HITRI plus
Heavy Ion Therapy Research Integration

CNAO Accelerator system, research and upgrades

MARCO PULLIA

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548

Research at CNAO

Besides clinical activity, CNAO has also research as institutional purpose.

Many reasearch activities on technical, preclinical and translational subjects

Typical research subjects carried out at CNAO are aimed at improving treatment

- Improving the understanding of biological mechanisms
- Improving the knowledge of basic physical processes
- Improving the technical performance of the accelerator system
- Improving the technical performance of the dose delivery
- Providing new types of radiation (new weapons to the clinician)

Collaborations with many institutions

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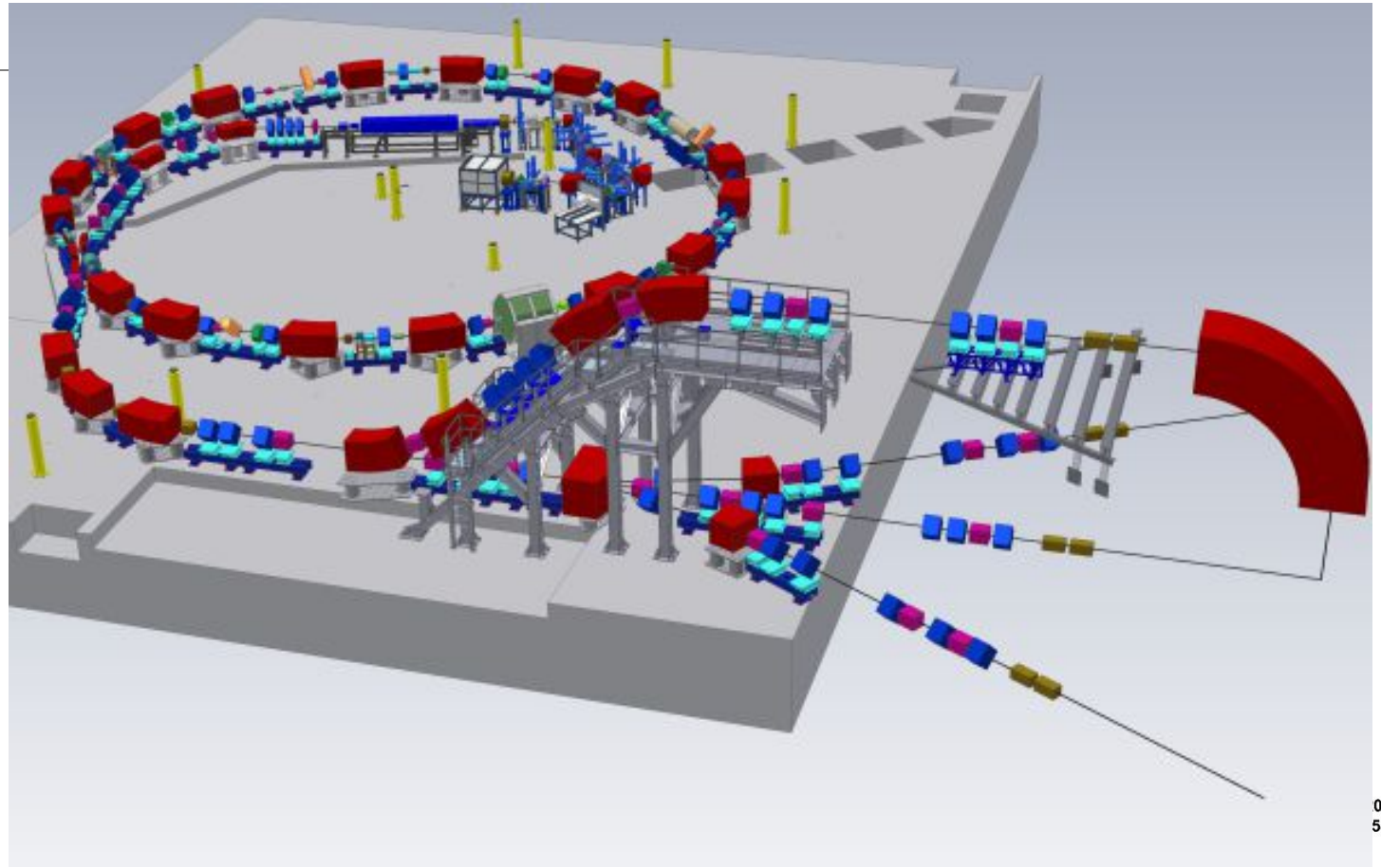
CNAO Accelerator system

7-250 MeV p
7-400 MeV/u C

3 treatment rooms
4 beamlines
for treatment



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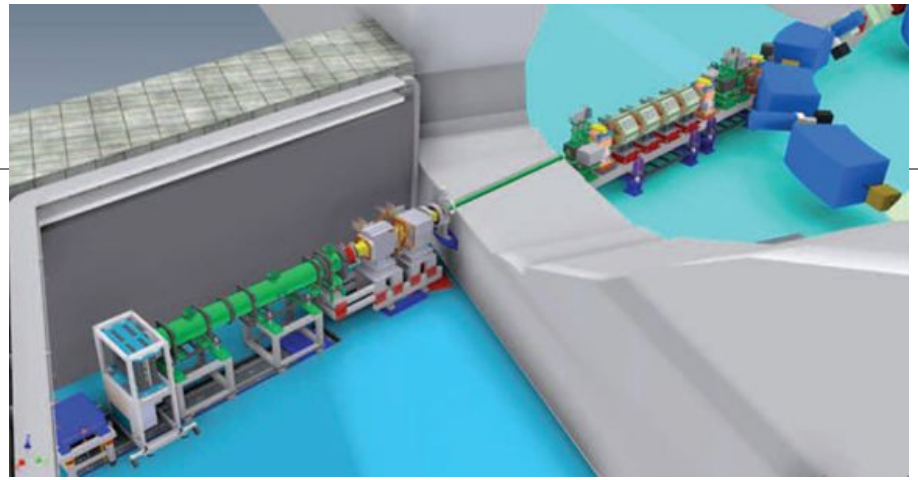
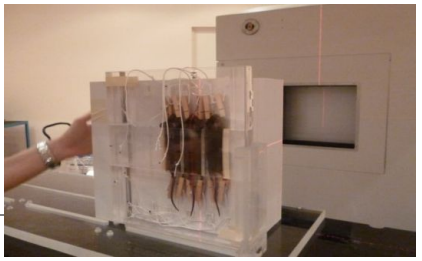
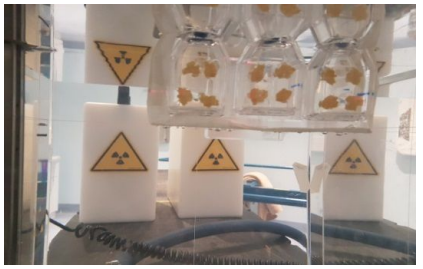
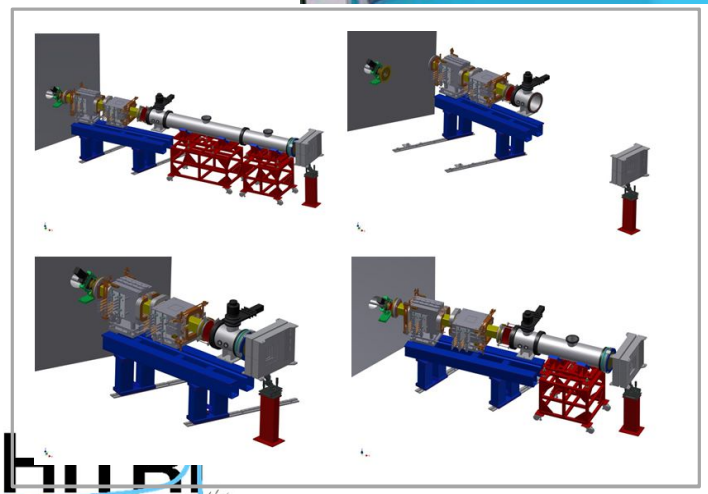
XPR









- Multiple configuration
- Accessible during treatment
- Experiments can be installed for many days
- DDS customization possible

Biological laboratory with all the necessary equipment to prepare and process cell samples is available on site.
Small animal irradiation is possible taking advantage of the nearby animal house facility of the University of Pavia

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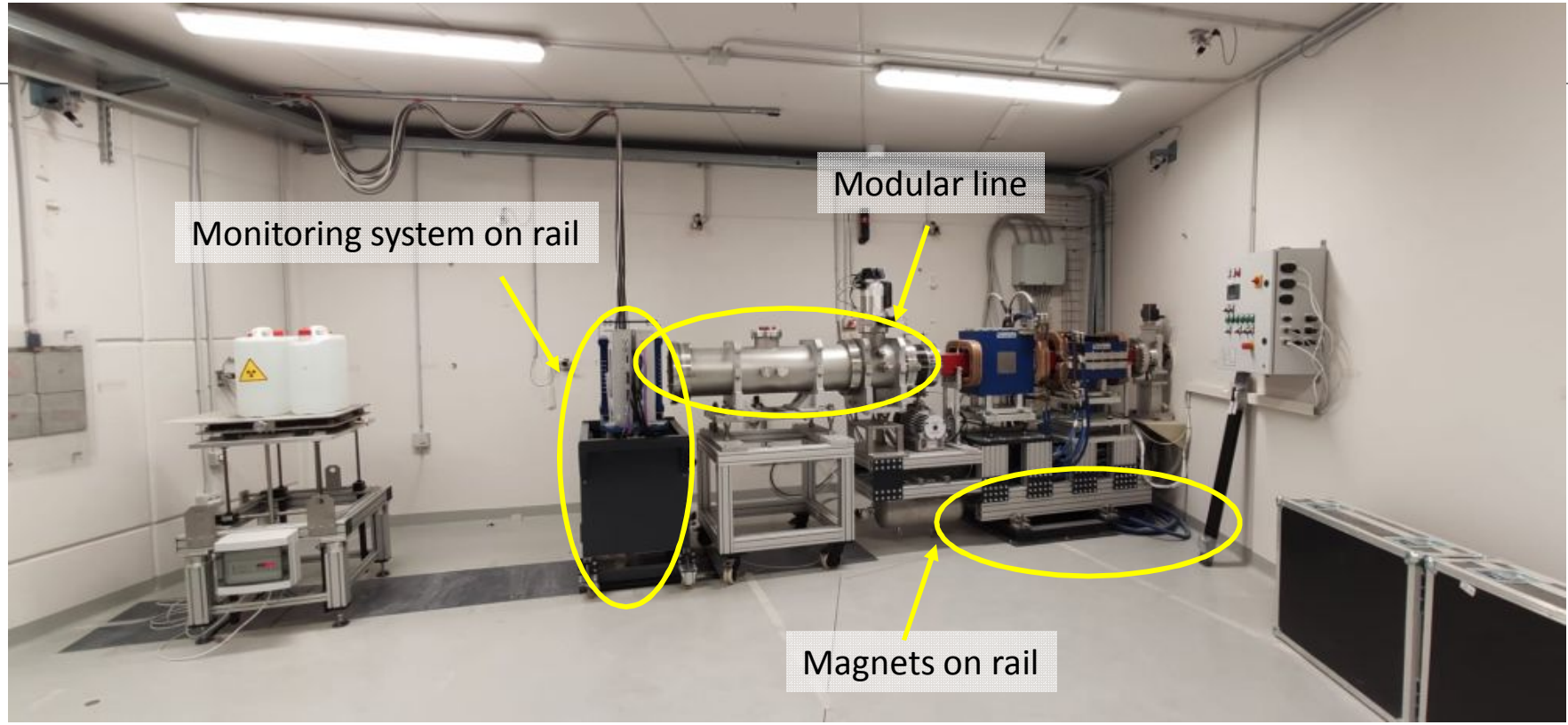
Experimental room open to external users



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Available beams

FWHM ~10 mm
(particle and energy dependent)

Irradiation field
< 200 x 200 mm^2
[iso4]

Max distance downstream target
< 5.5 m
[iso1]

Protons

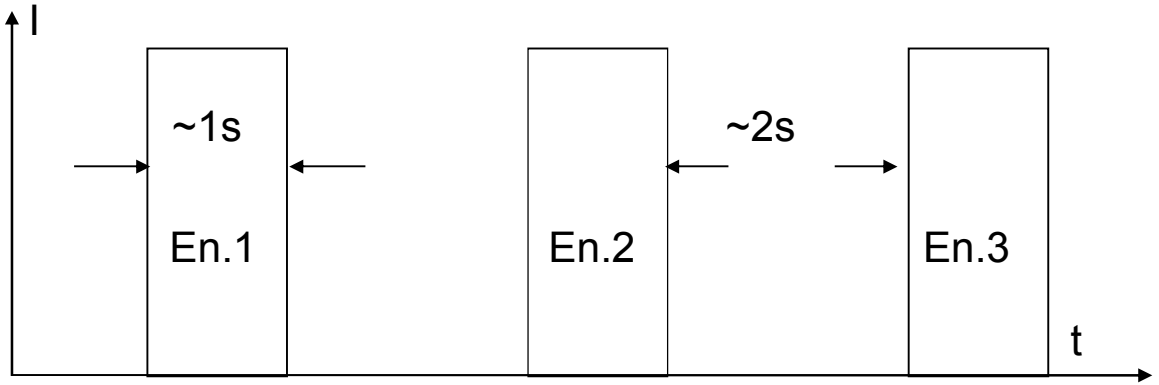
60-250 MeV

< 10^{10} p/spill

Carbon

120-400 MeV/u

< 4 x 10^8 C/spill



Low intensities (10^3 part/s) possible

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Research, development, upgrades

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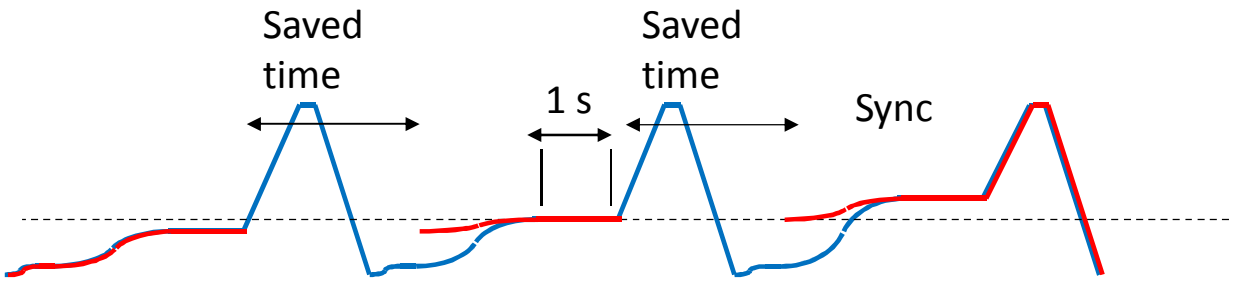
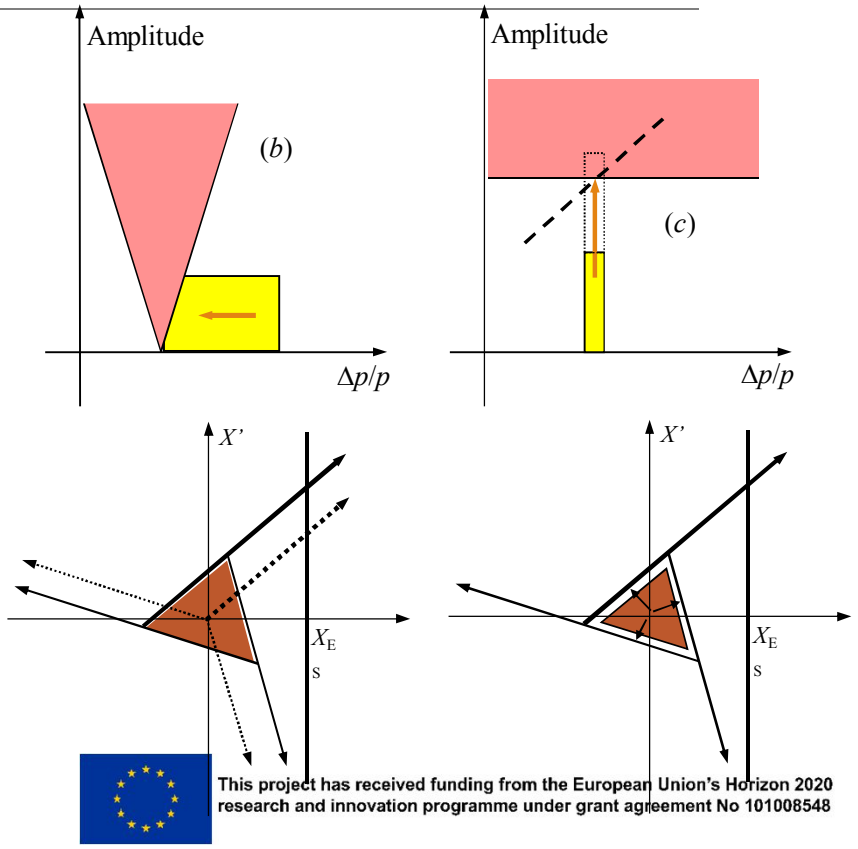
Research, development, upgrades

We have already seen RFKO and Multi Energy Extraction on Tuesday



Amplitude-momentum selection

RF-KO



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Range verification

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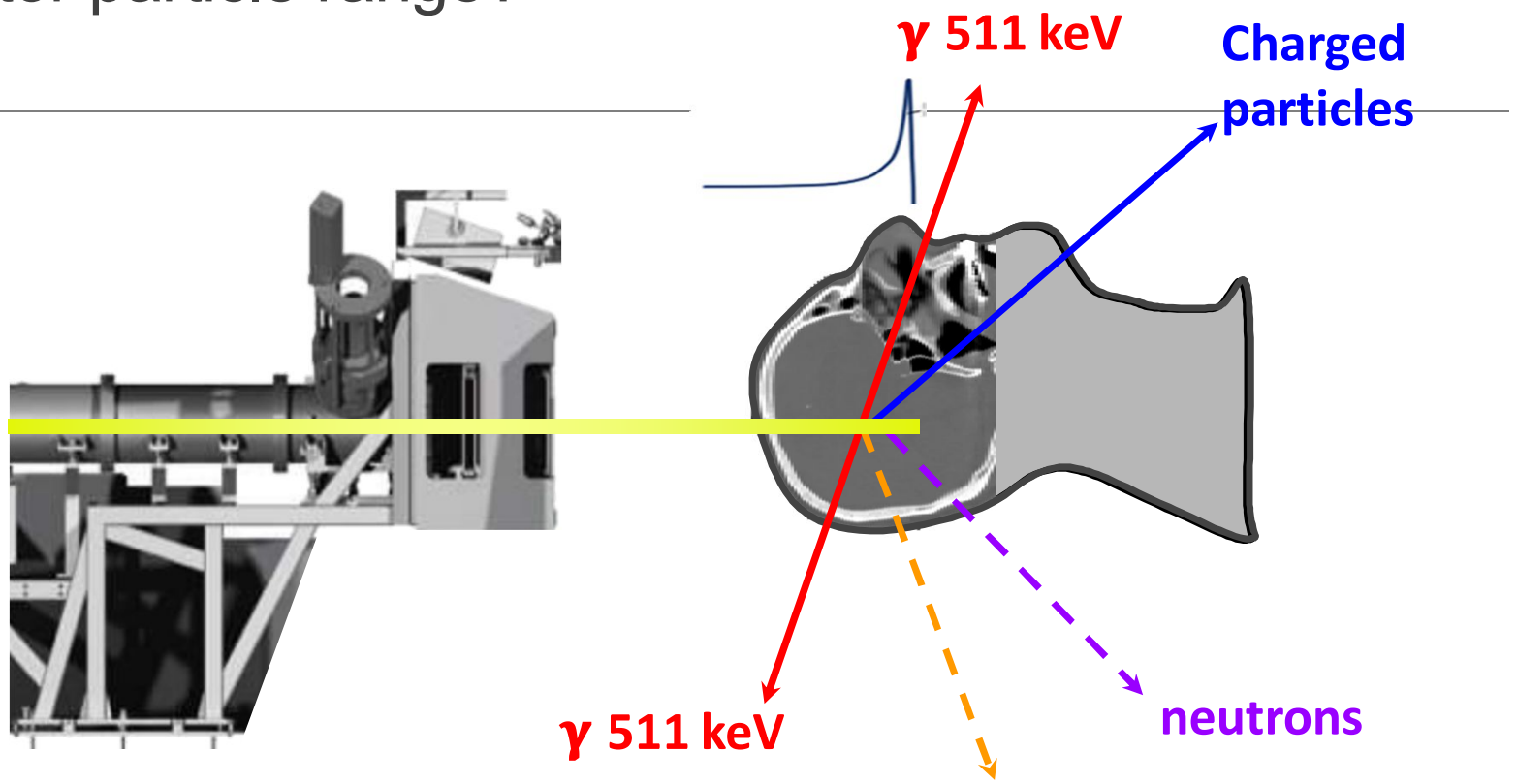
Range monitoring

How to monitor particle range?



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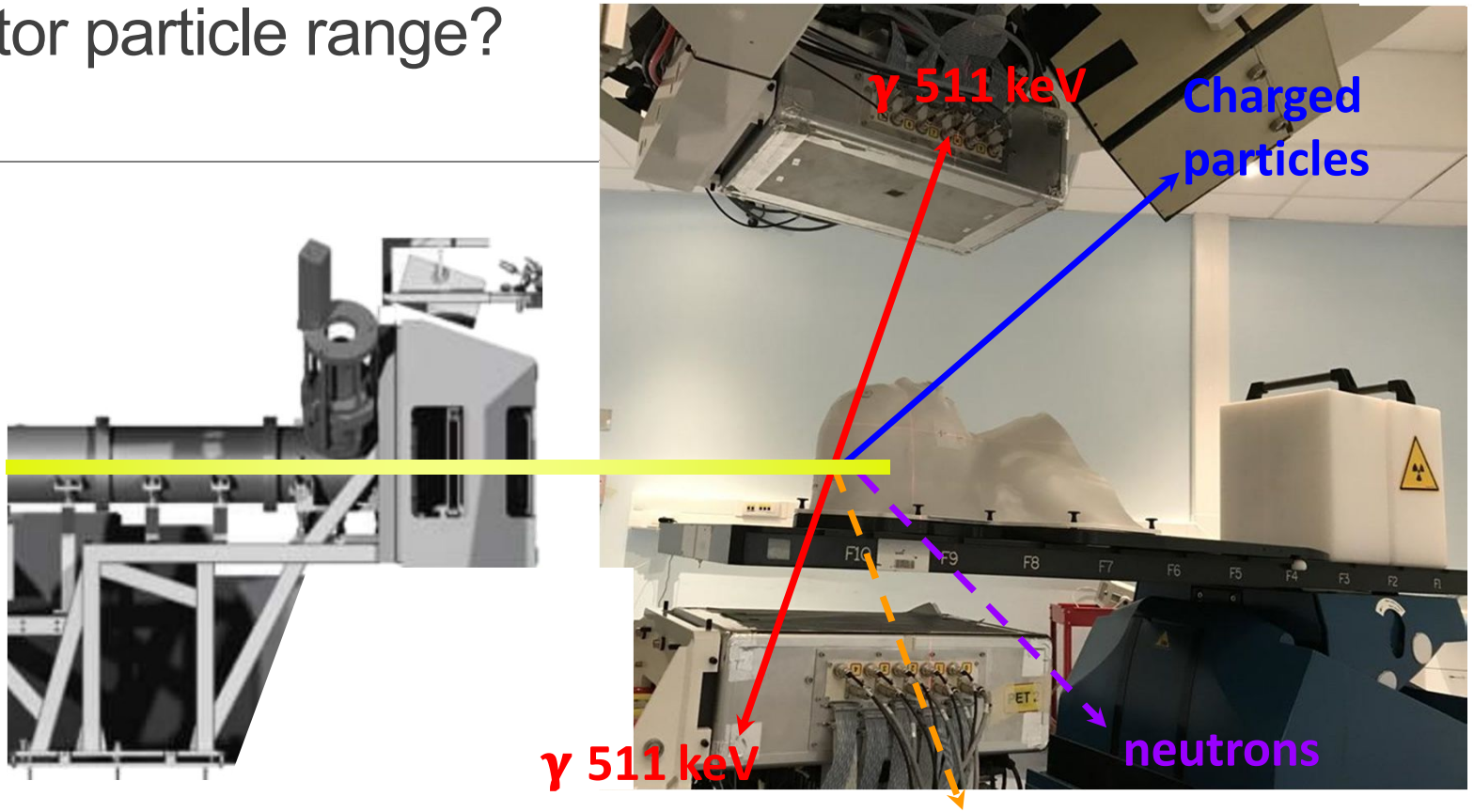
How to monitor particle range?



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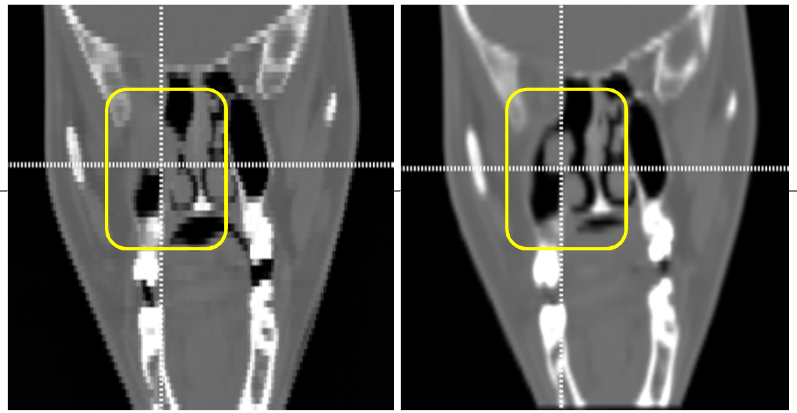
In beam PET



Patient ID: 006P: female, 39y, affected by ACC, treated with IMPT

dose released to CTV: 70 GyE in 35 fx (2.0 GyE/fx, 5 fx/week), two beams (15° - 175° IEC) // beam at 175° IEC monitored with INSIDE in-beam PET

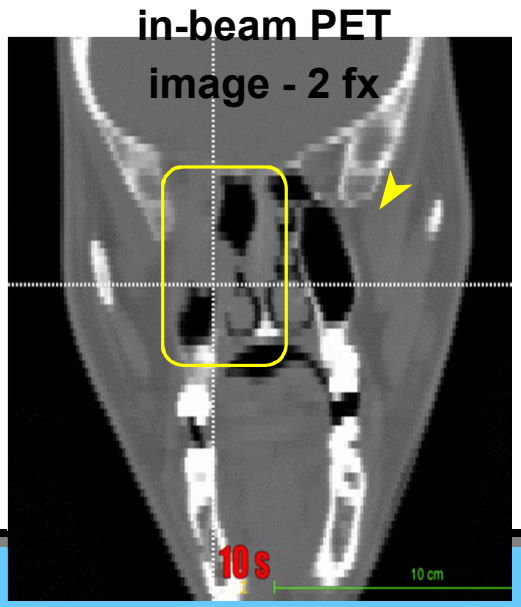
NOT REPLANNED

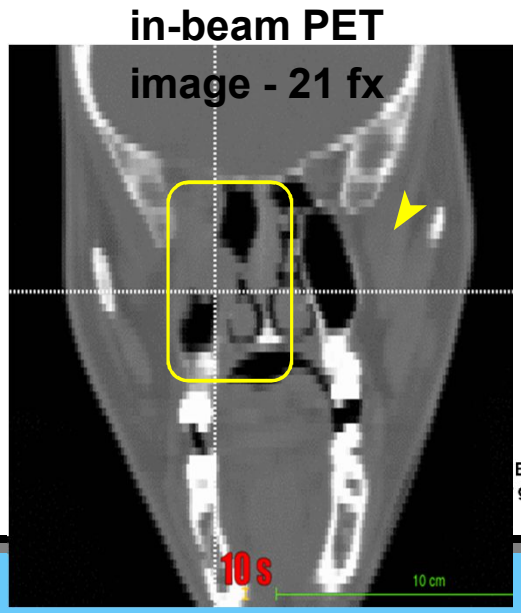
online in-vivo treatment verification

10 patients treated with carbon ions

9 patients treated with protons

sensitivity study and morphological changes detection





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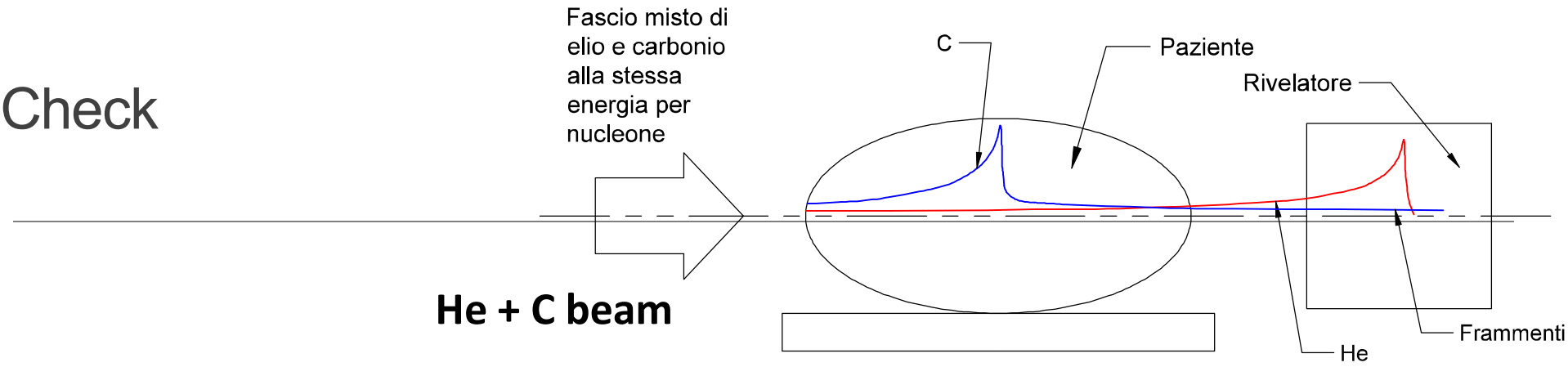
CLINICAL TRIAL

European Union's Horizon 2020 grant agreement No 101008548

HeCheck



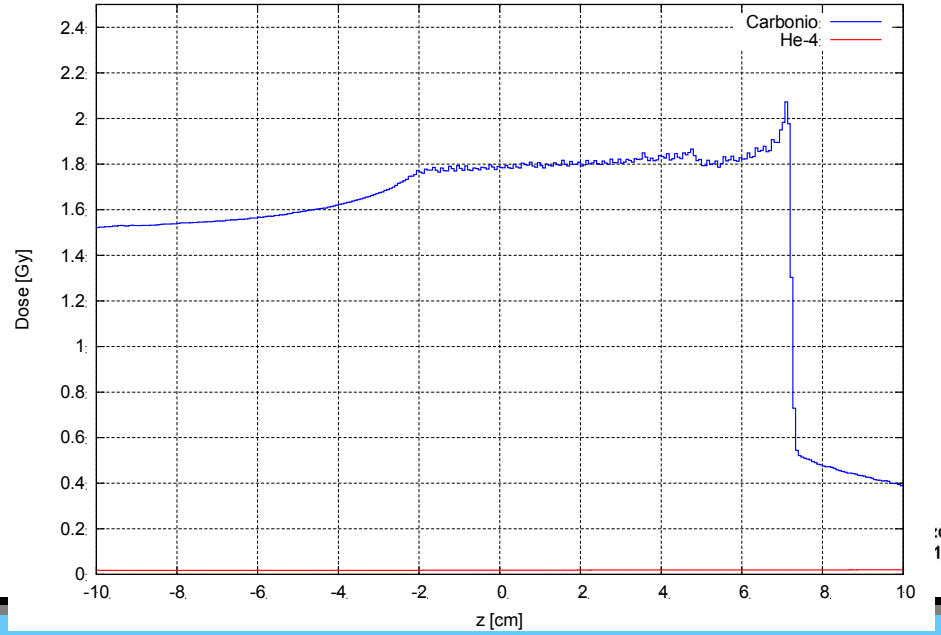
He + C beam

Proof of principle

He 10% in number wrt C

1% in dose

(C^{6+} source needed)



https://doi.org/10.1002/mp.13219

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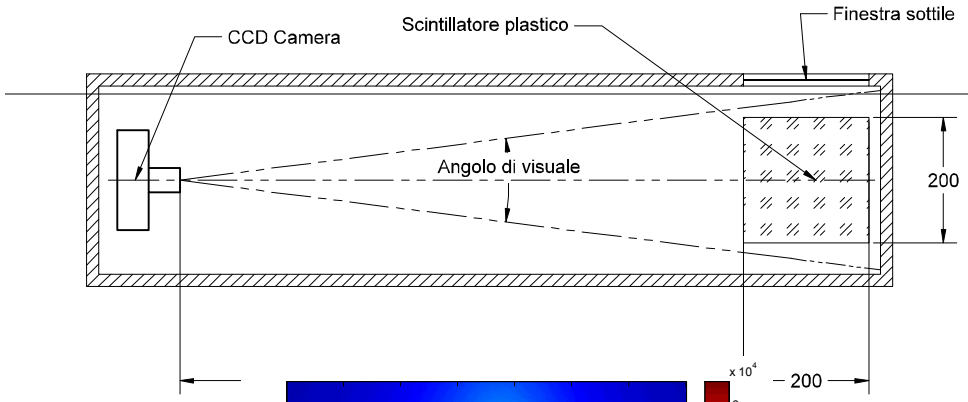
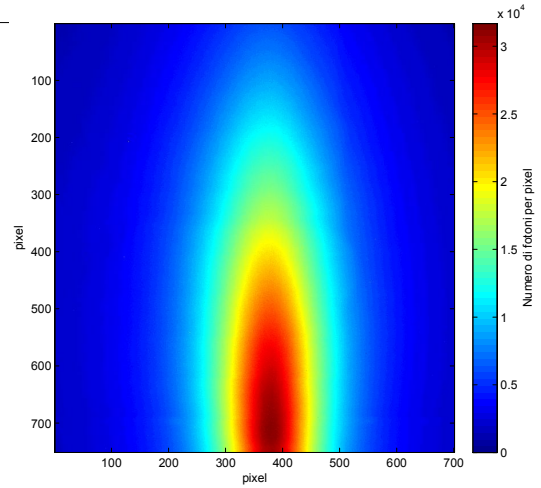
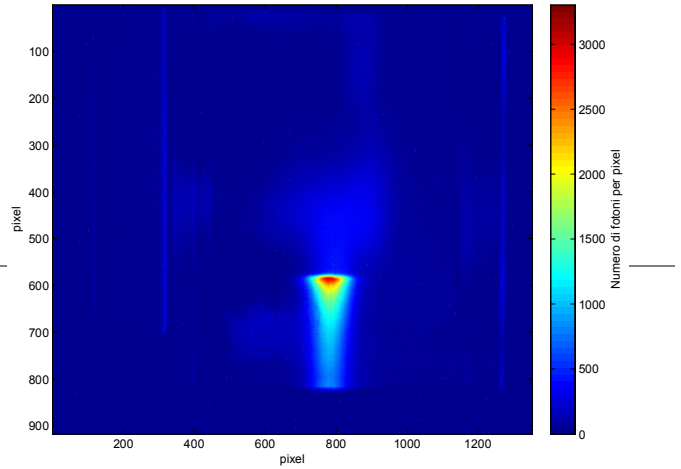
HeCheck

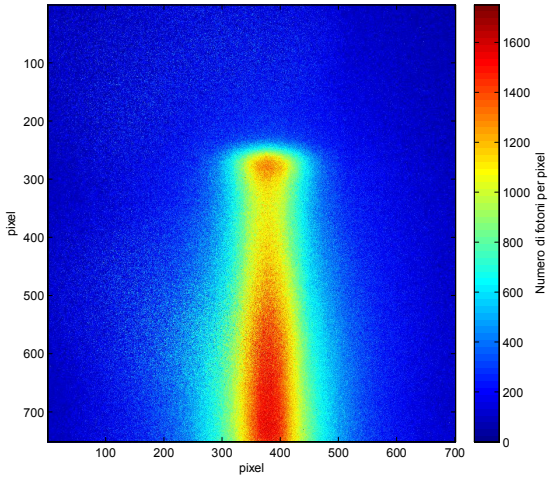




Fragments from 5x10^7 C ions at 280 MeV/u.



Protons, 81 MeV, 5x10^5 particles.



Protons (5x10^5) and carbon (5x10^6)

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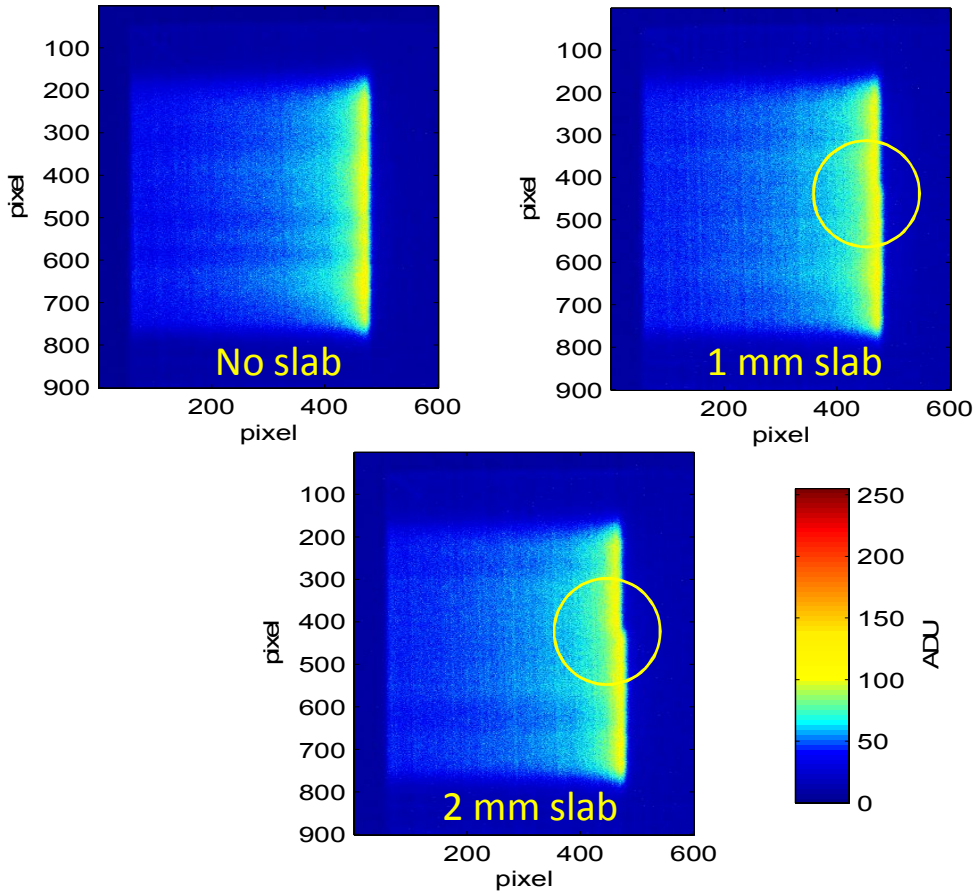
HeCheck

Resolution < 1 mm

Posizione n°	Range misurato senza slab [mm]	Range misurato con slab da 1mm [mm]	Range misurato con slab da 2mm [mm]
1.	100.524	99.244	98.732
2.	100.524	99.244	98.476
3.	100.524	99.500	98.732
4.	100.524	99.244	98.732
5.	100.524	99.500	98.732
6.	100.524	99.500	98.732
7.	100.524	100.268	100.268
8.	100.524	100.268	100.780
9.	100.524	100.524	100.780
10.	100.524	100.268	100.780
11.	100.524	100.524	100.780
12.	100.524	100.268	100.780
13.	100.524	100.524	100.524
14.	100.524	100.268	100.524
15.	100.268	100.012	100.524



Heavy Ion Therapy Research Integration

research and innovation programme under grant agreement No 101008548

Improved and new treatments

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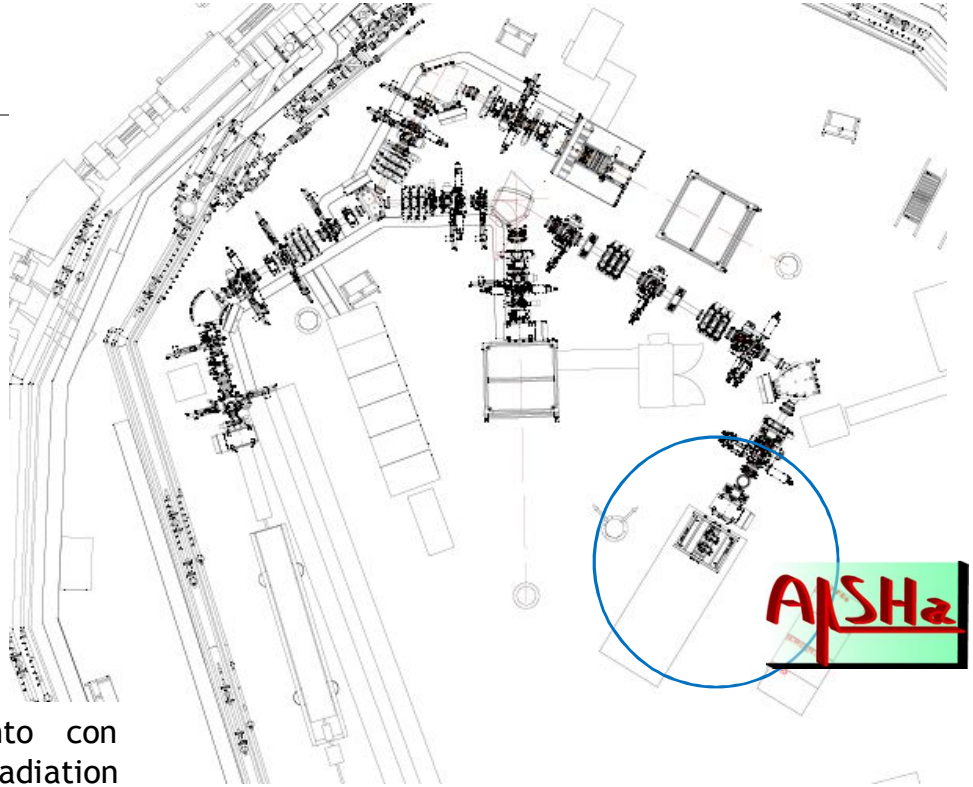
3rd Source – new ions - INSPIRIT

Several upgrades to CNAO machine:

- Revamping of critical components in order to speed some normal machine operations
- Revamping of critical components to increase machine reliability
- Upgrade of the radiobiology laboratory
- **New source** for Helium, Litium, Oxygen and Iron for new clinical protocols (He, O, Li) and biological or material experiments.

Opens path to
Multi ion treatments, LET painting, killing painting, …



A facility INnovativa di irraggiamento con Sorgente per Ioni per Ricerca e studi di radiation hardness con applicazioni IndusTriali e cliniche INSpIRIT – ID 1161908
Call HUB ricerca e Innovazione - EU/Regional funds

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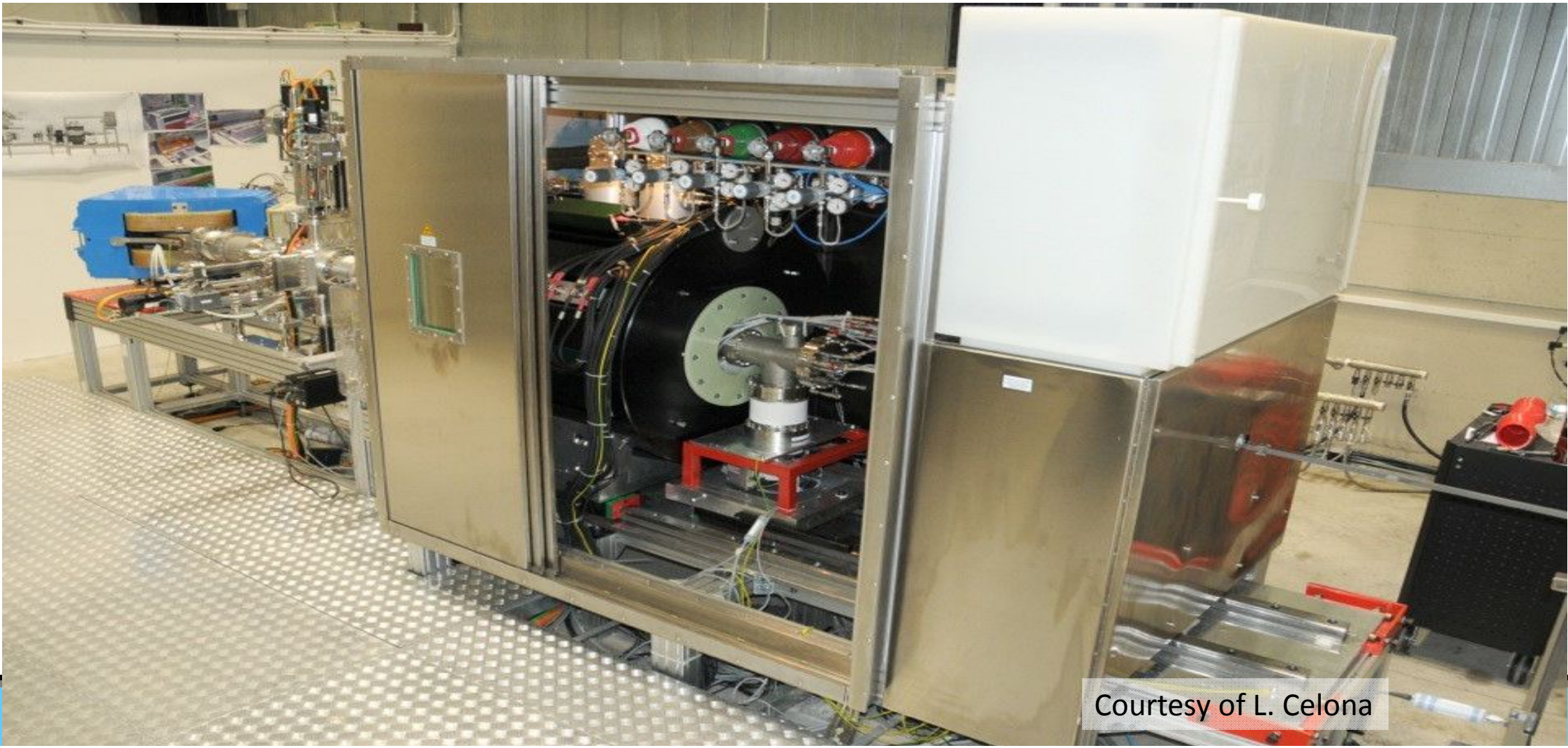
AISHA at LNS



Courtesy of L. Celona

Improved DDS

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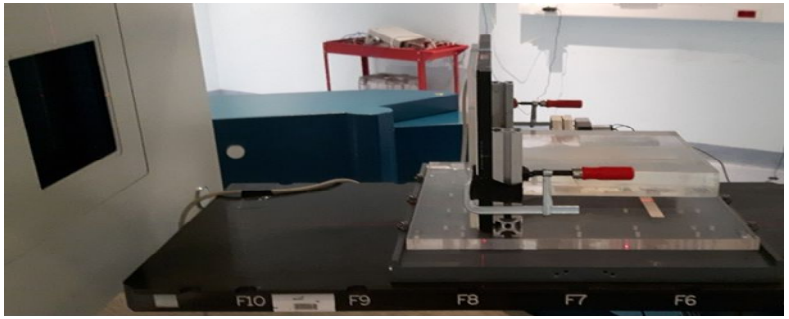
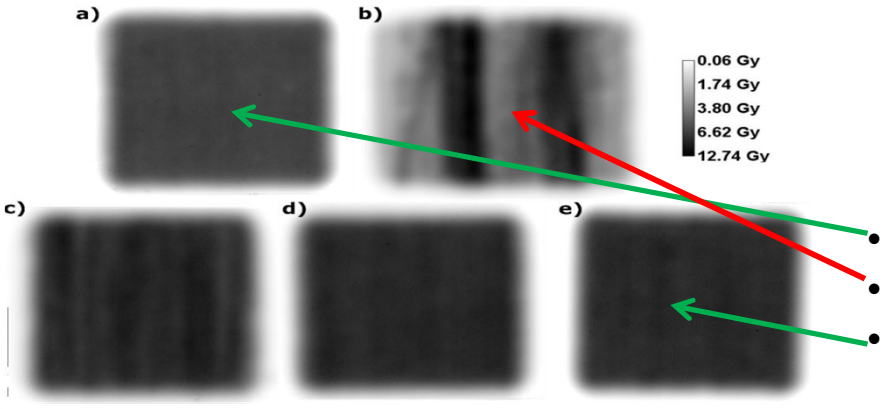
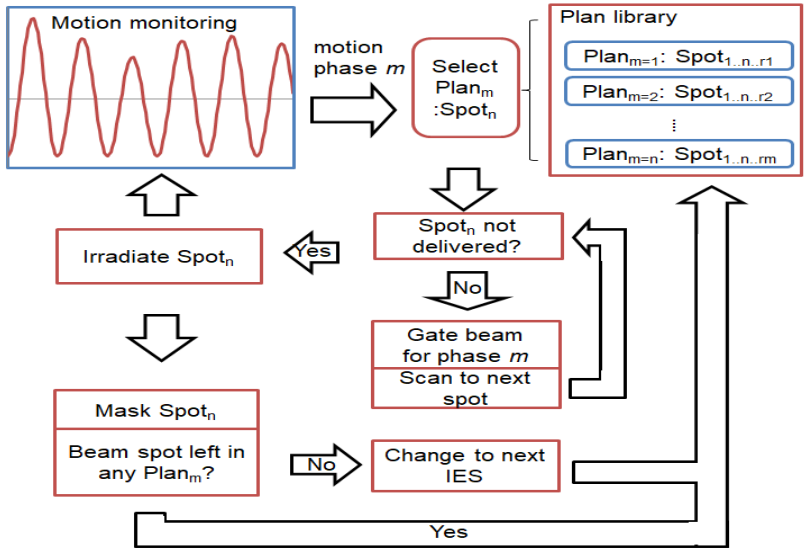
From gating to multi-phase 4D delivery

Collaboration with GSI for 4D treatment: compensation of breath related tumour movement. Subdivide treatment in respiratory phases.







- Standard treatment
- Standard treatment on moving detector
- Treatment subdivided in 10 phases

eceived funding from the European Union's Horizon 2020
vation programme under grant agreement No 101008548

M. Lis et al., A Modular System for Treating Moving Anatomical Targets With Scanned Ion Beams at Multiple Facilities: Pre-Clinical Testing for Quality and Safety of Beam Delivery, Front. Oncol. 11 (2021) 620388.

Radiobiology

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548

Radiobiology

The main topics for the present/next radiobiological research in CNAO comprise tissue, cell and molecular experimental activities aiming to investigate the mechanisms of response after particle irradiation:

- Mechanisms of radioresistance
- Healthy tissues and microenvironment response
- Effects of high let radiation in combination with other therapeutic modalities
- Low doses effects
- Other ion species: looking for the Optimal Particle Species. What is the optimal ion species for a given tumor / normal tissue combination?
- Biological markers (for tumor radioresistance and for individual sensitivity) in view of their potential ability to predict the outcome of cancer therapy and to customize the treatment to the single patient
- Late effects: secondary cancer induction (but not only…)

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CNAO Expansion

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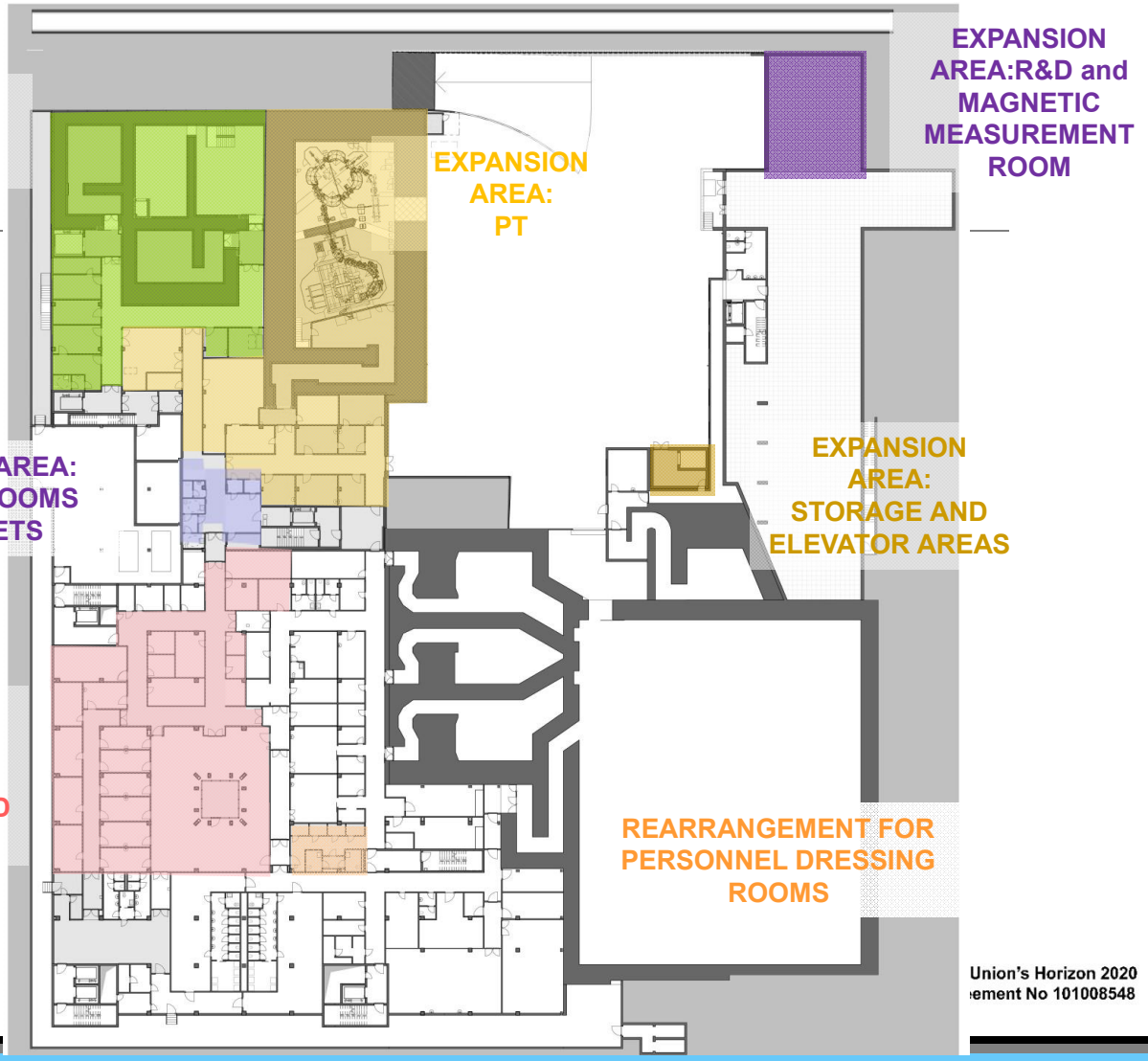
CNAO Expansion

Hitachi for proton Single Room Facility with a gantry

BNCT expansion agreement with TAE-TLS



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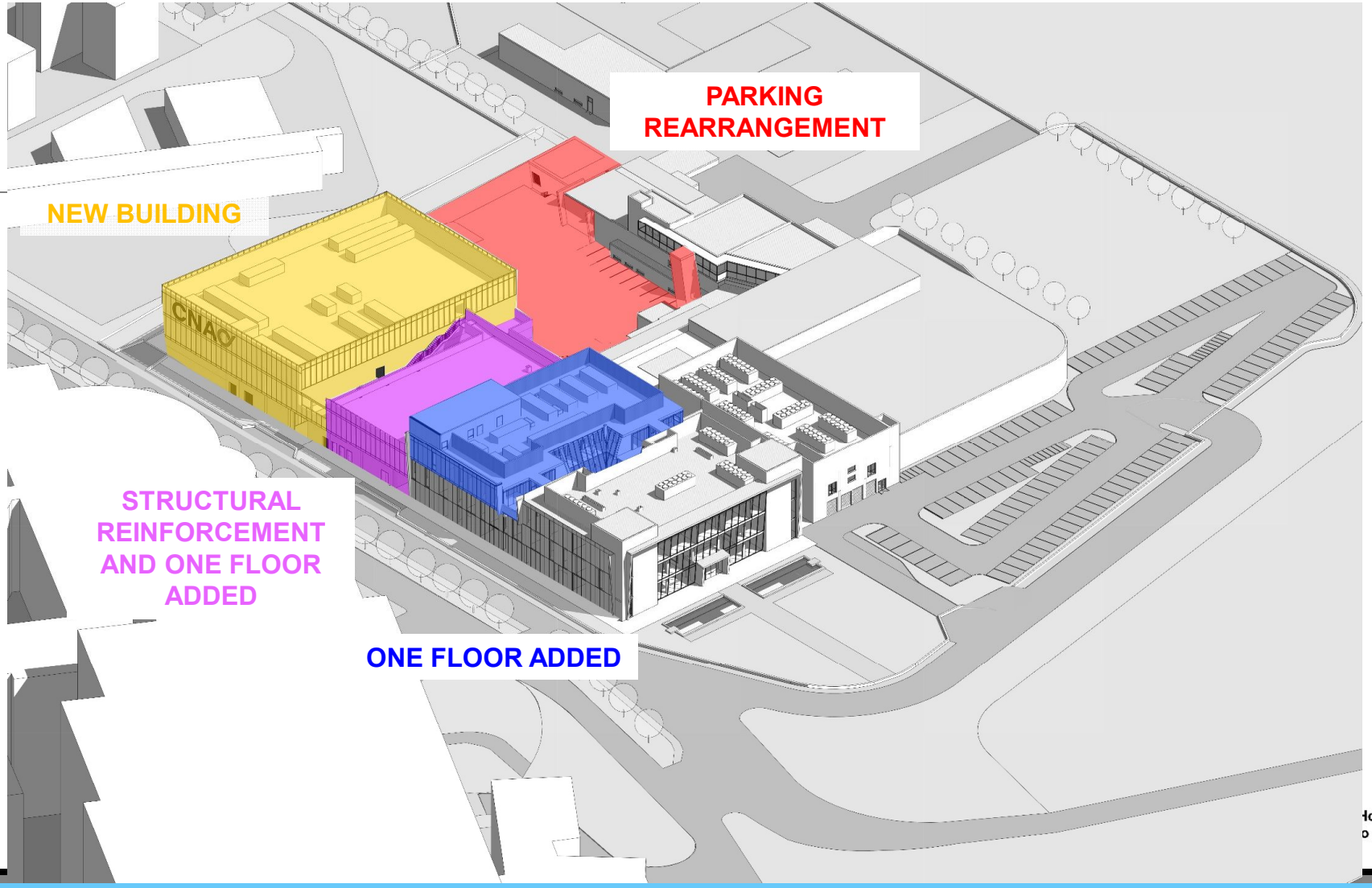

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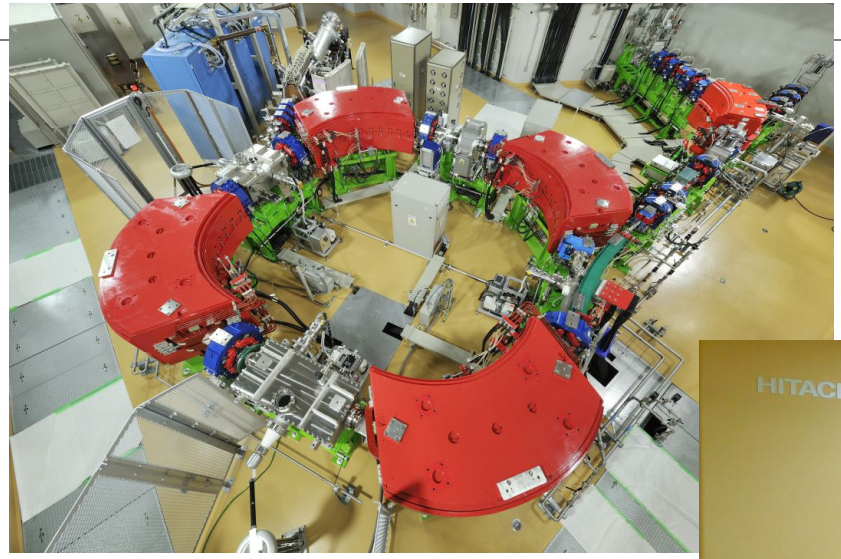
Hitachi Single Room Facility



Contract signed with Hitachi:
December 2019

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der grant agreement No 101008548

Accelerator based BNCT

Collaboration agreement signed
November 2020

Proton energy 2.5 MeV
Intensity 10-15 mA
p-Li reaction

tae LIFE SCIENCES

alpha beam™

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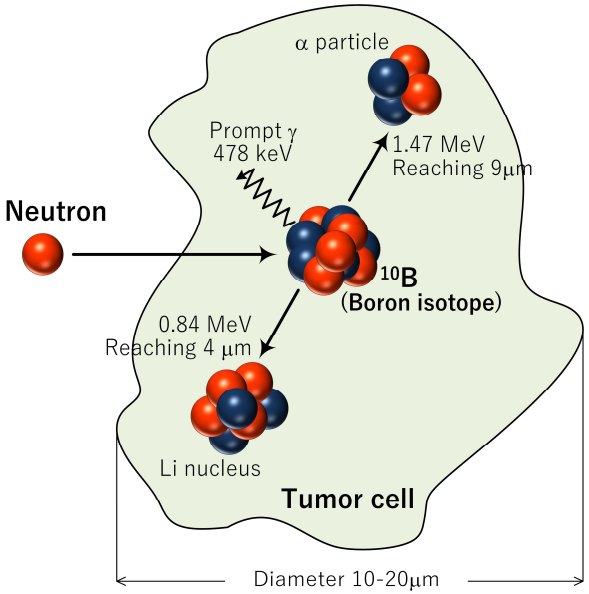
BNCT

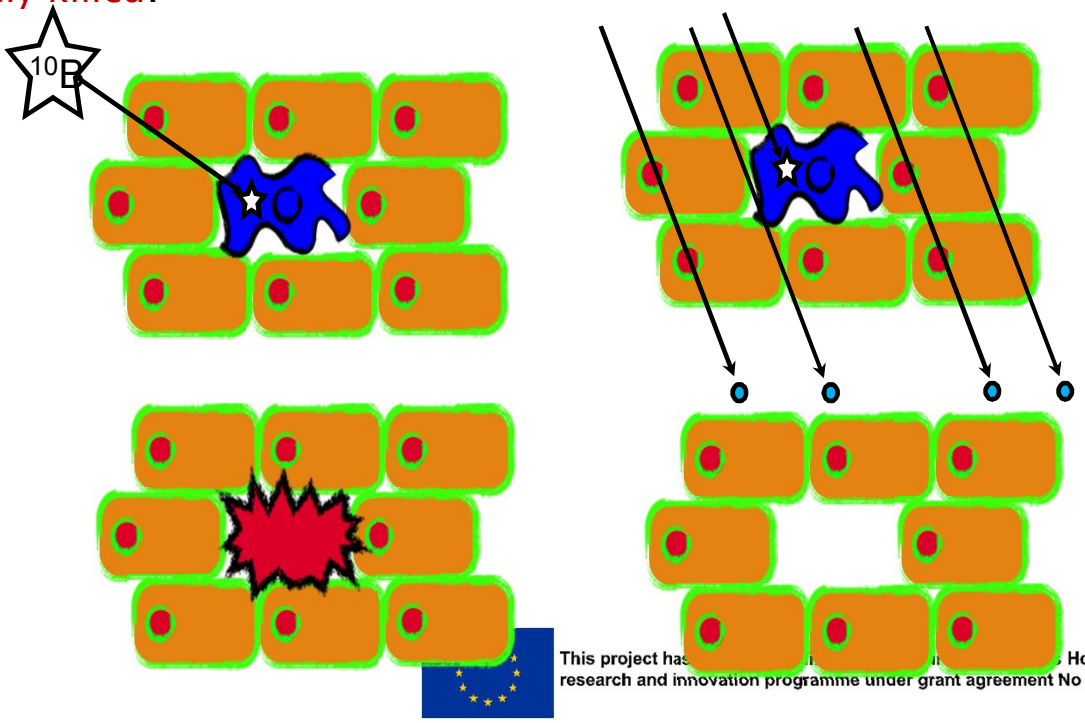
$^{10}_{5}\mathrm{B} + \mathrm{n} \rightarrow [^{11}_{5}\mathrm{B}] \rightarrow {}^{4}_{2}\mathrm{He}(\alpha) + {}^{7}_{3}\mathrm{Li} + 2.38\ \mathrm{MeV}$ for thermal neutron

Range of He and Li < 10 um which is within a tumor cell.

If the boron agent is accumulated in tumor cells,

the tumor cells can be selectively killed.





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CNAO further expansion

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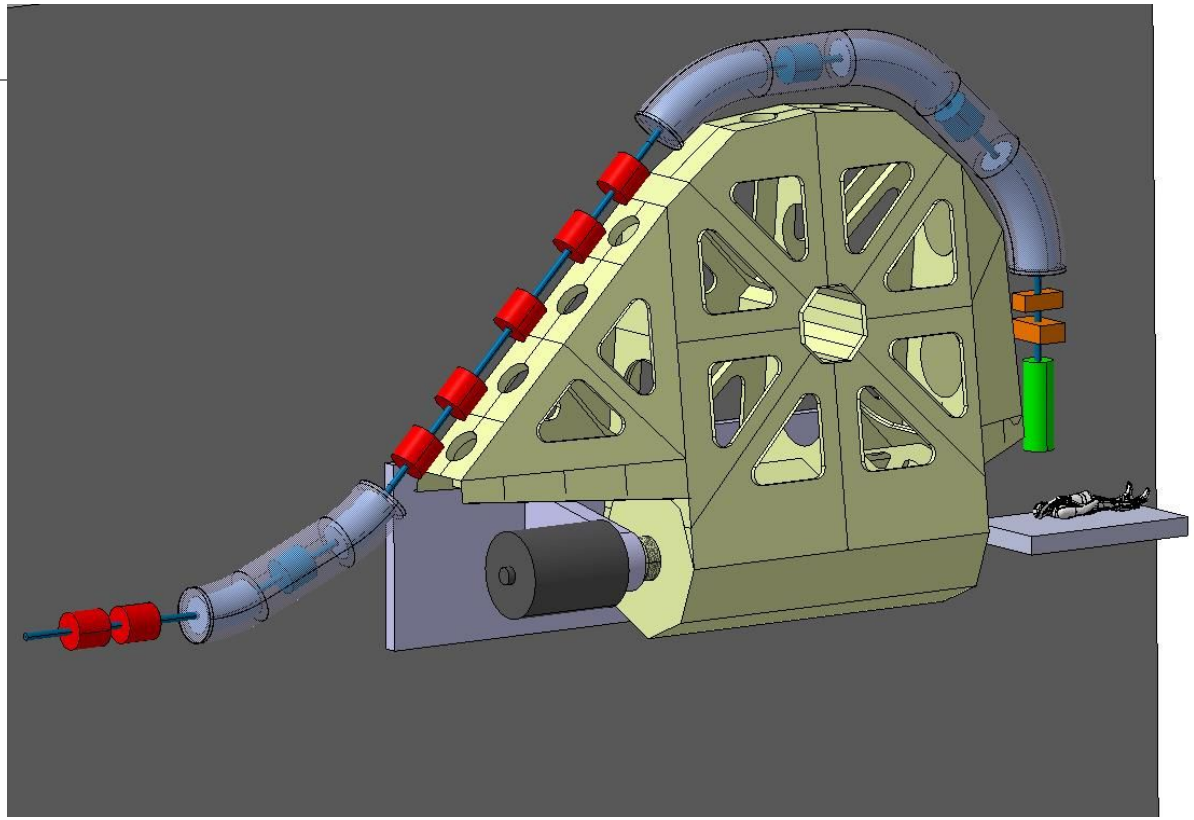
New carbon ion gantry design

CNAO-INFN-CERN-MedAustron collaboration under discussion

To be designed in 4 years and installed in 8-10 years at CNAO



U. Amaldi et al, SIGRUM
A Superconducting Ion Gantry with Riboni's Unconventional Mechanics

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Many other subjects were left out like dosimetry and microdosimetry, detector development, basic physical measurements useful for modelling (e.g. fragmentation cross section) etc.

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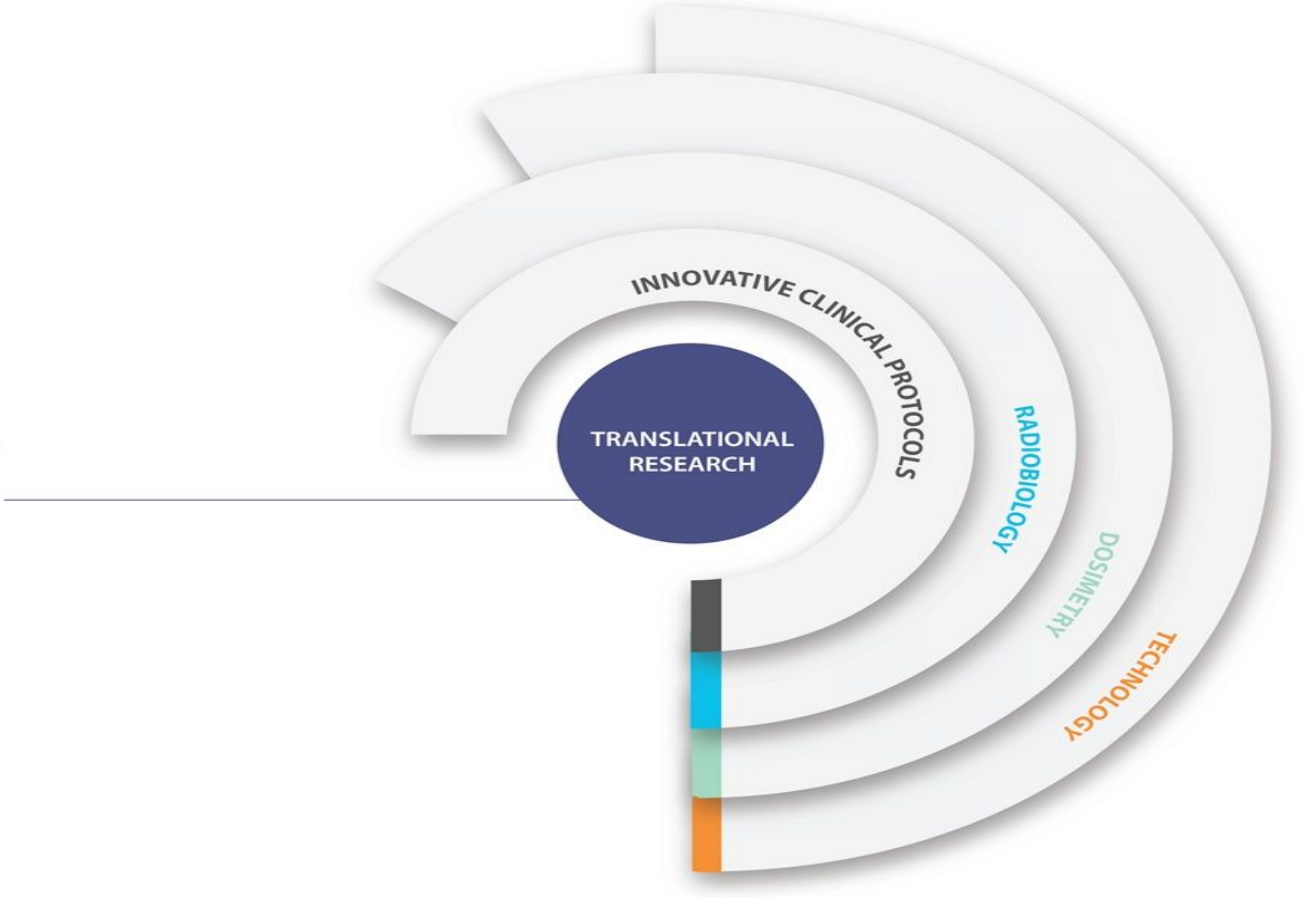
Research is a must to keep CNAO up-to-date to stay always at the cutting edge



HITR

ion's Horizon 2020
ment No 101008548

The Centre technology needs to evolve and adapt according to the research outcome: it is not a static "black box" producing beam, it is an evolving entity

Thank you for your attention

"Physics is like sex: sure, it may give some practical results, but that's not why we do it. "

R. Feynmann

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