

# Anthem

AdvaNced Technologies for Human-centEred Medicine

Atto costitutivo della Fondazione firmato il 9 novembre 2022 alle ore 12:00

## HUB: Università di Milano Bicocca

23 partners located throughout the country

8 public and 1 private universities

1 national public research centre

4 public hospitals

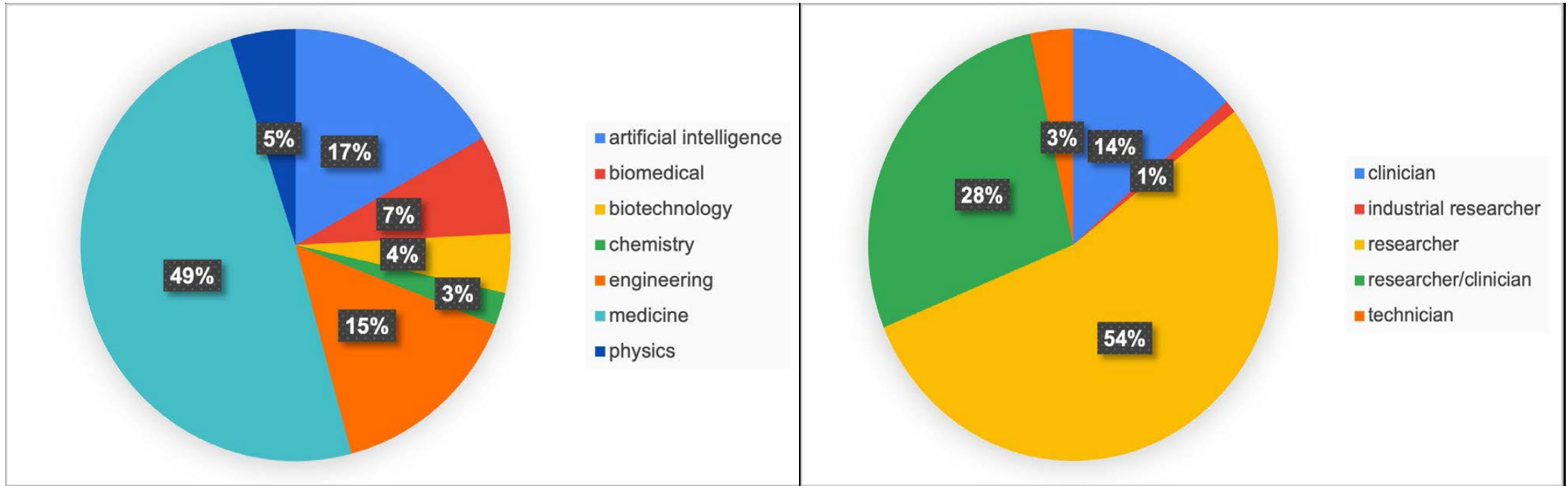
1 health agency

4 private research & healthcare institutes

4 private companies.

DENOMINAZIONE AFFILIATO	TIPOLOGIA SOGGETTO
HUB	Organismo di ricerca
Università degli Studi di Bergamo	Organismo di ricerca
Università degli Studi di Milano Bicocca	Organismo di ricerca
Università degli Studi di Messina	Organismo di ricerca
Università degli Studi della Campania "Luigi Vanvitelli"	Organismo di ricerca
Azienda Socio Sanitaria Territoriale di Bergamo Est	Organismo di ricerca
Fondazione Europea Ricerca Biomedica - Ferb Onlus	Impresa
Diapath S.p.A.	Impresa
Azienda Socio Sanitaria Territoriale Papa Giovanni XXIII	Organismo di ricerca
Istituto di Ricerche Farmacologiche Mario Negri	Organismo di ricerca
Azienda Socio Sanitaria Territoriale di Monza	Organismo di ricerca
Università degli Studi di Milano Bicocca	Organismo di ricerca
Università degli Studi di Bergamo	Organismo di ricerca
Università degli Studi della Calabria	Organismo di ricerca
Azienda Socio Sanitaria Territoriale Papa Giovanni XXIII	Organismo di ricerca
Agenzia di Tutela della Salute della Città Metropolitana di Milano	Organismo di ricerca
Artemide S.p.A.	Impresa
Azienda Socio Sanitaria Territoriale di Monza	Organismo di ricerca
Fondazione Europea Ricerca Biomedica - Ferb Onlus	Impresa
Azienda Socio Sanitaria Territoriale di Bergamo Est	Organismo di ricerca
Politecnico di Milano	Organismo di ricerca
Università Humanitas	Organismo di ricerca
Università degli Studi del Salento	Organismo di ricerca
Chiesi Farmaceutici S.p.A.	Impresa
Ab Medica S.p.A.	Impresa
Università degli Studi di Catania	Organismo di ricerca
Università degli Studi della Calabria	Organismo di ricerca
Università degli Studi di Messina	Organismo di ricerca
Università degli Studi della Campania "Luigi Vanvitelli"	Organismo di ricerca
Istituto Nazionale di Fisica Nucleare	Organismo di ricerca
Azienda Ospedaliera per L'Emergenza Cannizzaro	Organismo di ricerca
Università degli Studi del Salento	Organismo di ricerca
Politecnico di Milano	Organismo di ricerca
Università Humanitas	Organismo di ricerca
Biogem S.c.a r.l.	Impresa
Istituto Oncologico Del Mediterraneo S.p.A.	Impresa

The main scope of the project is to cover the existing gap in healthcare of **frail and chronic patients** within specific target territories and high-incidence, and orphan pathology-defined communities.



Our project vision considers AI as a key element in the implementation of our activities.

The motivation of this project is **technological**, because it is necessary both to develop new systems of diagnosis, monitoring and treatment and to adapt them to the context of territorial medicine and to the areas of intervention; **scientific**, because it is necessary to understand and analyse remote-collected parameters and data to make diagnoses and treatments as efficient as in a hospital context; **educational**, as both the medical and nursing community and the citizens must change their approach to the treatment of diseases.

**136.949.006,32 €** Costi complessivi

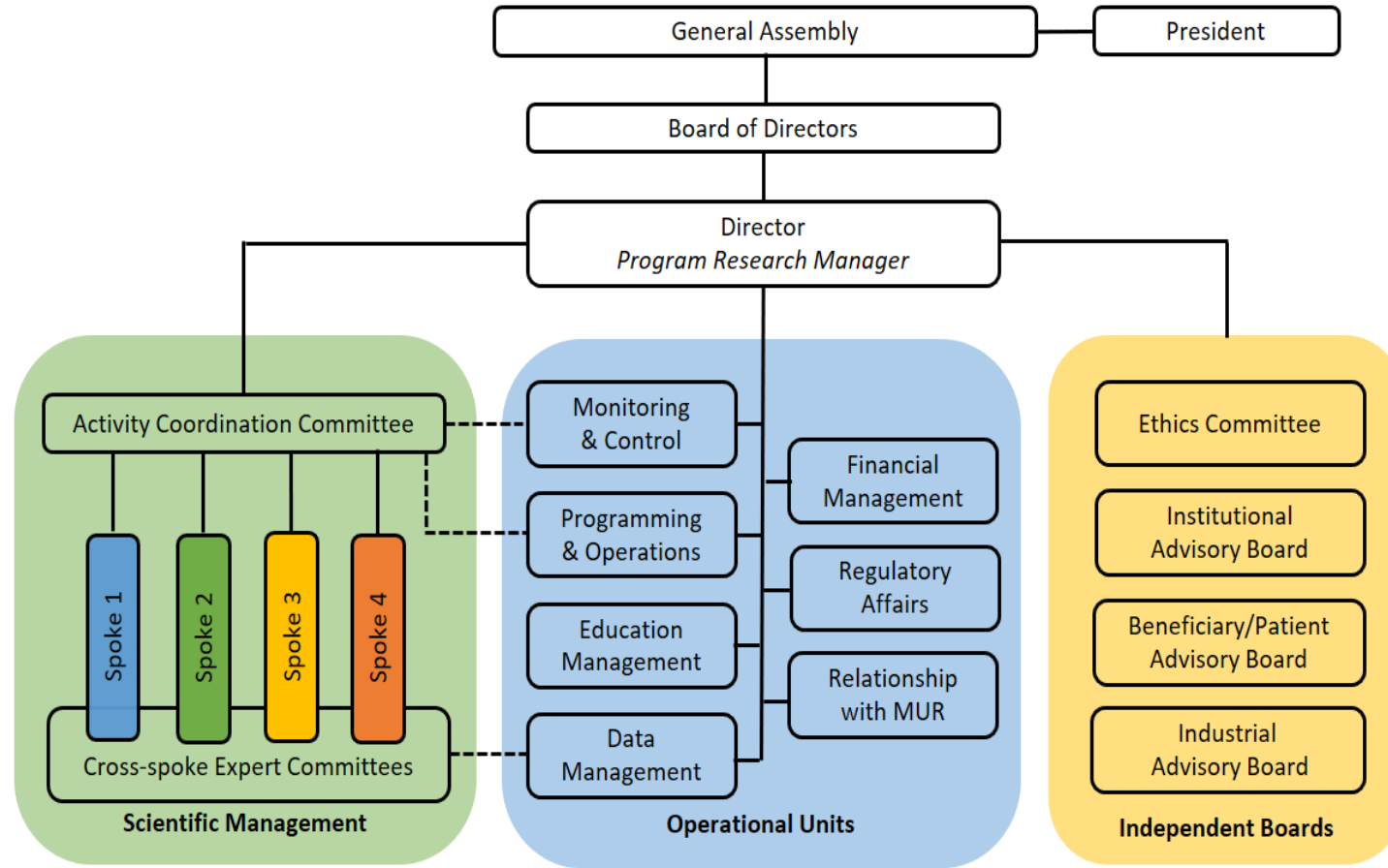
**125.841.999,39 €** Agevolazione attesa

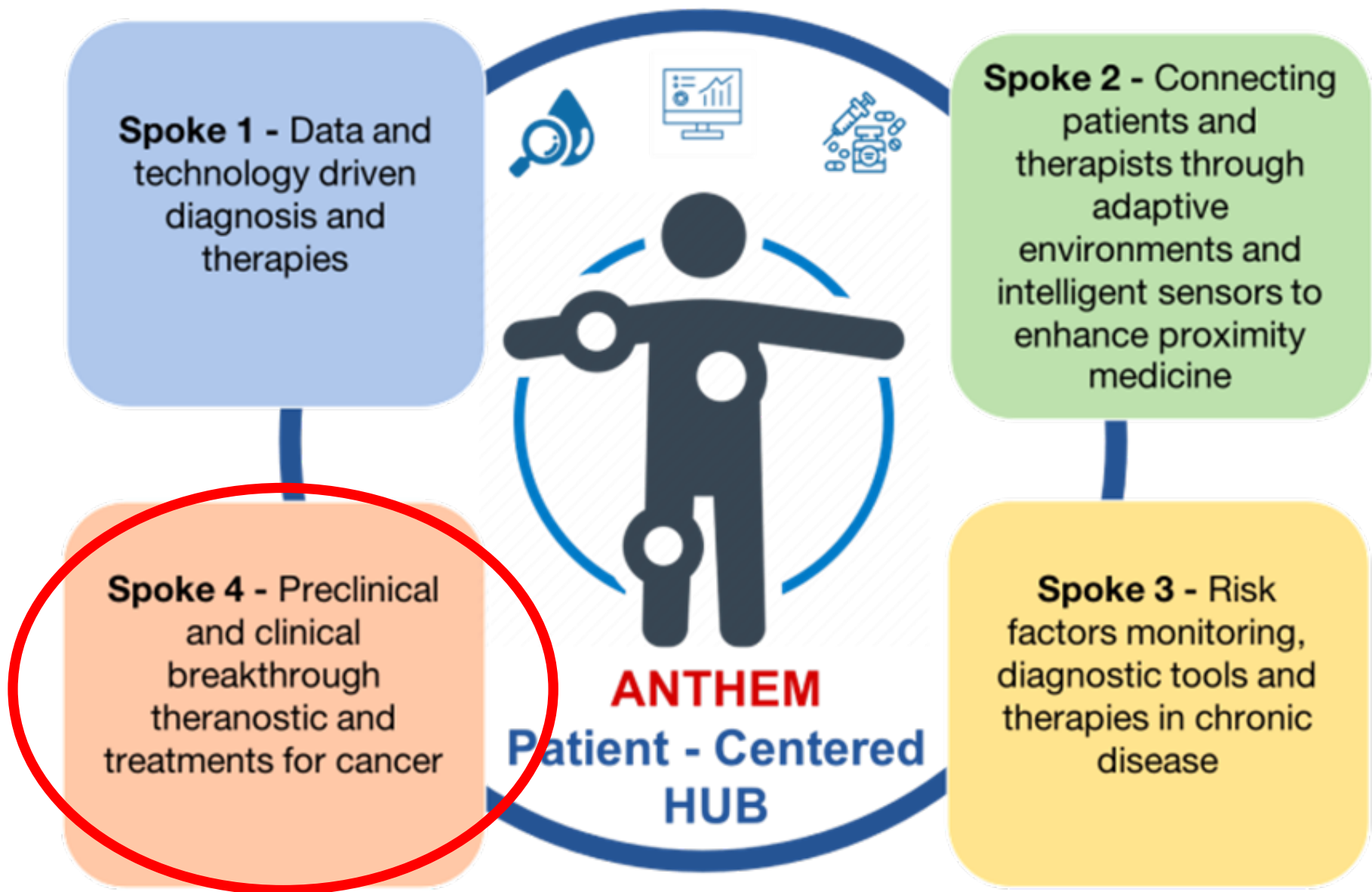
**123.000.000 €** Agevolazione negoziata

**12.500.000 €** INFN

**Call Budget 500.000.000 €, 4 Projects approved**

# ANTHEM Foundation





## Progetto Anthem

HUB Leader Mi-Bicocca

Spoke 4 Leader Uni CT

INFN Units of LNS, CT, NA, PV, LNL

Spoke 4:

Innovative radiotherapy techniques and imaging  
(Flash therapy & BNCT)

**PNRR-PE30**

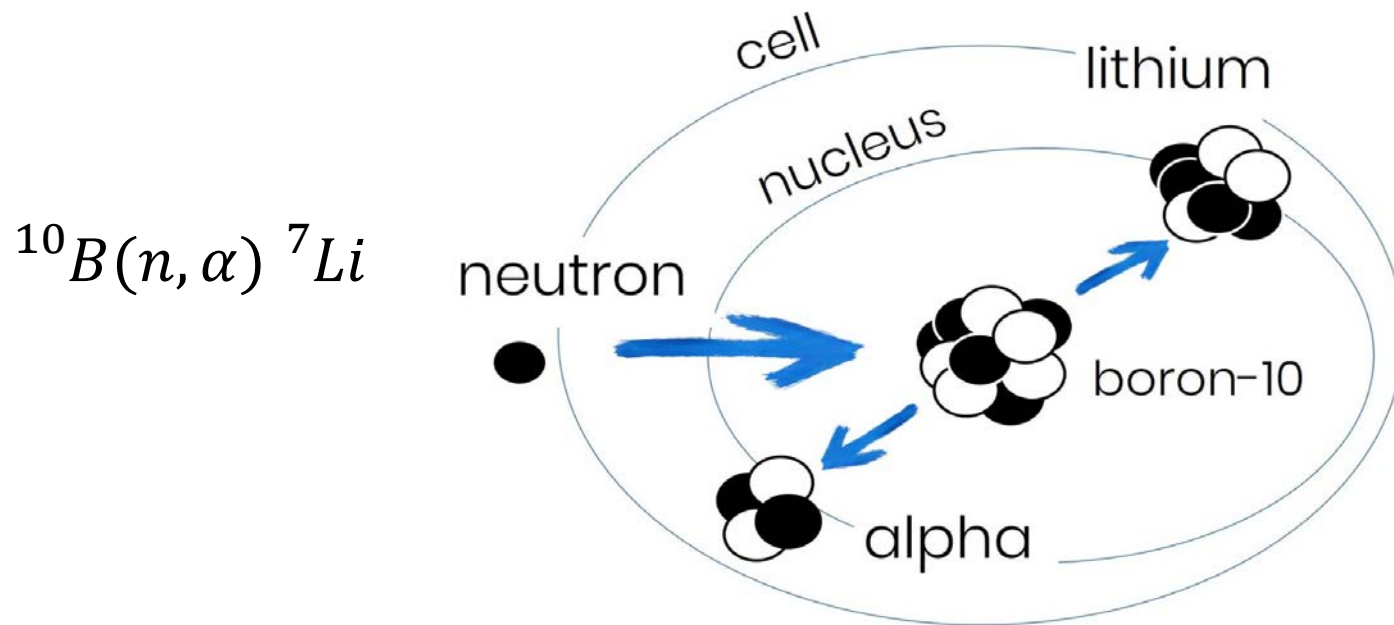
For FLASH: explore testing different types of particle beam detectors and monitoring systems, and define a dosimetric protocol for Flash regime beams of both electrons and protons

For BNCT: the accelerating system has unique performances, the best neutron beam and radiobiology studies concentrate on boron carriers and their ability to be internalised

# Boron Neutron Capture Therapy

A binary form of radiotherapy

- Administration of BORON
- Irradiation with low energy NEUTRONS



## Selectivity

Range of charged particles in tissue: around 10 micron.  
Biological targeting, selectivity at the cell level

## Effectiveness

High-LET radiation:  
high biological effectiveness



## PNRR PE30 Spoke 4

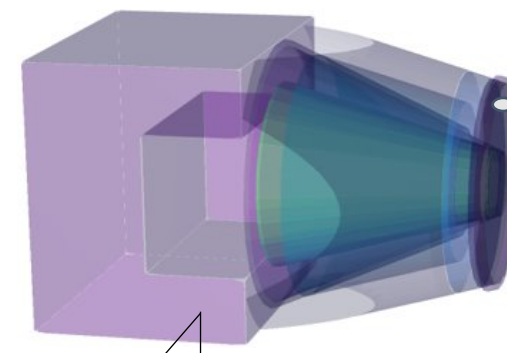
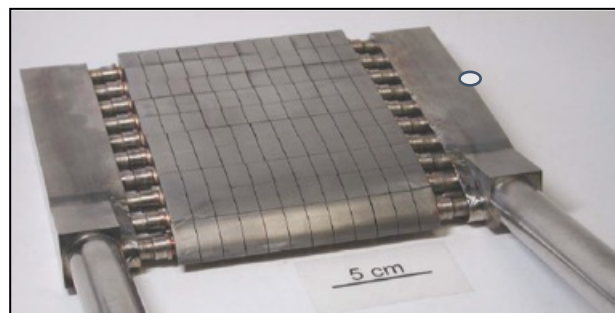
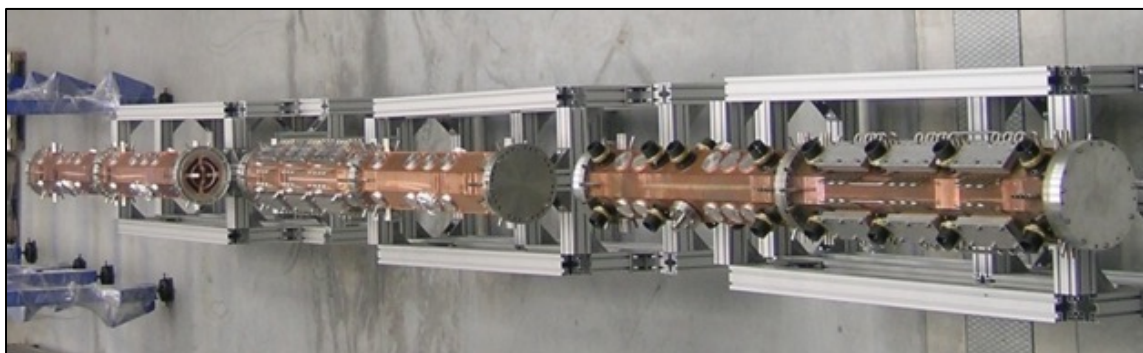
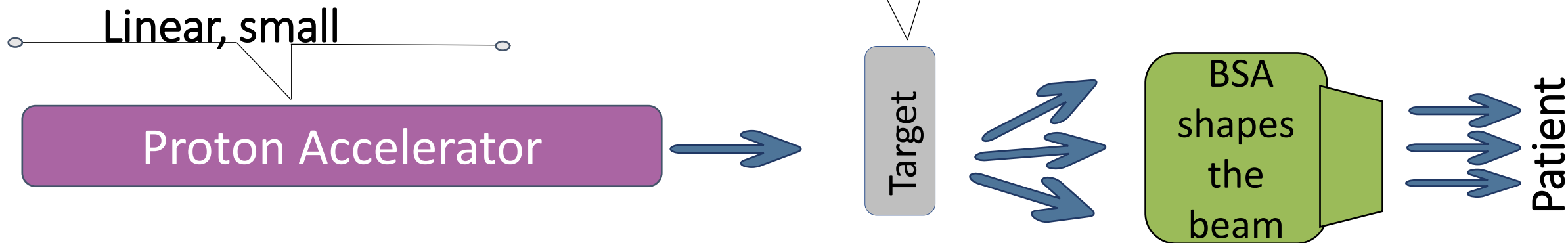
- Executive project for the installation of the high technology for a clinical centre BNCT@Caserta – [INFN](#)
- Preclinical studies (radiobiology-dosimetry-treatment planning): Univ. Vanvitelli + Polyclinic with support by [INFN](#)





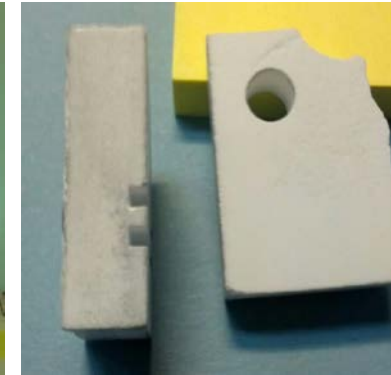
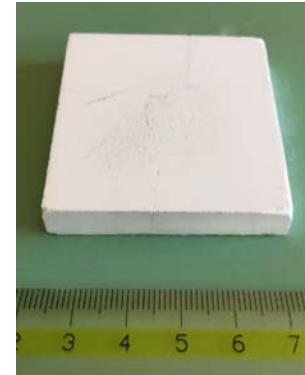
MUNES: Acceleratore RFQ 5 MeV, 30 mA, CW  
Target di Be sottile, BSA basato su AlF3

### Neutron production via nuclear reaction



Changes spectrum and collimates

# Densified $\text{AlF}_3$ and $\text{AlF}_3 + 2\% \text{LiF}$ High density ( $\sim 100\%$ )



Study of mechanical properties ongoing

Developed within R4I INFN Initiative

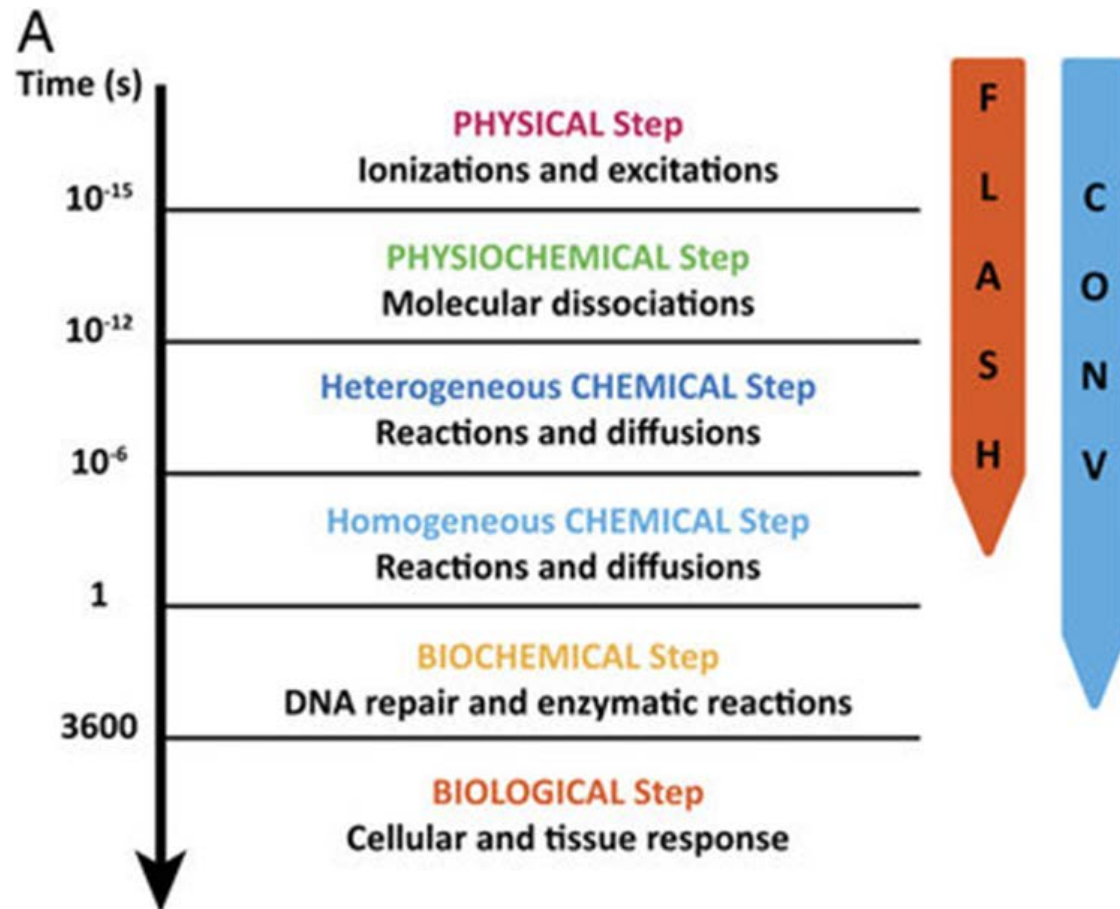
1 machine almost ready for LNL for target isotopes production

1 machine «sold» to Winsconsin for same purpose



# FLASH Therapy

Ultra-high dose rate (uHDR) shows promise to improve efficiency and efficacy



## PNRR PE30 Spoke 4

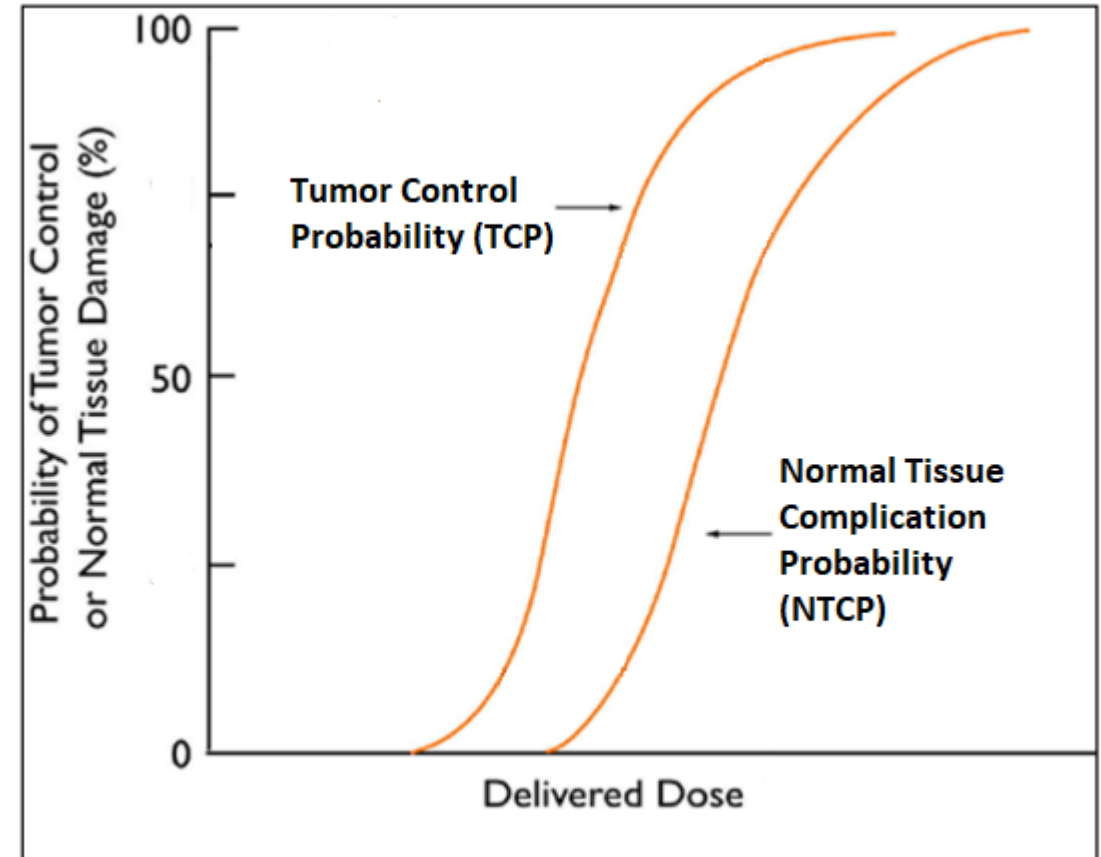
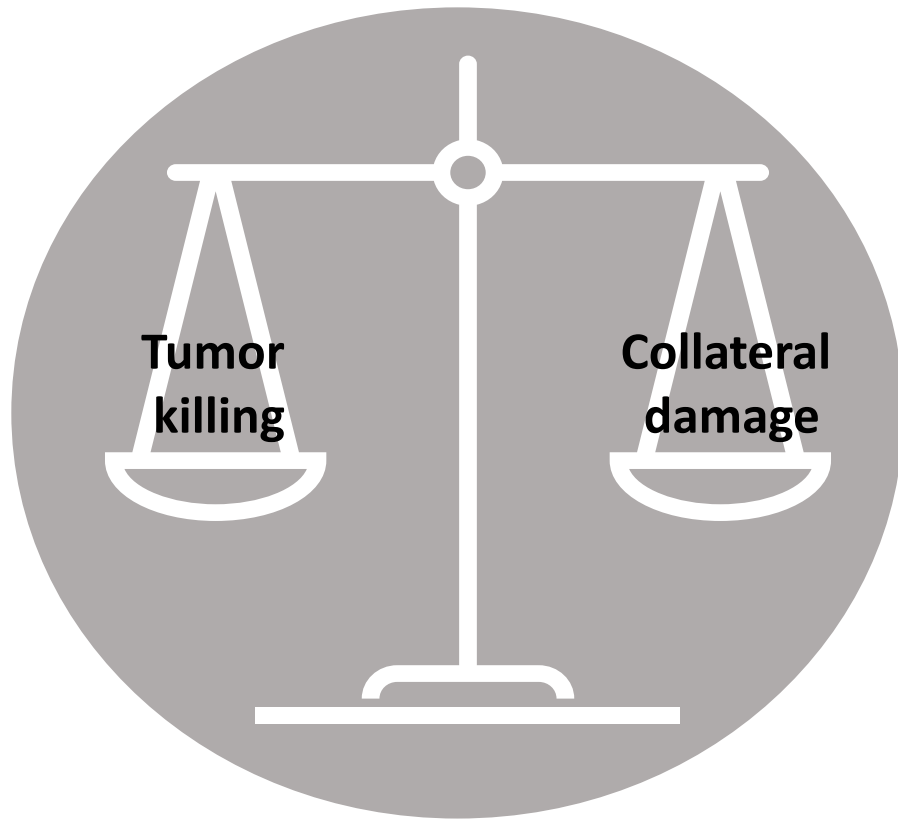
Study of FLASH therapy effect on glioblastoma (GBM) (UNICT, [INFN](#), CANNIZZARO, IOM, BIOGEM)

Achievement of a biological response to FLASH and ULTRA-FLASH therapies of tumour and healthy tissues by

1. 2D and 3D in vitro tumour and healthy cells response to therapy
2. in vivo tumour and healthy tissues response to therapy, in a murine GBM model
3. development of complementary therapies to improve the efficacy of treatment and quality of patient's life

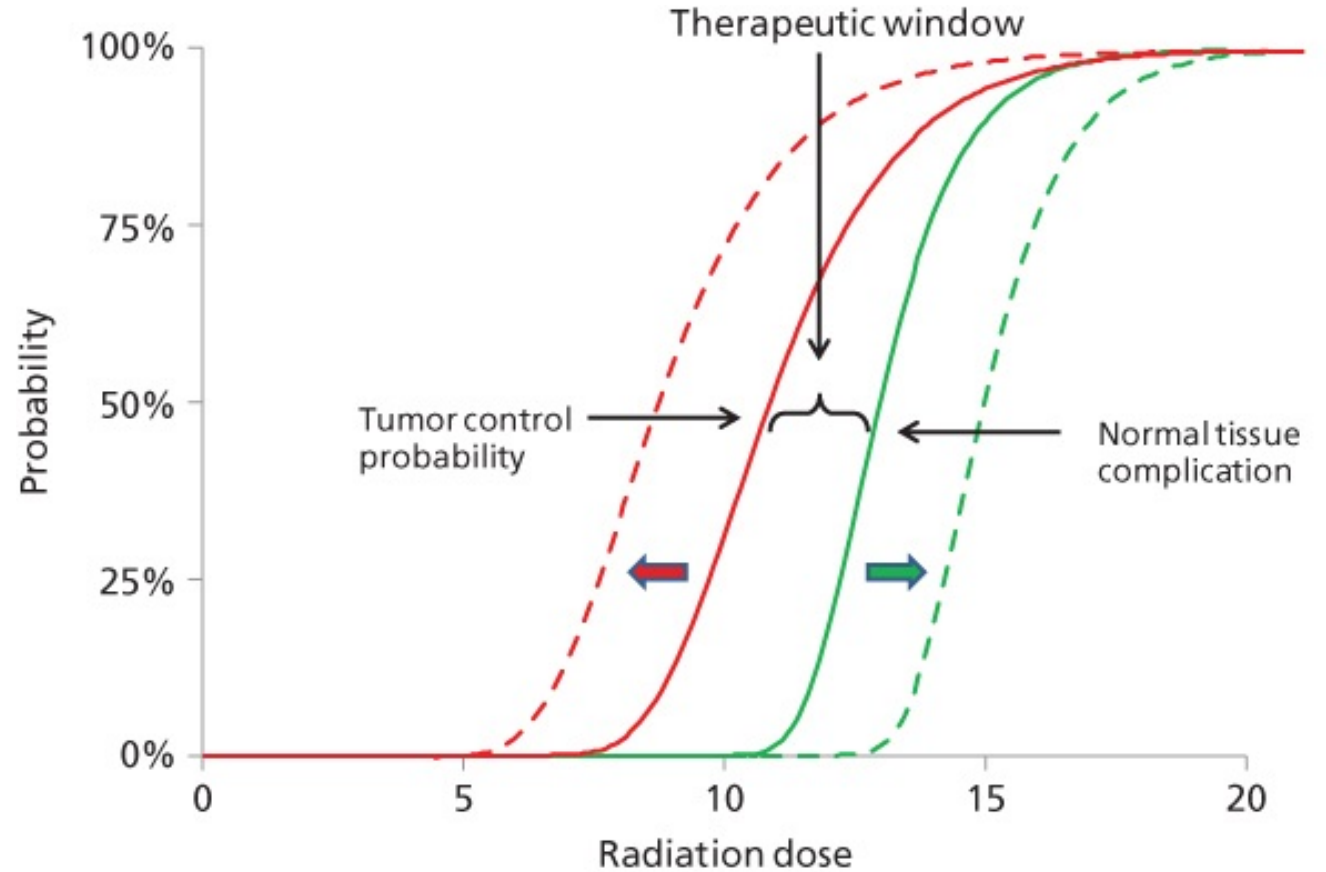
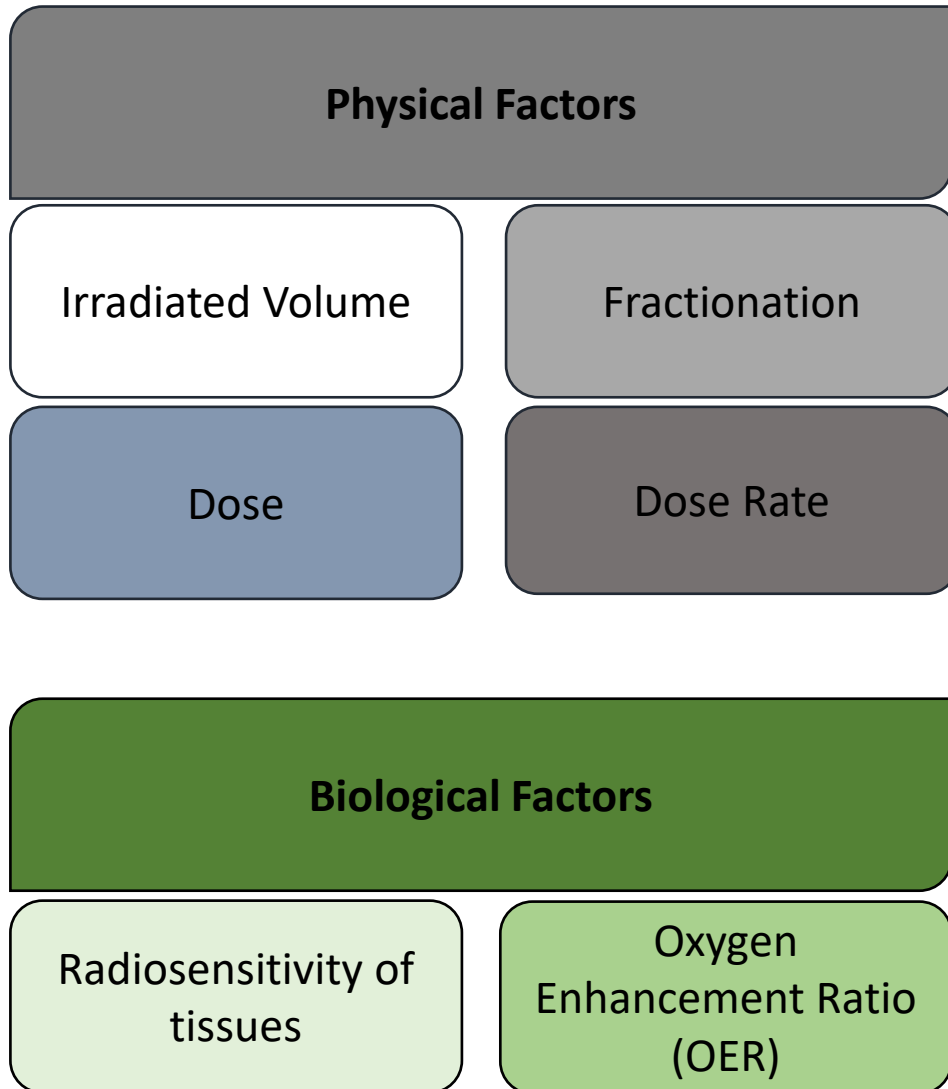
# Cancer therapy challenge

The purpose of radiotherapy is to **remove all the tumor cells** in the certain area completely, but it is impossible to give a high dose without seeing the effect on the surrounding normal tissue.



**Dose response curves** for tumors and normal tissues have to be considered.

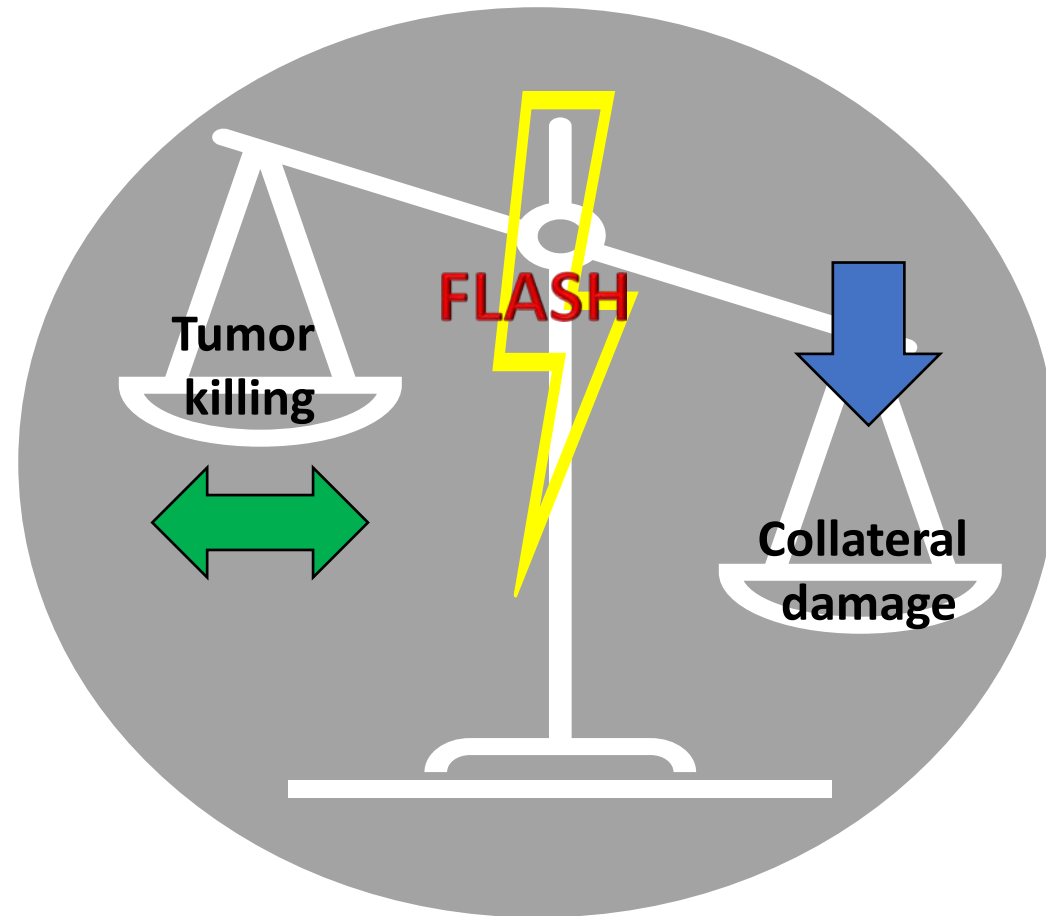
# Therapeutic window modifiers



# Ultra-High Dose Rate (FLASH) Radiotherapy

Irradiation at dose rates exceeding those currently used in clinical context reduce radiation-induced toxicities whilst maintaining an equivalent tumor response.

This is known as **FLASH effect**.





# THE RESEARCH NETWORK

## PRECLINICAL IMAGING AND RADIOBIOLOGICAL STUDIES



# FACILITIES



UNIVERSITÀ  
degli STUDI  
di CATANIA



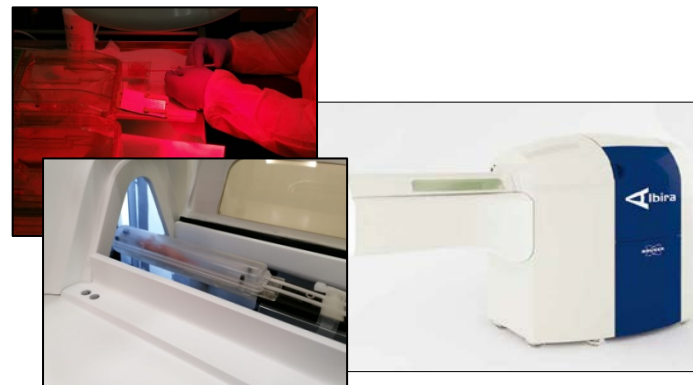
The network is composed by the collaboration among these institutions :

- Università degli Studi di Catania (UNICT) with the Center for Advanced in Vivo Research (CAPIR).
- Azienda Ospedaliera per l'Emergenza Cannizzaro di Catania (AOE-Cannizzaro).
- Istituto di Bioimmagini e Fisiologia Molecolare del Consiglio Nazionale delle Ricerche (IBFM-CNR).
- Laboratori Nazionali del Sud dell'Istituto Nazionale di Fisica Nucleare (INFN-LNS).

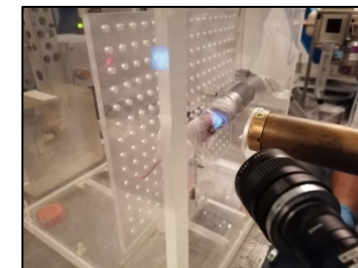
IT REPRESENTS A SYNERGISTIC NETWORK FOR RESEARCH ACTIVITIES  
FROM *IN VITRO* TO PRECLINICAL STUDIES



Cyclotron for the  
Radiotracer  
production



Molecular imaging analysis for animal models



"Catana Facility" for proton beams  
irradiation of animal models



## Equipment & skills UNIVERSITY OF CATANIA AND CAPIR

Two enclosures of 700 square meter are available with spaces, equipments and skills to relay mice, rats, guinea pigs and rabbits, as well as a room equipped with zebrafish tanks. The two enclosures also have got experimental surgery and microsurgery rooms, washing and sterilization locals, chemical and biological laboratories.



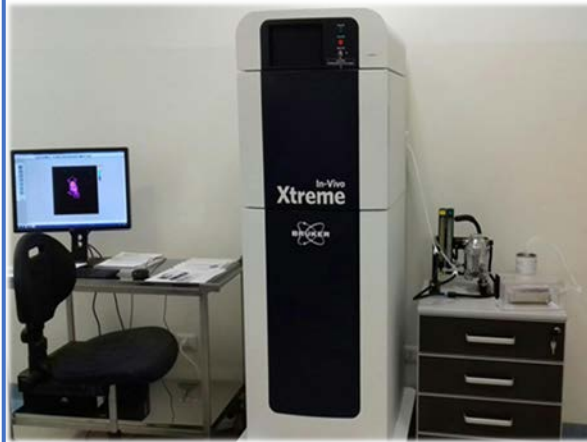
### **PET facility**

equipped with an integrated multimodal PET/CT Bruker ALBIRA for small animal, allowing the study of the progression of pathologies, the evaluation of the therapeutic efficacy of innovative molecules and to support research activities for the development of new drugs in the diagnostic and therapeutic area.



### **Optical Imaging facility**

equipped with an *in vivo* radiographic system "Bruker Xtreme" allowing the acquisition of traditional images in white light, fluorescence, luminescence and X-ray. It also allows screening of multiple animals at the same time, measuring the position and the biodistribution of the administered tracer/radiolabelling agent.



### **Ultrasound Imaging facility**

equipped with an ultrasound system "Vevo2100 Visualsonics", allowing to acquire functional and morphometric information of animal models compared to the evolution of the pathology studied.



## Equipment & skills AOE-Cannizzaro

Since 2005, it has been carried out Nuclear Medical Imaging activities, by the Nuclear Medicine and PET Center Operational Unit, that is capable of a Cyclotron for the radiopharmaceuticals production, a Radiochemistry Laboratory with a team for qualitative analysis of nuclear medical imaging and radiopharmaceuticals expertise of Nuclear Medicine area.



H-CANNIZZARO produces radiopharmaceuticals for clinical use: [18F] FDG - [11C] Colin - [11C] Methionine - [68Ga] DOTATOC.

It distributes [18F] FDG to approved facilities.

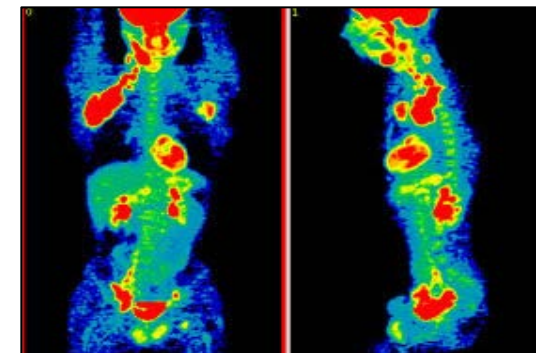
New Radiopharmaceuticals: [18F] FLT - [18F] MISO - [18F] Fluoride - [18F] Colin.

Multidisciplinary skills for *in vivo* tracers synthesis and biodistribution (nuclear physician, radio-pharmacist, physical physician, chemist).



Nuclear Medical Staff for the qualitative image analysis supported by nuclear medical opinion.

Physical Physician Staff for physical and dosimetric quantitative evaluations and support for image processing.



## Equipment & skills IBFM-CNR



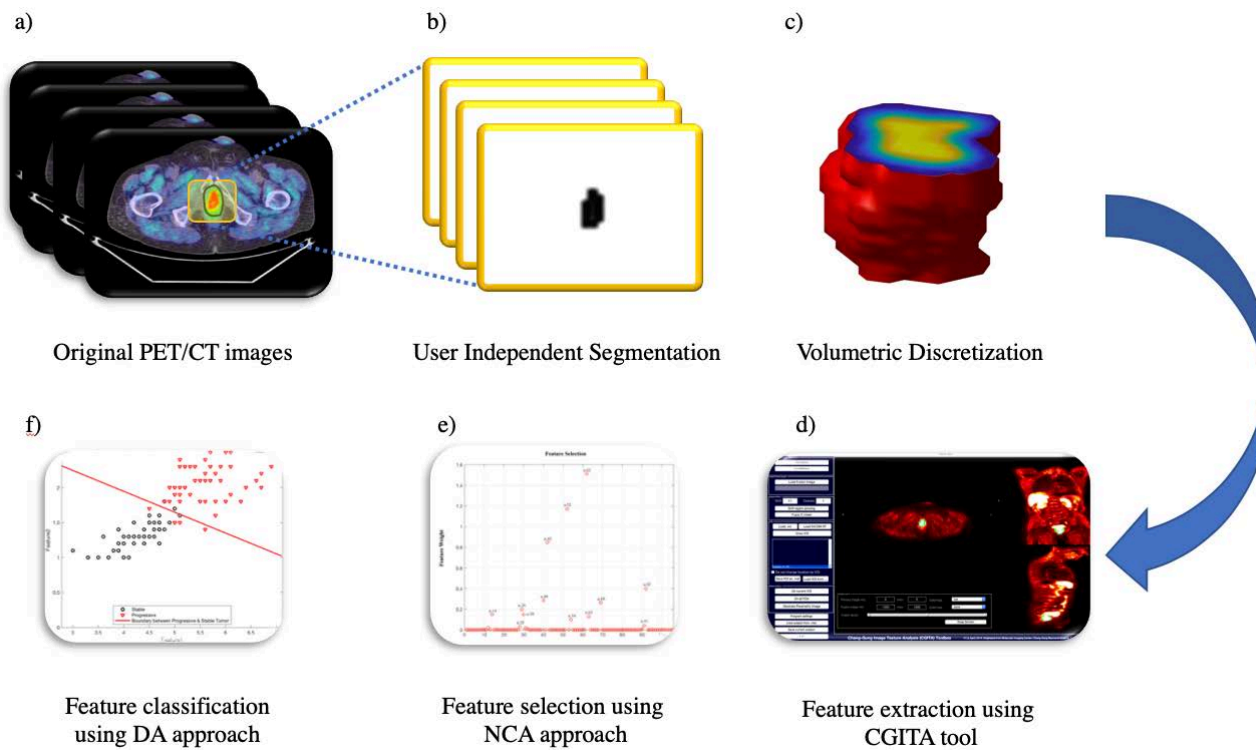
It develops *in vitro* and preclinical *in vivo* research activities in its secondary head office in Cefalù, having staff with animal experimentation, in bioimaging and in radioprotection expertise.



### Radiomic knowledge

It owns staff with competences in:

- ✓ Animal Experimentation with FELASA Cat-C
- ✓ Assistance for experimental design and support for animal management at LNS.
- ✓ Processing of bioimaging for signal quantification.







Coming soon....  
Thanks to ANTHEM project

ElectronFlash Accelerator

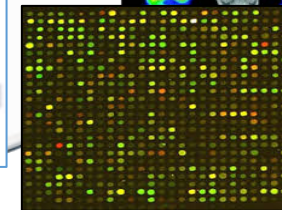
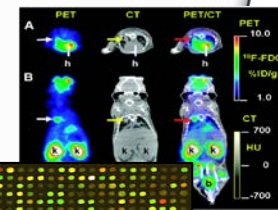
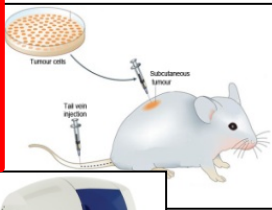
# ElectronFlash – Characteristics

- Energies: 7 and 9 MeV
- Collimator diameters: from 1 to 12 cm
- Dose Rate: from 0.005 Gy/s to 1500 Gy/s (10 cm collimator)
- Pulse duration: from 0.5 to 4 microSec
- Repetition frequency: from 1 to 350 Hz

# THE RESEARCH NETWORK

## PRECLINICAL IMAGING AND RADIOBIOLOGICAL STUDIES

Working progress





## *The biologically driven benefits from Flash Radiotherapy*

What alternative explanations are possible for the FLASH-effect?



- Possible dependence of the inflammatory/anti-inflammatory cell signaling????
- Sparing of circulating blood lymphocytes exposure???
- How survival/death balance works in such conditions?
- Different tissue capacities to maintain the redox balance??

*The real biological mechanisms need deeper studies*