Operation and patient treatments at CNAO facility

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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.

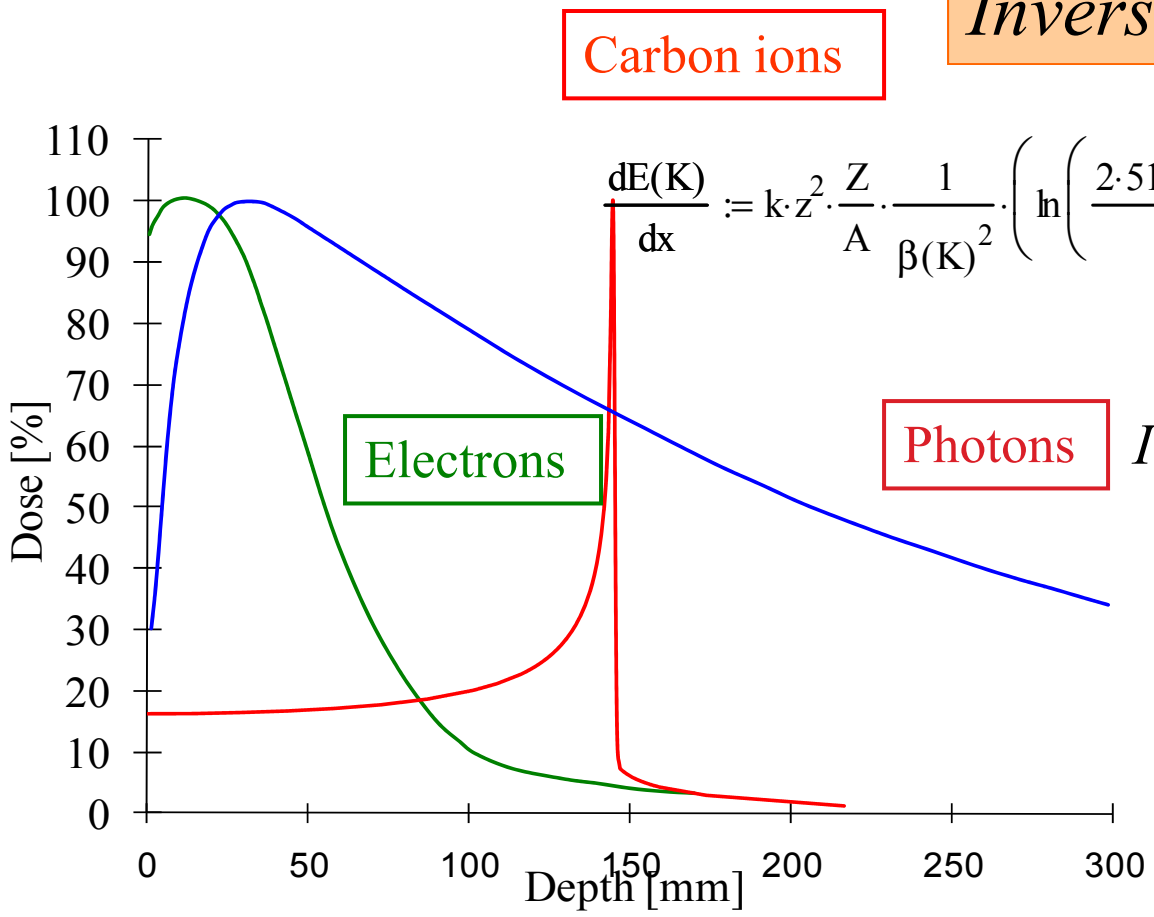
Hadrontherapy is a high precision kind of radiotherapy employing hadrons instead of the standard electrons and photons.

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

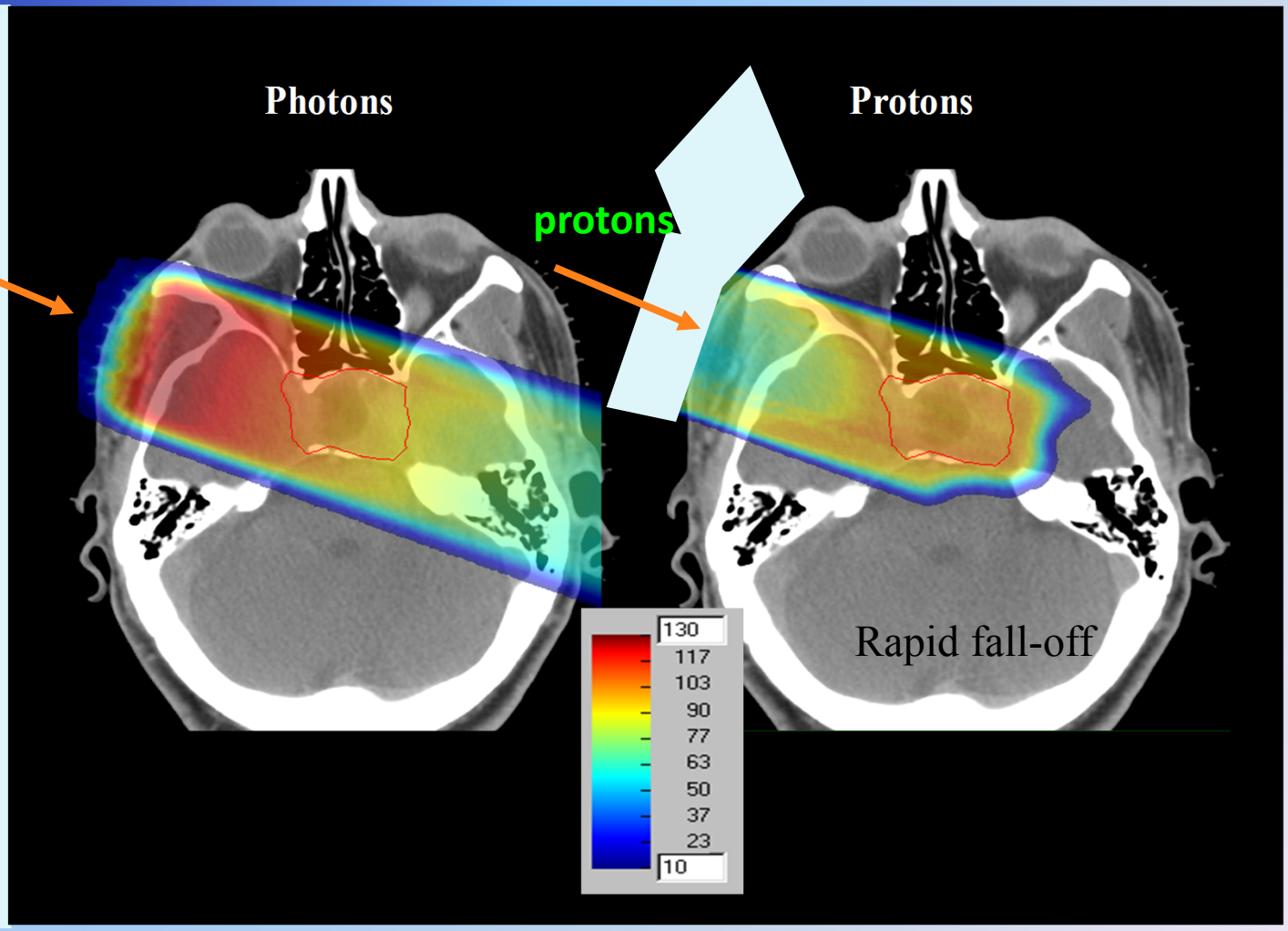
Inverse dose profile



$$\frac{dE(K)}{dx} := k \cdot z^2 \cdot \frac{Z}{A} \cdot \frac{1}{\beta(K)^2} \cdot \left(\ln\left(\frac{2 \cdot 511 \cdot \beta(K)^2 \cdot \gamma(K)^2}{I} \right) - \beta(K)^2 \right)$$

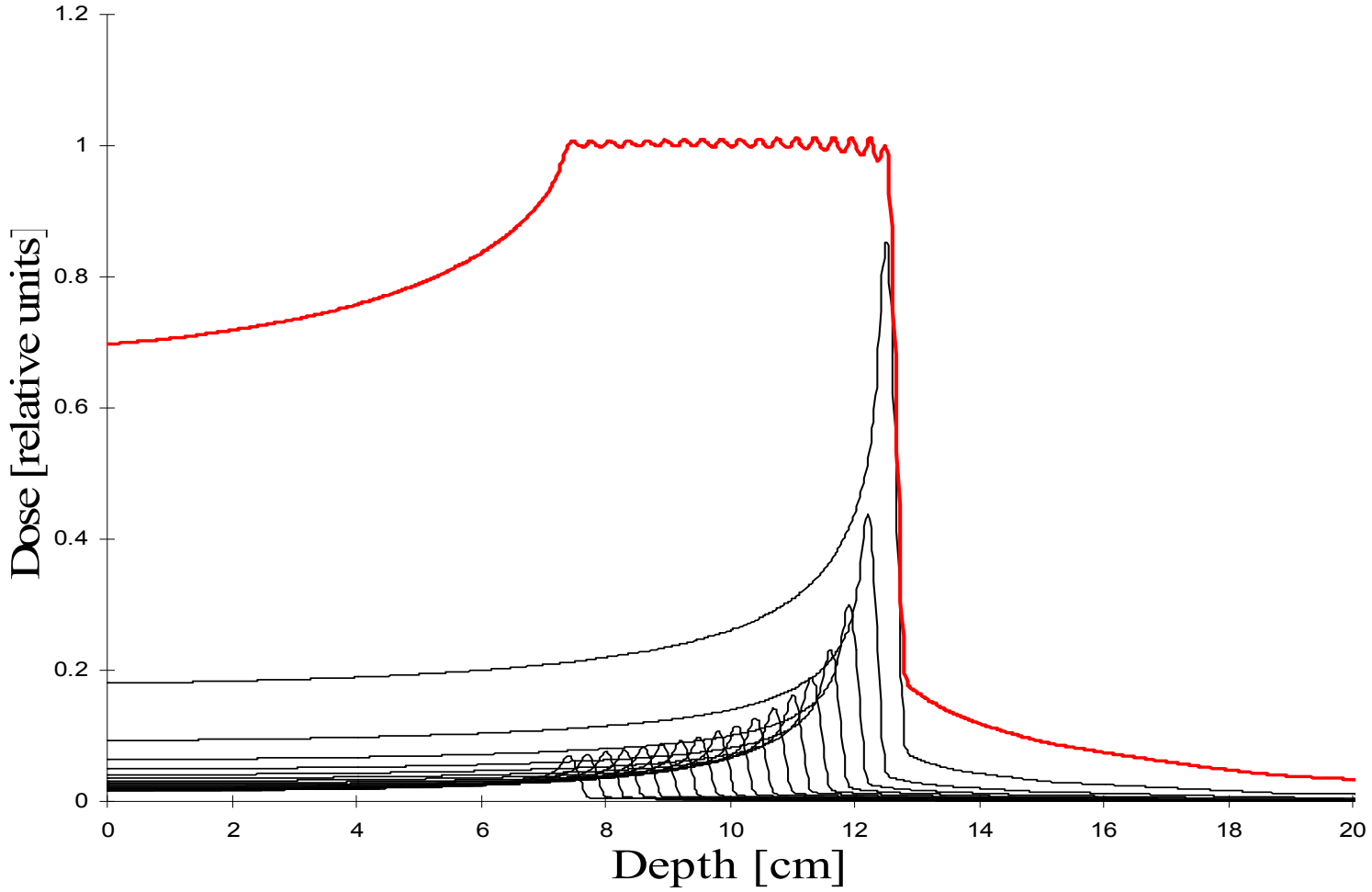
$$I = I_0 \cdot e^{-\mu \cdot x}$$

Comparison of dose distribution

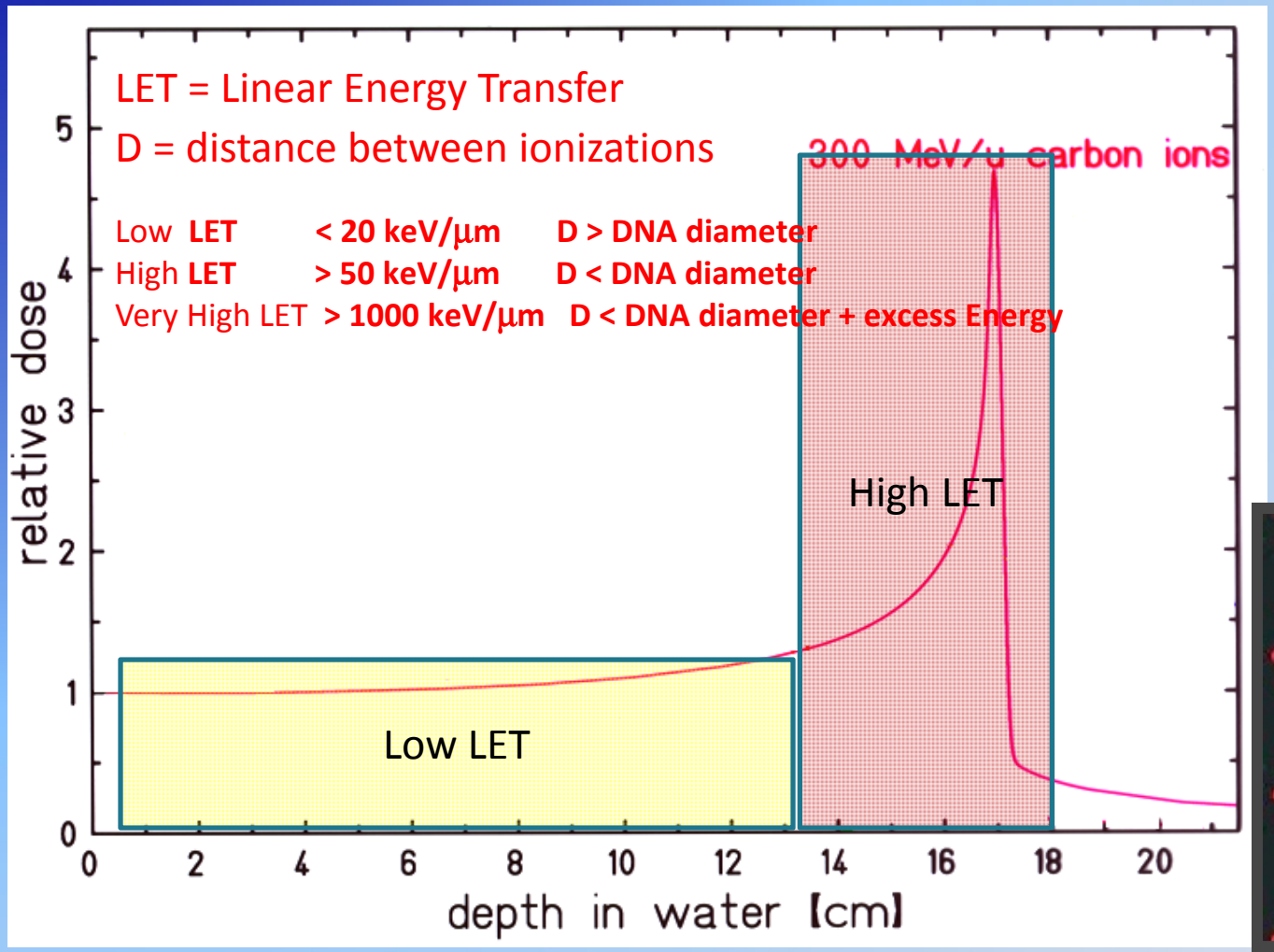


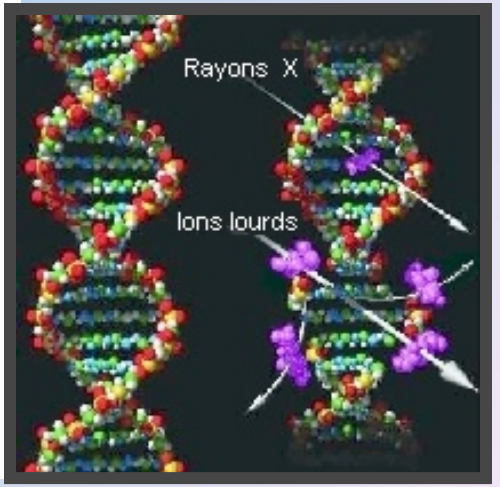
Spread Out Bragg Peak

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



Carbon ions have higher *LET* than protons





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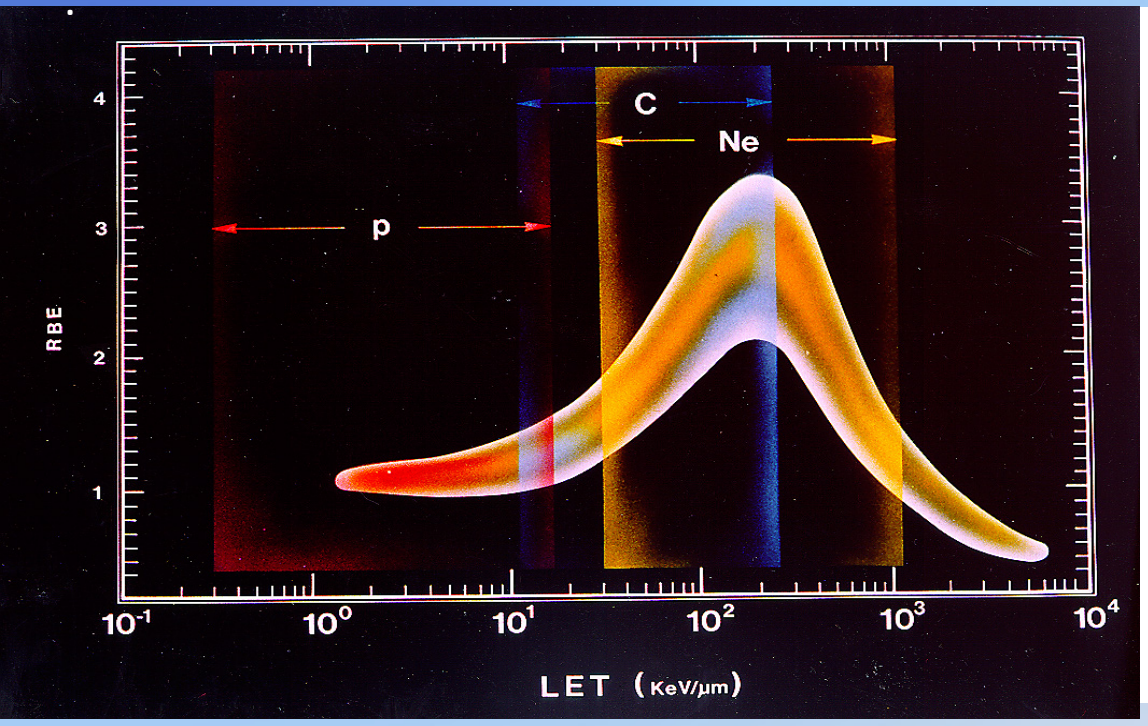
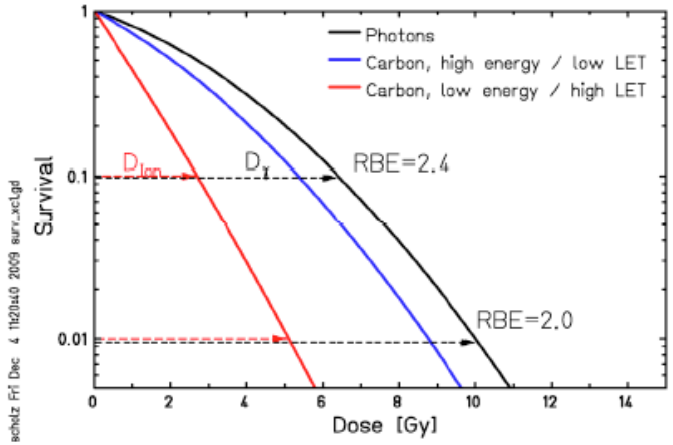
Why carbon ions?

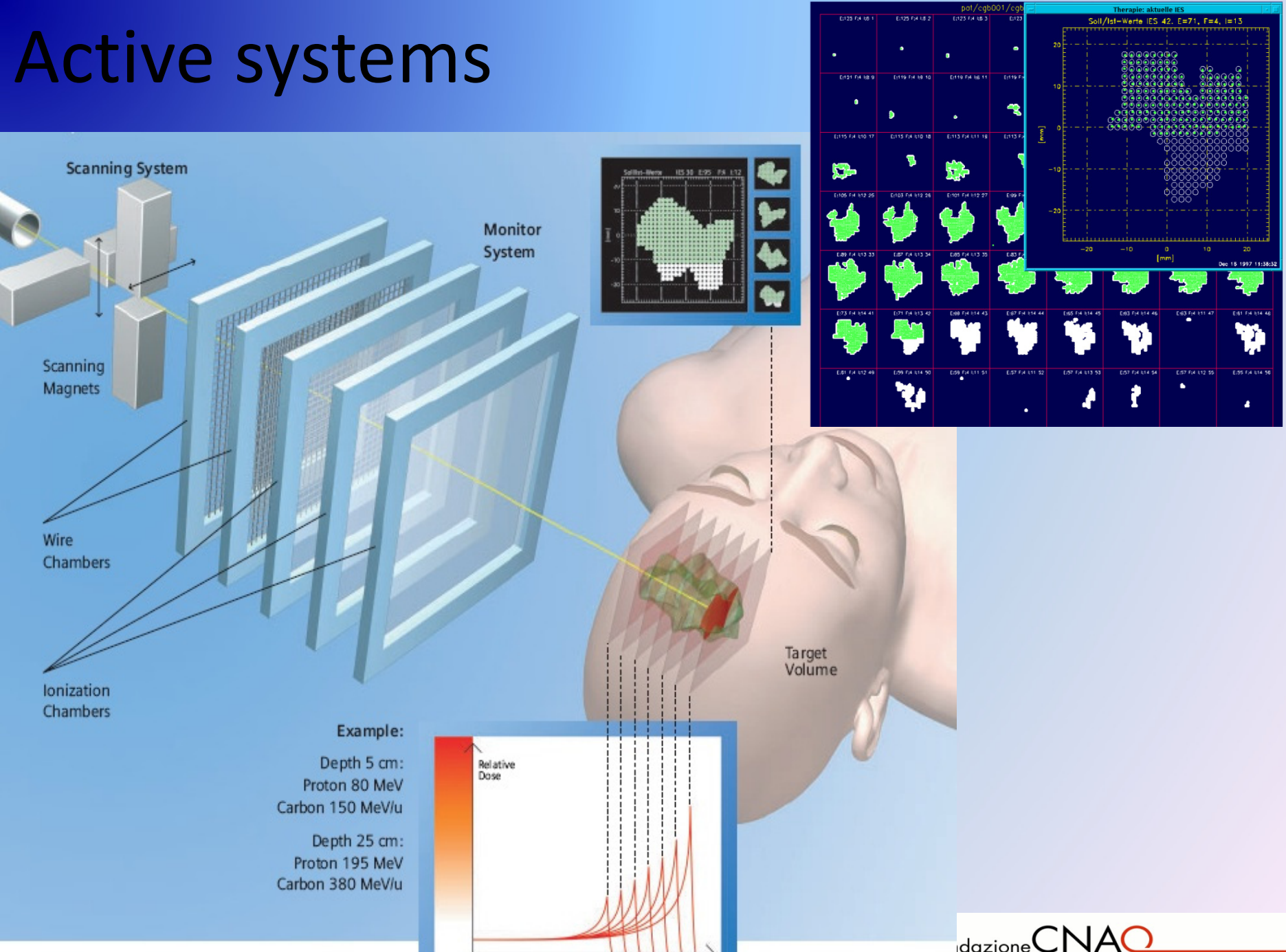
Qualitatively the energy deposited by carbon ions is more efficient, in terms of cell destruction, than the energy deposited by protons.
The higher efficiency in killing cells is expressed by the *relative biological effectiveness (RBE), which* is the ratio between the photon and the ion doses to produce 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



(Courtesy of Siemens Medical)

What is the CNAO Foundation

It is the first Italian center (second in Europe)
For hadrontherapy wih 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

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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**

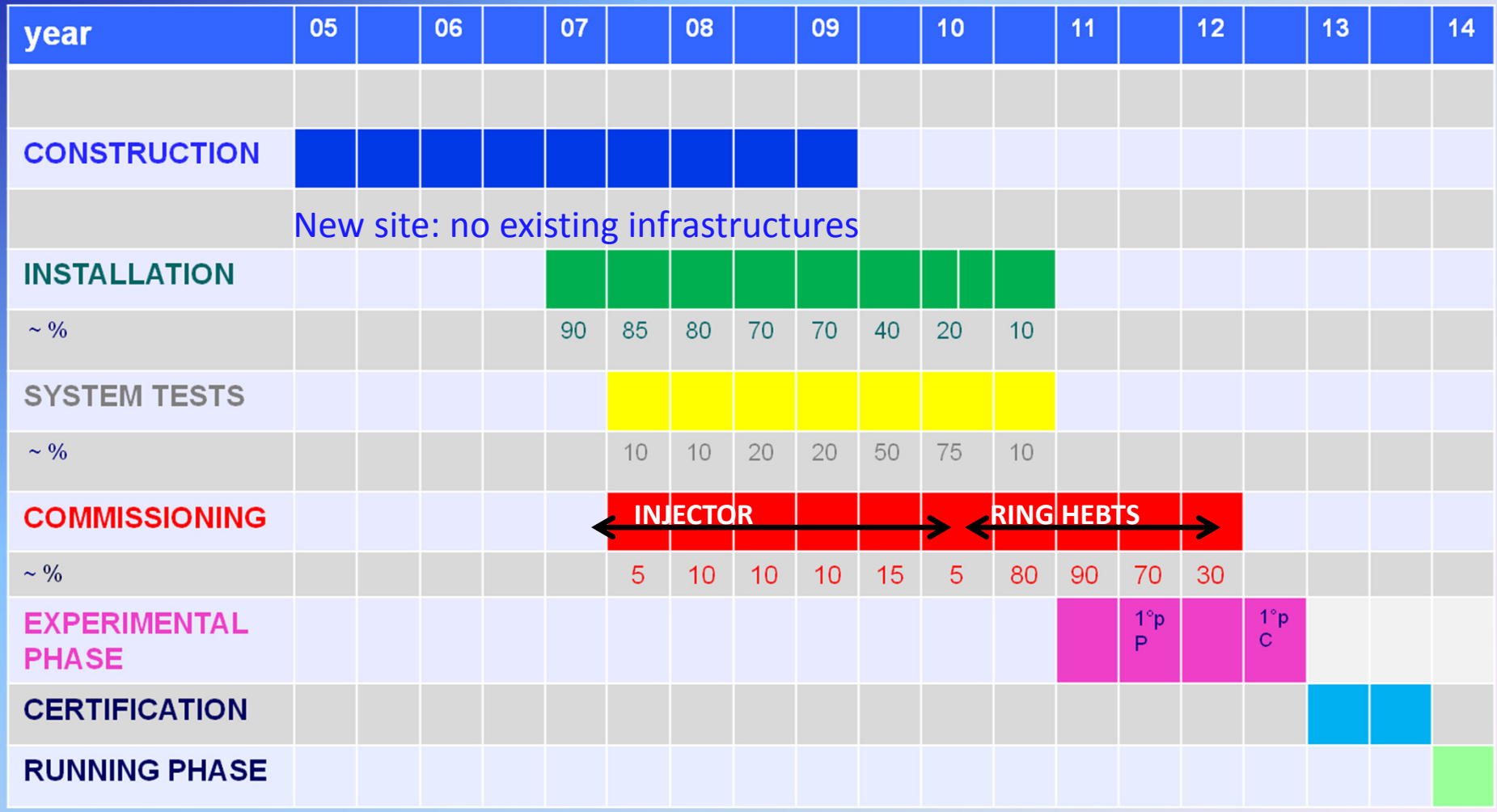
Steps of CNAO

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



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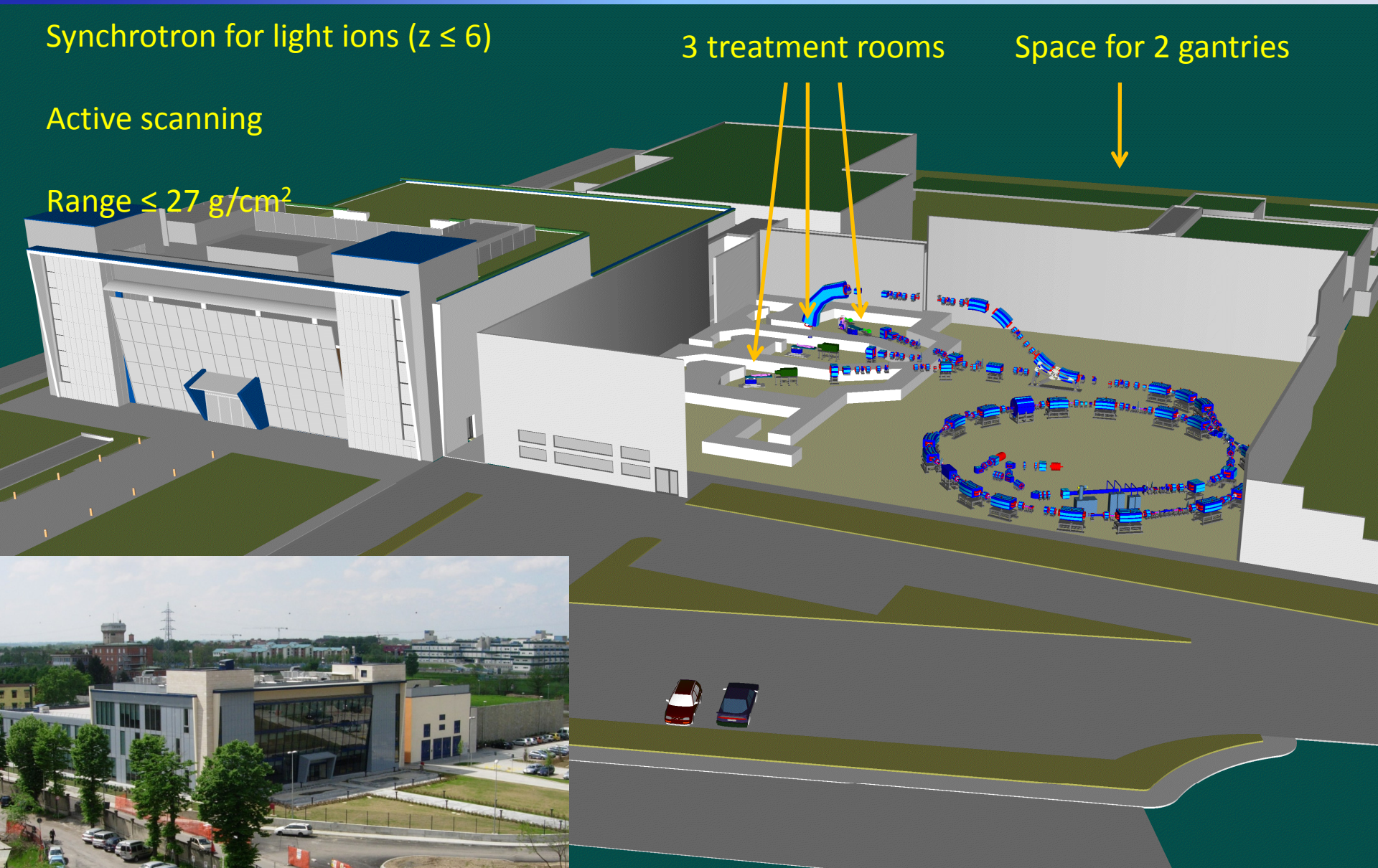
CNAO Site

Overview

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

Active scanning

Range ≤ 27 g/cm^2

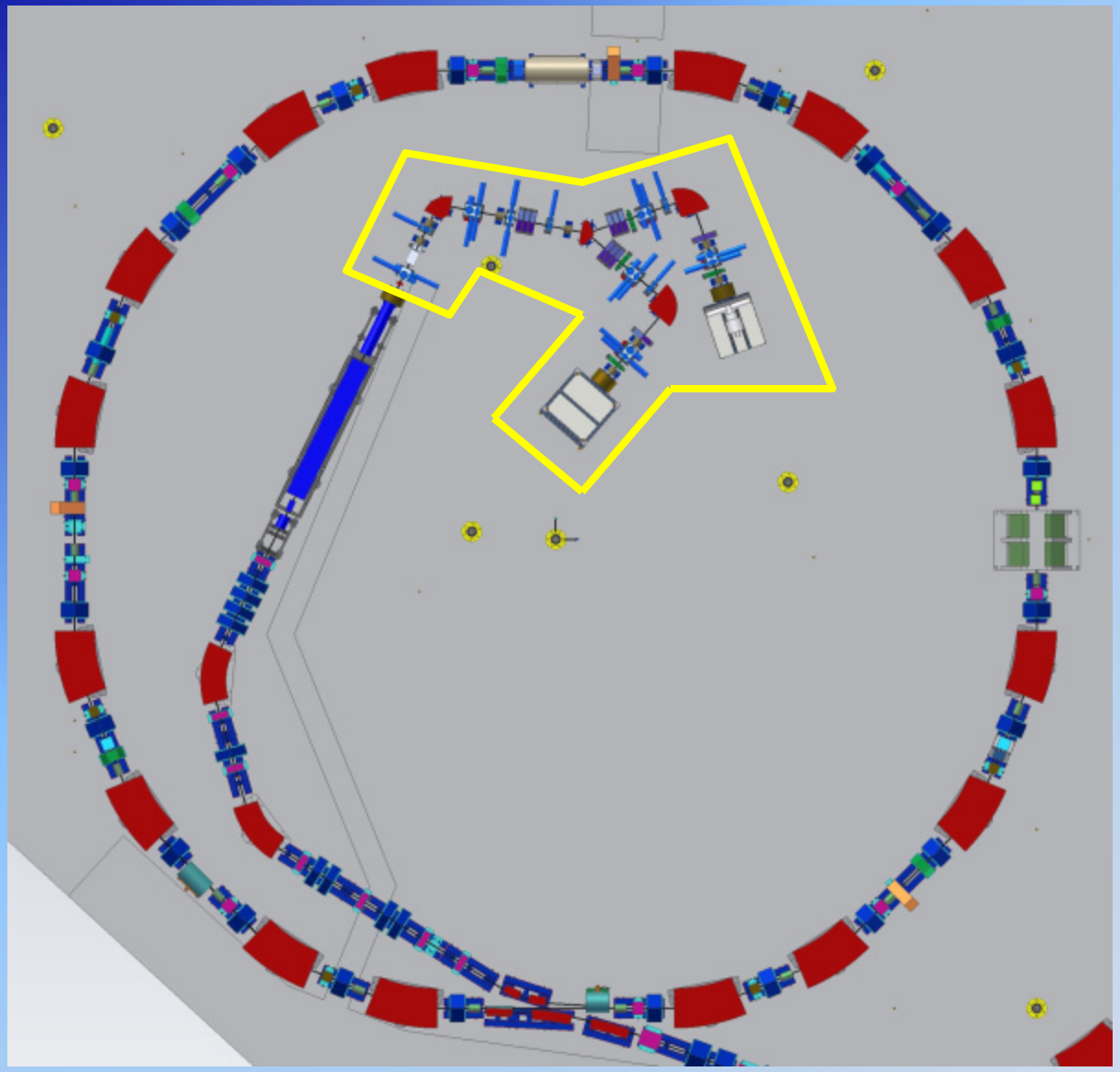


Basic Parameters I

Protons (< 10^{10} per spill)				
	LEBT (H_3^+)	MEBT	SYNC	HEBT
Energy [MeV/u]	0.008	7	7-250	60-250
Imax [A]	0.43×10^{-3}	0.7×10^{-3}	5×10^{-3}	7×10^{-9}
Imin [A]	0.43×10^{-3}	70×10^{-6}	0.12×10^{-3}	17×10^{-12}
$\varepsilon_{rms,geo}$ [π mm mrad]	35	1.9	0.67-4.2	0.67-1.43(V)
$\varepsilon_{tot,geo}$ [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
$(\Delta p/p)_{tot}$	±1.0‰	±(1.2-2.2)‰	±(1.2-3.4)‰	±(0.4-0.6)‰

Basic Parameters II

Carbon (< 4 10^8 per spill)				
	LEBT (C^{4+})	MEBT	SYNC	HEBT
Energy [MeV/u]	0.008	7	7-400	120-400
Imax [A]	0.16×10^{-3}	0.15×10^{-3}	1.5×10^{-3}	2×10^{-9}
Imin [A]	0.16×10^{-3}	15×10^{-6}	28×10^{-6}	4×10^{-12}
$\varepsilon_{rms,geo}$ [π mm mrad]	35	1.9	0.73-6.1	0.73-1.43(V)
$\varepsilon_{tot,geo}$ [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
$(\Delta p/p)_{tot}$	±1.0‰	±(1.2-2.0)‰	±(1.2-2.9)‰	±(0.4-0.6)‰



LEBT

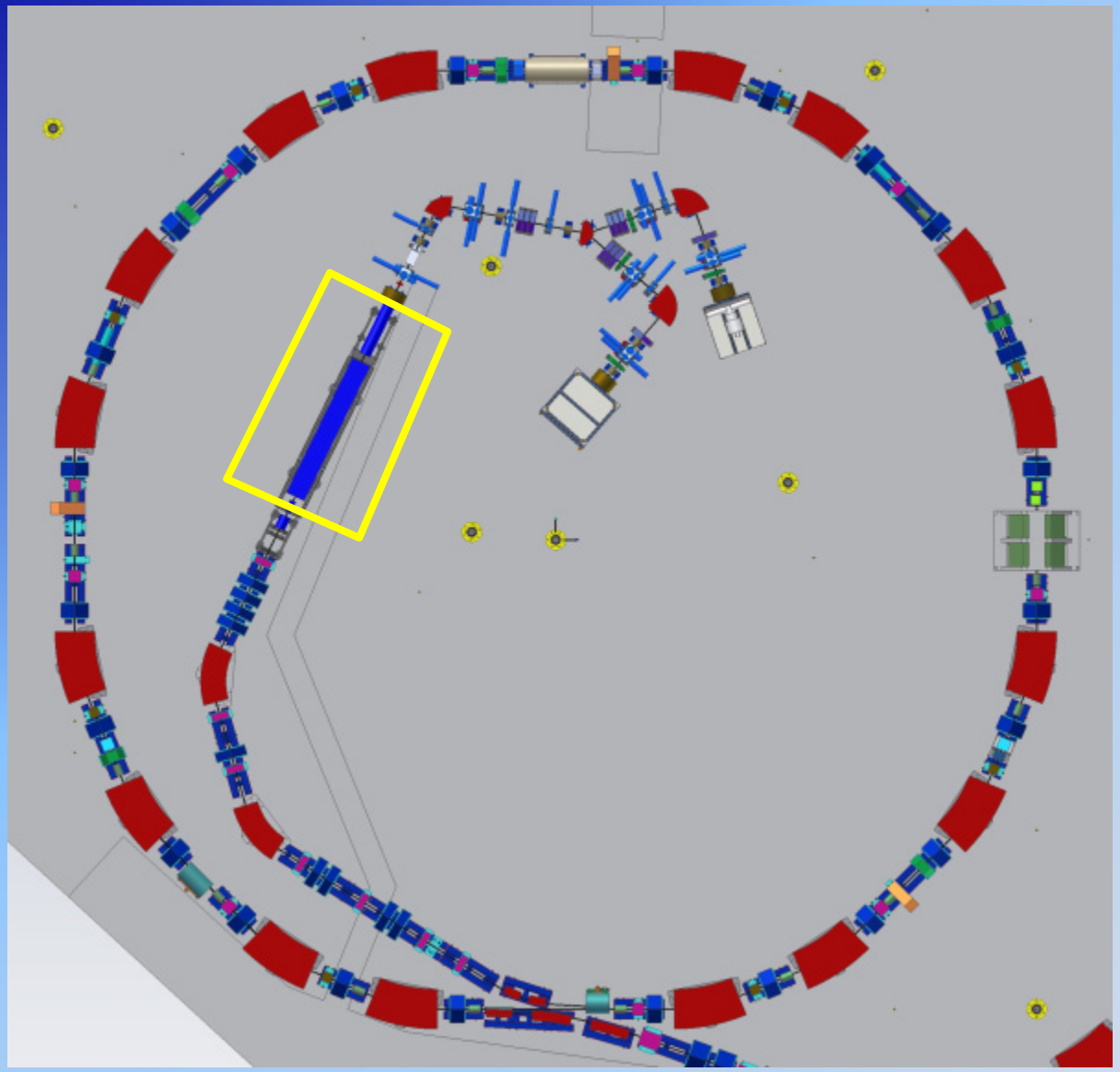
0.008 MeV/u H^{3+}
0.008 MeV/u C^{4+}

I ~ 0.5 mA (H^{3+})
I ~ 0.2 mA (C^{4+})

Two ECR sources (frequency tuning)

Continuous beam

LEBT Chopper

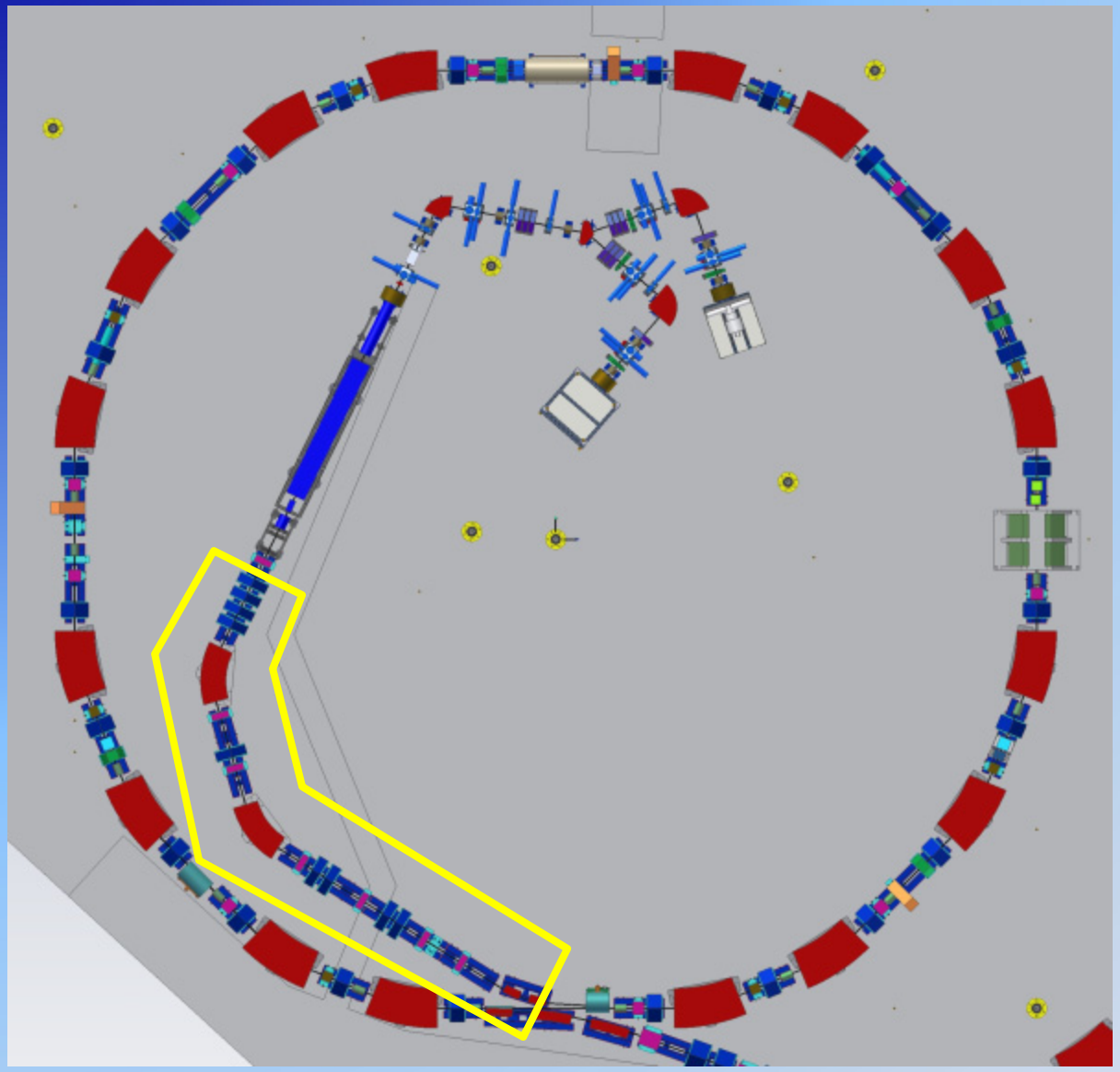


Linac=RFQ+IH

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 C^{6+}

I ~ 0.75 mA (p)
I ~ 0.15 mA (C^{6+})

Match betas

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

Stripping foil

Current selection

Debuncher

Emittance dilution

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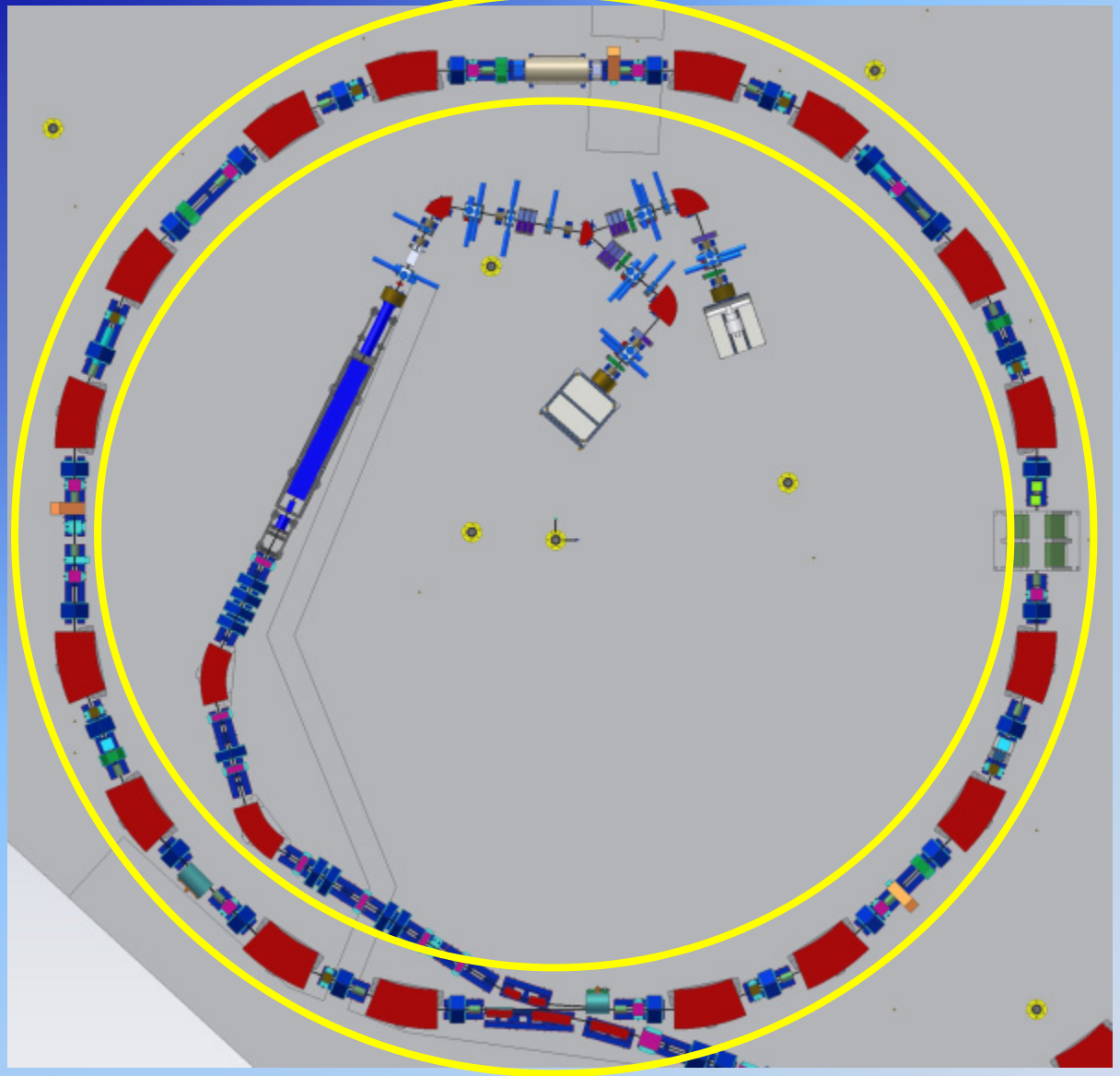

Synchrotron

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

I ~ 0.1-5 mA (p)
I ~ 0.03-1.5 mA (C)

Slow extraction

Betatron core

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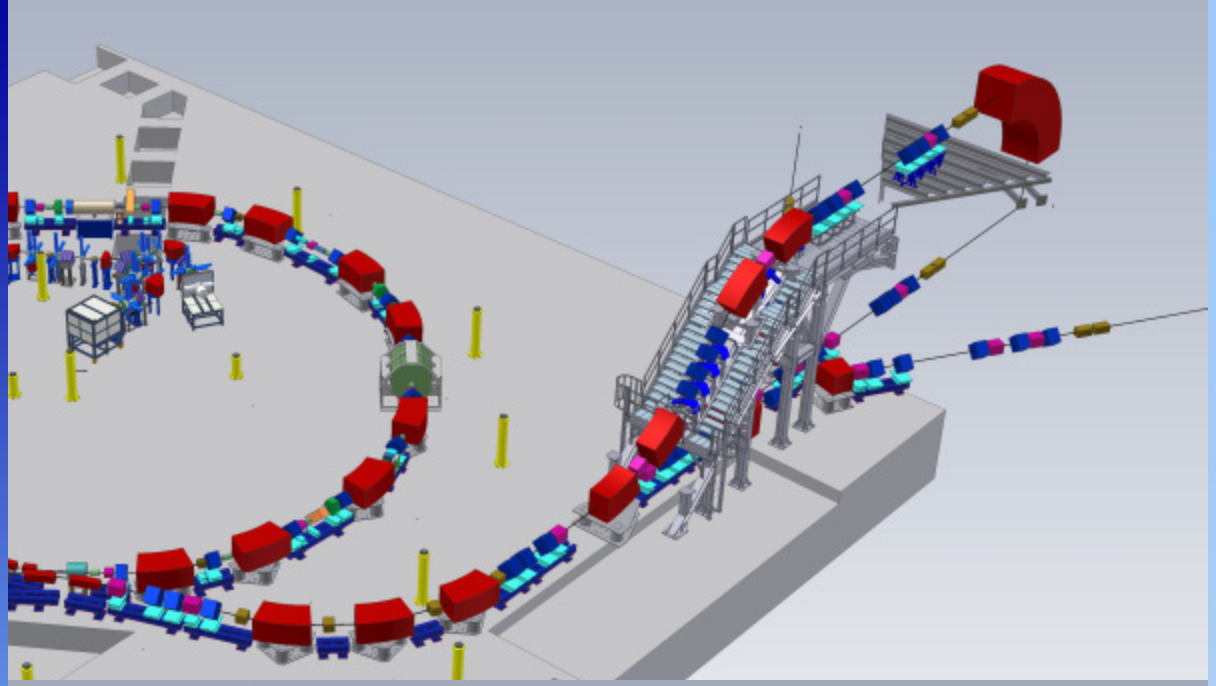
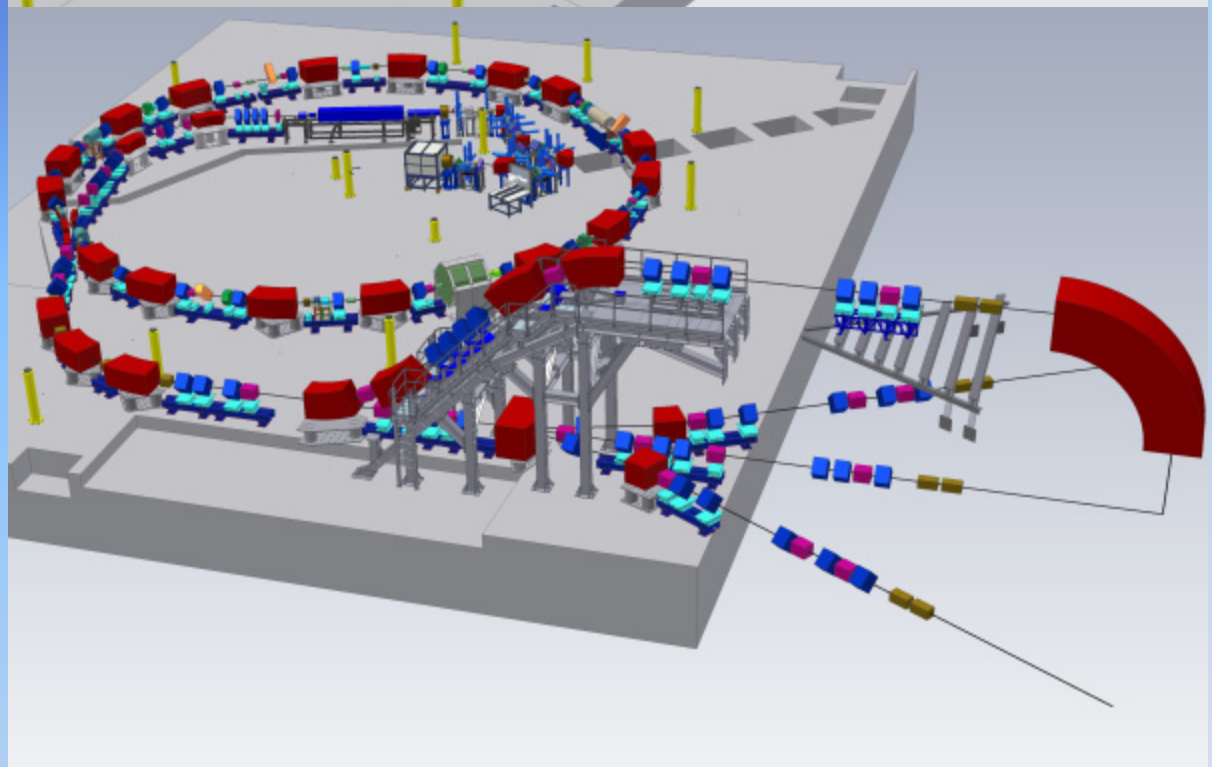




HEBT

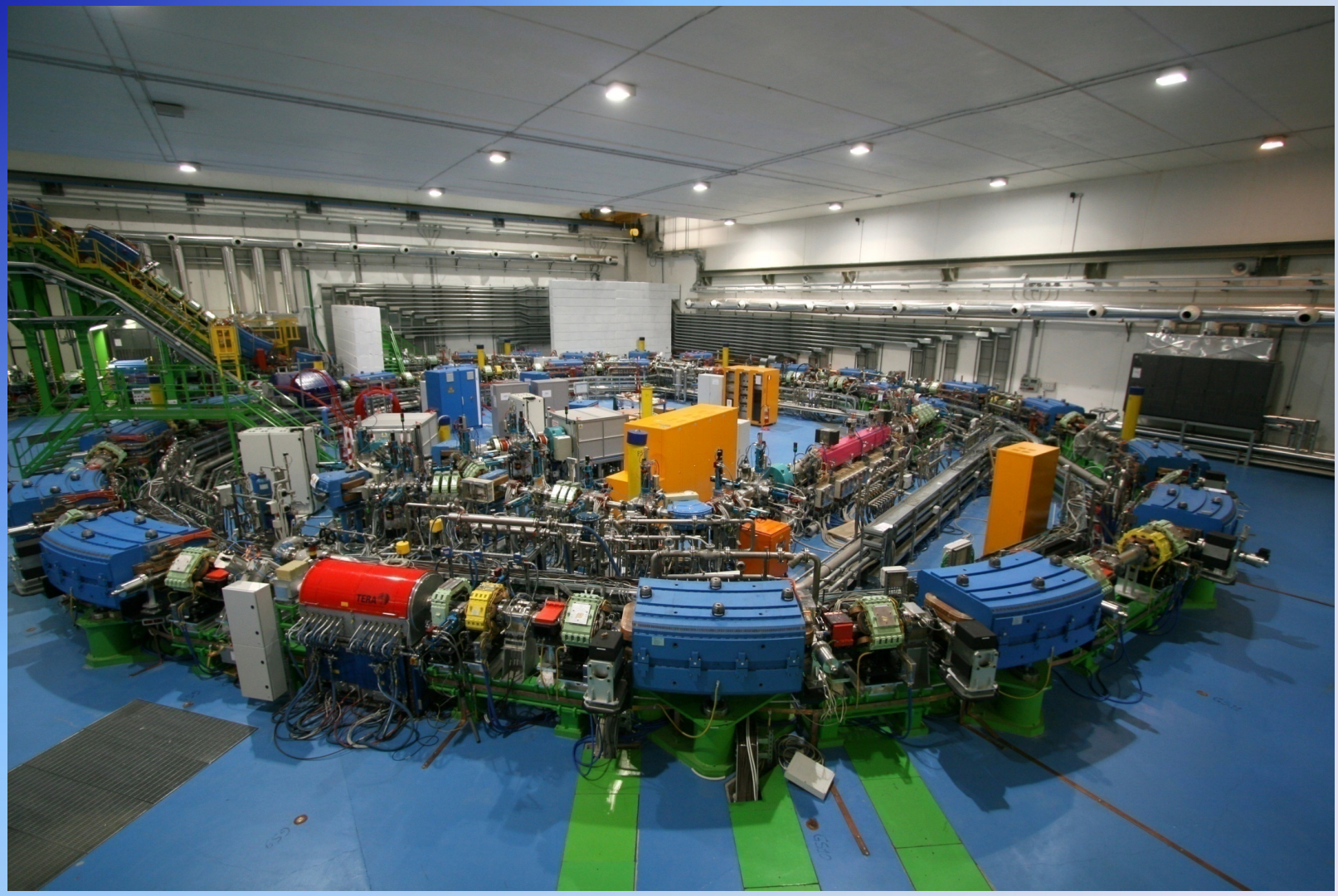
60-250 MeV p
120-400 MeV/u C

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

different settings for

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

Installation status



Accelerators and lines installation is finished

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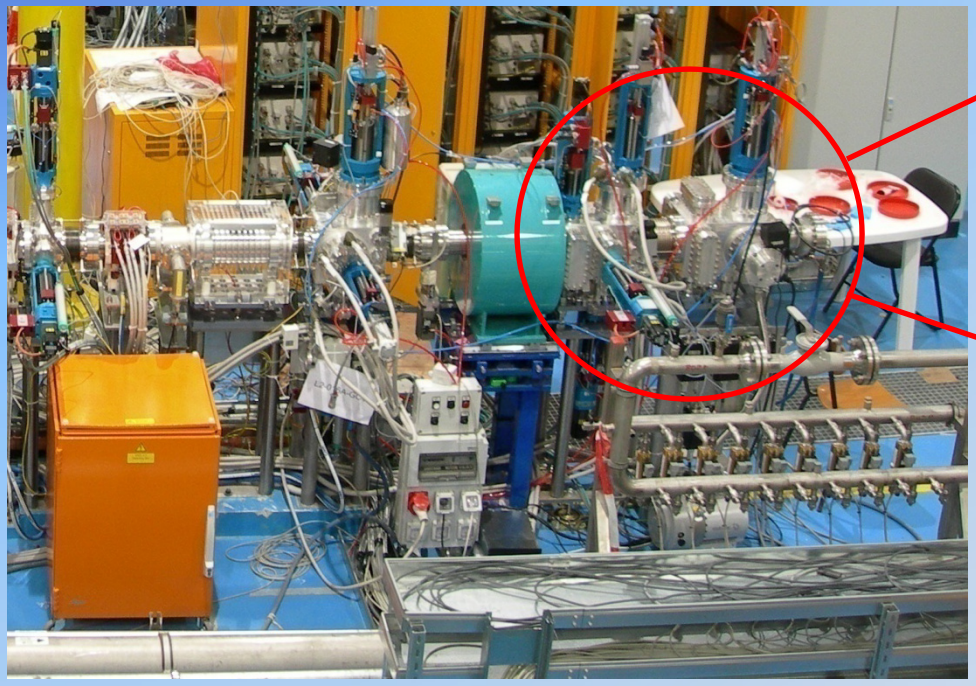
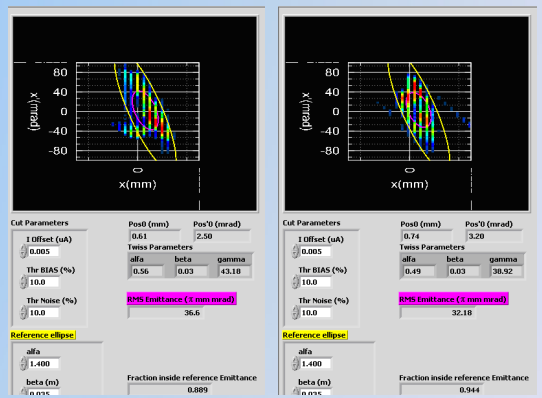
LEBT commissioning (2008)

Transmission up to 97%

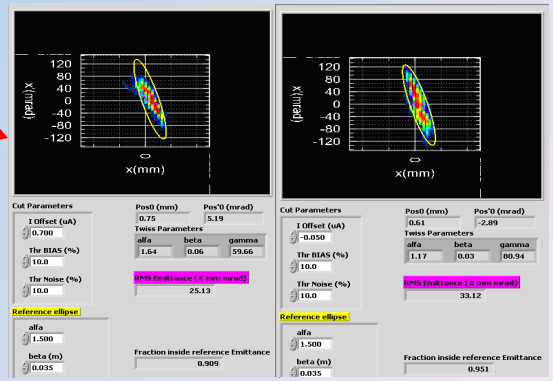
I_C up to 230 µA, I_{H3} up to 1.2 mA



Carbon H-V



H_3^+ H-V



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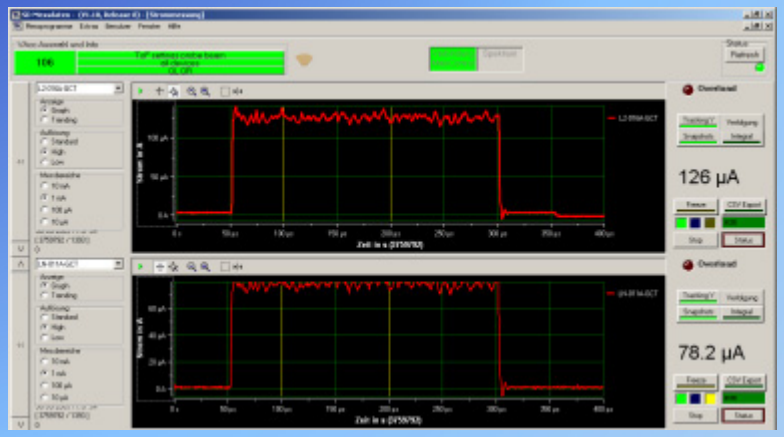
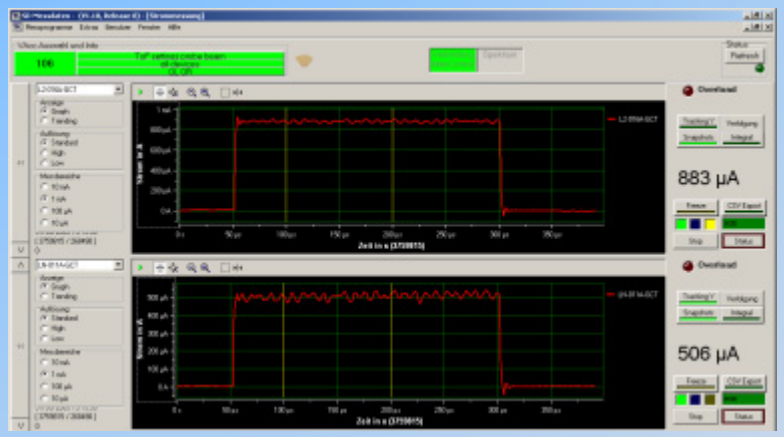
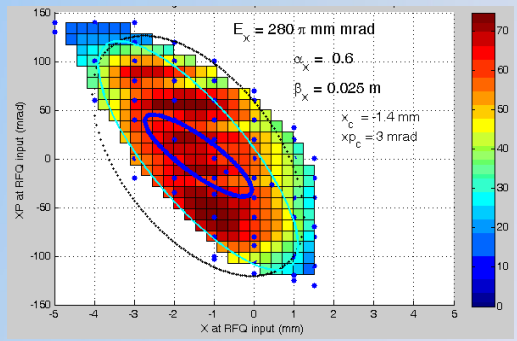
RFQ Commissioning (2009)

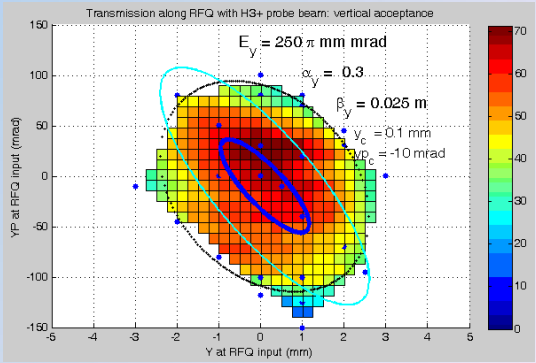
Transmission of 60%
(25% of losses longitudinal)





Acceptance of RFQ measured





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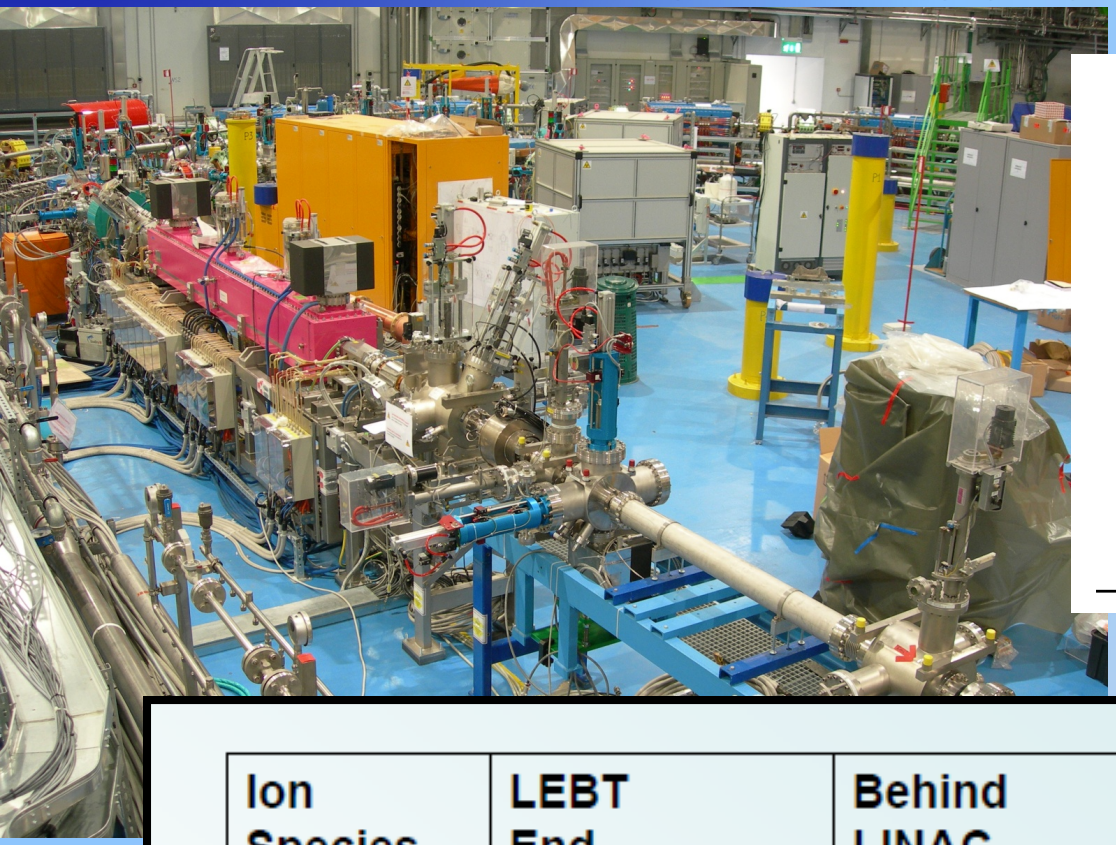
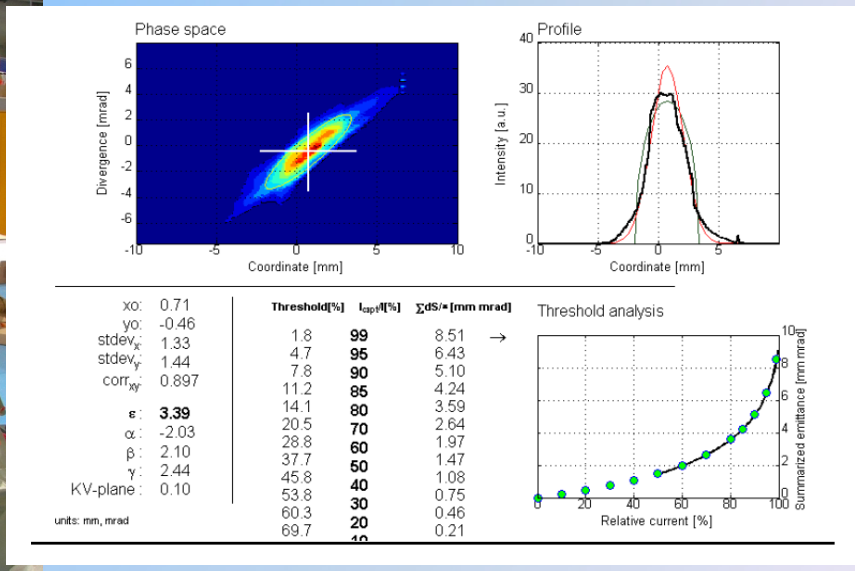
LINAC Commissioning (2009)



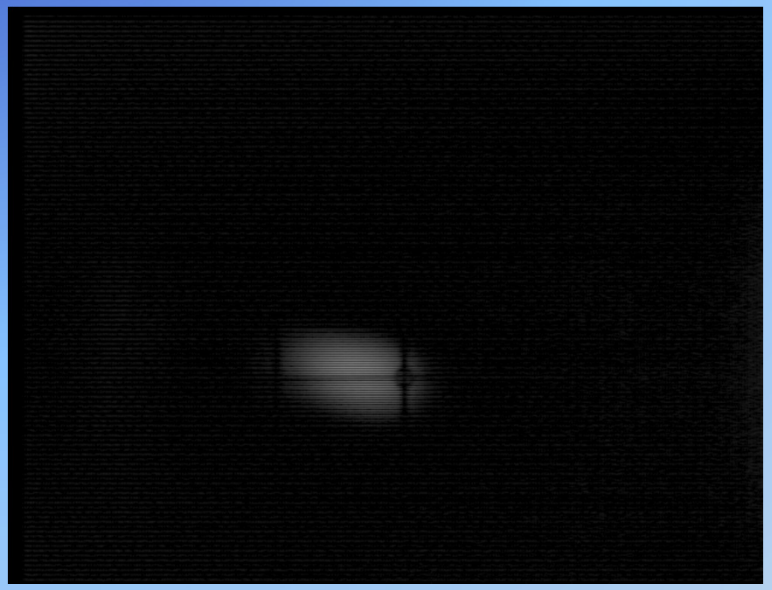


Ion Species	LEBT End	Behind LINAC	Max. LINAC Trans-mission	Behind Foil Stripper
C^{4+} / C^{6+}	≈ 170 µA	≈ 82 µA	48 %	≈ **115 µA**
H_3^+ / p	1.0 – 1.1 mA	≈ 400 µA	39 %	≈ **1.2 mA**
	710 µA	307 µA	46 %	≈ **900 µA**

First turn

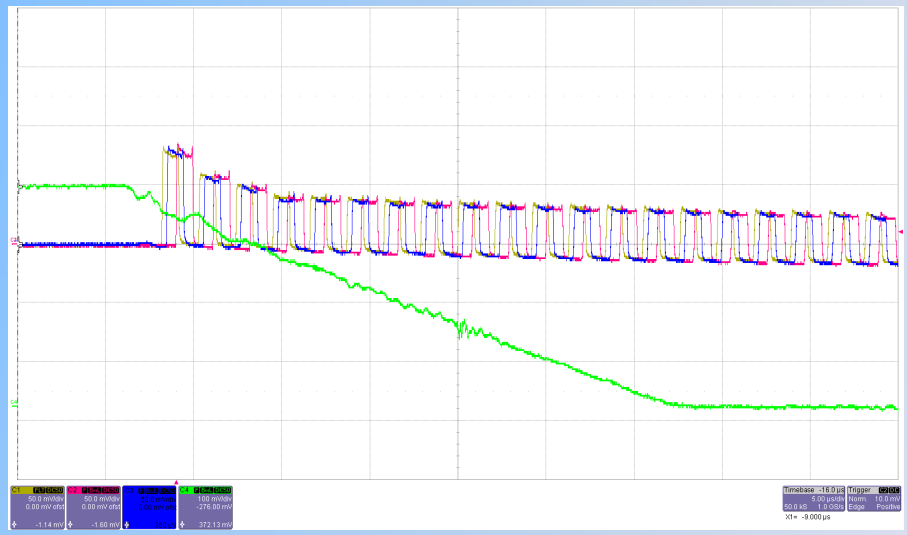
- 16 Dec 2009

Injection in synchrotron

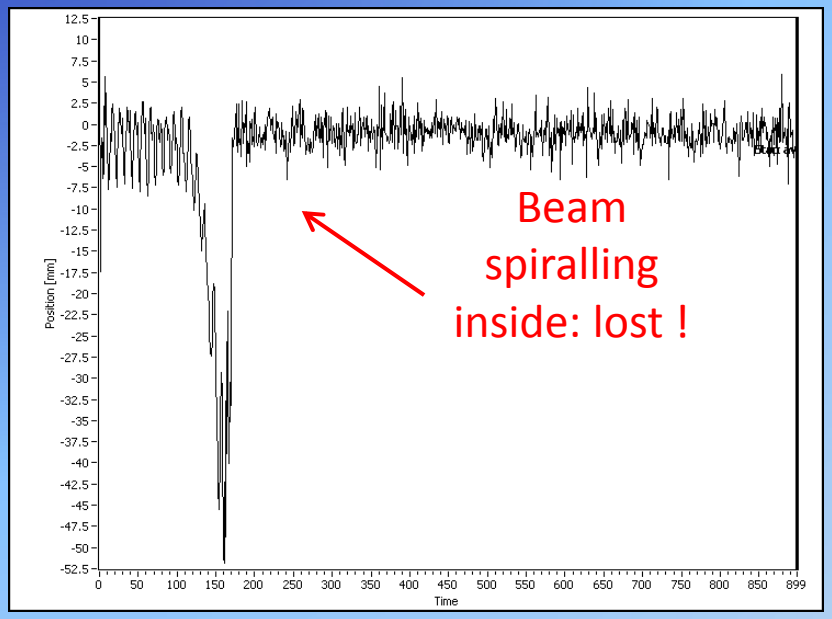


First turn

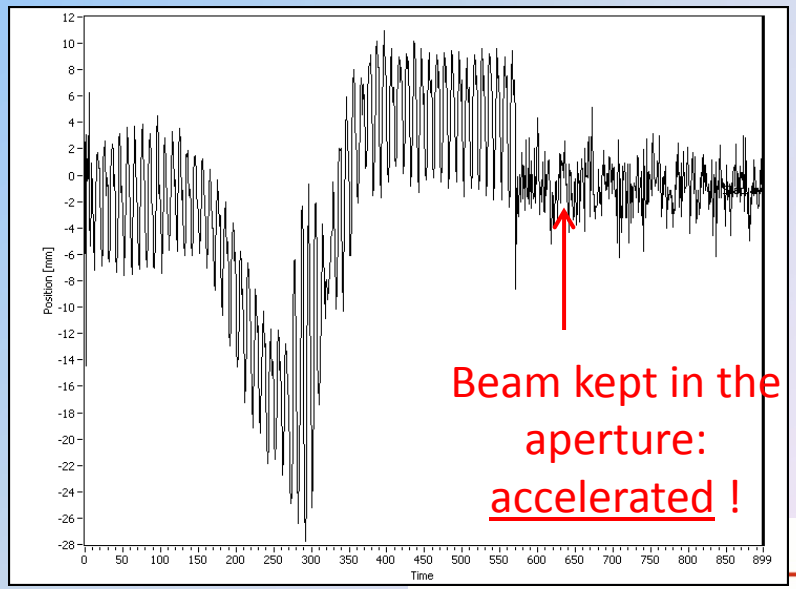
Multiturn injection: August 27, 2010



B field on – RF off

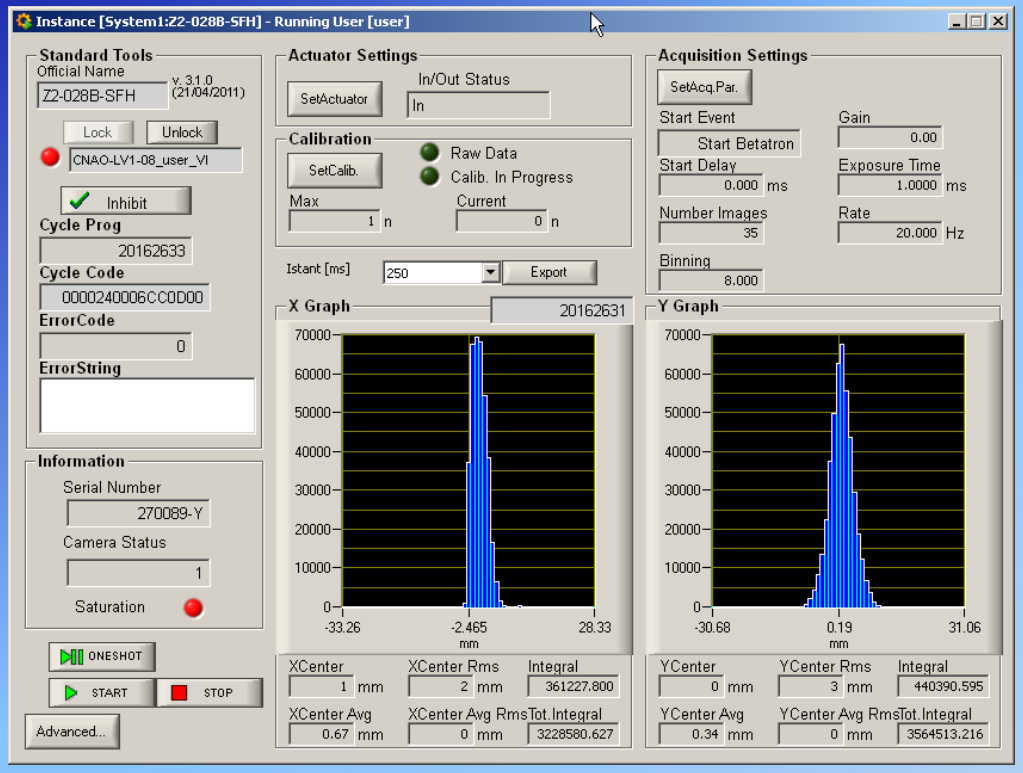


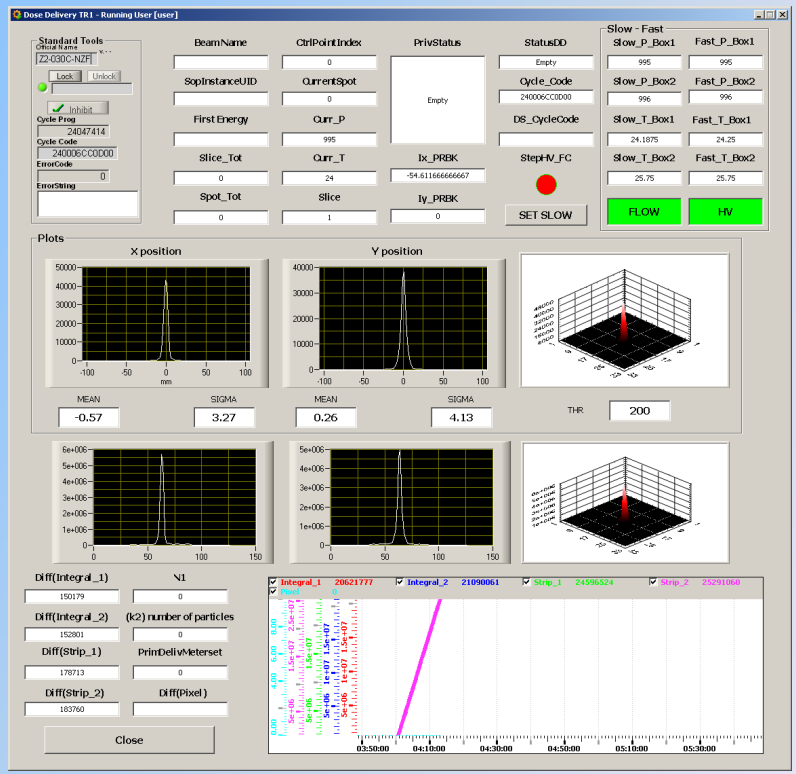
B field on – RF on



First beam acceleration September 17, 2010)

First extraction with Proton beam: November 2010





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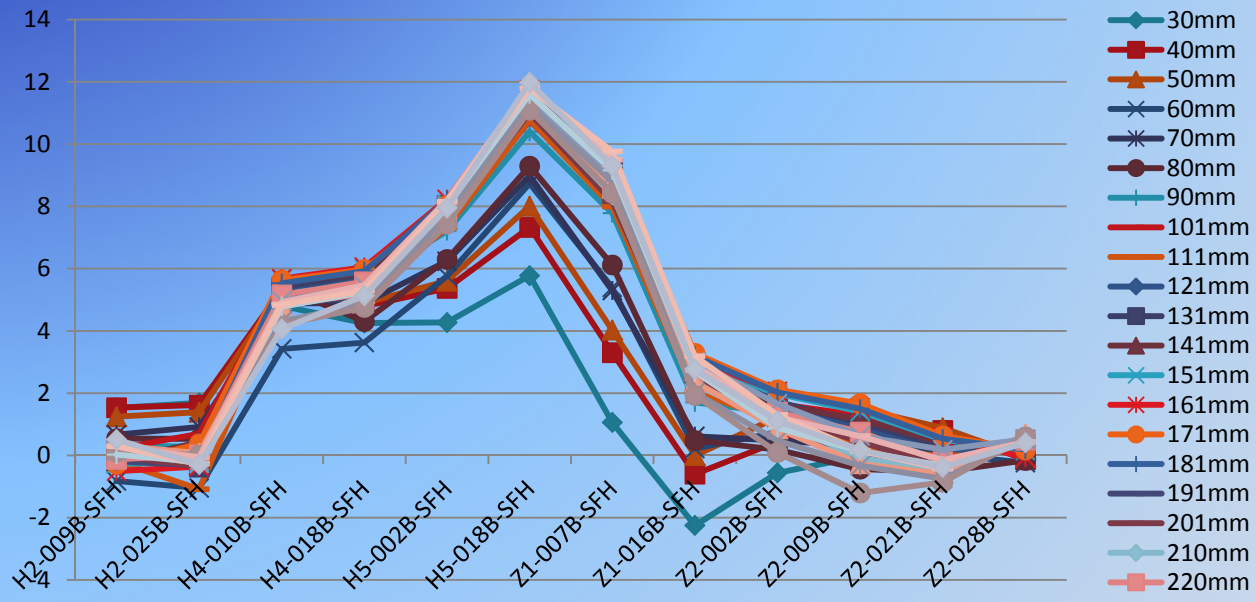
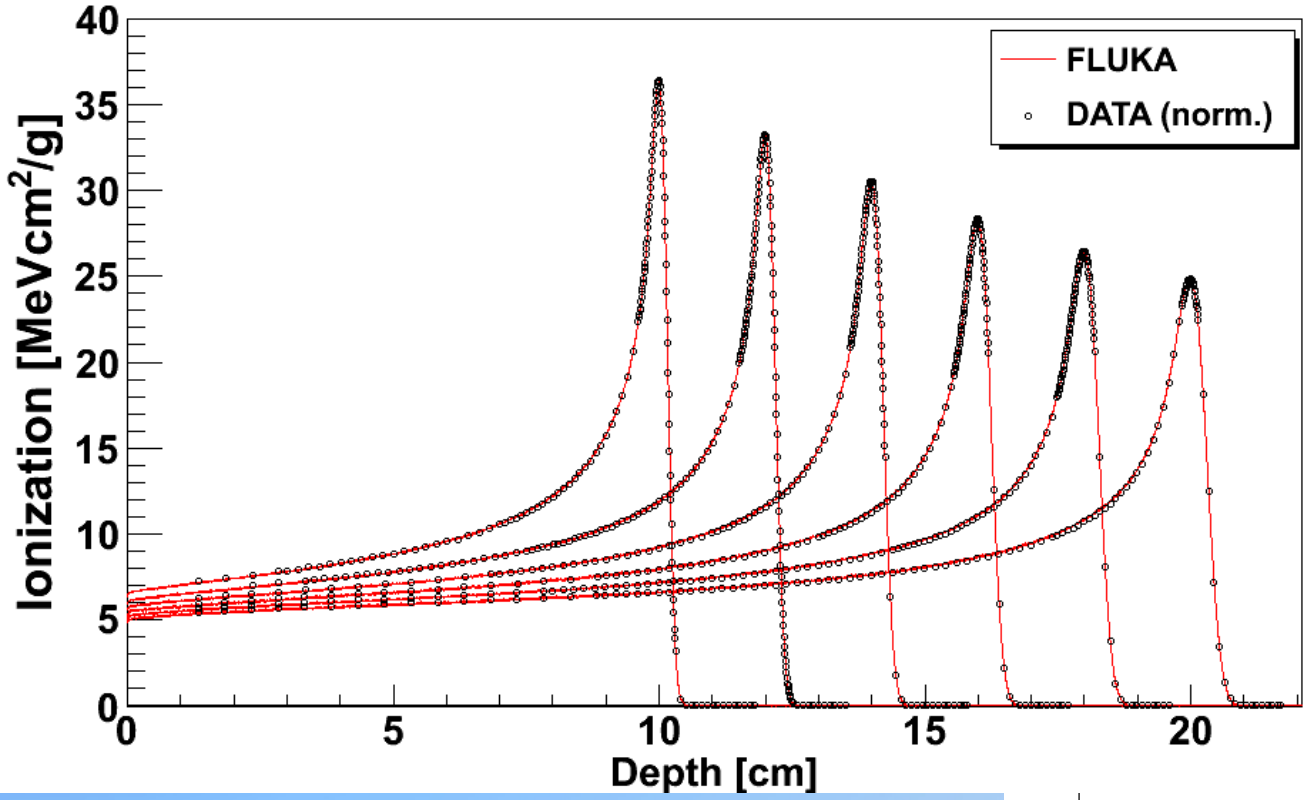
In 2011, after lots of studies and optimizations along the machine, proton beam has physically commissioned in the whole energy range in Z-line (60 MeV-220 MeV, that is 30 mm-320 mm of penetration depth in water) and delivered to medical staff for clinical commissioning.



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

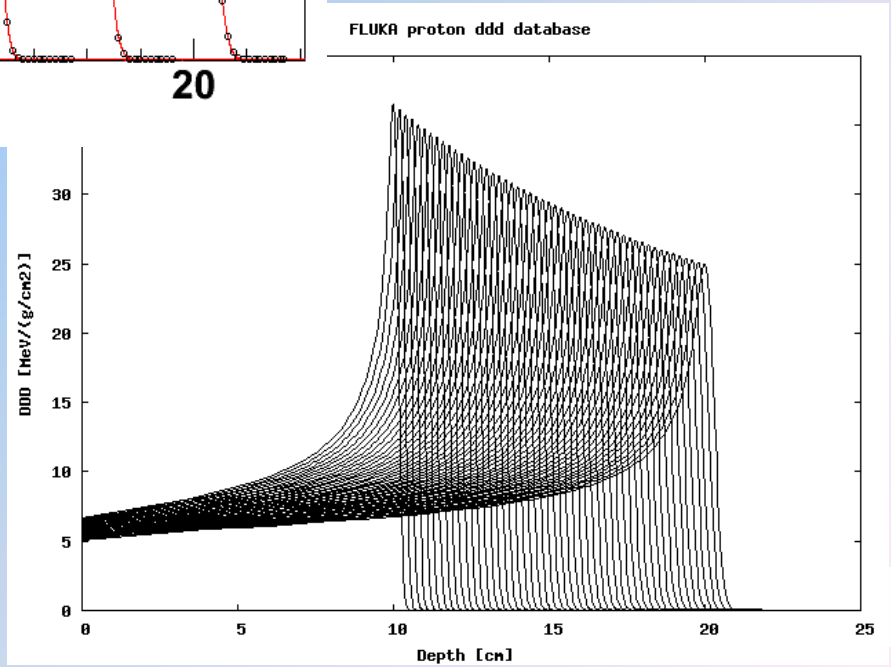
Proton Clinical characterization (1/3)



Bragg peak measurements

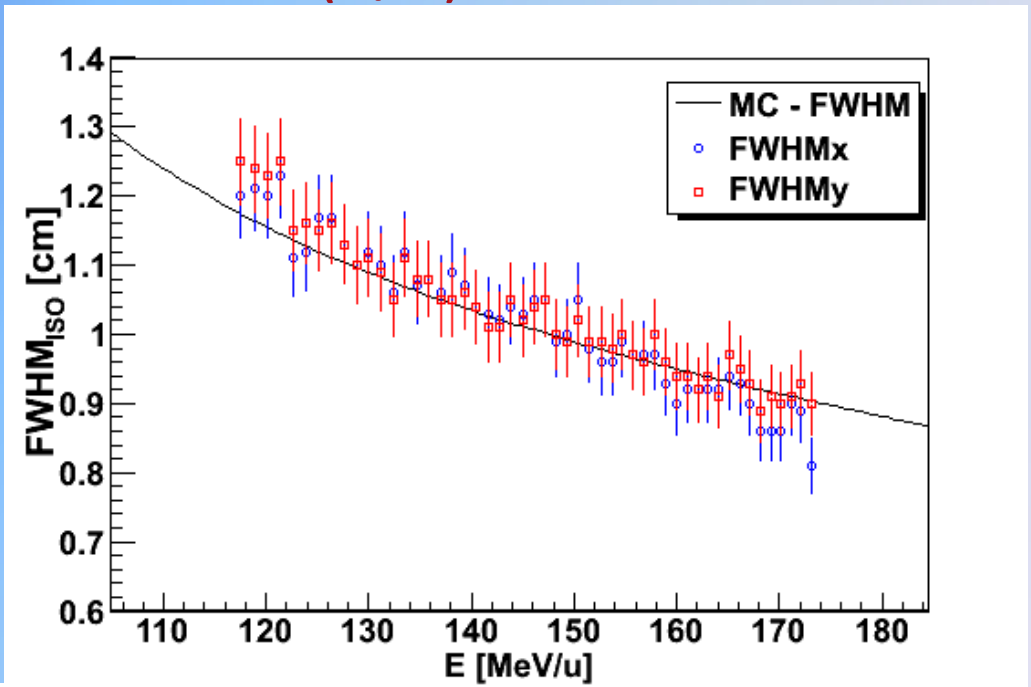
I_{pot} = 76.9 eV

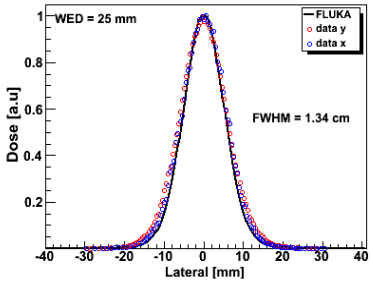
$|BP_{sperim} - BP_{FLUKA}| \leq 0.1$ mm

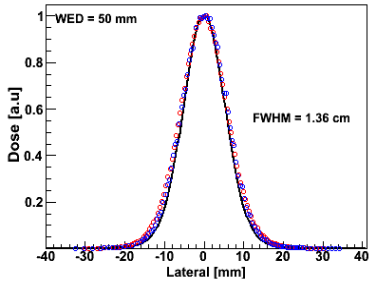


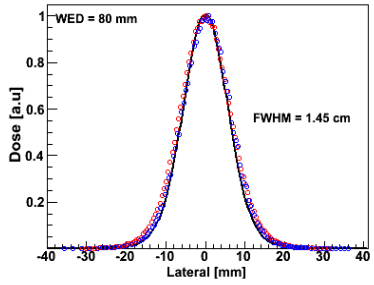
Proton Clinical characterization (2/3)

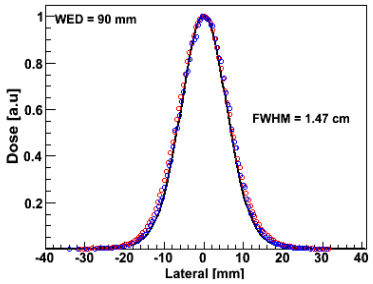
Spot dimensions measurements

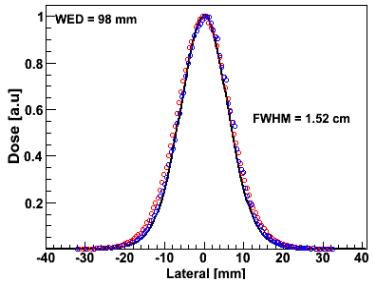


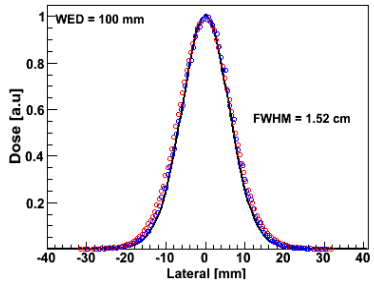












E = 117.54 MeV/u (100 mm BP)

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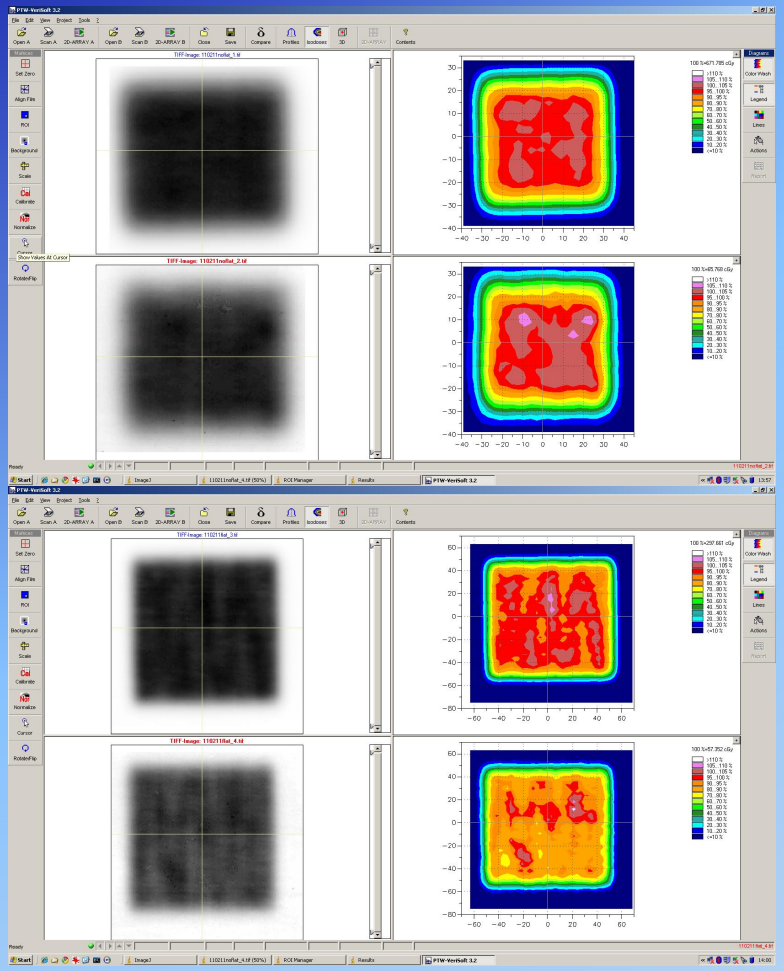
Proton Clinical characterization (3/3)

Dosimetric characterization



Homogeneity of 2.5%

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

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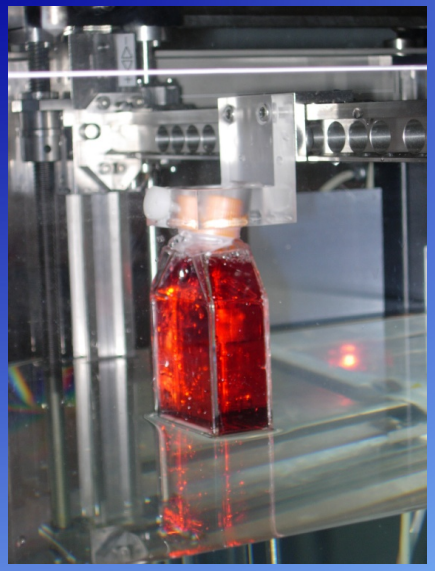
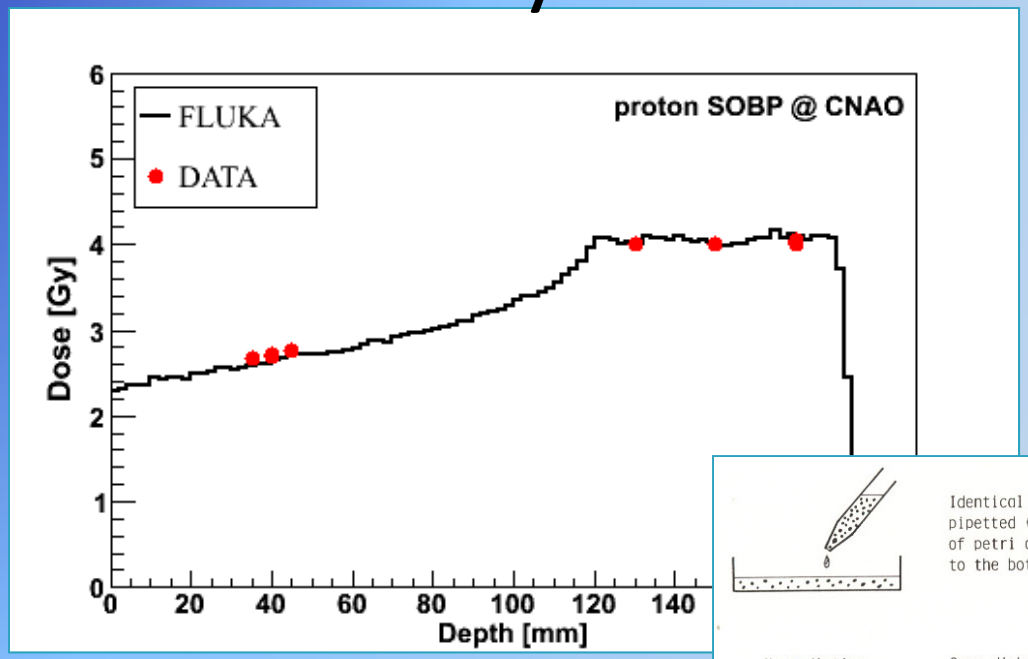
Dosimetry for RB



10x10 cm^2, 33x33 spots, 3 mm step)



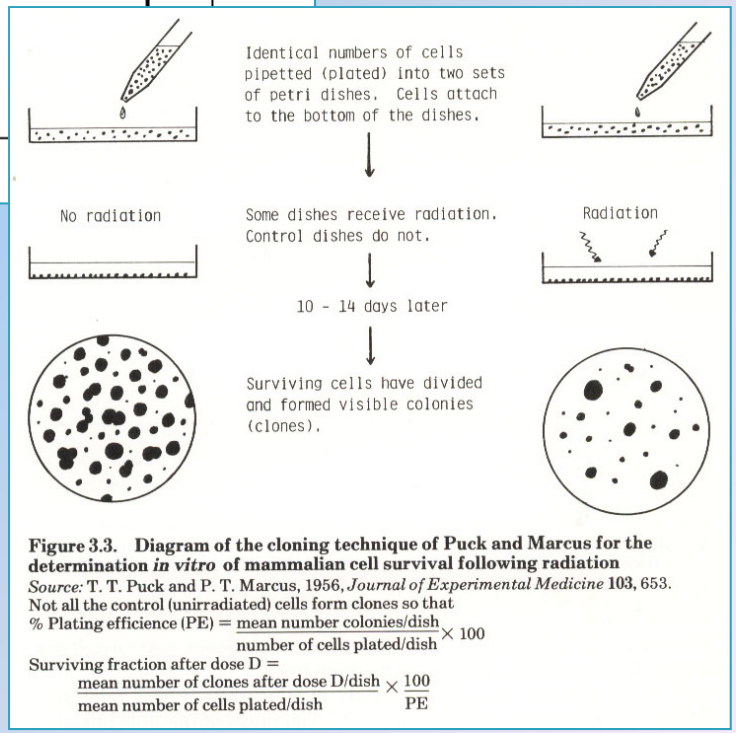


Figure 3.3. Diagram of the cloning technique of Puck and Marcus for the determination *in vitro* of mammalian cell survival following radiation

Source: T. T. Puck and P. T. Marcus, 1956, *Journal of Experimental Medicine* **103**, 653.

Not all the control (unirradiated) cells form clones so that

$$\% \text{ Plating efficience (PE)} = \frac{\text{mean number colonies/dish}}{\text{number of cells plated/dish}} \times 100$$

Surviving fraction after dose D =

$$\frac{\text{mean number of clones after dose D/dish}}{\text{mean number of cells plated/dish}} \times \frac{100}{\text{PE}}$$

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

(Courtesy of Roberto Cherubini)

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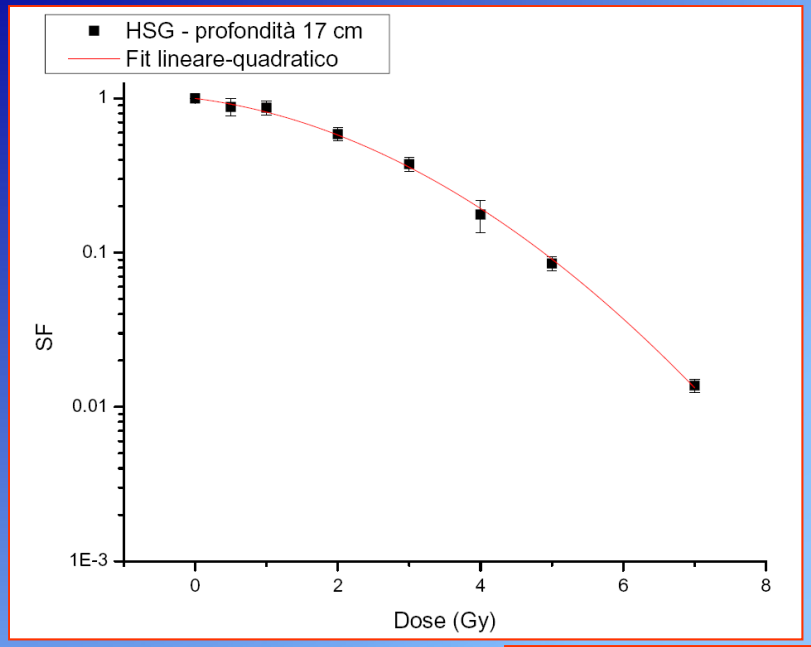
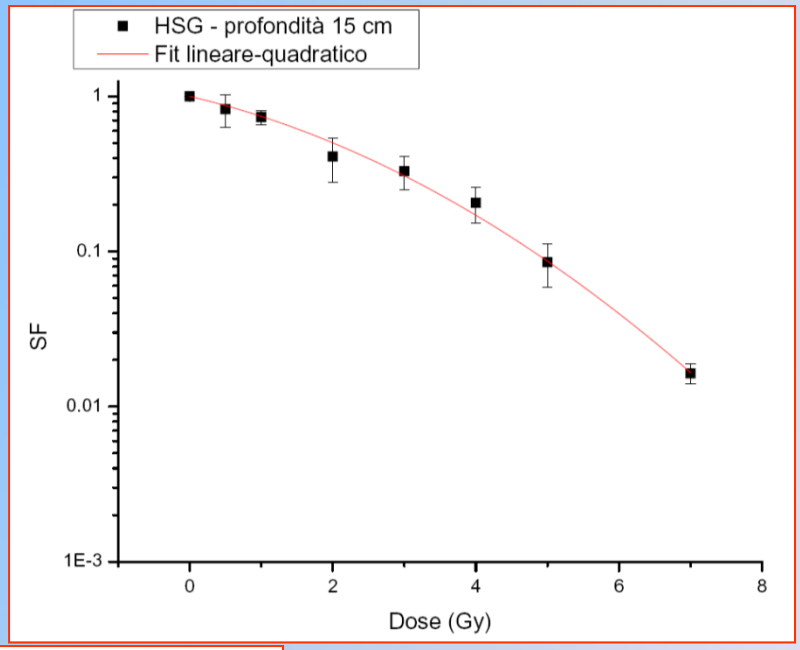
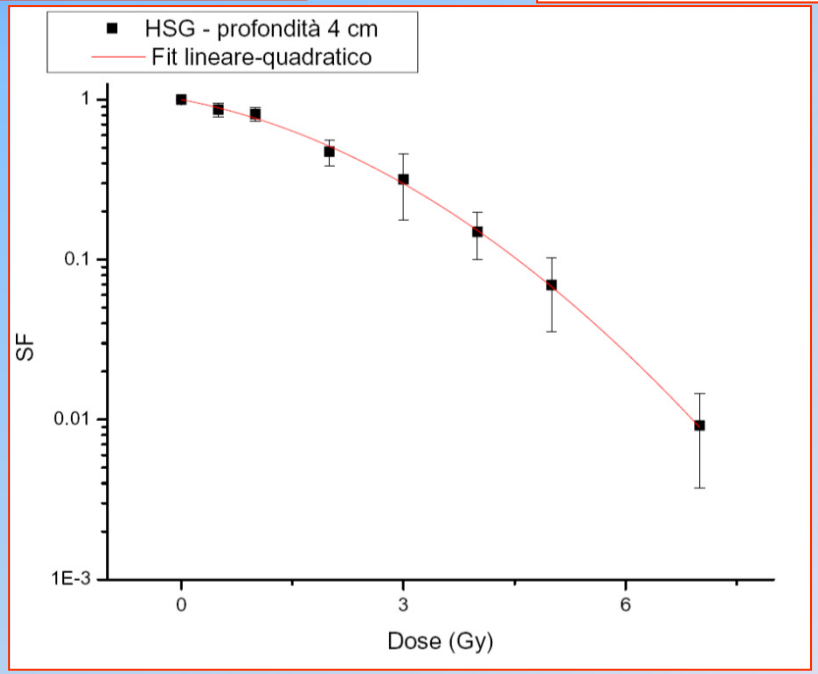
Survival curves– Proton: HSG cells







(Courtesy of Roberto Cherubini)

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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

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Start of medical activities

First patient with Proton beam
September 22, 2011)

Treatment rooms

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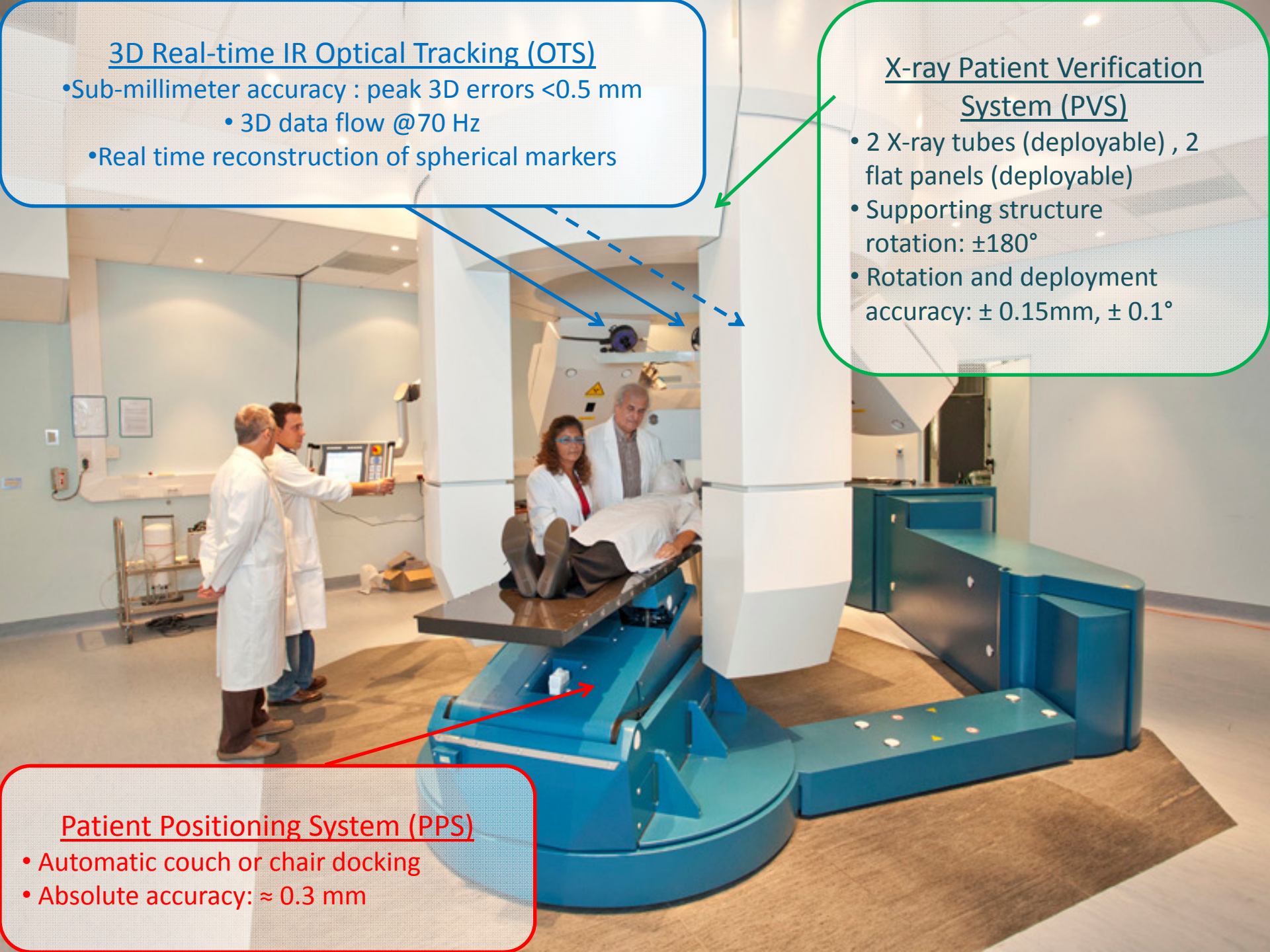
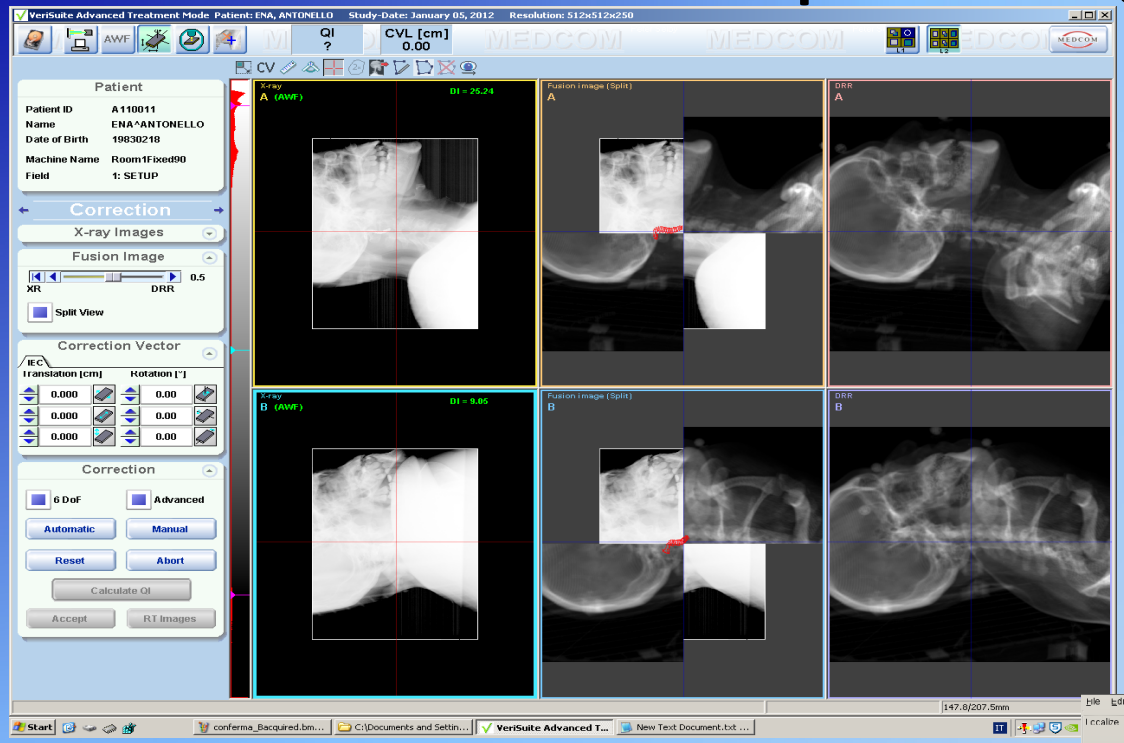
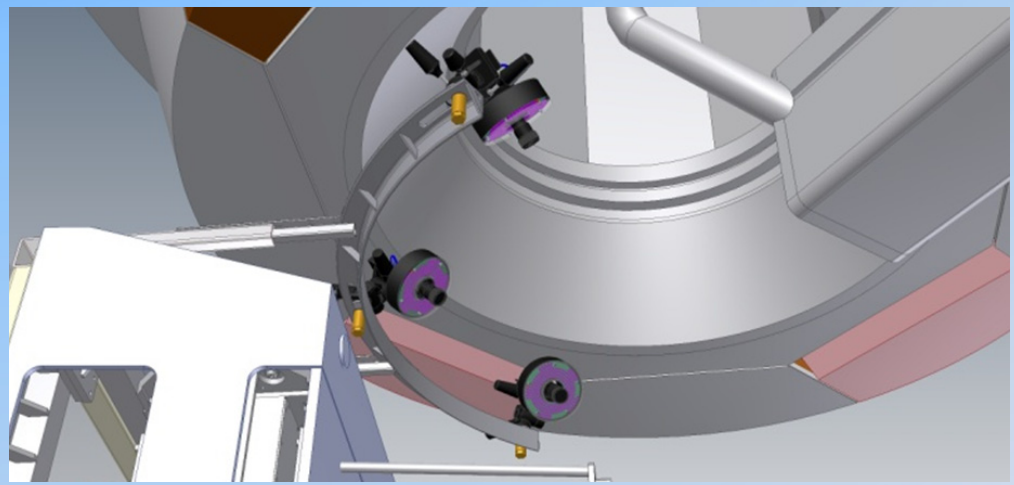
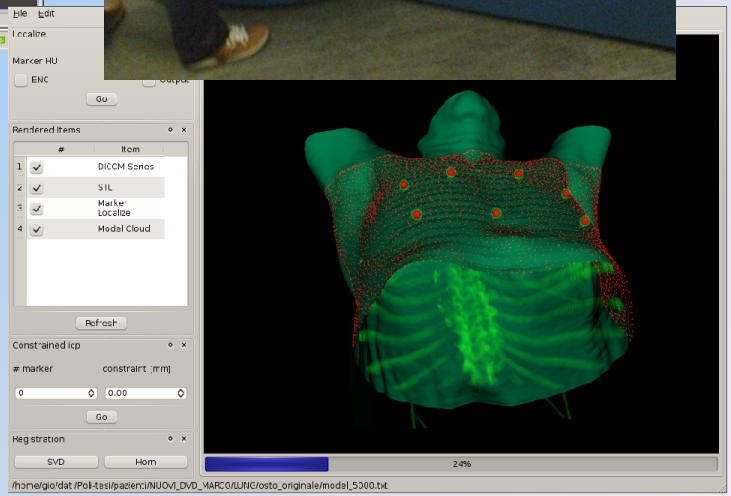

3D Real-time IR Optical Tracking (OTS)
•Sub-millimeter accuracy : peak 3D errors <0.5 mm
• 3D data flow @70 Hz
•Real time reconstruction of spherical markers
X-ray Patient Verification System (PVS)
• 2 X-ray tubes (deployable) , 2 flat panels (deployable)
• Supporting structure rotation: ±180°
• Rotation and deployment accuracy: ± 0.15mm, ± 0.1°
Patient Positioning System (PPS)
• Automatic couch or chair docking
• Absolute accuracy: ≈ 0.3 mm

Treatment planning system







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Possible pathologies at CNAO

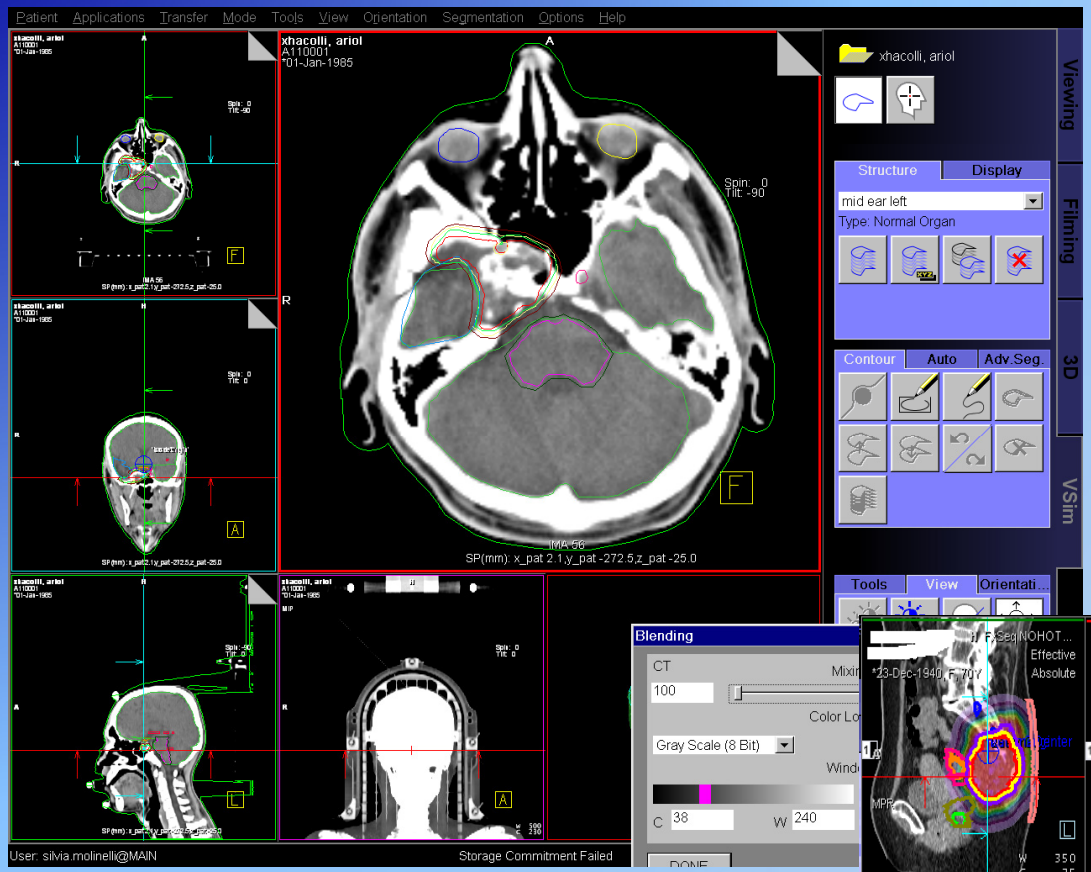
Proton beam

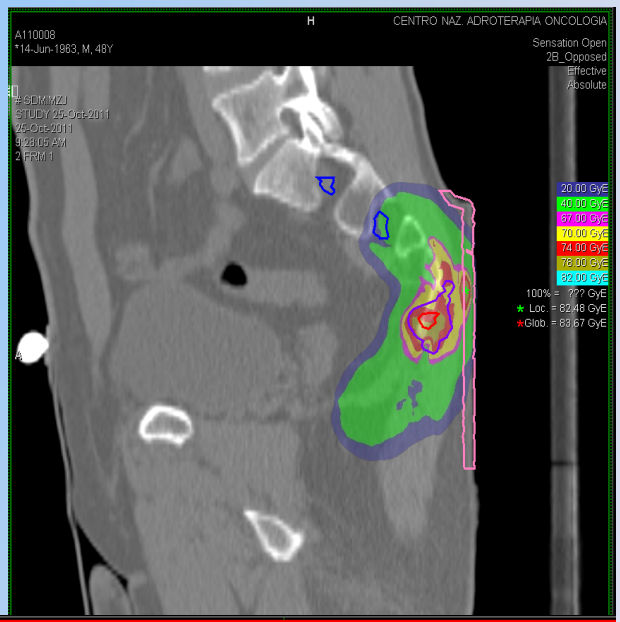
- Uveal melanoma
- Chordoma
- Chondrosarcoma (head, trunk)
- Meningioma (base of skull)
- Paranasal sinus cancer
- CNS schwannoma
- Pituitary adenoma

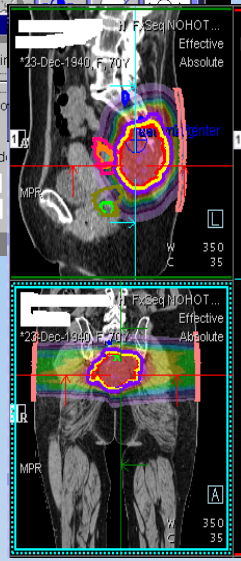
Carbon ion beam

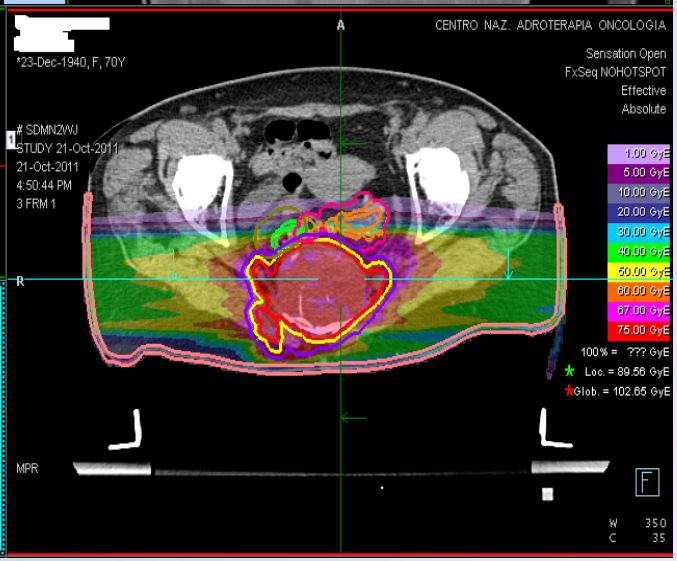
- Salivary gland tumors
- Mucosal melanoma (head & neck)
- Bone sarcoma
- Soft tissue sarcoma
- Prostatic carcinoma

Treatment planning system









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Orders of magnitude

Dose uniformity required: ±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 μs**

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

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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)

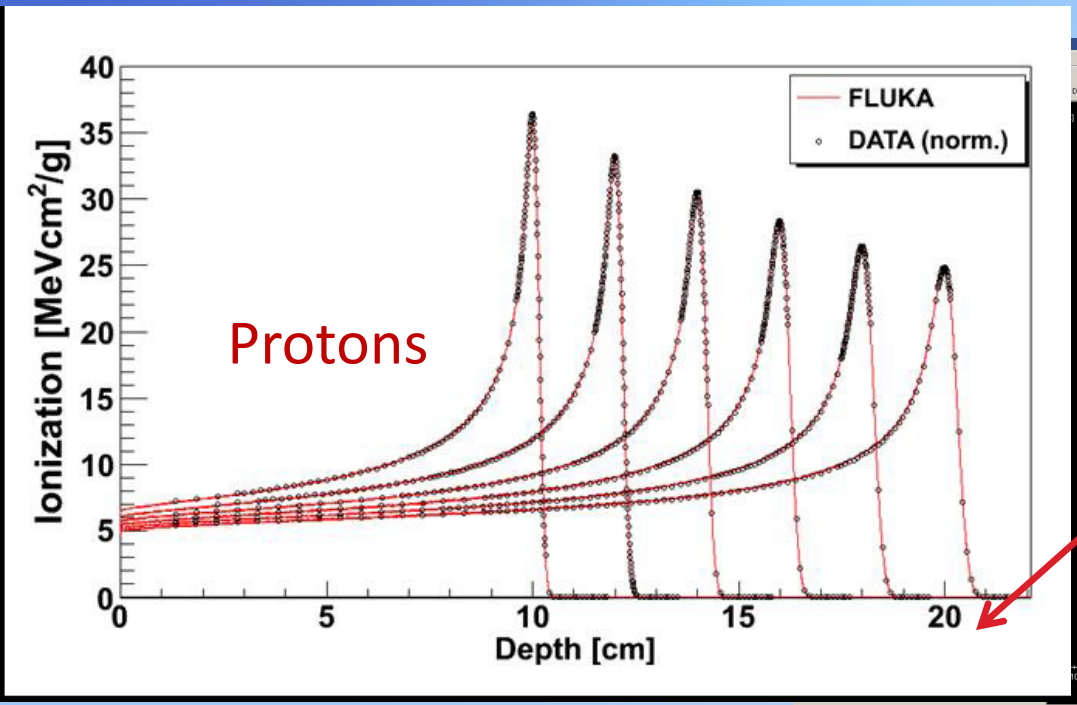
About maintenance..

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

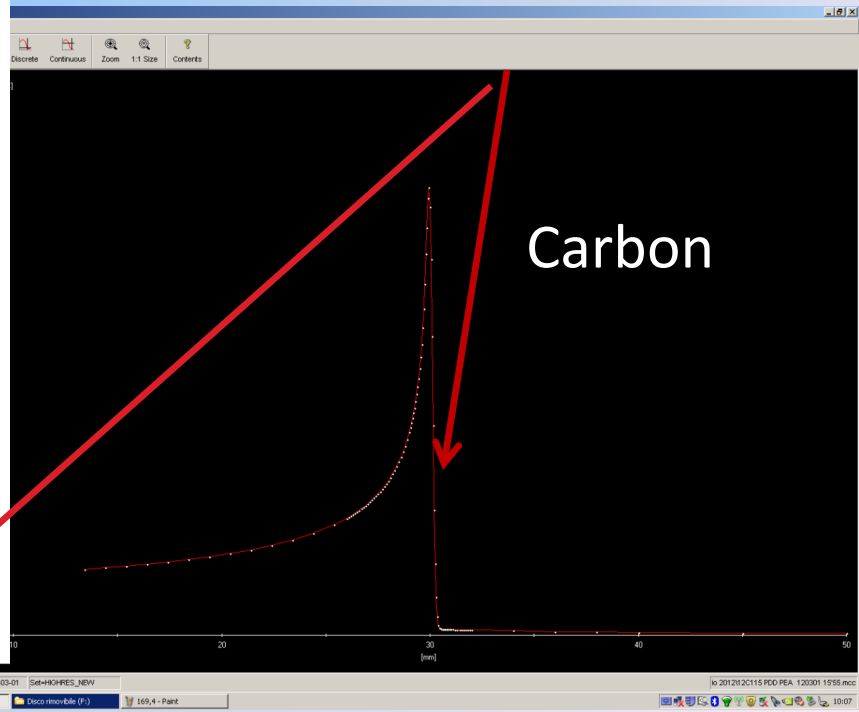
In this way the scheme of ramp down and ramp up of patients is avoided. In fact during a proton therapy a patient can sustain an interruption of 10 days.

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.

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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

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