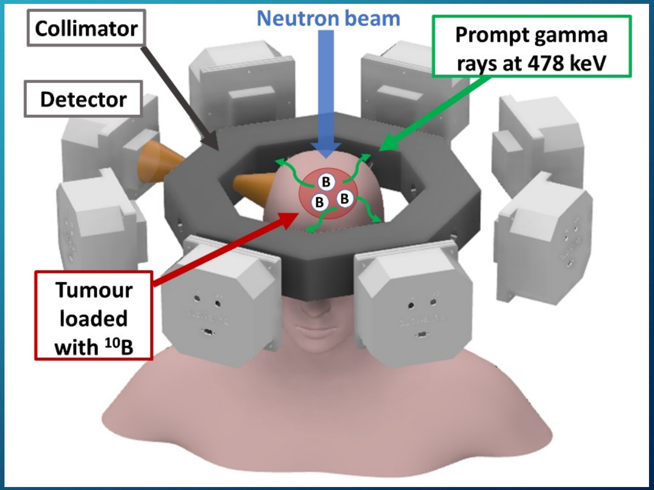
Aims of the Project



PROJECT GOAL: design a dedicated SPECT system for BNCT dose verification, build the first prototype (few modules), and test it with realistic irradiation conditions.

Proposed SPECT system:

- Detector: gamma camera based on LaBr3(Ce+Sr) square crystal + SiPMs
- Channel edge pinhole collimator
- Optimized detector shielding to avoid detector activation
- Unconventional scanner geometry due to constraints given by fixed neutron beam
- Modified image reconstruction algorithms to account for specific system geometry



SPOC - SPect for Online boron dose verification in bnCt
Collaboration, Project Organization – Milestones

Collaboration: 3 INFN Units Bari – Pavia – Milano (PI)

Project Organization: 4 Work Packages and 2 Milestones for each WP

- **WP1**: Simulations of irradiation neutron fields and of gamma and neutron fluxes on the detector. Study of shielding. Study of overall SPECT configuration (Polimi-Energia)
- **WP2**: Development of the gamma-ray detector, electronics, collimation system and algorithms for the gamma-ray position reconstruction. Development of the SPECT prototype. (Polimi-DEIB)
- **WP3**: BNCT dedicated tomographic reconstruction. (Bari)
- **WP4**: Beam tests at nuclear reactor and with accelerator-based sources. (Pavia)

Month:	1-3	3-6	7-9	10-12	13-15	16-18	19-21	21-24	25-27	28-30	31-33	34-36
WP1				M1		M5		M6				
WP2				M2						M8		
WP3				M3				M7				
WP4				M4								M9

2024 2025 2026

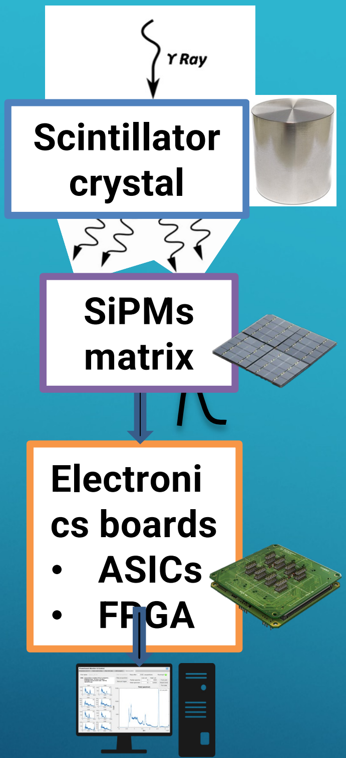
SPOC - SPect for Online boron dose verification in bnCt
INFN funds & Synergies

Funds: The 3 years project is funded by INFN for about 96k Euro

Synergies: The project will take profit of the synergy with the PRIN – PNRR project with the tittle "Development of a SPECT (Single Photon Emission Computed Tomography) detector prototype for dose measurements in BNCT (Boron Neutron Capture Therapy) . Duration of the project: two year (2024 – 2025) .
Collaboration: Politecnico di Milano (PI), Univeristà di Pavia, Politecnico di Bari
Bari Member: G. Pugliese (RU), G. Iaselli, D. Ramos
Funded for about 270k Euro

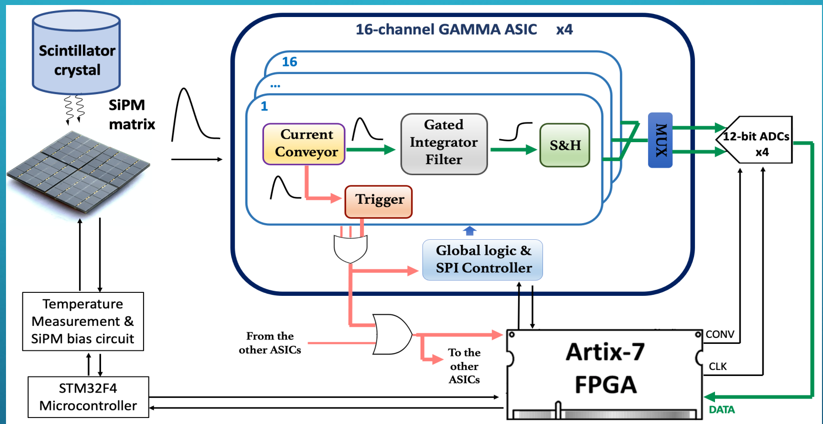
Preliminary Results

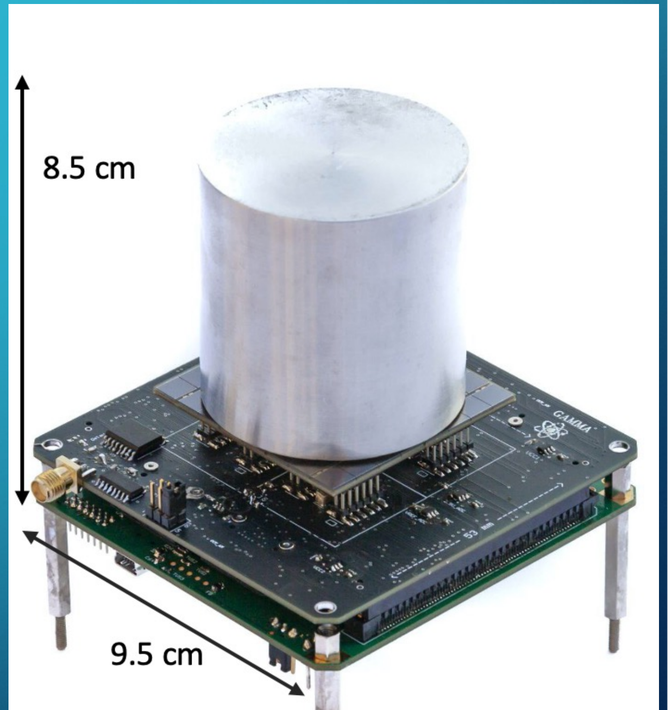
The V0 Detector Prototype



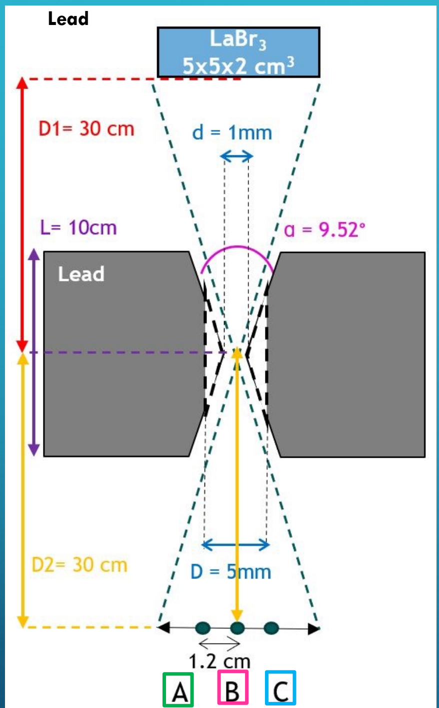
Gamma-ray detection module:

- 2" cylindrical LaBr3(Ce+Sr) scintillator crystal
- 4 arrays of 4x4 SiPMs
- 4 custom 16-channels GAMMA readout ASICs
- Data acquisition is managed by an FPGA.



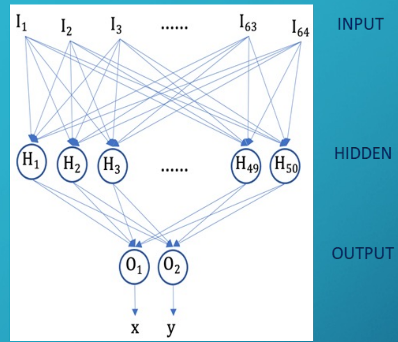


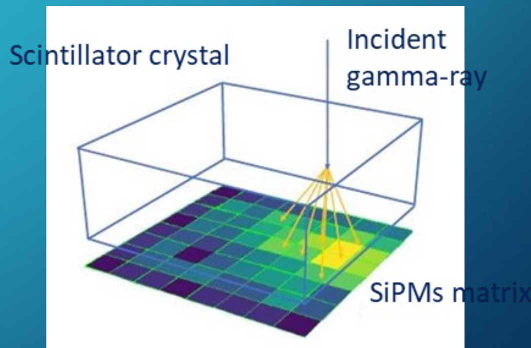
MC Simulations of Square Gamma Camera



Preliminary MC simulations performed to estimate imaging capabilities of a Gamma camera based on square $LaBr_3$:

- Channel edge pinhole collimator used for image acquisition
- Position estimation in the crystal performed with artificial neural networks (input: SiPM signals / output: x-y coordinates)
- Training of the network performed by scanning the crystal surface in 320 positions with a 1mm-collimated ^{137}Cs source (662 keV)
- The ANN is able to reconstruct the position of a 137Cs source in measurements acquired with the pinhole collimator with a spatial resolution of 3.25 mm





Overview of previous/ongoing projects

RIPARTI - Feasibility study for the development of advanced techniques in neutron beam radiotherapy

Bari task ⇆ synergy with ITEL Linearbeam s.r.l. facility for protontherapy

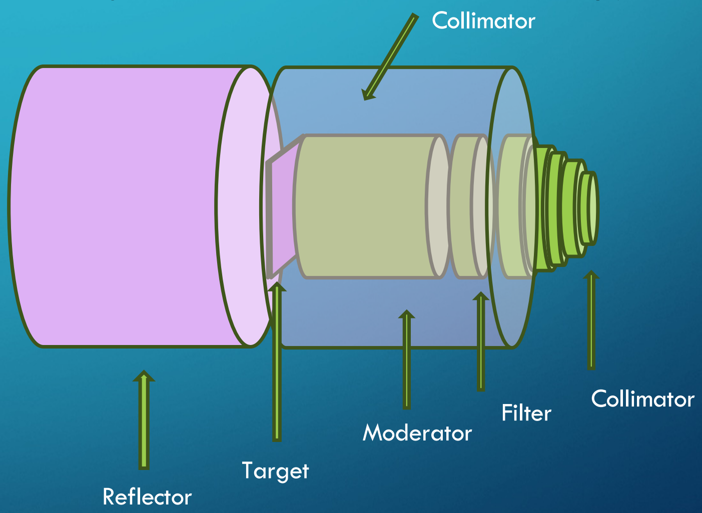
1 post-doctoral position

General goal: Feasibility study to become a protontherapy facility into Accelerator-based BNCT facility by introduction of a target system: Beam Shaping Assembly (BSA)

- Proposed target materials: **Lithium** and **Beryllium** → highest cross section for the reacctions p(^{9}Be,^{9}B)n and p(^{7}Li,^{7}Be)n, respectively.
- **Function:** Thermalize and moderate neutrons

Preliminary BSA layout

1. Moderator: AlF_3 , Al , MgF_2 , CaF_2, polyethylene
2. Filter: ^{7}LiF
3. Collimator: Pb, polyethylene
4. Reflector: Pb



Overview of previous/ongoing projects

SPOKE 8 - Development of a Processing Pipeline for Medical Images and Omics Data in Patients with Pancreatic Cancer

Objectives

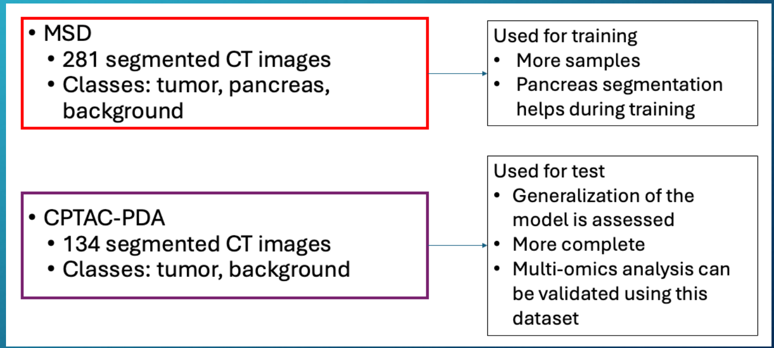
Image analysis for the study of neoplasms of internal organs with particular attention to pancreas neoplasms.
Extraction of data useful for the treatment of patients and to establish correlations with clinical data and genome.

Tools

Radiological images (before and after surgery), digitized biopsies, ultrasound, clinical picture, genomic sequencing.

Two main public datasets available as pipeline workflow input data

- Medical Segmentation Decathlon - Task07_Pancreas
- CPTAC-PDA



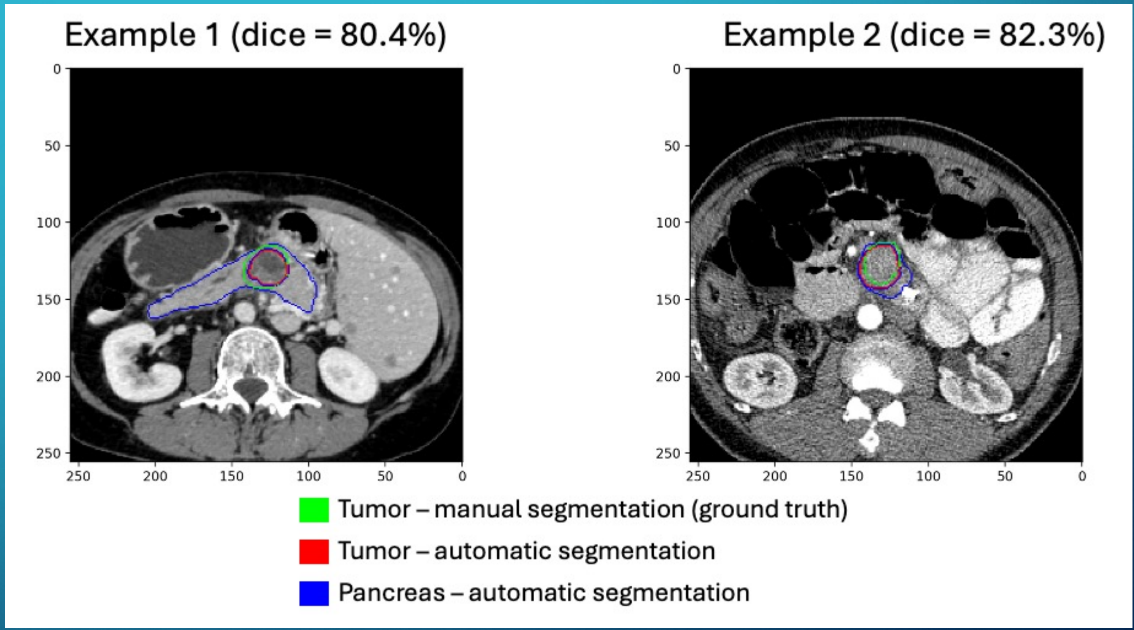
SPOKE 8 - Development of a Processing Pipeline for Medical Images and Omics Data in Patients with Pancreatic Cancer

Preliminary results from segmentation models

Mean dice score for the tumor class

	MSD validation set	Full CPTAC-PDA
SRSNet_v05 (ours)	37.5%	42.1%
nnU-Net (3d model)	53.1%	46.7%

examples from CPTAC-PDA



PROGETTI PNRR

PROGETTI CALCOLO IN AMBITO HEALTH – BARI

GIACINTO DONVITO

- Spoke8 - ICSC
- DARE
  - Già presentato in INFN-LS
- ITINERIS
  - Progetto sulla Biodiversità: INFN-Bari si occupa di fornire risorse di Calcolo e Servizio Cloud evoluti per supportare la comunità nazionale e internazionale che lavora nell'ambito del monitoraggio della biodiversità
- UNIBA come ReCaS-Bari partecipa ad altri progetti:
  - Centro Nazionale 3 (Omics)
  - ElixirXNextGenIT
    - Infrastruttura di ricerca per la realizzazione di una piattaforma nazionale di sequenziamento, analisi e gestione dati.
    - ReCaS-Bari fornisce risorse e tecnologie cloud

PROGETTI EU

- EuroScienceGateway:
  - START: 01/09/2022 || END 31/08/2025
  - Obiettivo:
    - Accessible e-Infrastructure resources for European scientists to enable pioneering data-driven research across scientific domains.
    - Support the varieties of analysis types and diverse usage patterns through efficient and smart job distribution to appropriate and sustainable infrastructures.
    - The application of FAIR principles to workflows and adoption of FAIR Digital Objects to stimulate reusable and reproducible research and enable the EOSC Interoperability Framework.
    - Adoption of the EuroScienceGateway by researchers in diverse scientific disciplines.
  - EuroScienceGateway will leverage a distributed computing network across 13 European countries, accessible via 6 national, user-friendly web portals, facilitating access to compute and storage infrastructures across Europe as well as to data, tools, workflows and services that can be customized to suit researchers' needs. At the heart of the proposal workflows will integrate with the EOSC-Core. Adoption, development and implementation of technologies to interoperate across services, will allow researchers to produce high-quality FAIR data, available to all in EOSC. Communities across disciplines -- Life Sciences, Climate and Biodiversity, Astrophysics, Materials science -- will demonstrate the bridge from EOSC's technical services to scientific analysis.

COLLABORAZIONI SCIENTIFICHE

- Elixir-IT
  - Una collaborazione fra 29 fra enti pubblici e università italiane con l'obiettivo di supportare la ricerca nel settore delle scienze della vita
- Lifewatch
  - Una collaborazione fra 35 fra enti pubblici e università italiane che hanno l'obiettivo di creare una infrastruttura per la ricerca sulla biodiversità e gli ecosistemi.

CERTIFICAZIONE ISO DATA CENTER

- Si sta lavorando ad una certificazione multi-sito (CNAF, Bari e CT) di una infrastruttura di Cloud computing evoluta per gestire servizi e data biomedicali e alte comunità con dati critici
- Per la prima volta si punta a servizi più evoluti che il solo IaaS

New scope

Coprogettazione, sviluppo e manutenzione di soluzioni software di DataCloud per il settore della ricerca.

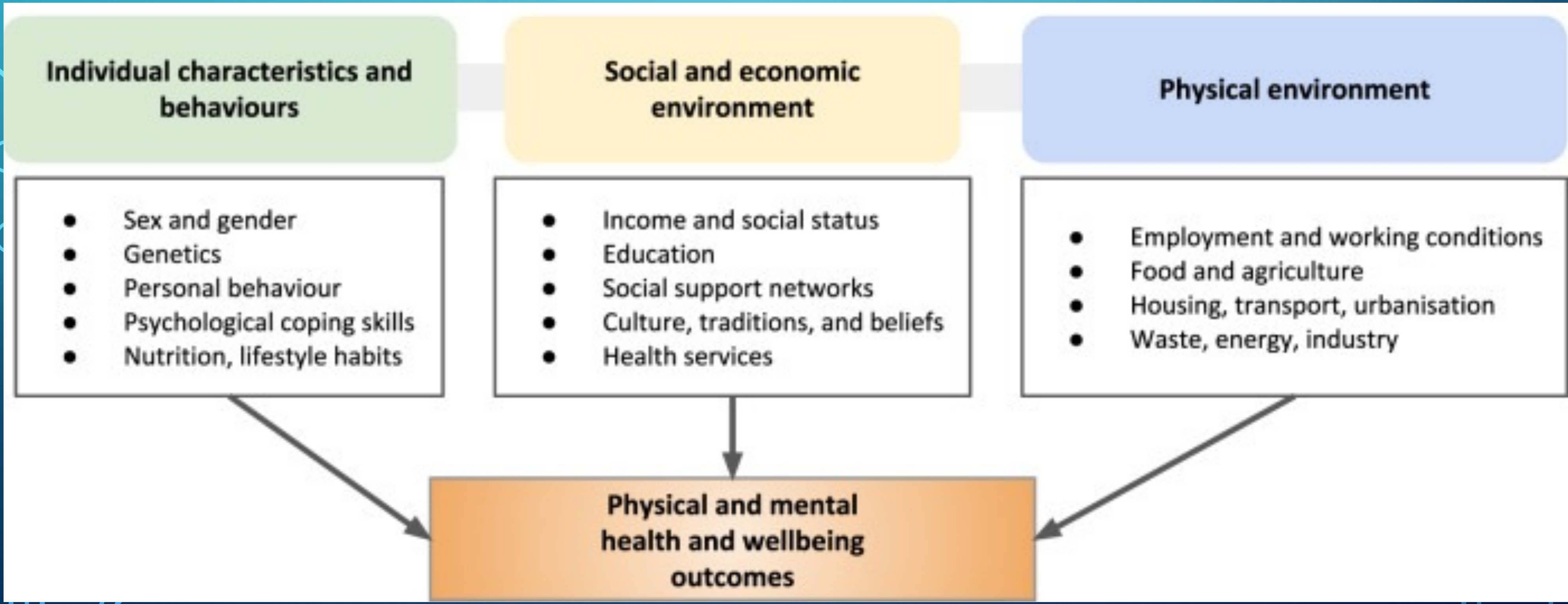
Erogazione di servizi di DataCloud IaaS, SaaS e PaaS in community deployment model.

Artificial intelligence for Medicine in digital age

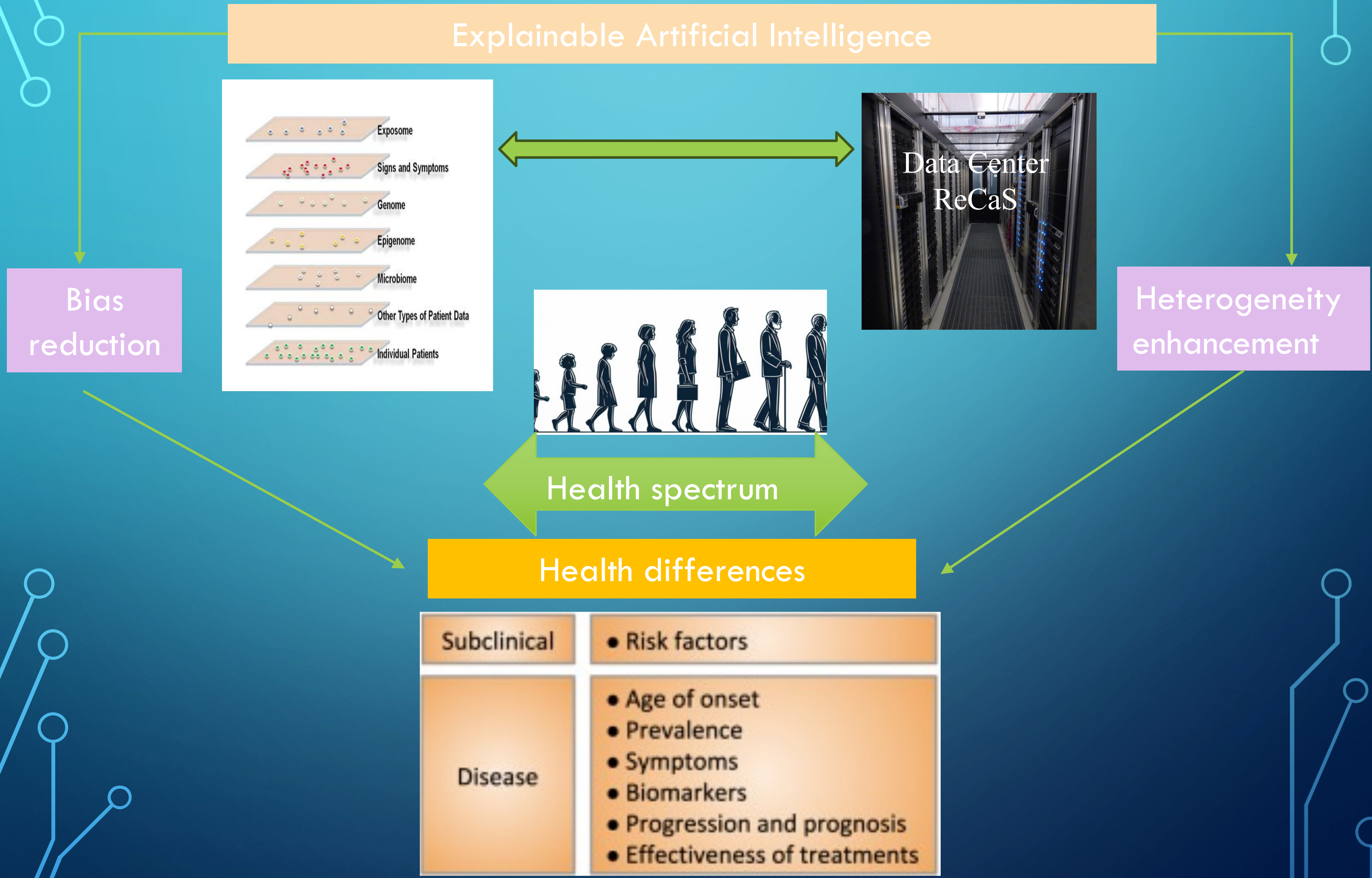
S. Tangaro, R. Bellotti, D. Diacono, A. Monaco, N. Amoroso, L. Bellantuono, M. Larocca, E. Pantaleo, …

DETERMINANTS OF PHYSICAL AND MENTAL HEALTH

Explainable Artificial Intelligence

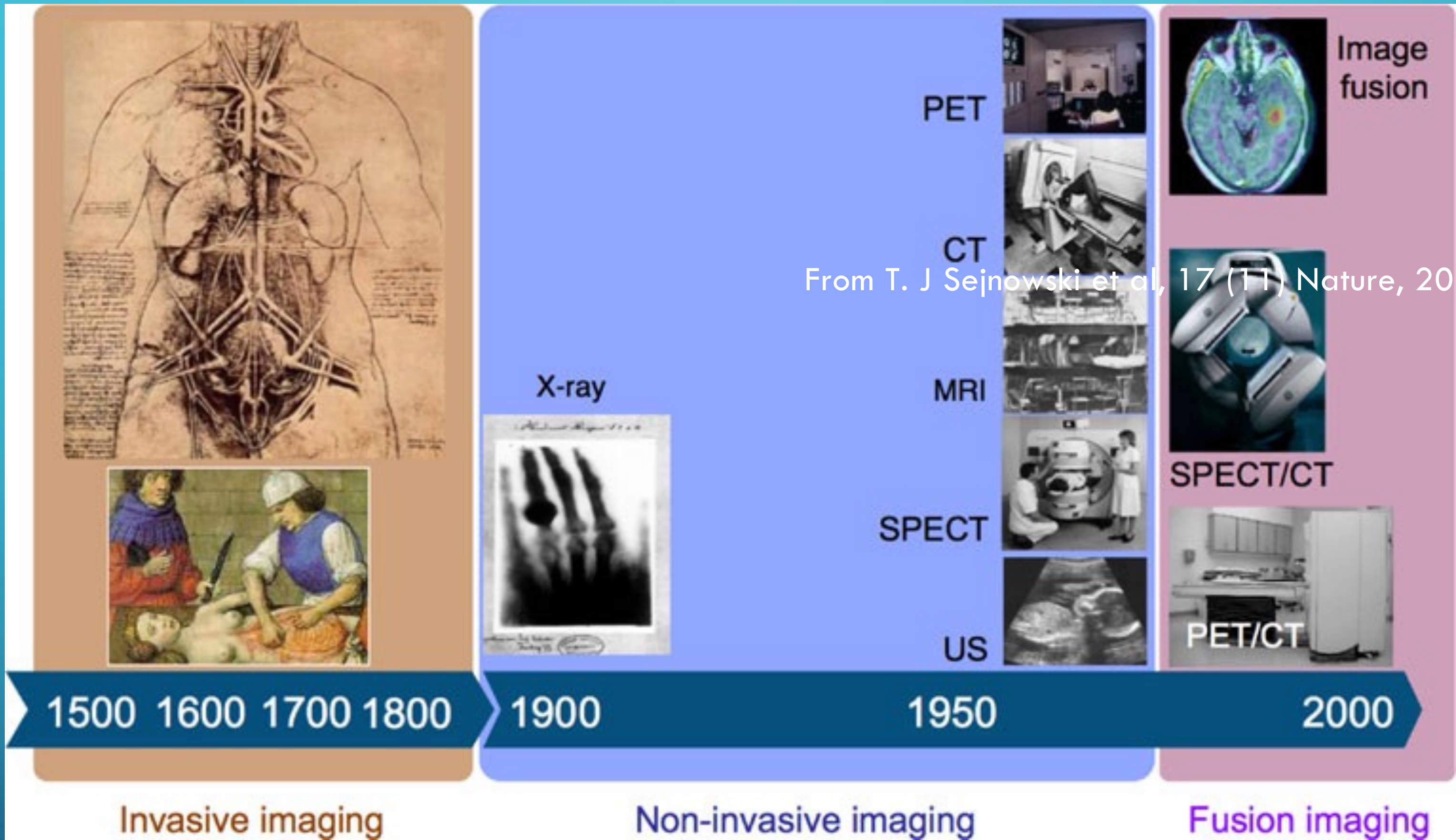


EXPLAINABLE ARTIFICIAL INTELLIGENCE FOR HEALTH APPLICATIONS

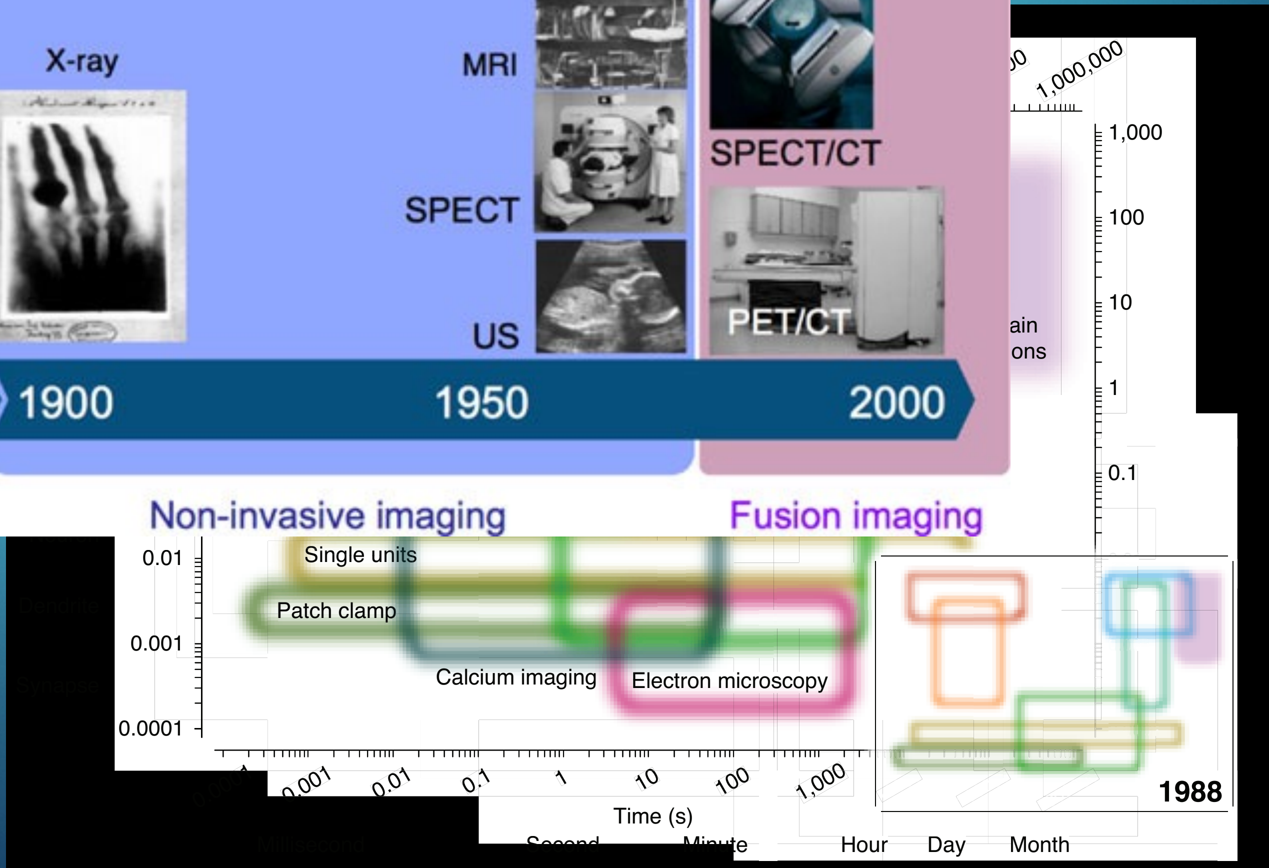


IMAGING ADVANCES

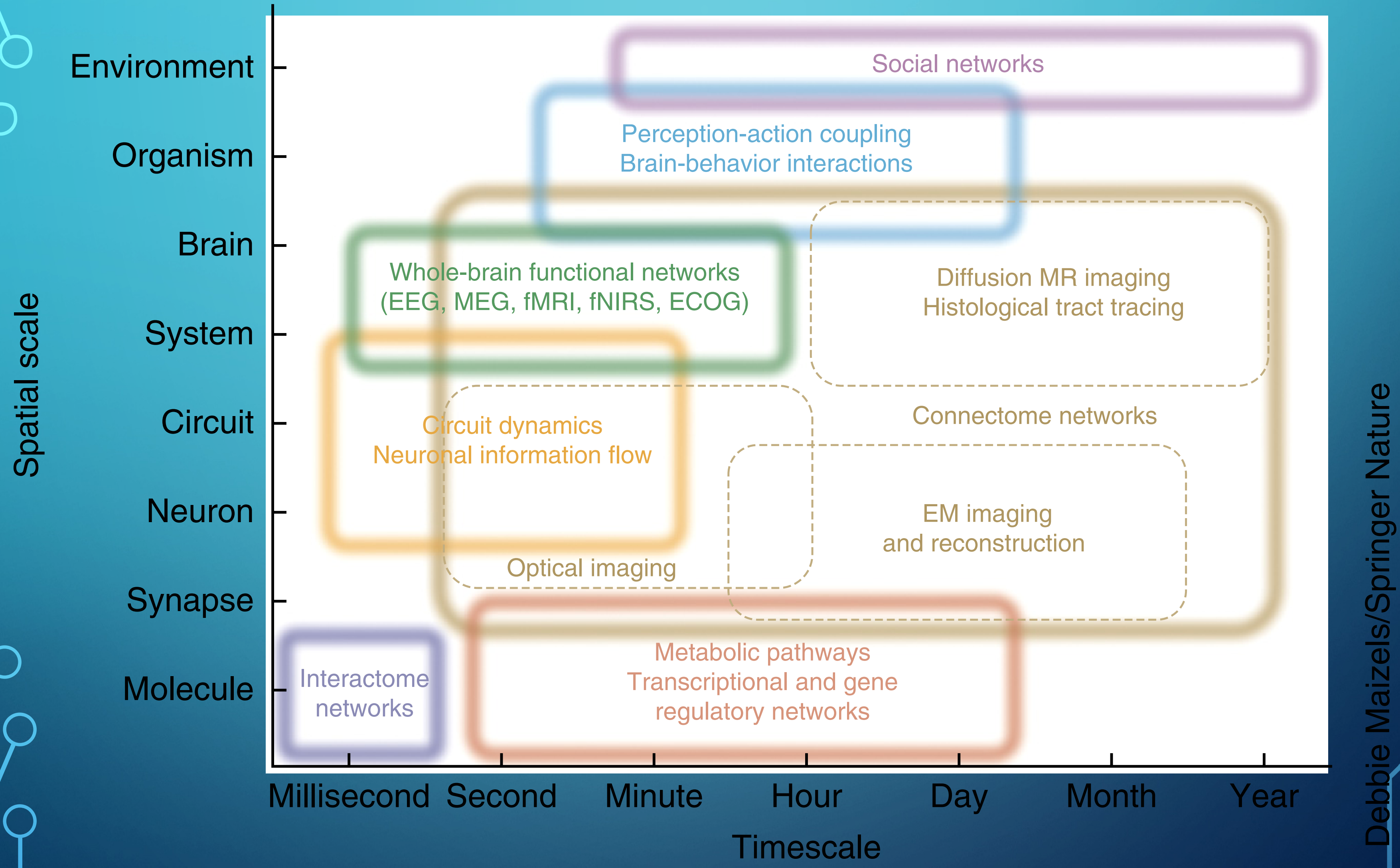
from T. Beyer et al., Insights Imaging (2011)



From T. J Sejnowski et al, 17 (11) Nature, 2014



NETWORK NEUROSCIENCE



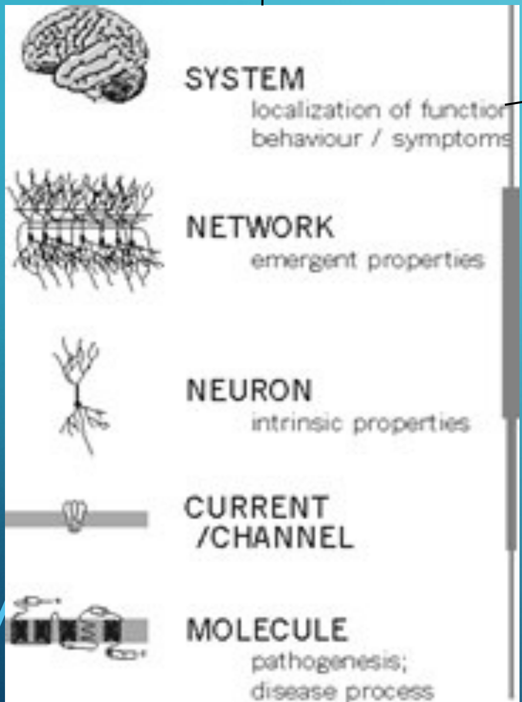
Danielle S Bassett & Olaf Sporns, 20 (3) Nature 2017

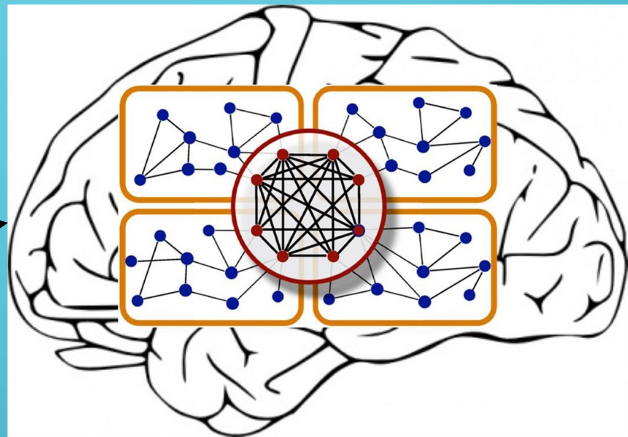
ARTIFICIAL INTELLIGENCE

- **Machine learning** (supervised or unsupervised)
  - **Data mining** (used also for Natural Language Process and Images classification)
    - Classification trees (for classifying/predicting discrete outcomes, e.g. bad/good)
    - Regression trees (for continuous outcomes, e.g. cost forecasting)
    - Belief networks (learning of probabilistic models)
    - Support vectors machines (learning of mathematical models)
    - Neural networks (learning of mathematical models)
      - » **Deep learning**
    - Conditional random fields
    - Reinforcement learning
  - **Process mining**
    - temporal pattern discovery
- **Complex Network and emergent behaviour** (physiological phenomena result from a complex series of interactions that occur hierarchically)
  - Dynamic interactions
  - Emergence

THE BRAIN AS A COMPLEX SYSTEM

Large – scale observations: neuroimaging/electrophysiological recordings





Complexity and emergent behaviour: cognitive and physiological phenomena result from a complex series of interactions that occur hierarchically.

- Many components
- Dynamic interactions
- Emergence

Public large-scale validation studies

Segmentation and classification results can be exploited to design computer aided detection systems.

The lack of an unbiased comparison among different studies has motivated in recent years a number of international challenges have been promoted to compare algorithms and methodologies within a common framework.

next_AIM - Artificial Intelligence in Medicine: *next steps*

INFN-CSN5

Project coordinator:
A. Retico, Pisa

13 Research Units:
- Bari (S. Tangaro)
- Bologna (D. Remondini)
- Cagliari (P. Oliva)
- Catania (M. Marrale)
- Ferrara (G. Paternò)
- Firenze (C. Talamonti)
- Genova (A. Chincarini)
- Lab. Naz. Sud (G. Russo)
- Milano (C. Lenardi)
- Napoli (G. Mettivier)
- Pavia (A. Lascialfari)
- Padova (A. Zucchetta)
- Pisa (M.E. Fantacci)

https://www.pi.infn.it/aim/

AIM [2019-2021]
next_AIM [2022-2024]

WP1 — Challenge I: no-so-big data

Strategies for efficient learning with limited data samples.

Evaluation of robustness and reliability of trained models.

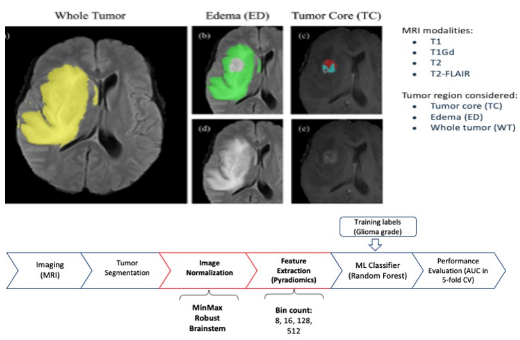
WP2 — Challenge II: explainable AI (XAI)

Make AI results understandable to humans.

Which image/data features are relevant to make a decision?

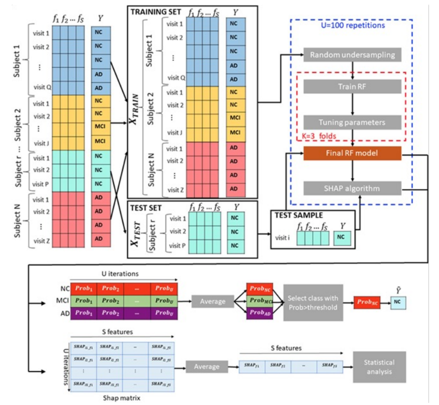
WP3 — Applications to real-world data samples include ....

Evaluation of the robustness of radiomic features in multiparametric MRI and its impact on predictive value of AI models



Ubaldi L, Saponaro S, Giuliano A, Talamonti C, **Retico A**. Deriving quantitative information from multiparametric MRI via Radiomics… *Phys Medica* 2023;107:102538 https://doi.org/10.1016/j.ejmp.2023.102538.

Robust implementation of explainable AI methods



Lombardi A, Diacono D, Amoroso N, Biecek P, Monaco A, Bellantuono L, … **Tangaro S**, Bellotti R. A robust framework to investigate the reliability and stability of explainable artificial intelligence …. *Brain Informatics* 2022; 9:17. https://doi.org/10.1186/s40708-022-00165-5.

WP4 — Computing resources and SW repository organization

ReCaS, IBiSCo, INFN-Cloud + local HW resources

WP5 — Exploitation of research results and communication

conferences, publications and outreach, collaboration with aifm

Long-standing collaboration with Italian centers (hospitals and IRCCS) and with international consortia for data sharing

ASSOCIAZIONE ITALIANA di FISICA MEDICA e SANITARIA
La Fisica al servizio della salute

POS 2

RN: P. Oliva

TELE-NEURART | Rete Nazionale Pediatrica per il tele-monitoraggio e la tele-riabilitazione dei disturbi e delle disabilità del neurosviluppo tramite l'individuazione e l'analisi di biomarker digitali, identificati tramite intelligenza artificiale

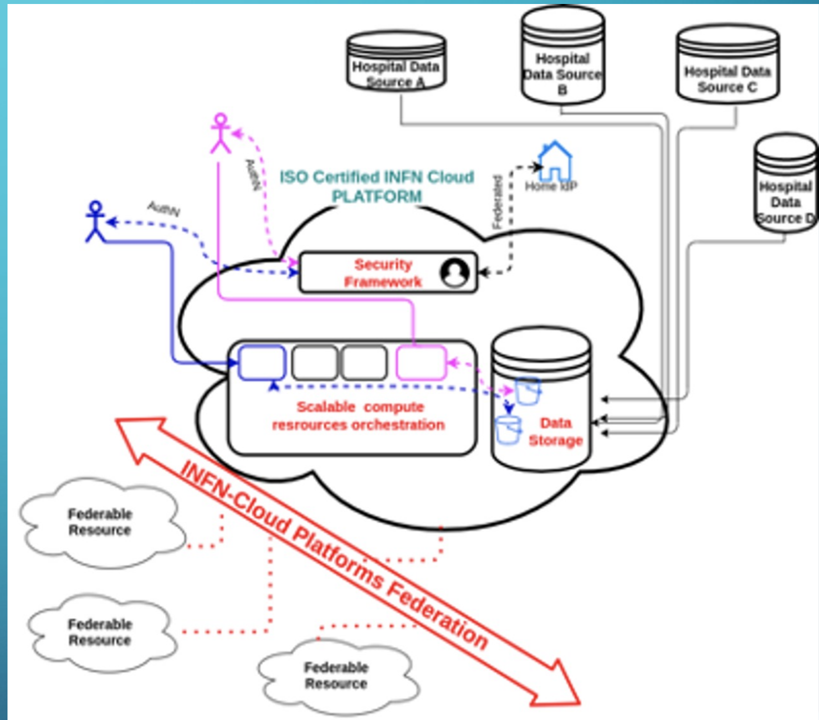
Design of a dedicated platform for medical data analysis with AI

The joint effort by the **Medical Physics and High Energy Physics communities** led to the design of a dedicated computing infrastructure which can link Clinical, Medical Research and Technical Research Centers.

The INFN-cloud based computing infrastructure is:

- **especially suited for training AI models**
- equipped with **secure storage and communication** systems (ISO/IEC 27001 27017 27018)
- **compliant with data protection regulation (GDPR)**

It would be able to accelerate the **development and extensive validation of AI-based solutions for Medical Imaging**.



[Retico A, Avanzo M, Boccali T, Bonacorsi D, Botta F, Cuttone G, et al. Enhancing the impact of Artificial Intelligence in Medicine: A joint AIFM-INFN Italian initiative for a dedicated cloud-based computing infrastructure. Phys Medica 2021;91:140–50. https://doi.org/10.1016/j.ejmp.2021.10.005.]

POS 3 - GENESIS ATI

Studio degli eventi GENEtici alla baSe della CarcInogeneSi in aree ad Alto Tasso di Inquinamento per tipologia produttiva

Obiettivo del progetto

Obiettivo del progetto è mettere in relazione i dati ambientali forniti da ARPA Sicilia, relativi alla presenza di sostanze chimiche e alla loro concentrazione in acque superficiali e profonde, con i dati clinici di pazienti oncologici, già presenti nel Registro Tumori gestito dall'ASP di Ragusa; oltre all'analisi retrospettiva dei dati già presenti nel database di ARPA Sicilia e nel Registro Tumori, il progetto prevede l'attivazione di studi clinici condotti dall'Università di Palermo e dallo IOR con il coinvolgimento di soggetti residenti a zone a rischio alto e basso, con lo scopo di creare un setting predittivo di potenziali malattie tumorali correlate o comunque condizionate dalla presenza di agenti ambientali inquinanti.

Conclusions (?)

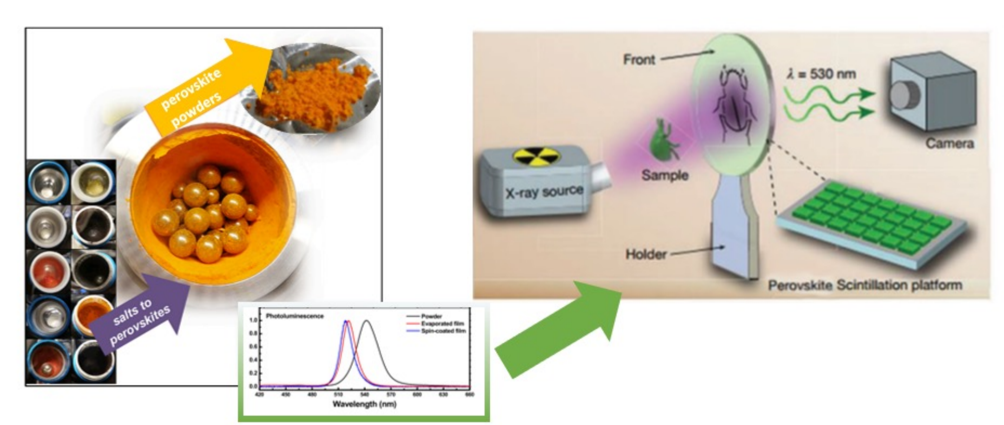
we are just at the beginning…

Further detail …

SHINE

Plastic Scintillators Phantom via additive manufacturing techniques

Anna Paola Caricato

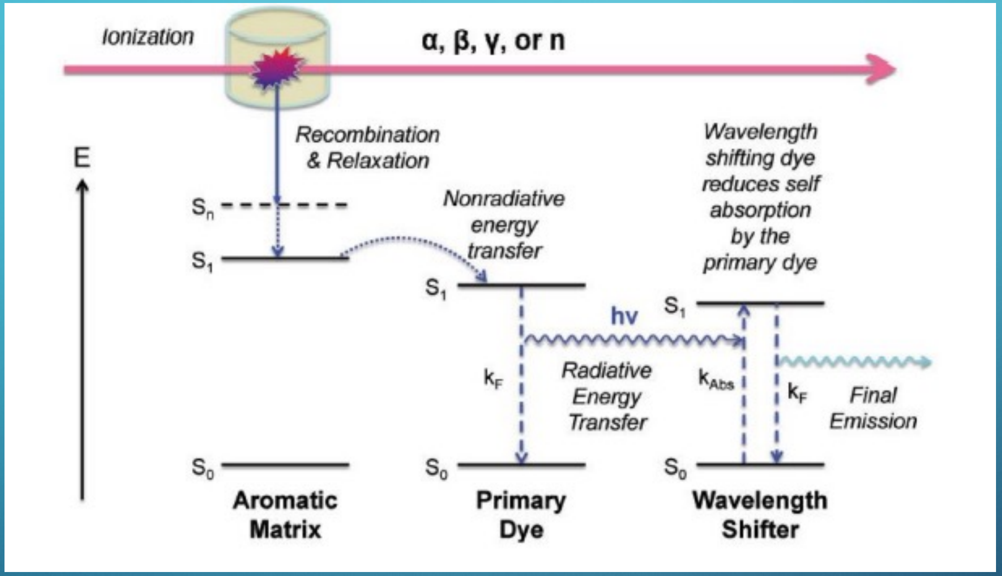


3 years experiment

INFN Units participating in SHINE: Lecce, Ba, LNL, TIFPA

Introduction/motivation

Plastic scintillator are of great interest in many application fields (security, medicine, HEP…)



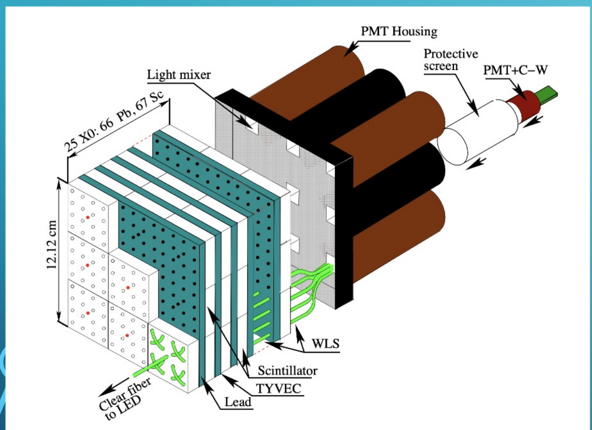
Plastic scintillator

Introduction/motivation

DEMAND: advanced scintillating materials with **high detection performances** and with **complex geometries and architectures.**

Future upgrades of the CERN LHC experiments have increased the interest in scintillators with high aspect ratio geometry

Now (SHASHLIK modules)



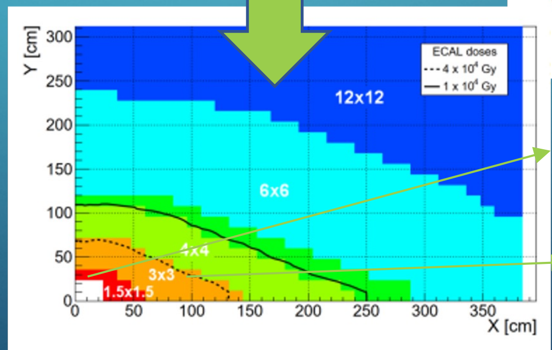
Ref: LHCb-PUB-2013-010

Polystyrene Scintillators and lead tiles + Polystyrene WLS fibers

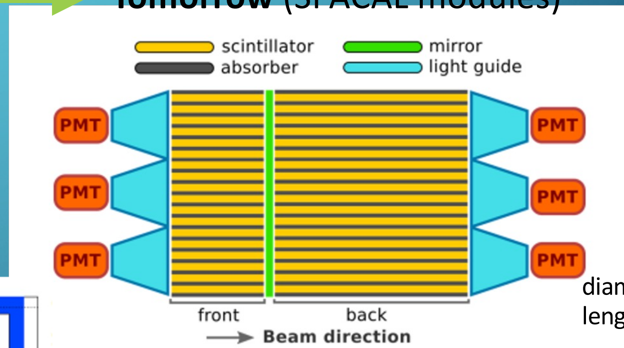
→ Rad-hard up to ~40 kGy

After LS4 (2035) increased luminosity

→ dose up to ~1MGy



Tomorrow (SPACAL modules)



diameter 1-2 mm, length 200-300 mm

Ref: LHCB-TDR-23

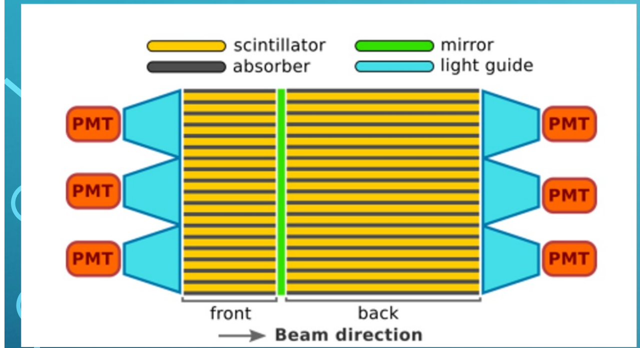
W absorber and inorganic crystal fibers (inner regions)

Pb absorber and organic fibers (near the inner region)

Introduction/motivation

DEMAND: advanced scintillating materials with **high detection performances** and with **complex geometries and architectures.**

Future upgrades of the CERN LHC experiments have increased the interest in scintillators with high aspect ratio geometry



SPACAL modules with Pb absorber and organic fibers (near the inner region)

challenging with conventional used materials

Requirements:

- **Radiation hard (up to 100 – 200 kGy) and performing scintillating materials** (comparable to commercial polystyrene based scintillators, e.g. SCSF-78Kuraray);
- **Low cost techniques;**

Introduction/motivation

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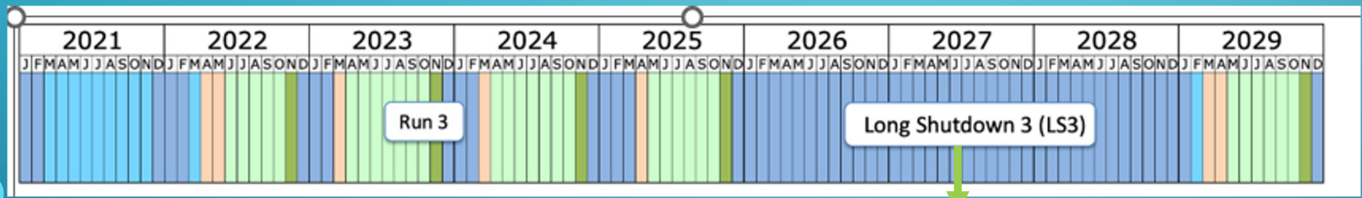
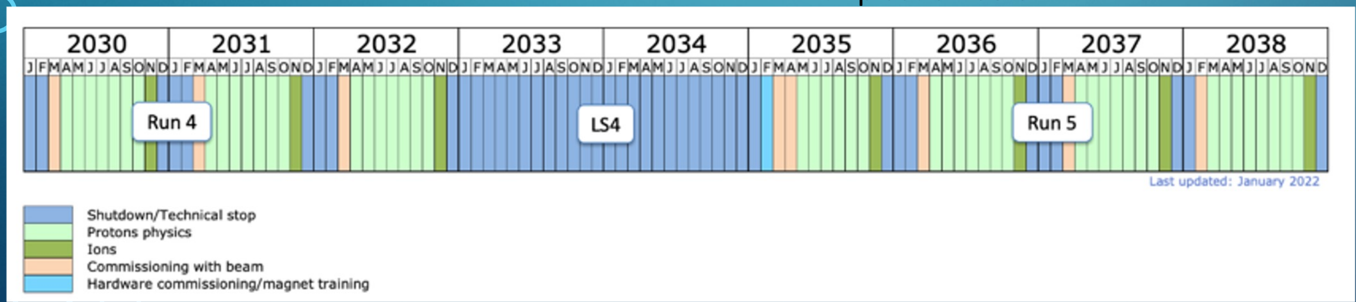
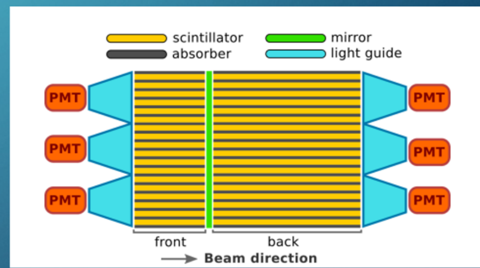
Future upgrades of the CERN LHC experiments have increased the interest in scintillators with high aspect ratio geometry

Longer term LHC schedule



setting of Pb and W SPACAL with plastic fibers



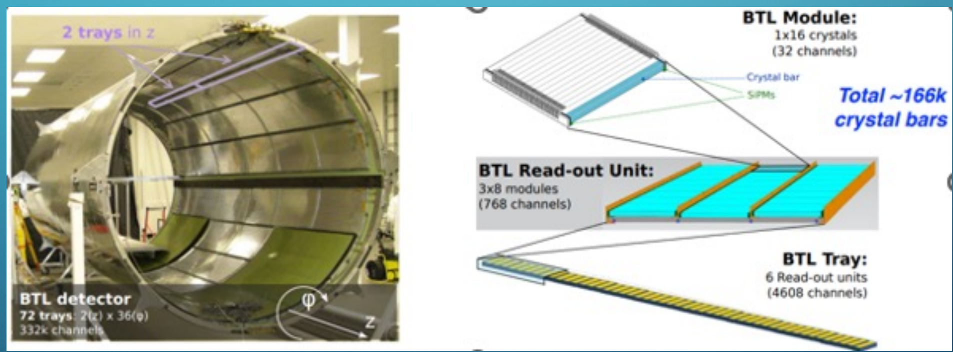


Introduction/motivation

DEMAND: advanced scintillating materials with **high detection performances** and with **complex geometries and architectures.**

Future upgrades of the CERN LHC experiments have increased the interest in scintillators with high aspect ratio geometry

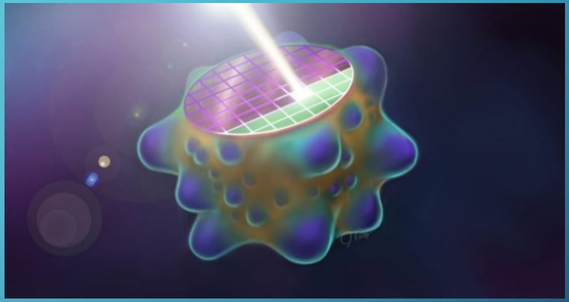
CMS experiment will employ LYSO bars of 3x3x57 mm^3 in the barrel to time-tag minimum ionizing particles with a precision of a few tens of ps



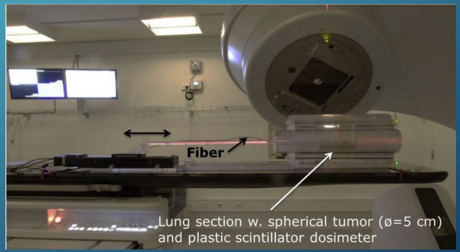
Introduction/motivation

DEMAND: advanced scintillating materials with **high detection performances** and with **complex geometries and architectures.**

Medicine: Modern delivery techniques of particle therapy (e.g. pencil beam scanning) requires to study the behavior of the energy deposition dynamics and dose released to the target possibly while it moves for higher accuracy in dose deposition to the target volume as well as improving the sparing of the surrounding healthy tissue .



Time-resolved dosimetry requires detectors with high spatial resolution coupled with the possibility to get online response



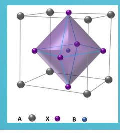
Introduction/motivation

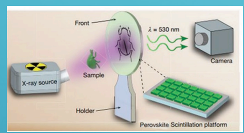
DEMAND: advanced scintillating materials with **high detection performances** and with **complex geometries and architectures**

INVESTIGATED SOLUTION :

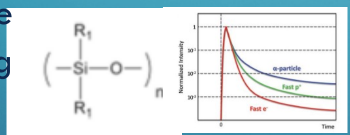
New and promising materials

- **Perovskite Material ABX_3**: large stopping power; high mobility-lifetime product; fast response (~ ns); large bulk resistance





- **Polysiloxane** have demonstrated interesting properties as scintillator



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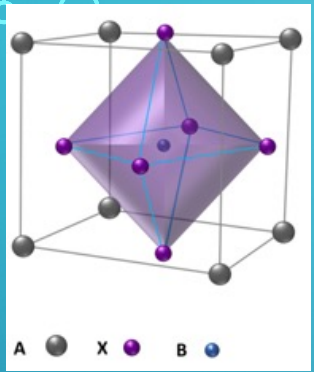
Advanced technologies

Additive manufacturing (AM) is a well-known technique for the fast fabrication of complex objects with different geometries and different polymers can be 3D

GOAL: realization of low cost, reproducible, high added value and innovative plastic scintillators by additive manufacturing using perovskite-polymer nanocomposite and polysiloxane materials for time-resolved dosimetry, high energy physics (LHCb).....

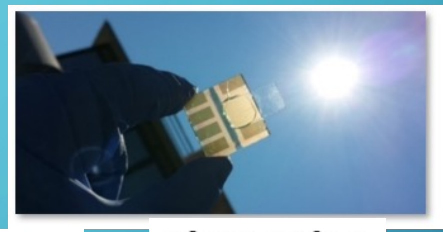
Perovskite (ABX_3)

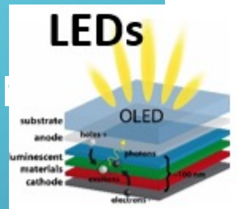


A: **cation,** organic (i.e. $CH_3NH_3^+$, $CH(NH_2)_2^+$) or inorganic (i.e. Cs^+, Rb^+)
B: **metal cation** (i.e. Pb^{2+}, Sn^{2+}, Ge^{2+})
X: **halogen anion** (i.e. F^-, Cl^-, Br^-, I^-)

- High photoluminescence (PL) quantum yields ;
- Long carrier diffusion lengths;
- defect tolerance;
- Low cost;
- Tunable band-gap with com
- -----

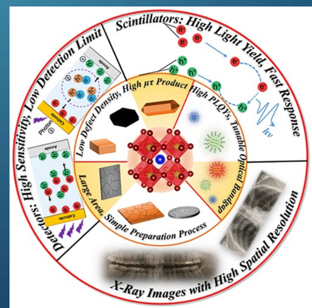
Photovoltaics





Photonics

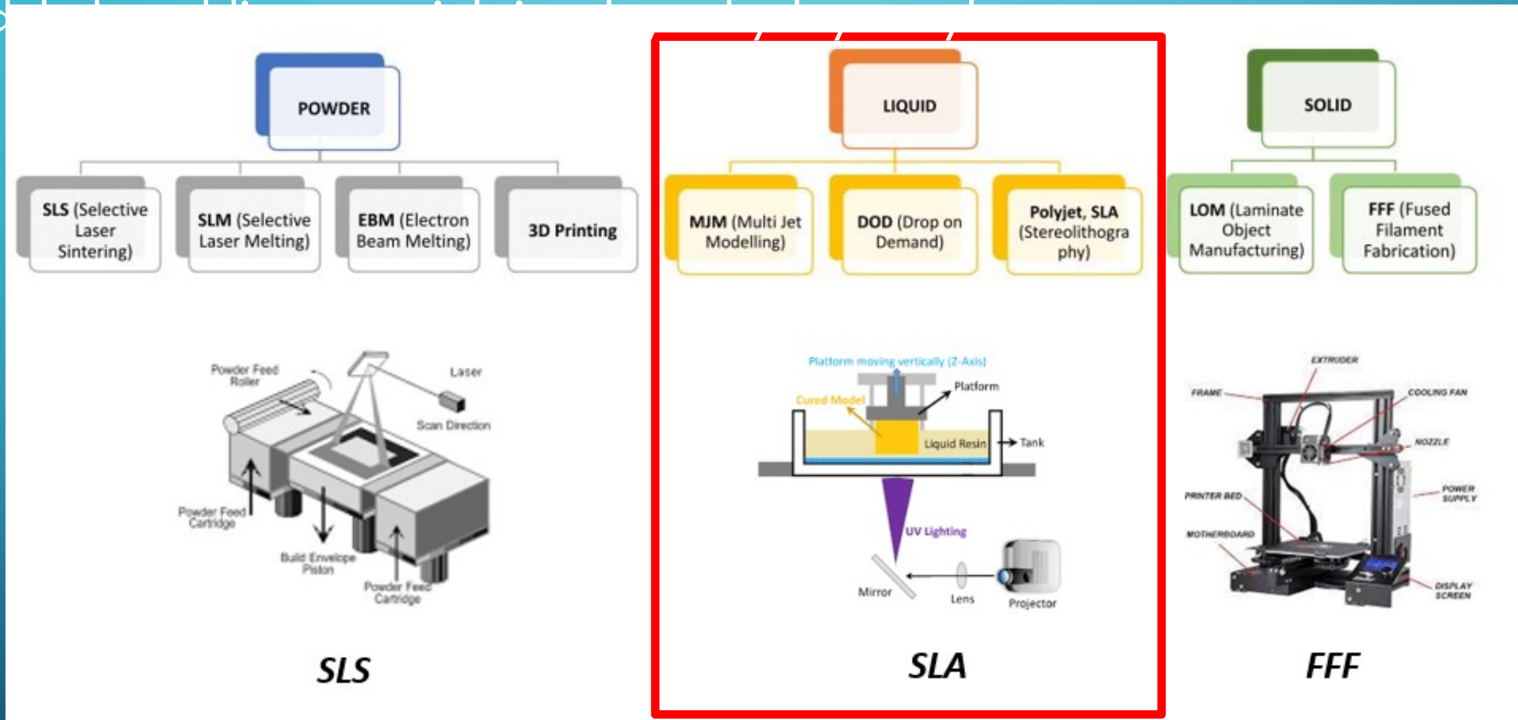
Ionizing Radiation detectors



In addition: large stopping power; high mobility-lifetime product; fast response (~ ns); large bulk resistance

Additive manufacturing (AM)

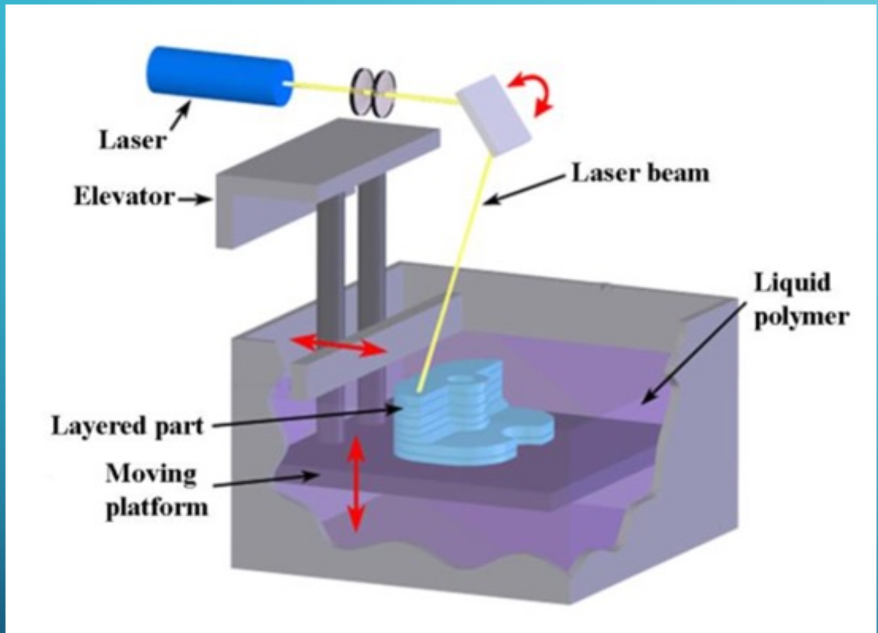
AM is a class of promising machineries that produce objects starting from computer-aided design (CAD) mod



Better resolution

Additive manufacturing (SLA)

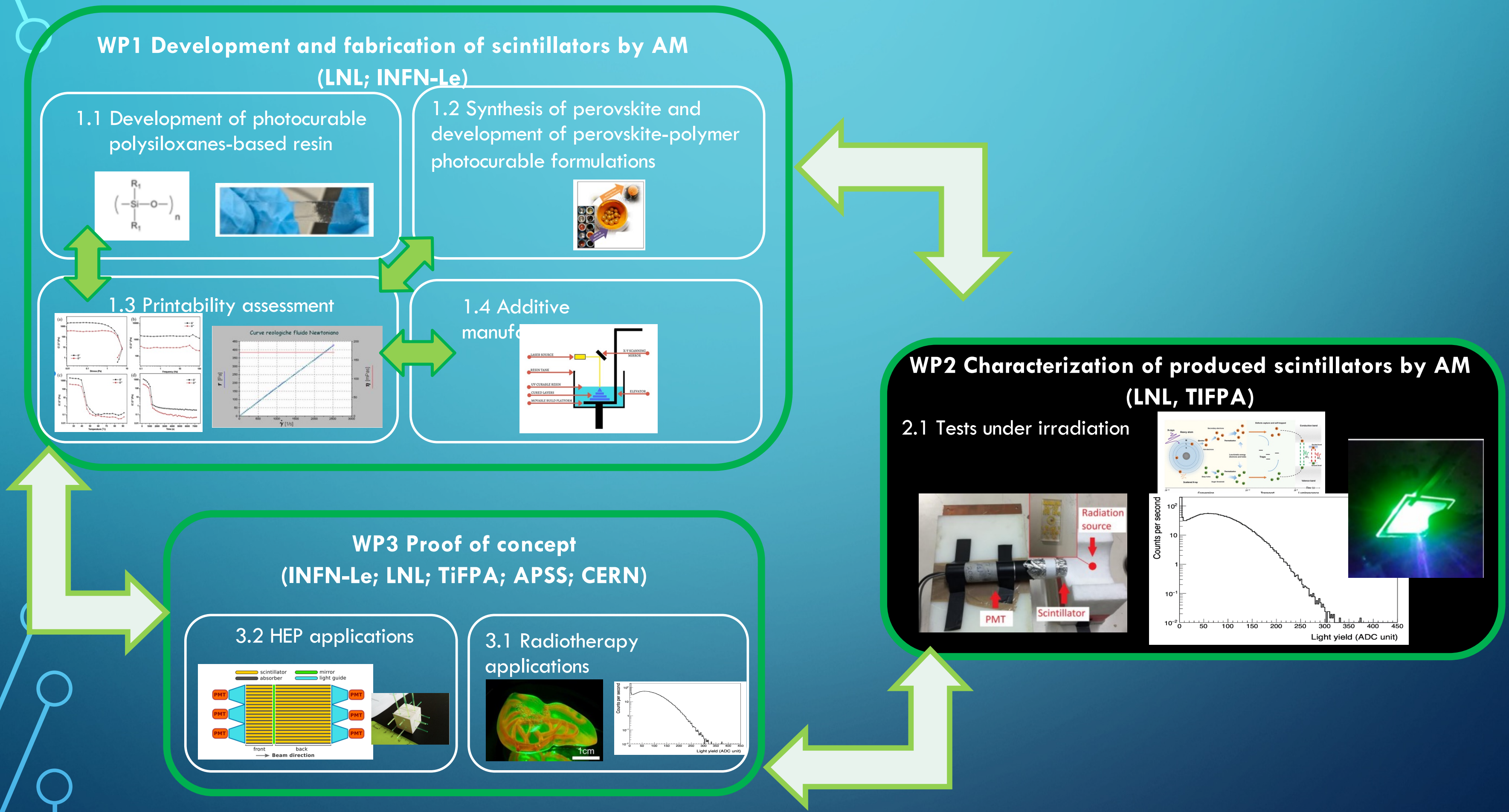
Stereolithography (SLA)



https://www.youtube.com/watch?v=5L5vdpkIrtU

2018. Antimicrobial modified hydroxyapatite composite dental bite by stereolithography Makvandi, P., **Corcione, C.E.**, Paladini, F., (...), Pollini, M., Maffezzoli, A., *Polymers for Advanced Technologies*, 29(1), pp. 364-371

Project organization and methodology



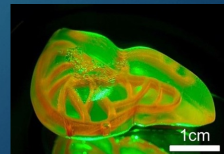
SUMMURIZING

FINAL GOAL: realization of low cost, reproducible, high added value and innovative plastic scintillators by additive manufacturing using perovskite-polymer nanocomposite and polysiloxane materials.

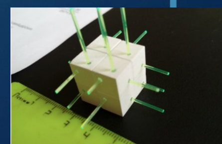
Preliminary goals:

- Synthesis of photocurable resins based on perovskite-polymer formulation or polysiloxane-based formulation with suitable properties (viscosity, times and speed of photopolymerization) for stereolithography;
- Transparent and reproducible composites with scintillating properties at least comparable with commercial scintillators

PROOF OF CONCEPT:



✓ detector with a typical shape of a radiotherapy target to be embedded on a dedicated phantom which can mimic the typical human movements (e.g.: breathing) and able to provide in real time a 3D information on the dynamics of the dose distribution delivered to the moving target.



✓ 3D-printed scintillators with fast timing capabilities and good light transport, featuring arbitrary geometries to match the physics requirements of particle detectors at future colliders and reduce the production costs (SpaCal configuration).

Project

AT-SVB

Airborne Transmission of SARS-CoV-2, Viruses and Bacteria in workplaces

2-year experiment (2021-2022)

INFN
Istituto Nazionale di Fisica Nucleare

INFN Units participating in AT-SVB: Lecce and Florence

The main goals of the AT-SVB Project

- Identify aerosol monitoring and analysis methods for the "early" identification of the presence of SARS-CoV-2 and other airborne pathogens in workplaces (laboratories, offices, etc.)
- Identify relationships between airborne pathogens, size distribution and composition of aerosol particles in relation to (1) **meteorological parameters** (e.g., temperature, relative humidity) and (2) **workplace aeration condition** (no aeration, air exchange, air ventilation, air conditioning system) to better define monitoring operation conditions
- Identify possible viral and bacterial transmission routes in areas outside the monitored workplaces by collecting both indoor and outdoor aerosol samples
- Develop automatic systems for bioaerosol monitoring at scheduled times

INFN Istituto Nazionale di Fisica Nucleare

Aerosol e Clima

CEDAD CEntro di Fisica applicata, DAtazione e Diagnostica

UNIVERSITÀ DEL SALENTO

AT-SVB Airborne Transmission of SARS-CoV-2, Viruses and Bacteria in Workplaces

Airborne bacteria characterization

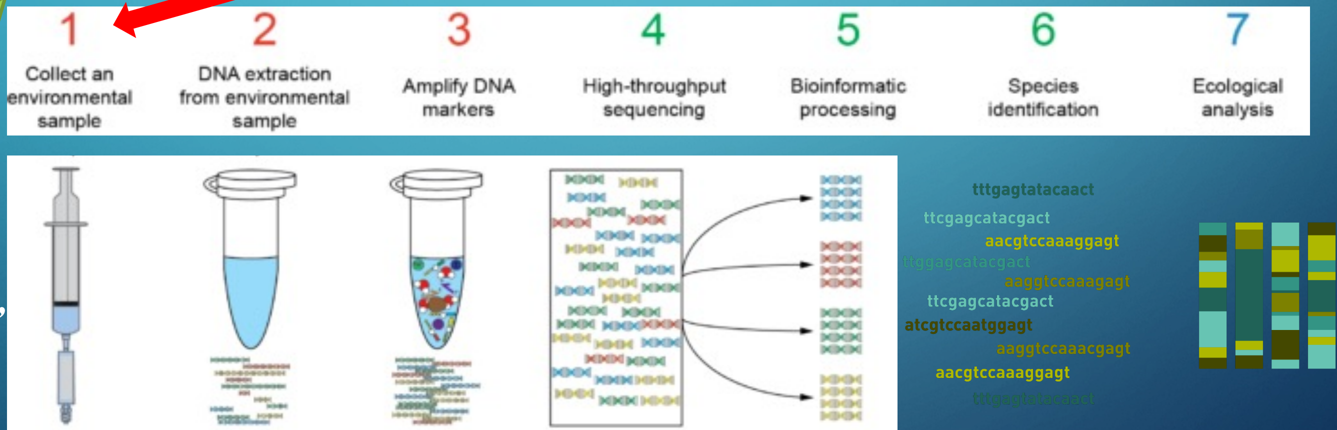
Sample elution foam (BOBCAT)

4-5 mL

aerosol monitoring and analysis methods for the identification of the presence of airborne pathogens

Genomix4Life
MICROARRAYS
SEQUENCING
BIOMARKERS
BIOINFORMATICS

quartz or Teflon filters



Metagenomic sequencing

Lab. Microbiologia, DISTEBA, University of Salento

Monitoring Campaign

Mathematics and Physics Department, University of Salento, Lecce

18 aerosol samples collected by means of the ACD-200 Bobcat **from September 2020 to January 2021**.

- **4 samples** in the **High Energy Laboratory** (denoted by "**AE**")
- **5 samples** in the **Electronics Laboratory** (denoted by "**R**")
- **4 samples** in the **corridors** of the Mathematics and Physics Department (denoted by "**C**").

- **5 samples** were, instead, collected from outdoor environments, namely the Department **roof**, and were denoted by "**F**".

MAIN GOAL

- Comparing the **airborne microbiome** from different indoor and outdoor locations and identify **potential pathogens** using a **compositional data approach**

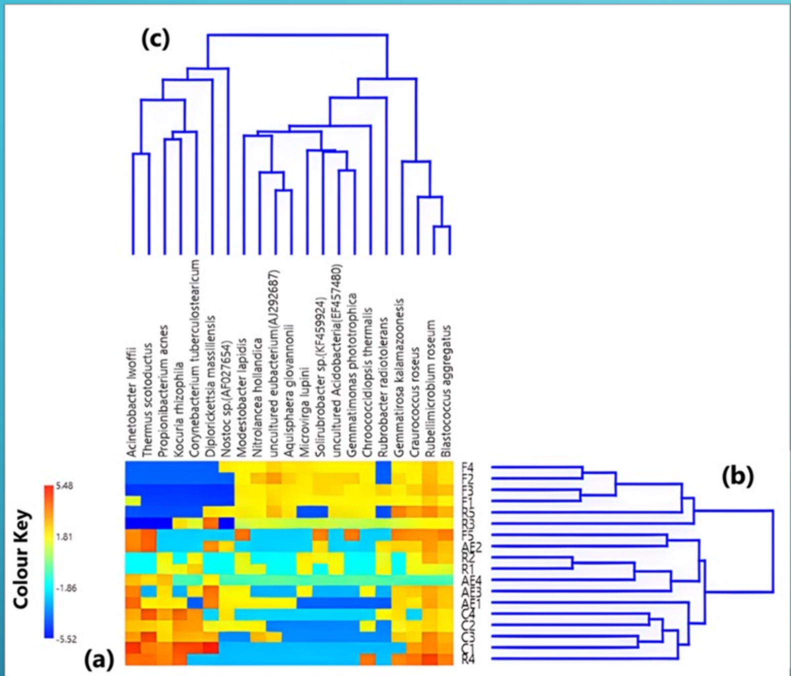
atmosphere MDPI

Article

Characterization of the Airborne Microbiome in Different Indoor and Outdoor Locations of a University Building Using an Innovative Compositional Data Analysis Approach

Mattia Fragola [1,2], Salvatore Romano [1,2,*], Dalila Peccarrisi [1], Adelfia Talà [3], Pietro Alifano [3], Alessandro Buccolieri [1,2], Gianluca Quarta [1,2] and Lucio Calcagnile [1,2]

Main Results



Both Dendrograms and Color Map are based on the 21 airborne bacterial species with the highest abundances

21 bacterial species (out of 5903 in total) were chosen among those characterized by the largest number of reads in every sample and detected at least in 40% of the 18 analysed samples.

CLUSTER 1

4 outdoor samples (F1, F2, F3, F4), in addition to **2 samples** from **Electronics laboratory** (R3, R5)

CLUSTER 2

1 outdoor sample (F5), as well as the other **3 samples** from **Electronics lab** (R1, R2, R4) and the **8 samples** from **High-Energy lab** and the **corridors**

Risultati e Conclusioni

1) Caratterizzazione delle comunità batteriche/virali presenti nei campioni di aerosol monitorati tramite codici numerici appositamente predisposti

2) Report sui campionamenti effettuati in ambienti indoor nel corso del progetto

3) Caratterizzazione della composizioni chimica, della struttura morfologica e della distribuzione dimensionale dell'aerosol

4) Realizzazione di una banca dati online con i risultati ottenuti nell'ambito delle campagne di monitoraggio

5) Test e messa a punto dei sistemi di controllo sviluppati per il monitoraggio da remoto

Pubblicazione

atmosphere MDPI

Article

Characterization of the Airborne Microbiome in Different Indoor and Outdoor Locations of a University Building Using an Innovative Compositional Data Analysis Approach

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Le attività di ricerca ed i risultati conseguiti dal progetto INFN AT-SVB avranno seguito nell'ambito dei seguenti progetti ed infrastrutture:

1) Progetto **BIO-MASTER** (*BIOaerosol Monitoring And classification: development of a Standardized procedure by integrating different data analysis Techniques and Experimental Research methodologies*) finanziato dal Ministero dell'Università e della Ricerca mediante il "Fondo per il Programma Nazionale di Ricerca e Progetti di Rilevante Interesse Nazionale (PRIN)" per il biennio ottobre 2023 – settembre 2025. Soggetti partecipanti: Università del Salento e CNR-IRET.

BIO-MASTER

2) Progetto **ITINERIS** - Italian Integrated Environmental Research Infrastructures System coordinato dal CNR-IMAA (triennio novembre 2022 – ottobre 2025)

ITINERIS
Italian Integrated Environmental Research Infrastructures System

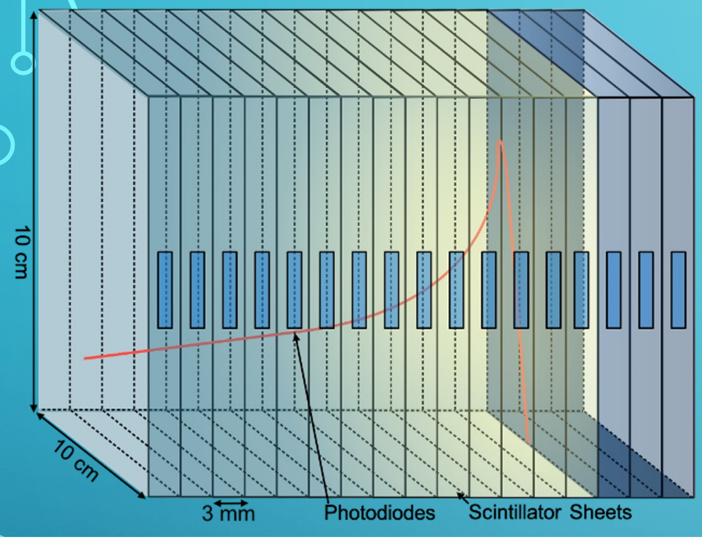
3) Infrastruttura di ricerca europea **ACTRIS** (*Aerosol, Clouds and Trace Gases Research Infrastructure*) ed Italiana **ACTRIS-IT**

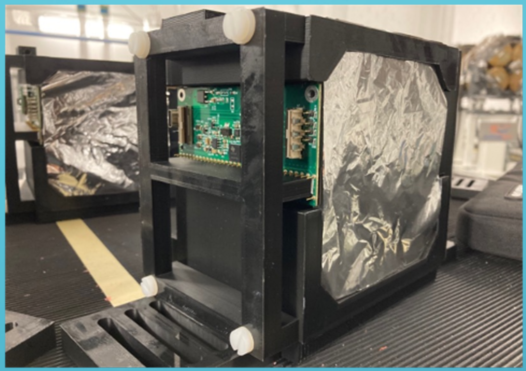
ACTRIS
Exploring the Atmosphere

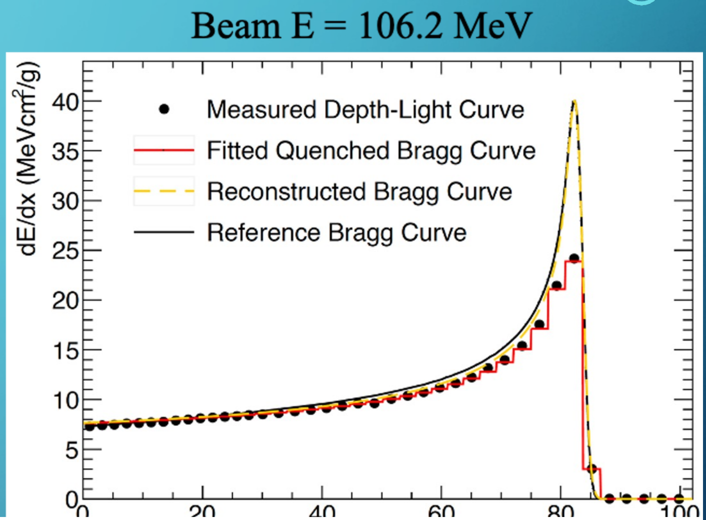
ACTRIS
ITALIA

BACKUP

RANGE MODULE







- Series of optically isolated polystyrene scintillator sheets of size: 10 cm×10 cm × 3 mm.
- Photodiodes coupled to fast, modular ADC electronics read light levels at over 5 kHz.
- Measure depth-*light* curve to reconstruct Bragg depth-*dose* and proton range with accuracy < 0.5mm.
- Modular design: one detector module (32 sheets, 96 mm total depth) can test pencil beam energies between 70–130 MeV. Possibility to daisy chain to cover the full clinical energy range.
- Real-time range reconstruction: 6 kHz data-rate, 40 Hz range fitting.

SCALING TO FLASH

- Dose-rate for FLASH estimated around 40 Gy/s.
  - Estimated delivery time of 100 ms
  - Corresponds to a current of 600 nA to the patient.
- Due to the nanosecond decay time of the plastic scintillator and the large dynamic range of the detector, range measurements are also possible at FLASH dose rates.
  - scintillation light output scales linearly with dose-*rate*.
- Clinical beam performed at UCLH in 2022 has 300 nA cyclotron current.
  - Approx. 1% transmission ratio to treatment room.
  - Expect 600/(300*1%) = 200 factor increase in light.

Range QA measurements for FLASH proton therapy using the Quality Assurance Range Calorimeter

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Abstract. The purpose of this work was to demonstrate the design and performance of a full-sized clinical prototype of the Quality Assurance Range Calorimeter (QuARC): a segmented large-volume scintillator-based detector for fast, accurate proton range quality assurance (QA) measurements. The detector used 128 scintillator sheets of size 105 × 105 × 3 mm arranged into 4 modules of 32 sheets, where each sheet was directly coupled to a photodiode. Fast analogue-to-digital conversion facilitated measurement of scintillator sheet light output to 20-bit precision at 6 kHz, with a dynamic range of up to 350 pC. Proton range measurements with the full-size detector were performed at The Christie at clinical (approx. 1 nA nozzle current) dose-rates, where the range accuracy of the QuARC was found to be within 0.4 mm of facility reference across the full clinical energy range. The QuARC was successfully able to perform range measurements of the 245 MeV beam at FLASH dose-rate (approx. 50 nA nozzle current), where the fitted range agreed with the clinical current measurement to 0.3 mm. Follow-up measurements with 2 detector modules at UMCG PARTREC investigated the linearity of the scintillator light output with beam current, which found non-linearity effects of up to 25% between beam energies of 60-150 MeV. Several convoluted variables are discussed as possible causes to this effect as well as improvements to the detector design for future experiments.

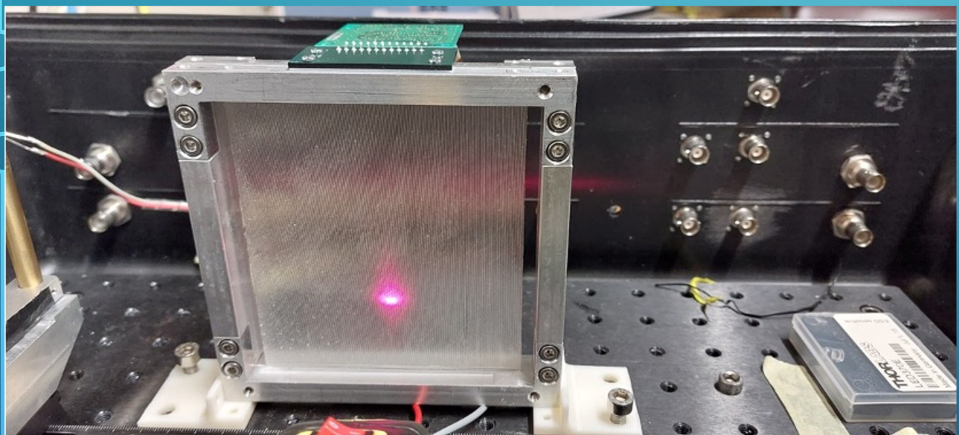
proton therapy, plastic scintillator, FLASH, quality assurance

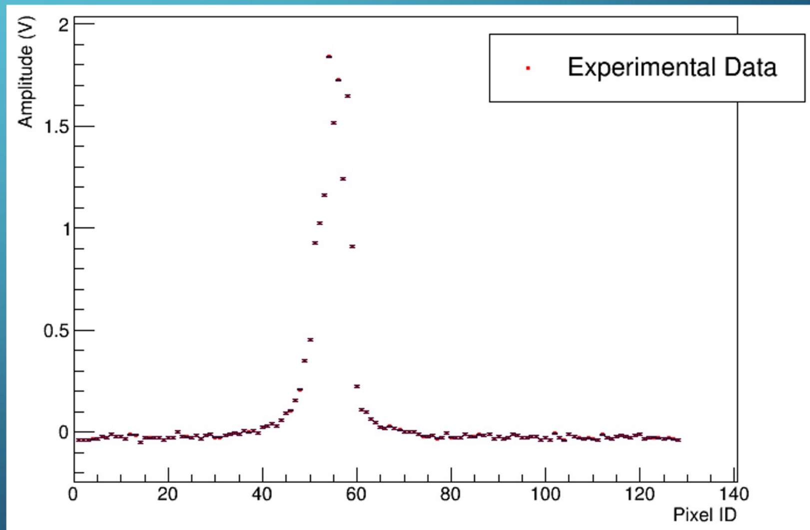
Submitted to: *Phys. Med. Biol.*

BEAM TRACKER

The potential for an integrated QA solution for FLASH PBT

- First detector prototype now produced in 2023 and under test @INFN-Bari
- 10 cm x 10 cm arrays made of BCF-60 plastic scintillating fibers by the Saint-Gobain, 0.50 mm diameter.
- emission peak at 530 nm.





Project Organization – Milestones

Milestones:
M1 (12m): Simulations of irradiation fields as well as signal and background on the detector.
M2 (12m): First prototype of the detector ready, including subcomponents for the detector procured (scintillator, SiPMs, ASICs) and DAQ system.
M3 (12m): First release of the Tomography reconstruction algorithm.
M4 (12m): Characterization of neutron beam at UNIPV LENA PGNAA facility using neutron activation measurements and Bayesian unfolding methods.
M5 (18m): Conclusion of shieldings studies and procurement.

Bari

Milestones:
M6 (24m): Simulations of the optimized scanner geometry.
M7 (24m): Tomography reconstruction algorithms ready.
M8 (30m): Development of further detector modules (up to 4 additional modules) concluded. Construction of SPECT prototype system concluded.
M9 (36m): Results from beam tests of the prototype in accelerator-based neutron sources. Final release of the BNCT-specific reconstruction algorithm.

Bari

Publications

Pubblicazioni:

1- D, Dayron, G. Pugliese, G. Iaselli, N. Amoroso, C. Gong, V. Pascali, S. Altieri, and N. Protti. 2023. "Study of Alternative Imaging Methods for In Vivo Boron Neutron Capture Therapy» Cancers 15, no. 14: 3582.
DOI: https://doi.org/10.3390/cancers15143582

2- D. Ramos on behalf of G. M. I. Pugliese, G. Iaselli, N. Protti, S. Altieri, C. Gong. 2023. "Monte Carlo study of 3D image reconstruction for boron dose distribution in BNCT with CZT-based Compton camera" IL NUOVO CIMENTO 46 C (2023) 73. DOI: 10.1393/ncc/i2023-23073-2

Overview of previous/ongoing projects

ENTER_BNCT

Bari task: Imaging methods for BNCT ⇆ synergy with University and INFN of Pavia

General goal: Develop an alternative method for a possible imaging protocol based on the measurement of the prompt gamma-ray of 478 keV with a **CZT Compton camera type detector**.

- Monte Carlo methods to simulate a **Compton image** data-set within a BNCT approach.
- Reconstruct the normalized simulated distributions using three methods: the classic **Maximum Likelihood Expectation Maximization (MLEM)** iterative method, a method based on **image processing operations**, and **Convolutional Neural Networks (CNN)** approach.

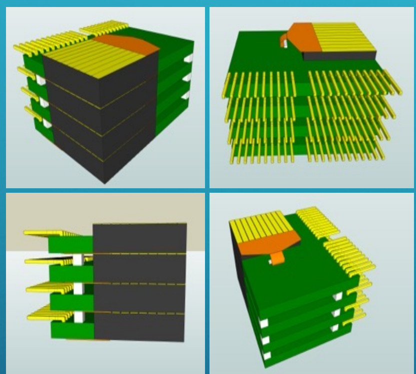
3D CZT detector

CZT single unit: 20x20x5 mm^3, planar transversal field (PTF), orthogonal drift strip electrodes

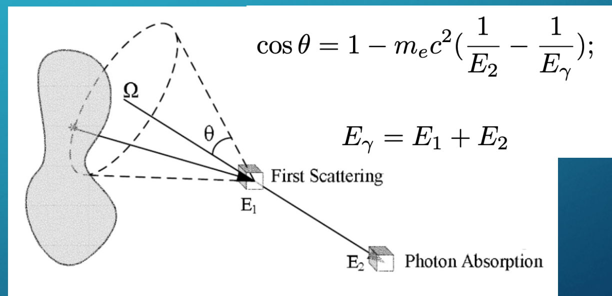
Room-temperature gamma-ray spectroscopic

Sub-millimetre spatial resolution and excellent energy resolution (<1% FWHM at 661.7 keV)

3D positioning



Compton camera principle



Reconstruction evaluation

$$\text{Accuracy} = \frac{TP}{TP + FP}$$

$$\text{Sensitivity} = \frac{TP}{TP + FN}$$

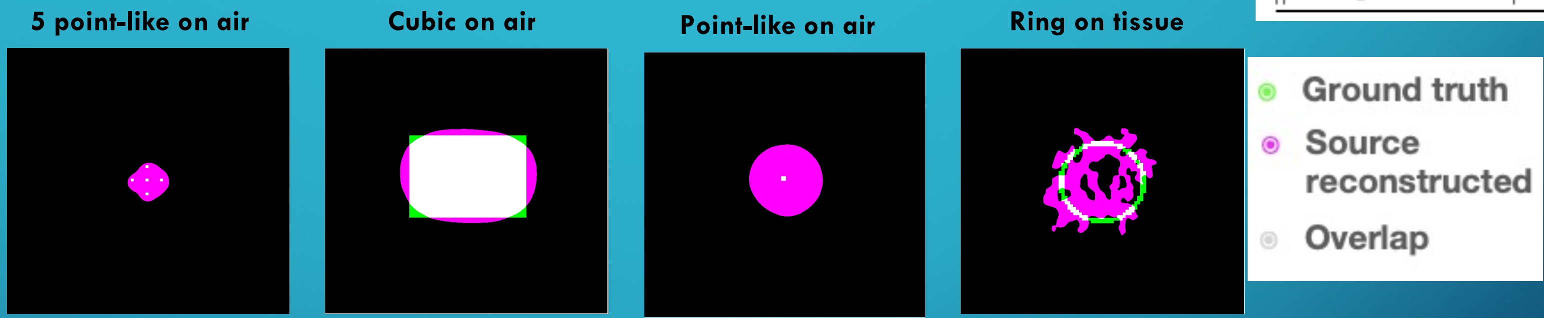
Overview of previous/ongoing projects
ENTER_BNCT

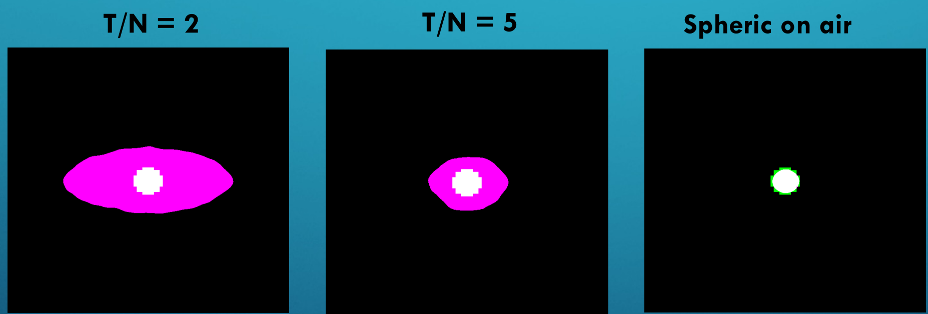
Data augmentation + Trasfer Learning

ResNet50 model

CNN layout

Property	Value
Layers	206 × 1 Layer
Connections	227 × 2 table
InputNames	1 × 1 cell
OutputNames	1 × 1 cell





	Accuracy	Sensitivity
5 point-like on tissue	3.81%	100%
Cubic on air	86.09%	96.27%
point-like on air	0.55%	100%
Ring on tissue	13.46%	59.20%
Spheric $T/N = 2$	4.83%	100%
Spheric $T/N = 5$	3.81%	100%
Spheric on air	99.73%	77.99%