

Workshop su Tecniche Avanzate di Radioterapia

# Adroterapia e BNCT al CNAO: il cuore degli atomi per la cura dei tumori complessi

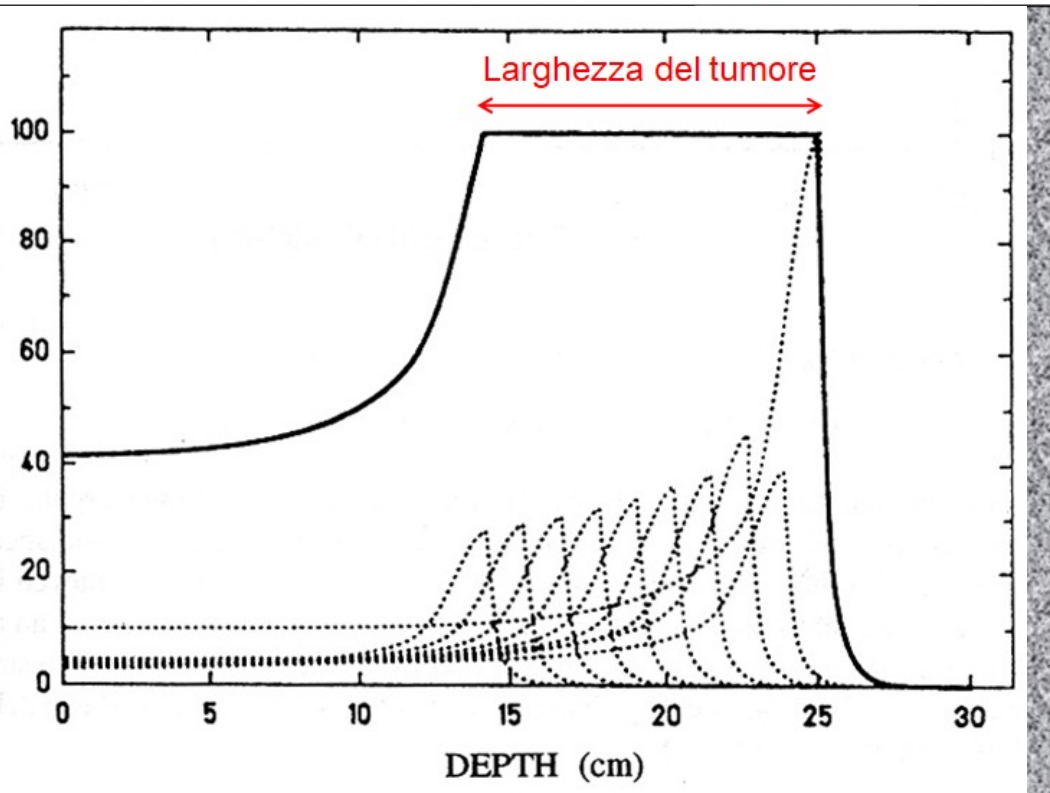
**Sandro Rossi**

*Fondazione CNAO*

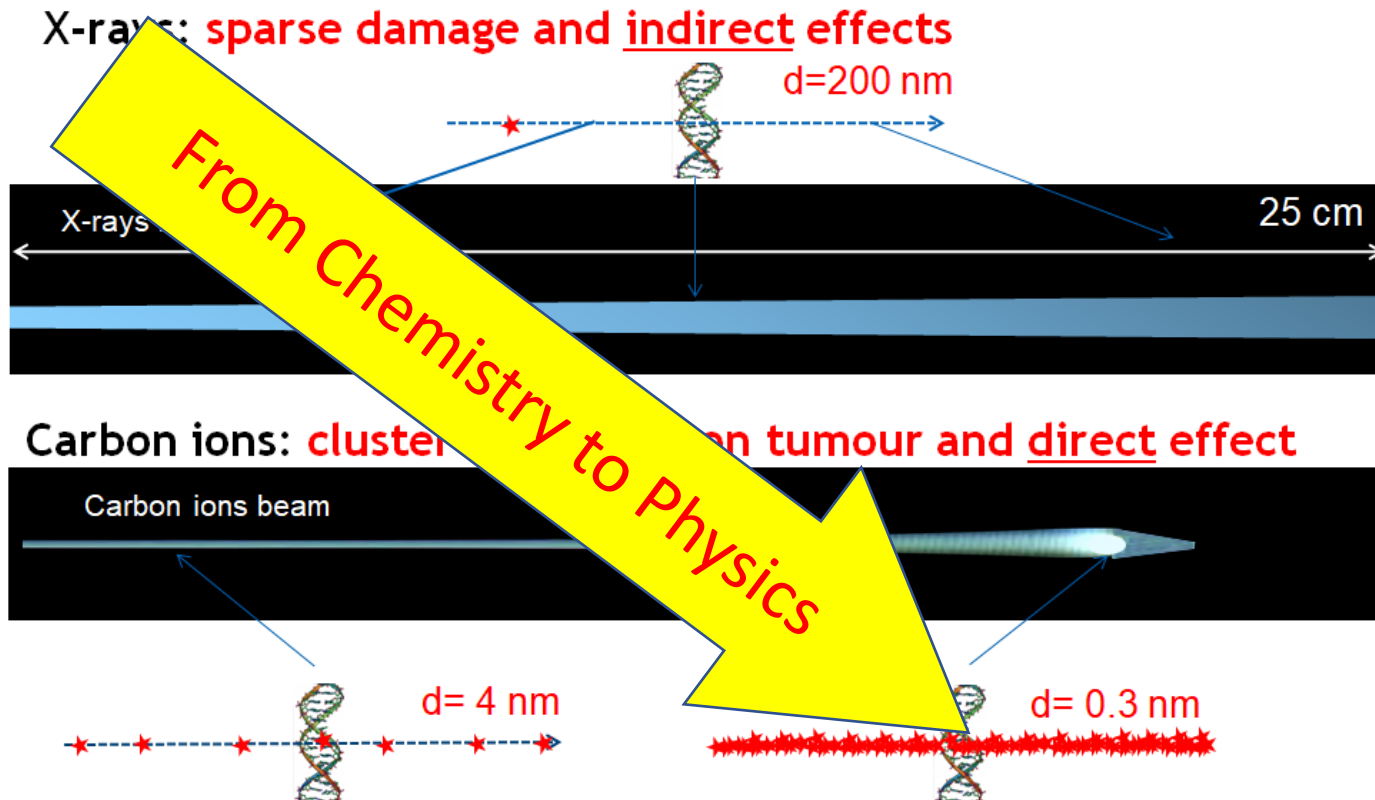
Bari, Campus Universitario  
15 Maggio 2024

# RATIONALE of hadrontherapy

## PRECISION - All hadrons



## EFFICACY - Carbon ions only

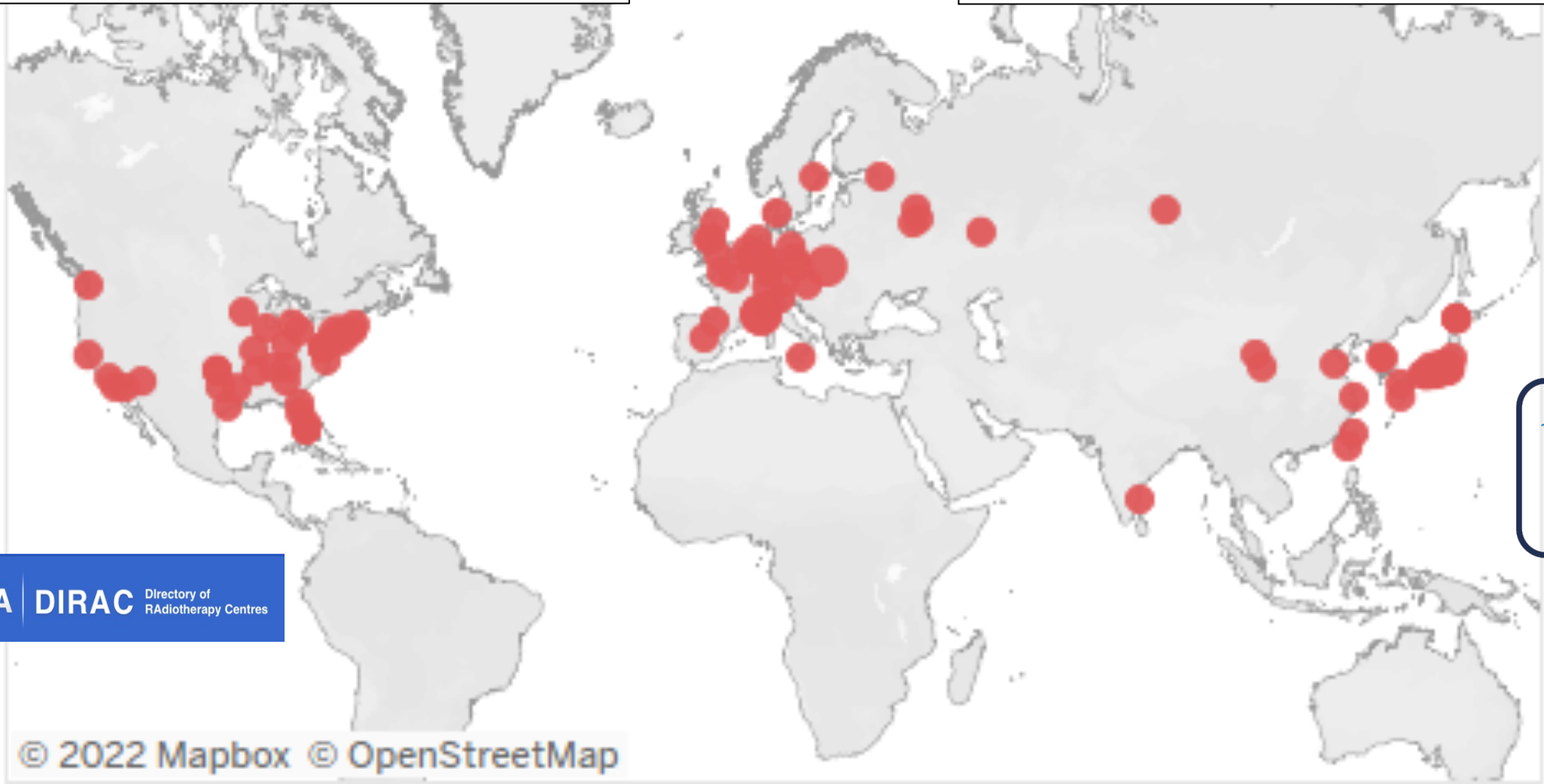


Difficult and rare tumours: ~5% of all tumours patients

# HADRONTHERAPY IN THE WORLD

107 centres with protontherapy  
(+40 in construction)

350.000 patients treated  
(+40.000/year)

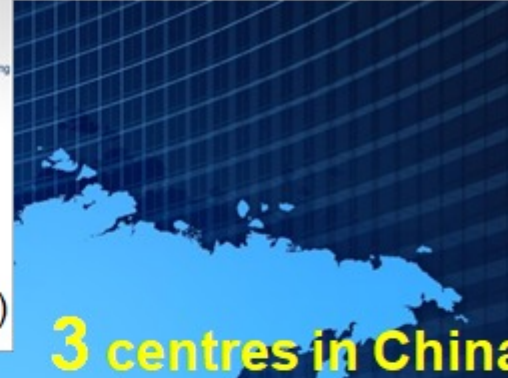
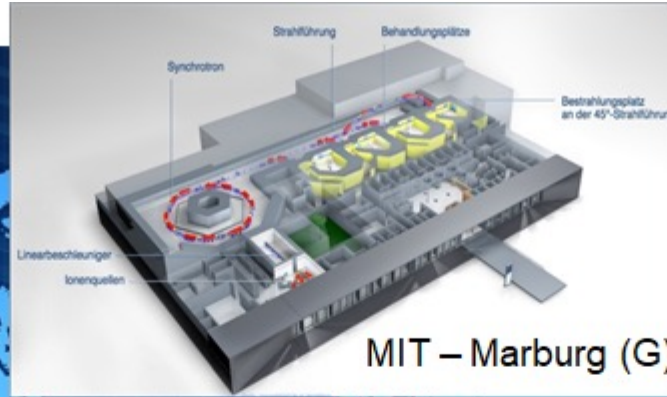


*P*article  
*T*herapy  
*C*o-  
*O*perative  
*G*roup



IAEA | DIRAC Directory of  
RAdiotherapy Centres

# HADRONTHERAPY IN THE WORLD



3 centres in China



6 centres in Japan

13 carbon ions centres  
(+5 in construction)  
6 of them multi-particle

50.000 patients treated  
(+5.000/year)



HIT – Heidelberg (G)

CNAO – Pavia (I)



MedAustron – Wien (A)



*P*article  
*T*herapy  
*C*o-  
*O*perative  
*G*roup



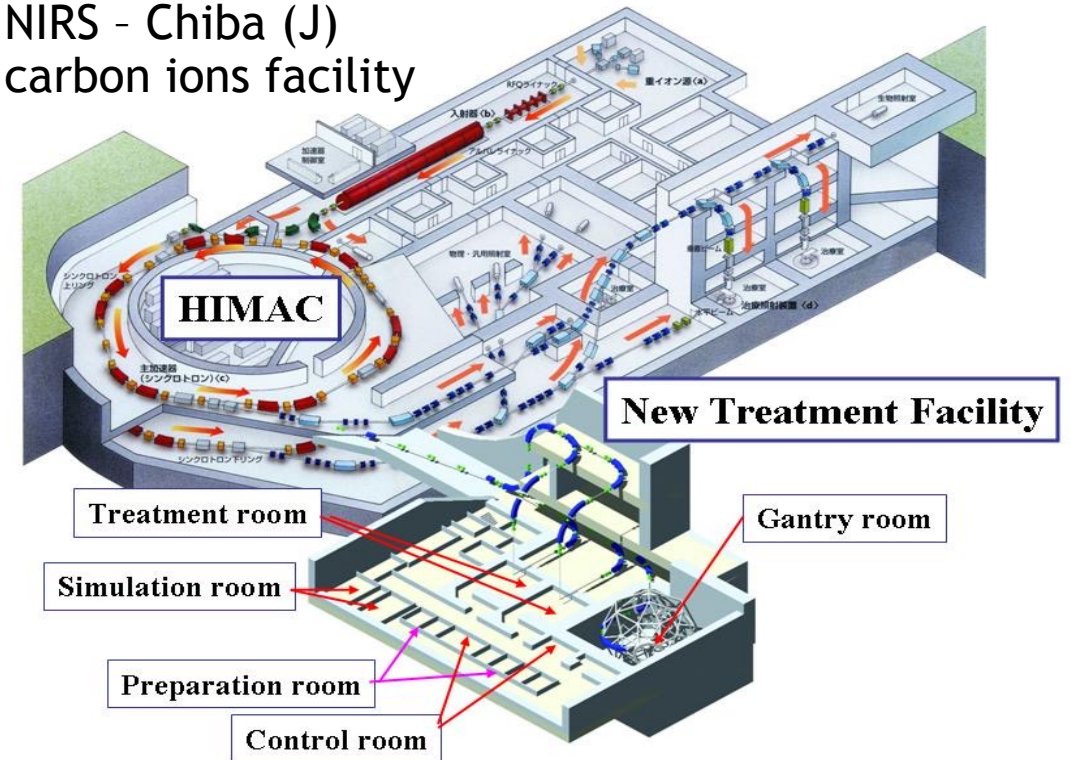
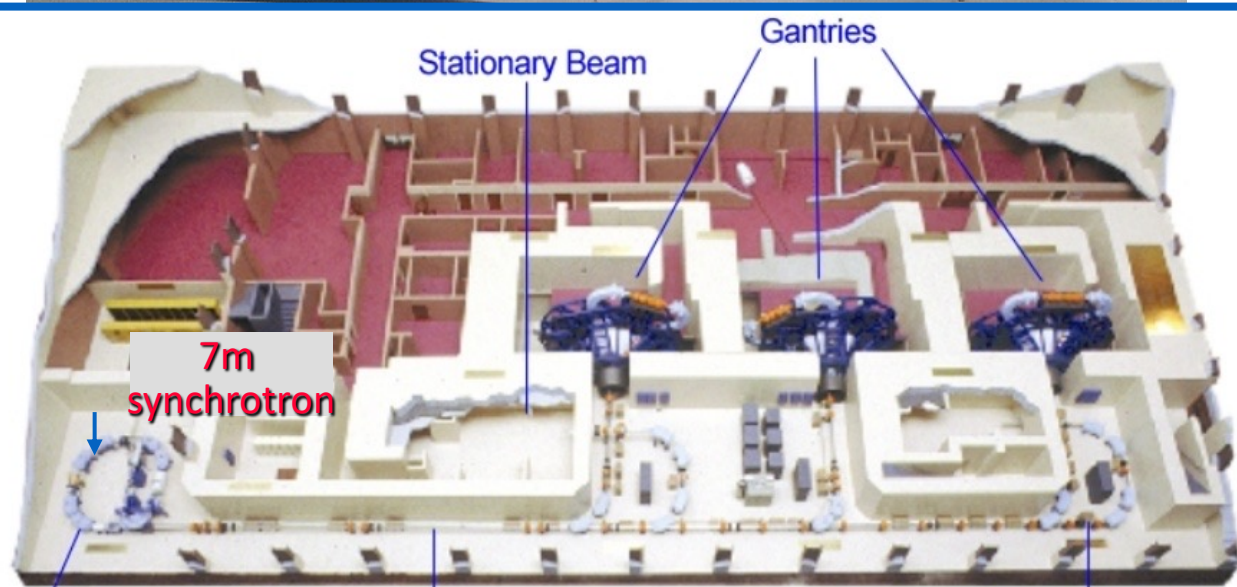
## Early nineties: first hospital based facilities...



Loma Linda - California (USA)  
proton facility



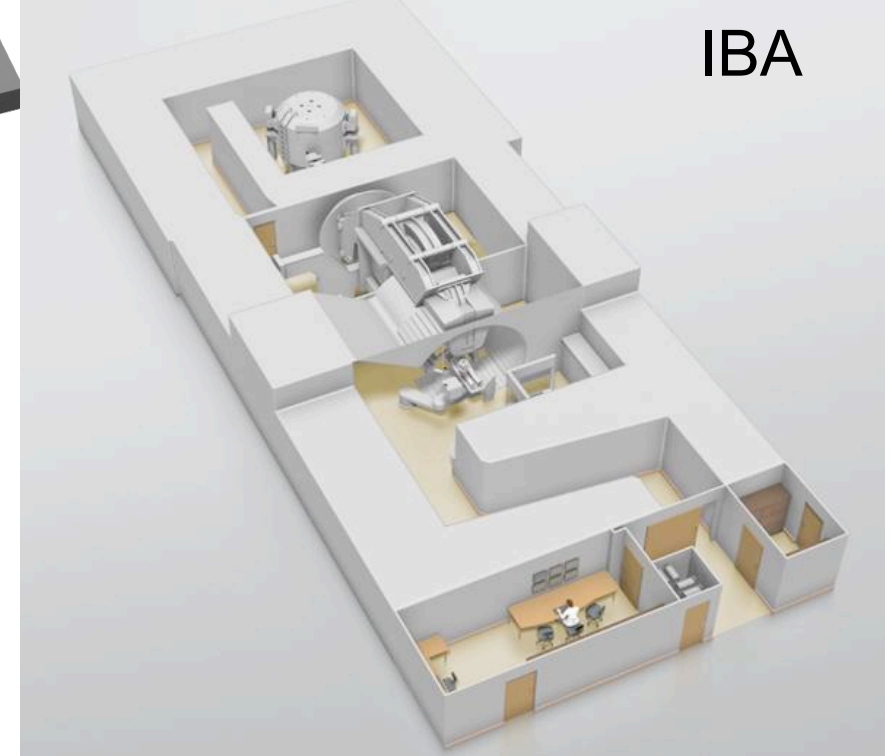
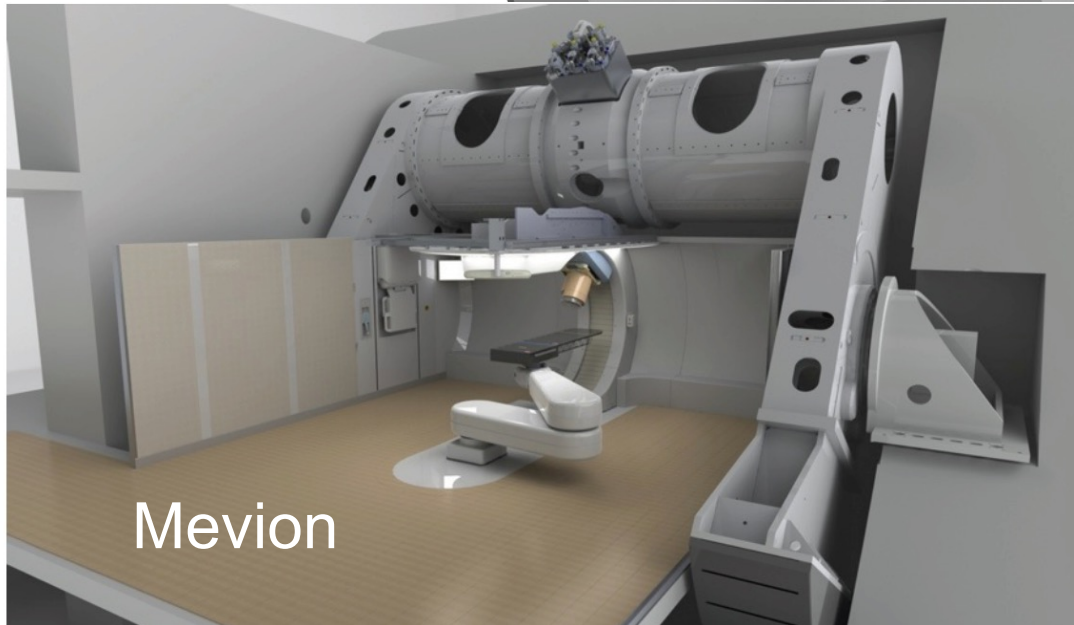
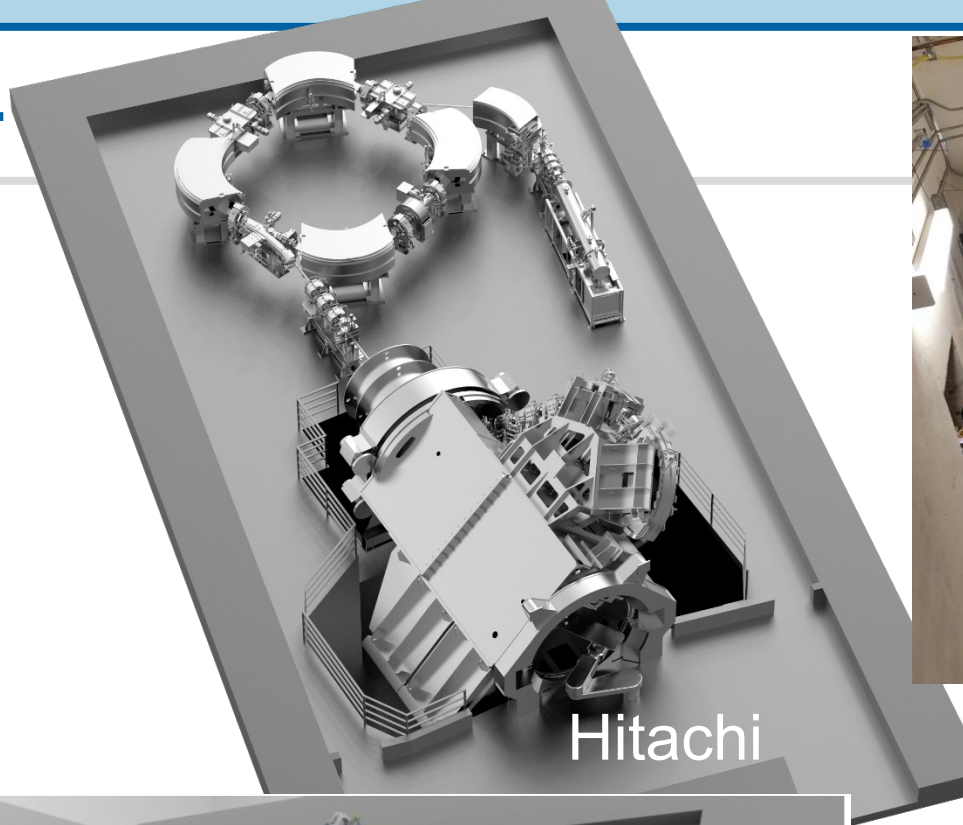
NIRS - Chiba (J)  
carbon ions facility





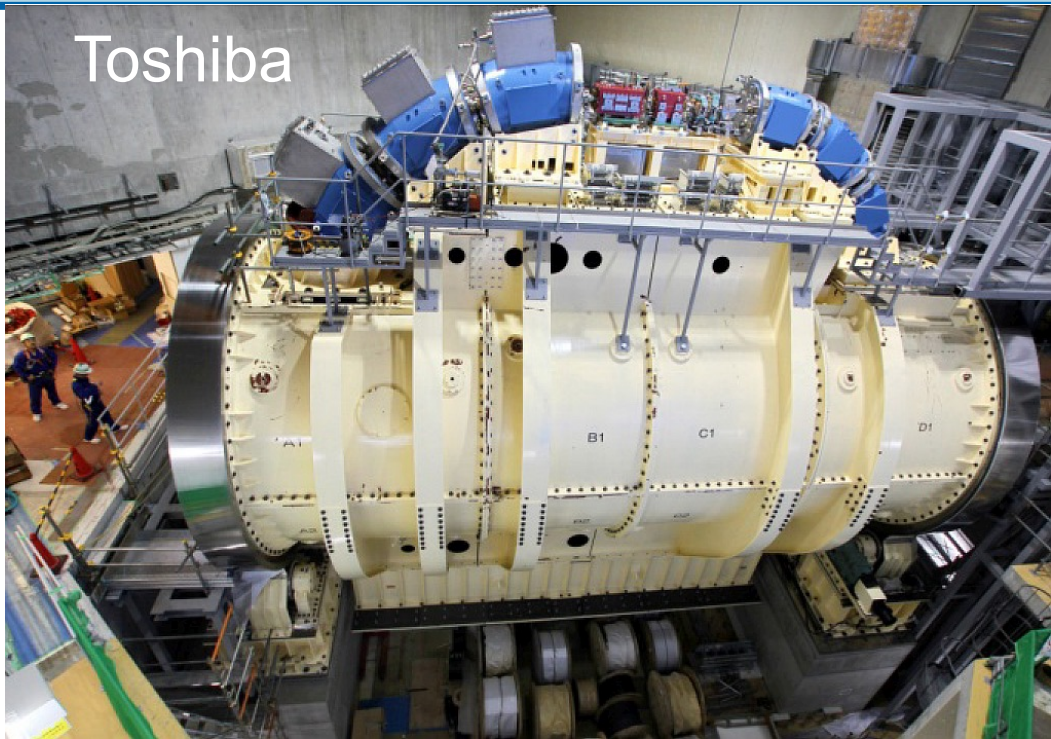
## Now, Companies...

- *Hitachi*
- *Varian Medical Systems*
- *IBA*
- *Protom*
- *Mevion*
- *Pronova*
- *Toshiba*
- *Sumitomo*
- *Mitsubishi*
- *LinearBeam*
- *Avo*
- *Bdot medical*
- *Optivus*





Now, Companies...





Located in Pavia (Italy)



**Not-for-profit private foundation**

**Created by the Italian Ministry of Health in 2001**

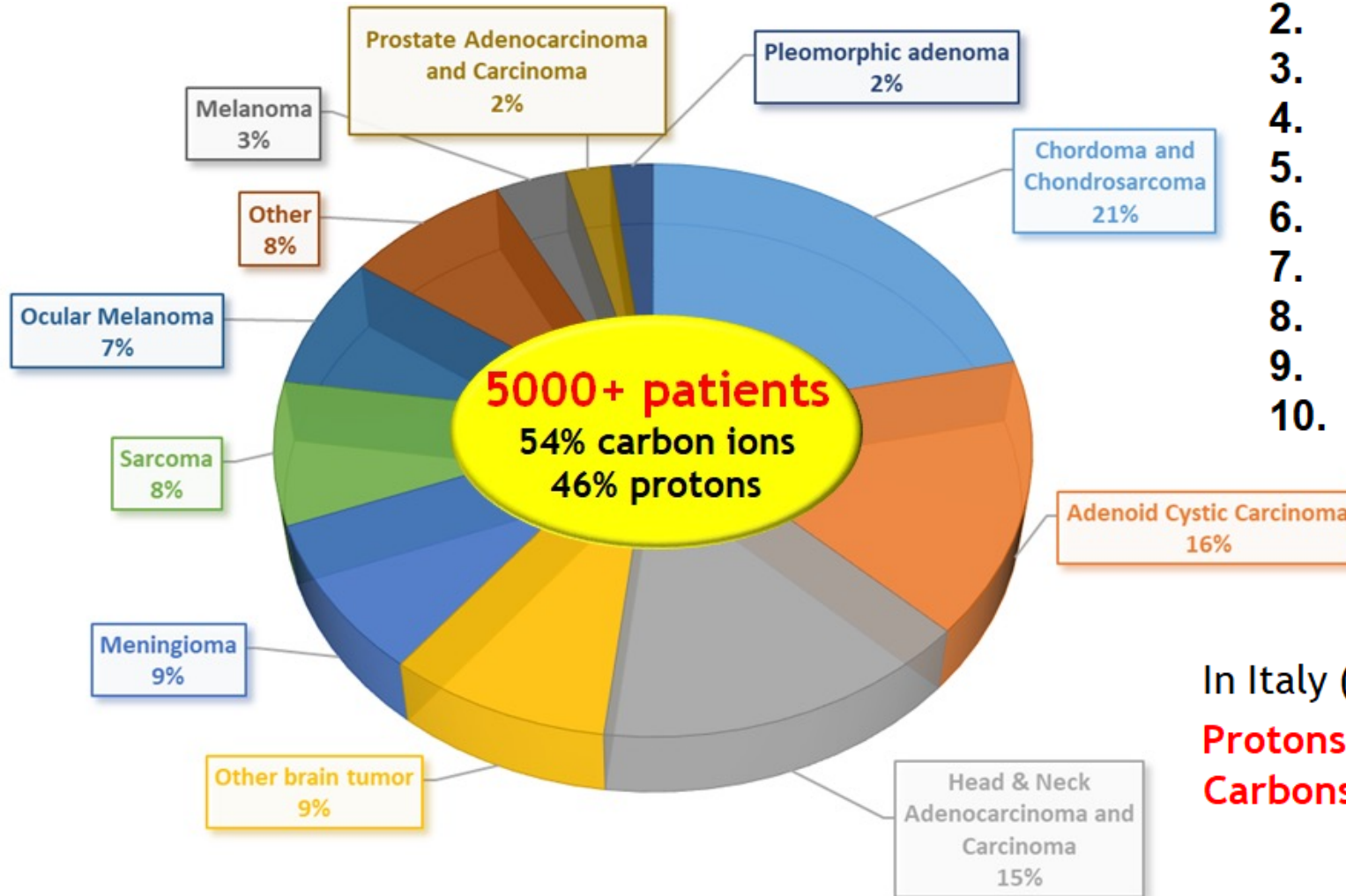
**With the purpose to introduce hadrontherapy in clinics, pursue research and formation**

**The Board is formed by 14 Institutions:**

- 5 hospitals
- 3 universities
- 2 research institutes
- 2 public entities (Ministry of Health and Town of Pavia)
- 2 bank foundations



# CLINICAL Activities at CNAO



1. Chordoma & chondrosarcoma base/spine
2. Meningiomas
3. Brain tumors (trunk)
4. ACC Salivary Glands
5. Orbit tumors including eye melanoma
6. Sinonasal carcinoma
7. Soft Tissue & bone Sarcoma (every sites)
8. Recurrent tumors (retreatment)
9. Patients with immulogical disorders
10. Pediatric solid tumors

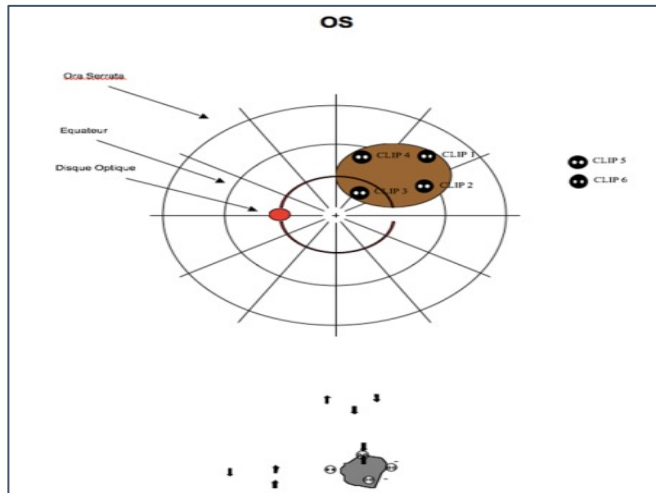
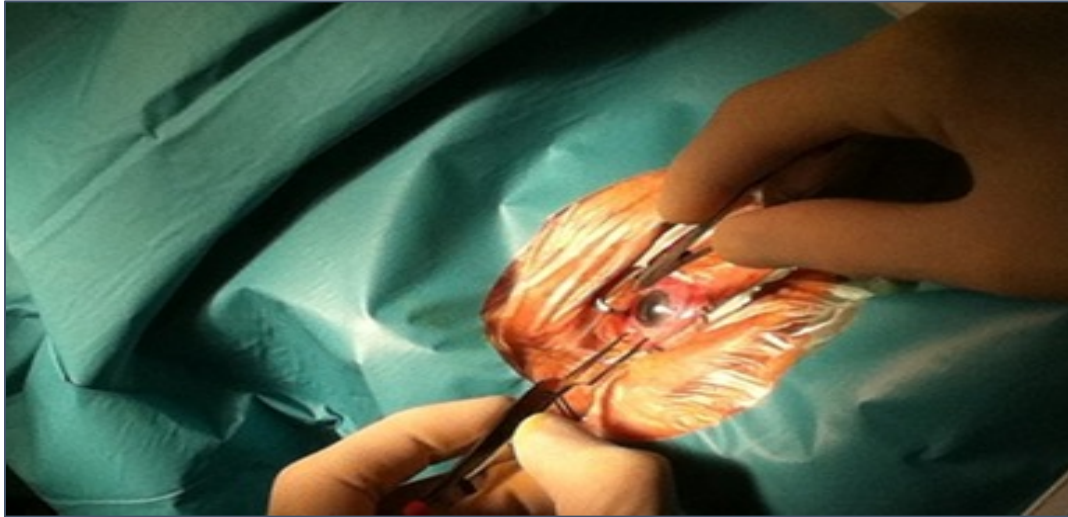
In Italy (60 million inhabitants) estimated cases 1-10:

**Protons:** about 5.000 patients/year

**Carbons:** about 1.000 patients/year

# Small volumes: ocular melanoma

Collaboration with INT - Milan:  
patient selection and tantalum clips

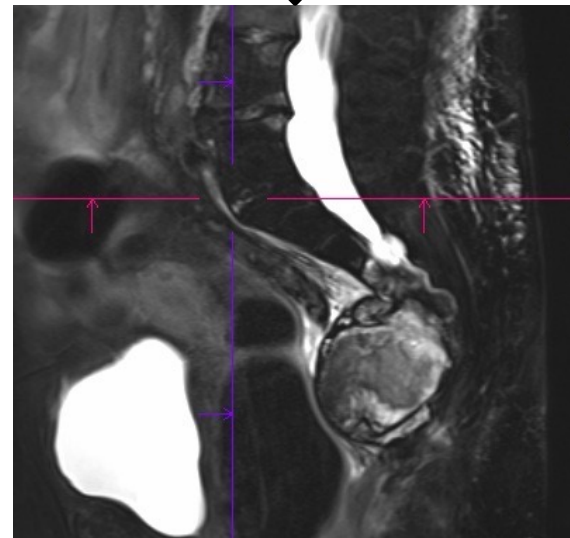
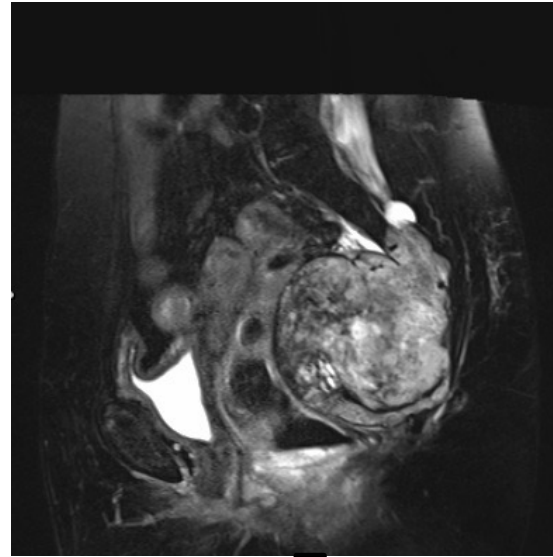
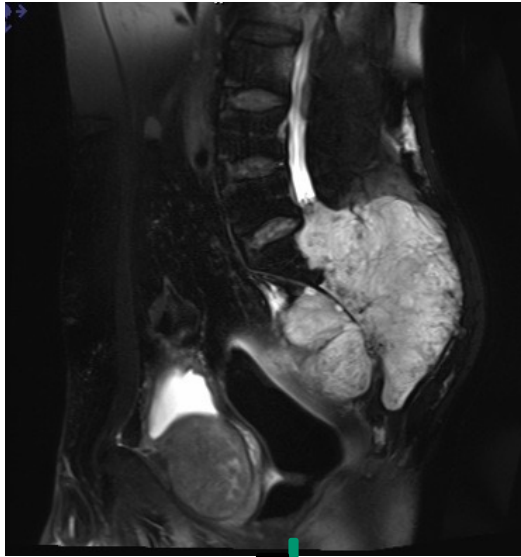


**> 450 patients**  
**Protons: 60 GyE (4 fx)**  
**Local Control >95%**  
**Eye preservation >90%**  
**Visual function >45%**

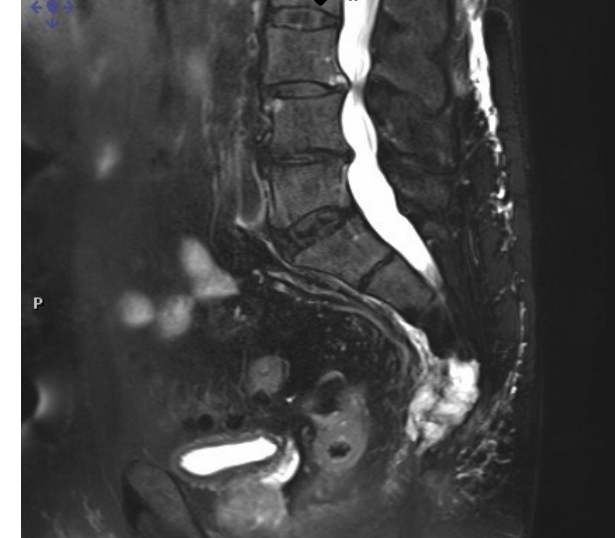
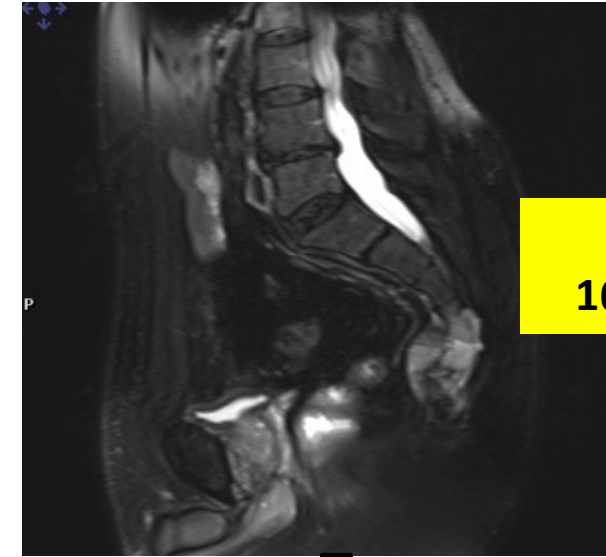


Collaboration with Politecnico Milano

## BIG volumes: sacral chordoma



After 1 year



CIRT 74 GyE  
16 fractions IMPT

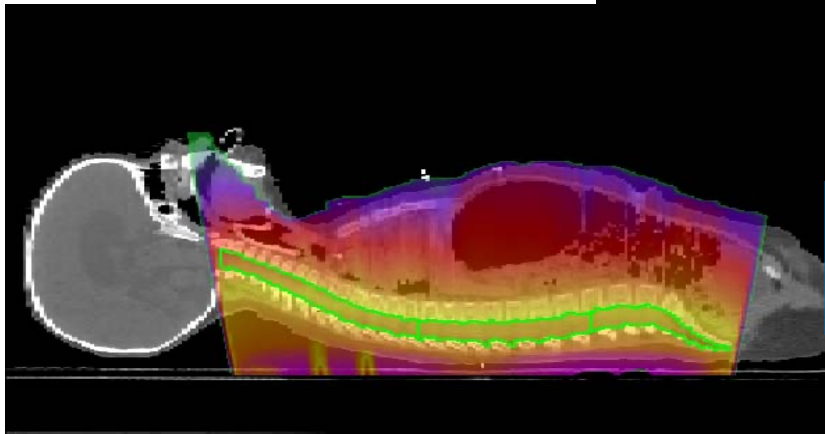
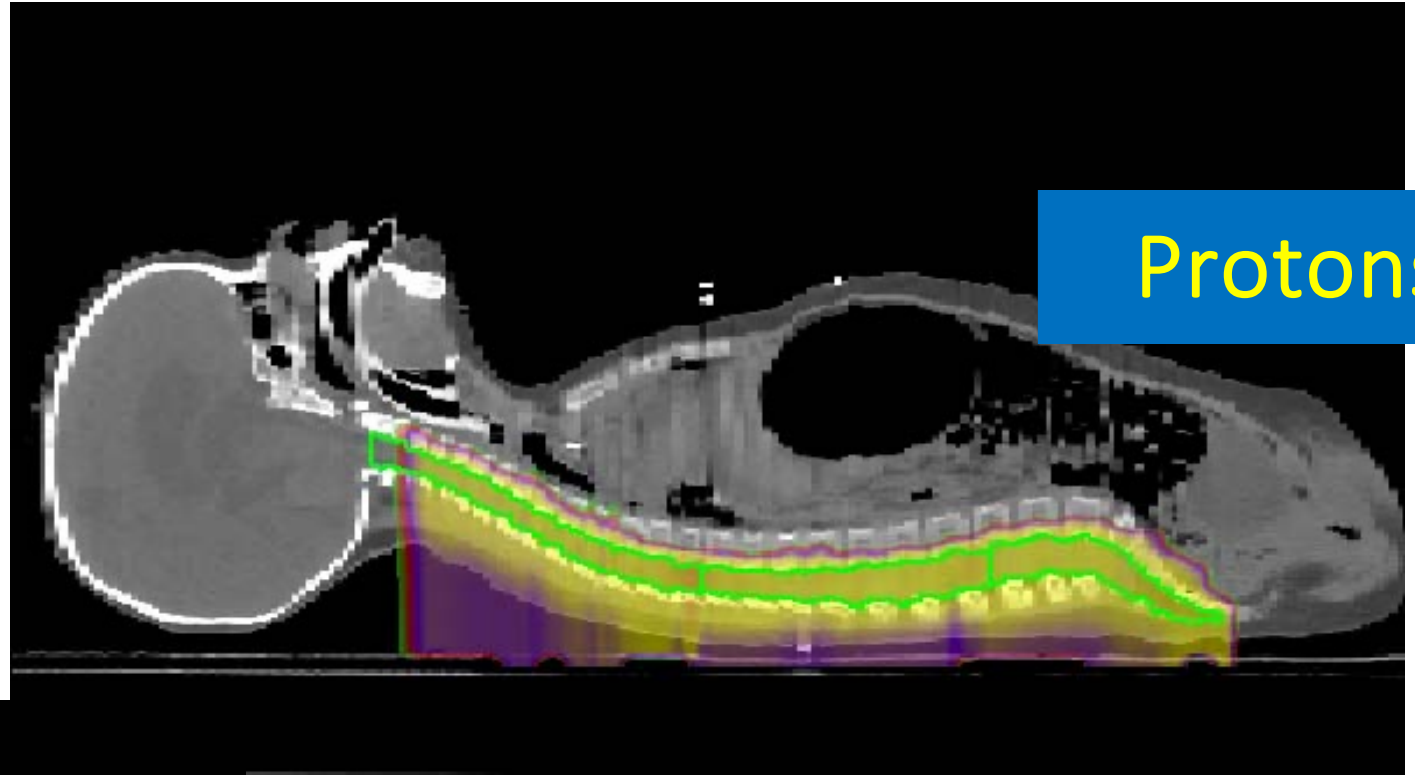


## Pediatric patients: elective for protons

Less dose to healthy tissues  
to reduce long term risks of secondary tumours

Year 2022: 46 pat  
(24 anaesthesia)

Year 2023: 62 pat  
(24 anaesthesia)

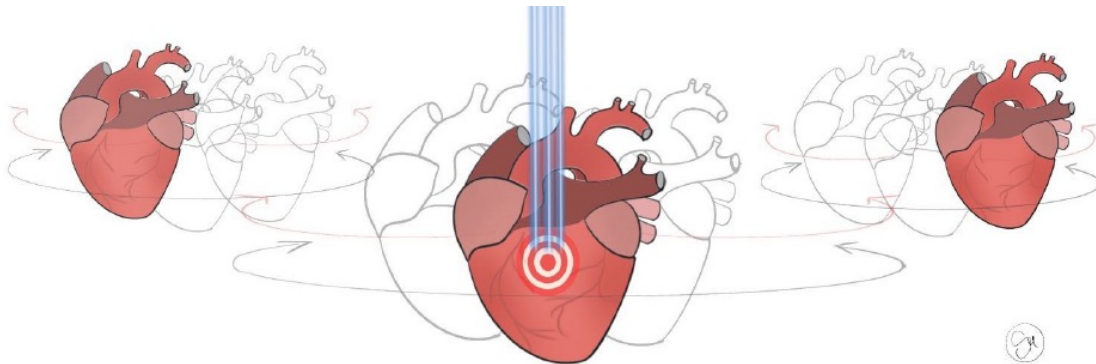
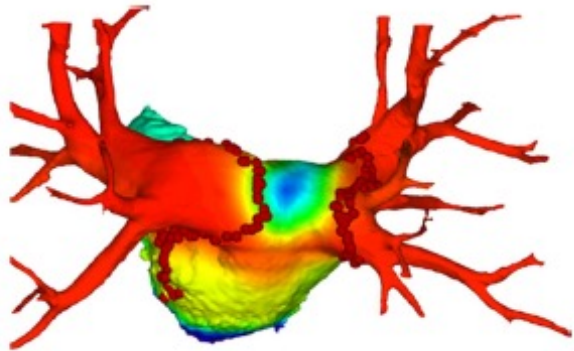


X-rays

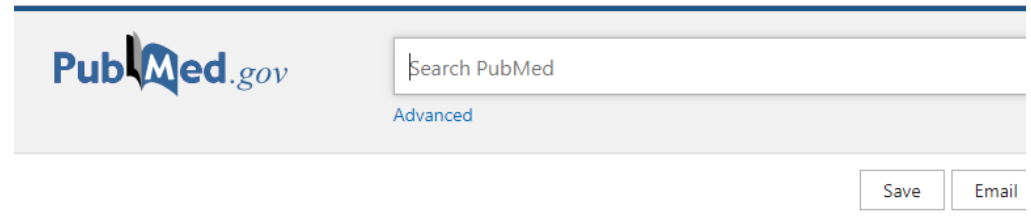


# Non oncological applications: ventricular arrhythmia

(Collaboration with San Matteo Hospital, Pavia)



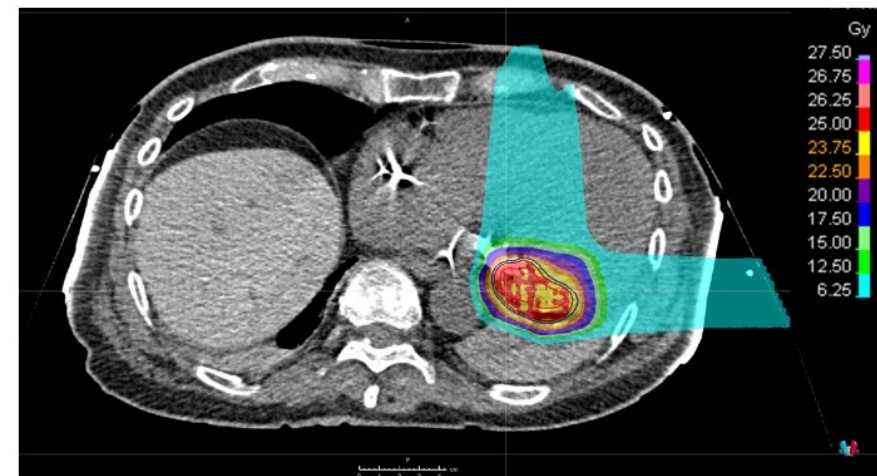
*Published on:*  
**European Journal of Heart Failure**



► [Eur J Heart Fail. 2020 Nov 12. doi: 10.1002/ejhf.2056. Online ahead of print.](#)

## The First-in-Man Case of Non-invasive Proton Radiotherapy to Treat Refractory Ventricular Tachycardia in Advanced Heart Failure

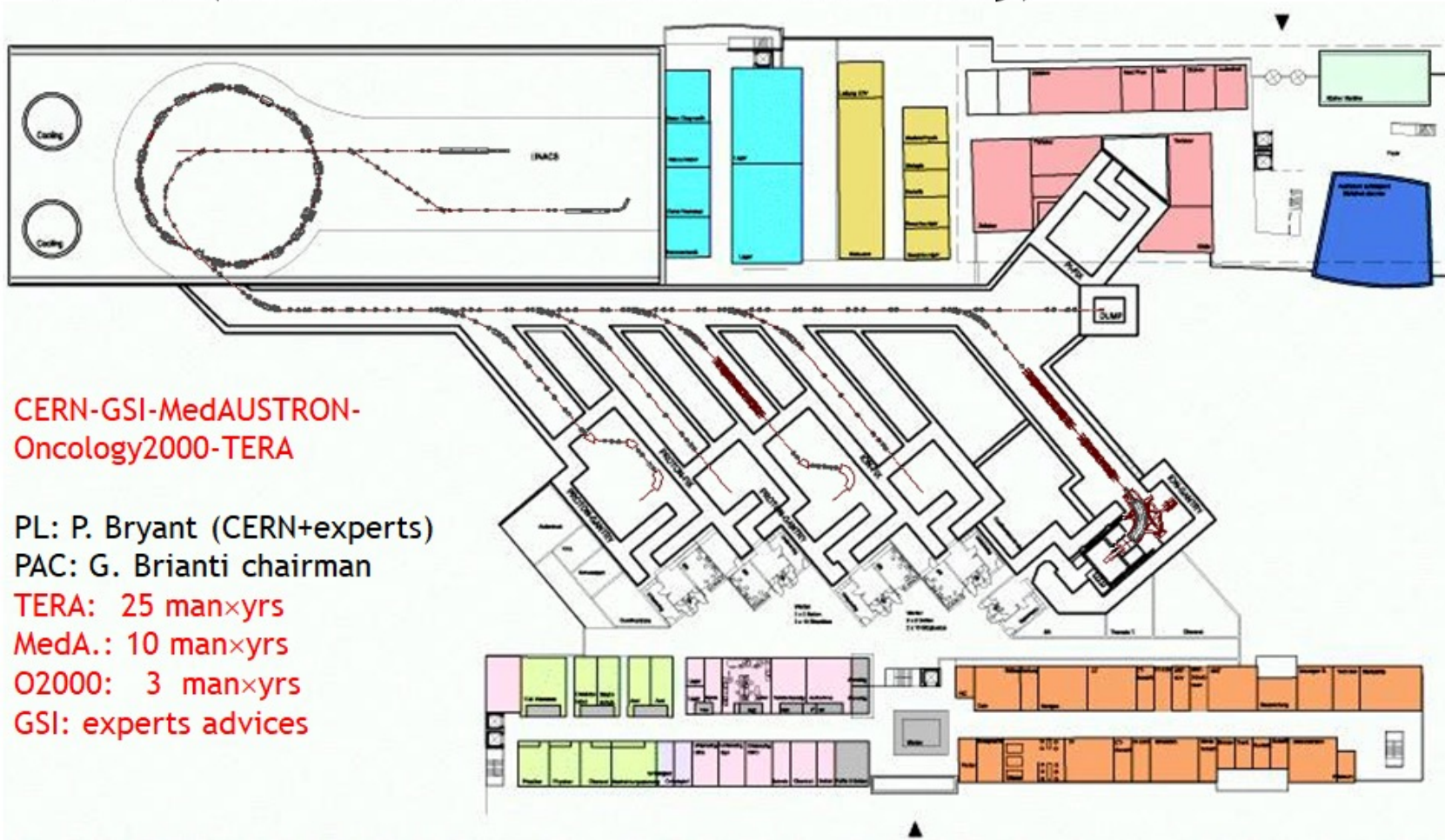
Veronica Dusi <sup>1 2</sup>, Viviana Vitolo <sup>3</sup>, Laura Frigerio <sup>1 4</sup>, Rossana Totaro <sup>1 4</sup>, Adele Valentini <sup>5</sup>, Amelia Barcellini <sup>3</sup>, Alfredo Mirandola <sup>3</sup>, Giovanni Battista Perego <sup>6</sup>, Michela Coccia <sup>2</sup>, Alessandra Greco <sup>4</sup>, Stefano Ghio <sup>4</sup>, Francesca Valvo <sup>3</sup>, Gaetano Maria De Ferrari <sup>7</sup>, Massimiliano Gneocchi <sup>1 2</sup>, Luigi Oltrona Visconti <sup>4</sup>, Roberto Rordorf <sup>1 4</sup>



# The origin of CNAO technology

**From 1996 to 1999 at CERN**

**PIMMS (Proton-Ions Medical Machine Study)**



**CERN-GSI-MedAUSTRON-  
Oncology2000-TERA**

PL: P. Bryant (CERN+experts)

PAC: G. Brianti chairman

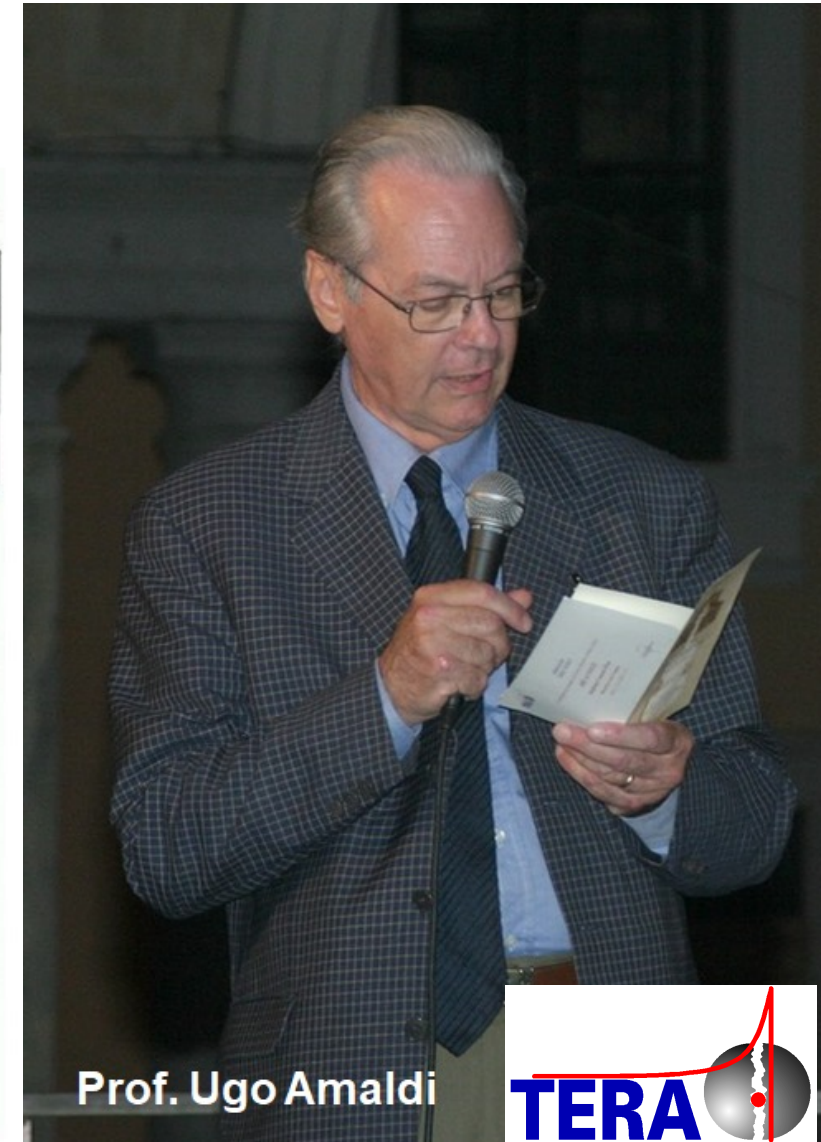
TERA: 25 man×yrs

MedA.: 10 man×yrs

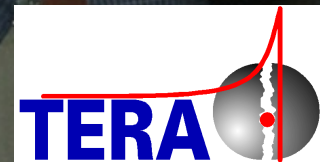
O2000: 3 man×yrs

GSI: experts advices

Objective: define the optimal hadrontherapy centre without constraints



Prof. Ugo Amaldi



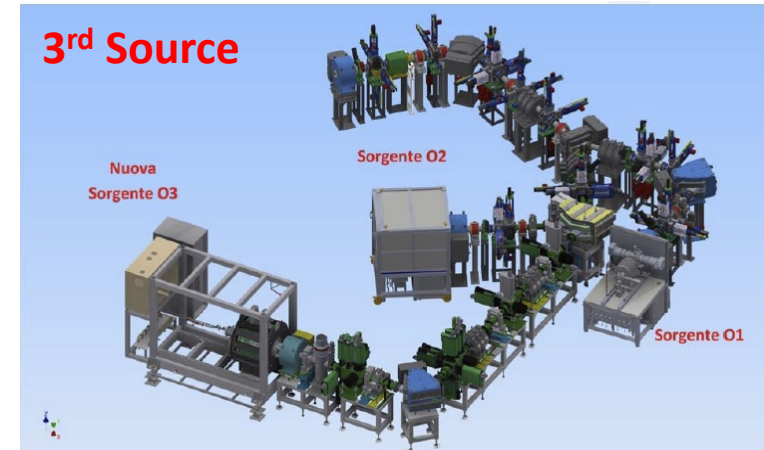
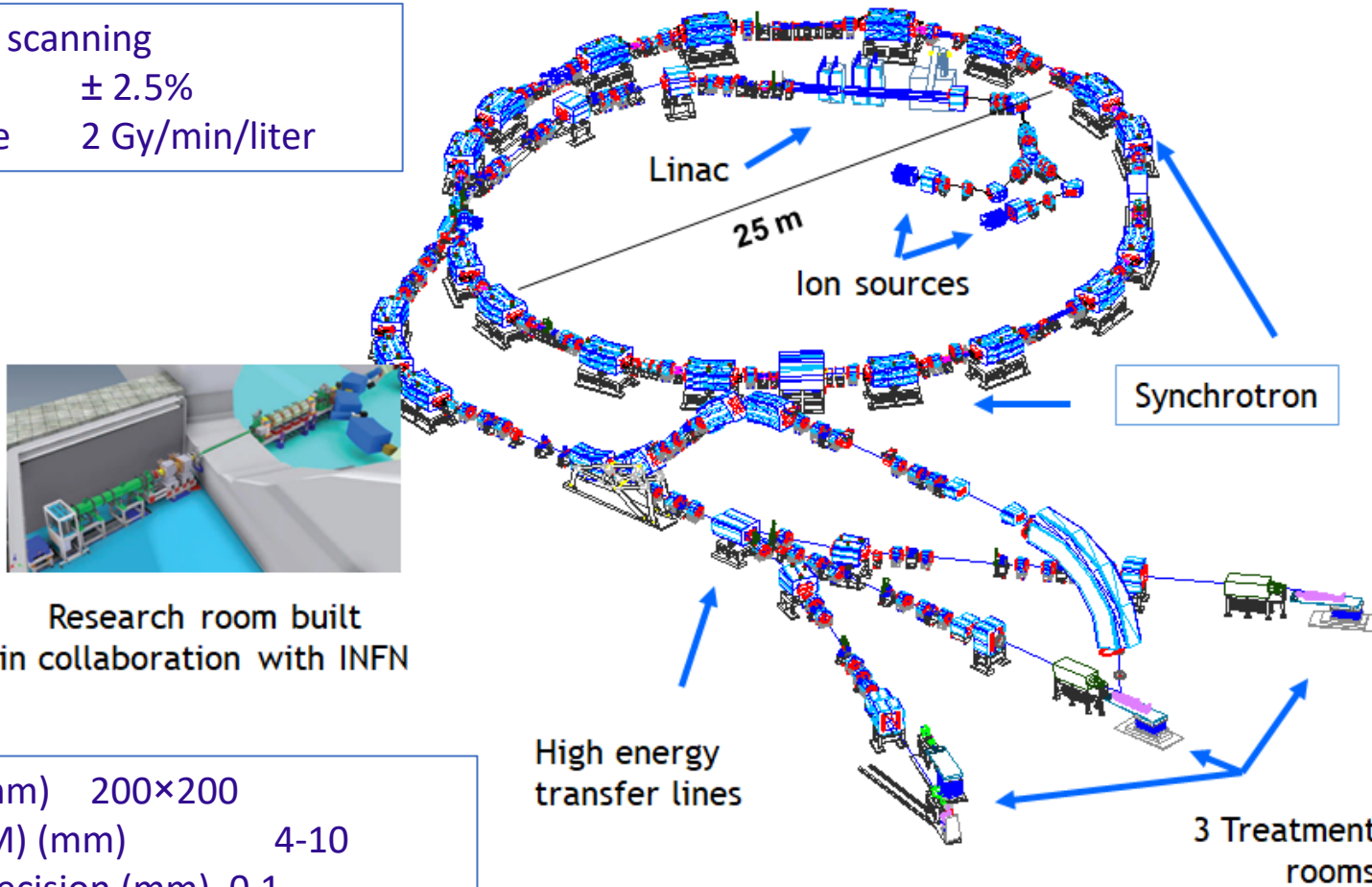


# THE CNAO SYSTEM FOR CLINICS AND RESEARCH

IP shared by CNAO, INFN, CERN

Accelerated ion p, C, He ...  
Energy range (MeV/u) 60-225 (p) (30-320mm)  
120-400 (C) (30-270mm)

Extraction Slow - scanning  
Dose uniformity  $\pm 2.5\%$   
Average dose rate 2 Gy/min/liter



Field size (mm×mm) 200×200  
Beam size (FWHM) (mm) 4-10  
Beam position precision (mm) 0.1



# THE HEARTH OF CNAO: THE SYNCHROTRON

Trasfer-lines  
tow. patients

Sources  
to generate

1 RF cavity  
to accelerate

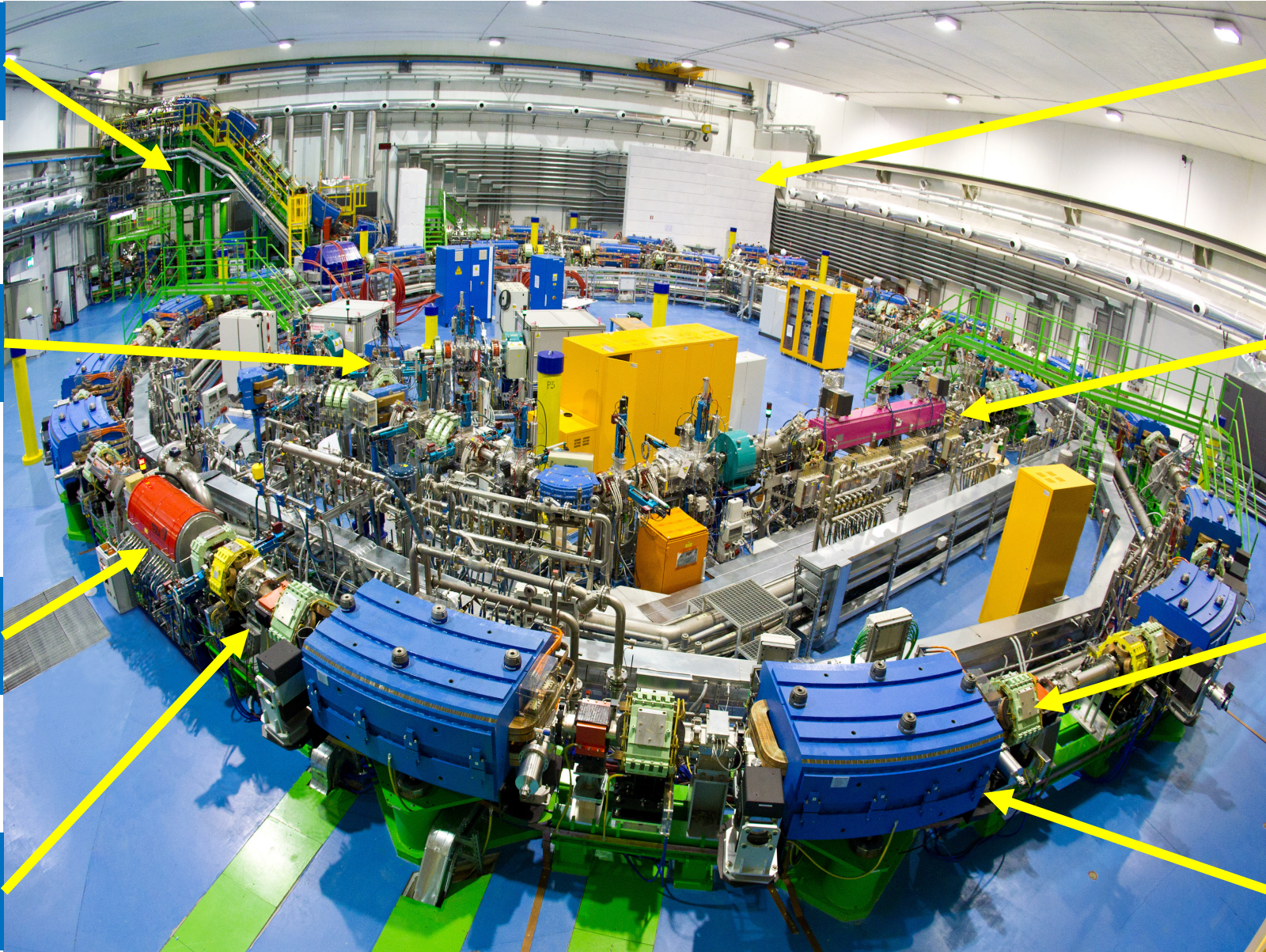
20 Correctors  
to steer

Power supplies  
room

Linac  
to pre-accelerate

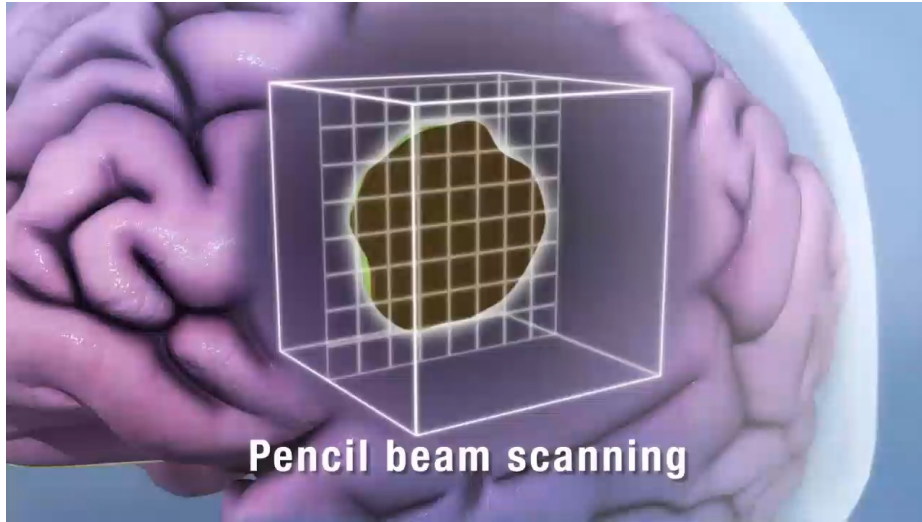
24 Quadrupoles  
to focus

16 Dipoles  
to bend





## Not only accelerators ...



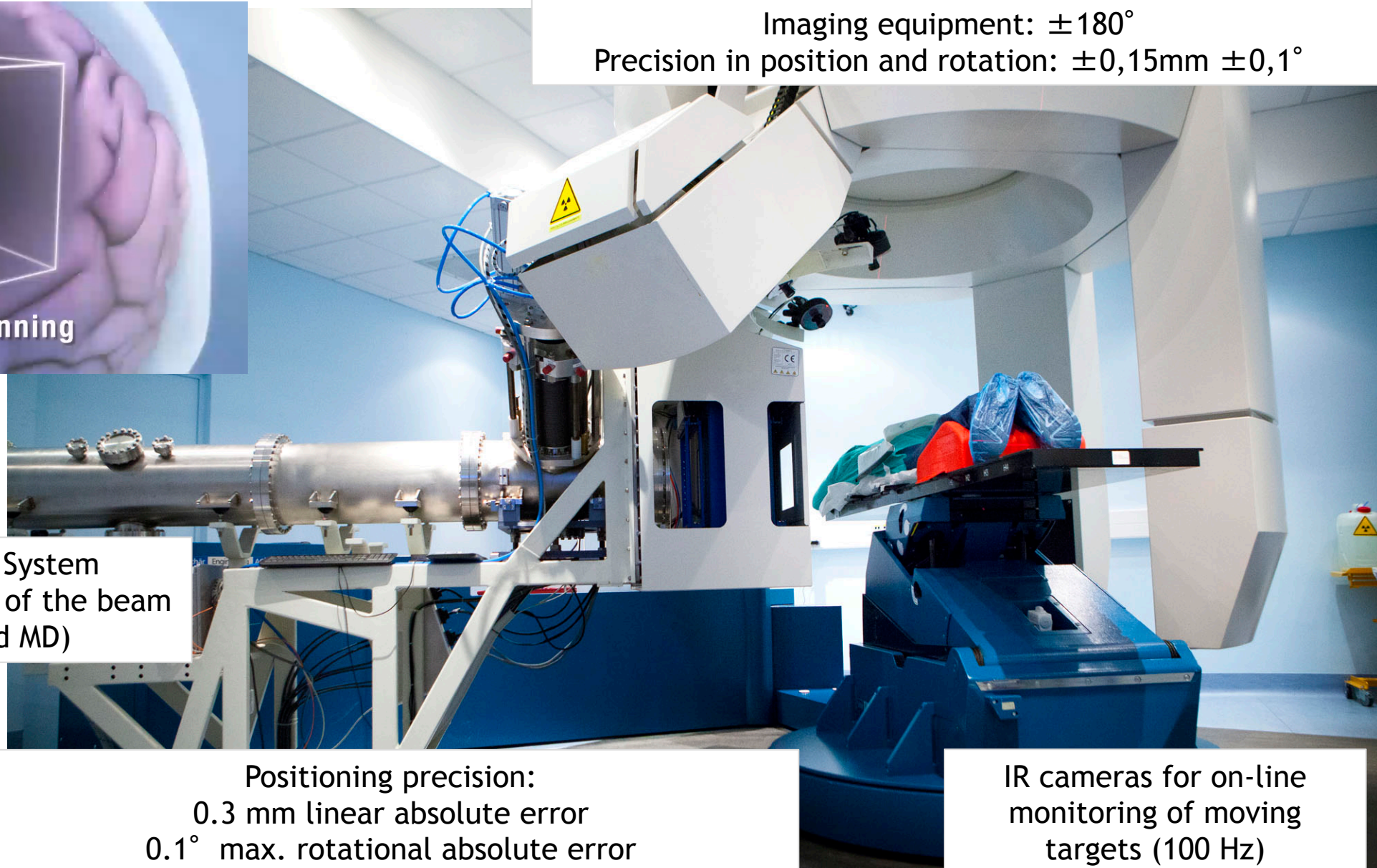
Pencil beam scanning

Imaging equipment:  $\pm 180^\circ$   
Precision in position and rotation:  $\pm 0,15\text{mm}$   $\pm 0,1^\circ$

Dose Delivery System  
for active scanning of the beam  
(CE certified MD)

Positioning precision:  
0.3 mm linear absolute error  
 $0.1^\circ$  max. rotational absolute error

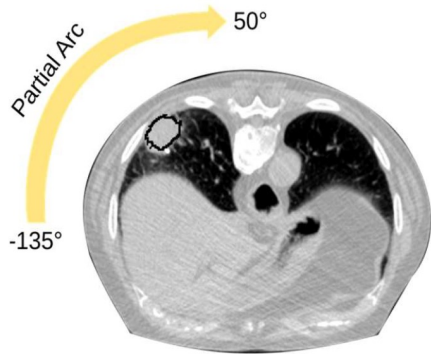
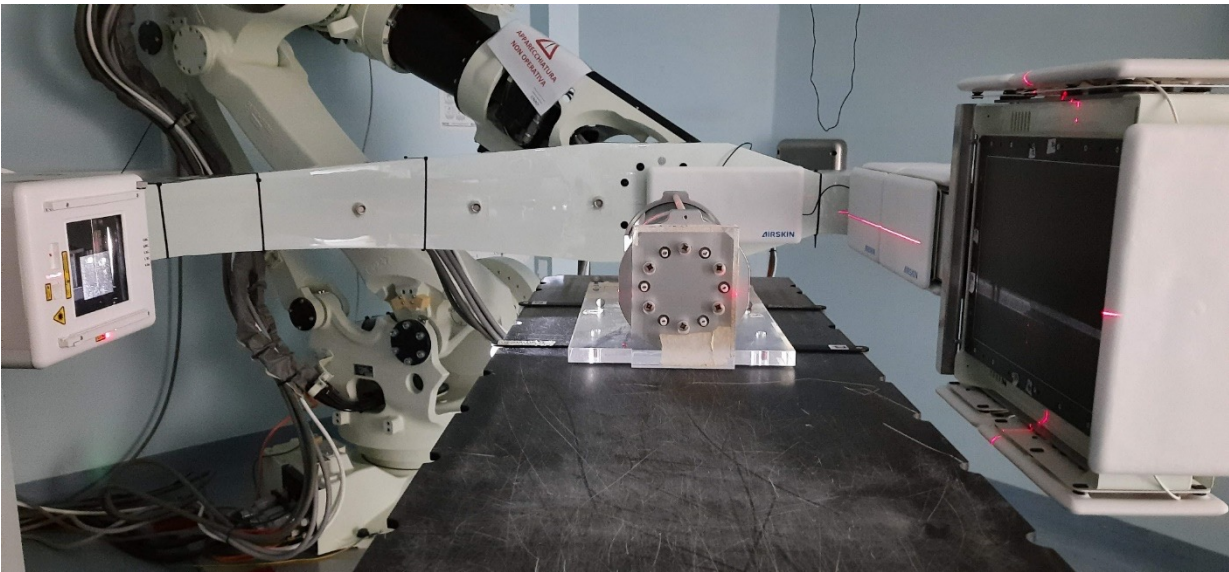
IR cameras for on-line  
monitoring of moving  
targets (100 Hz)



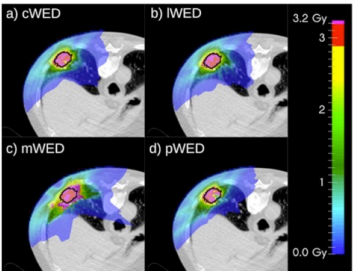
# Bioengineering: advanced patient positioning and verification systems

(Collaboration with G. Baroni - PoliMi)

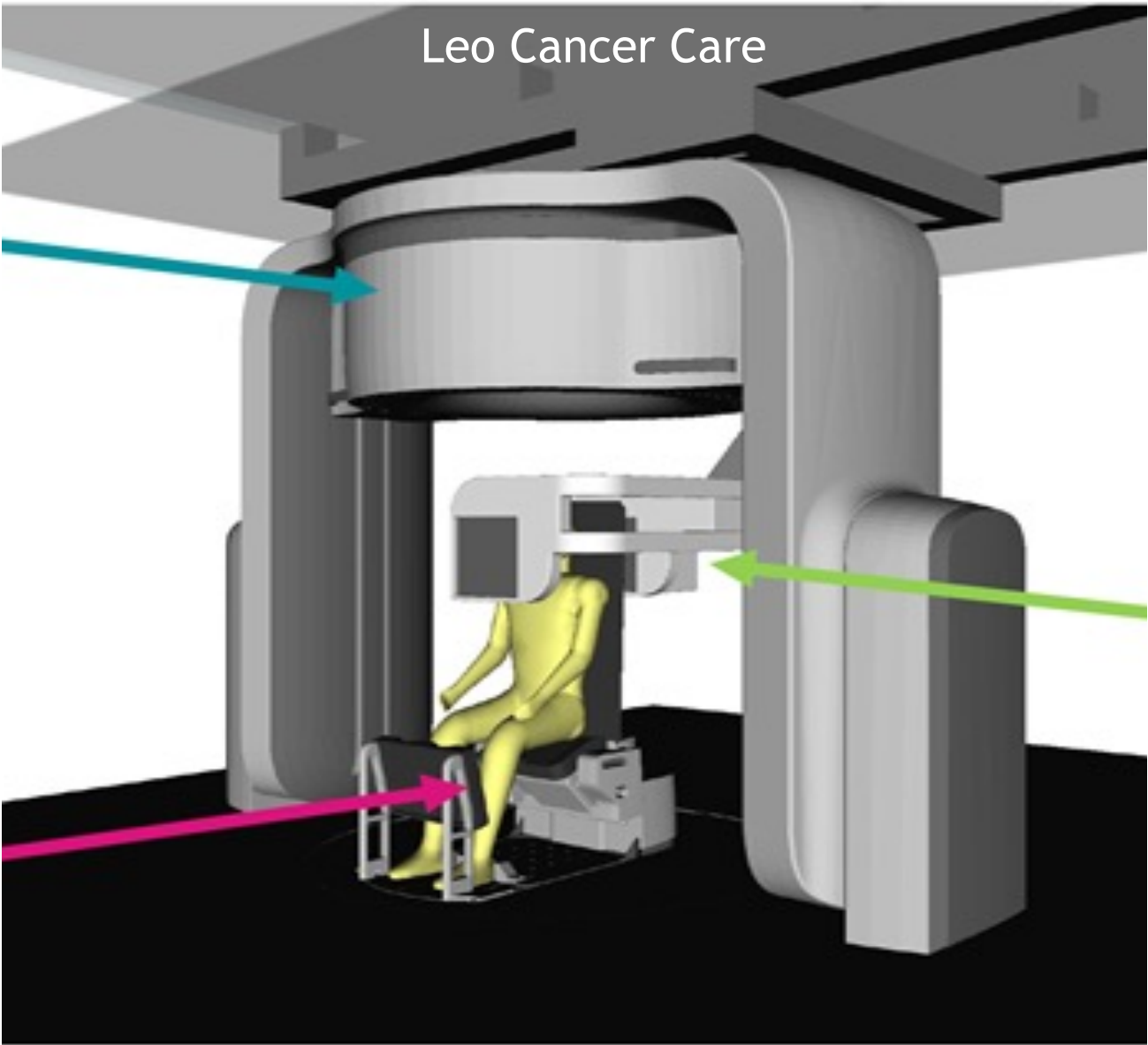
Robotic cone-beam CT



Arc therapy



(Collaboration with GSI)





# Operations and performances

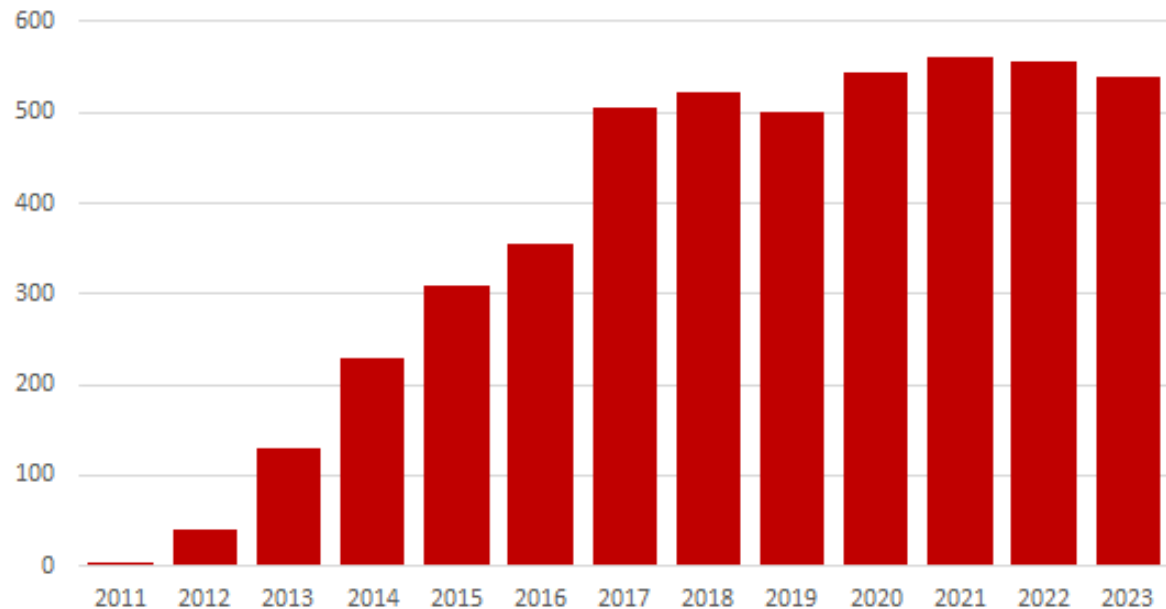
Machine running 24/7 - 3 shifts/day

4 maintenance stops per year of 5 days (Thursday to Monday included)

Patient treatments: 7:30 am - 9:30 pm from Monday to Friday

Night shifts and weekends for research, QA, upgrade and maintenance

Number of patients per year



## Years from 2011 to 2023

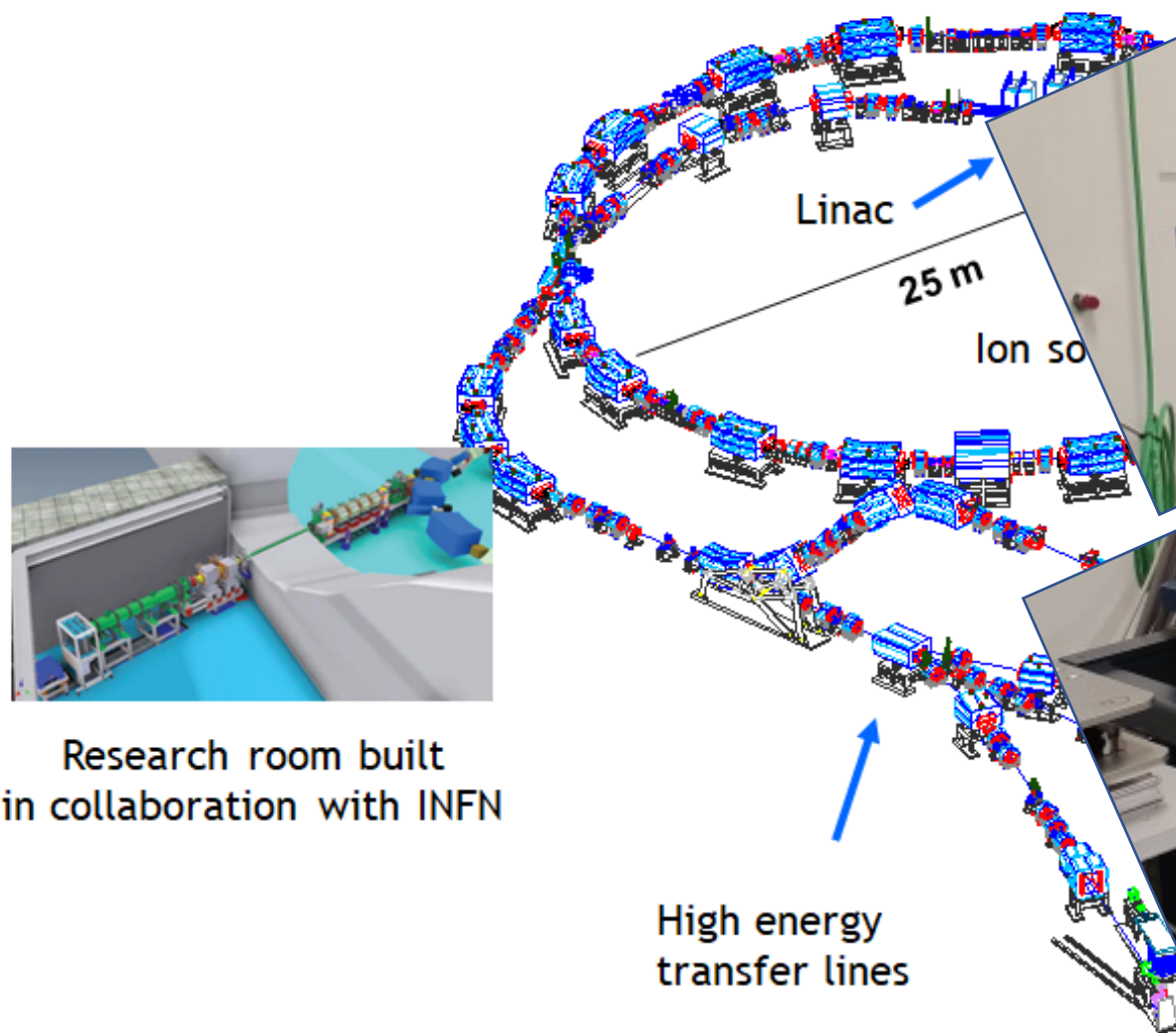
- 4062 running days
- 2985 treatment days
- 296dd ordinary maintainance
- 41 dd system breakdown
- **System availability: 90.6%**
- **System reliability (dd): 98.6%**
- **System reliability (sessions)**

## Year 2023

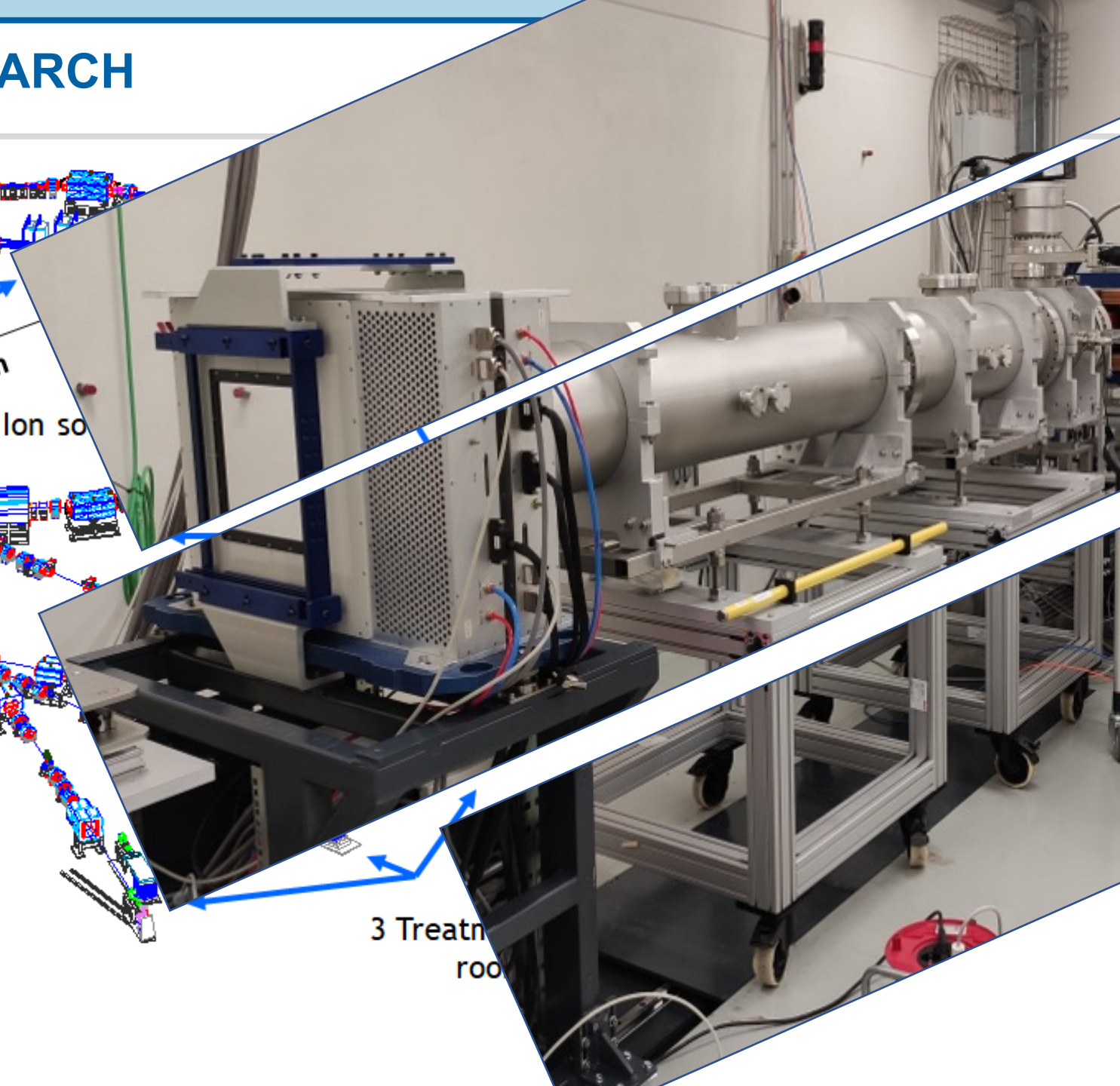
- 334 gg
- 241 gg
- 21 gg
- 0 gg
- **91.5%**
- **100%**
- **98.0 %**

204 (104+100) vs 9925

# BEAMTIME AND LABS FOR RESEARCH



Research room built  
in collaboration with INFN

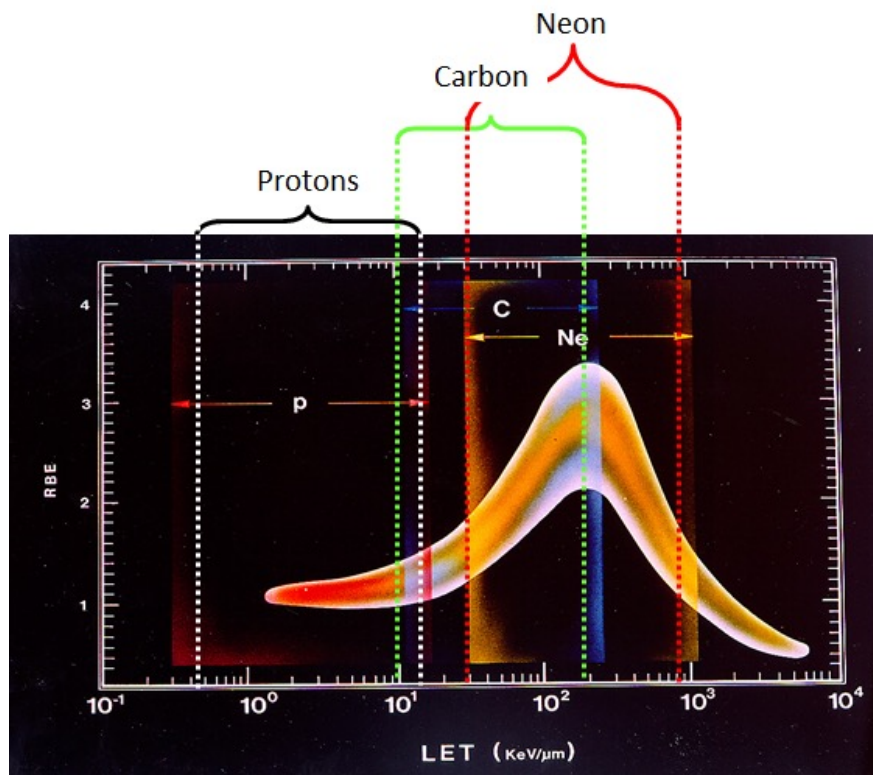


In 2023 more than 400 hours of  
beam time to external groups



# IONS: multi-parametric options for optimal individual treatment

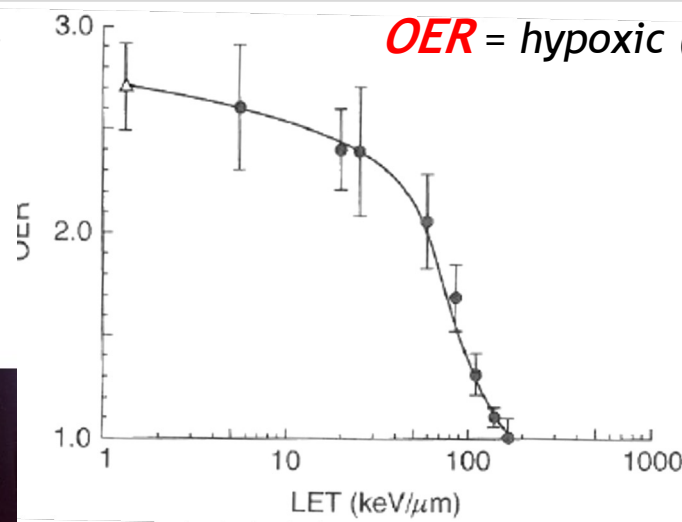
**Bragg peak** = maximum energy deposited at the end of the particle range



**Scattering (good>A)-Fragmentation (bad>A)**

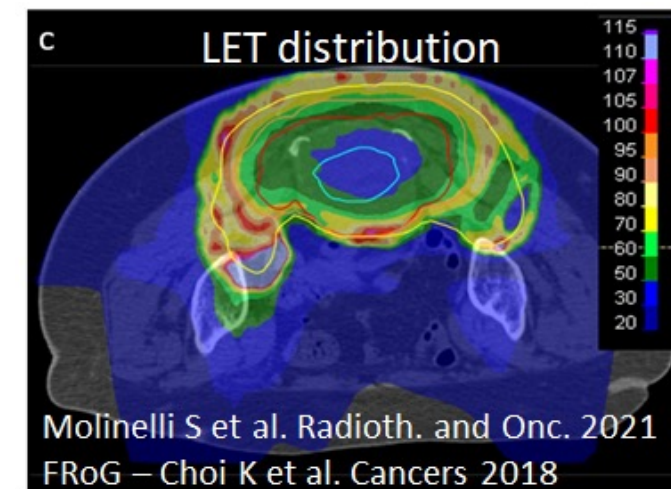
**RBE** = ratio between reference dose (X rays) and particle dose to obtain the same effect

**Immunotherapy + carbon ions** = combination increases clinical response

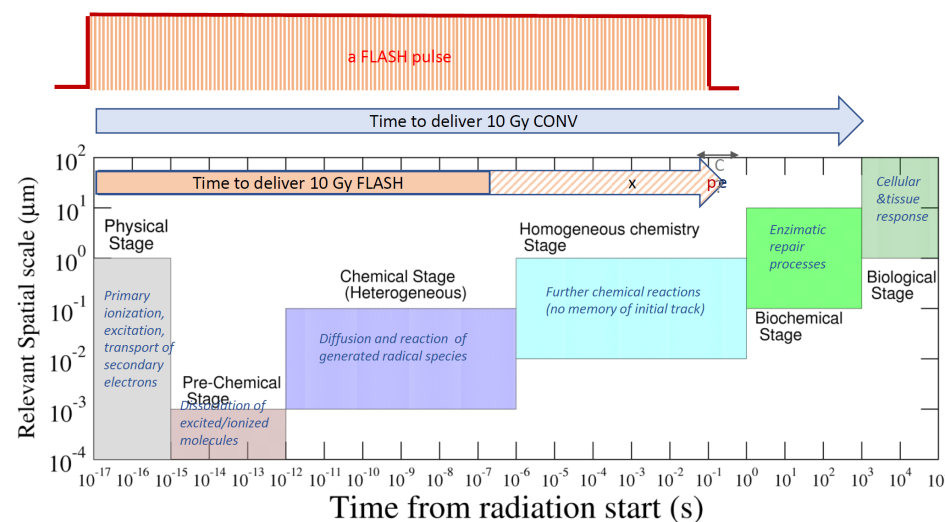


**OER** = hypoxic (0% pO<sub>2</sub>) vs oxic (20% pO<sub>2</sub>) conditions

**LET**

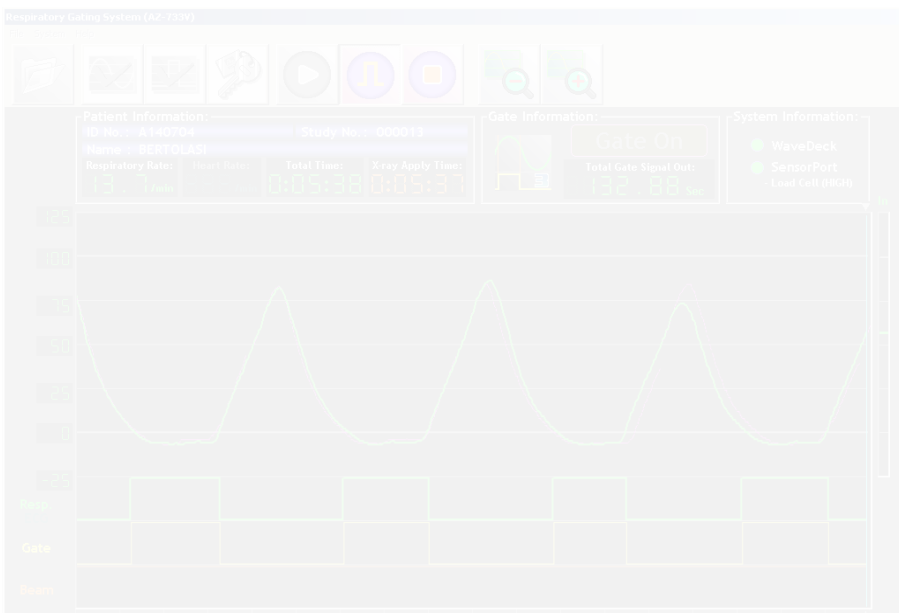


Spatiotemporal scales of radiation damage and FLASH



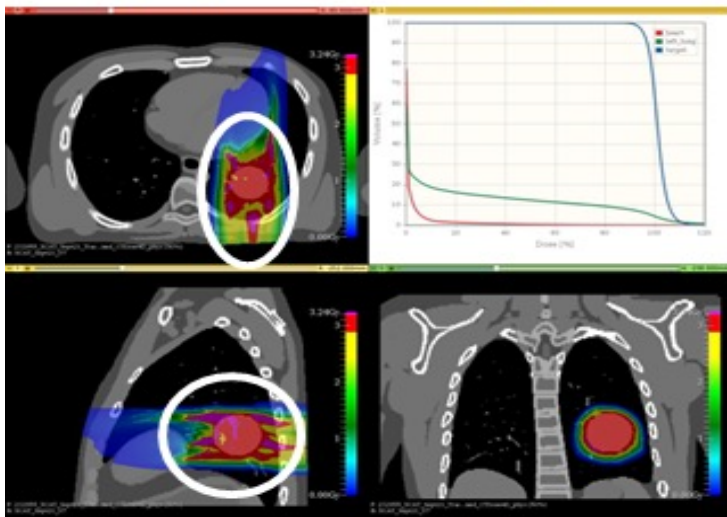
**FLASH THERAPY with ions**

# Tumours in moving targets



Accelerator cycle synchronized with patient

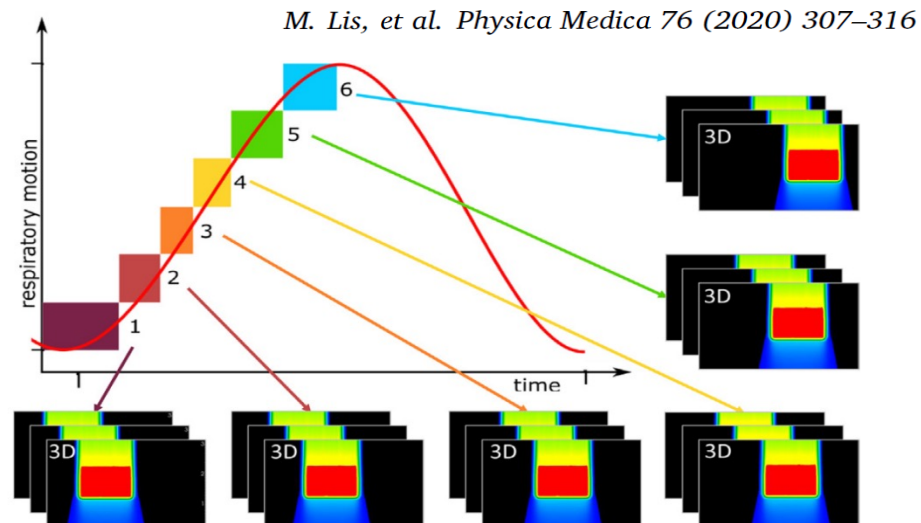
Single plan on moving tumor



Collaboration  
CNAO-GSI

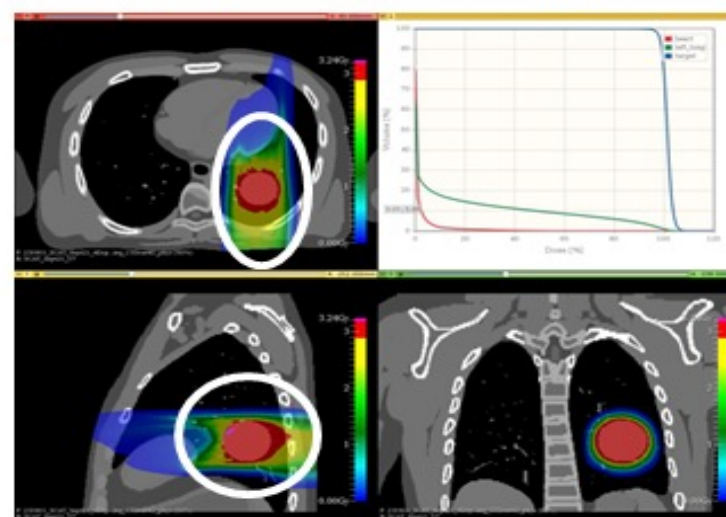
Dose calculations  
based on  
measurement  
results done  
In CNAO

DDS 4.0



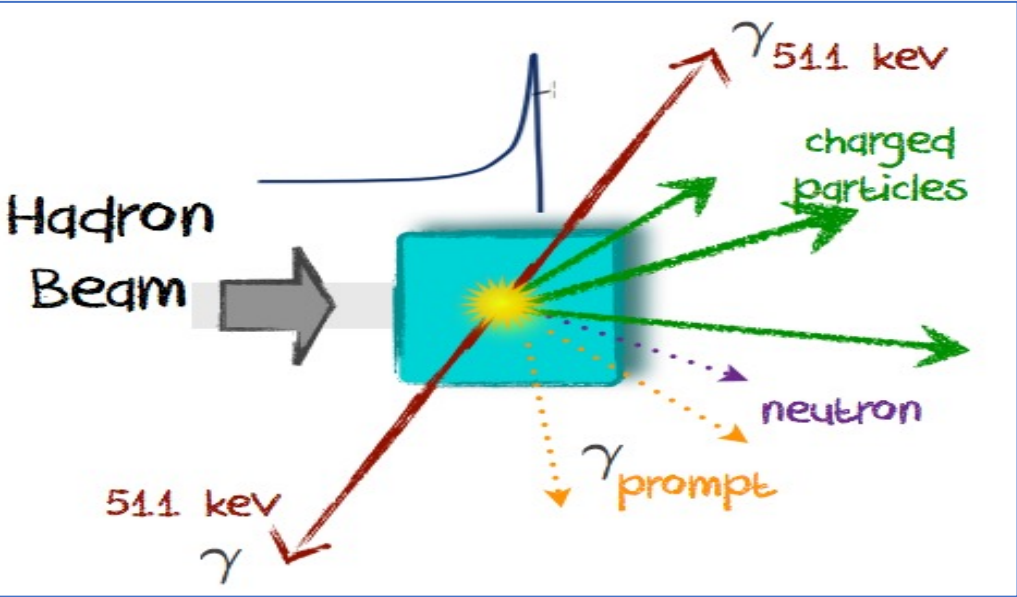
**Fig. 3.** A schematic depiction of the treatment plan library for an amplitude-based motion. Each individual plan is optimized on the motion phase-specific PTV, in an independent 3D-optimization. The beam spots in all of those plans are then scaled down, such that their total dose is the prescription dose.

Multiple plans on moving tumor



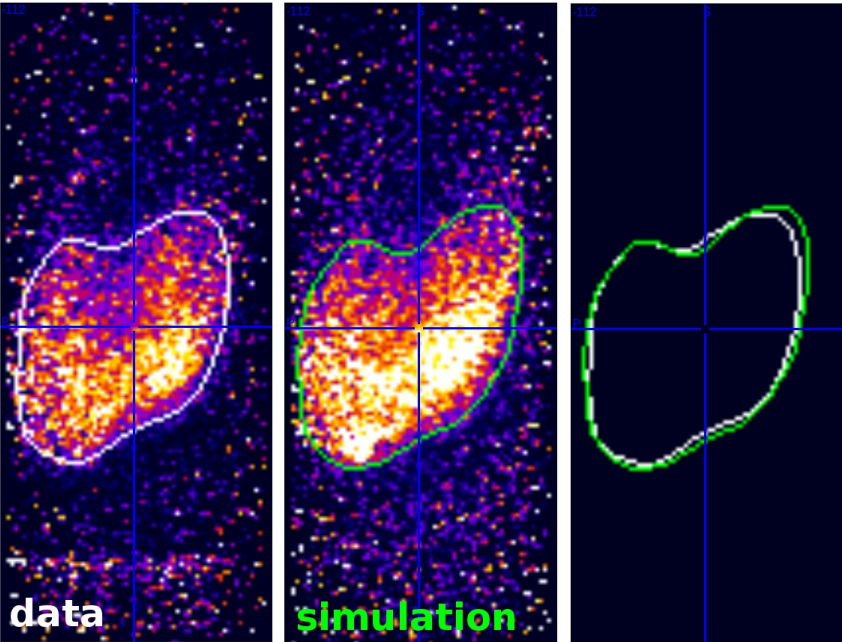


# Dose verification systems

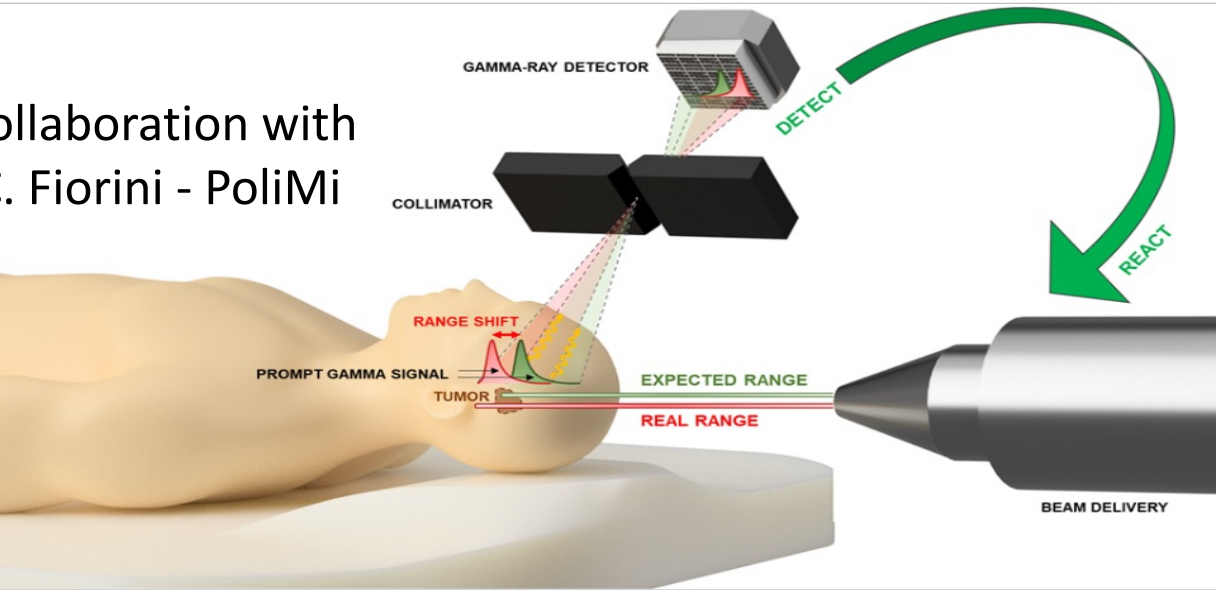


*Inside*

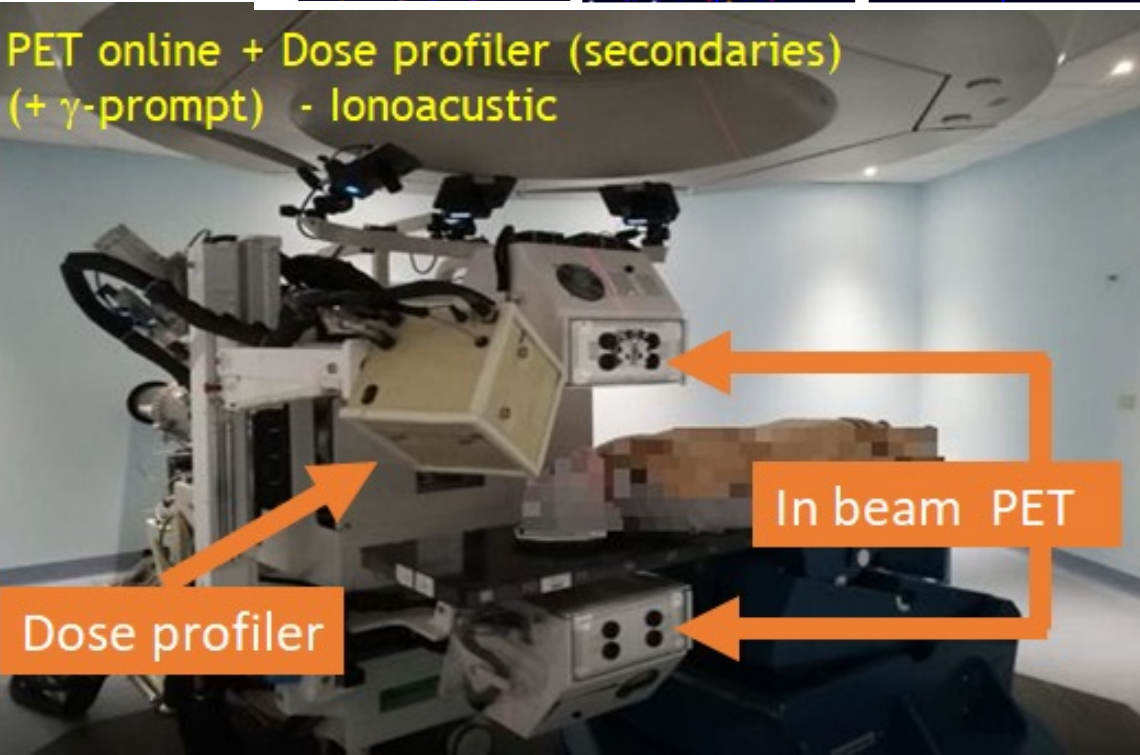
Collaboration with  
INFN, PoliMi, UniPi, UniTo



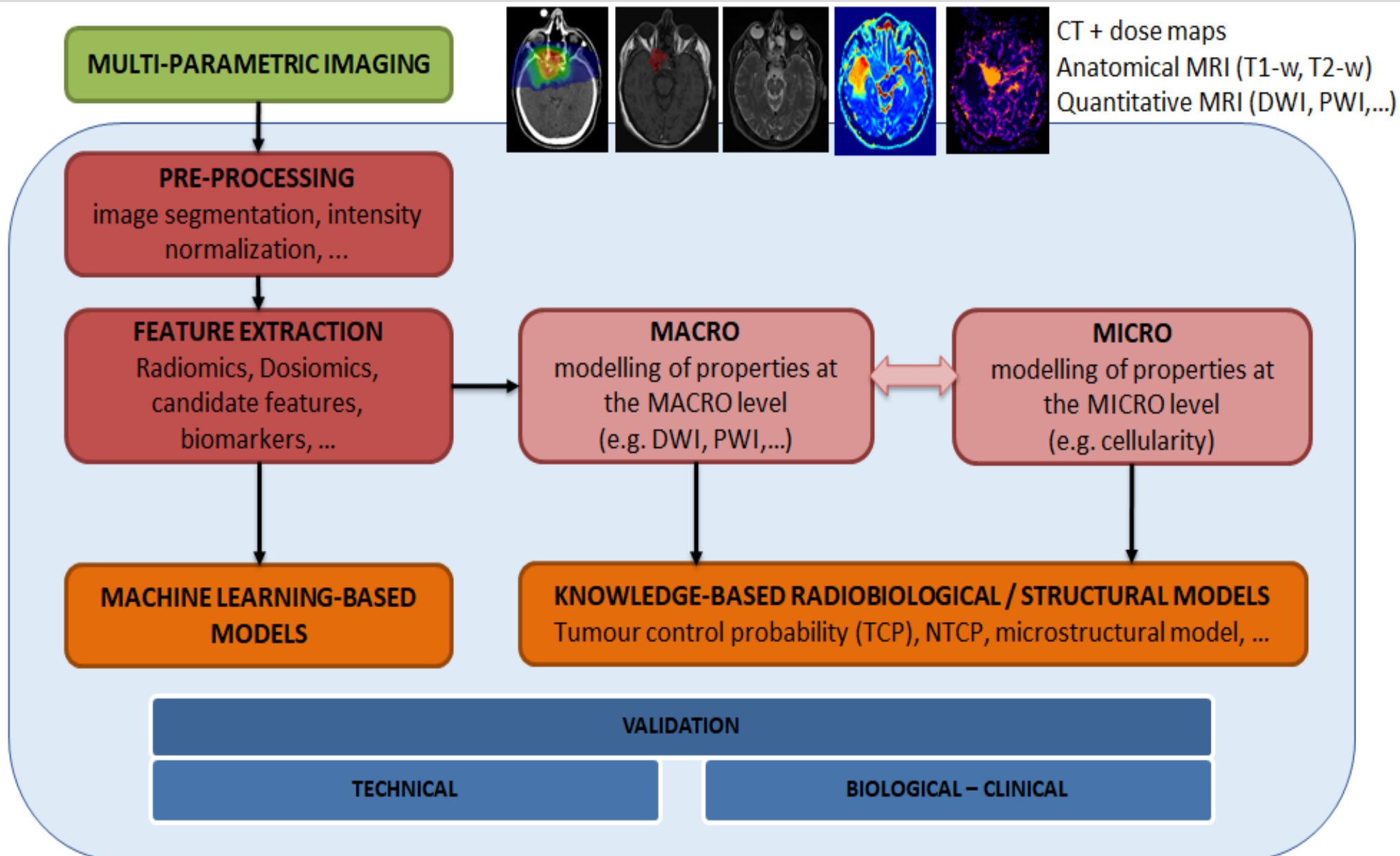
Collaboration with  
C. Fiorini - PoliMi



PET online + Dose profiler (secondaries)  
(+  $\gamma$ -prompt) - Ionoacoustic



## Technical framework







POLITECNICO  
MILANO 1863

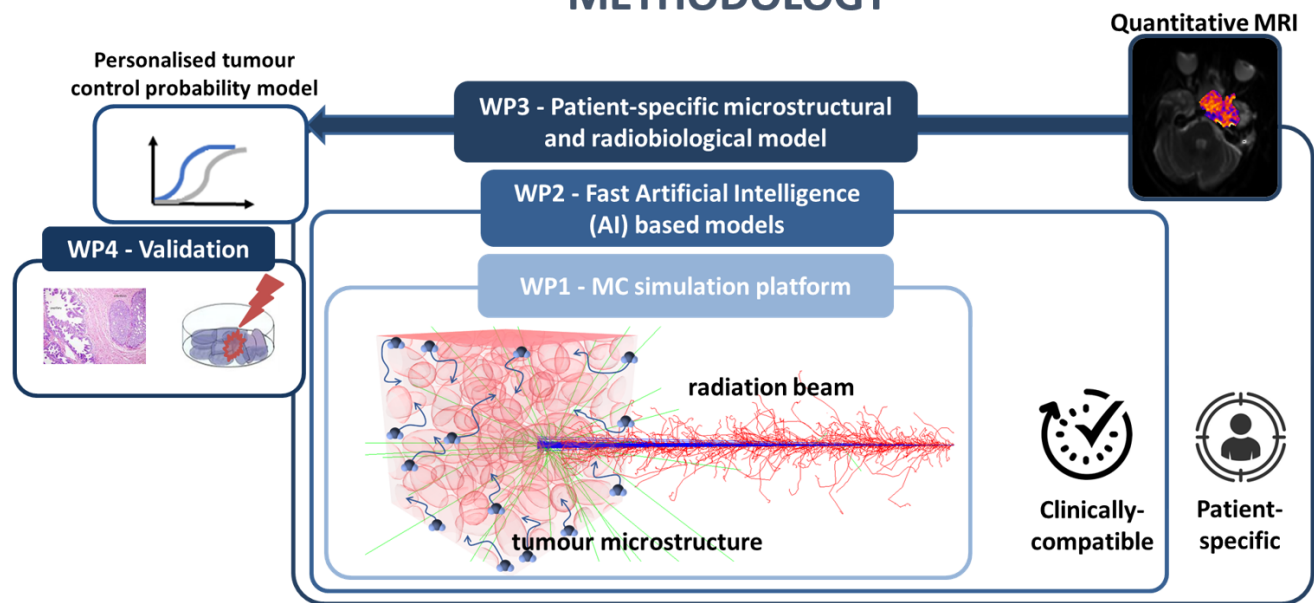


## Patient-specific **M**icrostructural and rad**i**obiological model for perso**N**alized external beam radiat**ION** therapy in localized tumour**S**

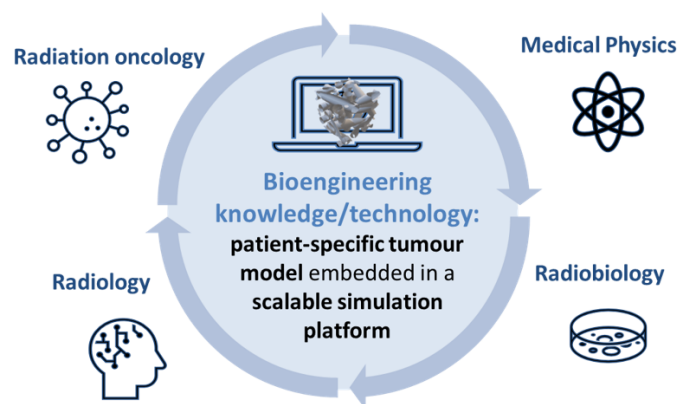
### VISION

Novel modellistic framework towards the implementation of biologically-guided radiotherapy treatments

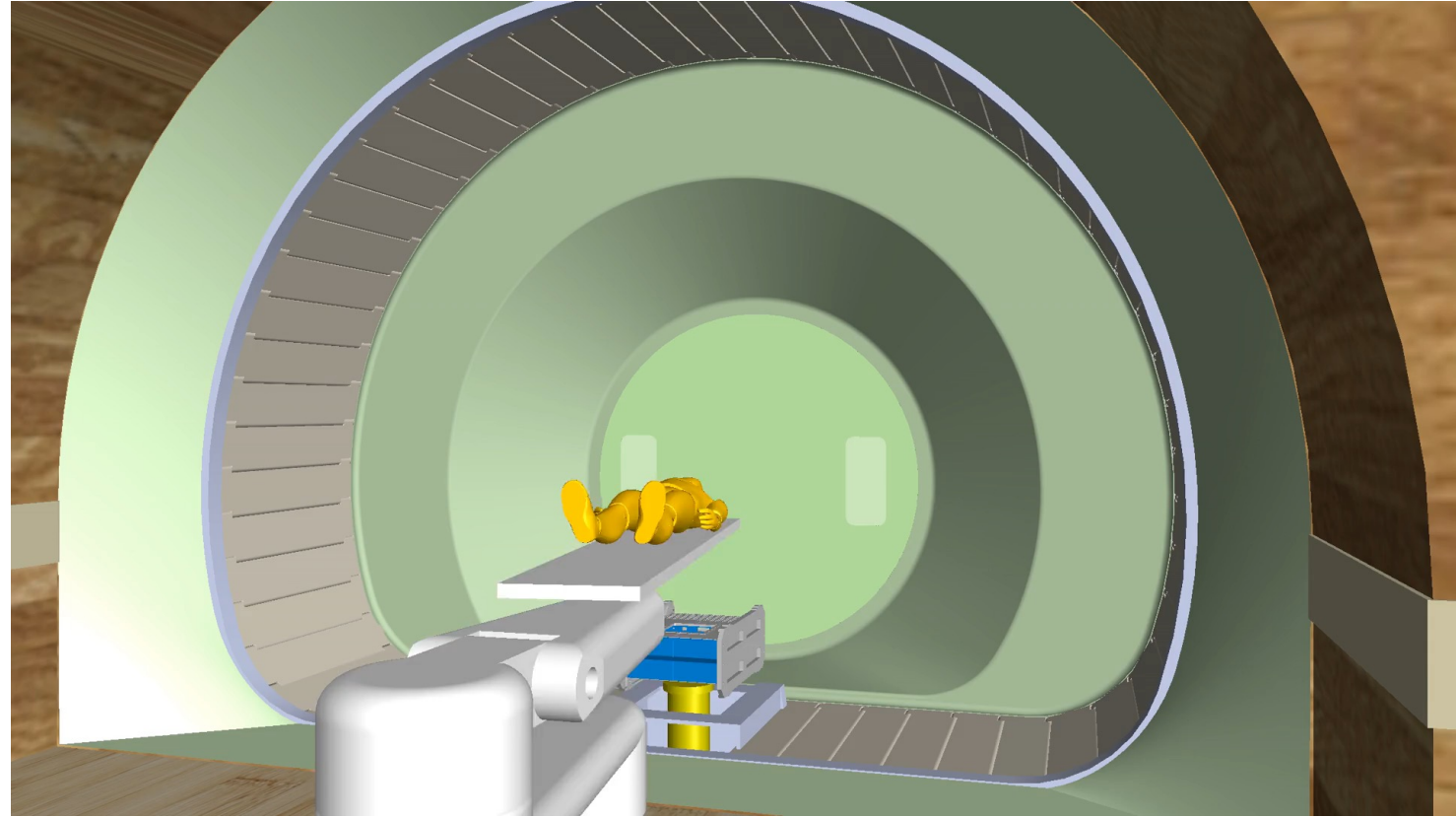
### METHODOLOGY



### RESULTS AND IMPACT



# Carbon ions gantry: a challenge

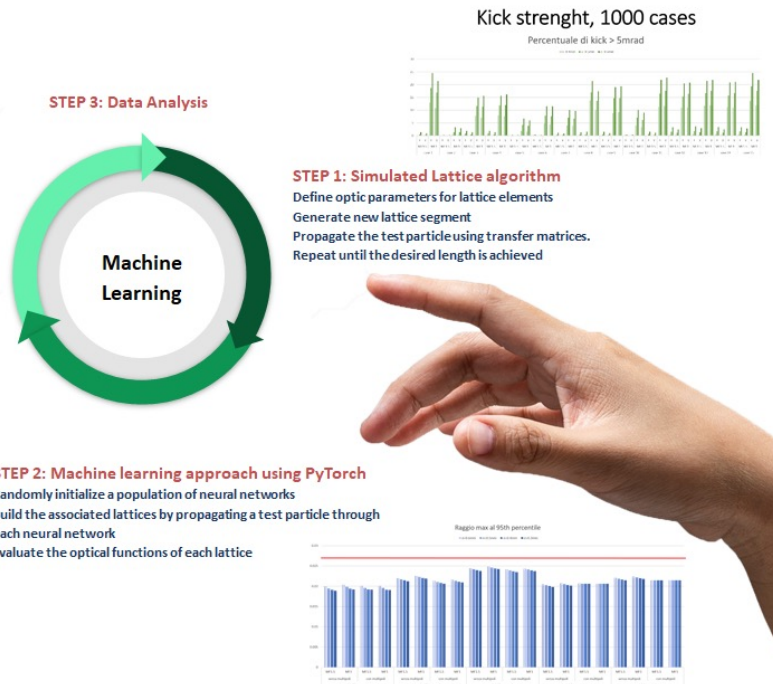
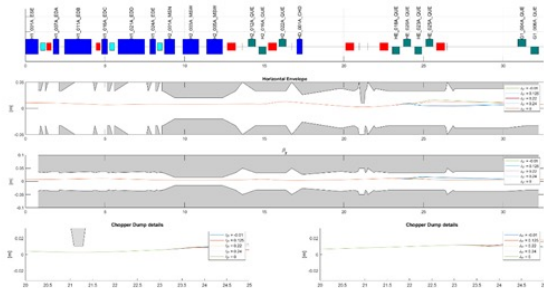
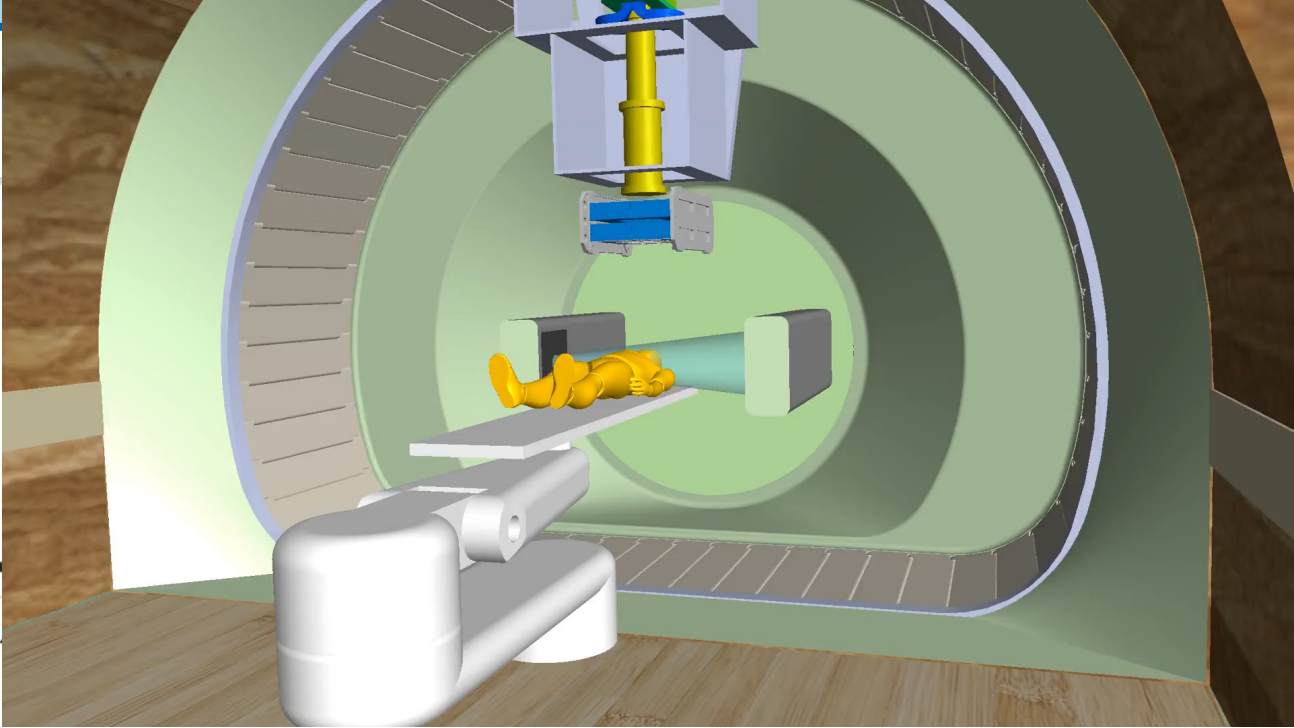
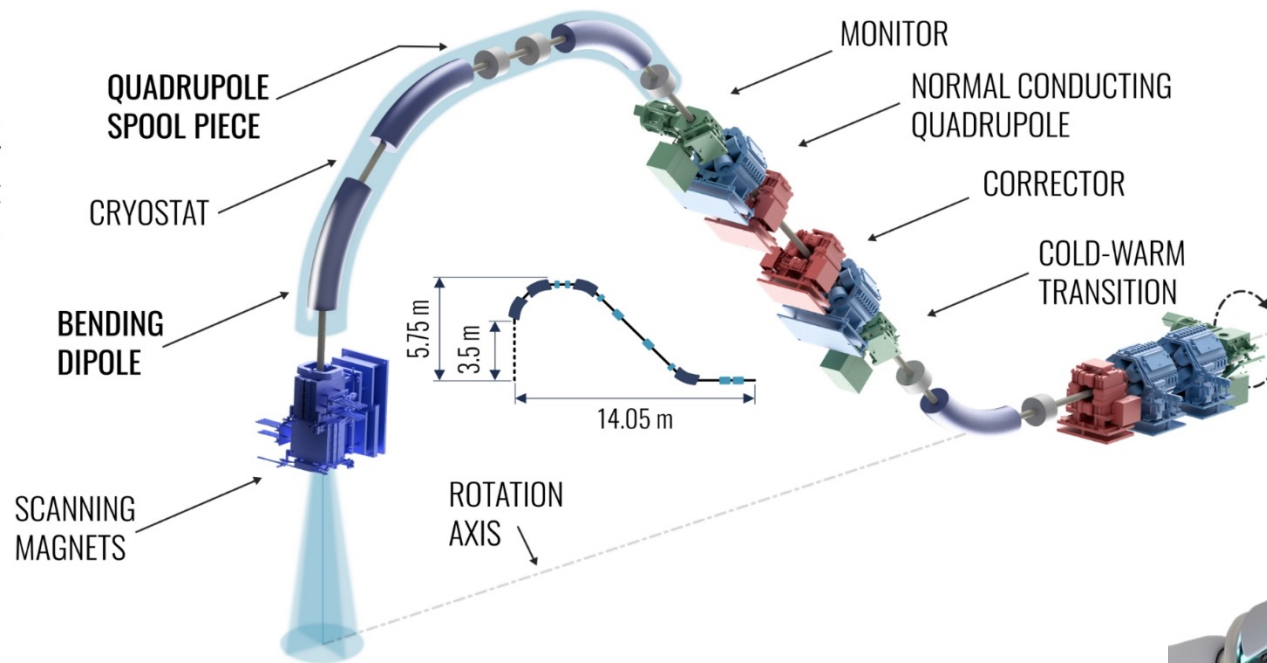


C-ions Gantries: radius 6...7 m - weight 350...670 tons

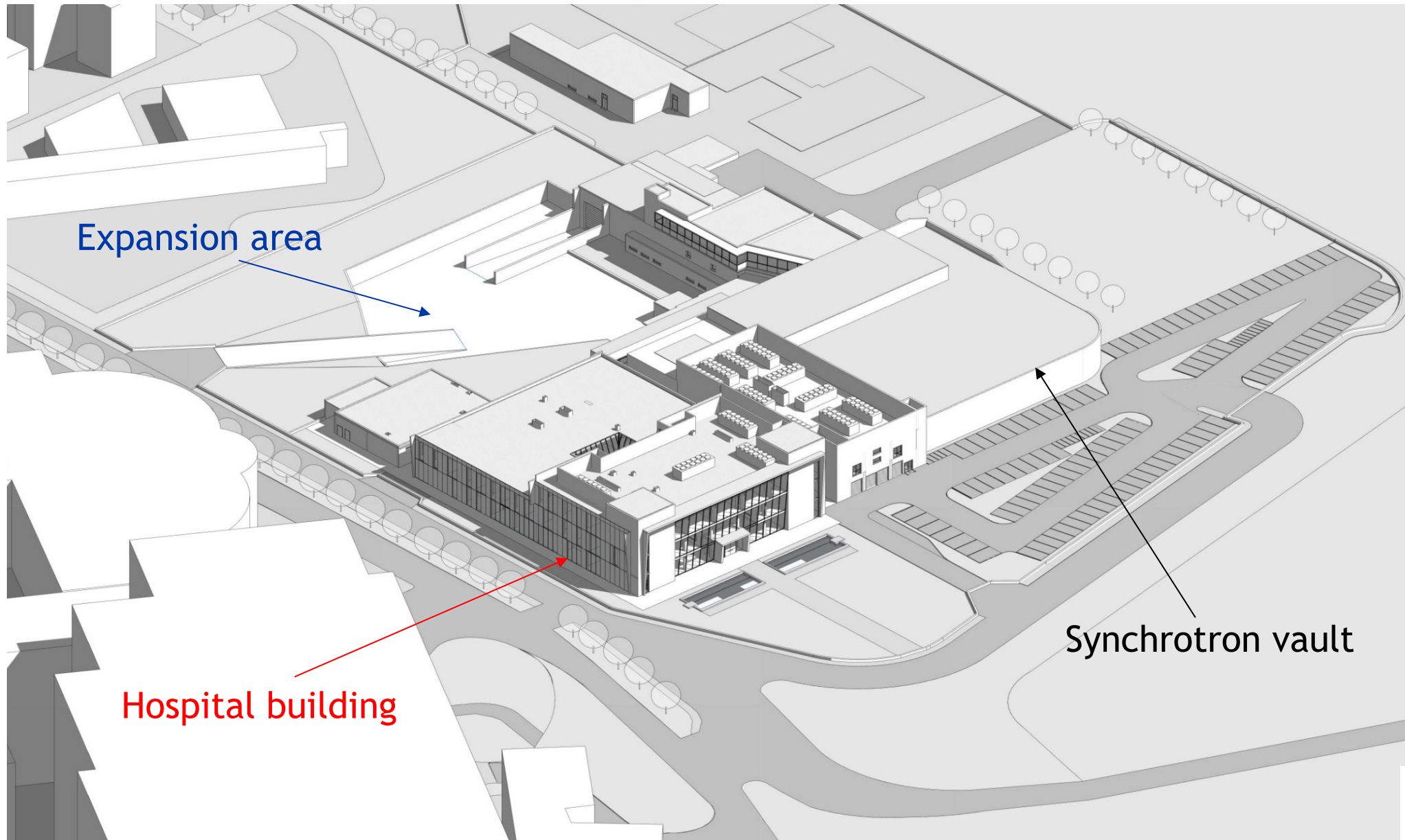
Only 3 operational worldwide: 1 Germany and 2 Japan



# EuroSIG: superconducting ion gantry

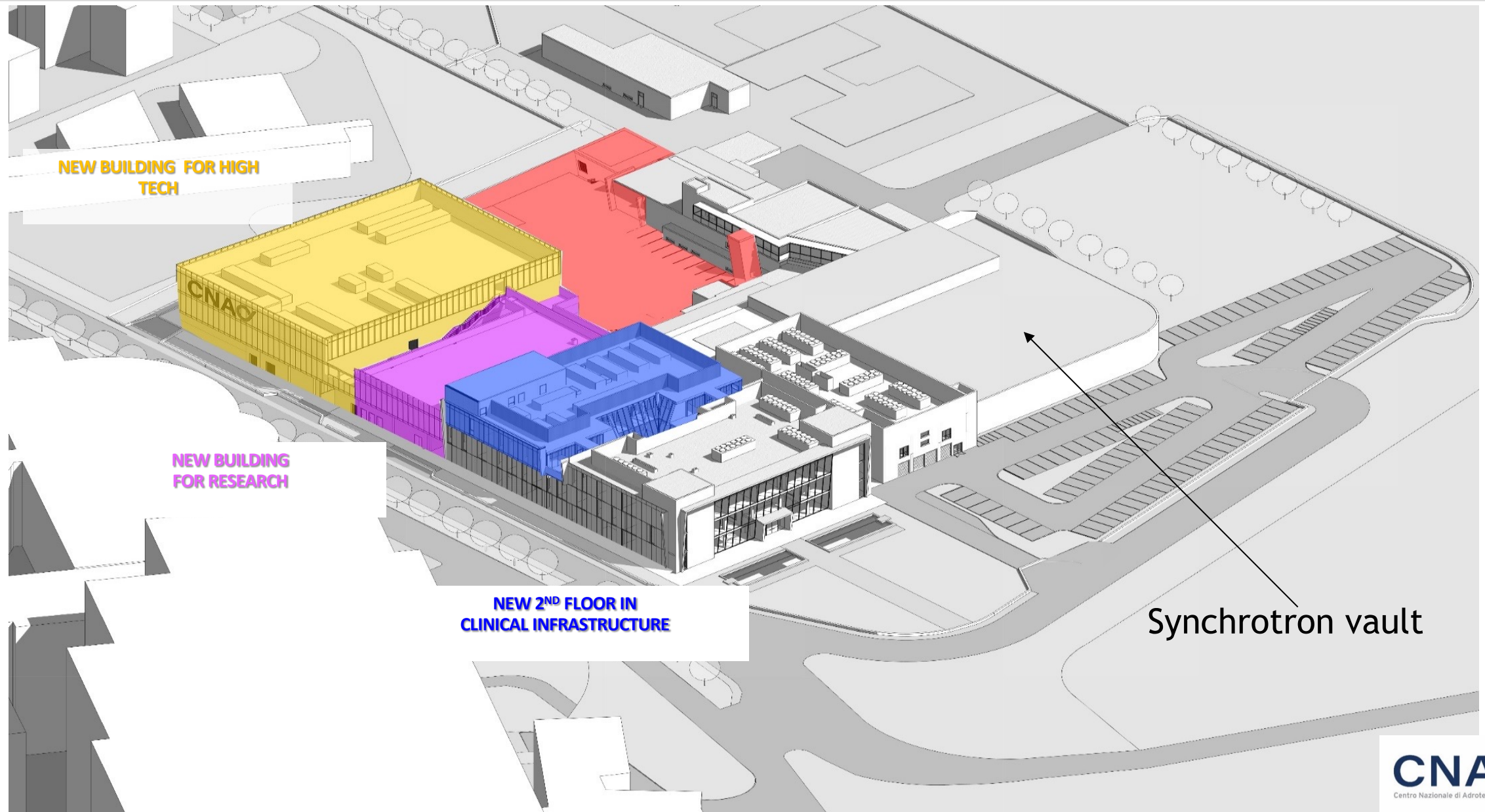


# CNAO Expansion Project: present layout

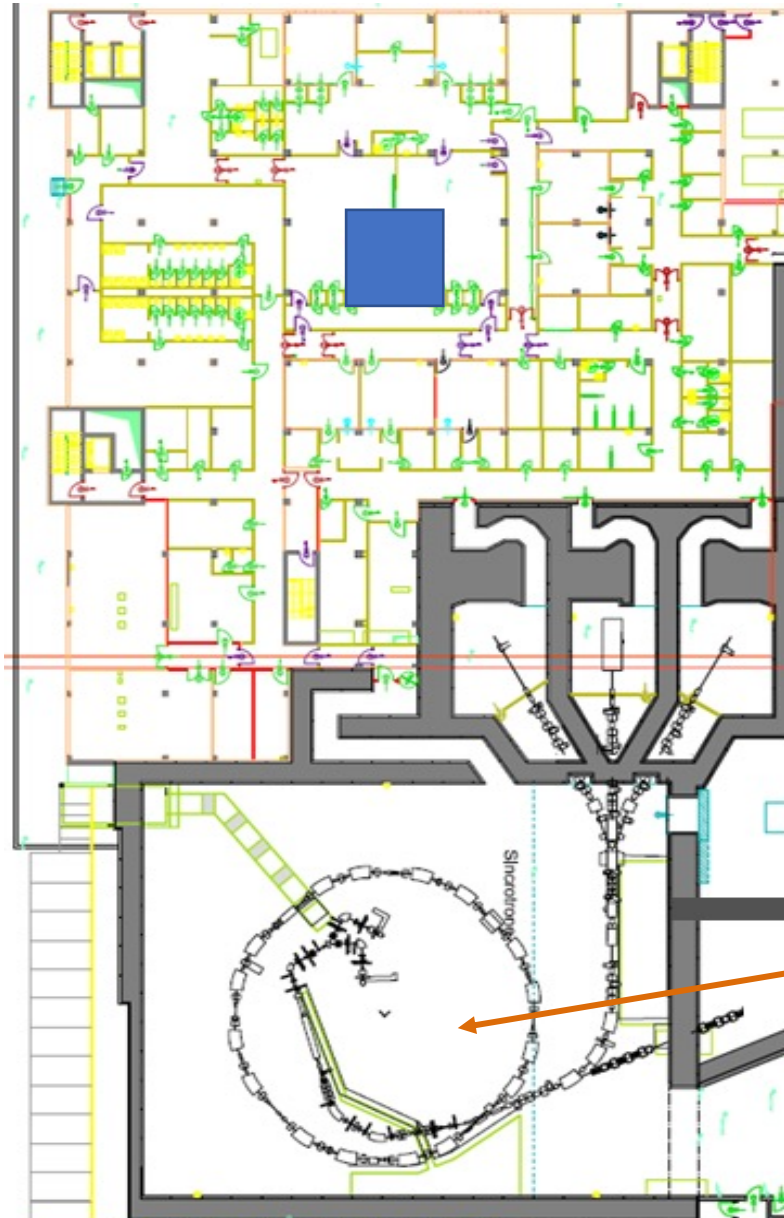




# CNAO Expansion Project: layout end 2024



## Level – 1: treatment area, experimental area and technical facilities



**Patient waiting area and services**

**3 Treatment rooms: 3H + 1V**

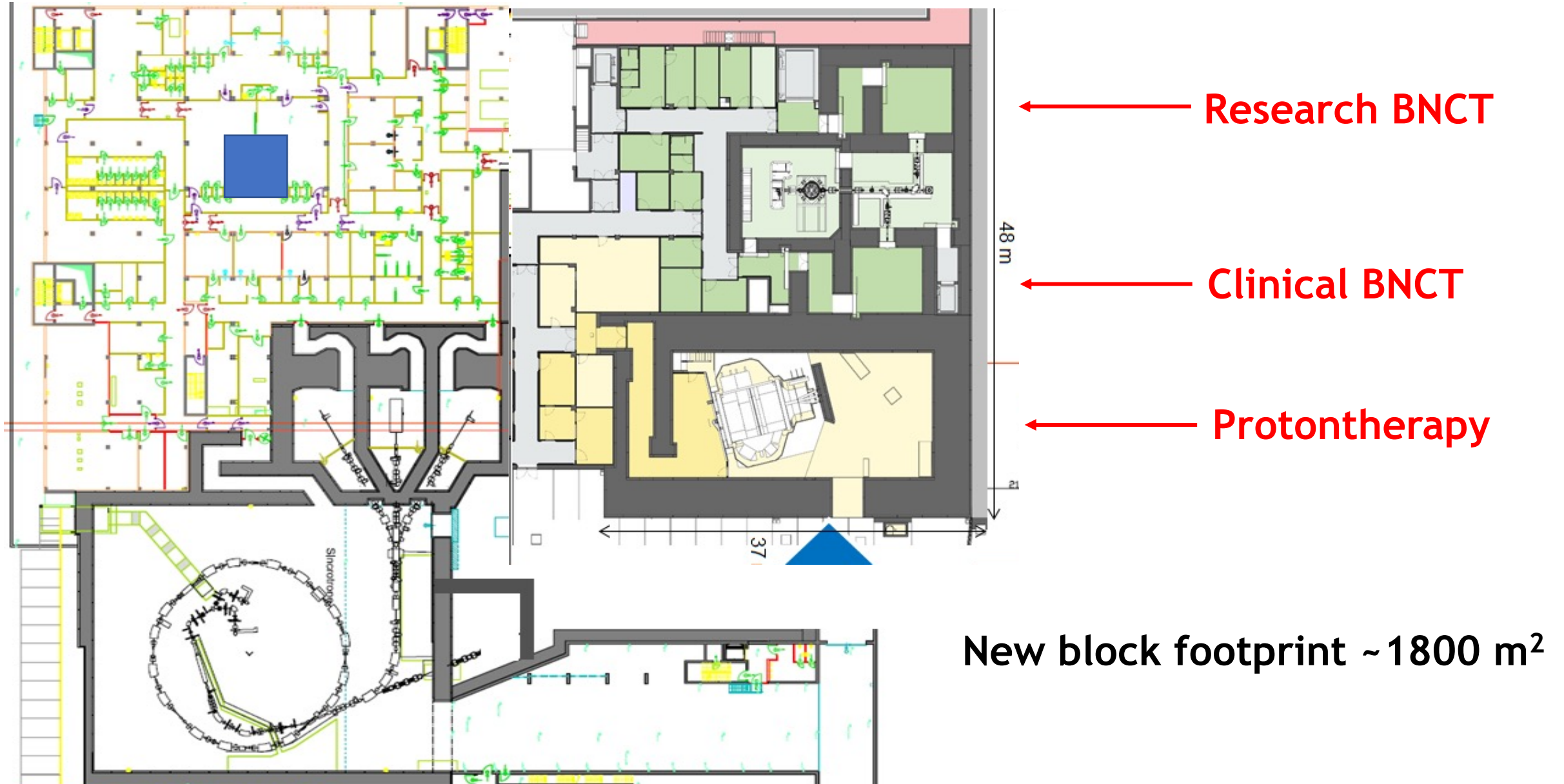
**Experimental room**

**Synchrotron vault**

**Main power supply room**



## NEW Level – 1: treatment area, experimental area and technical facilities





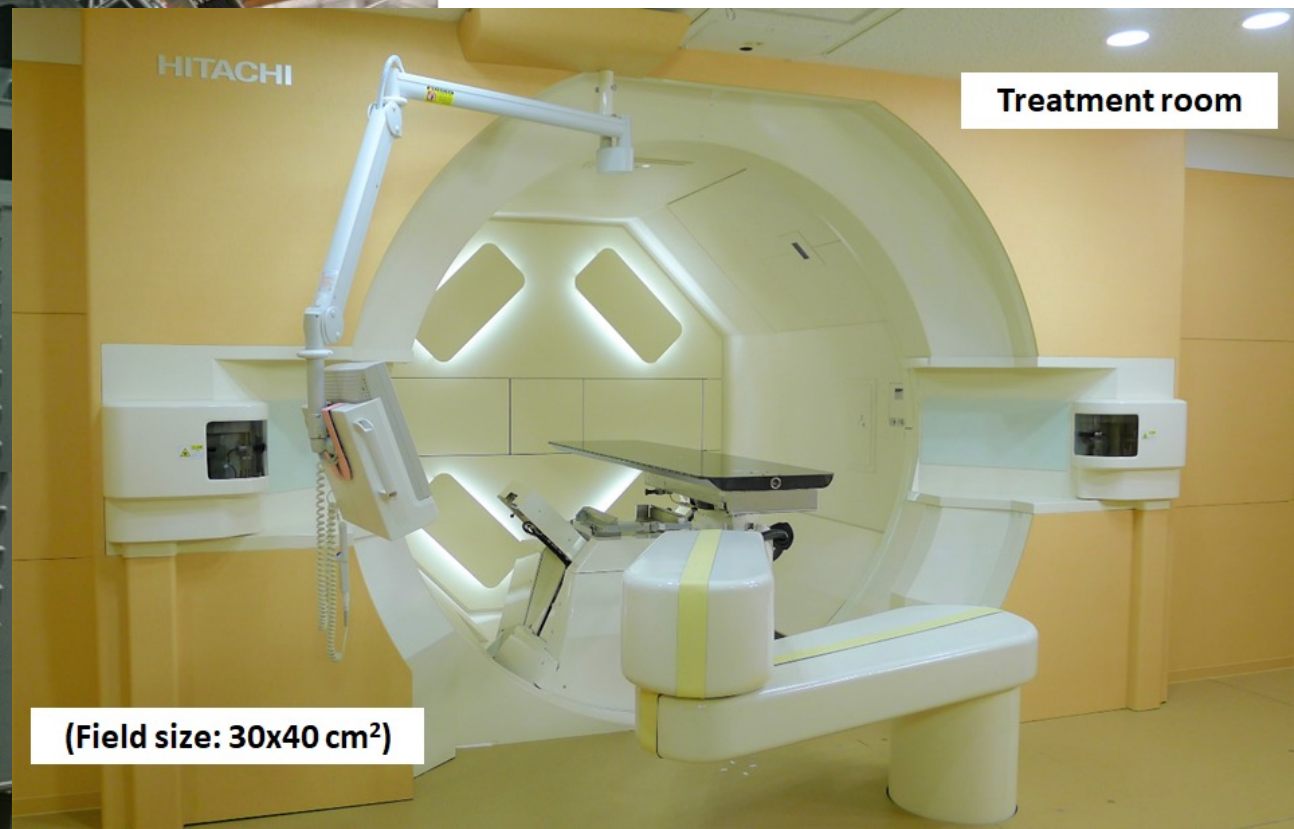
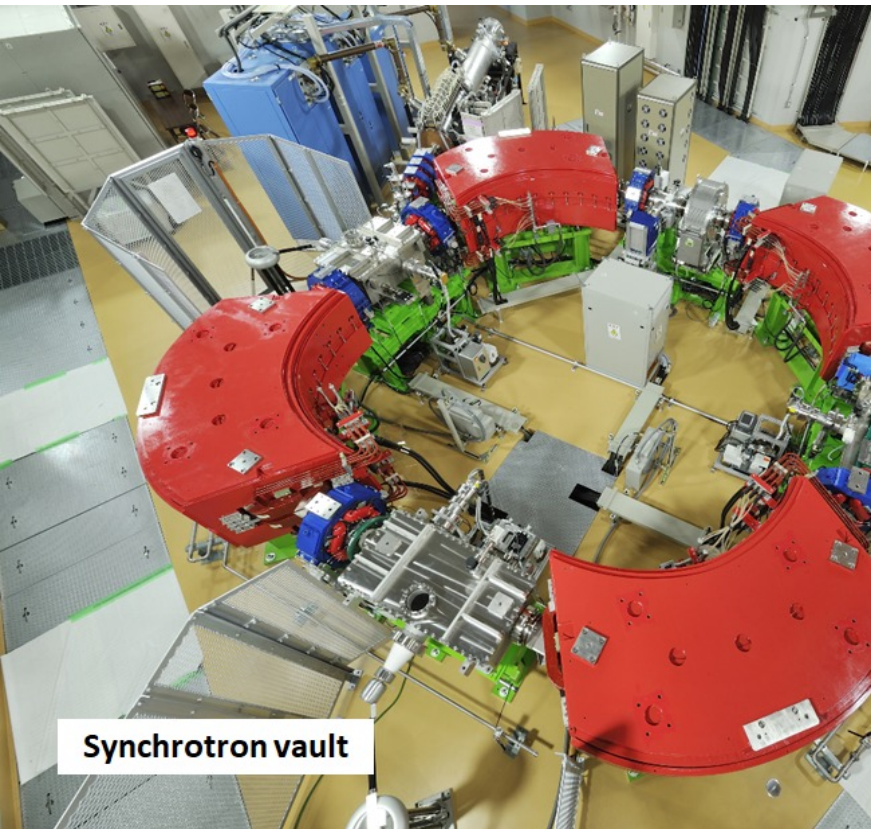


## Milestones:

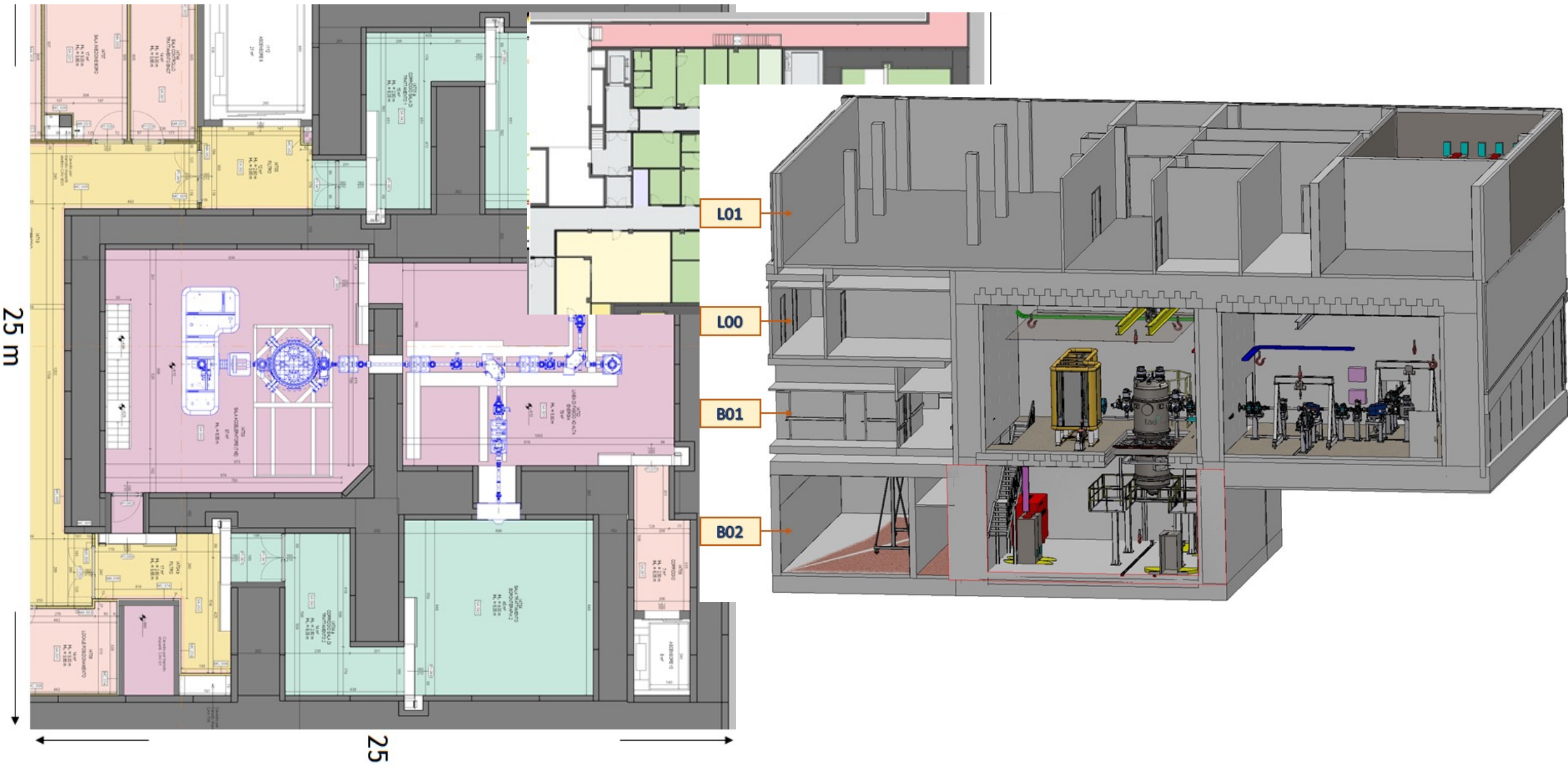
- ✓ Protontherapy installation starts middle 2024
- ✓ Building completed fall 2024
- ✓ BNCT installation starts fall 2024
- ✓ New technologies ready by fall 2025



## NEW Level – 1: HITACHI protontherapy



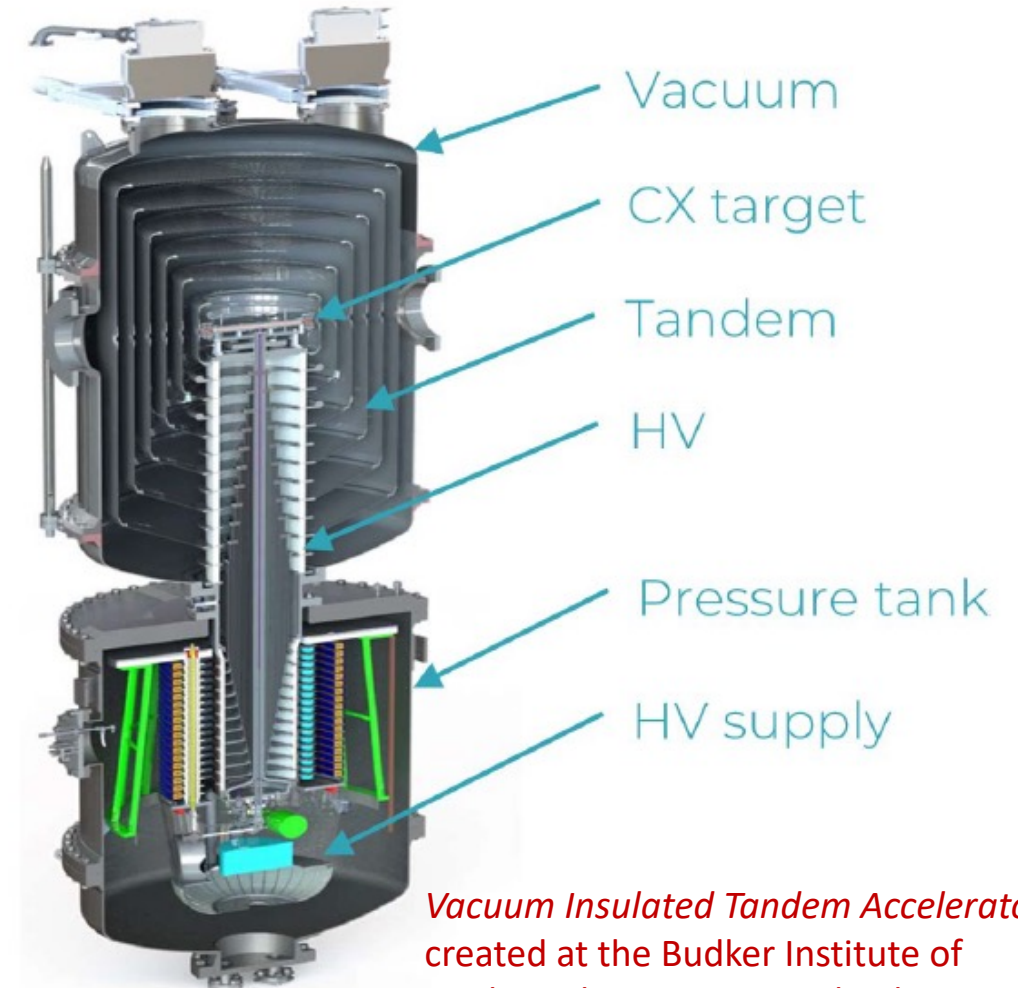
# NEW Level – 1: TLS - BNCT





## BNCT technology: tandem

The beam starts out as a negative hydrogen ion beam; we then pass it through the accelerator where we scrape the electrons off the hydrogen atom which makes it a proton beam and we accelerate it to the Mega Voltage energy range.

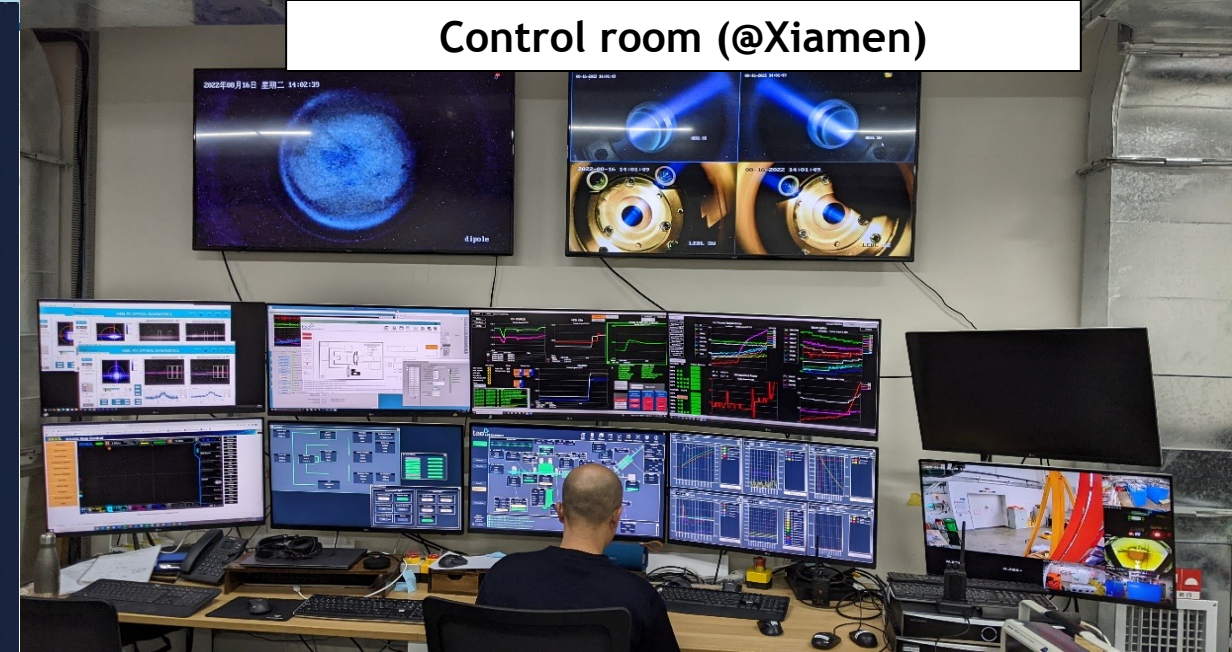


$$E_{\text{proton}} = 2.5 \text{ MeV}$$

Intensity = 10-15 mA - Lithium target

*Vacuum Insulated Tandem Accelerator  
created at the Budker Institute of  
Nuclear Physics in Novosibirsk, Russia*



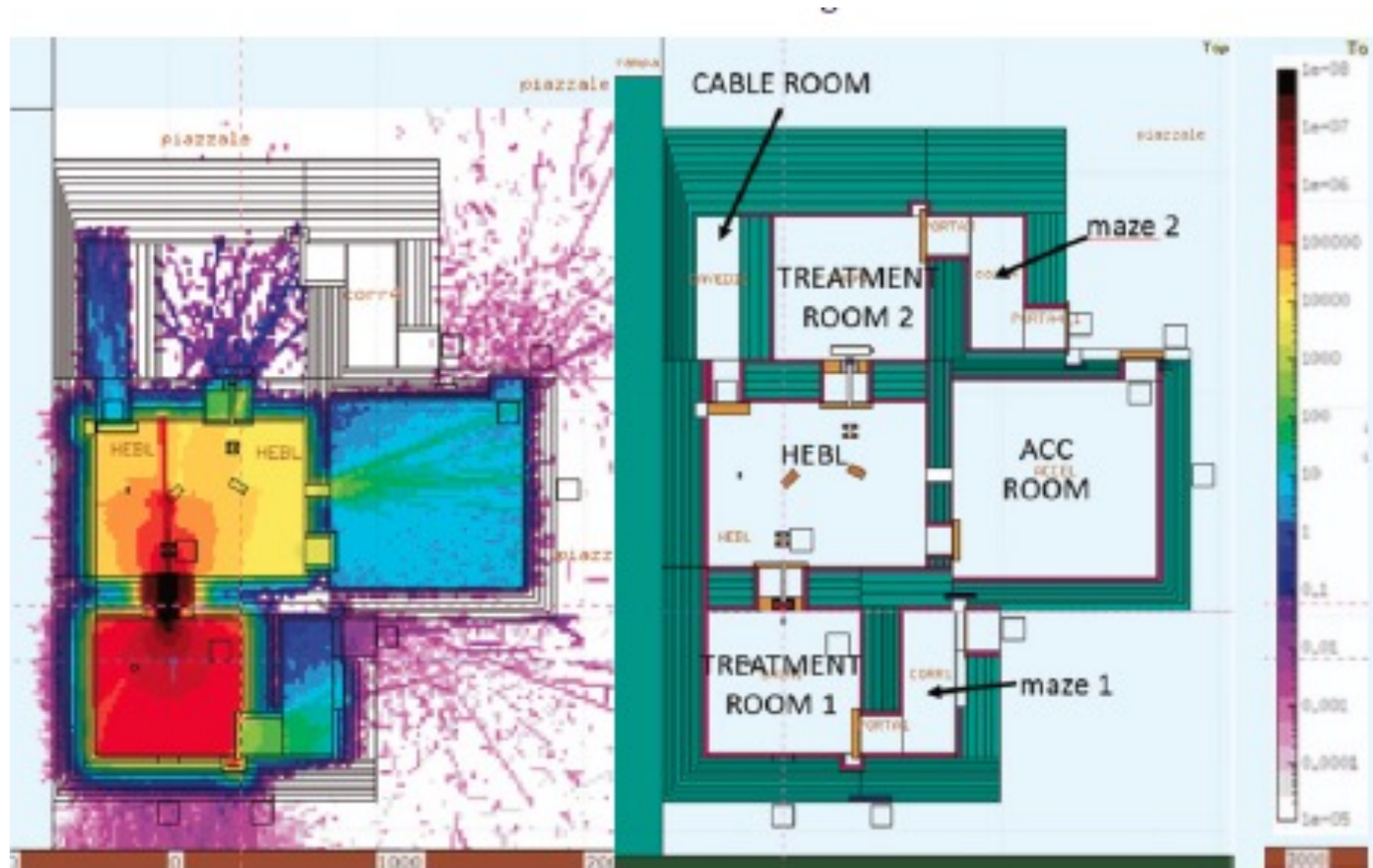


### Treatment room (@Xiamen)

**(Courtesy of TAE Life Sciences)**



# Radioprotection studies and authorization procedures



**CNAO**  
Centro Nazionale di Adroterapia Oncologica

## Valutazioni di radioprotezione sugli impianti del CNAO

Redatte ai sensi dell'All. XIV del D.Lgs 101/20 e  
s.m.i.

Pavia, 1 Marzo 2022  
Prot. 102

Relazione redatta dall'Esperto di Radioprotezione e acquisita e sottoscritta  
dal Direttore Generale ai sensi dell'art 109 comma II del D.Lgs 101/20

Ing. Michele Ferrarini  
Esperto di Radioprotezione  
III grado - n°30546

Dott. Sandro Rossi  
Direttore Generale

(Collaboration with  
S. Agosteo - PoliMi)

# The “White Book”



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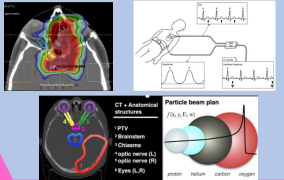
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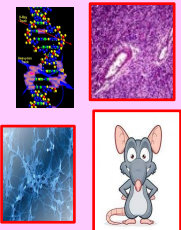
# FORMATION: PhD on risk and complexity in High Tech Medical Innovation

## BIOMEDICAL AREA

### Medical Physics



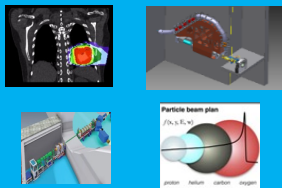
### Radiobiology



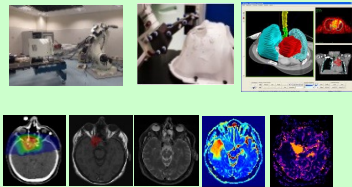
### Radioprotection



### Accelerator Physics

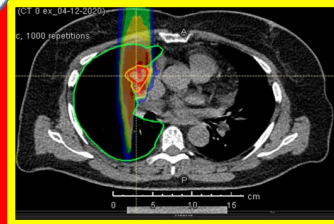


### Bioengineering

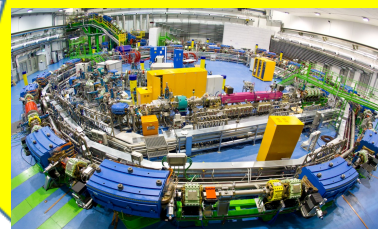


## TECNOLOGICAL AREA

### HADRONTHERAPY



### SYNCHROTRON



## HUMANITIES/SOCIAL AREA

### ETHICS



### COMPLEXITY



### LAW



### RISK



### INNOVATION



### Additional Training

- Informatics
- Linguistics
- Management of research and funding systems
- Valorization of results and intellectual property

New projects  
New particles  
BNCT  
Gantry



# FORMATION: PhD on risk and complexity in High Tech Medical Innovation

The PhD program cover a minimum of 3 years with a full-time commitment.

The educational path consists in both defining and carrying out a research project through advanced training activities, and individual in-depth analysis.

## Requirements:

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from the biomedical field (medical doctors, radiotherapists, medical physicists, biologists, biotechnologists),

from the technological field (physicists, engineers, data scientists),

from humanities and social areas (law, economy, philosophy, etc).

The Deadline to apply is: **June 2024**

The lessons start in **November 2024**



For Information : e-mail : [hadronacademy@cnao.it](mailto:hadronacademy@cnao.it)

# THANK YOU!



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