

Charged particles for cancer therapy
*International strategic review workshop:
what will be the unique advantages of laser driven charged particles*

CNAO status, latest developments and innovations

Sandro Rossi

Imperial College London, UK – February 27th, 2026
Online



CNAO

The National Center for Oncological Hadrontherapy

Not-for-profit founded and supported by:



Ministero della Salute

The Council: A Confluence of Italy's Leading Institutions

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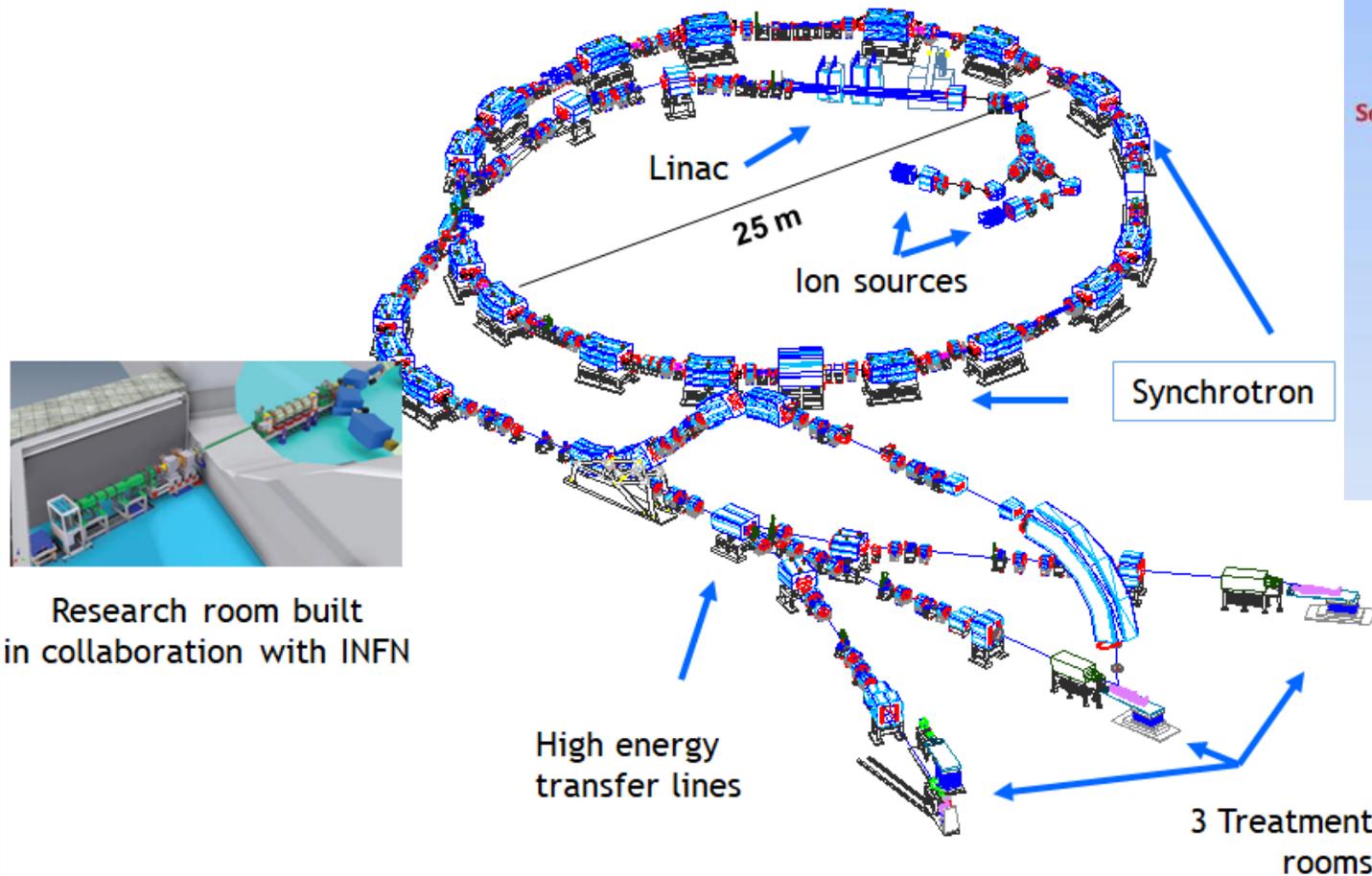
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Università di Milano
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Università di Pavia
Comune di Pavia

Partecipanti

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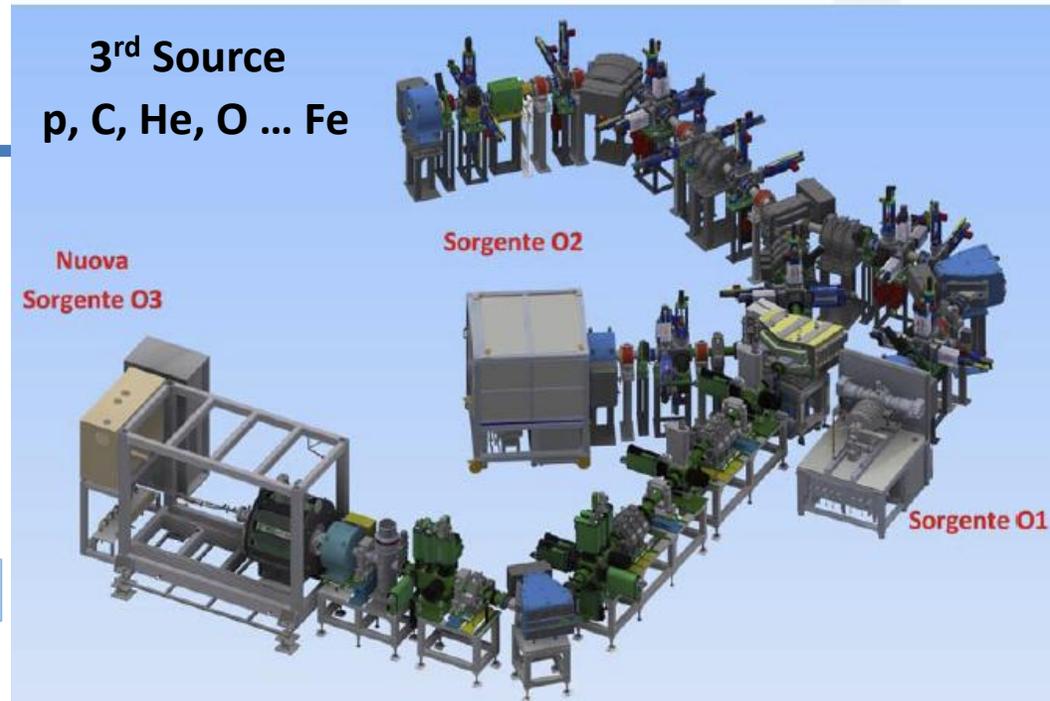
THE HEARTH OF CNAO



Research room built in collaboration with INFN

Intellectual property shared by CNAO - INFN - CERN

Built between 2005-2010
Treating patients since 2011
CE certified in 2014

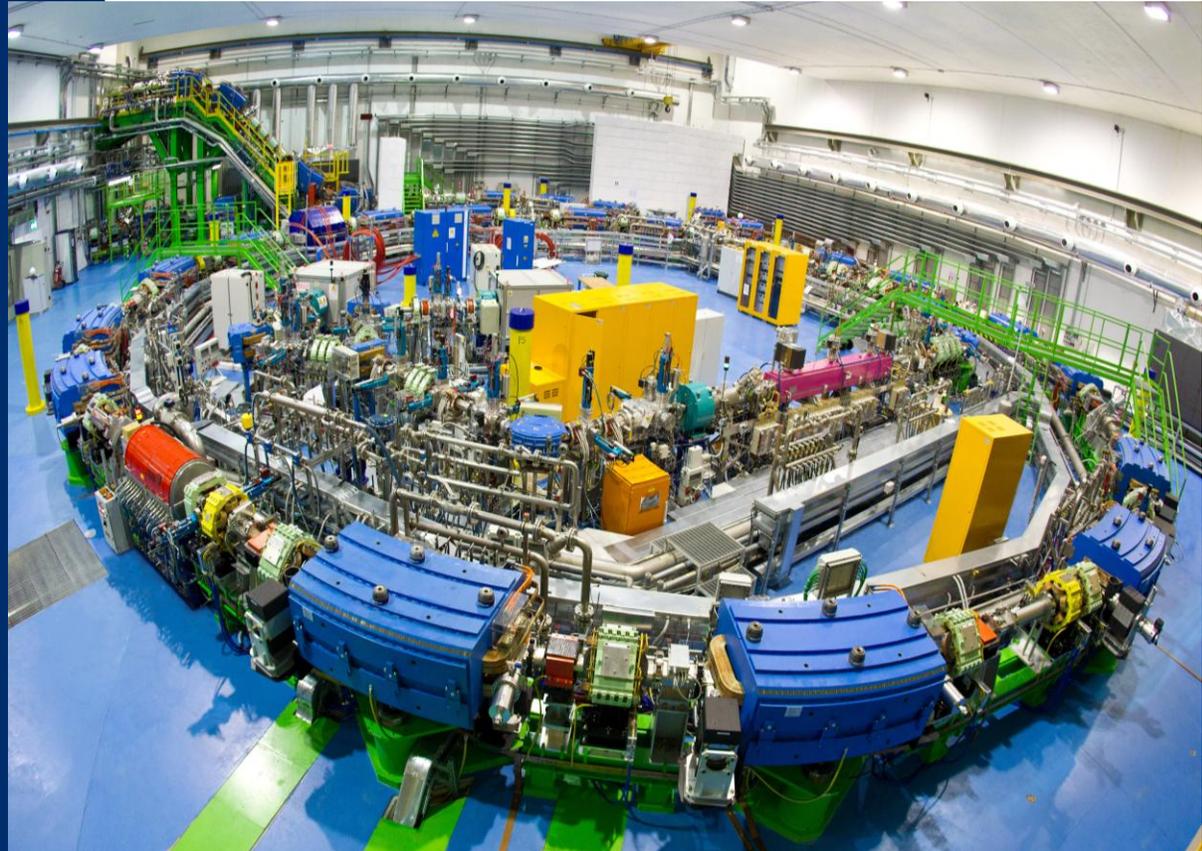


Accelerated ion	p, C, He ...
Energy range (MeV/u)	60-225 (p) (30-320mm) 120-400 (C) (30-270mm)

Extraction	Slow - scanning
Dose uniformity	± 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

CE CERTIFIED MEDICAL DEVICE



CNAO <small>Centro Nazionale di Adroterapia Oncologica</small>	
Dose Delivery System	
REF DDS/FIX	SN 0001/2015
V = 230 V ac P _{max} = 500 VA	I = 2 A f = 50 Hz
03/2015	Fondazione CNAO Via Erminio Borloni 1 - IT 27100 PAVIA ☎ +39 0382 0781 ✉ medicaldevice@cnao.it
UDI [01] 08054154660018 [21] 0001/2015	CE 0373

CNAO <small>Centro Nazionale di Adroterapia Oncologica</small>	
SISTEMA PER ADROTERAPIA	
REF CNAO-01	SN 0001/2012
05/2012	Fondazione CNAO Via Erminio Borloni 1 - IT - 27100 PAVIA ☎ +39 0382 0781 ✉ medicaldevice@cnao.it
UDI [01] 08054154660001 [21] 0001/2012	CE 0373



Organization Accredited
by Joint Commission International

2025 Center Efficiency Report



10,355
Patient Sessions Completed
Out of a total of 10,427 scheduled sessions for the year.



100%
of Scheduled Treatment Days Utilized
All 228 programmed treatment days saw activity.

91.3 %
Availability time

Analysis of Postponed Sessions

72 Total Sessions Postponed
Representing just 1% of the scheduled treatments.



Technical / Machine Faults
15
0.1%



Clinical / Patient Issues
57
0.5%

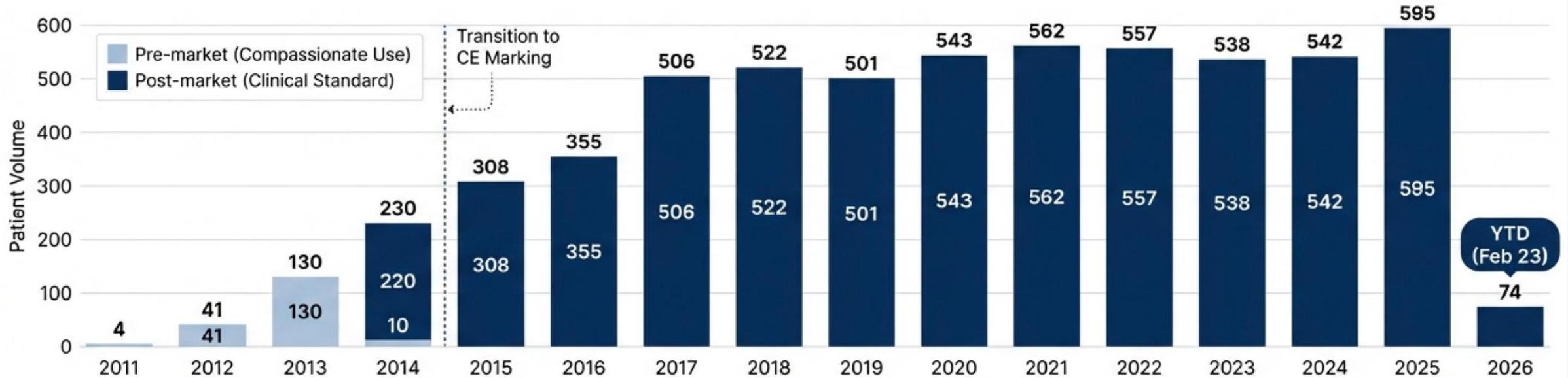
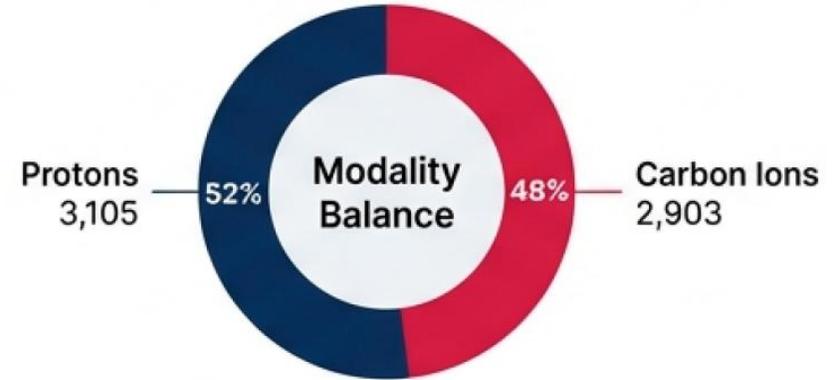
CNAO Clinical Activity Report: Cumulative Treatment Analysis (2011–2026)

Weekly Update - Data as of 23 February 2026

6,008

Total Cumulative Patients Treated

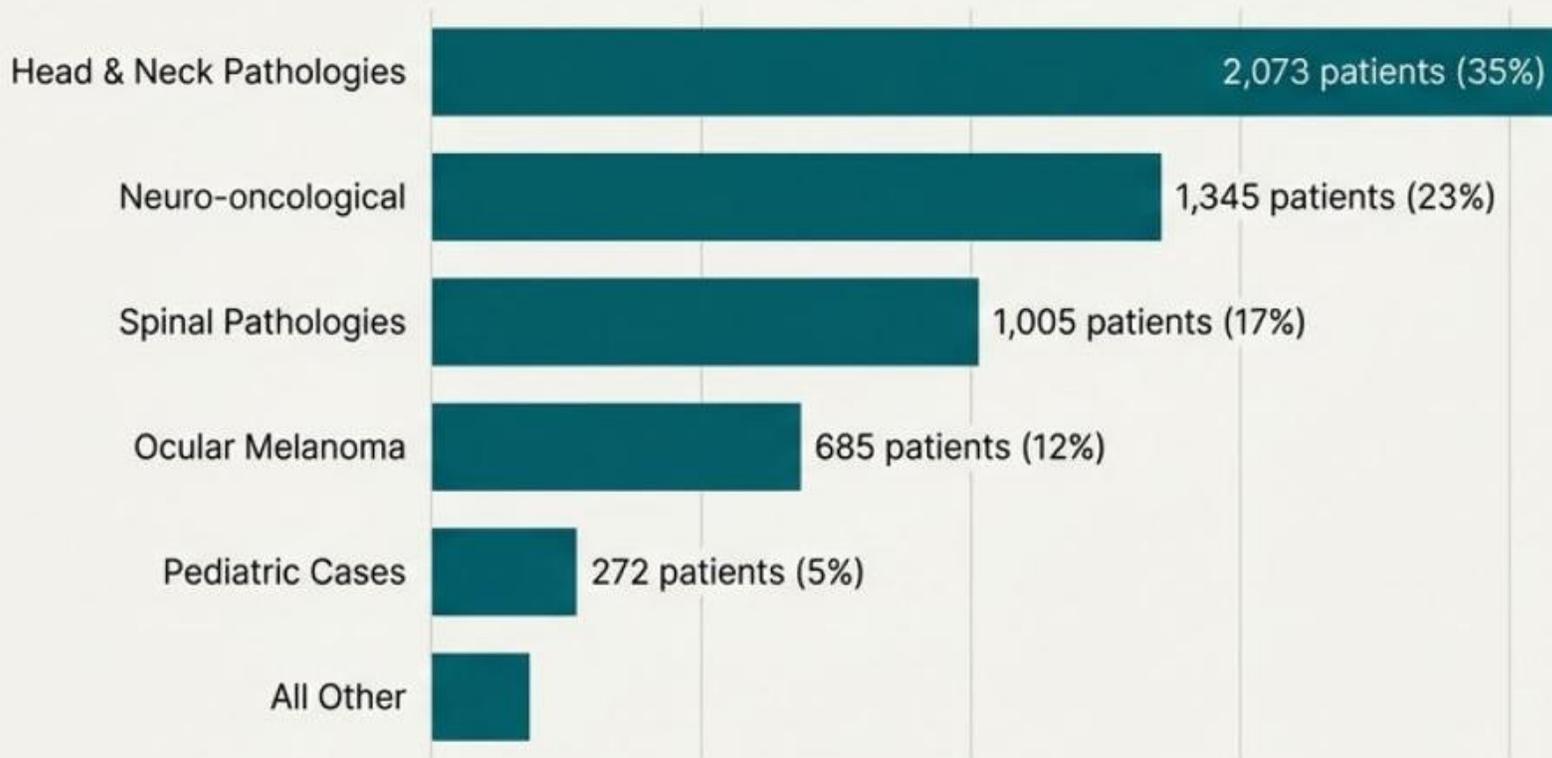
From inception (2011) to present



A Focus on the Most Complex and Radio-Resistant Tumors

Distribution of over 6,000 patients by treated pathology (PTA)

Distribution by Pathology



**A Critical Resource
for Children**

**272 Pediatric
Cases Treated**

Our expertise is concentrated in areas where conventional radiotherapy has known limitations, offering new hope for patients with complex cancers of the central nervous system, head and neck, and spine.

Redefining Outcomes: Data-Driven Proof of Efficacy

Comparing CNAO's clinical results for key pathologies against conventional X-Ray therapy benchmarks from medical literature.

Pathology & Endpoint	Conventional X-Ray Therapy	CNAO Particle Therapy
Adenoid Cystic Carcinoma 5-Year Local Control	25-39%	75% ↑
Mucosal Melanoma (Head & Neck) 3-Year Local Control	39%	85% ↑
Intracranial Meningioma (G1) 5-Year Local Control	73%	98% ↑
Skull Base Chordoma 5-Year Local Control	53-75%	71-84% ↑

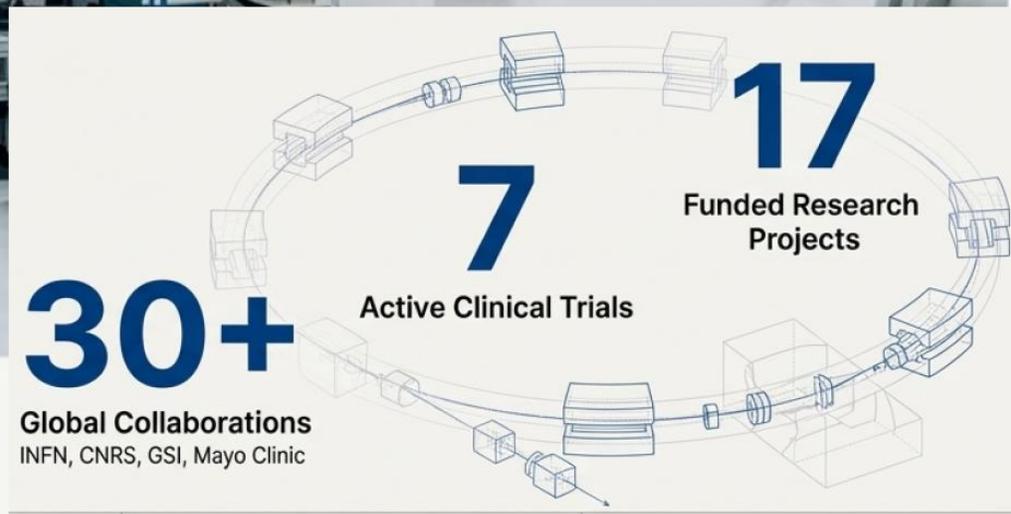
For some of the most challenging cancers, CNAO's hadron therapy provides a significant and decisive advantage in local tumor control, directly translating to better long-term outcomes for our patients.

The second pillar: Research

600+ hours of beamtime
to external users in 2025



Room built in collaboration with INFN

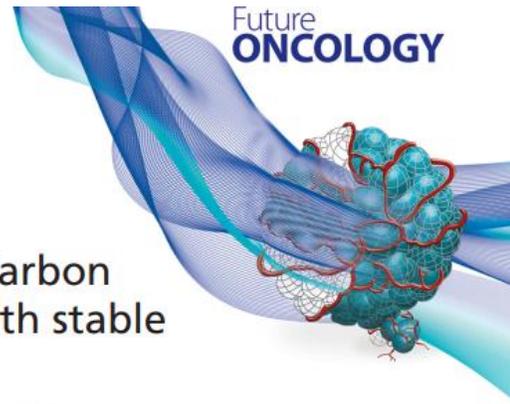


ICONIC STUDY: COMBINATION CARBON+IMMUNOTHERAPY

ICONIC study: **I**mmune checkpoint inhibitors and **C**arbon **iON** radiotherapy **I**n solid **C**ancers with stable disease

Clinical Trial Protocol

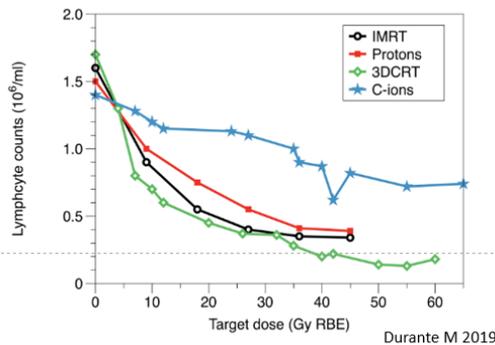
For reprint orders, please contact: reprints@futuremedicine.com



Immune checkpoint inhibitors and Carbon iON radiotherapy In solid Cancers with stable disease (ICONIC)

Stefano Cavaliere^{1,2}, Viviana Vitolo³, Amelia Barcellini^{*,3,4}, Sara Ronchi³, Angelica Facoetti⁵, Chiara Campo⁶, Catherine Klersy⁷, Silvia Molinelli⁸, Francesco Agustoni^{4,9}, Virginia Valeria Ferretti⁷, Annalisa De Silvestri⁷, Marco Platania¹⁰, Michele Del Vecchio¹⁰, Marco Durante¹¹, Alexander Helm¹¹, Claudia Fournier¹¹, Filippo de Braud^{2,10}, Paolo Pedrazzoli^{4,9}, Ester Orlandi^{*,3} & Lisa Licitra^{*,1,2,6}

Figure 3. Median values of lymphocyte count in esophageal cancer patients during the course of radiotherapy. Data for protons (1.8 Gy RBE/fraction) and IMRT (1.8 Gy/fraction) are from ref.⁴⁵ data for 3DCRT (1.6–2.0 Gy/fraction) and C-ions (2.7–3.6 Gy RBE/fraction) from ref.⁴¹



In vitro:

- Higher LET and RBE have greater impact on antigen release and less immune suppression increasing sensitivity to CTLs and induction of MDSC/T_H17
- PBT induces long-term inhibition of cell migration

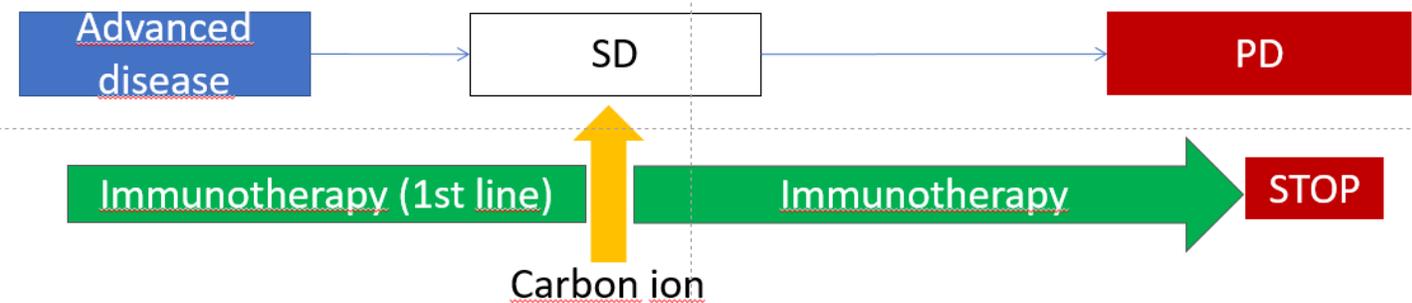
➤ Lower severe lymphopenia with protons

Primary endpoint: objective response rate (ORR) according to RECIST, assessed at least 8 weeks after CIRT

Co-primary endpoint: toxicity according to CTCAE version 5.0

Secondary endpoints:

- progression-free survival (PFS)
- overall survival (OS)
- objective response rate (ORR) according to irRECIST
- percentage of patients with disease progression as best response
- objective response of the metastatic lesion treated with CIRT
- disease control rate (DCR) according to RECIST, defined as ORR+SD



ICONIC study

Upfront hypofractionated CIRT (8GyE x 3 frs) to one measurable lesion previously untreated with local approaches

Immunological effects

Hi-ROC: targeting Hypoxia with heavy ions to gain control of RadiOresistant Cancers



Fondazione IRCCS
Istituto Nazionale dei Tumori



HEIDELBERG
UNIVERSITY
HOSPITAL



Neolys



LUXEMBOURG
INSTITUTE
OF HEALTH

CNAO

The National Center for Oncological Hadrontherapy



Maastricht University



POLITECNICO
MILANO 1863

Project start: 01.03.2025

Duration: 36 mesi

Kick off meeting 13-14 March 2025, in CNAO

- It aims to develop a **non-invasive biomarker to identify tumor hypoxia**, integrating genetic, imaging, and physiological data in order to guide the therapeutic choice between photon and carbon ion radiotherapy.
- A pilot study (Hyperion), supported by *in vitro* and *in silico* experiments, will validate the most promising biomarker.
- The project also involves the creation of a medical device prototype for the non-invasive assessment of hypoxia and the exploration of "digital twins" to **optimize personalized radiotherapy planning**.



MULTI-PARAMETRIC IMAGE GUIDANCE IN PARTICLE THERAPY

Patient stratification and treatment plan optimization

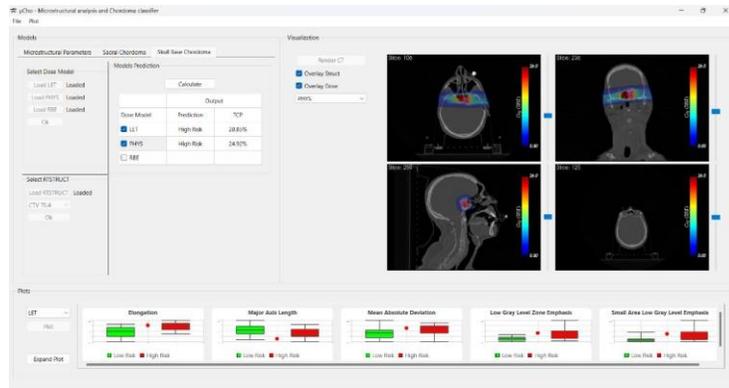


Macroscopic Modelling

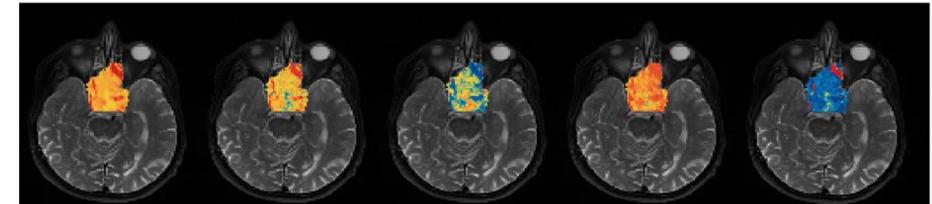
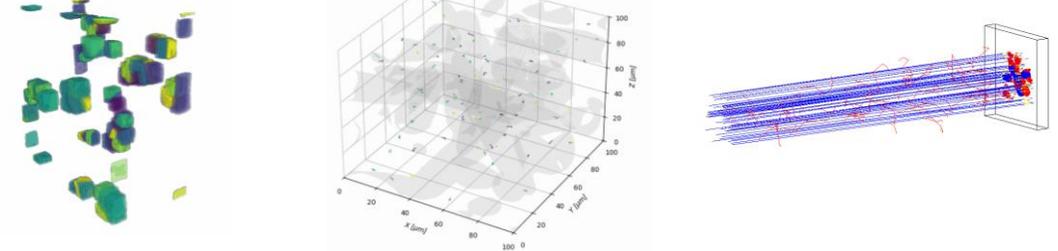


Microstructural Modelling

- Dosimetrics & LET in skull base and sacral chordoma

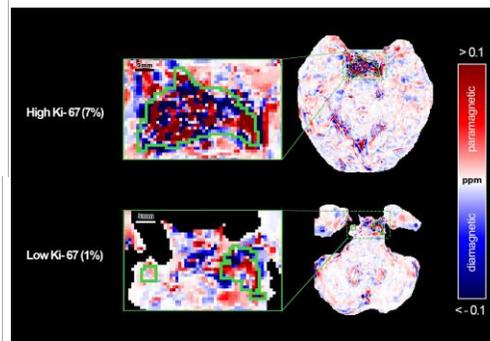
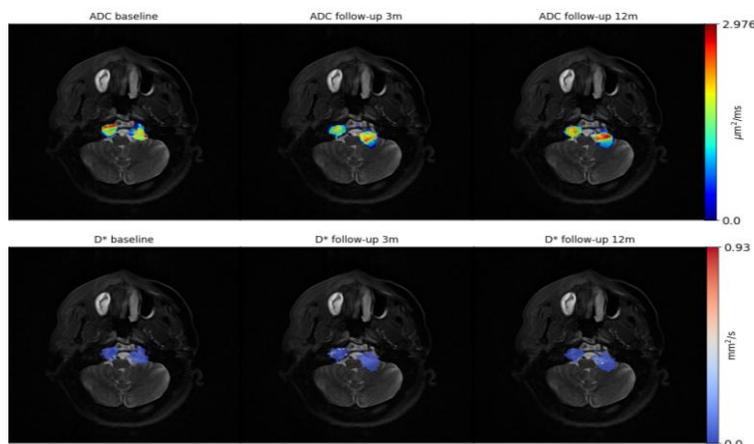


- In-silico modelling / Microstructural modelling (sub-voxel analysis)

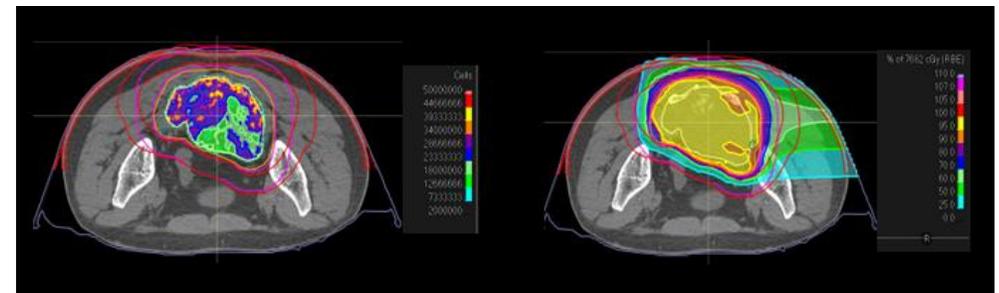


ADC ($\mu\text{m}^2/\text{ms}$) R (μm) vf (a.u.) D ($\mu\text{m}^2/\text{ms}$) ρ_{app} ($1/\mu\text{m}^3$)

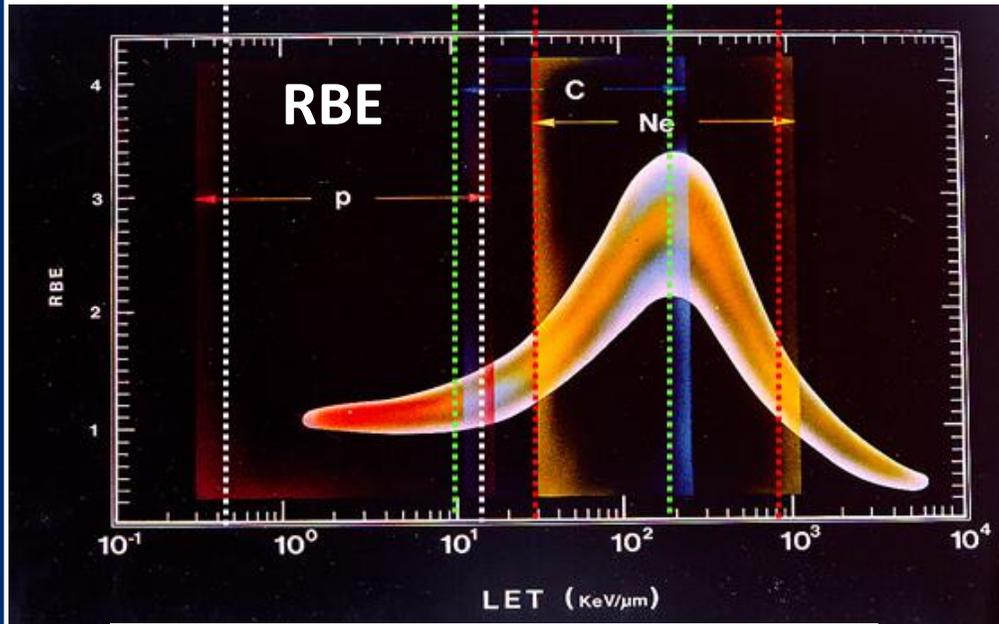
- Quantitative MRI modelling (voxel-scale analysis)



- Dose Painting



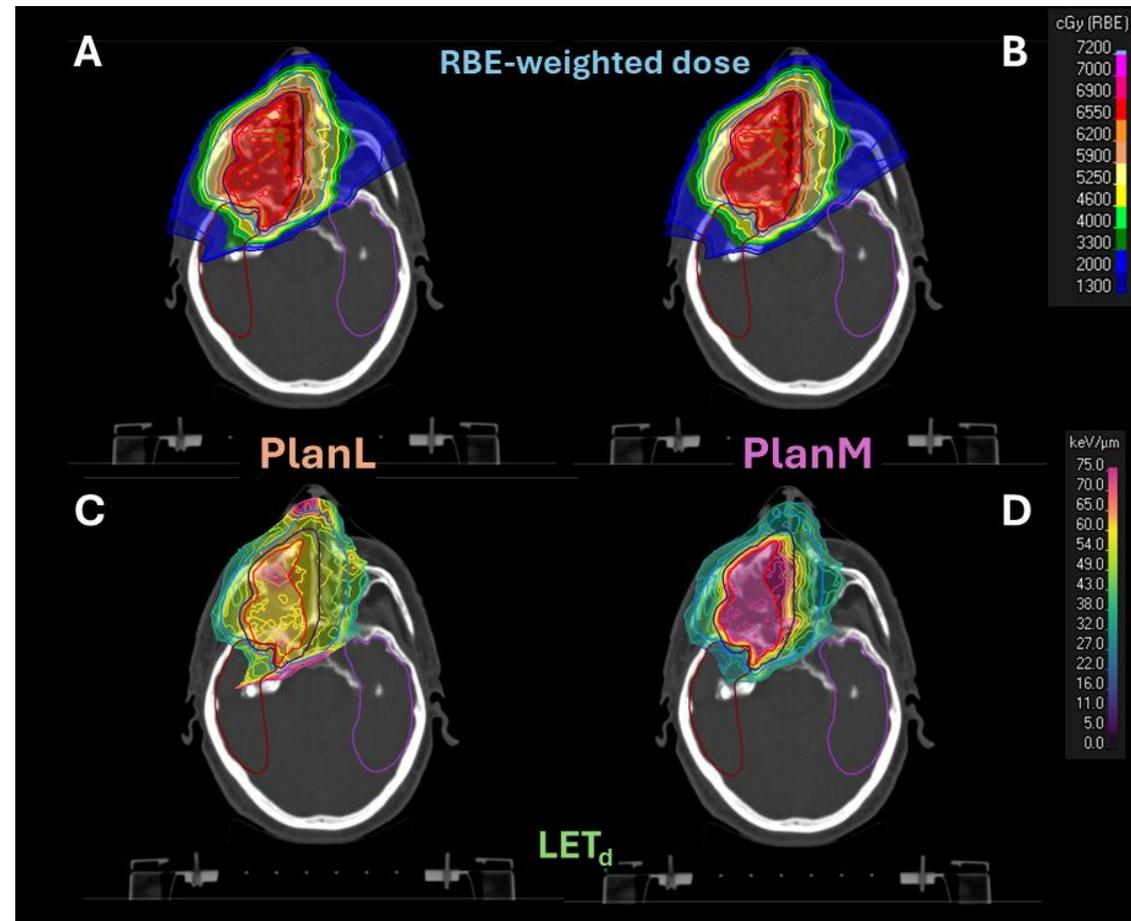
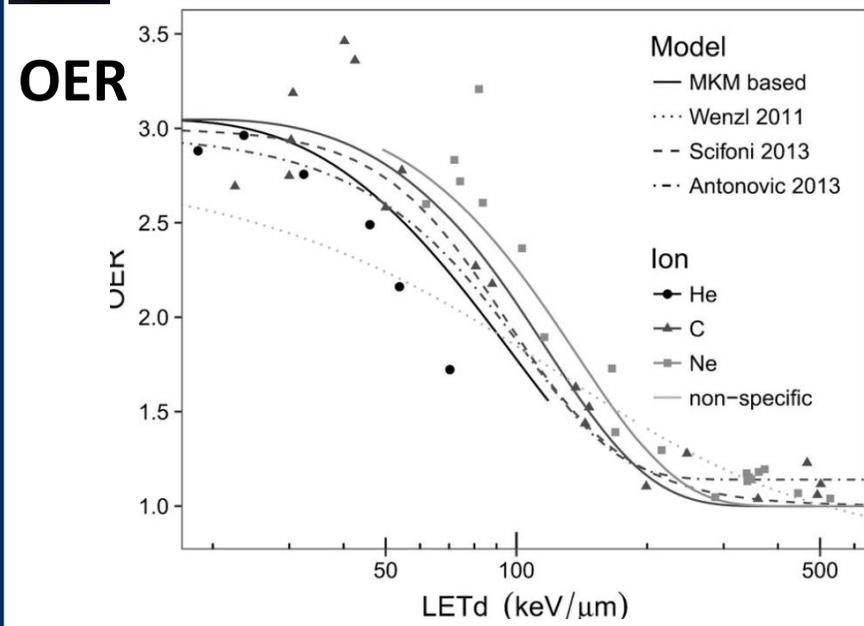
MULTI-IONS: “NEW DRUGS” FOR OPTIMAL PERSONALIZED TREATMENTS



Minimum LETd to the GTV:

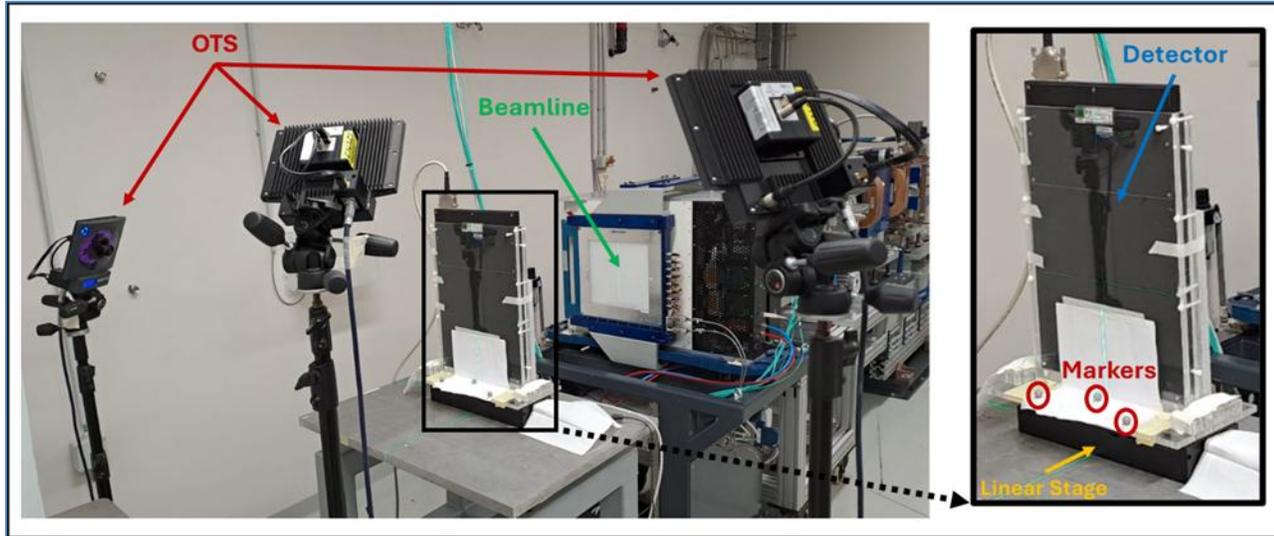
- Clinical CIRT: 40 ± 4 keV/μm
- PlanL CIRT-LET optimized: 56 ± 4 keV/μm
- Plan M MIRT: 68 ± 3 keV/μm

**Multi-ion
(p, He, C, O)
LETd painting**



4D C.A.P.H.

Experimental validation at CNAO XPR



- **Ionization Chamber** (IC) 2D-array (PTW Octavious 1500XDR)
- Programmable **Linear Stage** moving perpendicular to the beamline, **regularly/irregularly** – amplitude variations and/or baseline drifts
- Amplitude $\sim 14\text{mm}$, period $\sim 3\text{-}5\text{ sec}$

4DCT (8 phases)

- CNAO patient
- Hepatic tumor

Treatment Plans (TriP98)

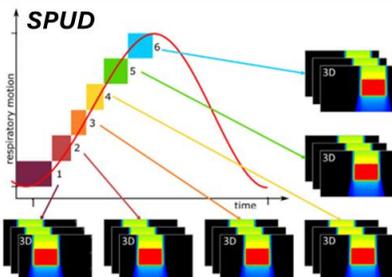
- Static
- Gating (*min 25k particl.*)
- Gating + 3xRescanning (**75k**)
- Multi-phase (SPUD) (**200k**)

Linear Stage motion idealized

- **Not actual patient motion**
- Dose reconstruction: **new DVFs first built** then employed to **characterize** the **adopted motion pattern**

Dose Delivery

- **Detector measurements VS plan**
- **DVH analysis**
- 5D-RIDOS reconstruction

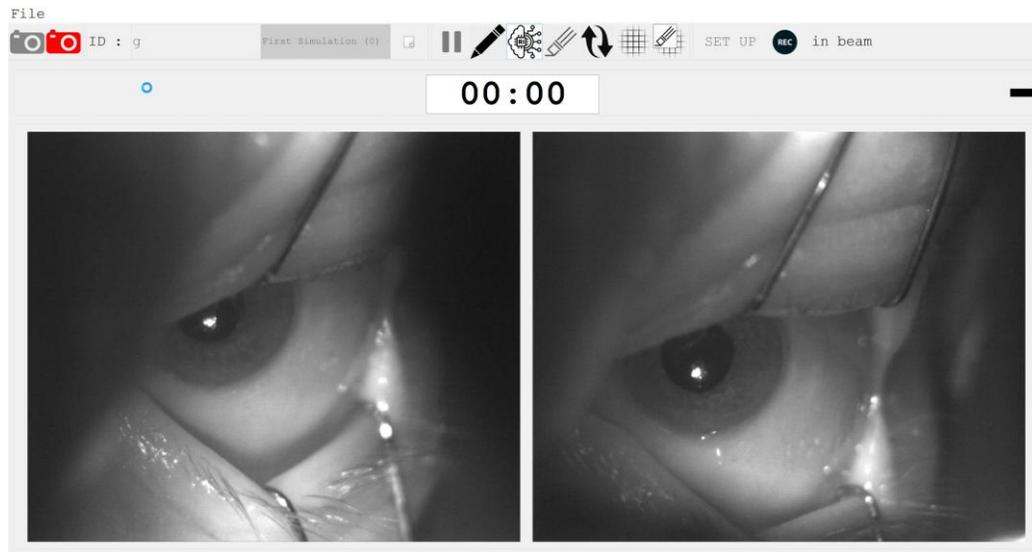


Experiments repeated with **Linear Stage** as **ground-truth** monitoring system
[Steinsberger et al., 2023] [Lis et al., 2020]

Manuscript submitted to IJROBP

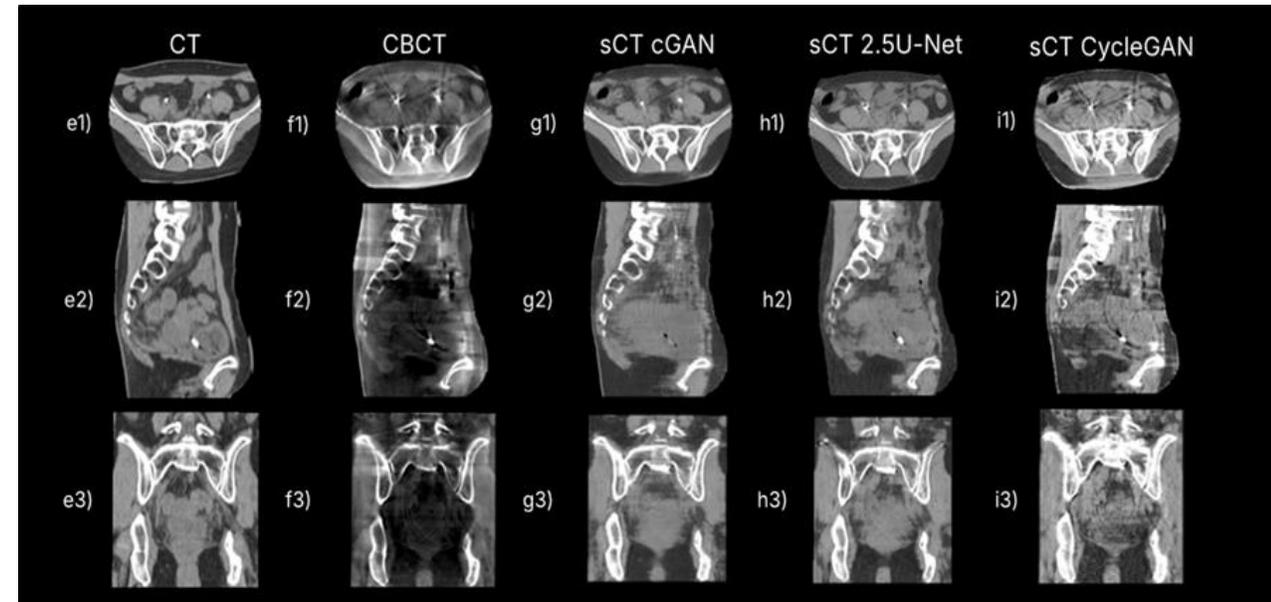
ARTIFICIAL INTELLIGENCE PROJECTS

Integration of **MedFormer** for eye structures segmentation in Eye Tracking System clinical application



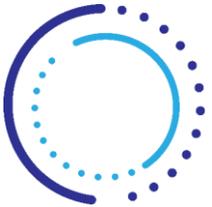
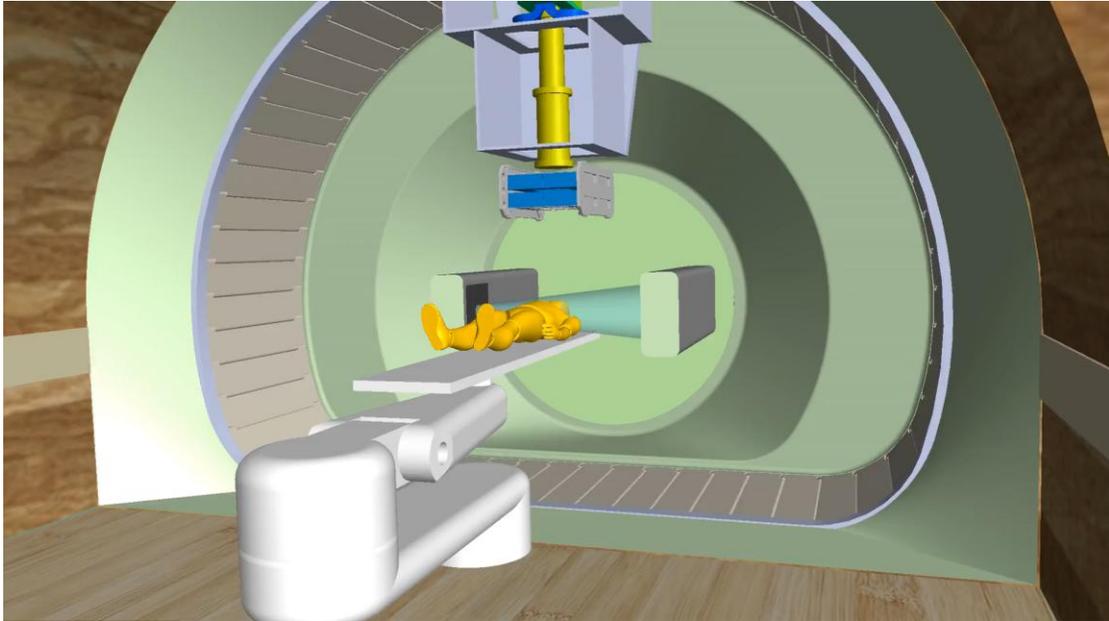
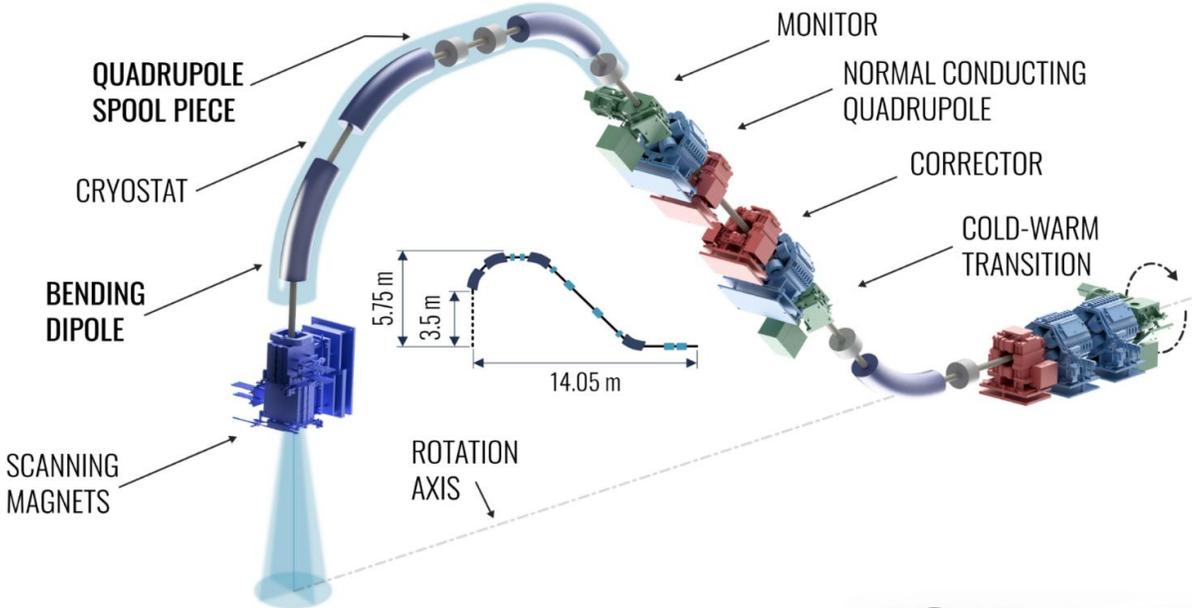
Video captured from user interaction with ETS clinical SW application demonstrating the real-time segmentation capabilities of the implemented MedFormer.

Deep learning for replanning synthetic CT generation from CBCT in abdominal district



Examples of synthetic CTs generated by three different networks (conditionalGAN, 2.5D U-Net, and CycleGAN) on the axial, sagittal and coronal planes from CNAO CBCT data acquired in Room #2.

SUPERCONDUCTING ION GANTRY



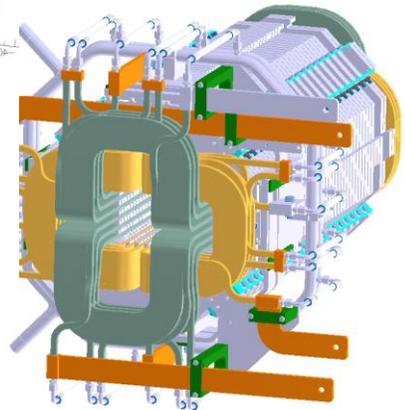
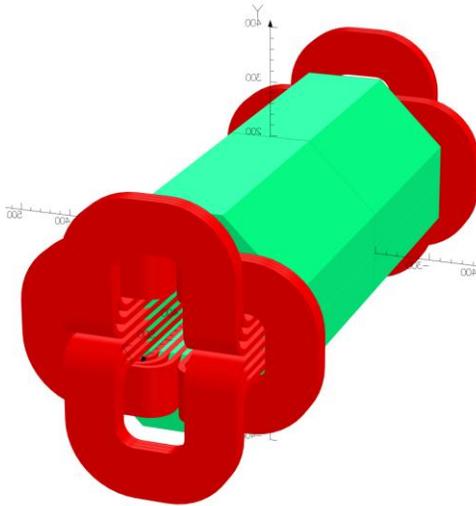
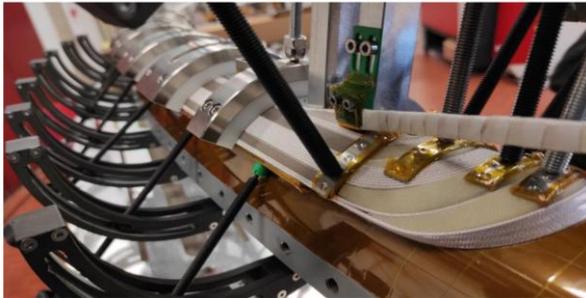
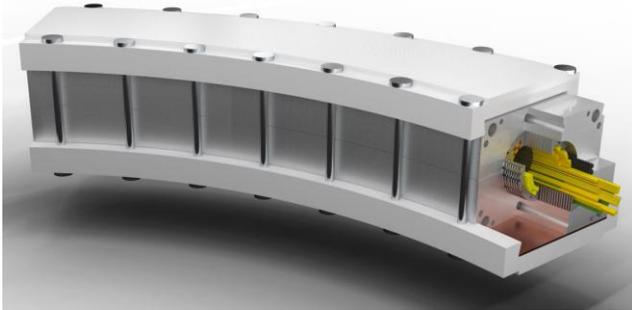
EuroSIG
European
Superconducting
Ion Gantry



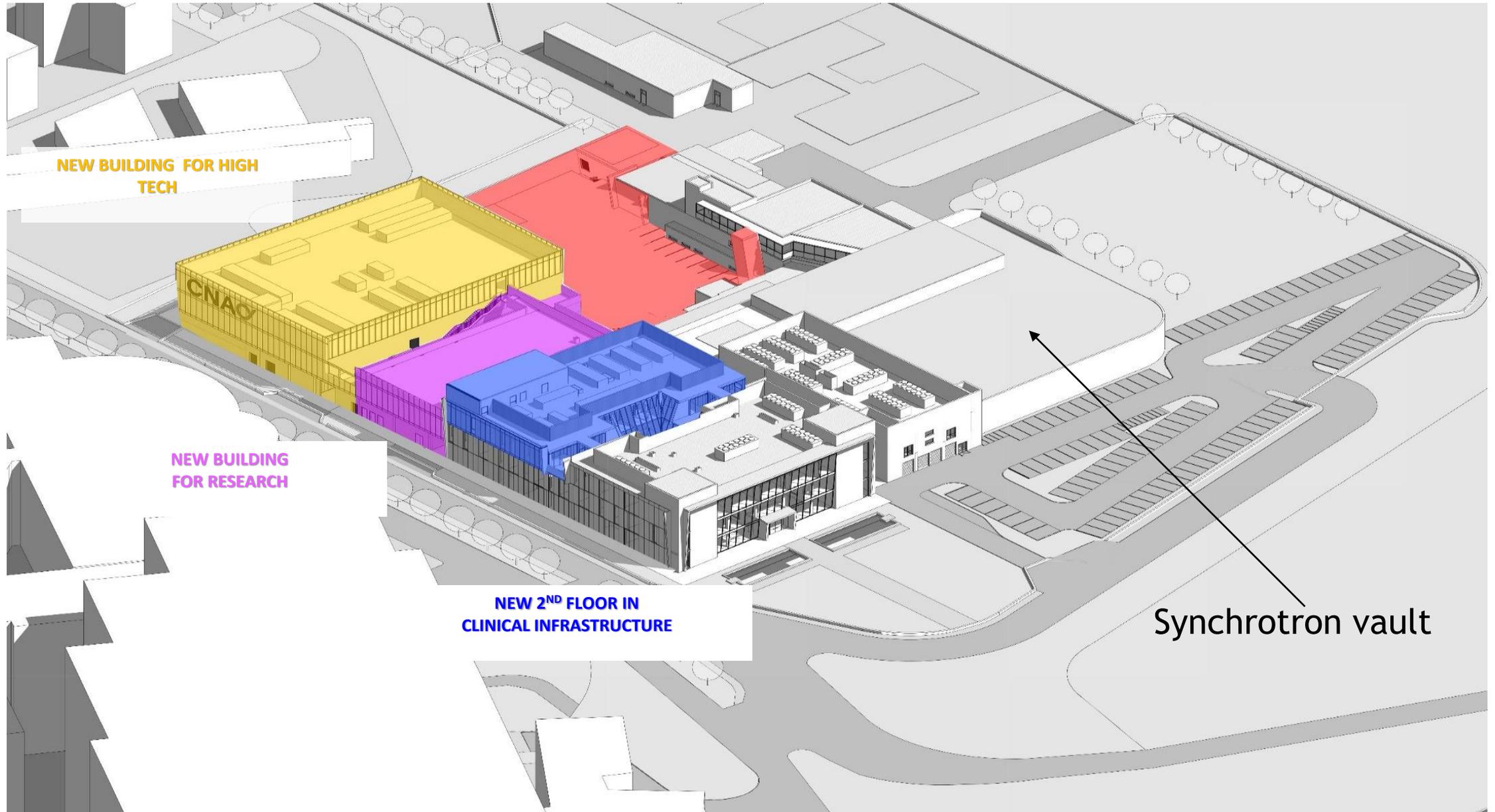
The National Center for Oncological Hadrontherapy



Istituto Nazionale di Fisica Nucleare



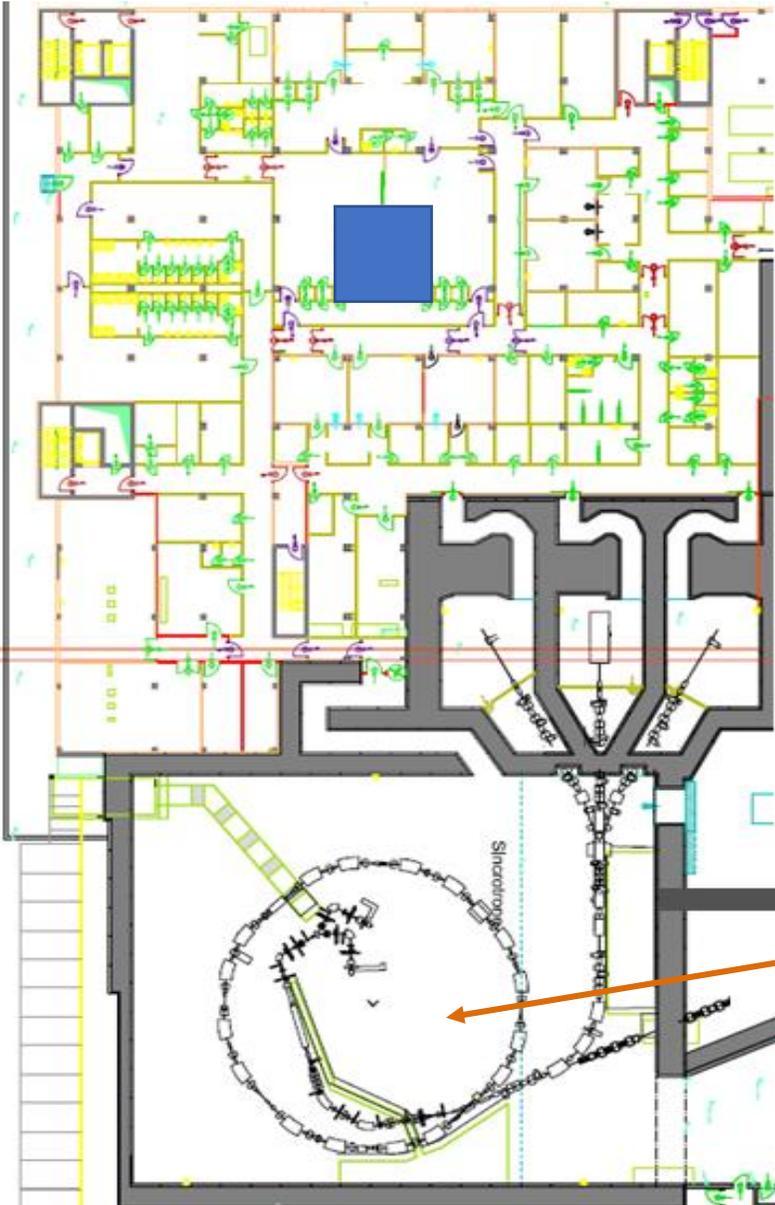
EXPANSION PROJECT



EXPANSION PROJECT



ORIGINAL LAYOUT



← Patient waiting area and services

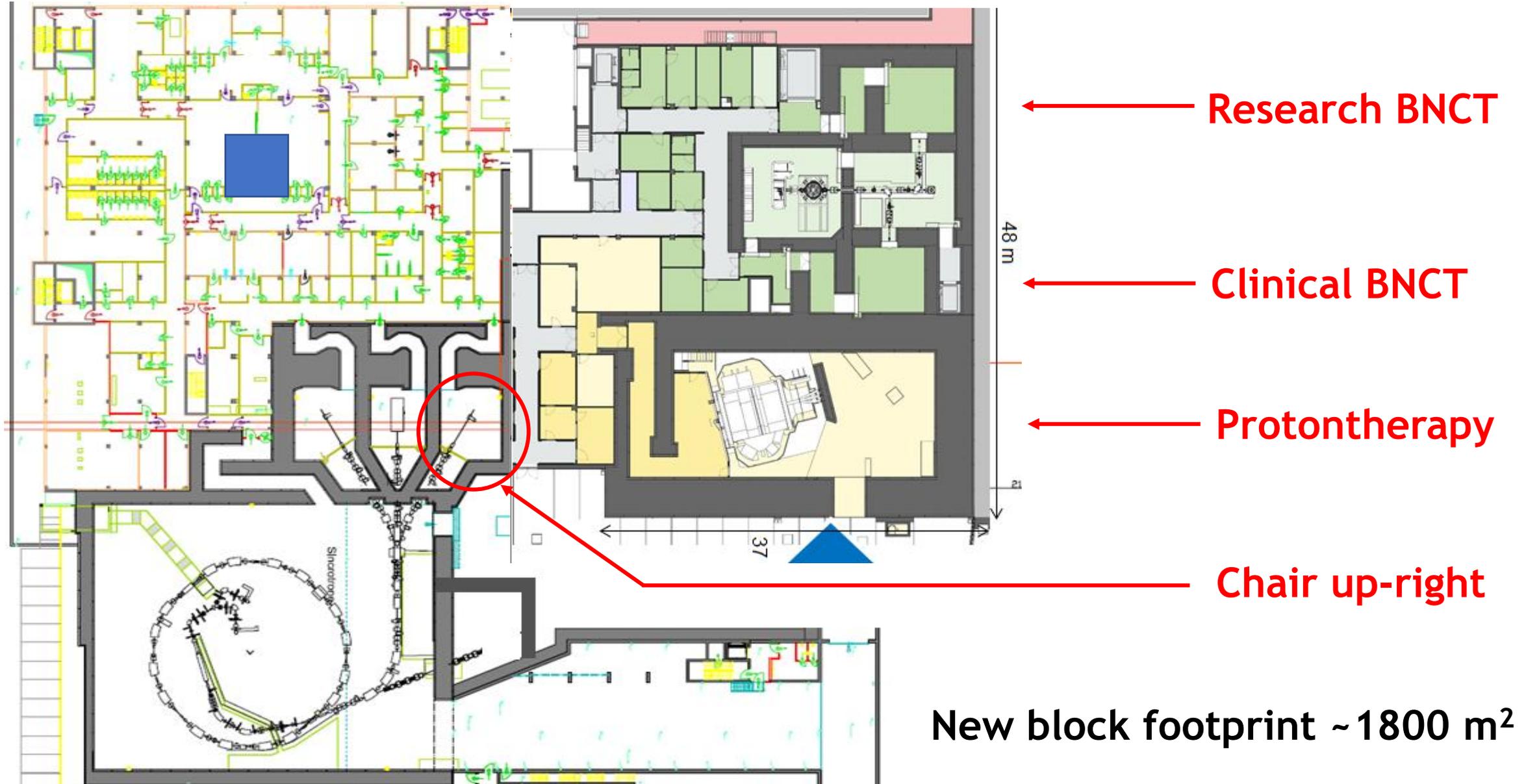
← 3 Treatment rooms: 3H + 1V

← Experimental room

← Synchrotron vault

← Main power supply room

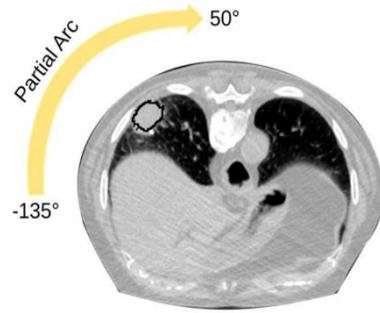
NEW LAYOUT



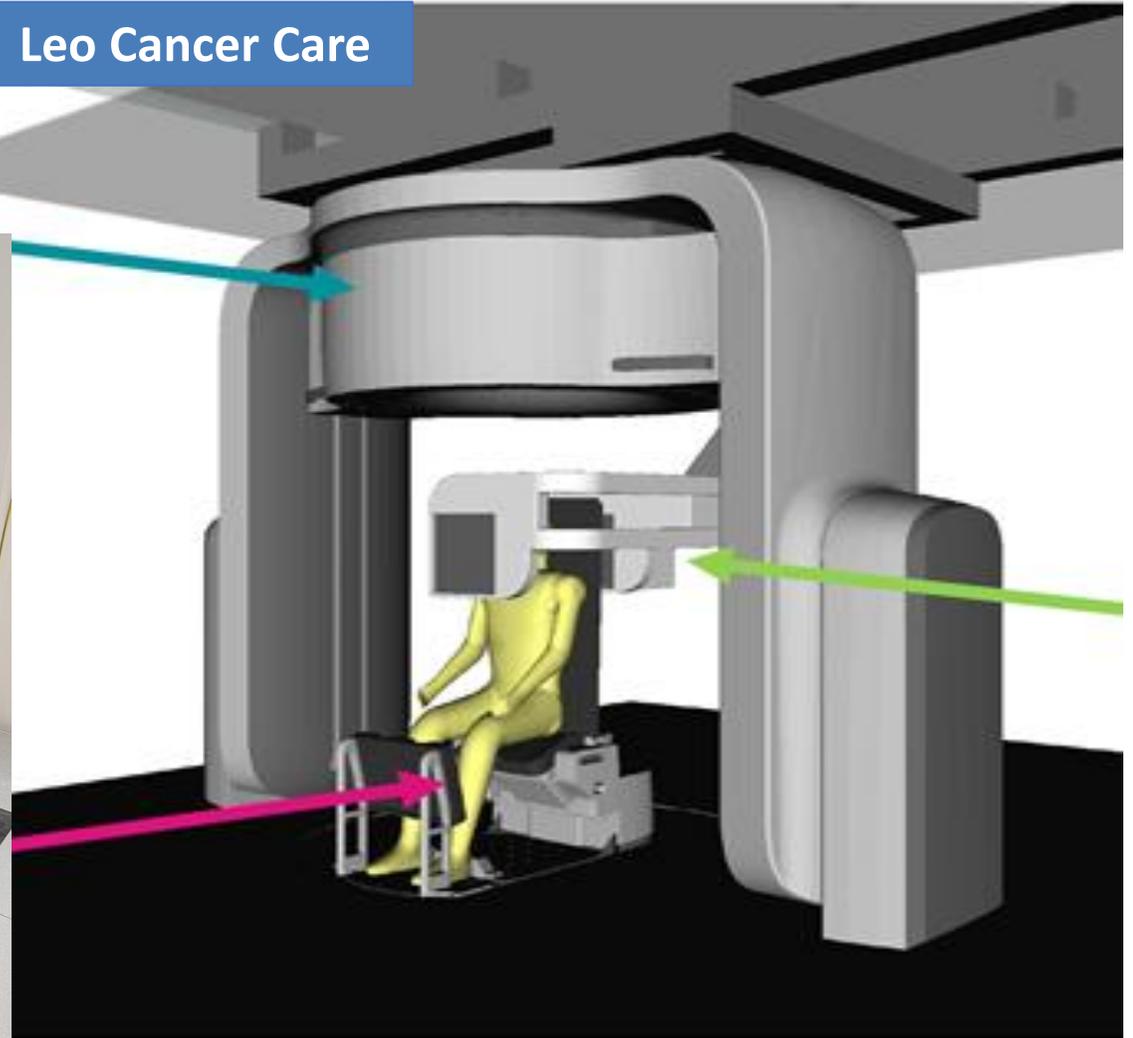
NEW PATIENT POSITIONING IN ROOM #3

Arc therapy

Collaboration with GSI



Leo Cancer Care

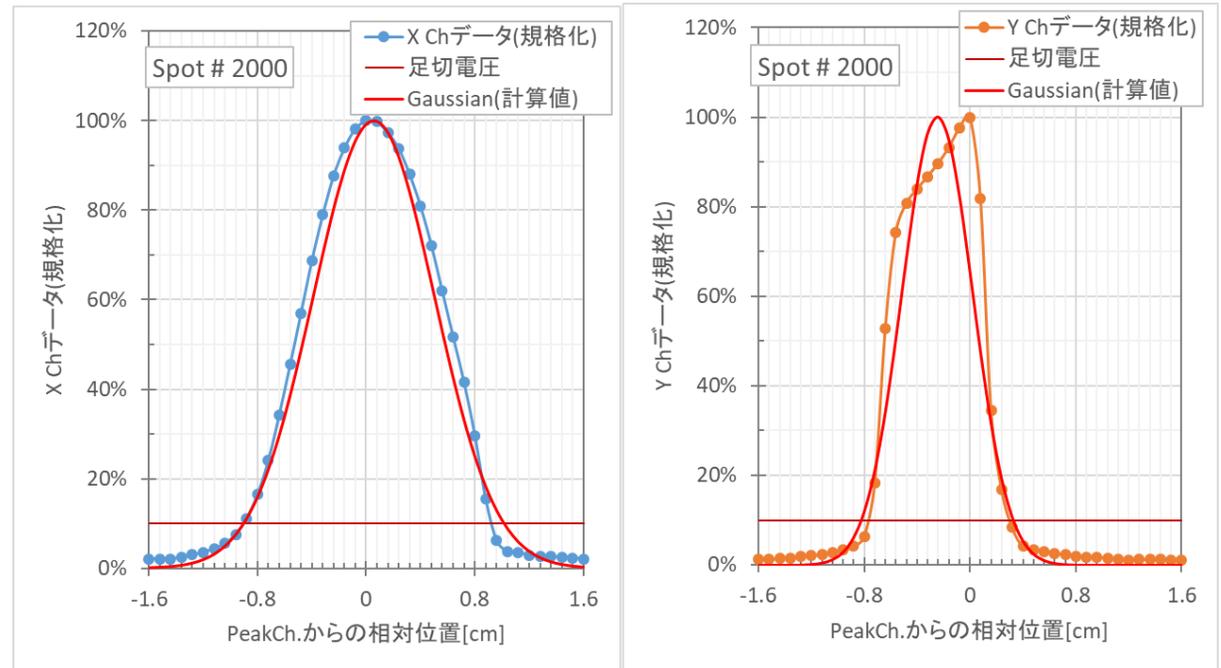


Installation fall 2026

PROTON MACHINE + GANTRY (HITACHI)



Commissioning ongoing
First patient fall 2026



Profiles of a spot measured at the Dose Monitor in the nozzle of the Hitachi gantry.

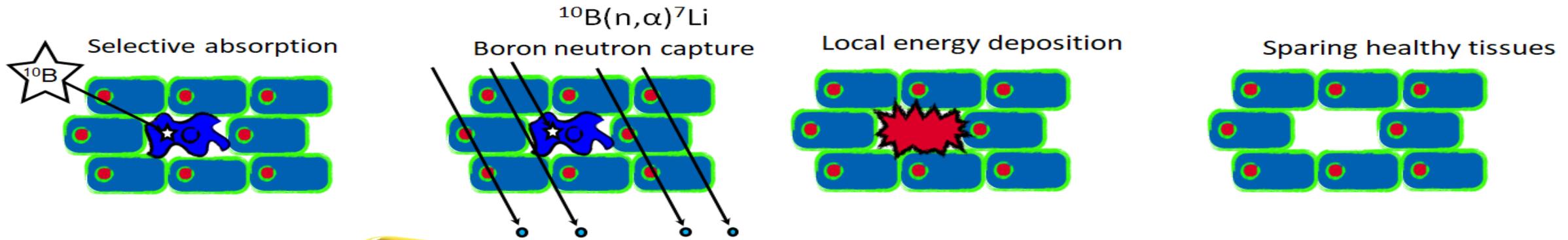
The measured profile is shown together with a gaussian fit. In the accelerator horizontal plane the bar of charge distribution is visible.

Gantry at 90° (horizontal beam)

Beam energy 228 MeV

$1.25 \cdot 10^{10}$ protoni/spill (nominal $3 \cdot 10^{10}$)

BORON NEUTRON CAPTURE THERAPY (BNCT)



BNCT@CNAO Collaboration
CNAO - INFN - PoliMi - UniPv - SMatteoPv



E_{proton} 2.5 MeV
Intensity 10-15 mA
Target p-Li

tae LIFE SCIENCES

Pre-clinical testing in 2027

PERSONNEL



Total Number: 172

Women: 96

Men: 76

Mean age: 43

Graduates: 76% (40% PhD + Master)

Positions: 28

Disciplines: 19

<i>February 2026</i>	<i>N</i>
Director General and Services	28
Scientific Directorate and Clinical Trial Centre	5
Clinical Department	77
Administration and Finance Department	18
Technical Department	38
R&D Department	8
Total	172

COLLABORATIONS

International

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Med-Austron (Wien)
NIRS (Chiba)
HIT (Heidelberg)
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Istituto Tecnico Cardano

THANK YOU!



www.cnao.it

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