

Operation and patient treatments at CNAO facility

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IPAC 2012, New Orleans

May 24th, 2012

Overview

- Hadrontherapy and History of CNAO
- Commissioning of high technology
- Clinical commissioning
- Medical experimentation

The hadrontherapy idea

Radiotherapy is the clinical technique used in the 40% of the cases of cures from the cancer.

Hadrontherapy is a high precision kind of radiotherapy employing hadrons instead of the standard electrons and photons.

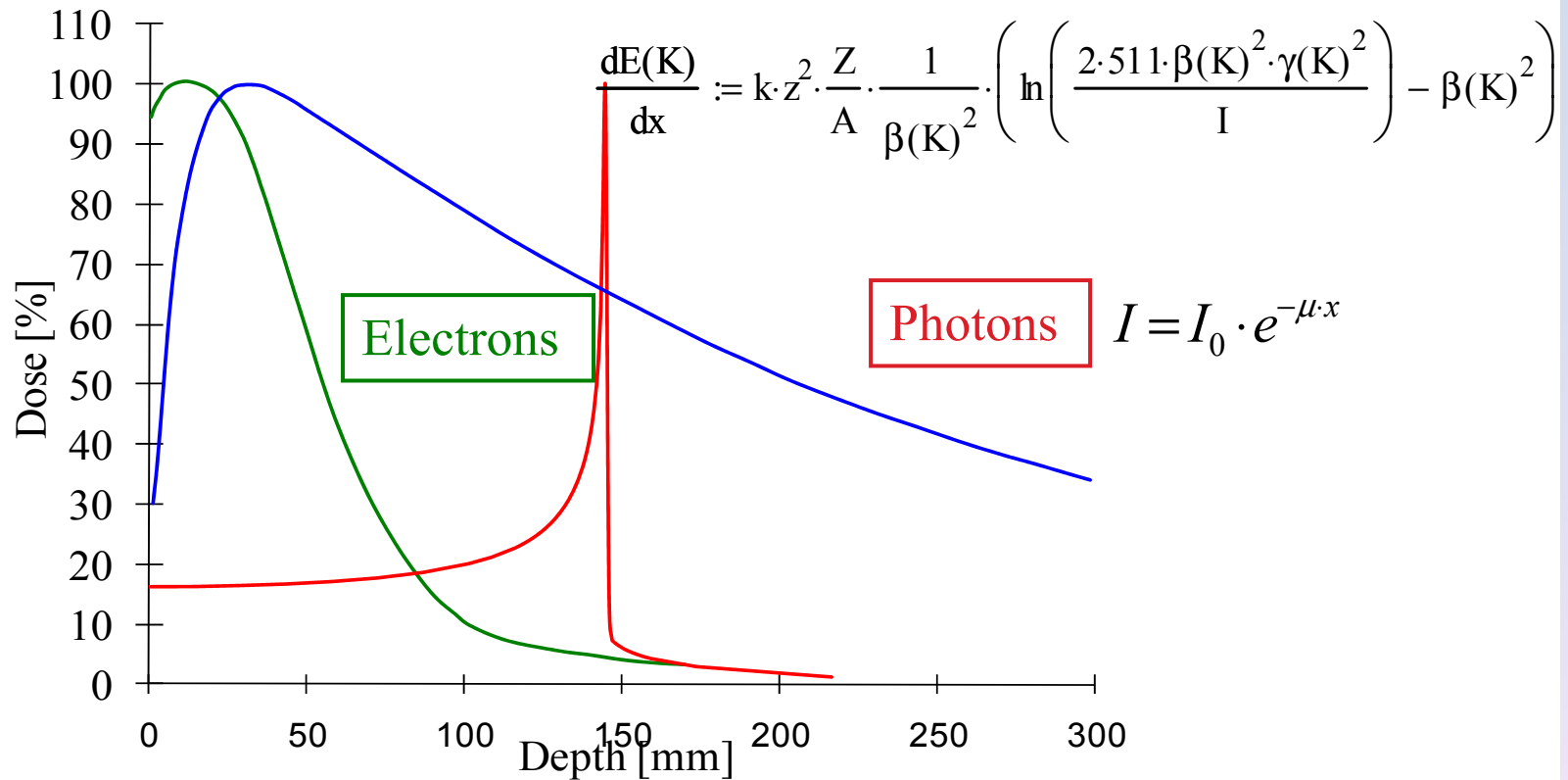
Proton and carbon ions have important advantages:

- beams penetrate the patient without diffusion
- they deposit their maximum energy totally at the end of their range. In this way the beam is able to produce severe damage to the diseased DNA and the traversed healthy tissue is preserved
- due to the charge, the beams can be scanned: any part of a tumor can be accurately and rapidly irradiated.

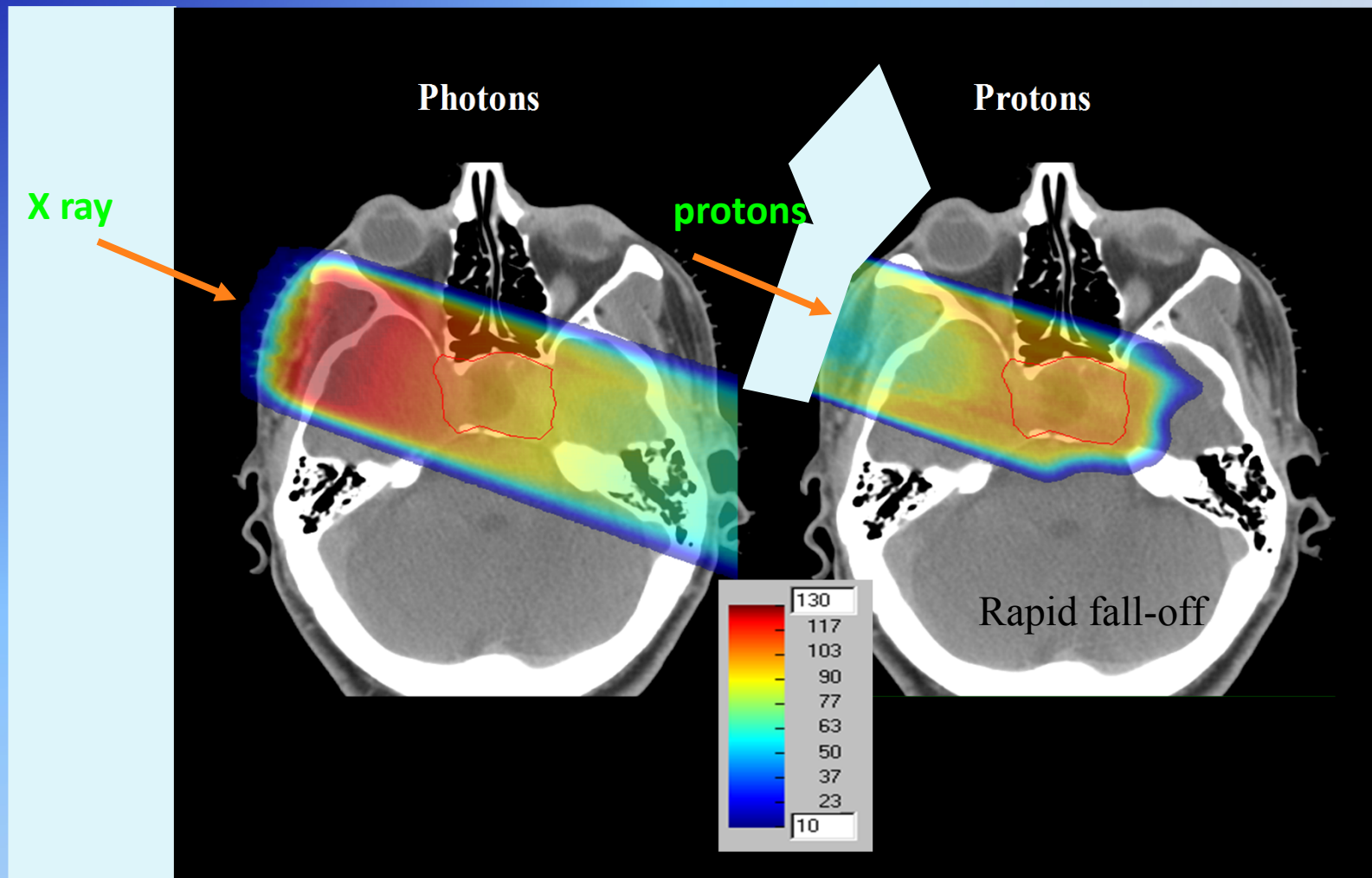
Comparison of the depth dose profiles

Inverse dose profile

Carbon ions

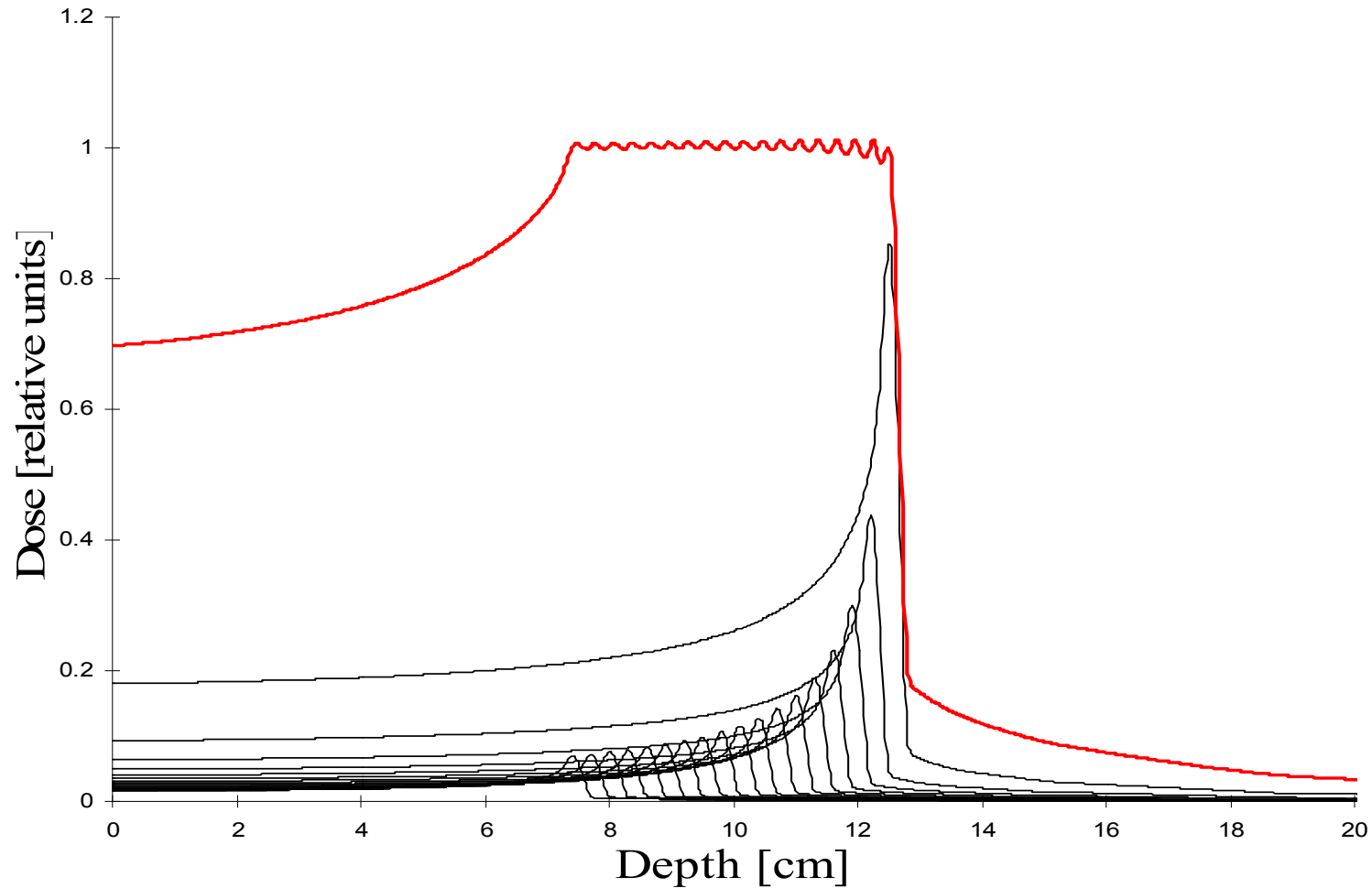


Comparison of dose distribution

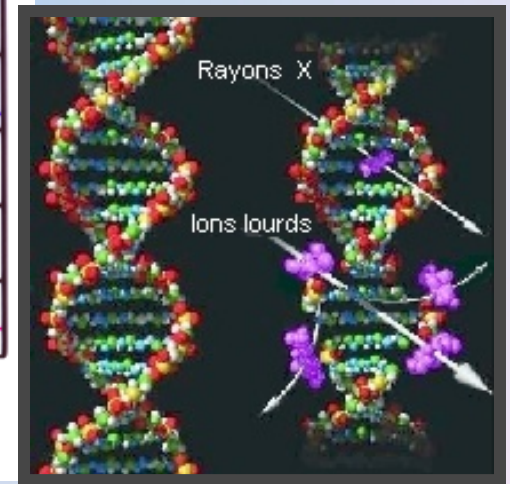
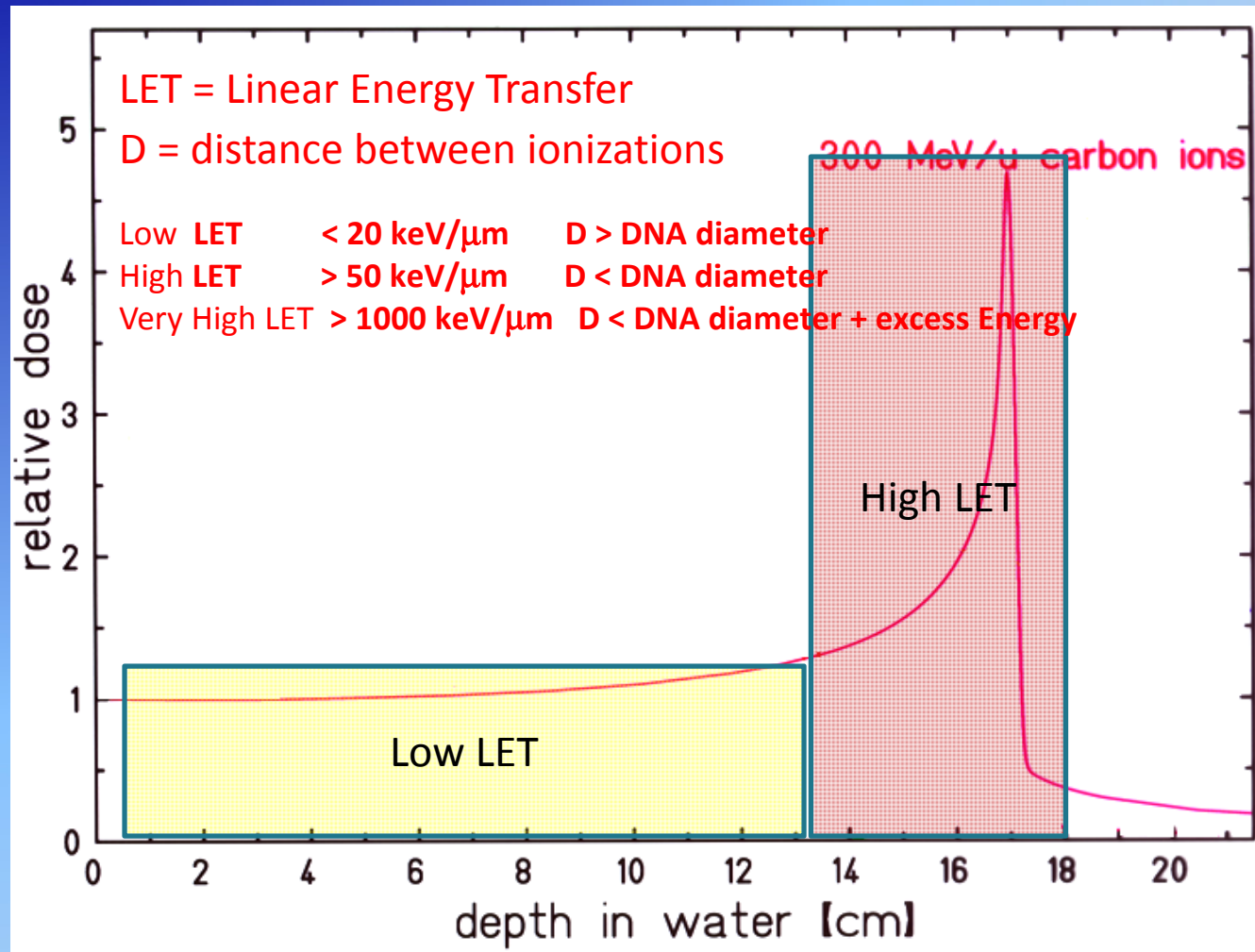


Spread Out Bragg Peak

Using different energies the so called Spread out Bragg Peak (SOBP) is obtained.



Carbon ions have higher *LET* than protons

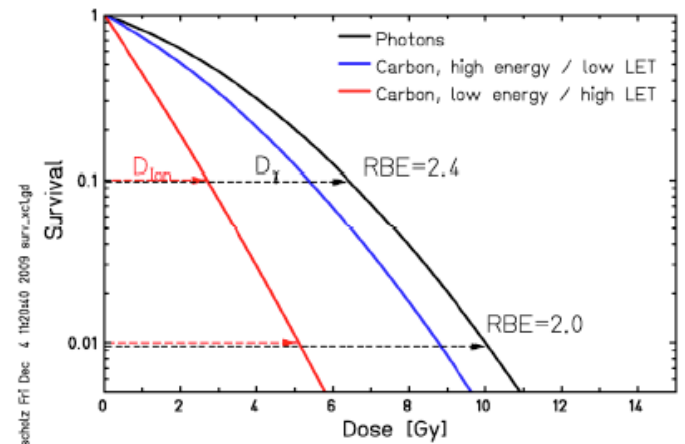
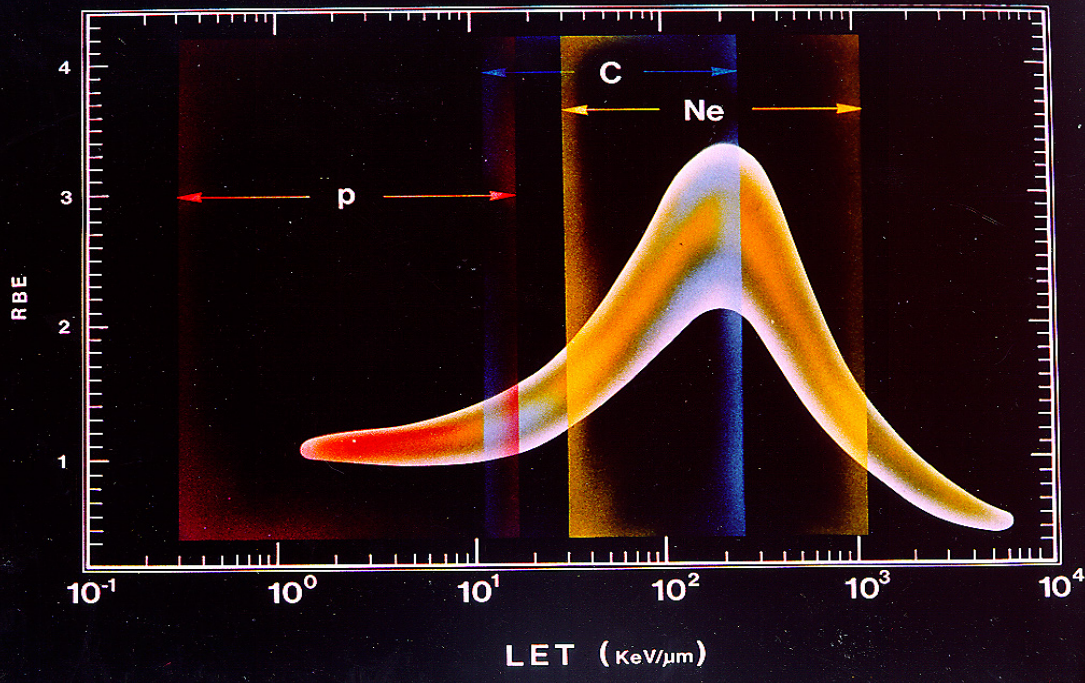


Why carbon ions?

Qualitatively the energy deposited by carbon ions is more efficient, in terms of cell destruction, than the energy deposited by protons.

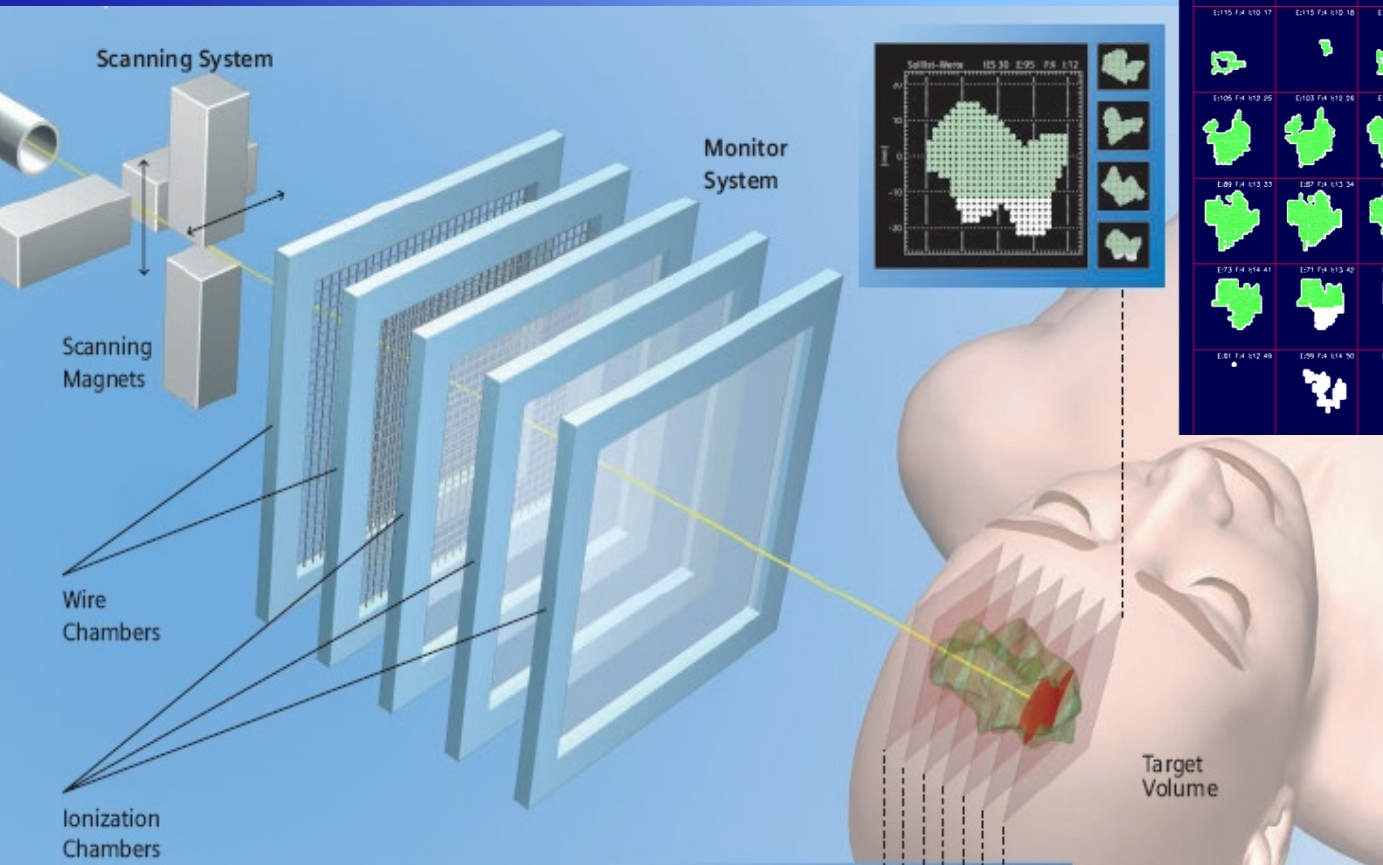
The higher efficiency in killing cells is expressed by the *relative biological effectiveness (RBE)*, which is the ratio between the photon and the ion doses to produce the same biological effect.

Carbon RBE > 3 in the Bragg peak region
>= 1 in the entry channel.



The survival curve for the target cells for late injury is "curvier" than that for acute effects

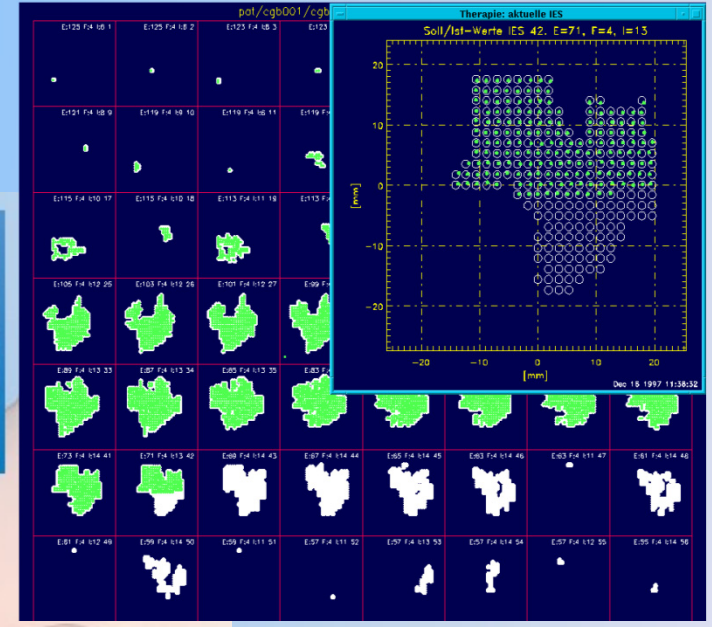
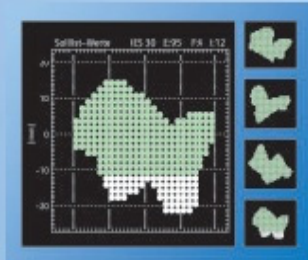
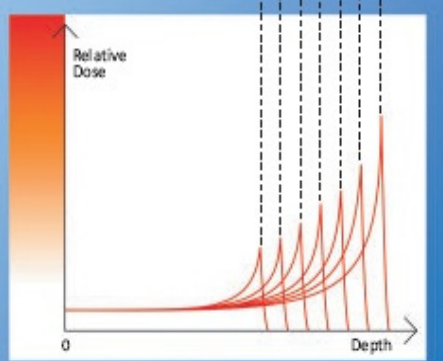
Active systems



Example:

Depth 5 cm:
Proton 80 MeV
Carbon 150 MeV/u

Depth 25 cm:
Proton 195 MeV
Carbon 380 MeV/u



(Courtesy of Siemens Medical)

What is the CNAO Foundation

It is the first Italian center (second in Europe)
For hadrontherapy with protons and Carbon ions.
It is located in Pavia, near Milan

It is a no profit organisation (Foundation) created
with the financial law 2001 and it comes from the
PIMMS (Proton Ions Medical Machine Studies)
project performed by TERA Foundation at CERN

Collaborations

NATIONAL

INFN

co-direction, involvement/responsibility in many technical issues, formation

Town of Pavia

land and authorisations

University of Milan

medical coordination and formation

Polytechnic of Milan

patient positioning, radioprotection and authorisations

University of Pavia

electrical plant, power supplies and betatron, safety, formation

Province of Pavia

logistics and authorisation

University of Turin

interface beam-patient, TPS

INTERNATIONAL

CERN

special magnets, dipole measurements and diagnostics
(+ PIMMS heritage)

GSI

linac and special components

LPSC (Grenoble)

betatron, low-level RF

NIRS (Chiba)

medical activities, formation

Steps of CNAO

Step 1: construction

 Years: 2005 - 2009

Step 2: beam commissioning

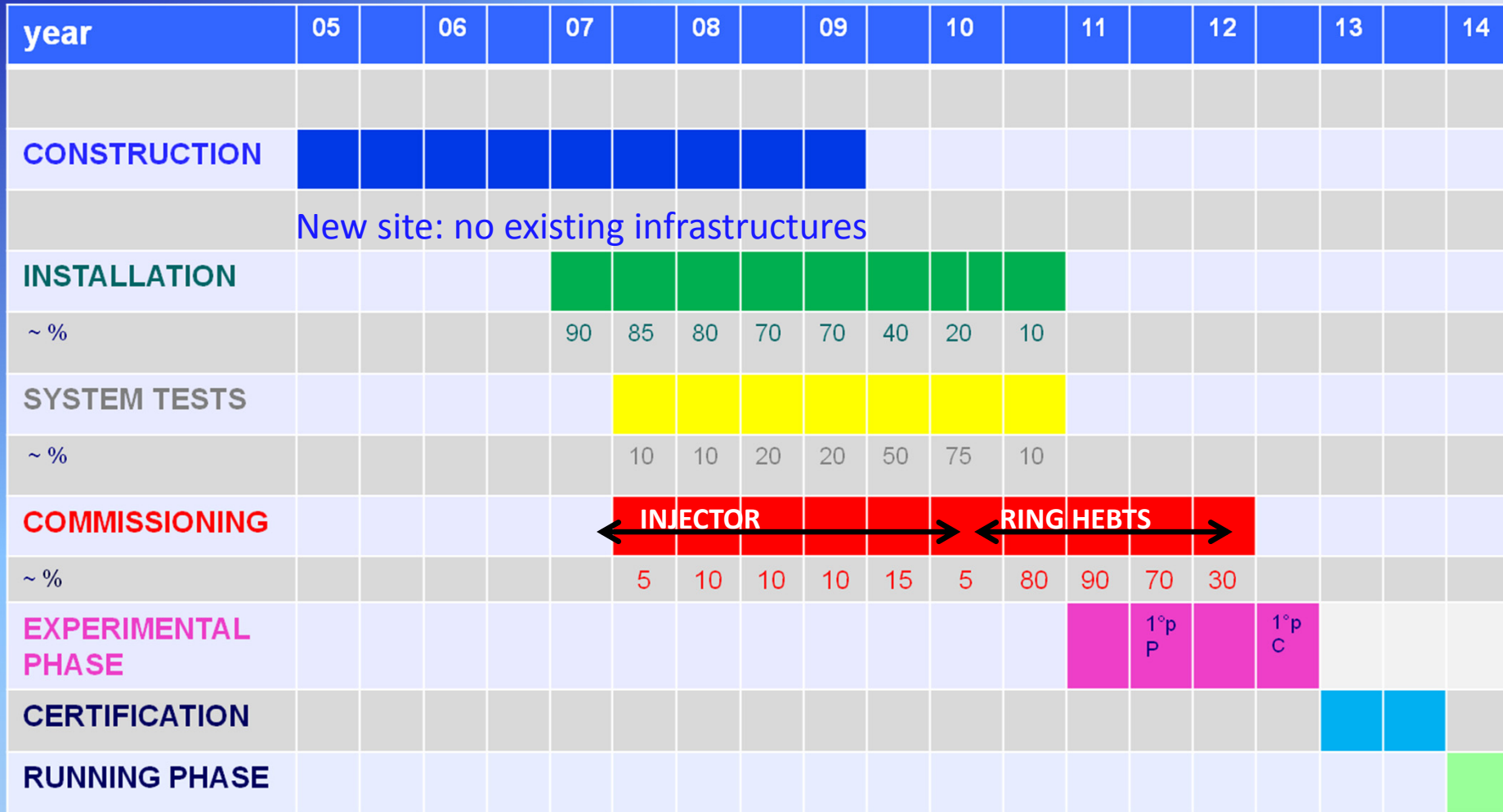
 Years: 2005 - 2009

Step 3: experimentation

 Years: 2011 - 2012

Phase 4: start-up

 Years: 2012 - 2013



CNAO Site

November 2005



October 2009



Overview

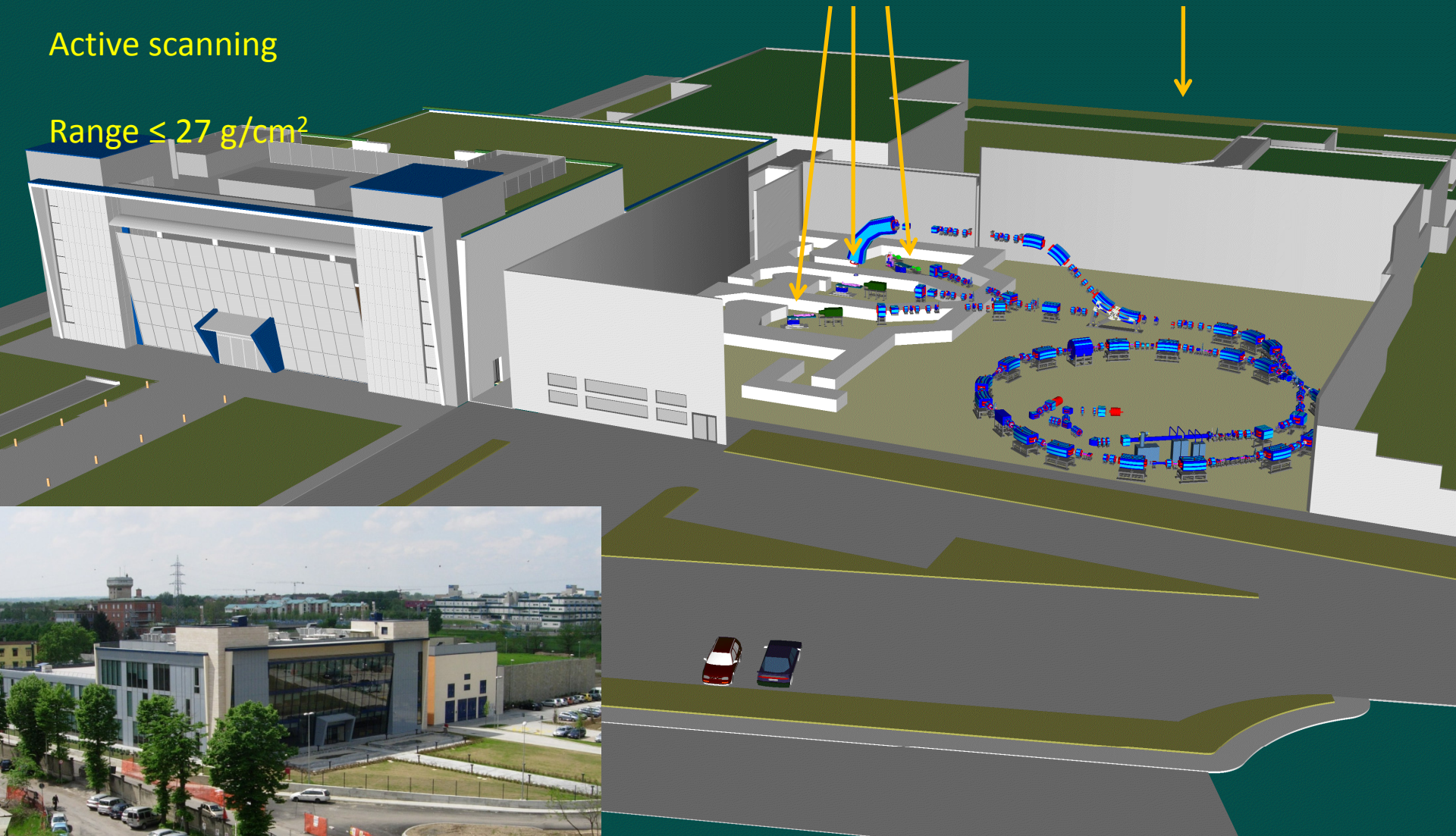
Synchrotron for light ions ($z \leq 6$)

Active scanning

Range $\leq 27 \text{ g/cm}^2$

3 treatment rooms

Space for 2 gantries



Basic Parameters I

Protons ($< 10^{10}$ per spill)				
	LEBT (H_3^+)	MEBT	SYNC	HEBT
Energy [MeV/u]	0.008	7	7-250	60-250
I_{max} [A]	0.43×10^{-3}	0.7×10^{-3}	5×10^{-3}	7×10^{-9}
I_{min} [A]	0.43×10^{-3}	70×10^{-6}	0.12×10^{-3}	17×10^{-12}
$\epsilon_{rms,geo}$ [π mm mrad]	35	1.9	0.67-4.2	0.67-1.43(V)
$\epsilon_{tot,geo}$ [π mm mrad]	180	9.4	3.34-21.2	3.34-7.14 (V) 5.0 (H)
Magnetic rigidity [T m]	0.039	0.38	0.38-2.43	0.38-2.43
$(\Delta p/p)_{tot}$	$\pm 1.0\%$	$\pm(1.2-2.2)\%$	$\pm(1.2-3.4)\%$	$\pm(0.4-0.6)\%$

Basic Parameters II

Carbon ($< 4 \cdot 10^8$ per spill)				
	LEBT (C ⁴⁺)	MEBT	SYNC	HEBT
Energy [MeV/u]	0.008	7	7-400	120-400
I _{max} [A]	0.16×10^{-3}	0.15×10^{-3}	1.5×10^{-3}	2×10^{-9}
I _{min} [A]	0.16×10^{-3}	15×10^{-6}	28×10^{-6}	4×10^{-12}
$\epsilon_{\text{rms,geo}}$ [π mm mrad]	35	1.9	0.73-6.1	0.73-1.43(V)
$\epsilon_{\text{tot,geo}}$ [π mm mrad]	180	9.4	3.66-30.4	3.66-7.14 (V) 5.0 (H)
Magnetic rigidity [T m]	0.039	0.76	0.76-6.34	3.25-6.34
$(\Delta p/p)_{\text{tot}}$	$\pm 1.0\%$	$\pm(1.2-2.0)\%$	$\pm(1.2-2.9)\%$	$\pm(0.4-0.6)\%$



LEBT

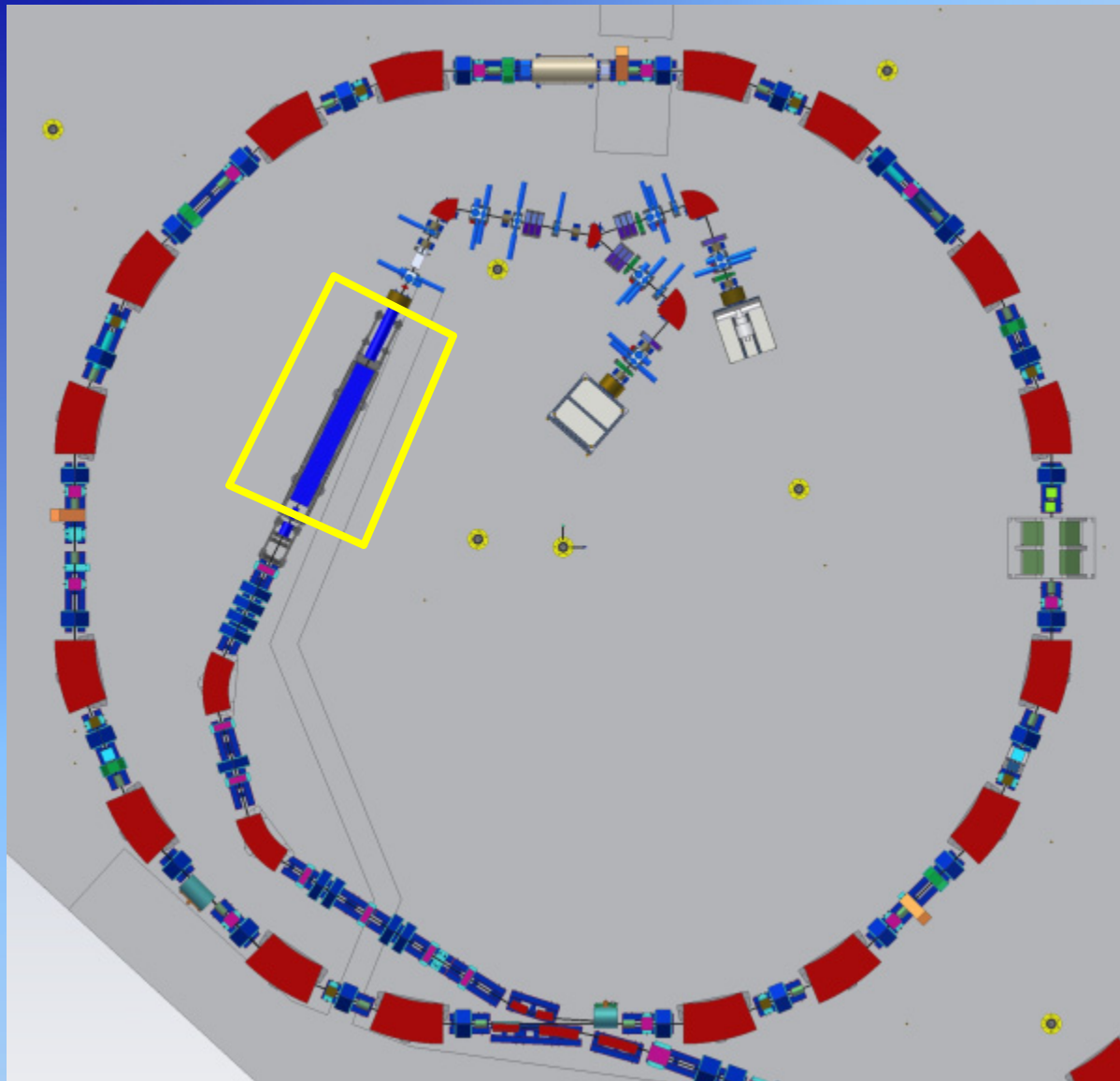
**0.008 MeV/u H^{3+}
0.008 MeV/u C^{4+}**

**$I \sim 0.5$ mA (H^{3+})
 $I \sim 0.2$ mA (C^{4+})**

**Two ECR sources
(frequency tuning)**

Continuous beam

LEBT Chopper



Linac=RFQ+IH

217 MHz

RFQ

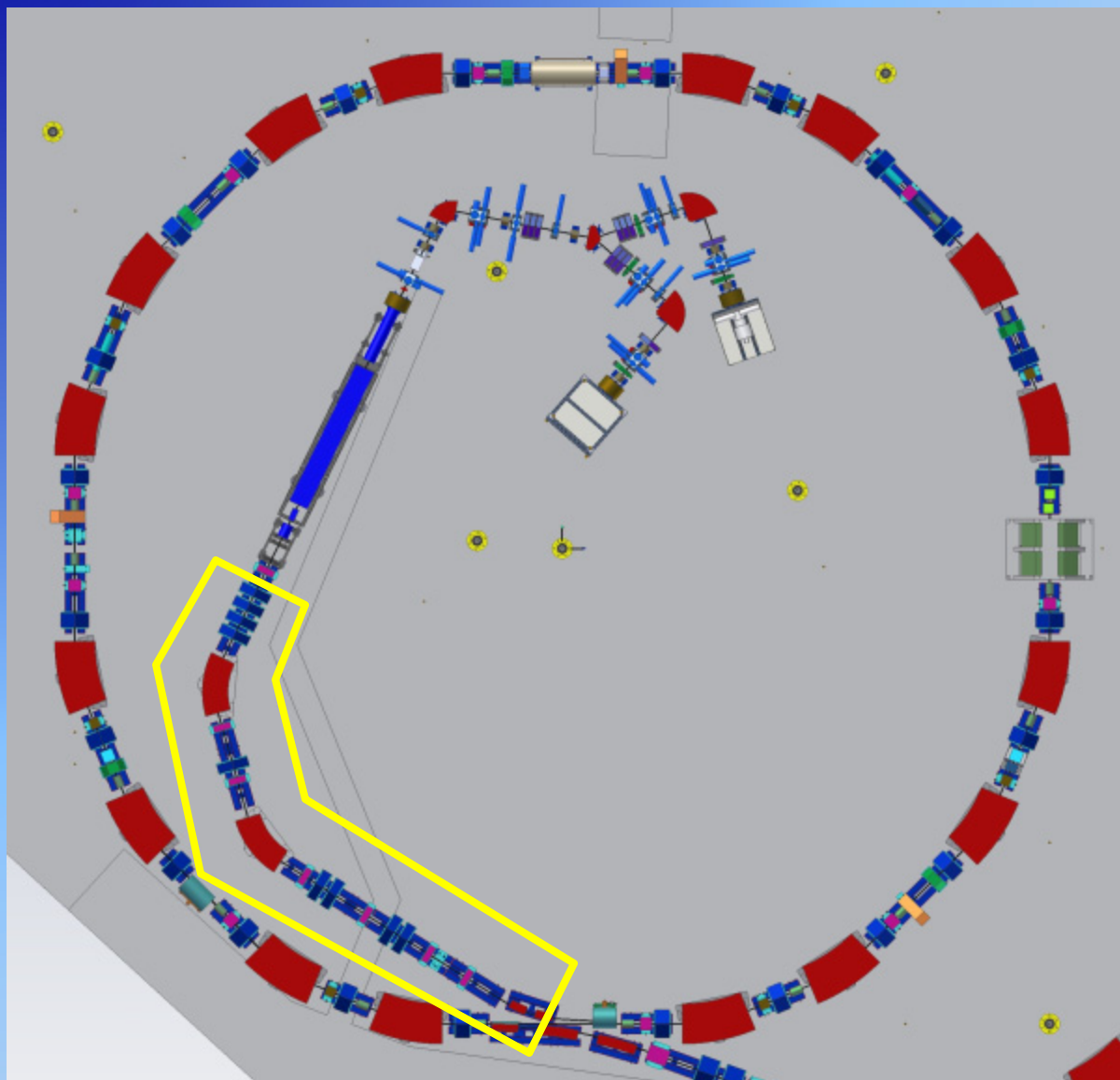
0.008-0.4 MeV/u H^{3+}

0.008-0.4 MeV/u C^{4+}

IH

0.4-7 MeV/u H^{3+}

0.4-7 MeV/u C^{4+}



MEBT

7 MeV p
7 MeV/u C⁶⁺

$I \sim 0.75$ mA (p)
 $I \sim 0.15$ mA (C⁶⁺)

Match betas

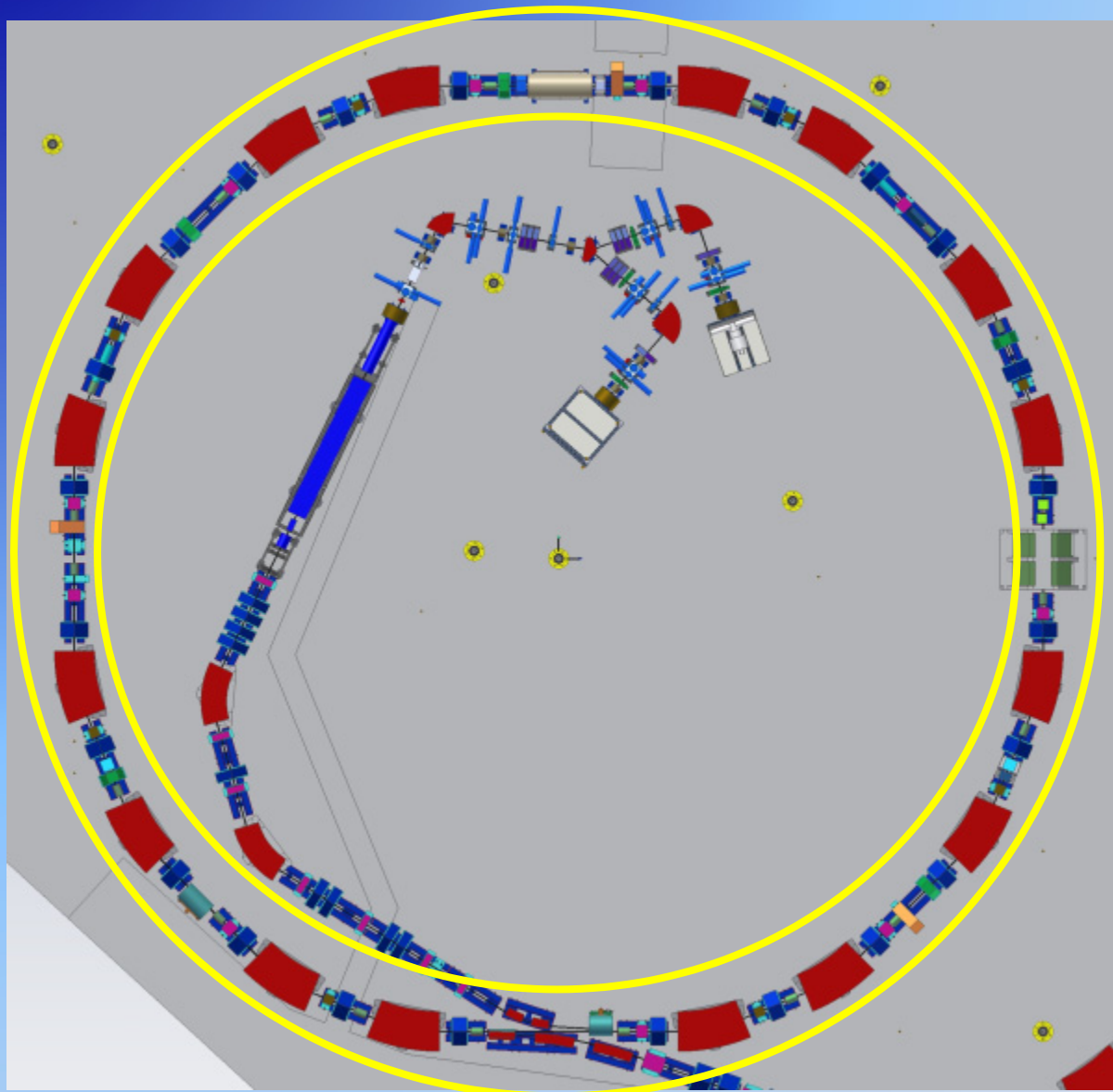
$(x, x')_{inj}$

Stripping foil

Current selection

Debuncher

Emittance dilution



Synchrotron

7-250 MeV p

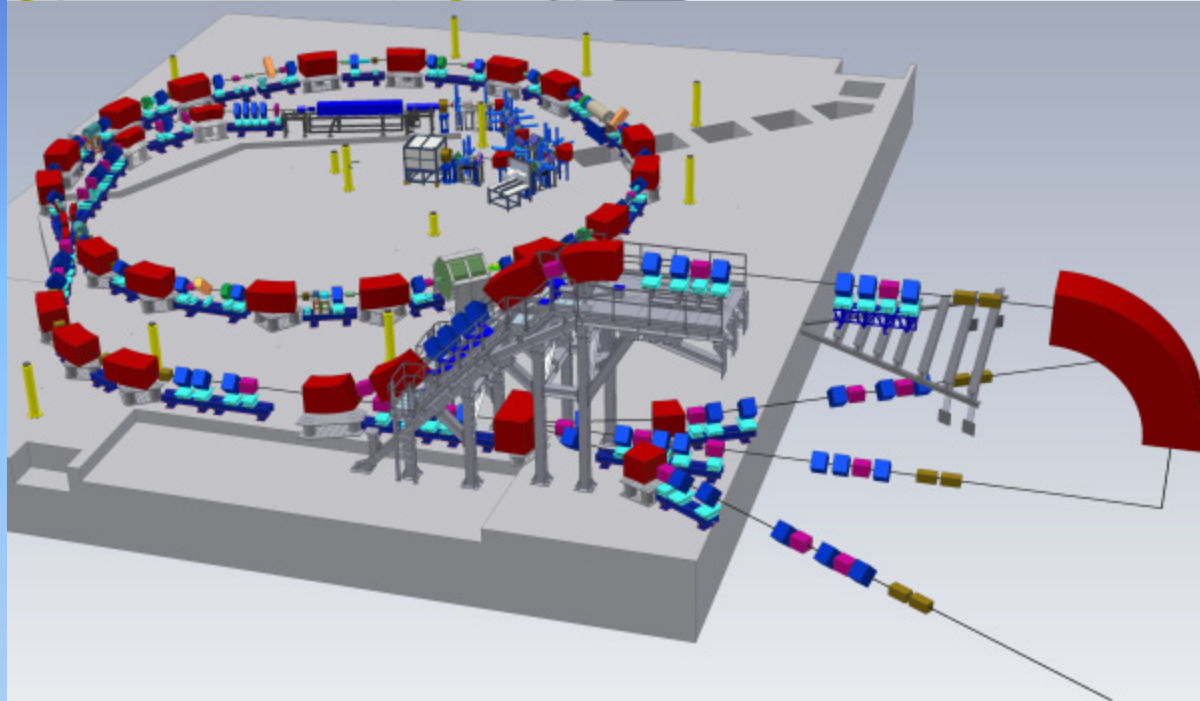
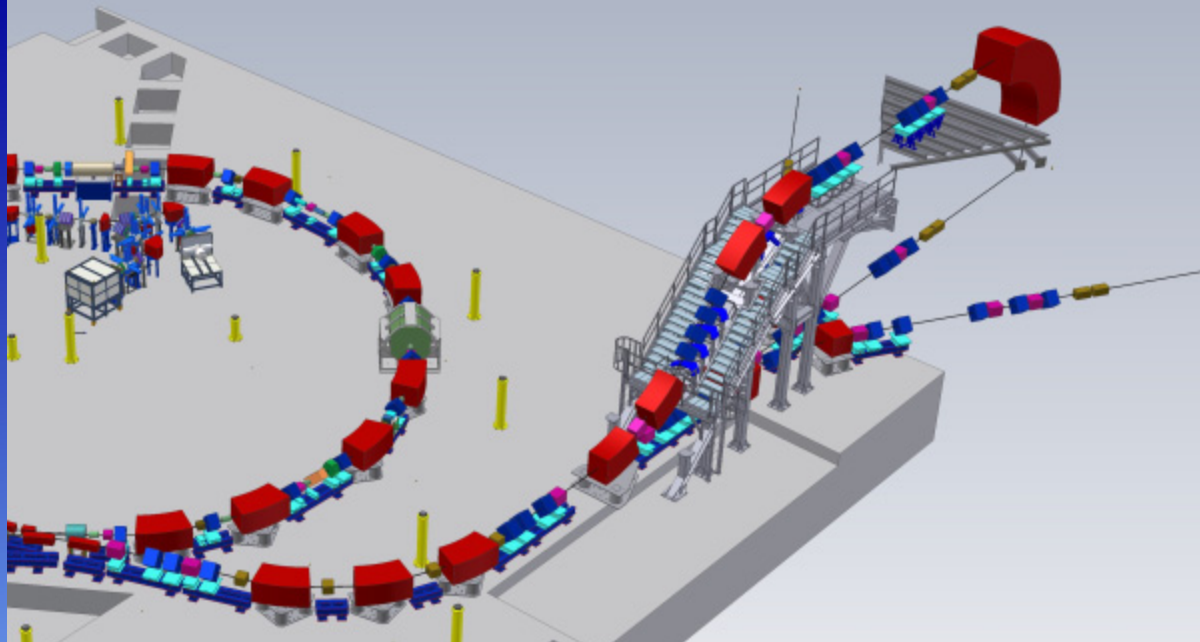
7-400 MeV/u C

$I \sim 0.1-5 \text{ mA (p)}$

$I \sim 0.03-1.5 \text{ mA (C)}$

Slow extraction

Betatron core



HEBT

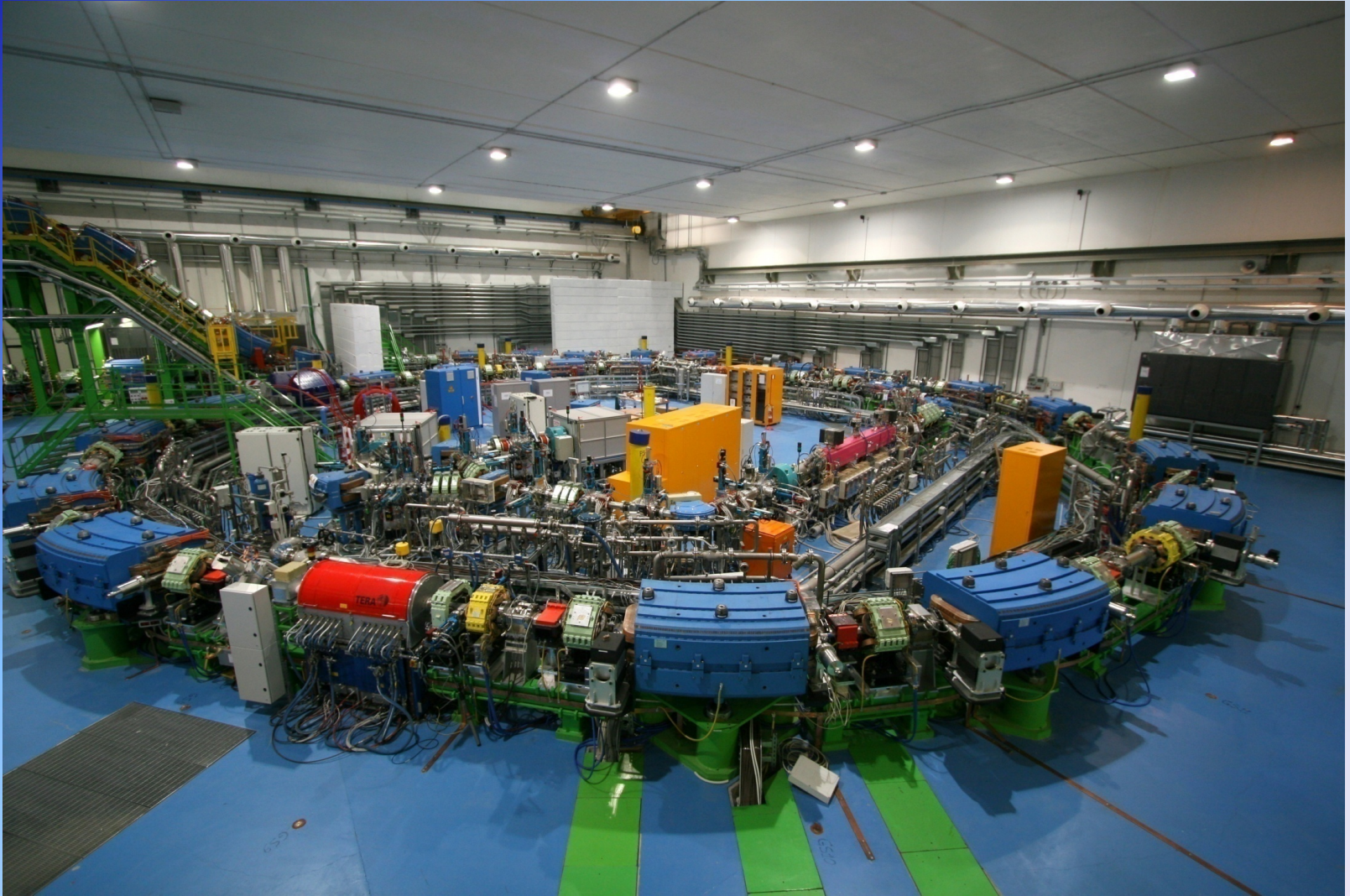
60-250 MeV p
120-400 MeV/u C

10^{10} p/spill (~ 2 nA)
 $4 \cdot 10^8$ C/spill (~ 0.4 nA)

different settings for

- Treatment Line
- Horizontal beam size
- Vertical beam size
- Extraction energy

Installation status



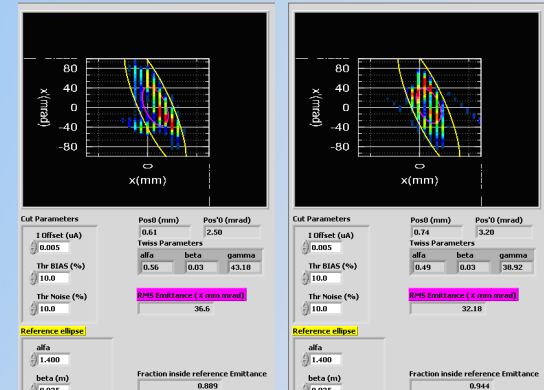
Accelerators and lines installation is finished

LEBT commissioning (2008)

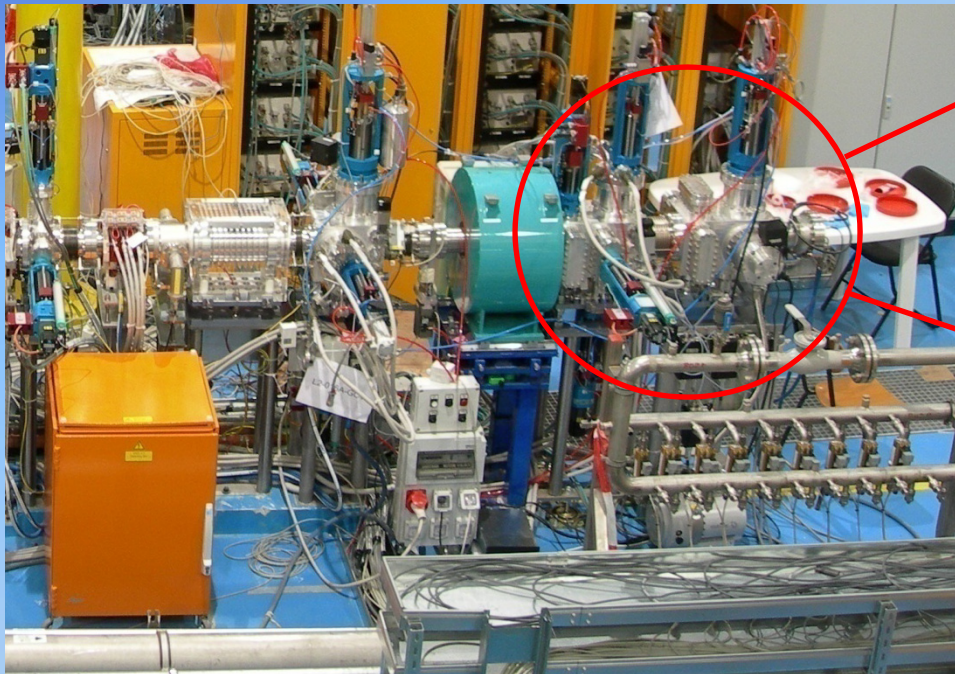
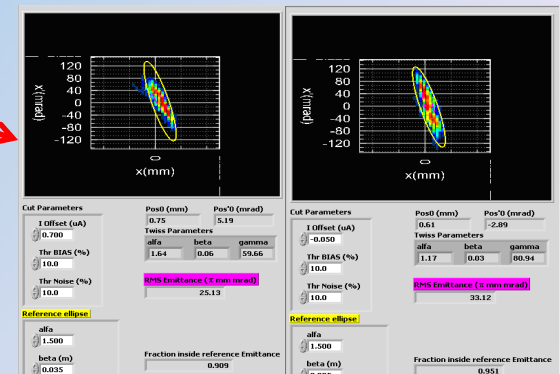
Transmission up to 97%

I_C up to $230 \mu\text{A}$, I_{H3} up to 1.2 mA

Carbon H-V



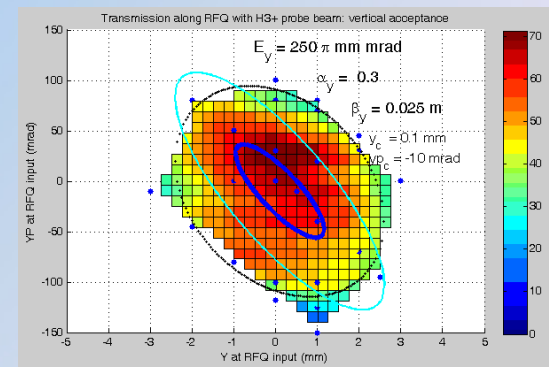
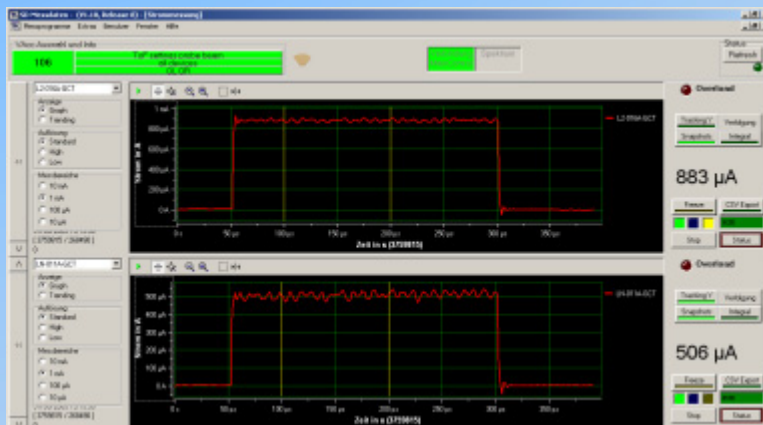
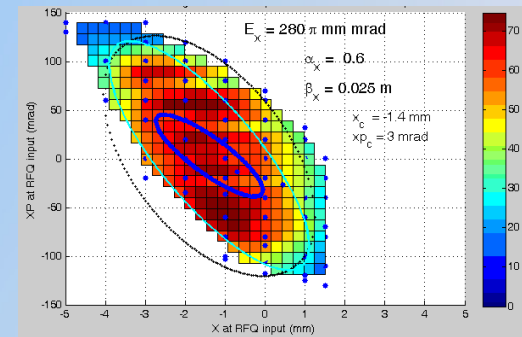
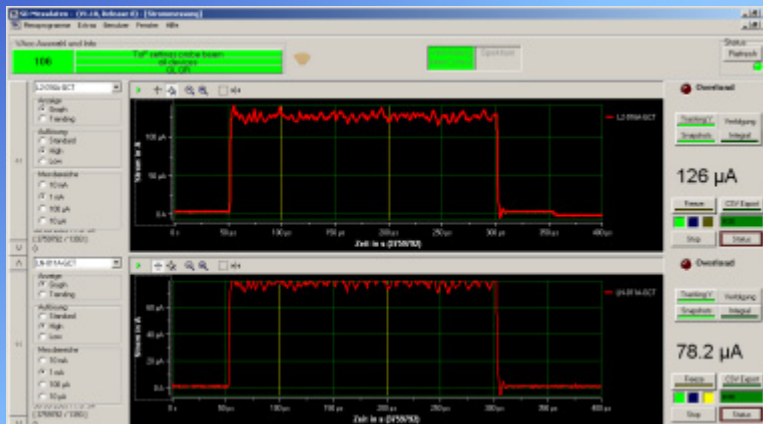
H₃⁺ H-V



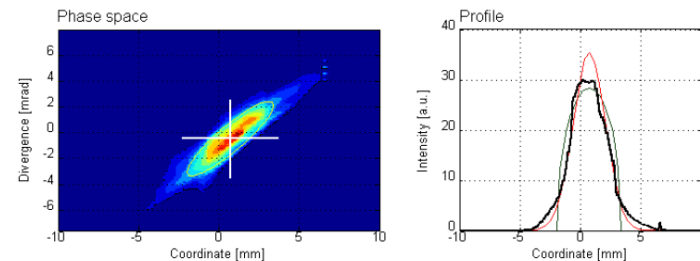
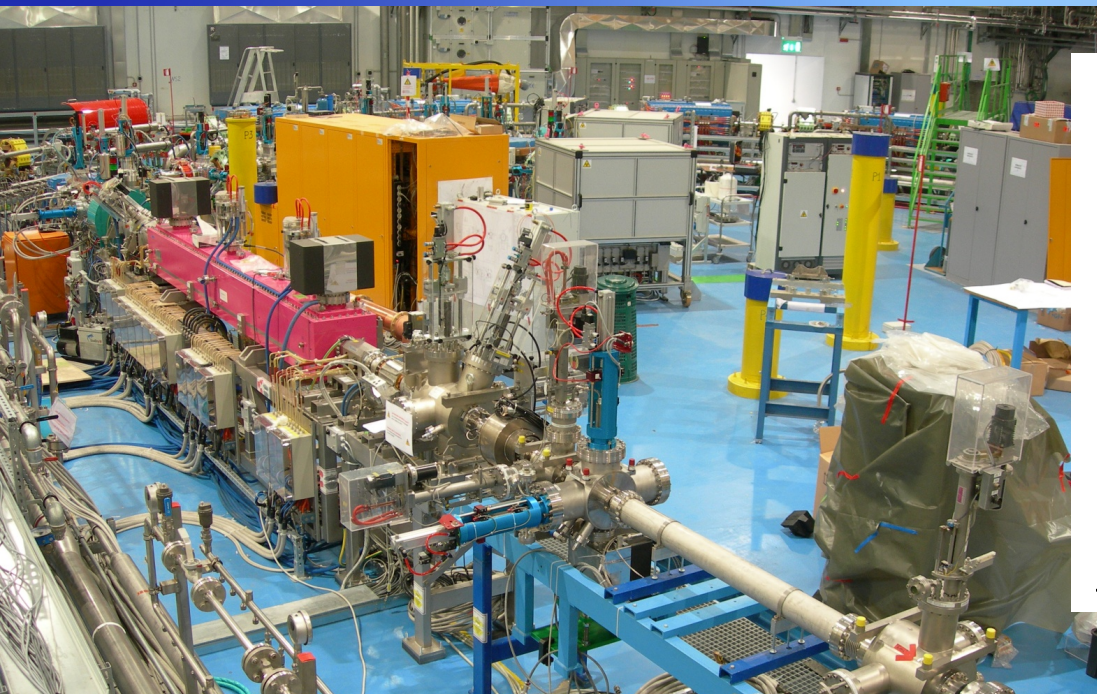
RFQ Commissioning (2009)

Transmission of 60%
(25% of losses longitudinal)

Acceptance of RFQ measured



LINAC Commissioning (2009)

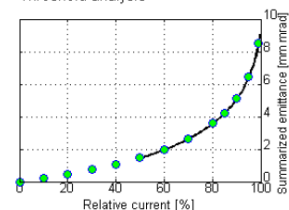


xo: 0.71
 yo: -0.46
 stdev_x: 1.33
 stdev_y: 1.44
 corr_{xy}: 0.897
 ε: **3.39**
 α: -2.03
 β: 2.10
 γ: 2.44
 KV-plane: 0.10

units: mm, mrad

Threshold[%]	I _{app} [%]	ΣdS/*[mm mrad]
1.8	99	8.51
4.7	95	6.43
7.8	90	5.10
11.2	85	4.24
14.1	80	3.59
20.5	70	2.64
28.8	60	1.97
37.7	50	1.47
45.8	40	1.08
53.8	30	0.75
60.3	20	0.46
69.7	10	0.21

Threshold analysis



Ion Species	LEBT End	Behind LINAC	Max. LINAC Transmission	Behind Foil Stripper
C⁴⁺ / C⁶⁺	≈ 170 μA	≈ 82 μA	48 %	≈ 115 μA
H₃⁺ / p	1.0 – 1.1 mA	≈ 400 μA	39 %	≈ 1.2 mA
	710 μA	307 μA	46 %	≈ 900 μA

First turn

- 16 Dec 2009

Injection in synchrotron

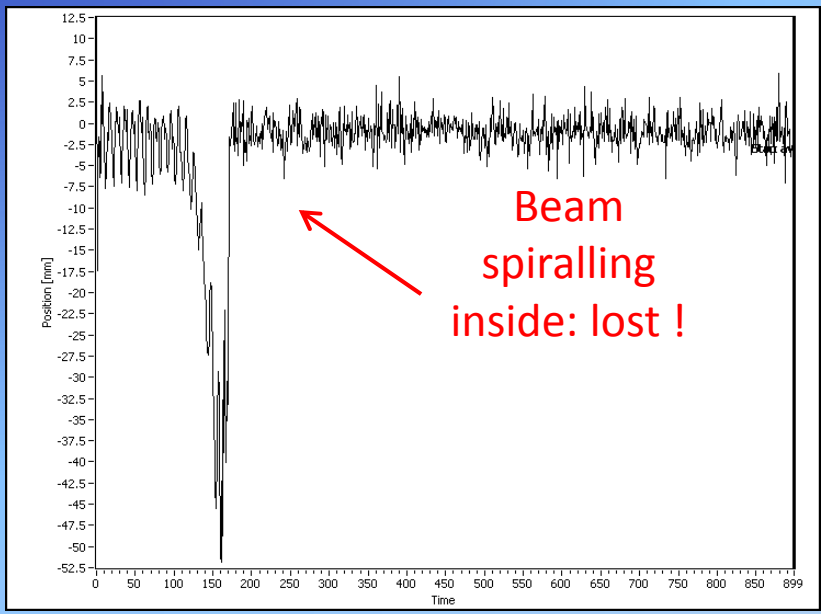


First turn

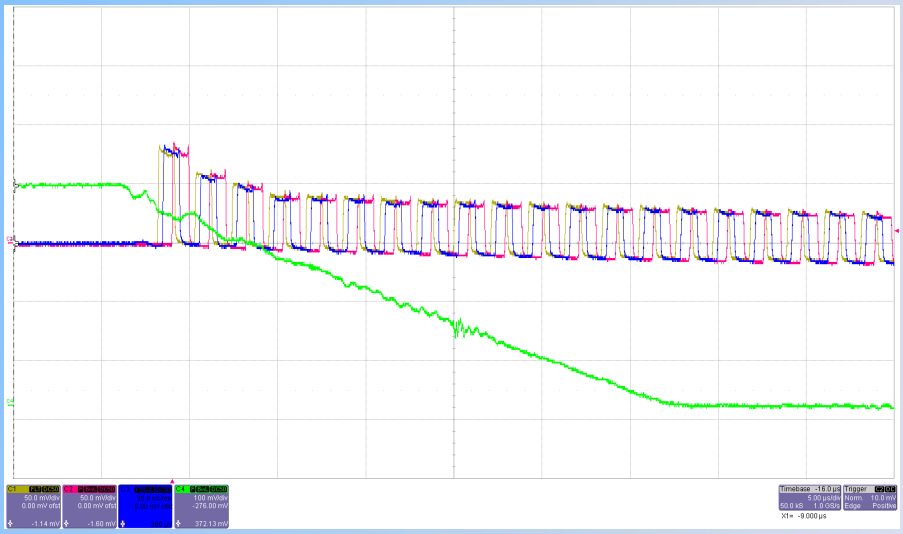


Multiturn injection: August 27, 2010

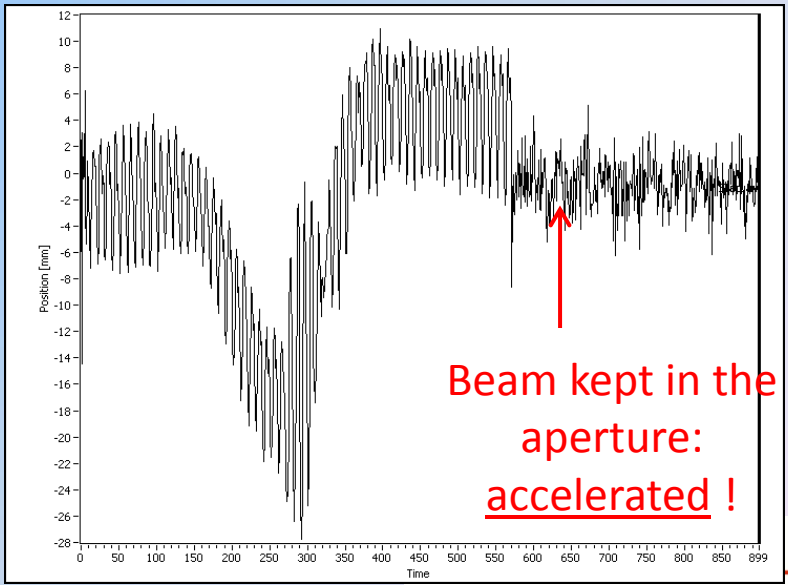
B field on – RF
off



First beam acceleration
September 17, 2010)



B field on – RF
on



First extraction with Proton beam: November 2010

Instance [System1:Z2-028B-SFH] - Running User [user]

Standard Tools

Official Name
Z2-028B-SFH v. 3.1.0 (21/04/2011)

Lock Unlock

CNAO-LV1-08_user_VI

Inhibit

Cycle Prog
20162633

Cycle Code
0000240006CCDD00

Error Code
0

Error String

Information

Serial Number
270089-Y

Camera Status
1

Saturation

ONESHOT

START STOP

Advanced...

Actuator Settings

In/Out Status
In

SetActuator

Calibration

Raw Data
 Calib. In Progress

SetCalib

Max 1 n Current 0 n

Istant [ms] 250 Export

Acquisition Settings

SetAcq.Par.

Start Event Gain 0.00

Start Betatron Exposure Time 1.0000 ms

Start Delay 0.000 ms Rate 20.000 Hz

Number Images 35

Binning 8.000

X Graph 20162631

XCenter	XCenter Rms	Integral
1 mm	2 mm	361227.800
XCenter Avg	XCenter Avg RmsTot	Integral
0.67 mm	0 mm	3228580.627

Y Graph

YCenter	YCenter Rms	Integral
0 mm	3 mm	440390.595
YCenter Avg	YCenter Avg RmsTot	Integral
0.34 mm	0 mm	3564513.216

Dose Delivery TRI - Running User [user]

Standard Tools

Official Name
Z2-030C-NZF

Lock Unlock

Inhibit

Cycle Prog
24047414

Cycle Code
240006CCDD00

Error Code

Error String

BeamName
SopInstanceUID
First Energy
Slice_Tot
Spot_Tot

CrtpointIndex
CurrentSpot
Curr_P
Curr_T
Slice

PrivStatus
Ix_PREK
Iy_PREK

StatusADD
Cycle_Code
DS_CycleCode
StepN_FC

Slow - Fast
Slow_P_Box1
Slow_P_Box2
Slow_T_Box1
Slow_T_Box2

Fast_P_Box1
Fast_P_Box2
Fast_T_Box1
Fast_T_Box2

SET SLOW

FLOW HV

Plots

X position

MEAN: -0.57 SIGMA: 3.27

Y position

MEAN: 0.26 SIGMA: 4.13

THR: 200

Diff(Integral_1) N1

150179 0

Diff(Integral_2) (k2) number of particles

152801 0

Diff(Strip_1) PrinDelivMeterSet

178713 0

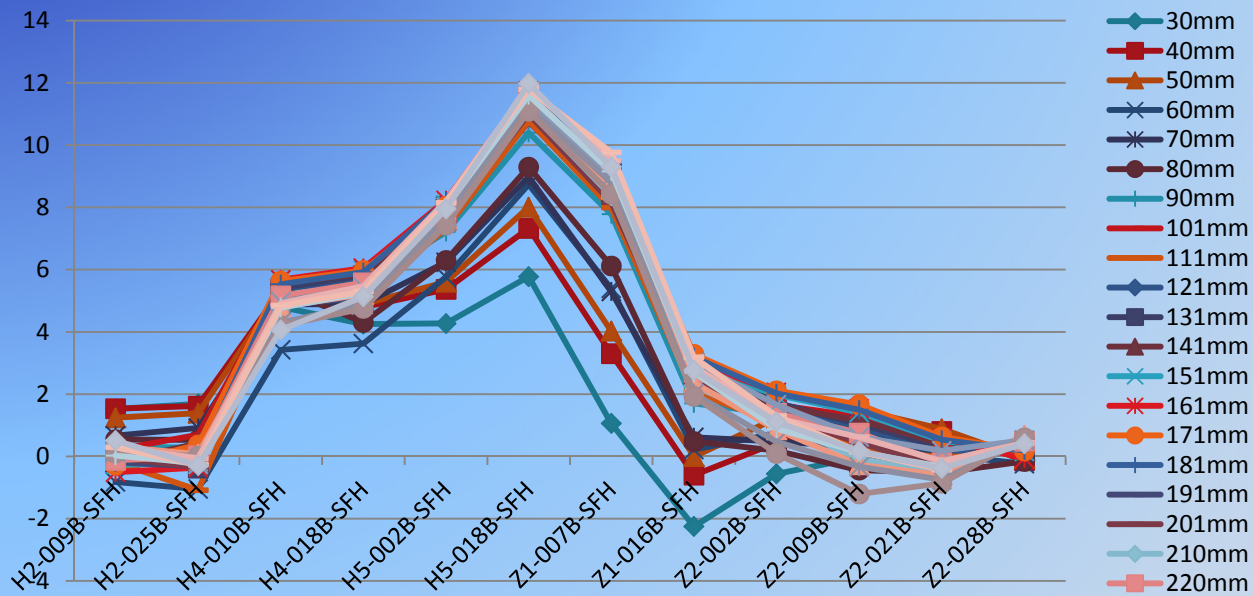
Diff(Strip_2) Diff(Pixel)

183760 0

Close

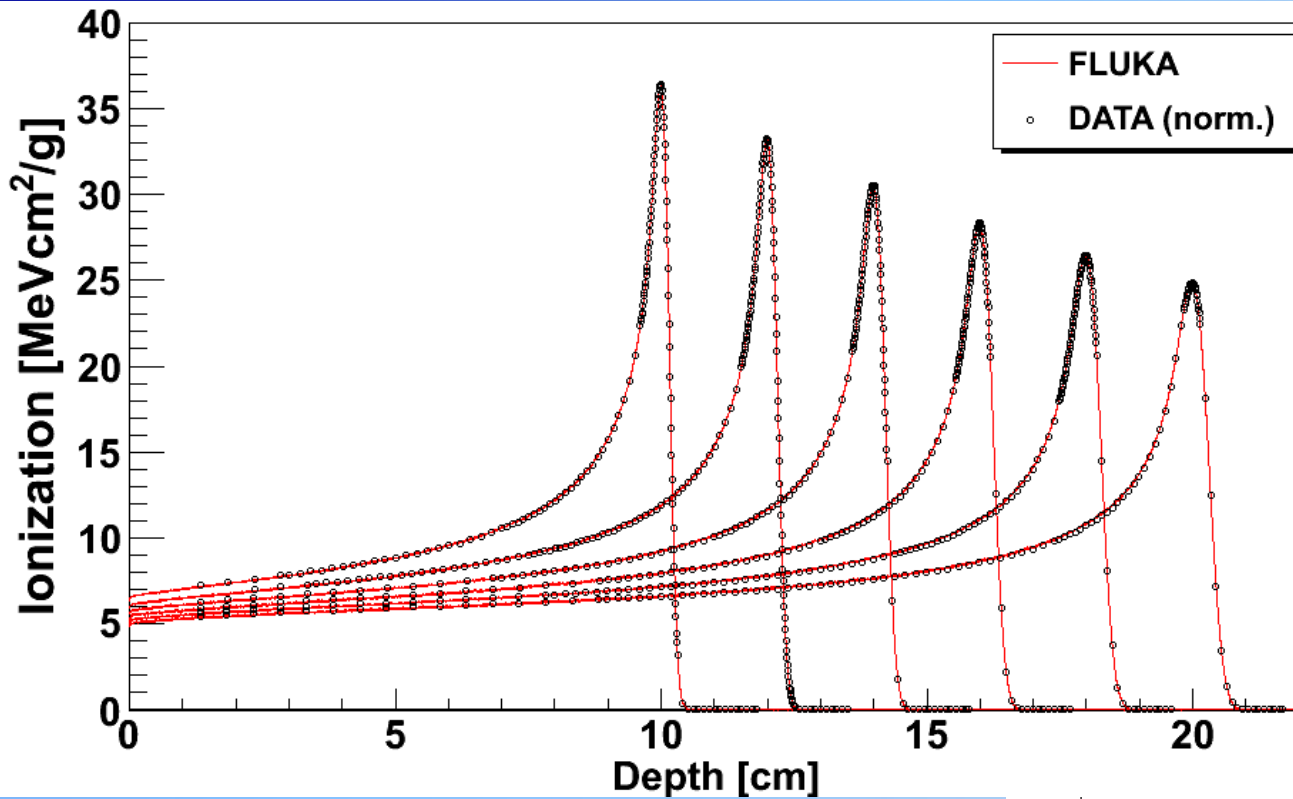
Integral_1 20621777 **Integral_2** 21990061 **Strip_1** 24596524 **Strip_2** 25791980

In 2011, after lots of studies and optimizations along the machine, proton beam has physically commissioned in the whole energy range in Z-line (60 MeV-220 MeV, that is 30 mm-320 mm of penetration depth in water) and delivered to medical staff for clinical commissioning.



Horizontal beam Trajectories along HEBT as a function of energy (measured in mm-depth)

Proton Clinical characterization (1/3)

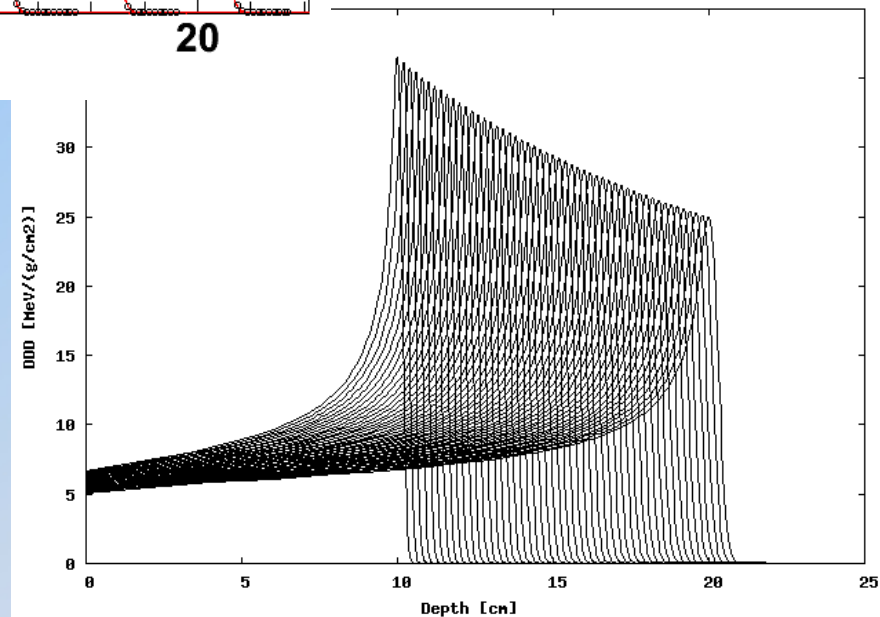


Bragg peak measurements

FLUKA proton ddd database

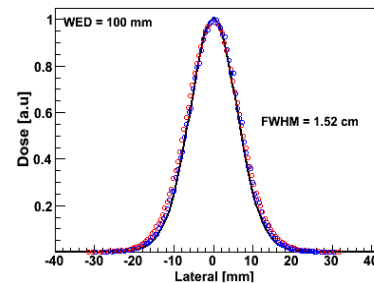
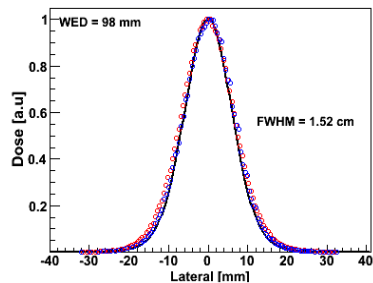
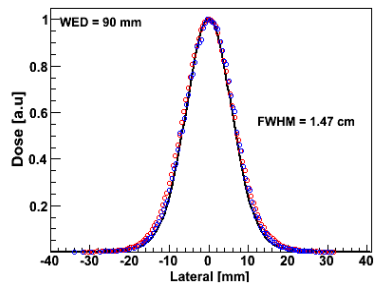
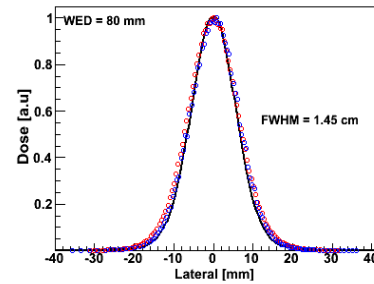
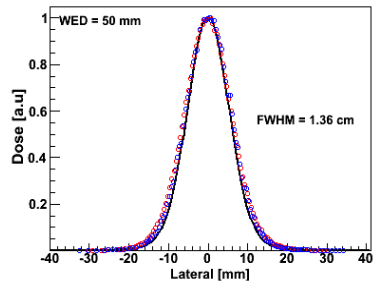
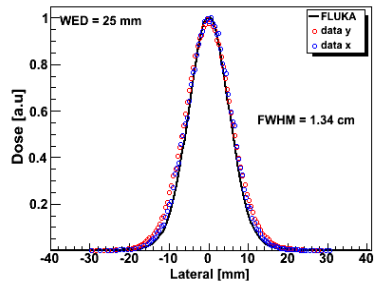
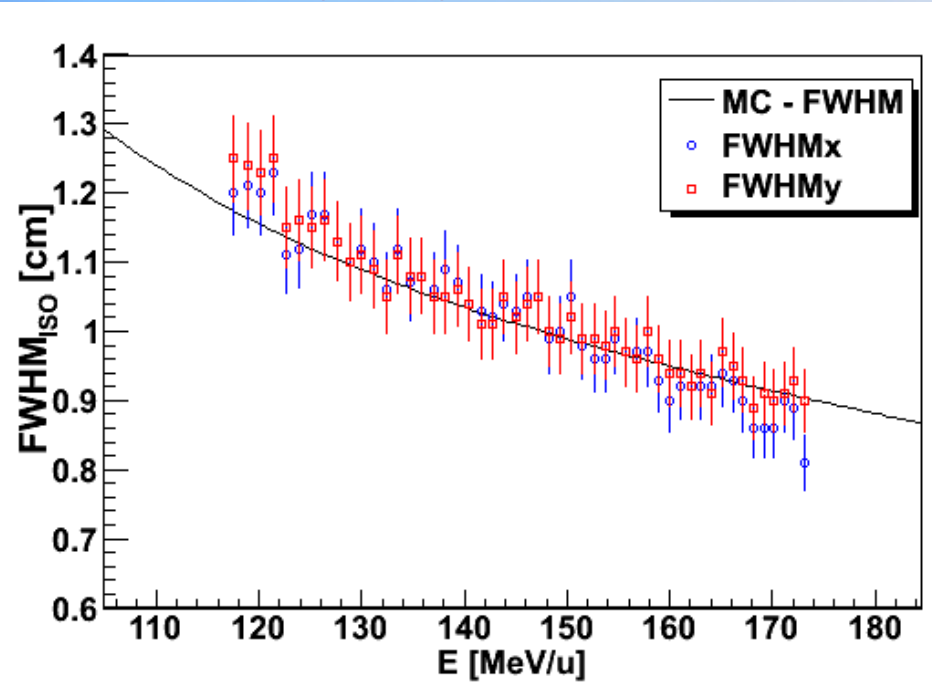
$$I_{\text{pot}} = 76.9 \text{ eV}$$

$$|BP_{\text{sperim}} - BP_{\text{FLUKA}}| \leq 0.1 \text{ mm}$$



Proton Clinical characterization (2/3)

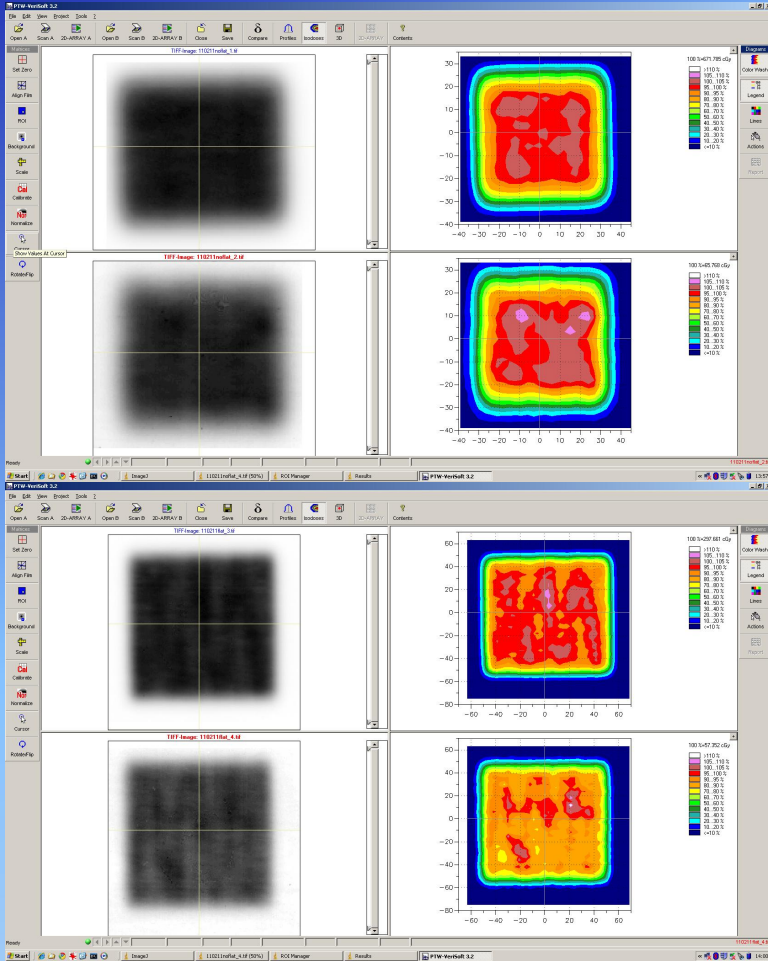
Spot dimensions measurements



E = 117.54 MeV/u (100 mm BP)

Proton Clinical characterization (3/3)

Dosimetric characterization



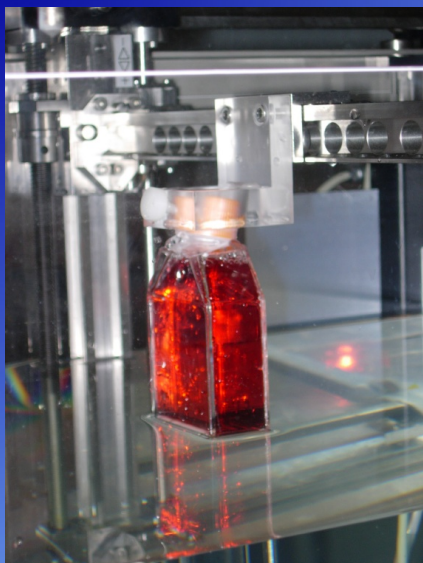
Homogeneity of 2.5%



G. Garibaldi

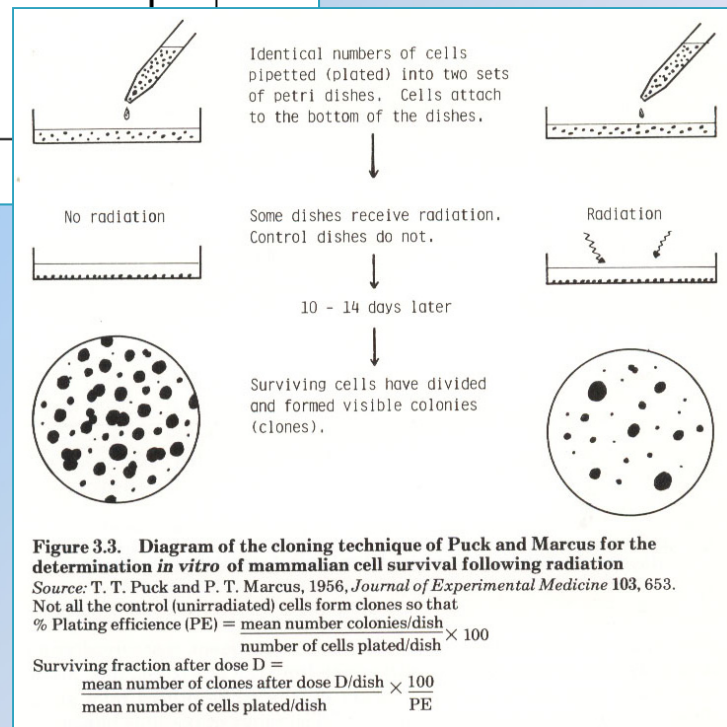
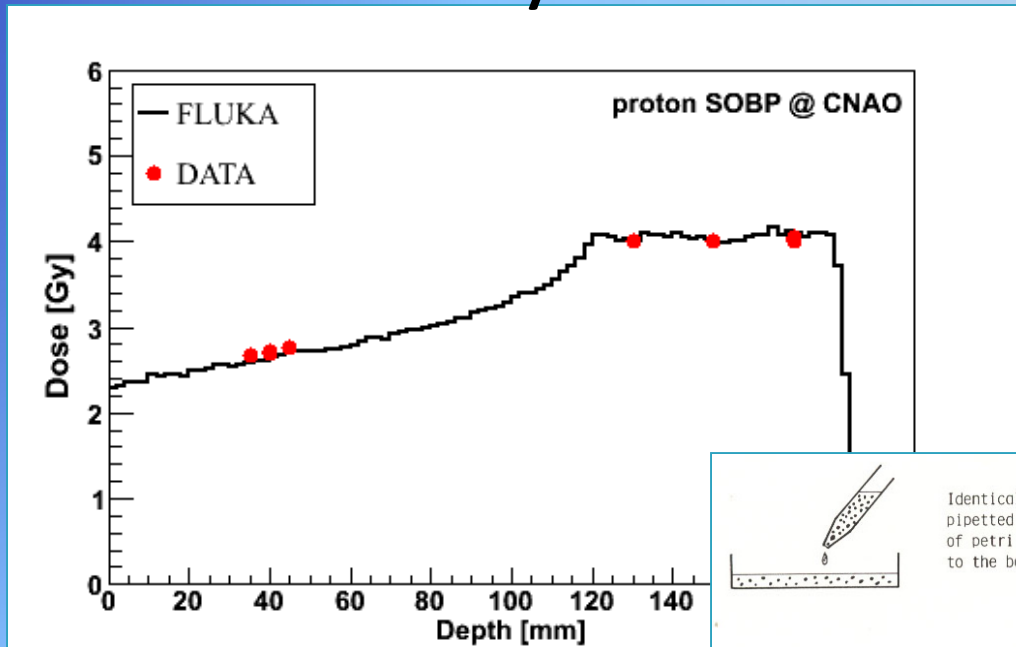
2011 – one of the first scanning exercise in honour of 150 Italian anniversary

Dosimetry for RB

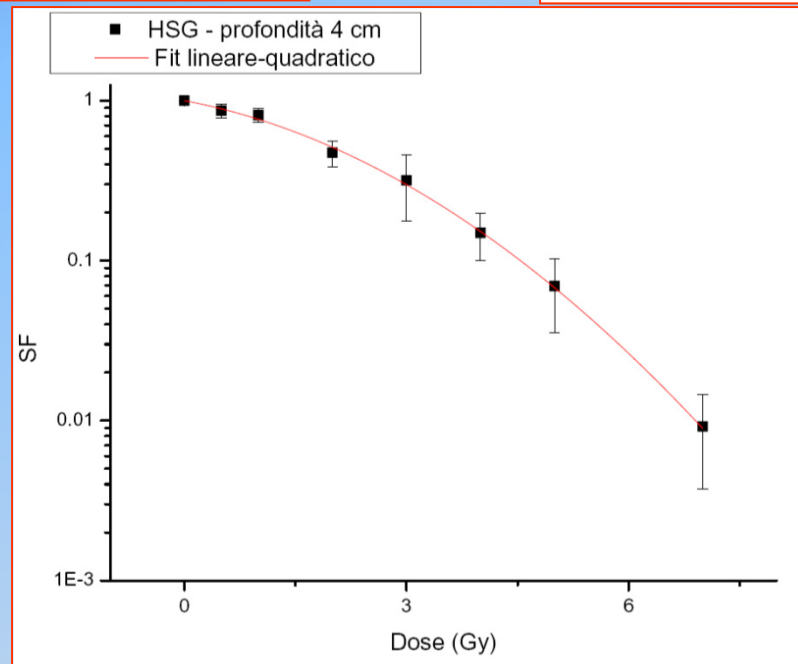
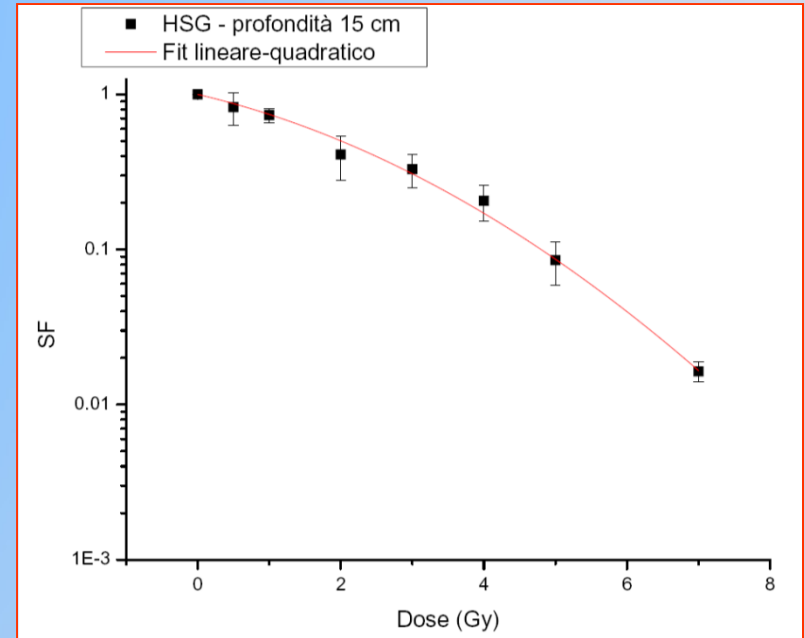
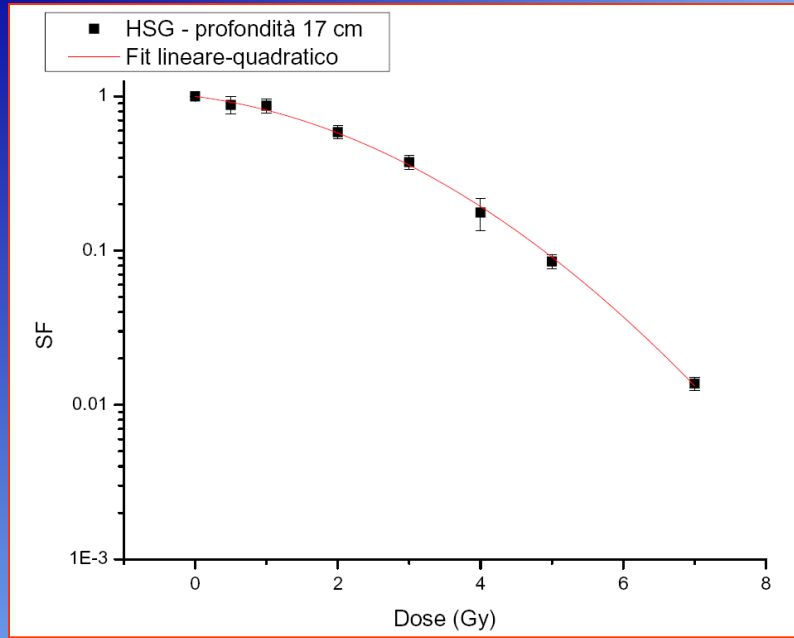


10x10 cm², 33x33 spots, 3 mm step)

- HSG (Human salivary gland tumor)
- T98G (human glioblastoma)
- V79 (Chinese hamster lung fibroblast)



Survival curves– Proton: HSG cells



(Courtesy of Roberto Cherubini)

PROGETTO DI SPERIMENTAZIONE CLINICA

A CURA DI:

Erminio Borloni – Presidente
Roberto Orecchia – Direttore Scientifico
Sandro Rossi – Segretario Generale e Direttore Tecnico



IL CENTRO NAZIONALE DI ADROTERAPIA ONCOLOGICA

Strada Privata Campeggi – 27100 Pavia



Sedi: Via Caminadella, 16 - 20123 Milano
Iscrizione al Registro delle Persone Giuridiche della Prefettura di Milano n. 192
P.IVA n. 03491780965
Codice Fiscale n. 97301200156

Presented to:

- Italian Ministry of Health
- Region Lombardy

Main Tasks:

- Dosimetry characterisation
- Radiobiology characterisation
- Patient treatments

Start of medical activities

*First patient with Proton beam
(September 22, 2011)*



Treatment rooms



3D Real-time IR Optical Tracking (OTS)

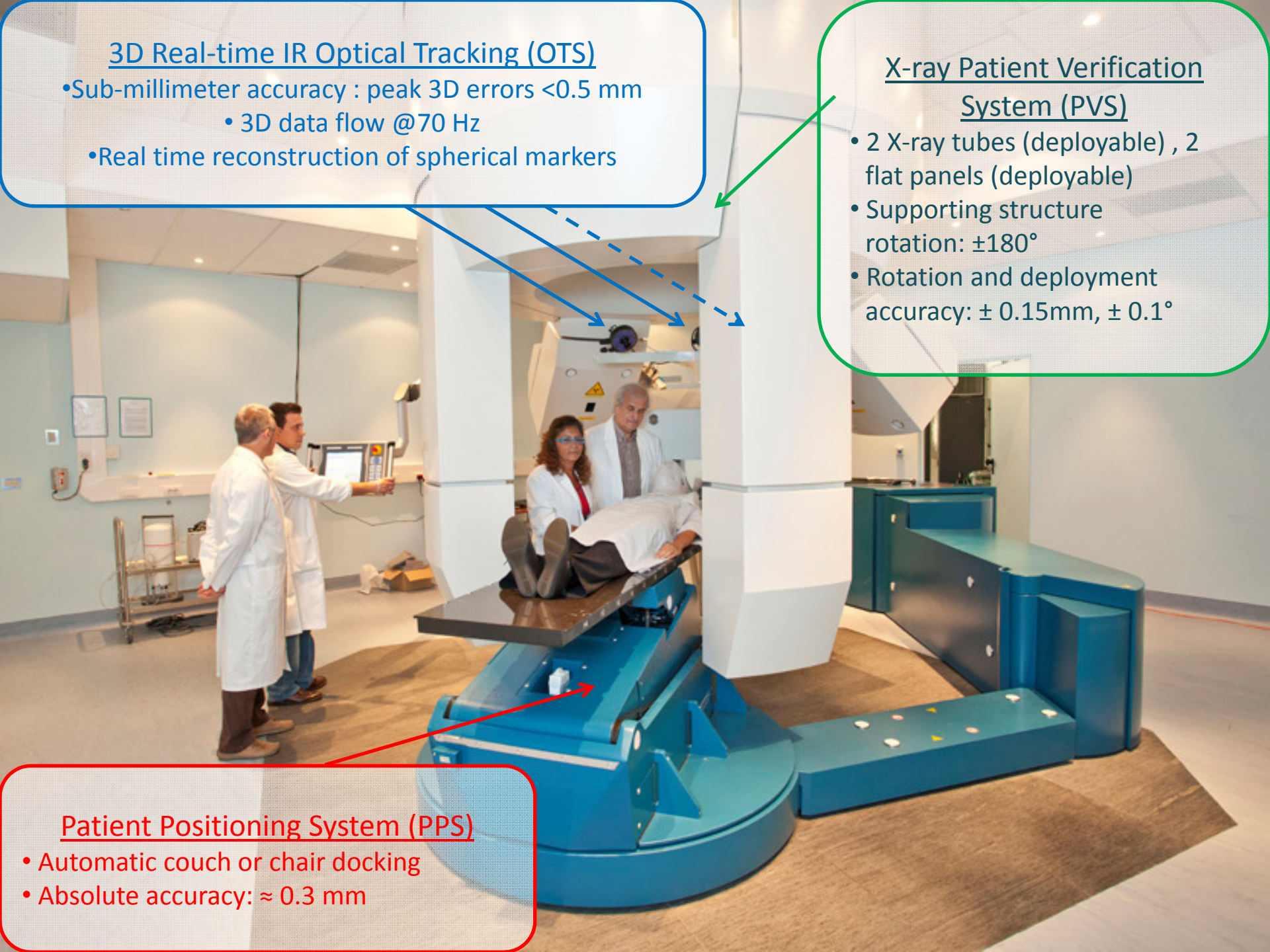
- Sub-millimeter accuracy : peak 3D errors <math>< 0.5 \text{ mm}</math>
 - 3D data flow @70 Hz
- Real time reconstruction of spherical markers

X-ray Patient Verification System (PVS)

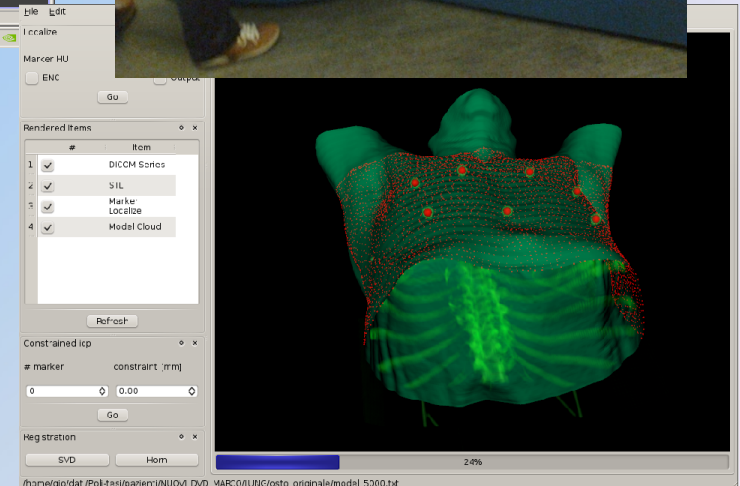
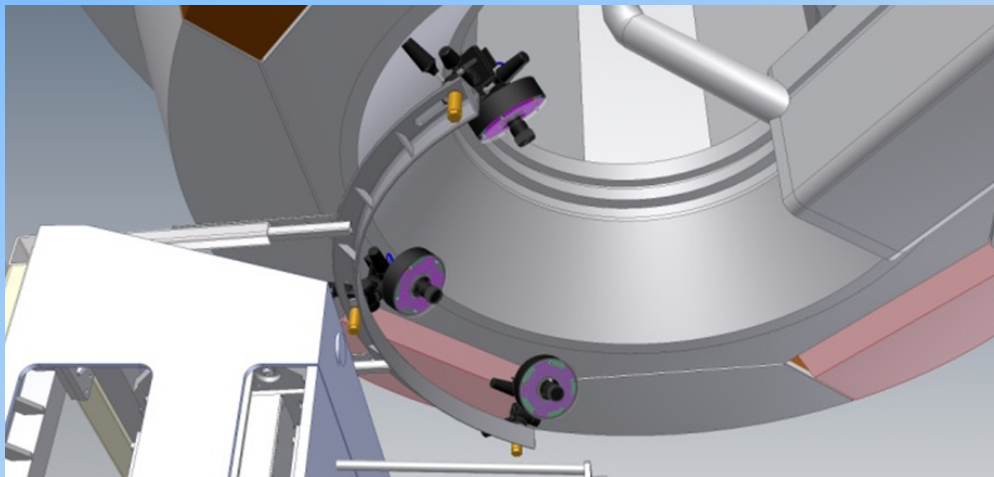
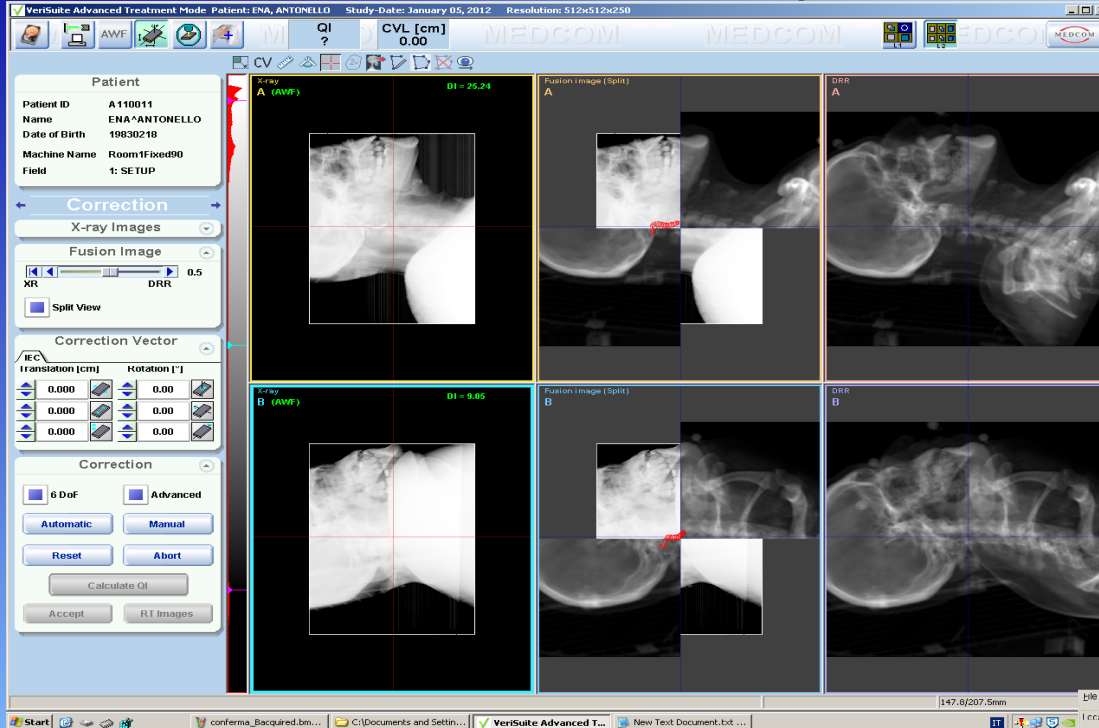
- 2 X-ray tubes (deployable) , 2 flat panels (deployable)
- Supporting structure rotation: $\pm 180^\circ$
- Rotation and deployment accuracy: $\pm 0.15 \text{ mm}$, $\pm 0.1^\circ$

Patient Positioning System (PPS)

- Automatic couch or chair docking
- Absolute accuracy: $\approx 0.3 \text{ mm}$



Treatment planning system



Possible pathologies at CNAO

Proton beam

- Uveal melanoma
- Chordoma
- Chondrosarcoma (head, trunk)
- Meningioma (base of skull)
- Paranasal sinus cancer
- CNS schwannoma
- Pituitary adenoma

Carbon ion beam

- Salivary gland tumors
- Mucosal melanoma (head & neck)
- Bone sarcoma
- Soft tissue sarcoma
- Prostatic carcinoma

Treatment planning system

The screenshot displays a comprehensive radiation therapy treatment planning system interface. The main window is divided into several functional areas:

- Top Left:** Patient information and menu options (Patient, Applications, Transfer, Mode, Tools, View, Orientation, Segmentation, Options, Help). Patient details include "xhacoll, ariol", "A110001", and "01-Jan-1985".
- Top Center:** A large axial CT scan of the head with various colored contours (green, blue, yellow, red) representing different anatomical structures and target areas.
- Top Right:** A vertical toolbar with icons for "Viewing", "Flipping", "3D", and "VSim". Below it is a "Structure" and "Display" panel with a dropdown menu set to "mid ear left" and "Type: Normal Organ".
- Bottom Left:** Three smaller CT scan views (axial, sagittal, and another axial) showing different slices of the patient's head.
- Bottom Center:** A "Blending" panel with sliders for "CT" (set to 100) and "Color Look" (set to "Gray Scale (8 Bit)"). It also includes a "Window" section with "C: 38" and "W: 240".
- Bottom Right:** Two large panels showing dose distribution maps. The top panel is a sagittal view of the neck with a color-coded dose distribution. The bottom panel is an axial view of the neck with a similar dose distribution. Both panels include a legend on the right with dose levels (e.g., 20.00 GyE, 40.00 GyE, 67.00 GyE, 75.00 GyE) and a color scale.
- Bottom Far Right:** A vertical toolbar with icons for "Tools", "View", and "Orientati...".

At the bottom left, the user name "User: sylvia.molinelli@MAIN" and a "Storage Commitment Failed" message are visible.

Orders of magnitude

Dose uniformity required: $\pm 2.5\%$

Treatment session duration: 20 - 30 min

Irradiation duration: 2 - 3 min

Slice thickness: 3 - 5 mm

Spot size: 4 - 10 mm

Position precision: 0.1 mm

Spot duration: 5 - 10 ms

Beam current: 0.1 - 1 nA

Measurement time: $< 100 \mu\text{s}$

74 CGE, 37 fractions for patient with Protons

Treated Patients at CNAO by July 2012: 17

Experimentation phase

230 patients

150 patients

Carbon ions

80 patients

Protons

Typical day at CNAO

- 6:00 Start of daily QA of Proton beams
- 8:30 start of treatments
- 14:00 start of Carbon ions commissioning
- 3:00 start of typical measurement with Proton beam (summary of machine status)

Scheduled maintenance activities during the night (up to 3:00)

About maintenance..

Each year four shutdowns of 1 week are foreseen for the ordinary maintenance of the high technology devices

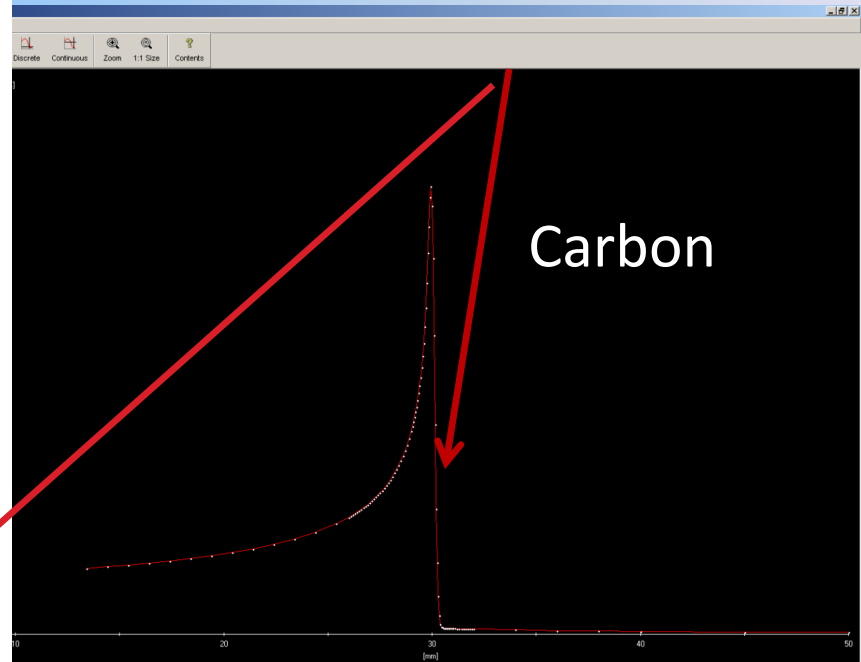
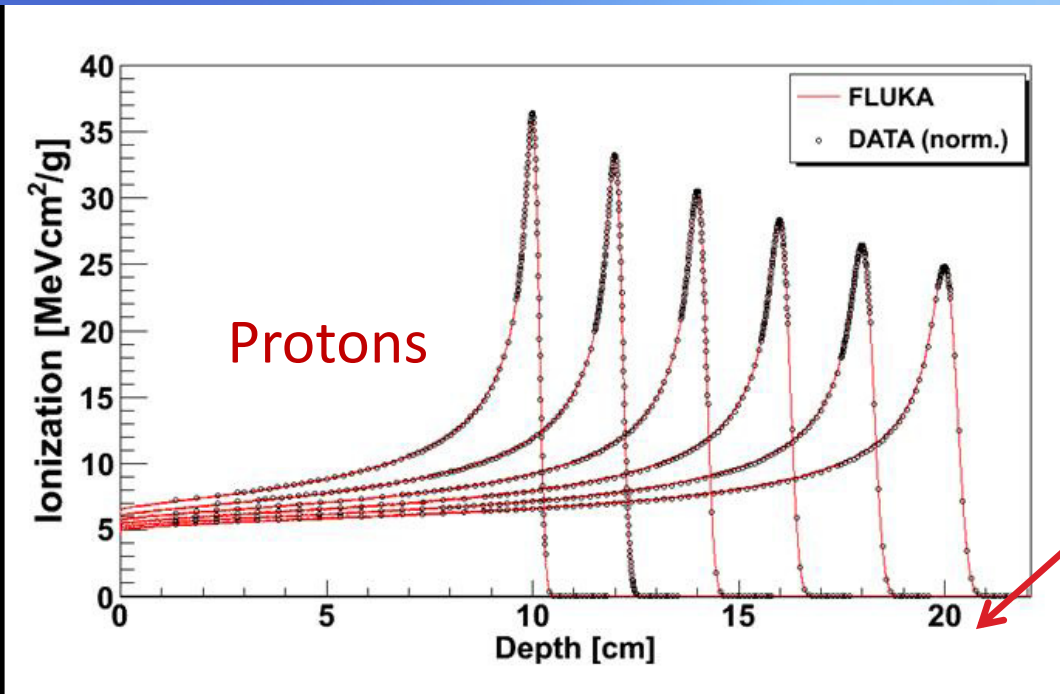
In this way the scheme of ramp down and ramp up of patients is avoided. In fact during a proton therapy a patient can sustain an interruption of 10 days.

About Carbon ions

Carbon ions have been physically and clinically commissioned using T line
Radiobiological characterization (in vivo on mice and in vitro experiments)
will start on May 25, 2012.

First patient with Carbon ions beam is foreseen in September 2012

Different fall-out



The other beam lines with both the species will be operative in the next months: this will allow
To increase the number of patients.

Conclusions

- CNAO construction is finished
- Accelerator commissioning is in progress
- Medical Physics activities with Proton and Carbon ion beam (Imaging, Treatment planning, instrumentation acquisition, workflow specification, etc.) have started
- Many research programs are in progress (internal activities, collaborations with international partners, ULICE)



Thank you for your attention