HITRI*plus*

Heavy Ion Therapy Research Integration

Ion Therapy Centre (CNAO) and HITRI*plus* opportunities

Sandro Rossi

Director General - CNAO Foundation

HITRI*plus* Coordinator

25th IPPOG Meeting in Sofia

12-13th May 2023

CNAO

Centro Nazionale di Adroterapia Oncologica

CNAO = National Centre for Oncological Hadrontherapy

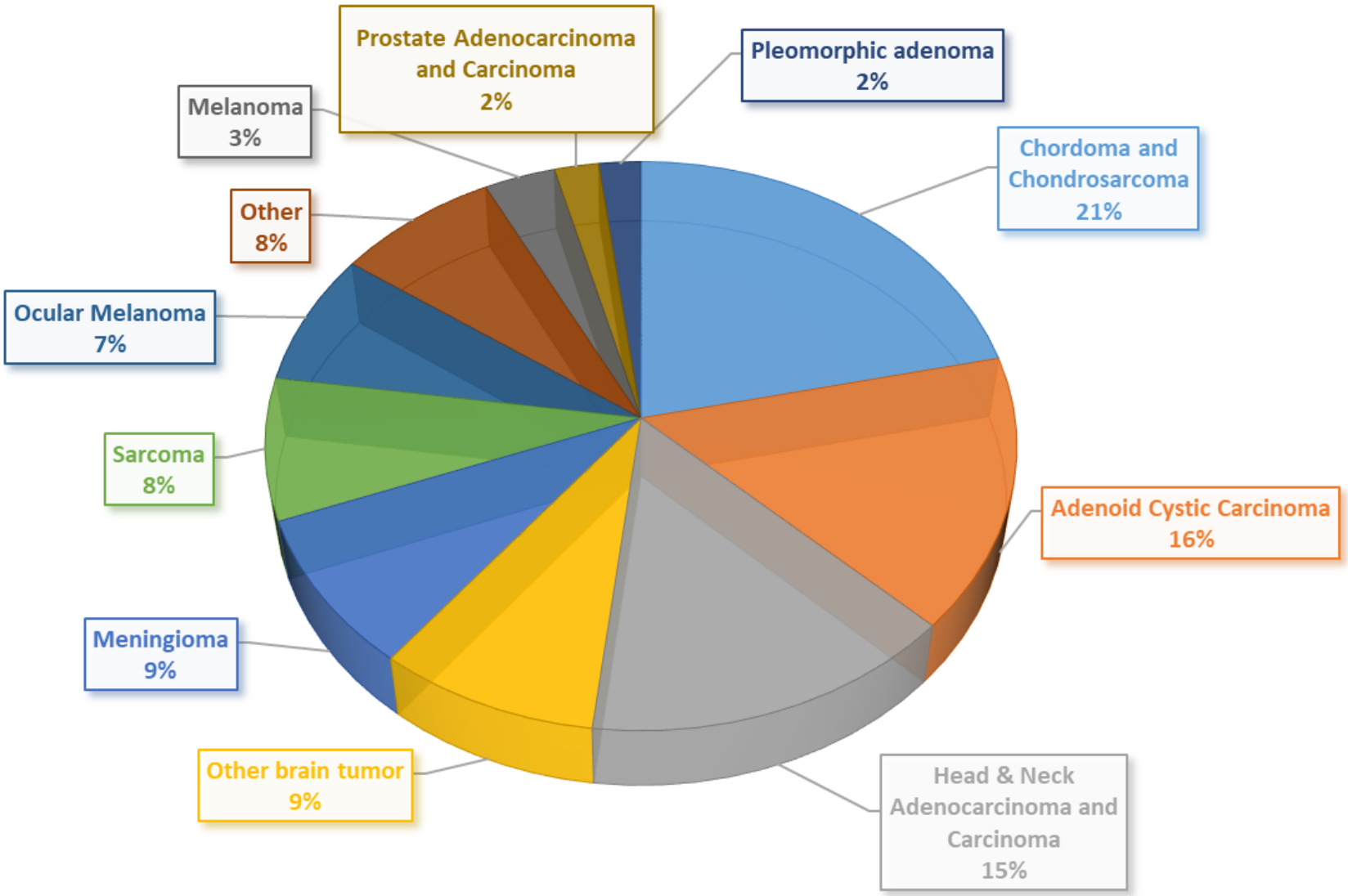
Not-for-profit private Foundation

Created by the Italian Ministry of Health in 2001

with the purpose to build and run a hadrontherapy Centre

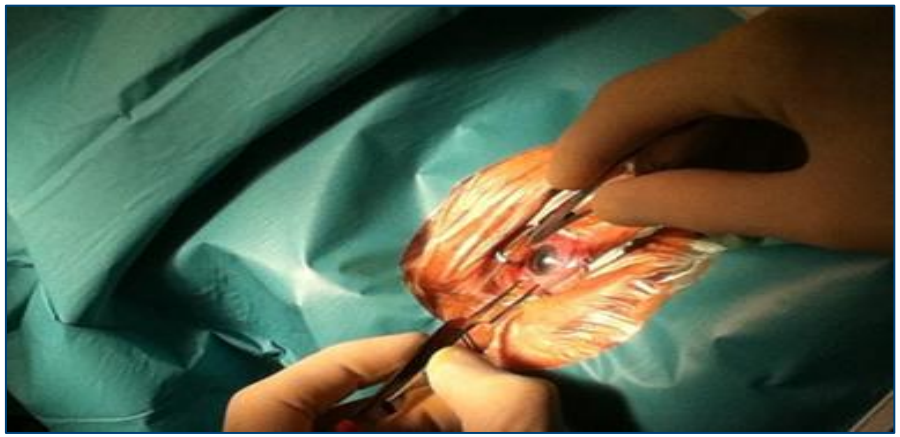
CNAO: >4400 patients

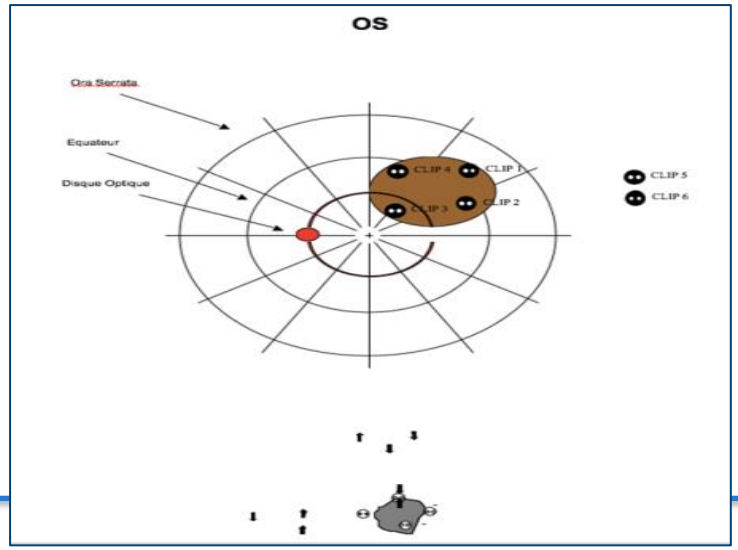
54% carbon ions- 46% protons



Ocular melanoma: small volumes

INT – Milan + Galliera – Genova:
patient selection and tantalium clips



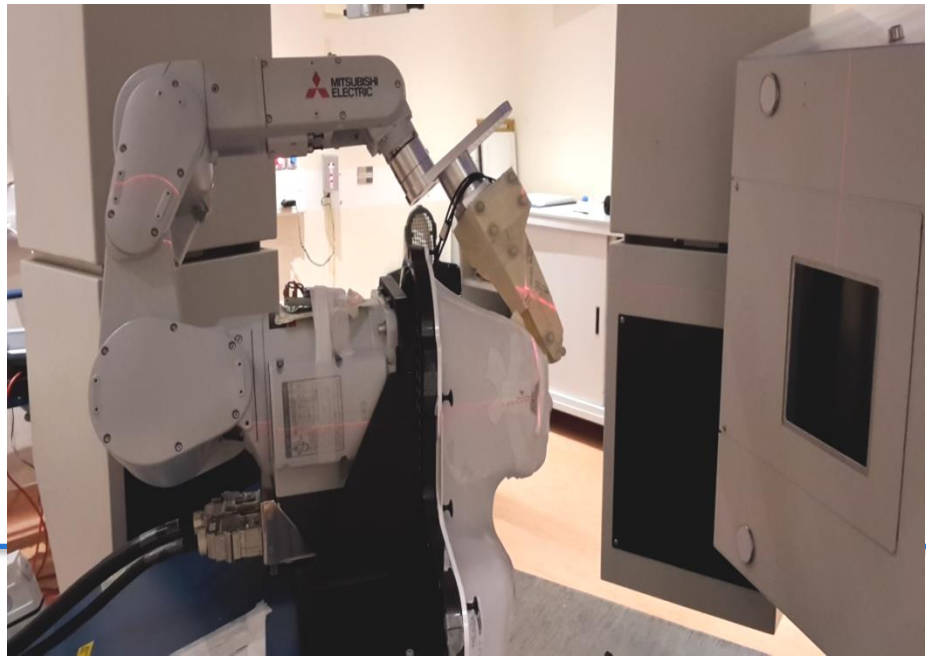


> 400 patients

Protons: 60 GyE (4 fx)

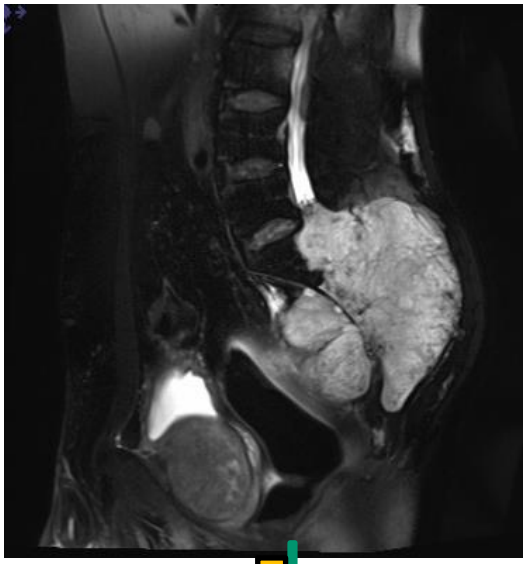
Local Control >95%
Eye preservation >90%
Visual function >45%

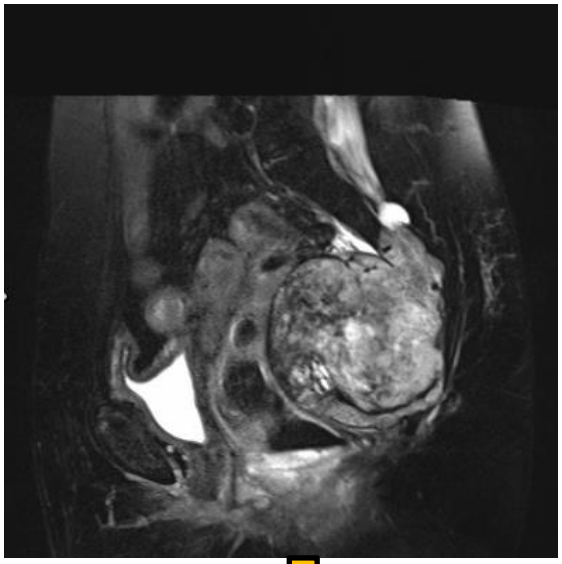
Collaboration with Politecnico Milano

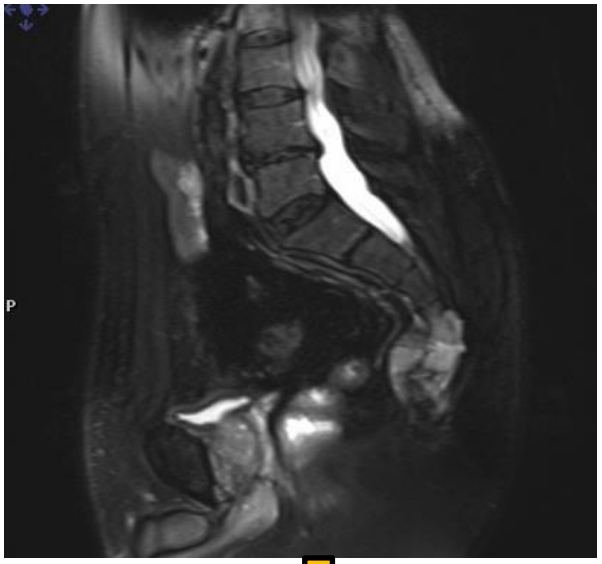


Sacral Chordoma: big volumes

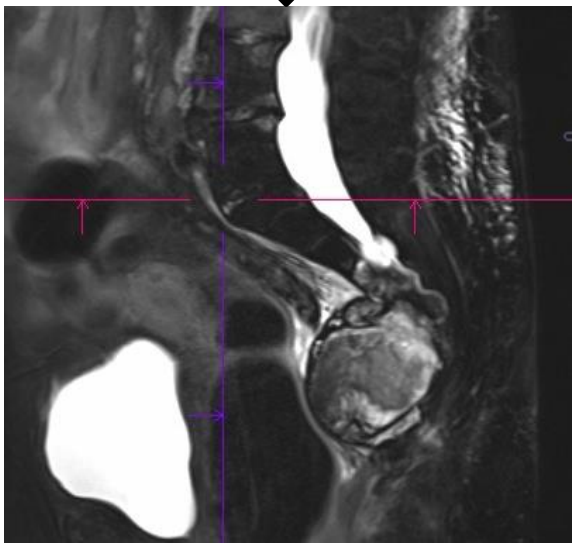
CIRT 74 GyE
16 fractions IMPT

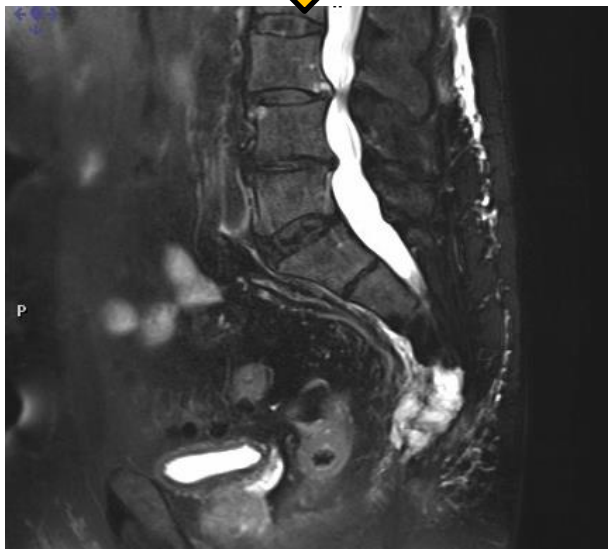






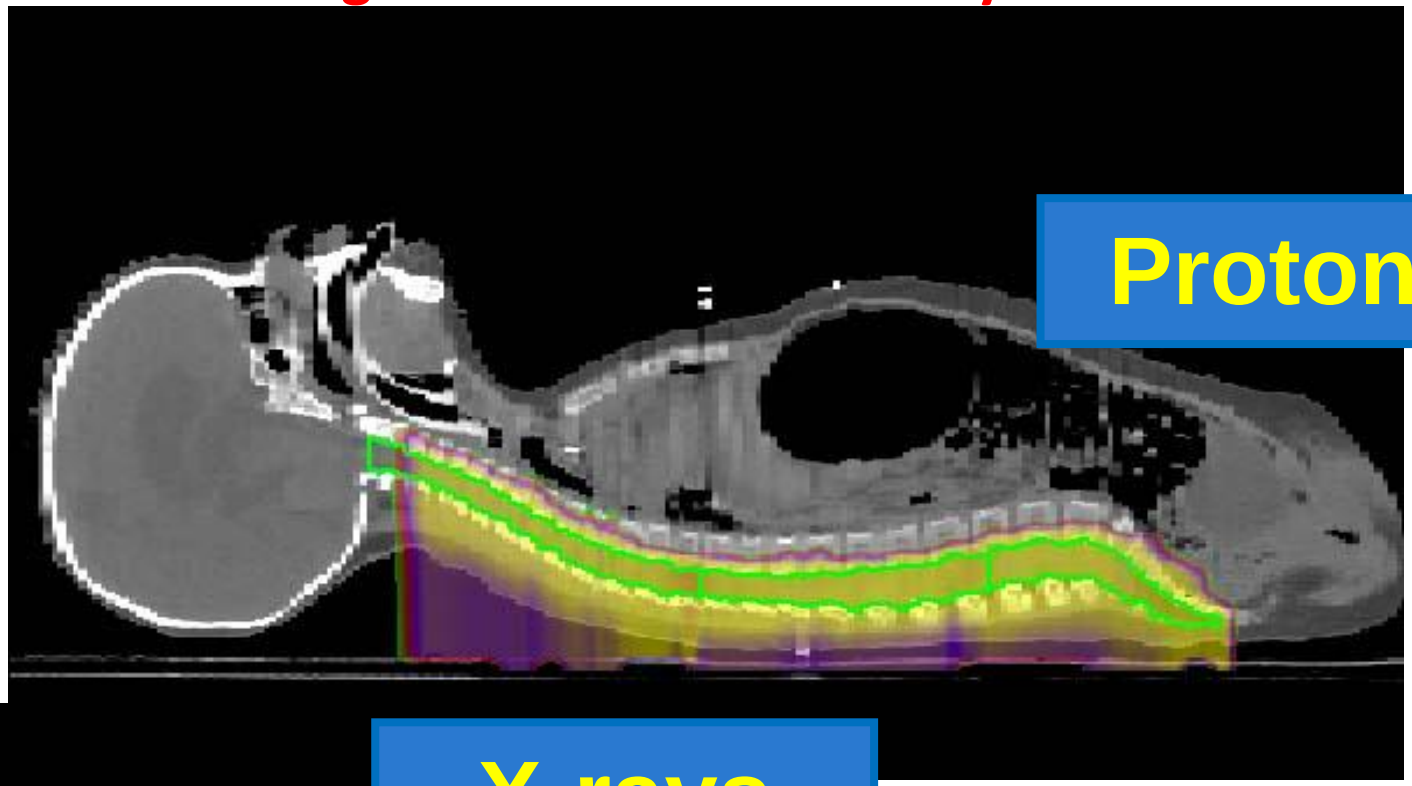
After 1 year

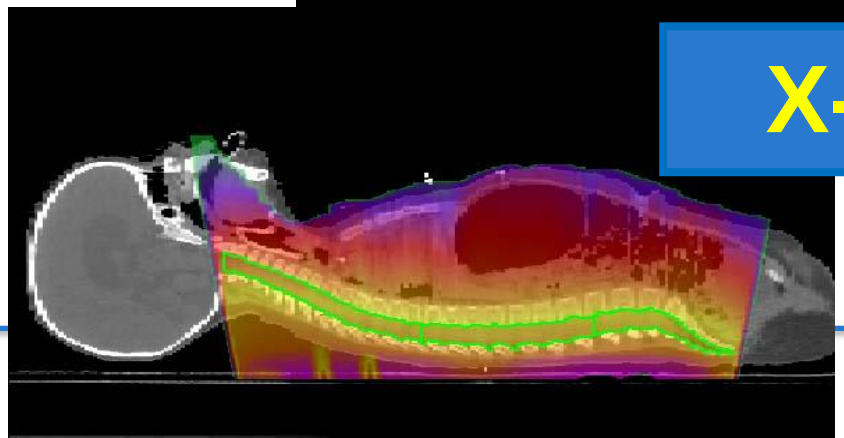




Pediatric patients elective for protons

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





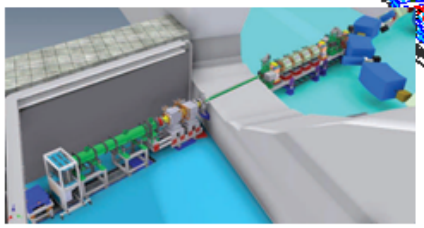

Technology at CNAO

The CNAO system: compact design for ions

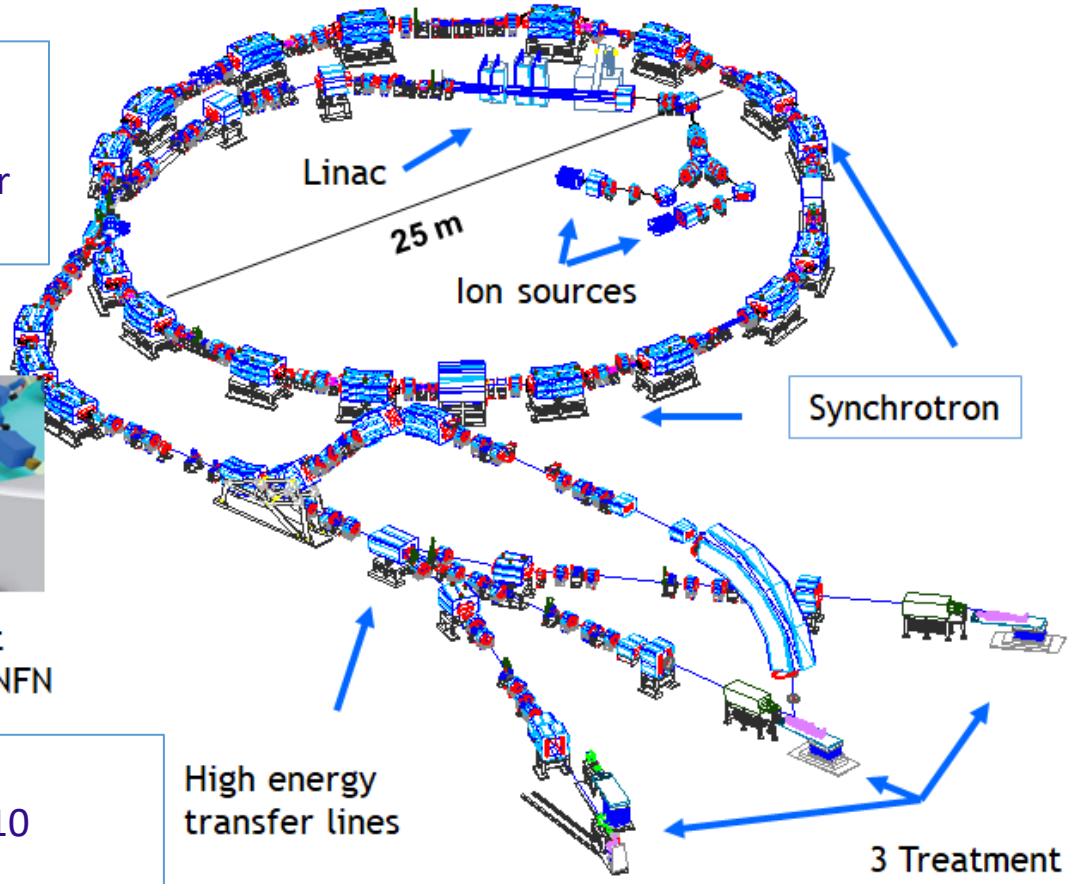
Intellectual property shared by CNAO – INFN - CERN

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

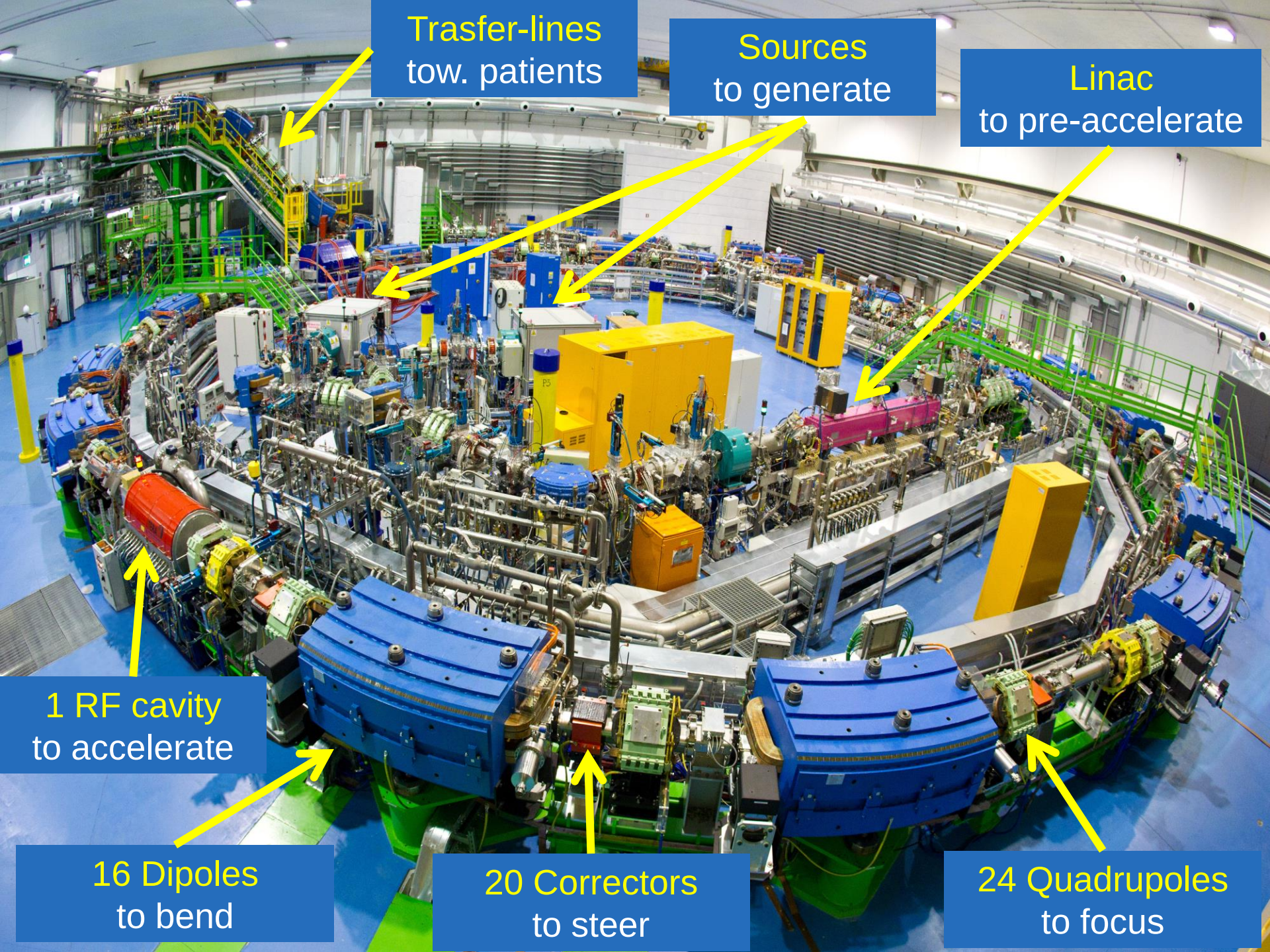
Extraction	Slow
Dose uniformity	± 2.5%
Average dose rate	2 Gy/min/liter



Research room built
in collaboration with INFN

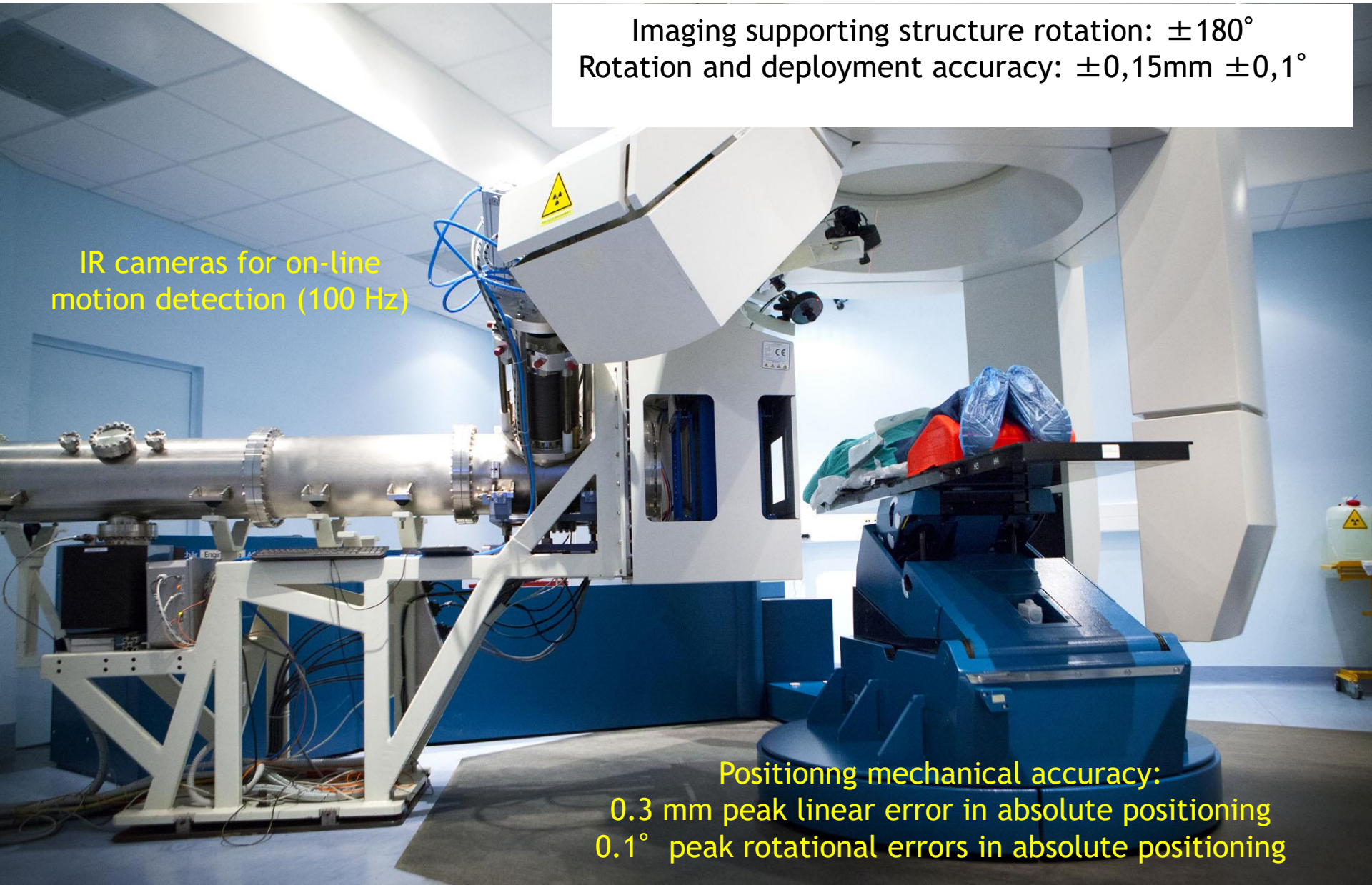


Field size (mm × mm)	200 × 200
Beam size (FWHM) (mm)	4-10
Beam position precision (mm)	0.1

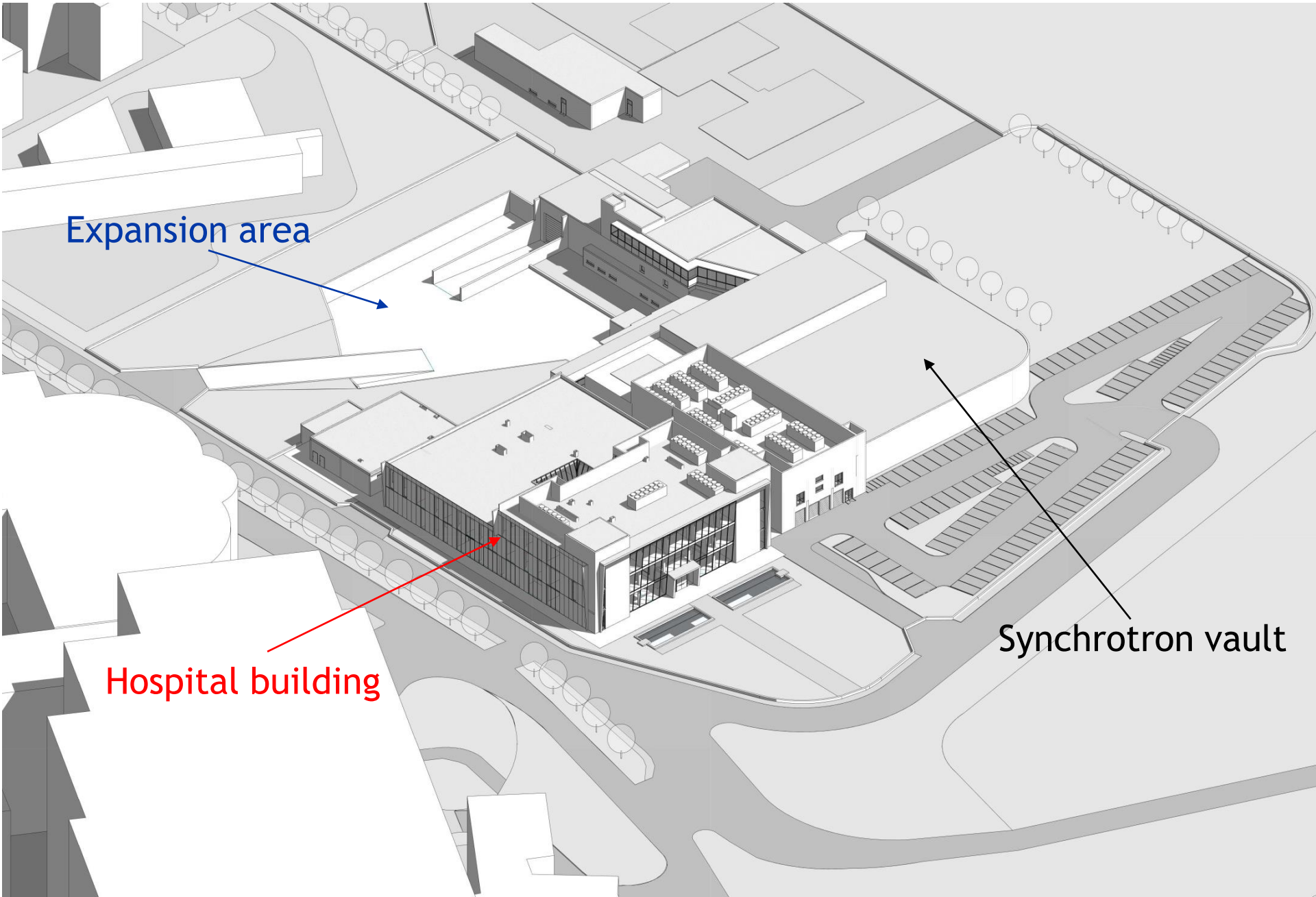

Trasfer-lines
tow. patients
Sources
to generate
Linac
to pre-accelerate
1 RF cavity
to accelerate
16 Dipoles
to bend
20 Correctors
to steer
24 Quadrupoles
to focus

Positioning and verification systems

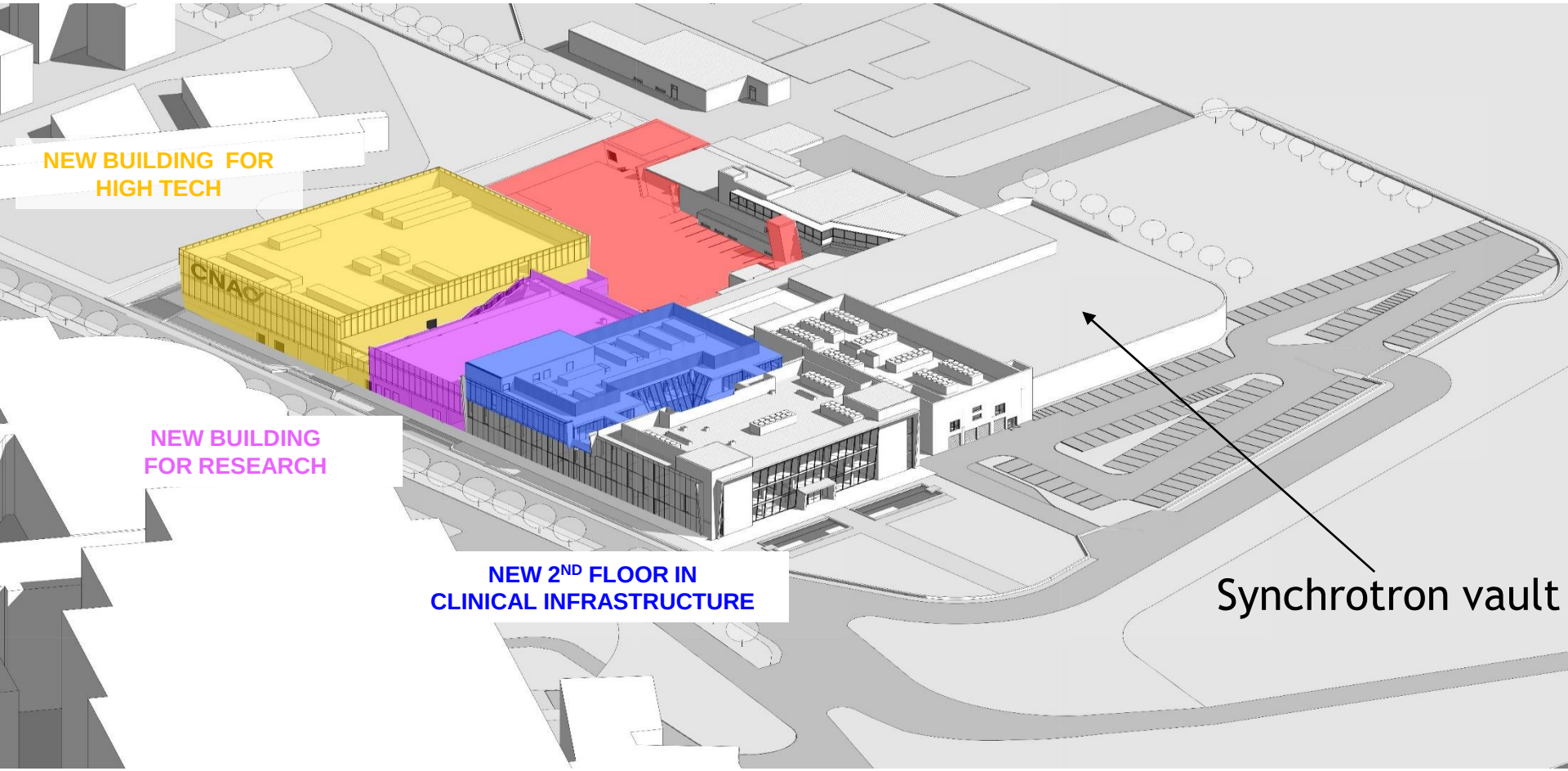
Imaging supporting structure rotation: ±180°
Rotation and deployment accuracy: ±0,15mm ±0,1°



Present layout



CNAO 2.0

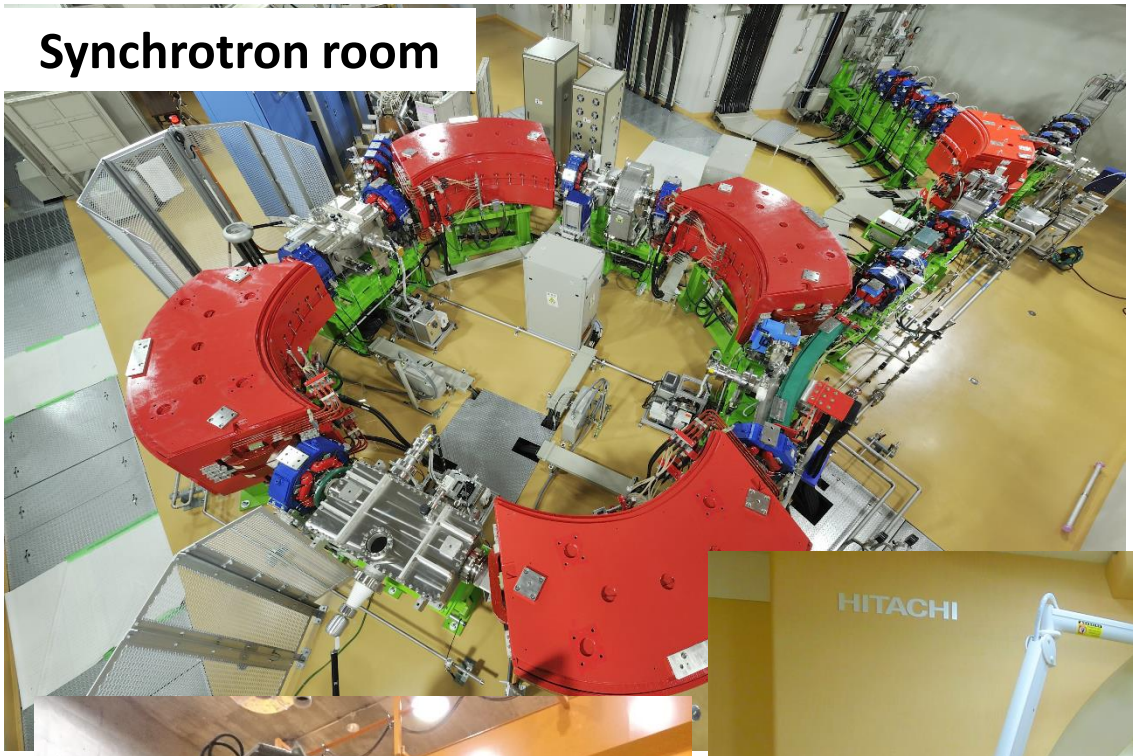


Layout by end 2023


SERMAC
MUSSELLI

New single-room for protons

Synchrotron room



Start installation end 2023

360° isocentric gantry
(Field size: 30x40 cm²)

Treatment room

BNCT: proton tandem accelerator

Start installation Q1/24

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

alpha beam™

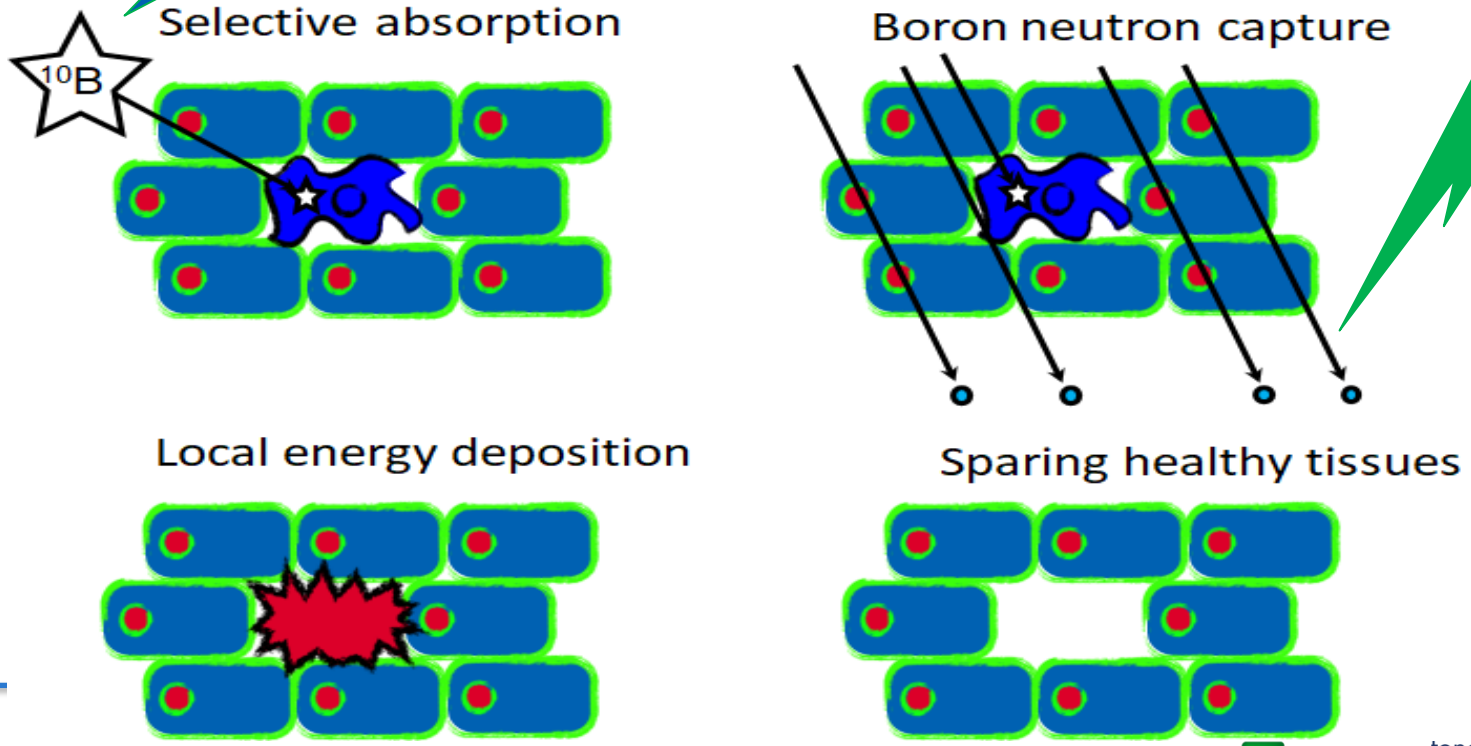
tae LIFE SCIENCES

BNCT: Boron Neutron Capture Therapy

2-steps research approach for metastasized tumours

Boronated drug that selectively reaches the tumour cells and avoids the healthy tissues

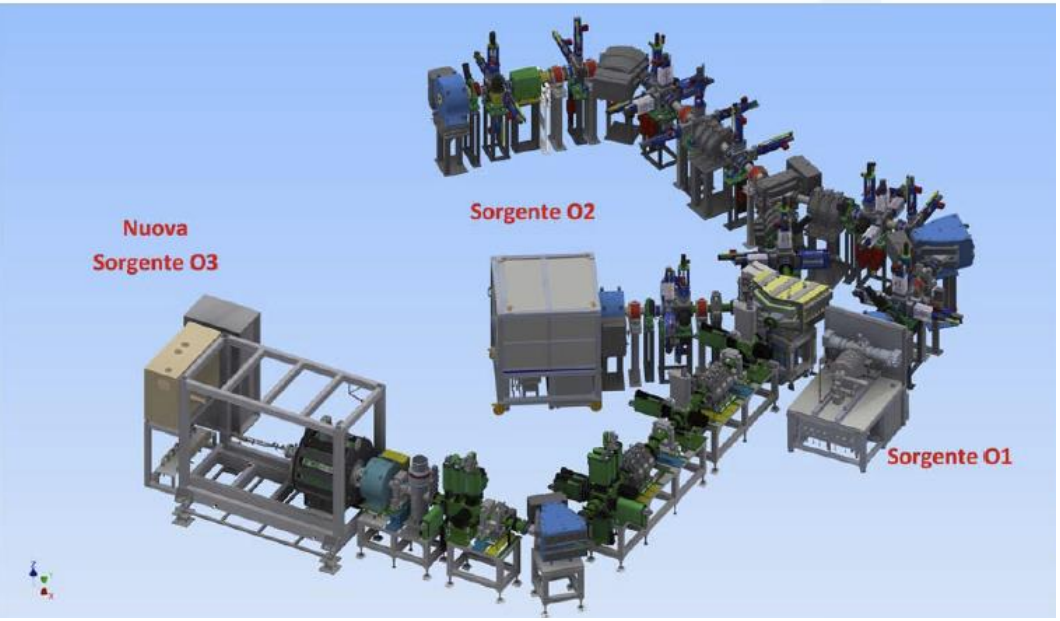
Accelerator driven neutron production




Research at CNAO

INSpIRIT: new ion source

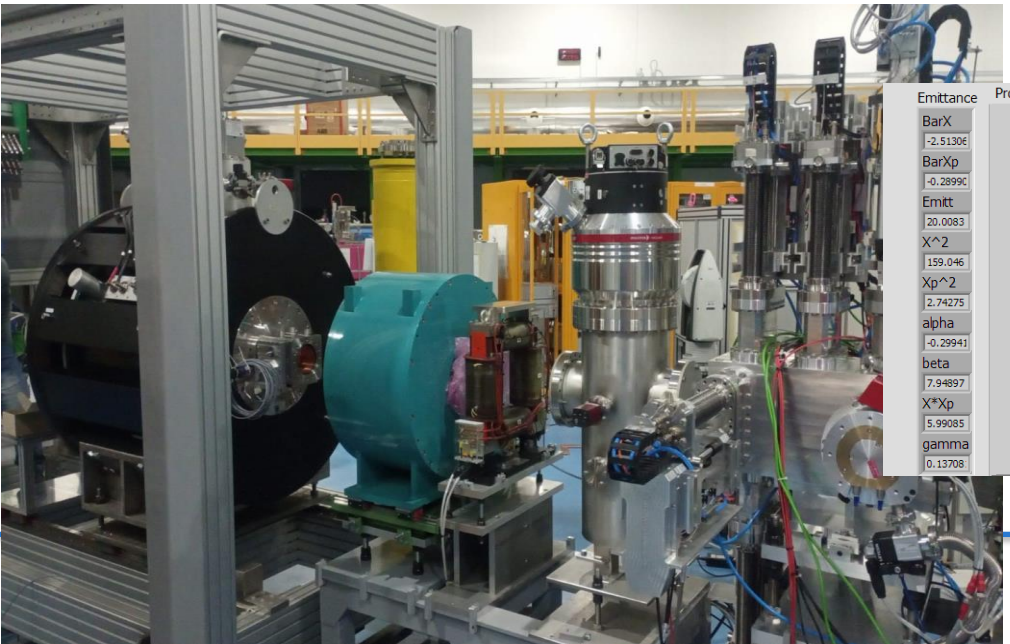
Collaboration CNAO-INFN-HiFuture

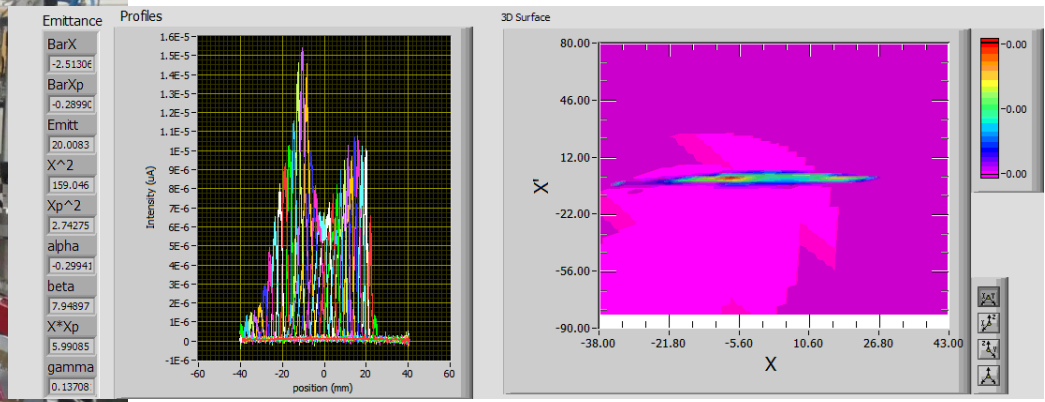


Expected currents

Ion beam production (eμA)

Ion	Supernanogan (14 GHz)	AISHa (18 GHz + TFH)
H^+	2000	4000
H_2^+	1200	2000
H_3^+	1000	1500
$^3He^+$	800	2000
$^{12}C^{4+}$	250	800
$^6Li^{2+}$ - $^7Li^{2+}$	//	800
$^{10}B^{3+}$ - $^{11}B^{3+}$	//	600
$^{18}O^{6+}$	400	1000
$^{21}Ne^{7+}$	120	500
$^{36}Ar^{12+}$	20	150





Vertical emittance Helium beam

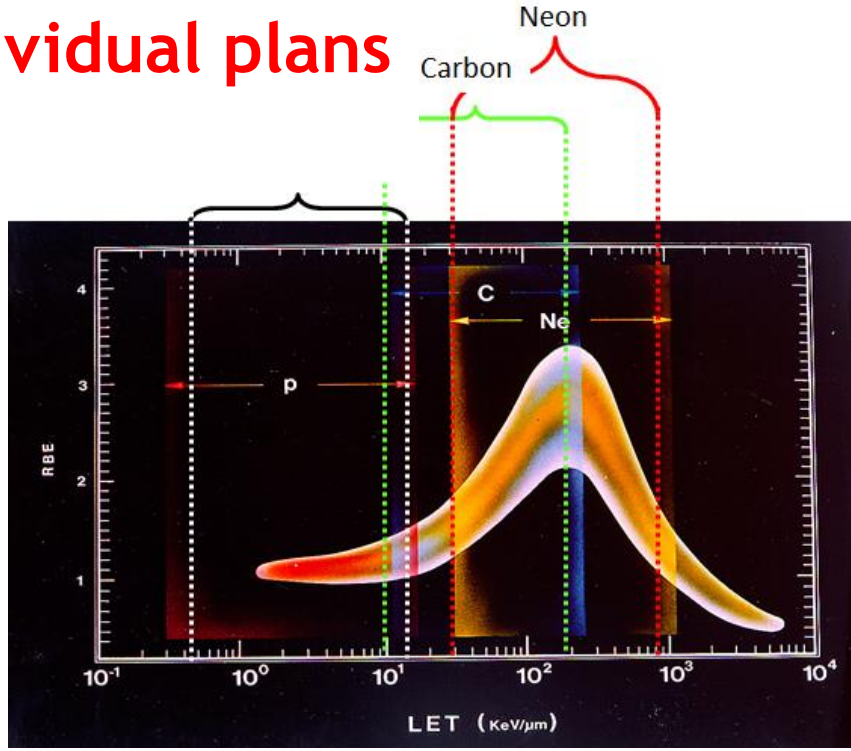
Multi-ion treatment for best individual plans

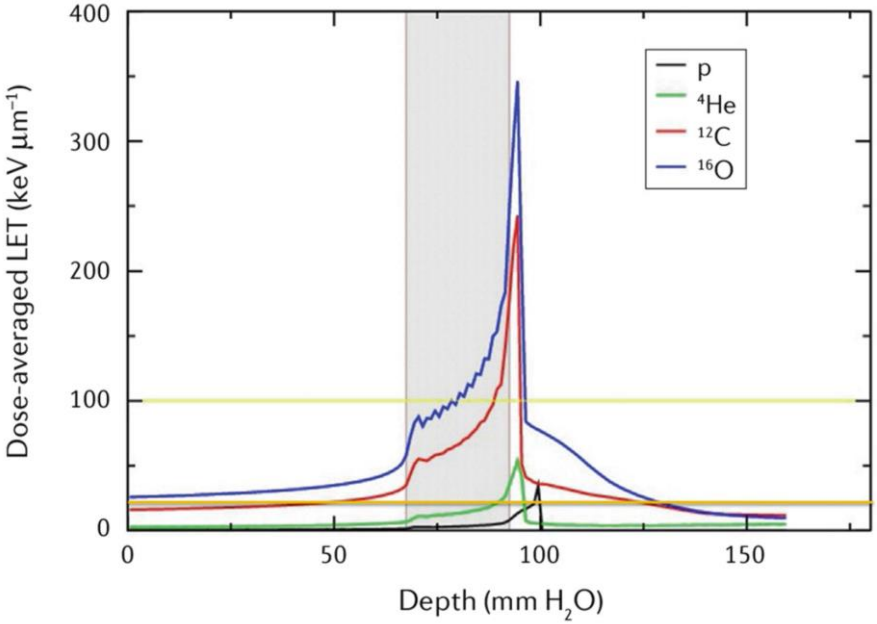
proportional to the square of the ion charge, inversely proportional to the square of particle velocity

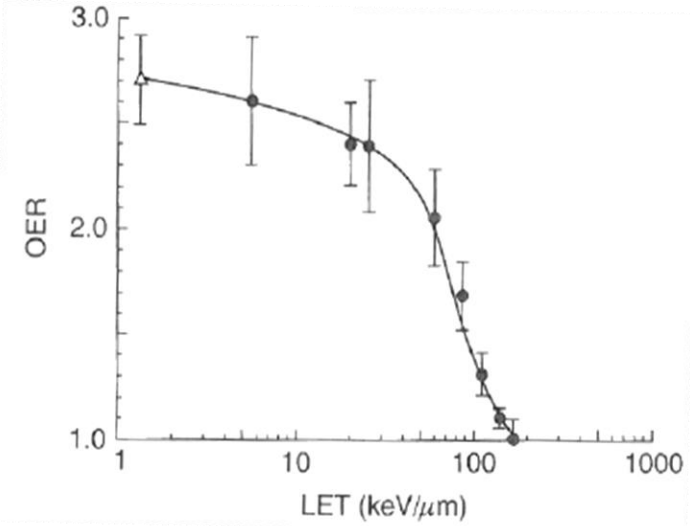
***Scattering** (good>A) – **Fragmentation** (bad>A)*

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

***OER** = ratio of the doses producing the same effect in hypoxic (0% pO_2) and oxic (20% pO_2) conditions*

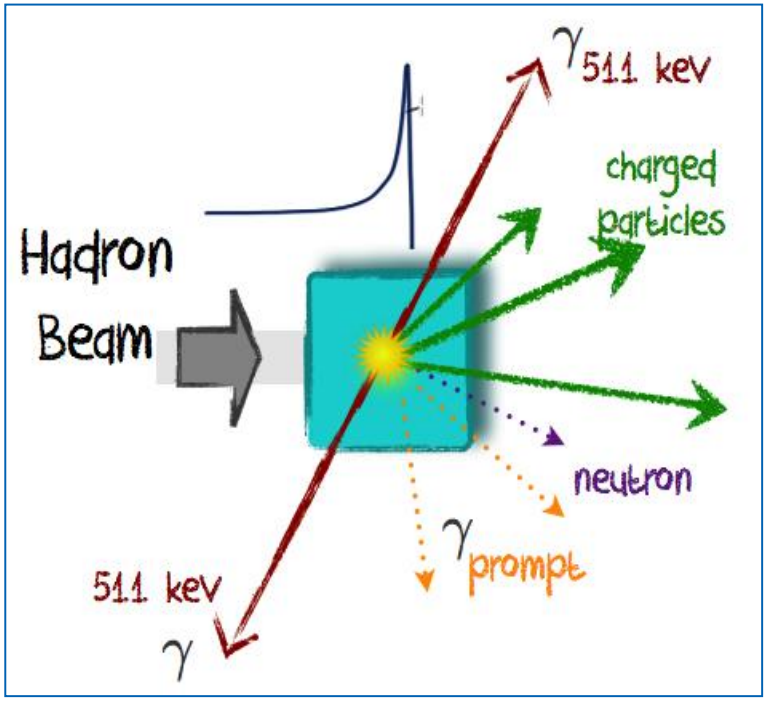






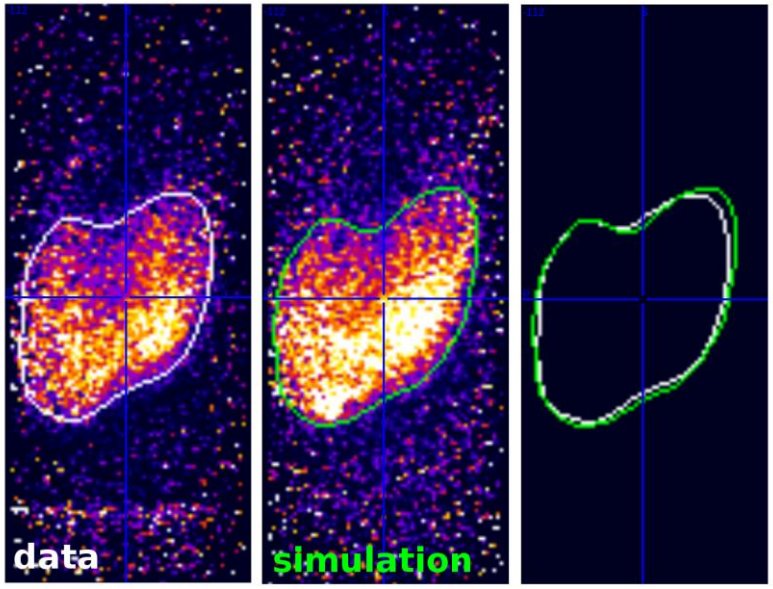
RADIOBIOLOGY EXPERIMENTS: IN-VITRO & IN-VIVO

Dose and Beam range monitoring



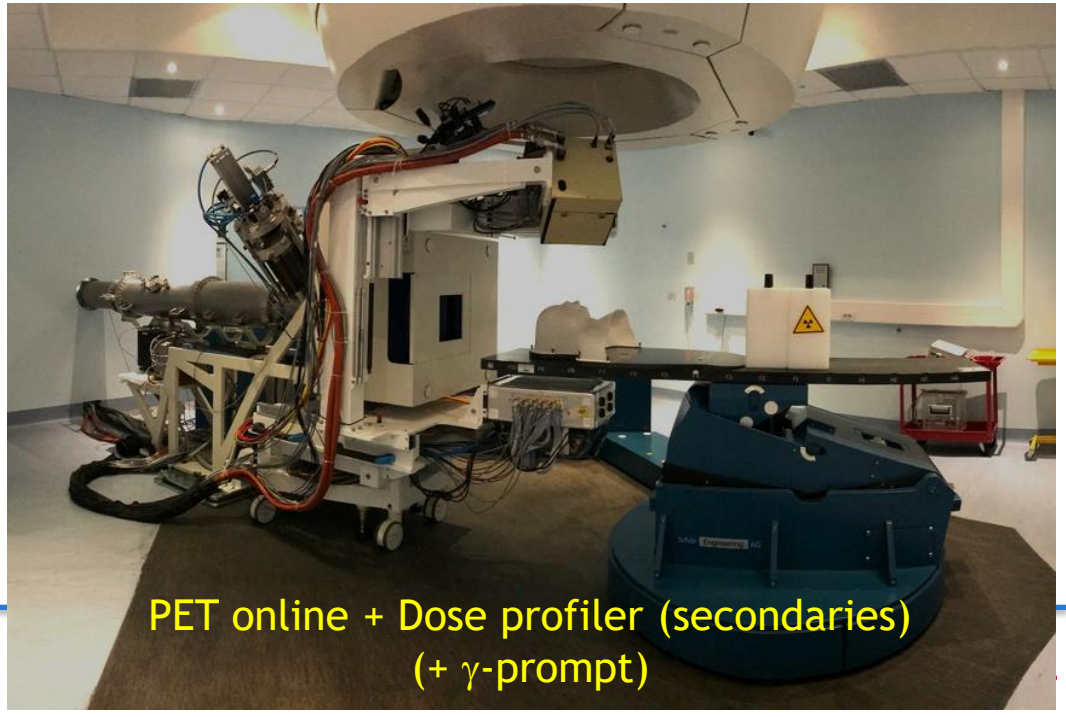
Patient - 01/12/2016
Proton beam
4 min treatment + 1min after

InSide



Goal: dose monitoring pre-treatment range assessment

(Collaboration with INFN UniPi - UniTo)



R&D: new carbon ion gantry

Collaboration CNAO-INFN-CERN-MedAustron

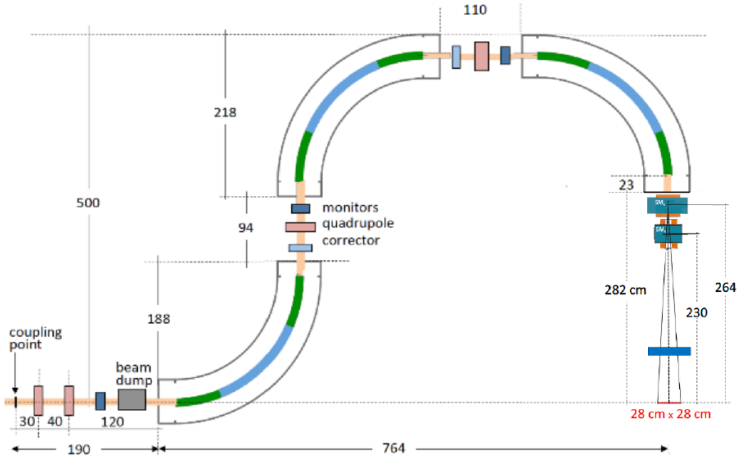
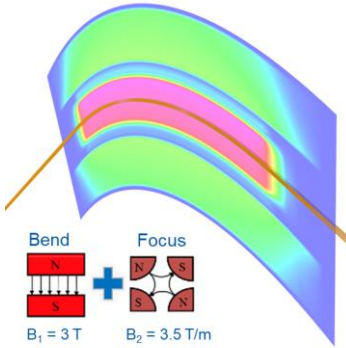
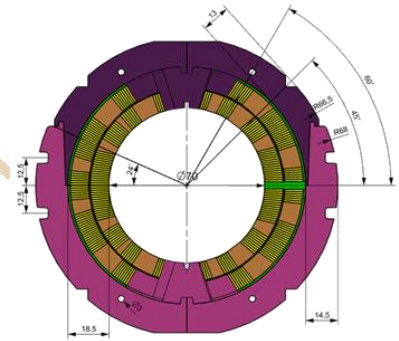


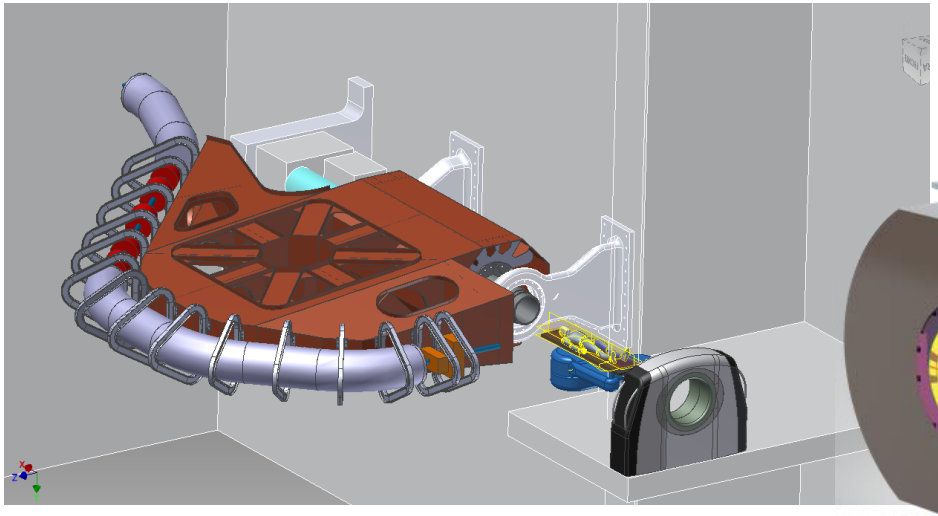
Figure 1. *Layout of the gantry and the scanning system based on 90° canted cosine theta magnets running at 4 T.*

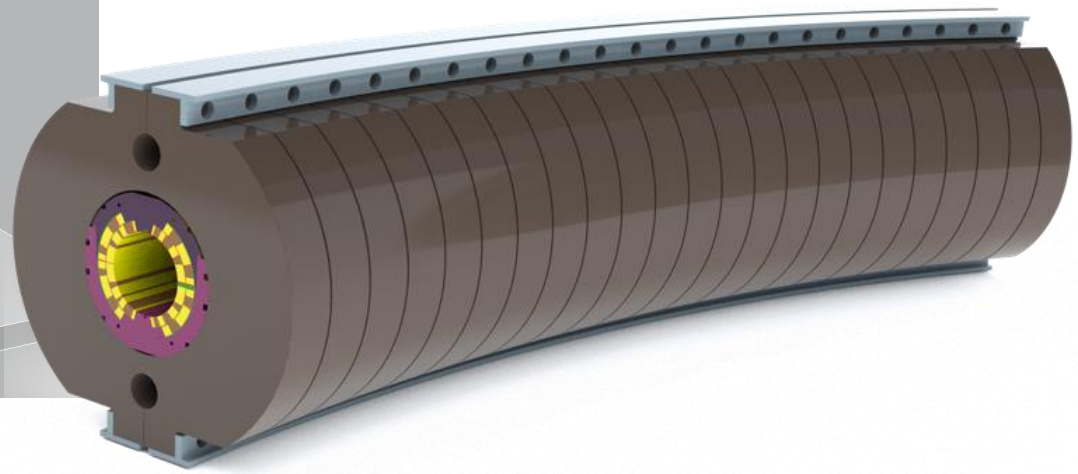
Superconducting Magnet Design



Final design: Dip+Quad
= combined funtion







Radiomics, Dosiomic …

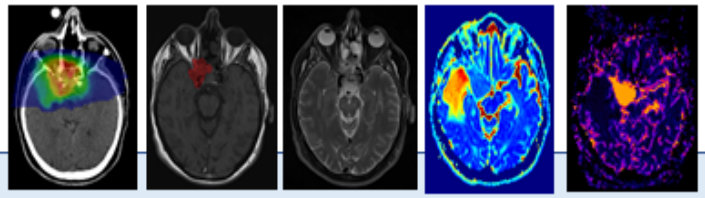
strategies for individual treatment optimization

and outcome prediction (Collaboraboration with PoliMi)

AIRC IG-2020 n. 24946
PI: Prof. Baroni G.

Technical framework

MULTI-PARAMETRIC IMAGING



CT + dose maps
Anatomical MRI (T1-w, T2-w)
Quantitative MRI (DWI, PWI,…)

PRE-PROCESSING
image segmentation, intensity normalization, …

FEATURE EXTRACTION
Radiomics, Dosiomics, candidate features, biomarkers, …

MACRO
modelling of properties at the MACRO level (e.g. DWI, PWI,…)

MICRO
modelling of properties at the MICRO level (e.g. cellularity)

MACHINE LEARNING-BASED MODELS

KNOWLEDGE-BASED RADIOBIOLOGICAL / STRUCTURAL MODELS
Tumour control probability (TCP), NTCP, microstructural model, …

VALIDATION

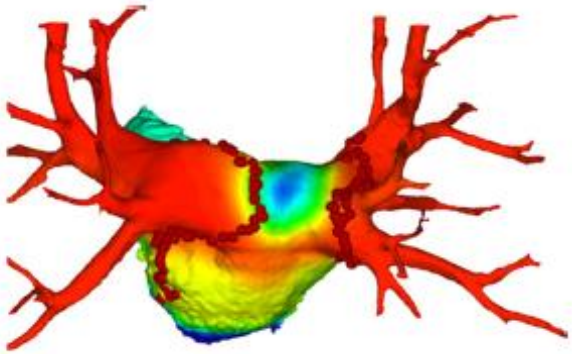
TECHNICAL

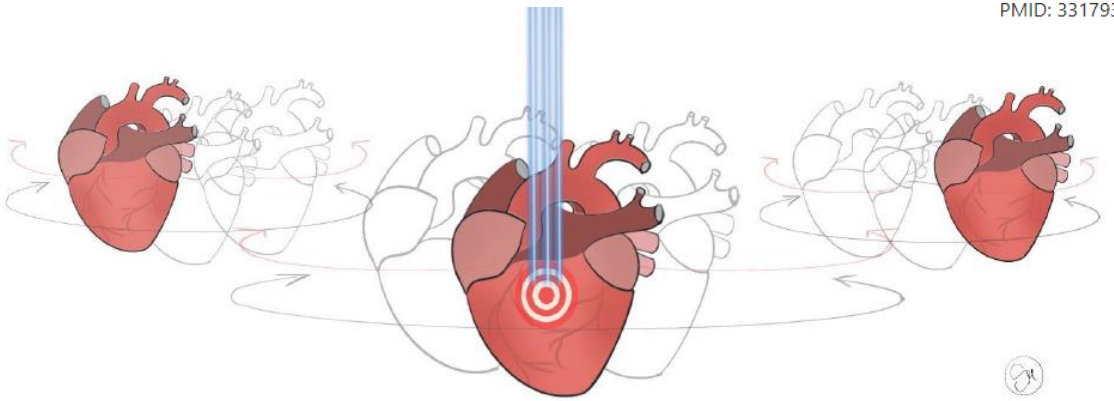
BIOLOGICAL – CLINICAL

Non oncological application: ventricular arrhythmia

(Collaboration with San Matteo Hospital, Pavia)

Published on:
European Journal of Heart Failure





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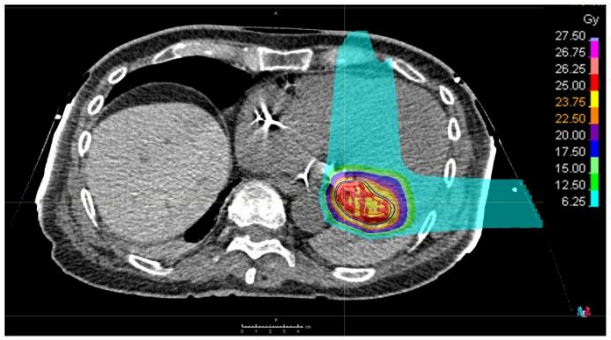
Eur J Heart Fail. 2020 Nov 12. doi: 10.1002/ejhf.2056. Online ahead of print.

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

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

Affiliations + expand

PMID: 33179329 DOI: 10.1002/ejhf.2056



HITRIplus PARTNERS

CNAO
BEVATECH
cea
CERN European Organisation for Nuclear Research
Laboratorio Nacional de Fusión Ciemat
COSYLAB
GSI Helmholtzzentrum für Schwerionenforschung
INFN Istituto Nazionale di Fisica Nucleare
MedAustron
PAUL SCHERRER INSTITUT PSI
1862 RIGA TECHNICAL UNIVERSITY
SEE ST South East European International Institute for Sustainable Technologies
UKGM UNIVERSITÄTSKLINIKUM GIESSEN UND MARBURG
UNIVERSITÄTSKLINIKUM HEIDELBERG
L-Università ta' Malta
Philipps Universität Marburg
UPPSALA UNIVERSITET UPPSALA UNIVERSITY SWEDEN
wigner
KLINIČKI CENTAR Crne Gore
Jožef Stefan Institute
SENTRONIS a SENIS company magnetic & current measurement
Cyril and Methodius University in Skopje

23 Institutes - 14 EU Countries

(4 CIRT centres, 11 research institutions, 5 universities, 3 SMEs)

4.5 years Project: 1st April 2021 – 30th September 2025

WP1: Management
WP13: Ethics Requirement

WP2: Networking and Communication, Dissemination and Outreach

WP3: Clinical networking

WP4: Innovation, technology transfer, industry relation

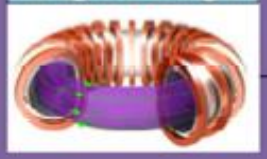
WP5: Education and Training

JRA
Joint Research Activities

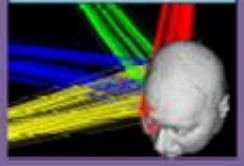
TNA
WP6
Transnational Access

WP7: Advanced accelerator and gantry design

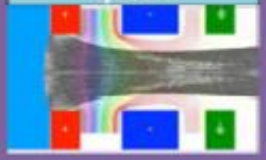
WP8: Superconducting magnets design



WP9: Advanced beam delivery

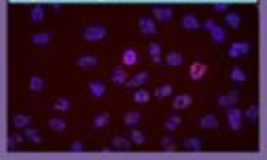


WP10: Multiple energy extraction system



WP11: Controls and safety

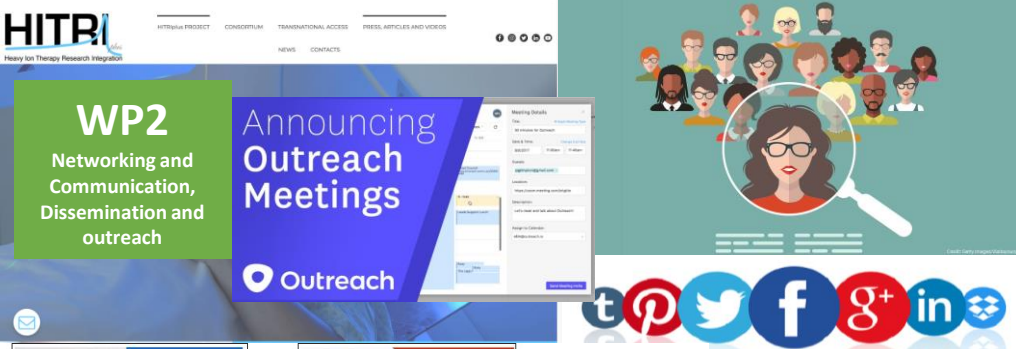
WP12: Radiobiology and quality assurance



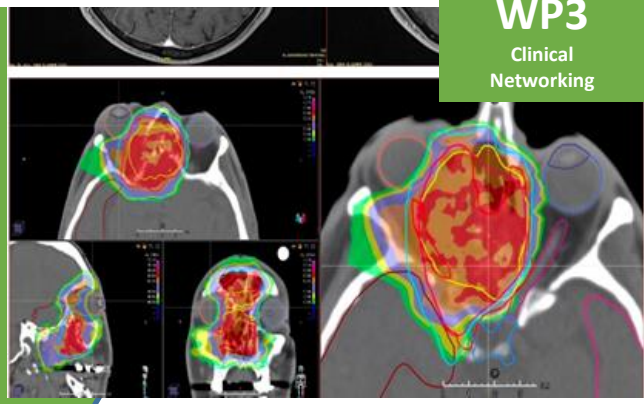
HITRI*plus* NA

- ✓ Design **one trial** as a template for bringing innovative heavy ion therapy approaches in the clinics
- ✓ Set up a **European registry** to collect data on rare cancers treated with heavy ion therapy
- ✓ Review existing data on **OARs dose costraints** in use in the clinical facilities

WP2
Networking and Communication, Dissemination and outreach



WP3
Clinical Networking



WP5
Education and Training

WP4
Innovation, Technology transfer, Industry relation

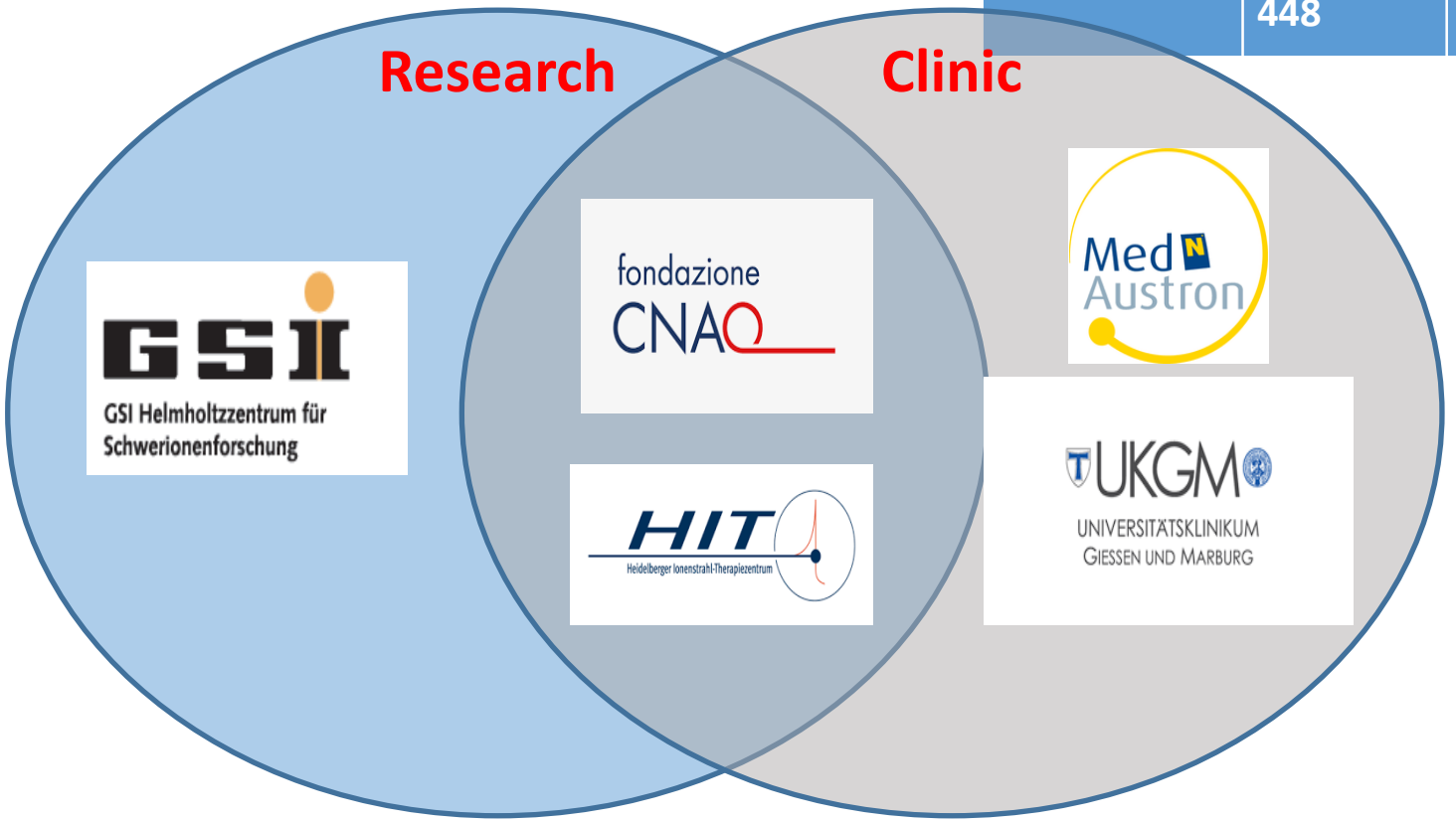
Education and training – international specialised course on **Clinical Aspects of Heavy Ion Cancer Therapy Research**

From the **3th to the 7th of July 2023**, online on zoom; https://indico.cern.ch/event/1248018/
This school will cover clinical aspects and it is primarily intended for **medical students specialising or who are considering to specialise in oncology as well as clinicians of all levels in radiotherapy and particle therapy.** The course will be delivered by over 35 world-leading clinicians in the field and will focus on head and neck, sarcoma, prostate, liver, pancreas, gynae and rare indications, re-irradiation, innovative methods, organ motion, treatment planning, present and future clinical trials and radiobiology.
The course also includes a "train-the-trainer" session based on the professional, open-source, research toolkit **matRad**, tailored to students' and researchers' requirements in treatment planning.

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

WP6: Transnational Access

	Res. [h]	Clin. [accesses]	Total
CNAO	80	12	92
GSI	296	-	296
UKHD/HIT	72	10	82
MEDA	-	12	12
MIT	-	16	16
	448	**50**	**498**



HITRI*plus*
Heavy Ion Therapy Research Integration

JOIN HITRI*plus* THE EUROPEAN HEAVY ION THERAPY RESEARCH COMMUNITY

PLAY YOUR PART IN THE COMMUNITY AND WORK TOGETHER THE MOST EXPERIENCED CLINICIANS AND RESEARCHERS

500 hours of transnational access (TNA) at one of the **four heavy ion centres in Europe** and at the worldwide leading accelerator facility of the GSI

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

HITRI*plus*
Heavy Ion Therapy Research Integration

www.hitriplus.eu

CLINICAL RESEARCH ACCESS

REFER PATIENTS TO THESE FACILITIES AND PERSONALLY PARTECIPATE TO CLINICAL RESEARCH.
IMPROVE YOUR KNOWLEDGE ON HEAVY ION THERAPY

CNAO, HIT, Marburg, MedAustron will be glad to welcome physicians, oncologists, radiotherapists and medical physicists willing to perform clinical research:

- discussing the eligibilities
- comparing treatment plans
- taking part in research clinical trials

THE BEST OF CLINICAL RESEARCH ON:

- Chordoma & chondrosarcoma base/spine
- Meningiomas
- Brain tumors (trunk)
- ACC Salivary Glands
- Orbit tumors including eye melanoma
- Sinonasal carcinoma
- Soft Tissue & bone Sarcoma (every sites)
- Recurrent tumors (retreatment)
- Immulogical desorders

CLINICAL RESARCH IN HADRONTHERAPY AT NO COST FOR SCIENTIFIC PROGRESS AGAINST CANCER:

- Choose the treatment facility
- Stay at the centre with a group of 2-3 clinical researchers for up to one week
- Reimbursement for travel and accommodation

SCAN AND APPLY

RESEARCH ACCESS

SHARE RESEARCHERS HIGH LEVEL KNOWLEDGE AND BE INVOLVED IN PRECLINICAL RESEARCH AND NEW CHALLENGES

CNAO, GSI, HIT will be glad to welcome members of universities, research centres, and hospitals for carrying out research activities with heavy ion beams.

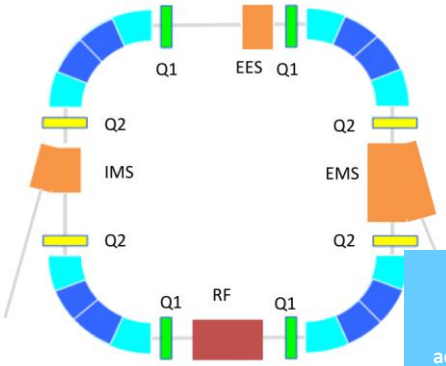
SUBMIT YOUR PROPOSAL FOR A NEXT LEVEL RESEARCH PROJECT ON:

- radiation biology for heavy ions radiotherapy
- medical physics of heavy ions
- nuclear physics applied to particle therapy
- new model systems for pre-clinical experiments with heavy ions

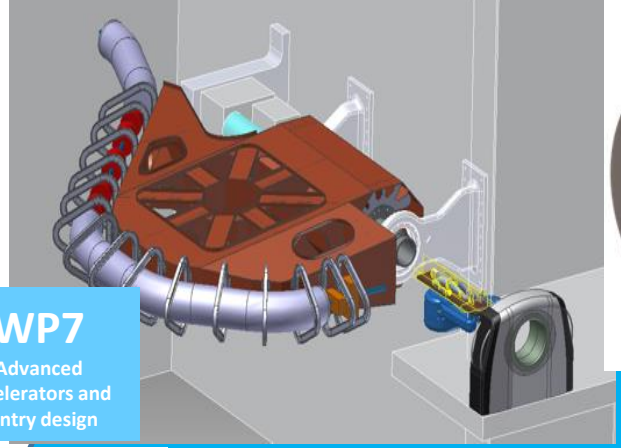
ION BEAMS AT NO COST:

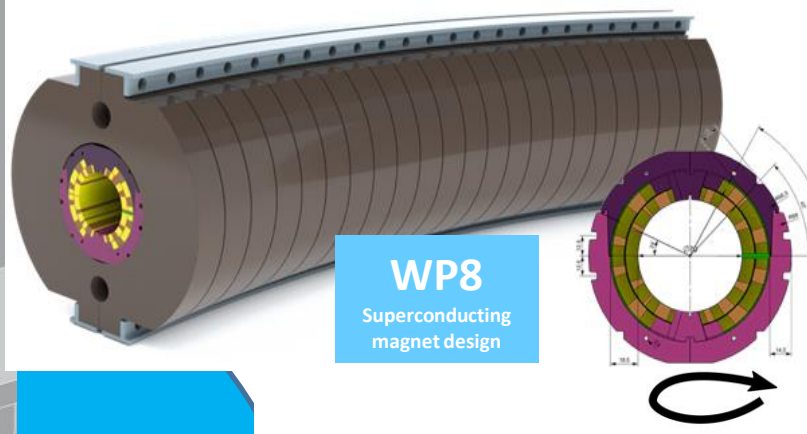
- Choose the research facility and plan your experiments with the experts
- Reimbursement for travel and accommodation

SCAN AND APPLY



WP7
Advanced accelerators and gantry design

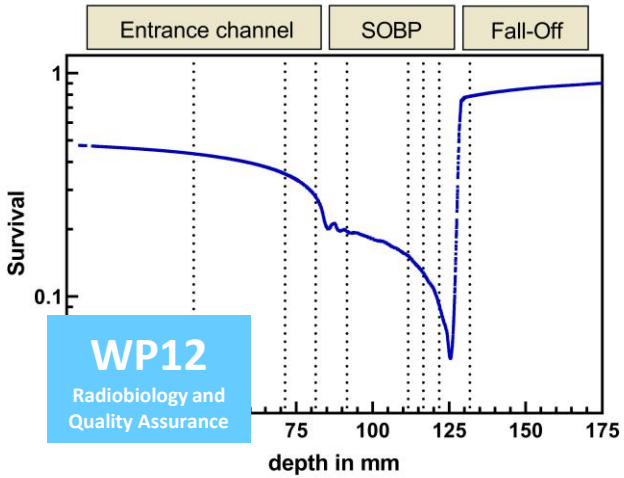




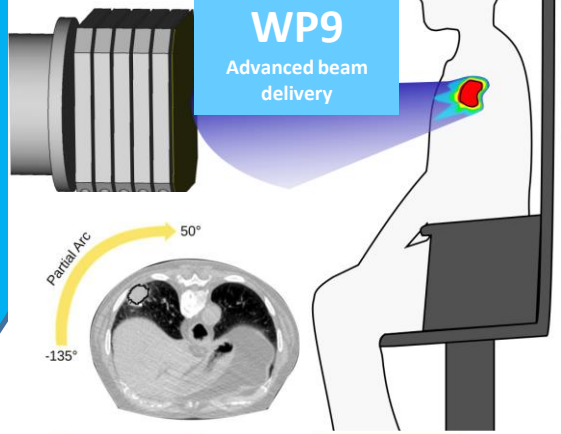
WP8
Superconducting magnet design

HITRI*plus*

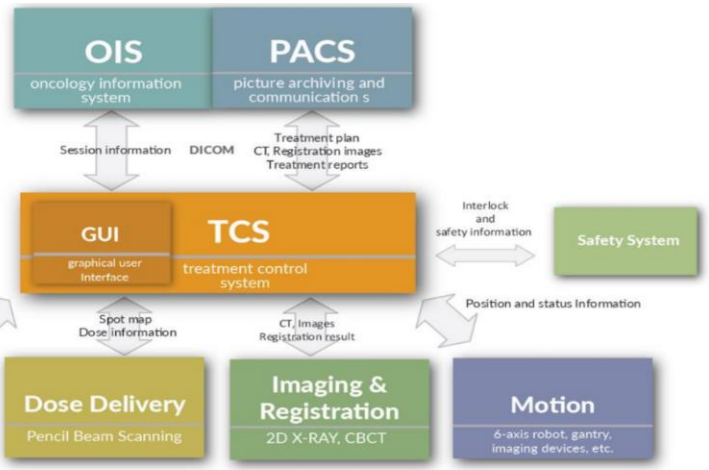
JRA



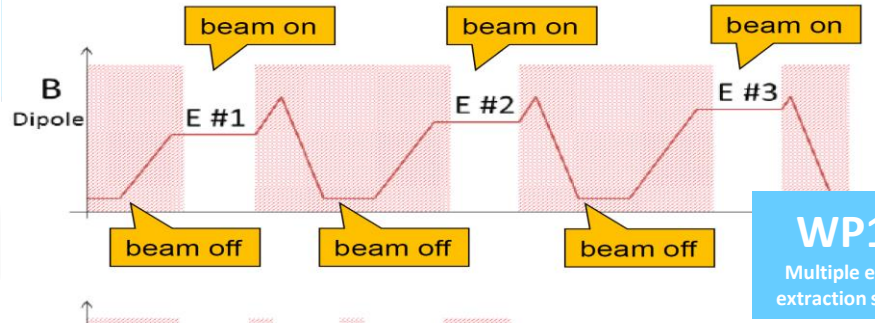
WP12
Radiobiology and Quality Assurance

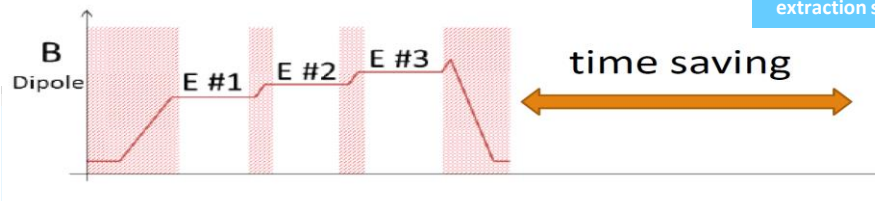


WP9
Advanced beam delivery



WP11
Controls and Safety





WP10
Multiple energy extraction system

CNAO
Centro Nazionale di Adroterapia Oncologica

THANK YOU!

https://www.hitriplus.eu/

https://www.cnao.it/

HITRI plus
Heavy Ion Therapy Research Integration

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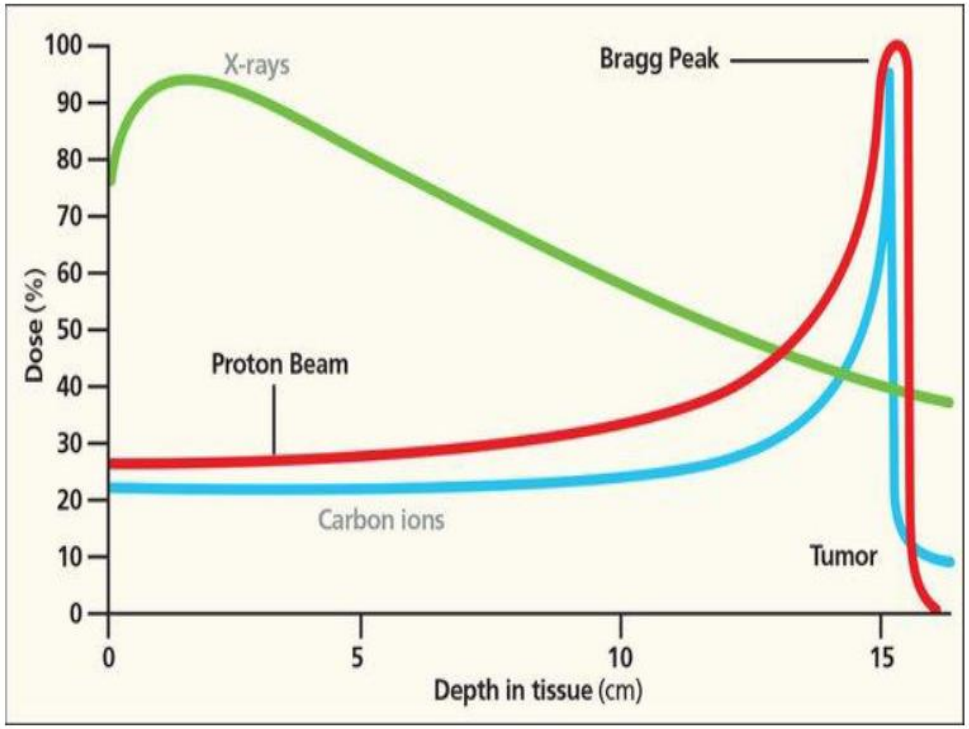
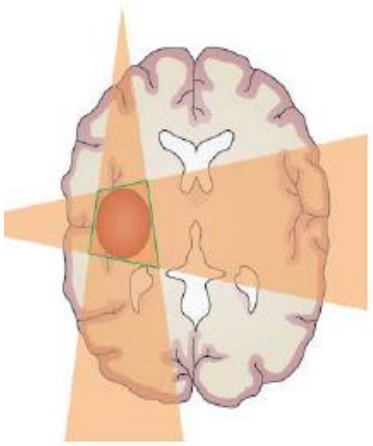
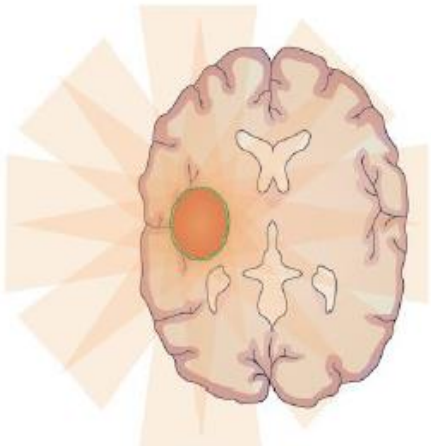
Hadrontherapy to treat ‘difficult’ cases: **Physics**

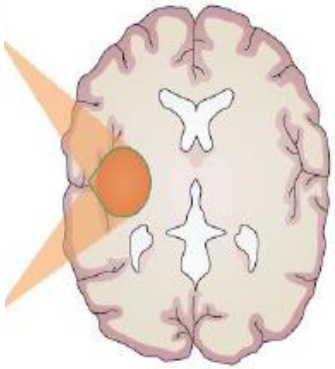




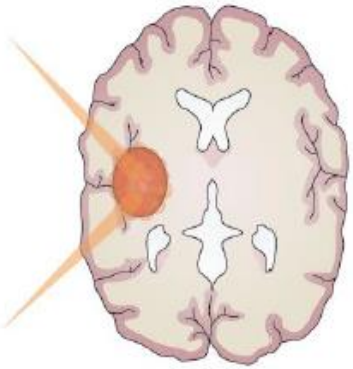
Conventional photon radiotherapy



Intensity modulated radiotherapy



Proton beam therapy



Pencil beam scanning proton therapy

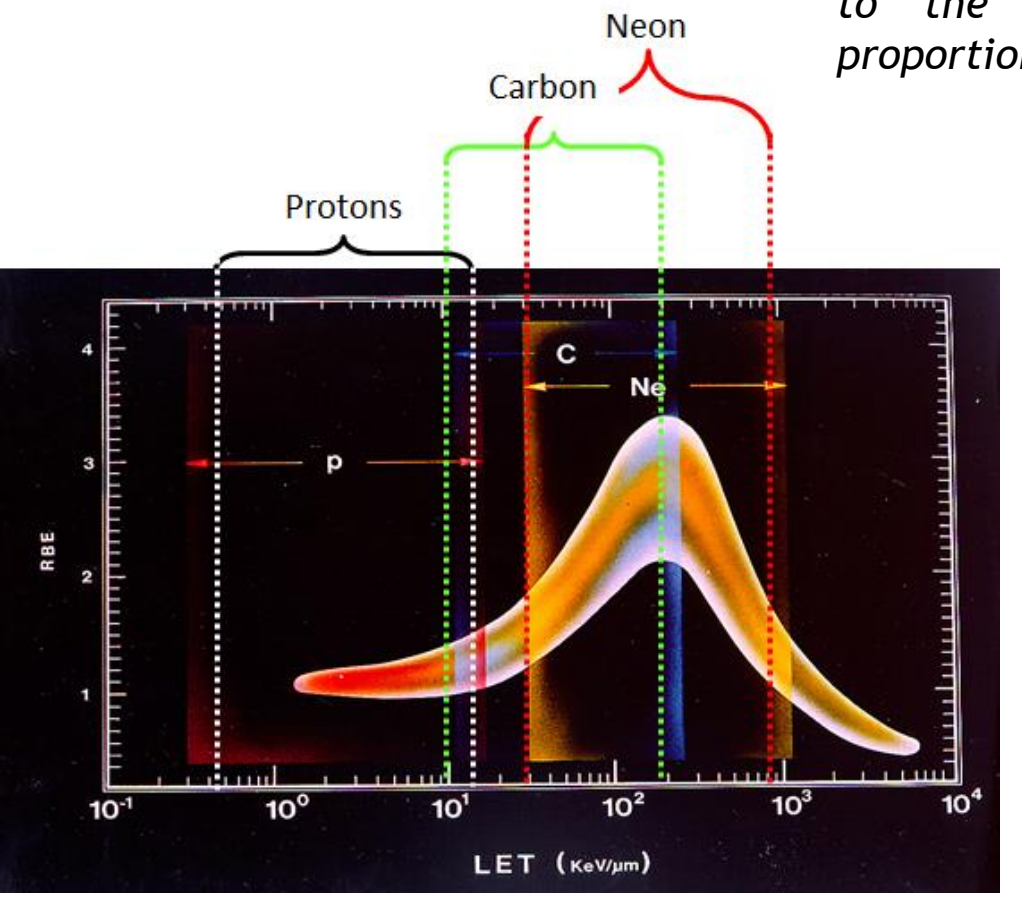
dosimetric benefit

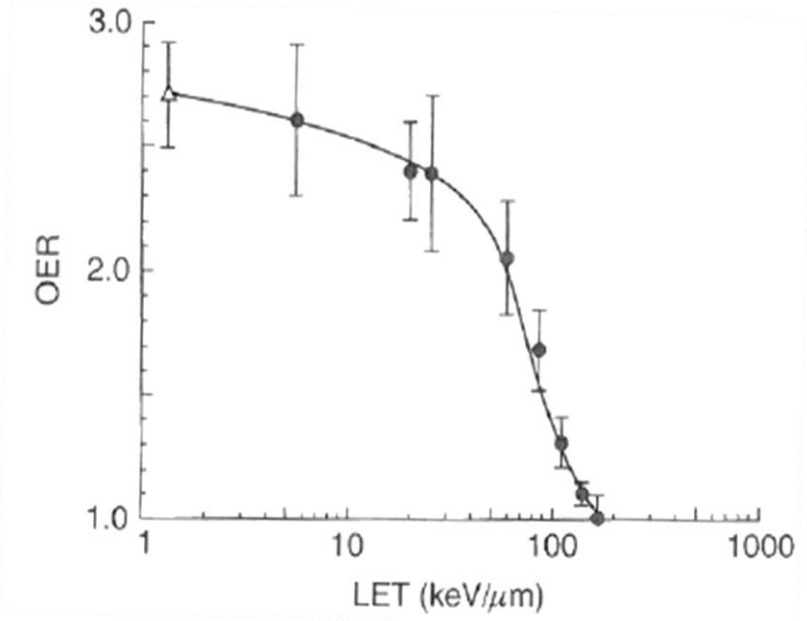
conditio sine qua non

clinical benefit

Hadrontherapy to treat 'difficult' cases:
Radiobiology

LET *= energy loss per unit mass lenght: proportional to the square of the ion charge, inversely proportional to the square of particle velocity*





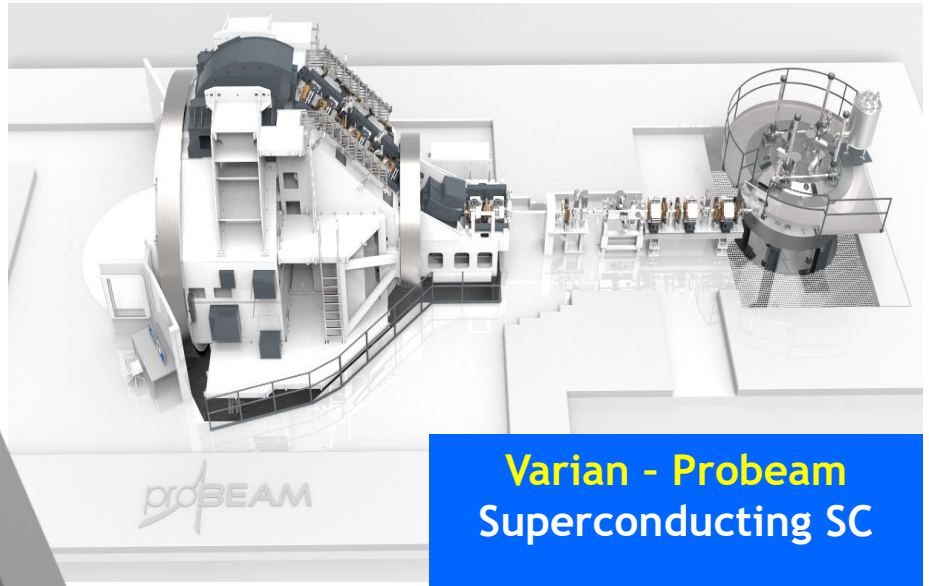
RBE *= ratio between reference dose (X rays) and particle dose to obtain the same effect*

OER *= ratio of the doses producing the same effect in hypoxic (0% pO_2) and oxic (20% pO_2) conditions*

96 centres with protontherapy (+30 in construction)

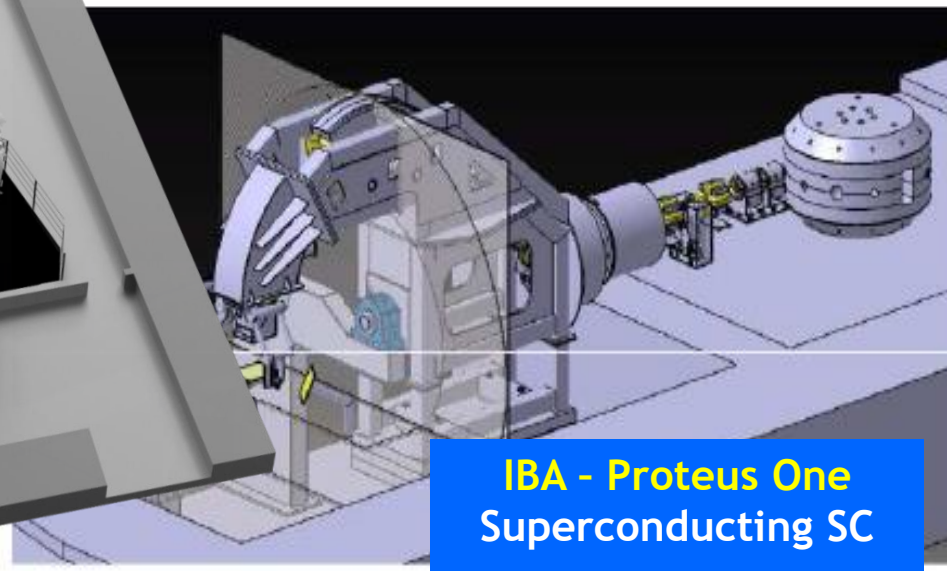
330.000 patients treated (+40.000/year) [www.ptcog.ch]

MEVION S250
Superconducting



Varian - Probeam
Superconducting SC

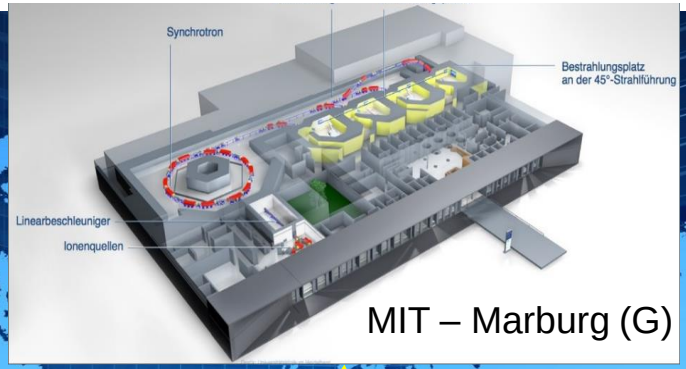
HITACHI
Synchrotron



IBA - Proteus One
Superconducting SC

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

45.000 patients treated (+5.000/year) [www.ptcog.ch]



MIT – Marburg (G)

HIT – Heidelberg (G)

3 centres in China

6 centres in Japan

CNAO – Pavia (I)

MedAustron – Wien (A)