

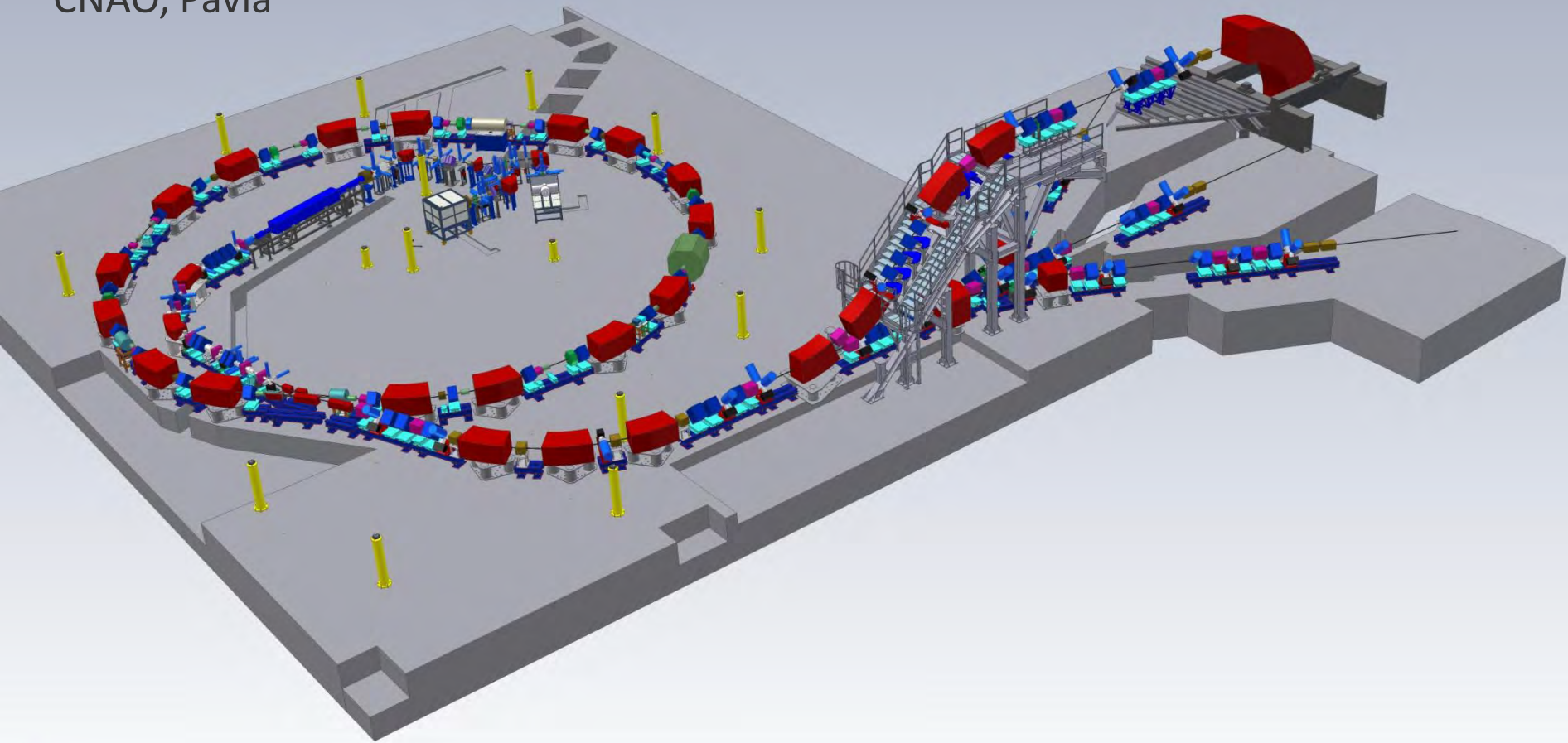
# CNAO, the Italian Hadrontherapy Project

Caterina Biscari

on behalf of the CNAO team

LNF-INFN, Frascati

CNAO, Pavia



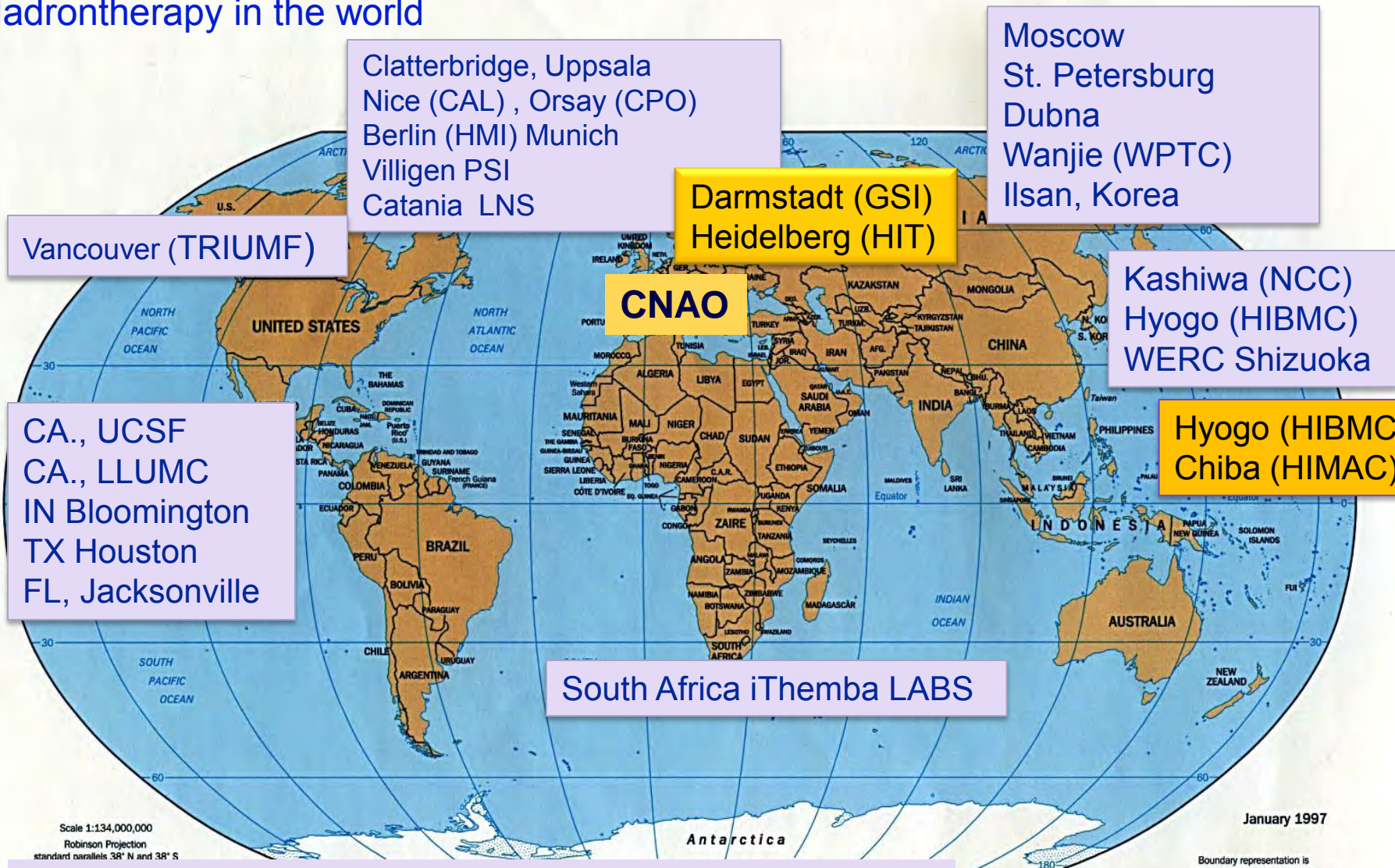
# CNAO team

- S. Alpegiani, G. Baccaglioni, G. Balbinot, R. Basso, G. Bazzano, D. Bianculli, J. Bosser, E. Bressi, G. Burato, G. Butella, M. Caldara, L. Casalegno, E. Chiesa, V. Chimenti, G. Ciavola, G. De Filippi, R. Diegoli, M. Donetti, L. Falbo, D. Fiocchi, L. Frosini, M.A. Garella, F. Generani, F. Gerardi, S. Gioia, L. Grilli, L. Lanzavecchia, R. Monferrato, V. Mutti, M. Necchi, M. Nodari, A. Parravicini, M. Pelliccioni, M. Pezzetta, C. Priano, G. Primadei, **M. Pullia**, **S. Rossi**, S. Savazzi, M. Scotti, S. Sironi, A. Smaldore, M. Spairani, S. Toncelli, E. Vacchieri, G. Venchi, S. Vitulli, C. Viviani, **CNAO-Pavia**
- C. Biscari, L. Celona, R. Cirio, A. Clozza, C. De Martinis, P. Fabbricatore, G. Franzini, S. Gammino, S. Giordanengo, F. Marchetto, L. Pellegrino, A. Pisent, R. Ricci, C. Roncolato, C. Sanelli, M. Serio, F. Sgamma, A. Stella, **INFN**
- M.E. Angoletta, J. Borburgh, M. Buzio, R. Chritin, D. Cornuet, J. Dutour, T. Fowler, K. Metzmacher, L. Sermeus, **CERN**
- G. Clemente, C.M. Kleffner, M. Maier, A. Reiter, B. Schlitt, W. Vinzenz, H. Vormann, **GSI**

Not exhaustive list



# Hadrontherapy in the world



61122 patients treated with protons

5342 with carbon ions

02 March 2009, PTCOG

Scale 1:134,000,000  
Robinson Projection  
standard parallels 38° N and 38° S

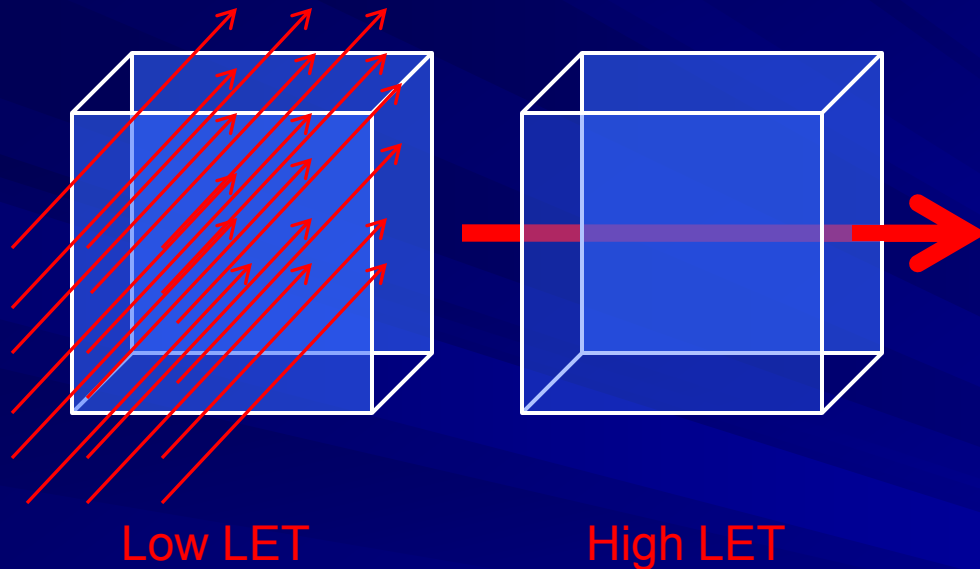
January 1997

Boundary representation is not necessarily authoritative.

802543 (R00352) 1-97

# Why carbon ions?

## Hadrontherapy biological basis

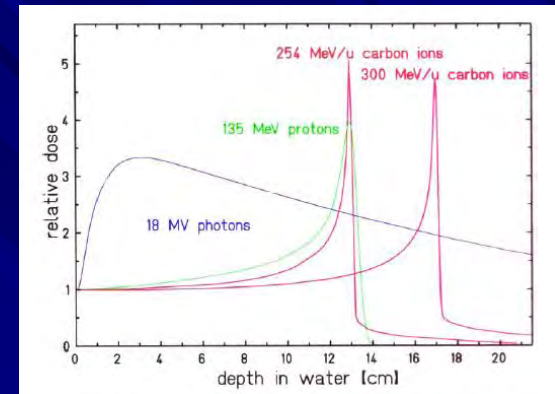


Low LET

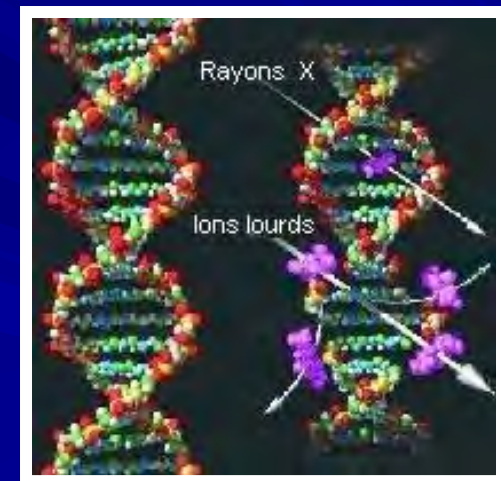
High LET

D = distance between ionizations

Low LET	<20 keV/ $\mu\text{m}$	D > DNA diameter
High LET	> 50 keV/ $\mu\text{m}$	D < DNA diameter
Very High LET	>1000 keV/ $\mu\text{m}$	D < DNA diameter + excess Energy



Energy deposition in matter





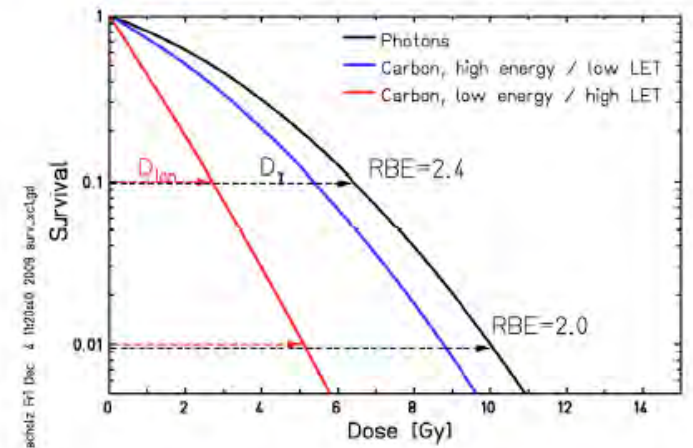
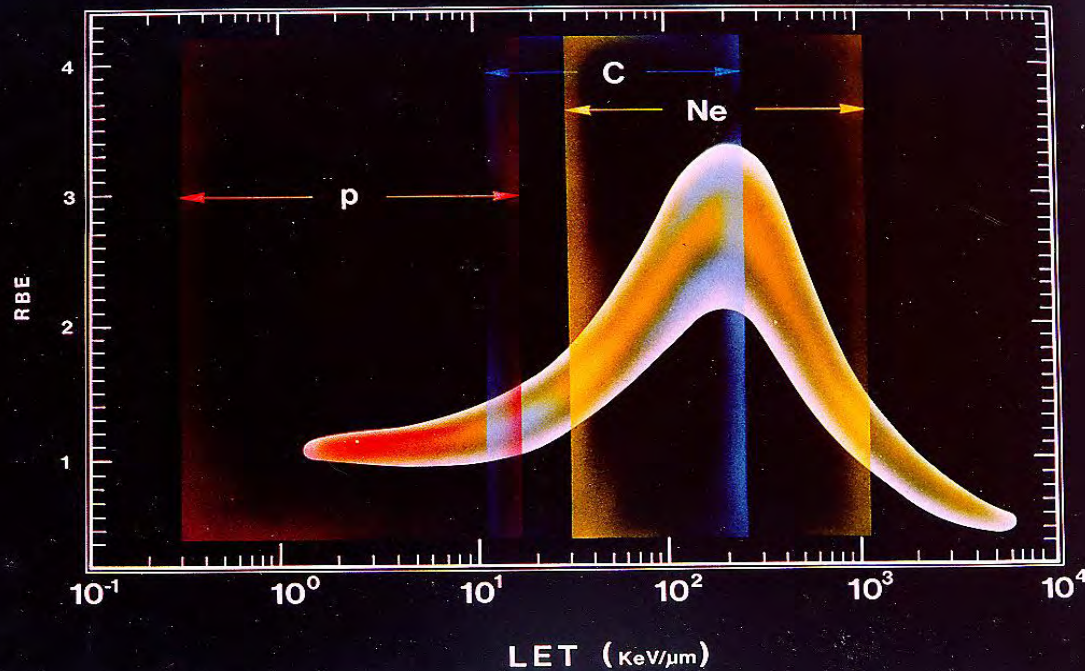
# Why carbon ions?

Carbon ions have higher *LET* than protons

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 which are necessary for producing the same biological effect.

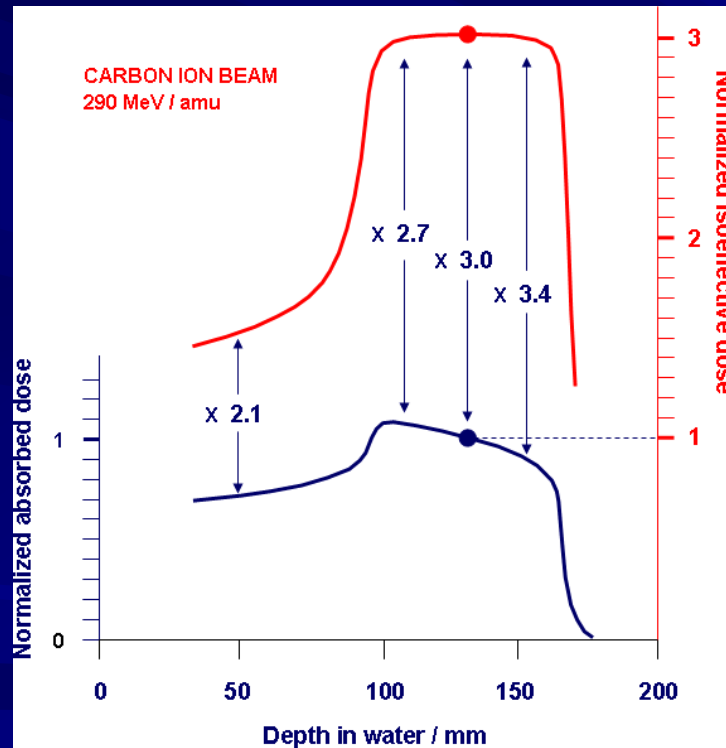
Carbon RBE > 3 in the Bragg peak region  
>= 1 in the entry channel.



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

When planning the treatment, RBE must be considered :  
Concept of “biological dose”:

physical dose distribution necessary for obtaining a flat biological dose



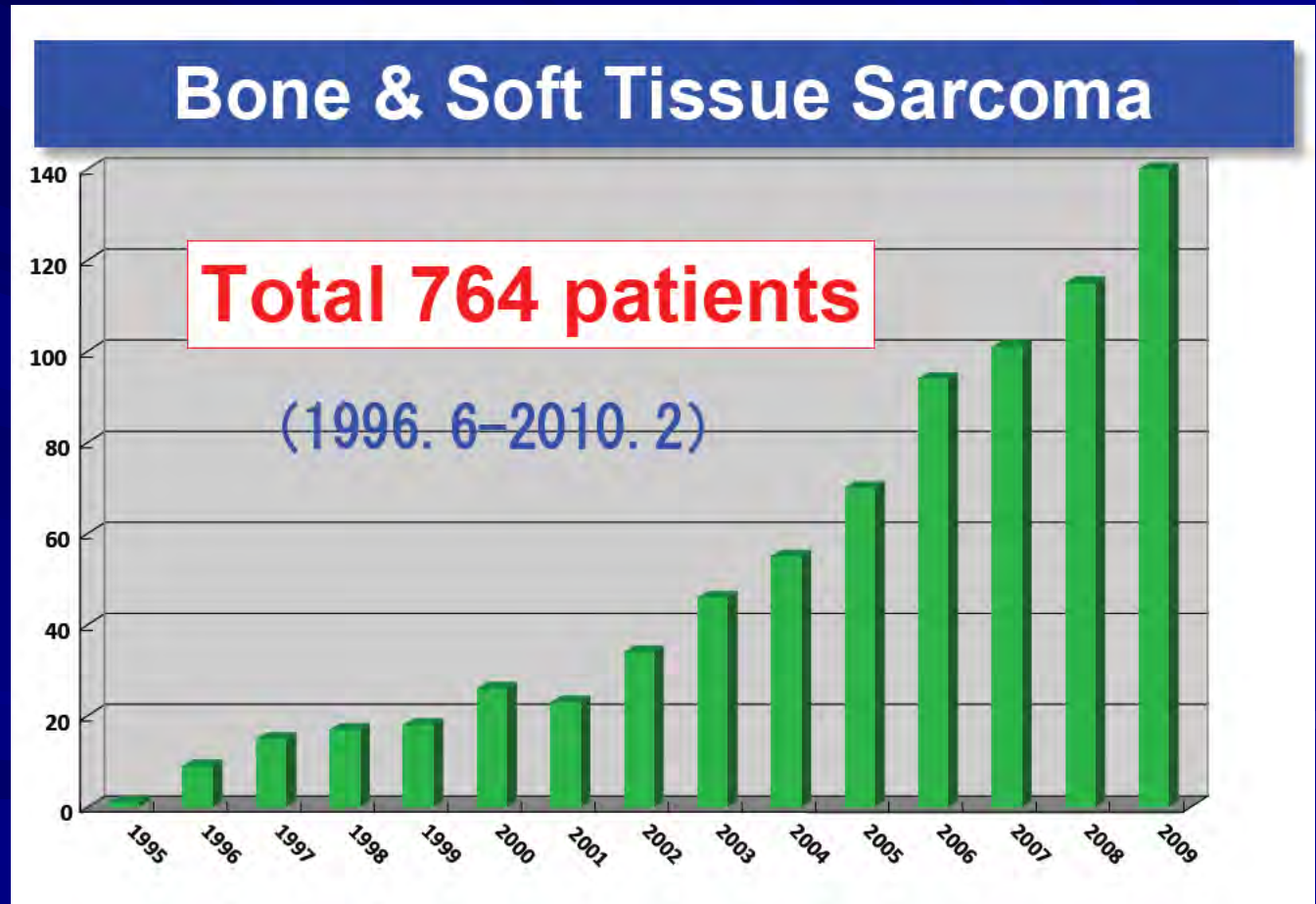
Other parameters: cell type, blood perfusion, oxygenation  
Hypoxic tumours resistant to photons and protons  
Carbons drawback : dose deposition after Bragg peak -  
Protons drawback : lateral diffraction

# CLINICAL comparison between different methods

## Statistics

„Few Carbon treated patients → Experimental phase

Example :



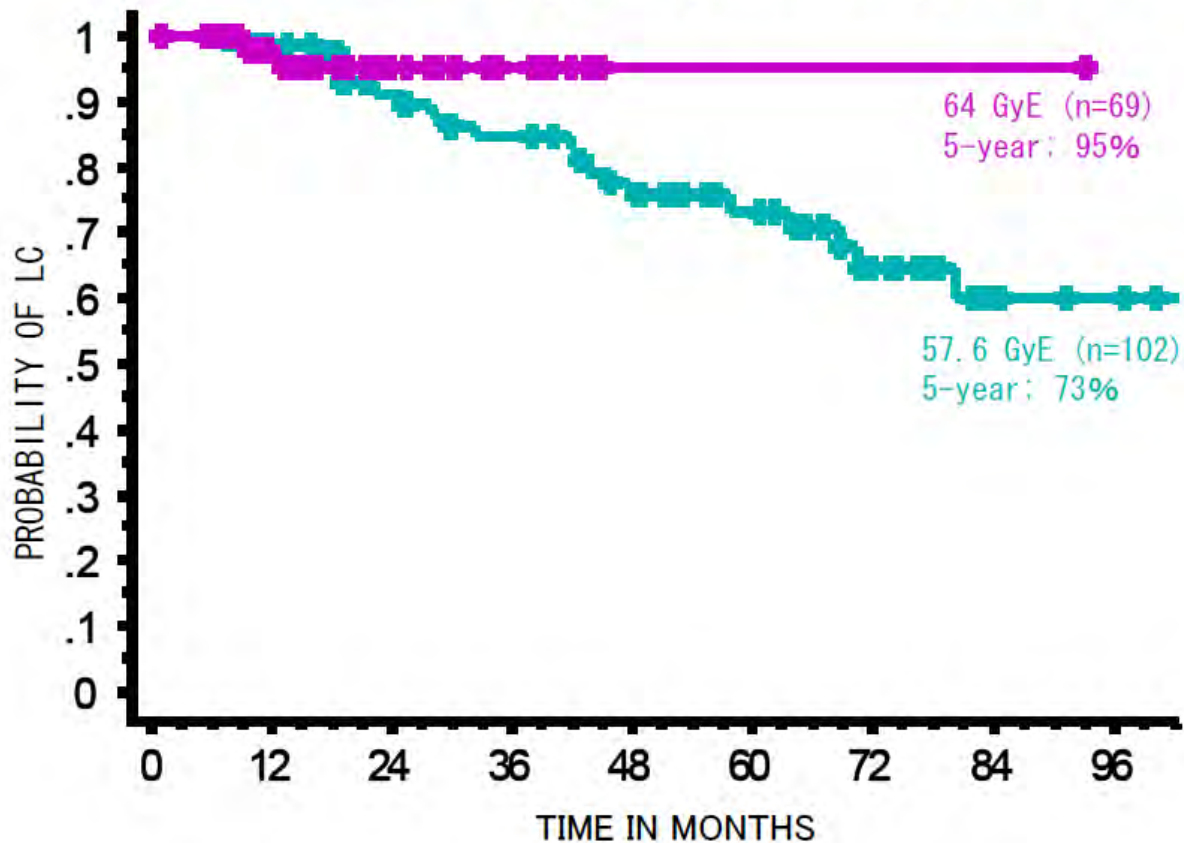


# Time

Analysis of results - example

## Phase II (9602) for Malignant Head-and-Neck Tumors

Local Control of ACC (n=129) according to Carbon ion Dose



# Tracking patients and exchanging data within different institutions

## Morbidities after Carbon Ion Therapy (2000.4~2008.2)

	No.	Grade					
		0	1	2	3	4	5
<b>Skin</b>							
Early	427	1	385	38	3	0	0
Late	420	4	389	20	6	1	0
<b>GI tract</b>							
Early	380	375	5	0	0	0	0
Late	374	373	1	0	0	0	0
<b>Lung</b>							
Early	33	33	0	0	0	0	0
Late	33	31	2	0	0	0	0
<b>Edema</b>	<b>18</b>	<b>14</b>					
<b>Spinal cord</b>	<b>39</b>	<b>38</b>					

**64GyE : 29, 67.2GyE:53, 70.**

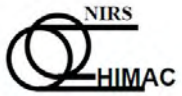
### ESTIMATING SEVERITY GRADE

For abnormalities NOT found elsewhere in the **Toxicity** Tables use the scale below to estimate grade of severity:

<b>GRADE 1</b>	<b>Mild</b>	Transient or mild discomfort (< 48 hours); no medical intervention/therapy required
<b>GRADE 2</b>	<b>Moderate</b>	Mild to moderate limitation in activity - some assistance may be needed; no or minimal medical intervention/therapy required
<b>GRADE 3</b>	<b>Severe</b>	Marked limitation in activity, some assistance usually required; medical intervention/therapy required, hospitalizations possible
<b>GRADE 4</b>	<b>Life-threatening</b>	Extreme limitation in activity, significant assistance required; significant medical intervention/therapy required, hospitalization or hospice care probable

## “Conclusion”

**Carbon ion radiotherapy  
is a safe and effective  
local treatment for inoperable  
bone and soft tissue sarcoma  
without  
acceptable morbidity.**



### *New Treatment Facility Project at HIMAC*

*Koji Noda*

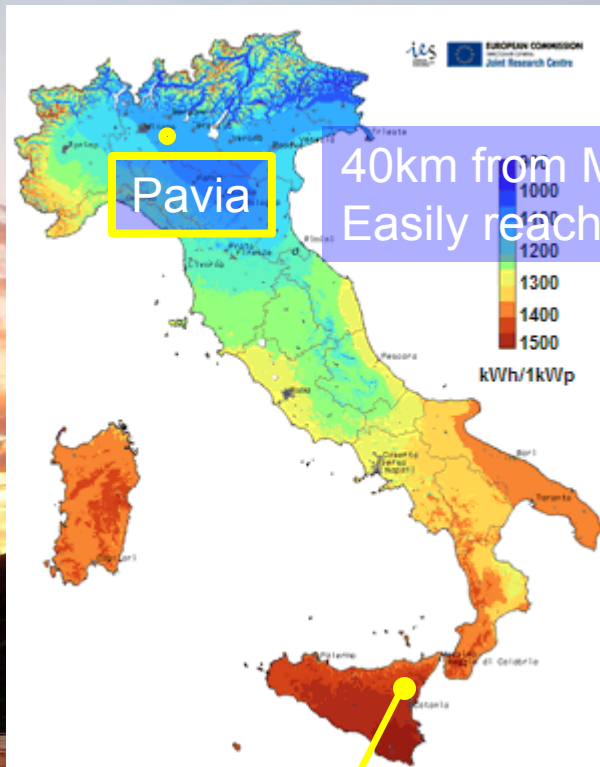
*Research Center for Charged Particle Therapy  
National Institute of Radiological Sciences*

*2<sup>nd</sup> NIRS-CNAO Sympo., Pavia, Italy, 21<sup>st</sup> March, 2010*





# CNAO in Pavia



40km from Milan

Easily reachable from all Italy and from most European airports

CATANA:  
in operation since 2002  
150 patients treated



Certosa di Pavia - 1400

# CNAO Foundation

In 2001 CNAO is created as no profit organisation (Foundation) created with the financial law 2001 to build the national center for hadrontherapy designed by TERA Foundation

At the end of 2003 CNAO acquires the TERA project and hires the design group

## Collaborations

NATIONAL: INFN, Univ of Pavia, Milano, Torino, Politecnico of Milano, Town of Pavia

INTERNATIONAL: CERN, GSI, LPSC, NIRS

# The Phases of CNAO

Phase 1: construction

 Years: 2005 - 2009

Phase 2: experimentation

 Years: 2010 - 2011

Phase 3: start-up

 Years: 2012 - 2013



# CNAO SCHEDULE

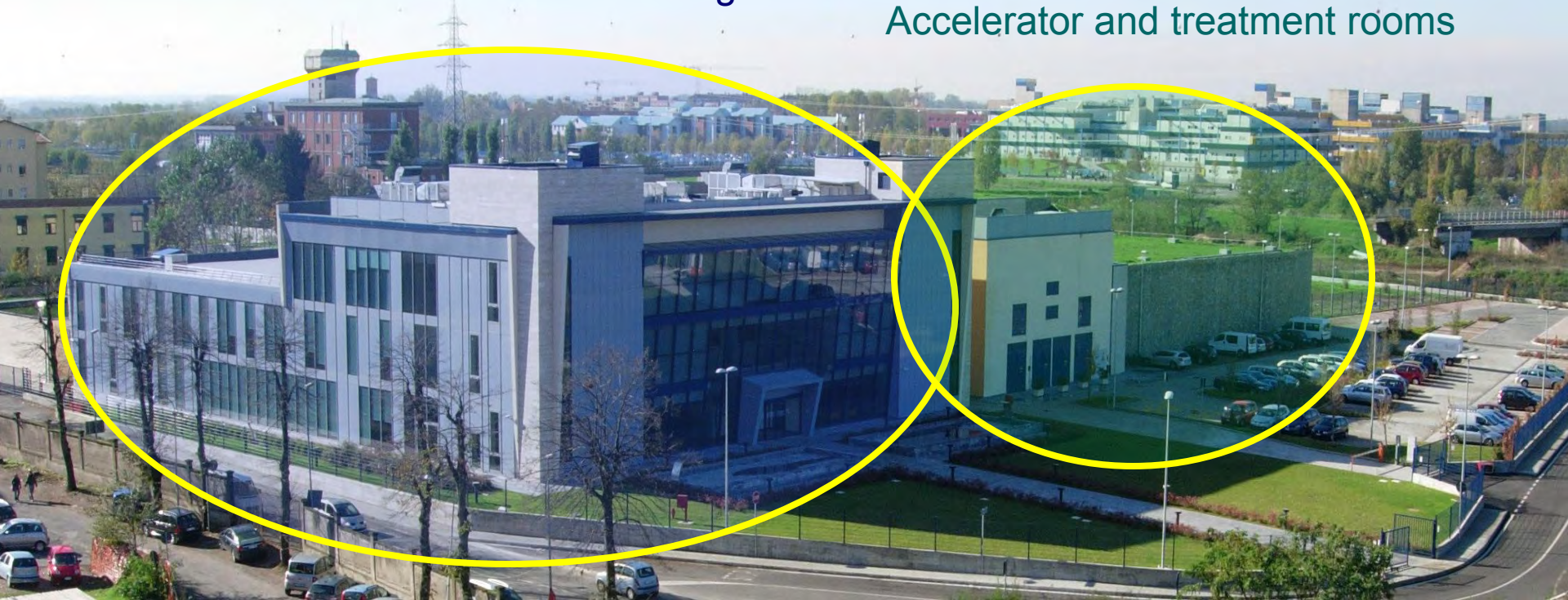
*today*

year	05		06		07		08		09		10		11		12
<b>CONSTRUCTION</b>															
	New site: no existing infrastructures														
<b>INSTALLATION</b>															
~ %					90	85	80	70	70	40	20	10			
<b>SYSTEM TESTS</b>															
~ %															
<b>BEAM COMMISSIONING</b>															
~ %															
<b>EXPERIMENTAL PHASE</b>															



Medical and Administrative buildings

Accelerator and treatment rooms



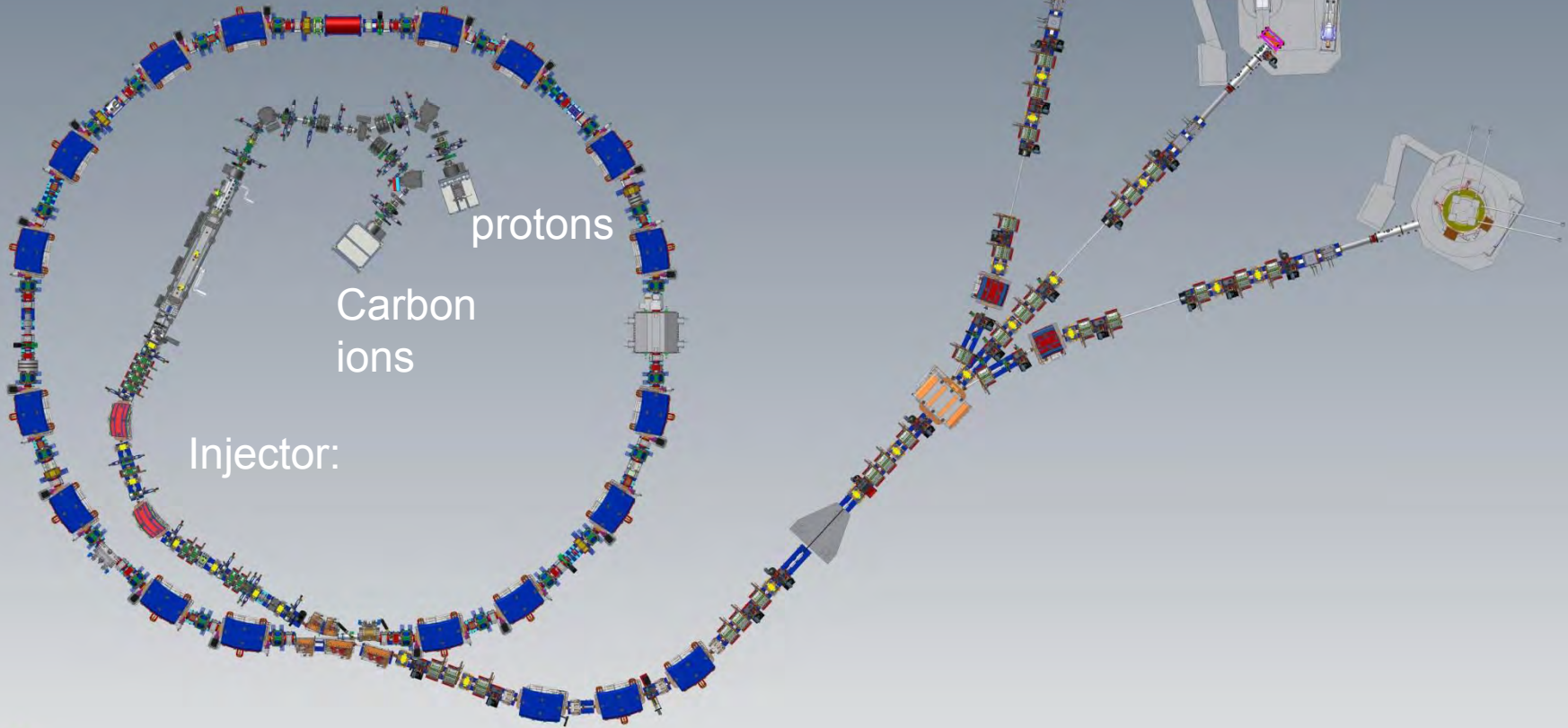
# ACCELERATOR

Synchrotron

P : 60 – 250 MeV

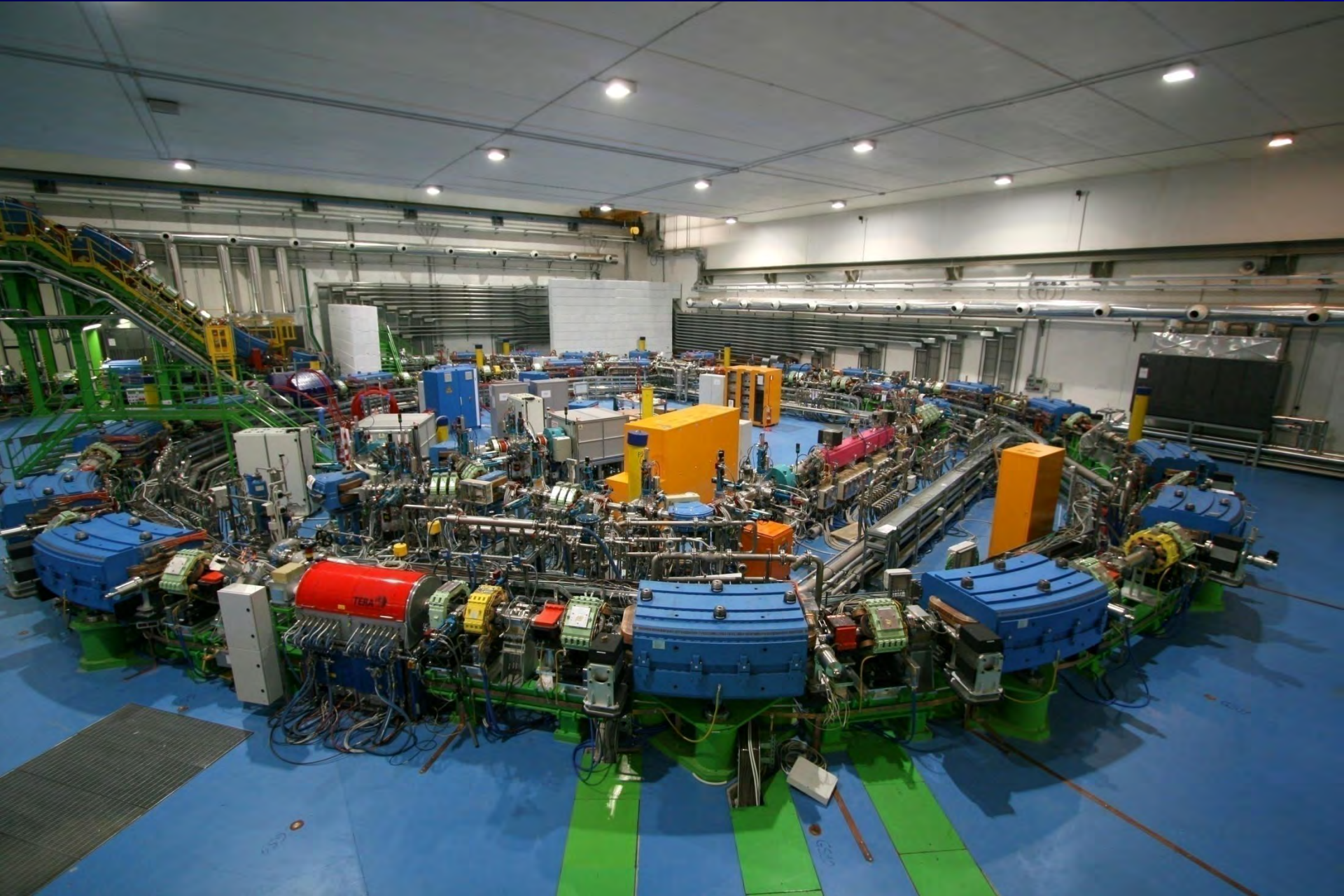
C6+ : 120 - 400 MeV

3 Treatment rooms





# Synchrotron hall today



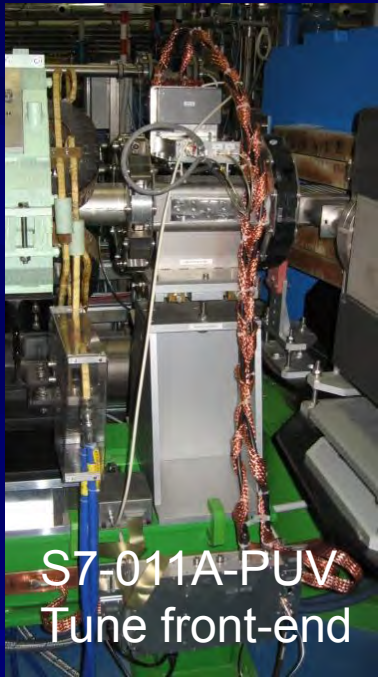


# Vertical dipole installation

05-09



# Some examples of the most recent beam diagnostic installations



S7-011A-PUV  
Tune front-end

Synchrotron



H3-011B-QPM  
Qualification Monitor Installation

HEBT

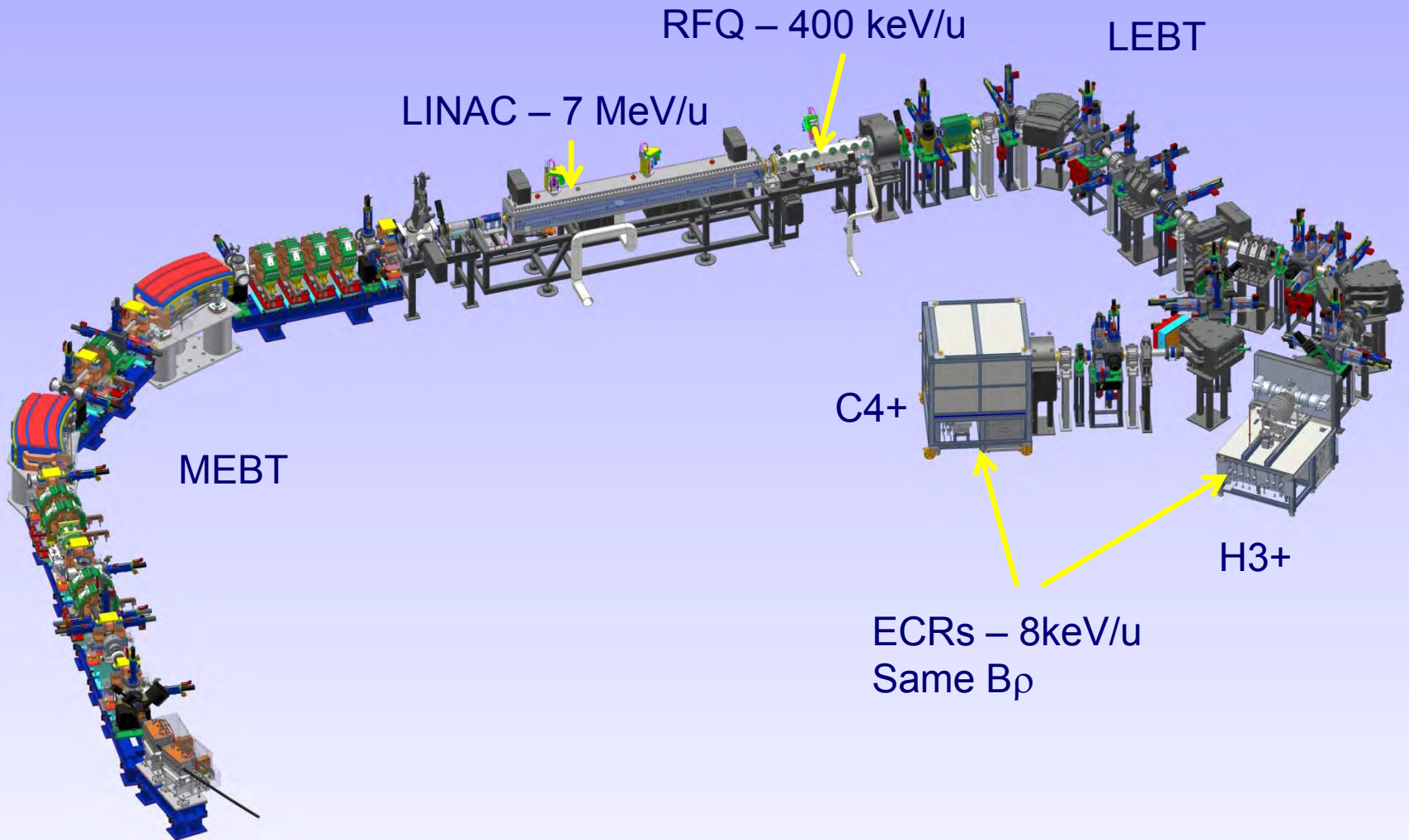


Z2-028A-SFH  
Long Fibers SFH

Treatment room



# INJECTOR

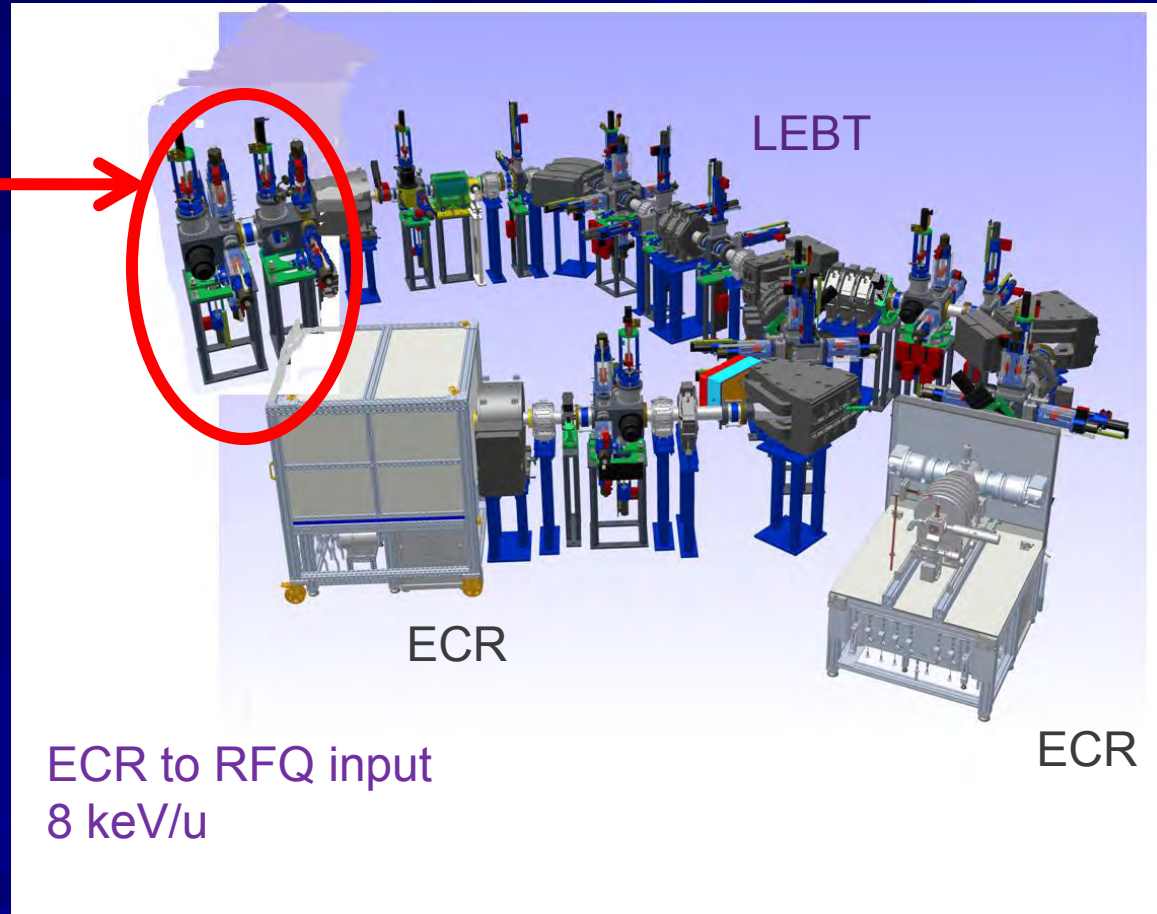


# INJECTOR commissioning strategy

TB0

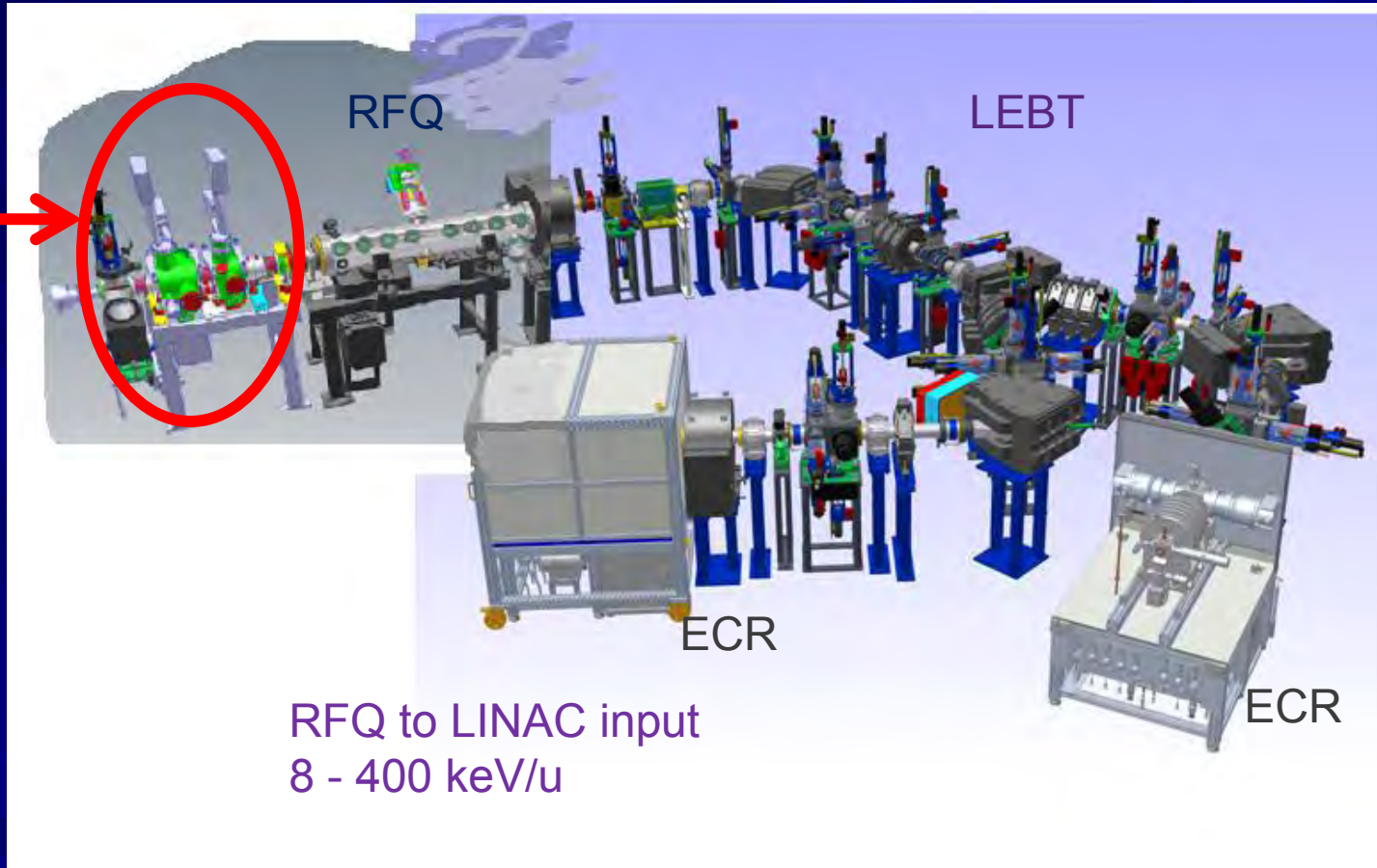
Diagnostic tank

- Intensity
- Dimensions
- Profile
- Emittance



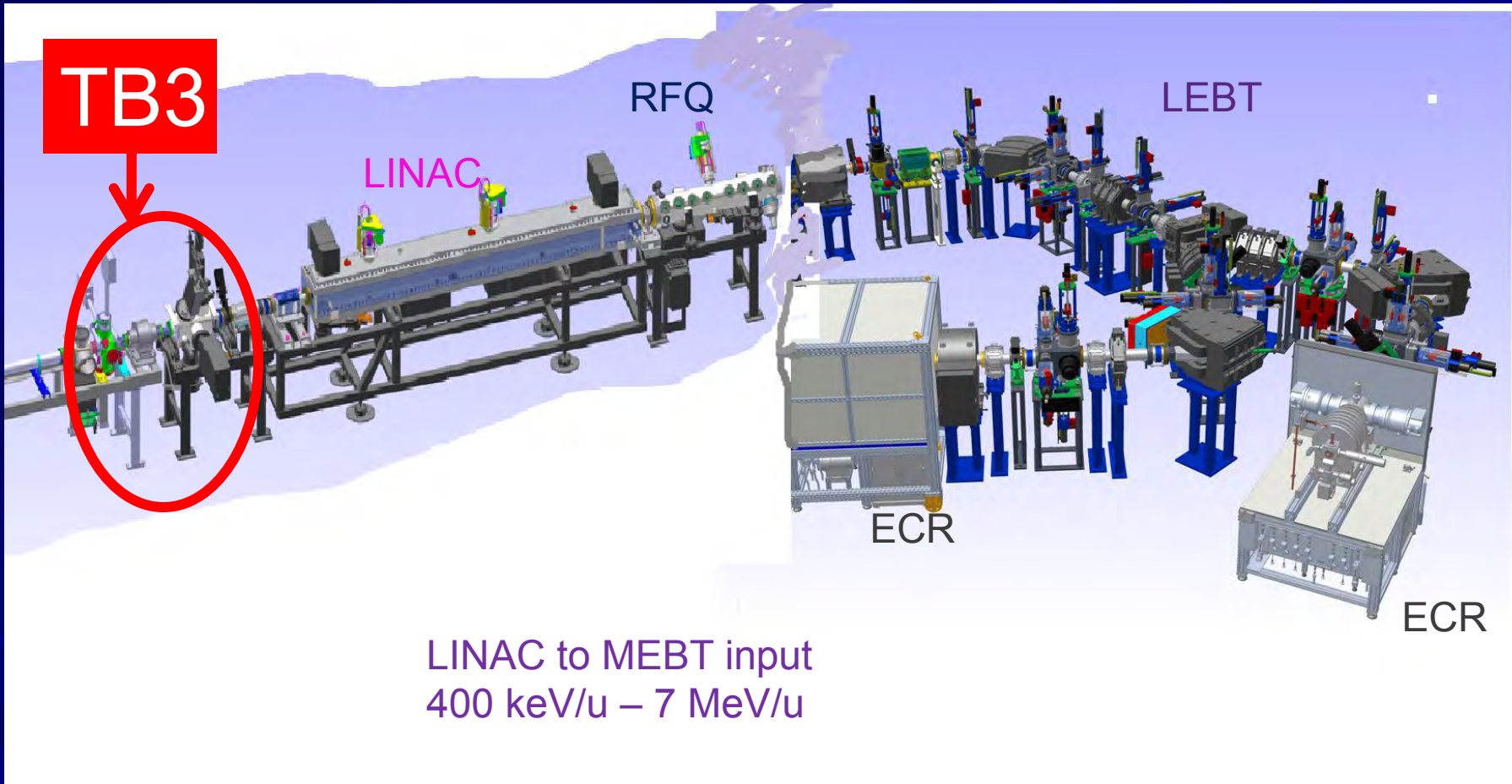
# INJECTOR commissioning strategy

TB2





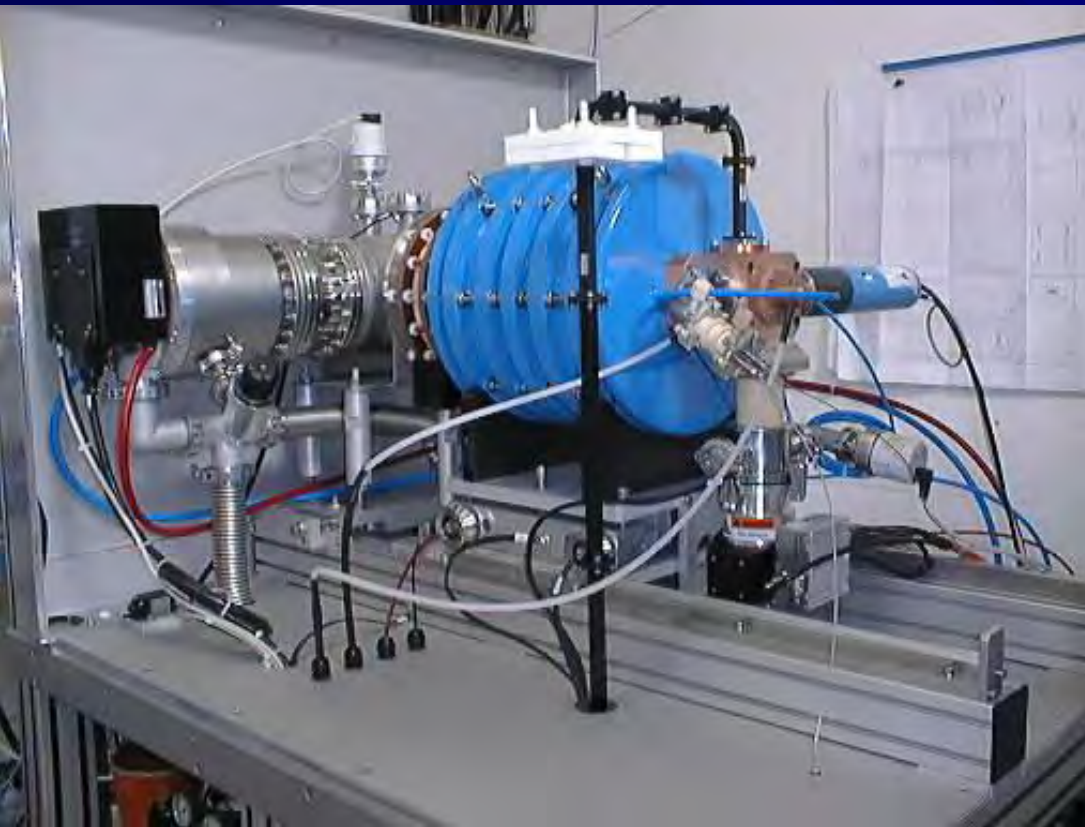
# INJECTOR commissioning strategy



# ECR Ion Sources

Both can deliver H<sup>3+</sup>, C<sup>4+</sup> and other species  
14.5GHz

MEBT

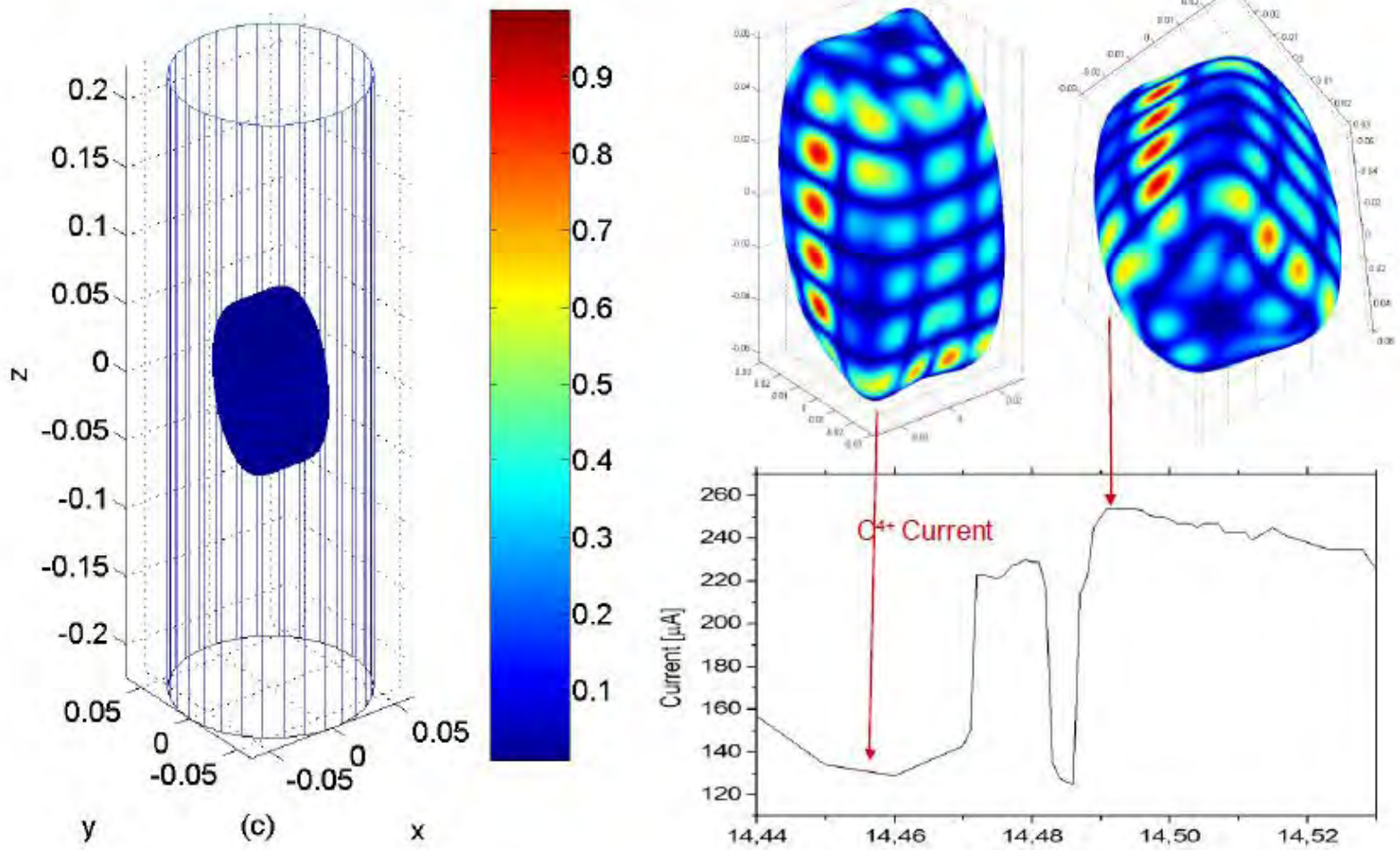


- Double wall, water cooled plasma chamber with 7 mm diameter aperture for beam extraction.
- **Permanent magnets** system providing the axial and radial confinement (axial field from 0.4 to 1.2 T, radial field 1.1 T)
- A copper made “magic cube” for the microwave injection system which consists of a waveguide to coaxial converter with a tuner to minimize the reflected power.
- An RF window for the junction between the magic cube at high vacuum and the waveguide at atmospheric pressure coming from the generator.
- A gas injection system.
- A DC bias system to add electrons to the plasma and decrease the plasma potential.
- An RF generator of about **400 W** at 14.5 GHz (the effective power used in operation is below 300W).
- **Flexible frequency variable travelling wave tubes amplifiers (TWTA)** .

Built by Pantechnic on INFN-LNS Design

# FREQUENCY TUNING EFFECT

Increase of the extracted current by 30-50 %



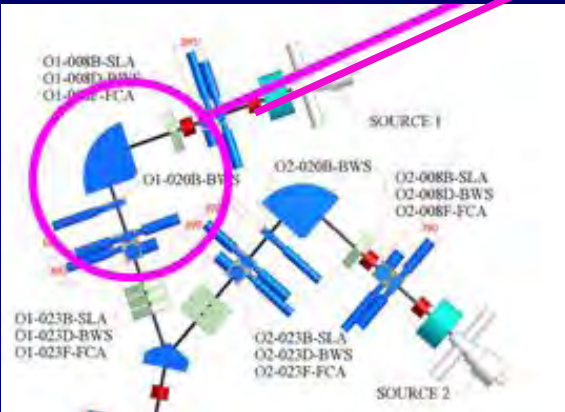
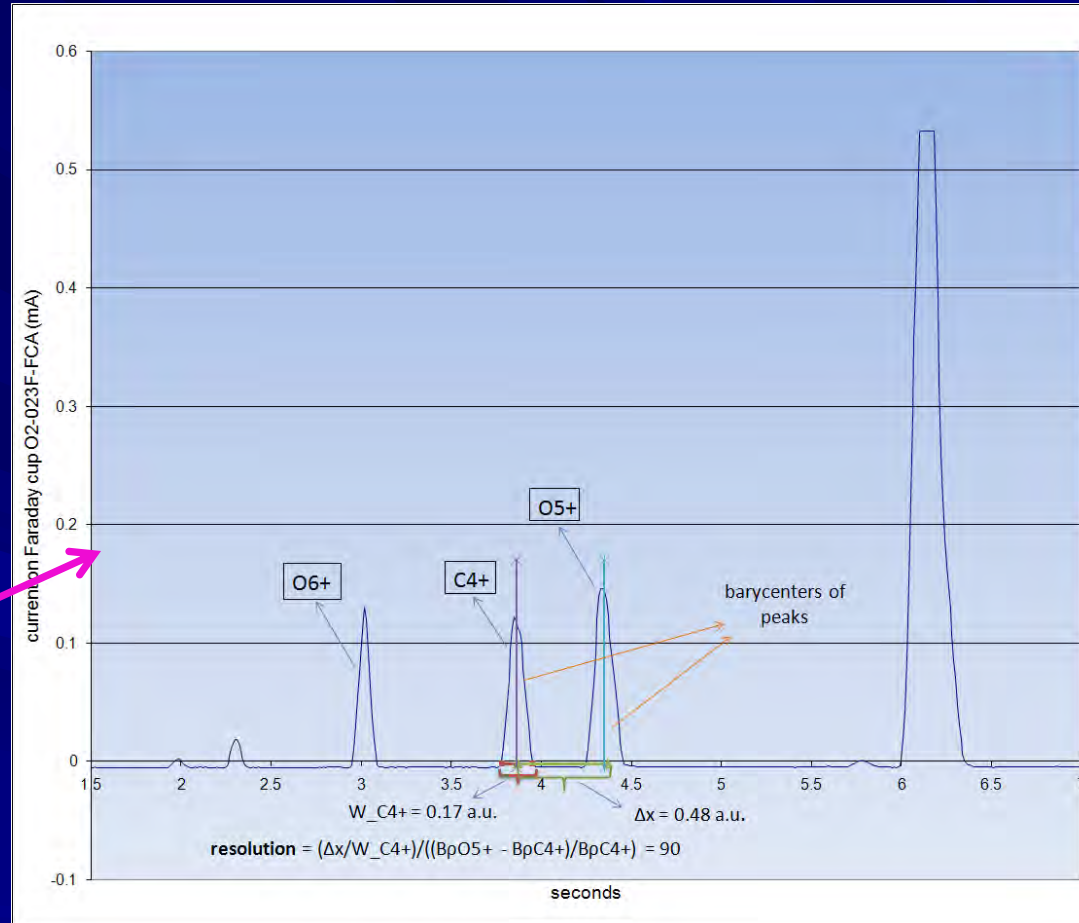
Slight variations of the exciting frequency produce strong changes in the electric field distribution over the resonance surface – S. Gammino



# Spectra of source

$$R = \frac{\left(\frac{\Delta x}{W}\right)}{\left(\frac{(B\rho_{O^{5+}} - B\rho_{C^{4+}})}{B\rho_{C^{4+}}}\right)}$$

Minimum resolution to separate C4+ from O5+:  
 $R \approx 30$

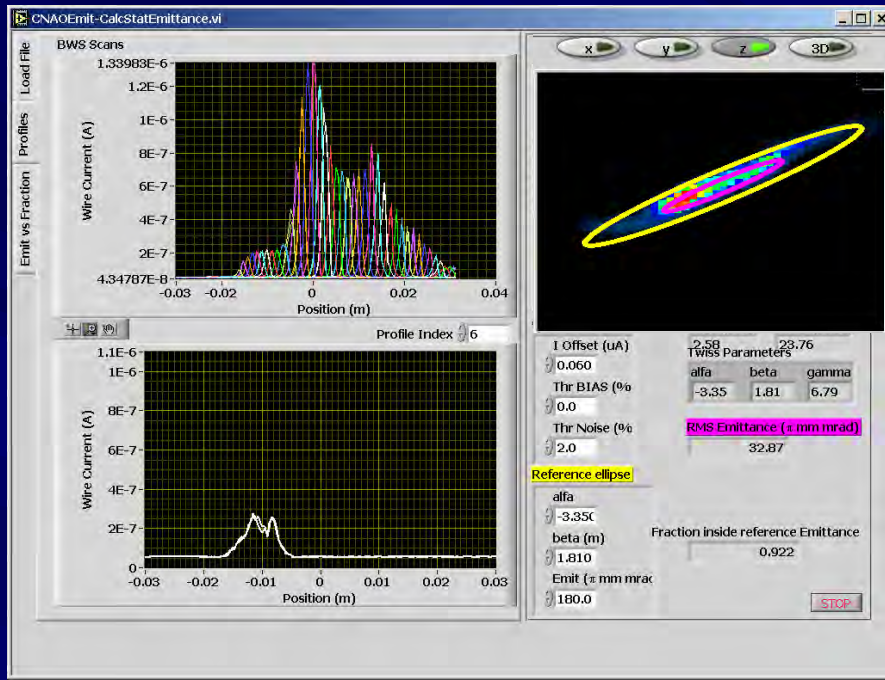


Measurement performed  
 with a fixed gap of slits (2 mm).

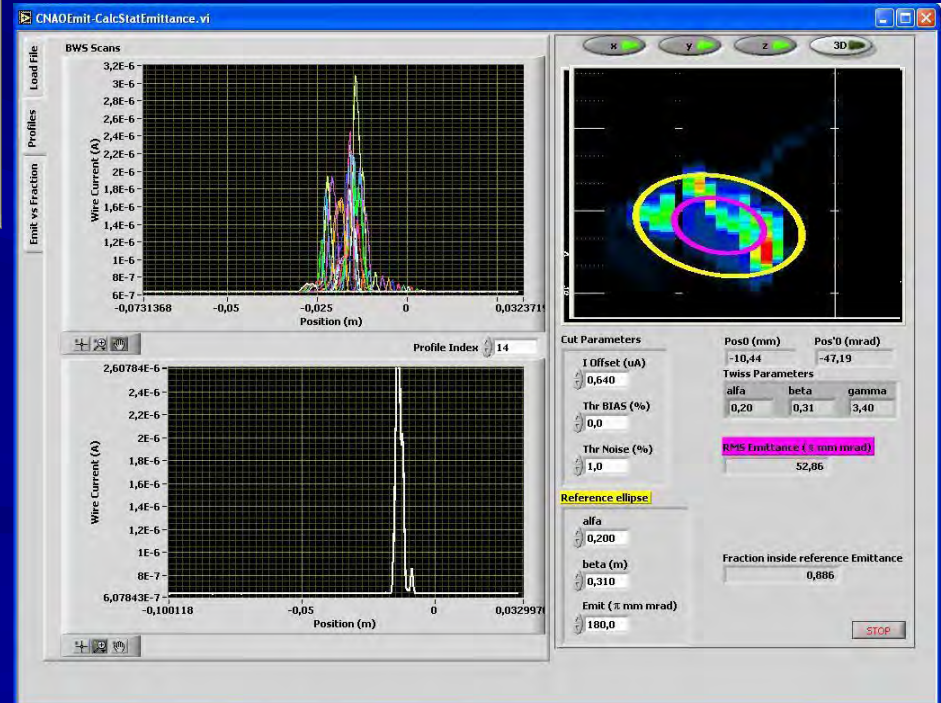
# Sources currents and emittances

$H_3^+$ , 1.4mA  
(design = 800  $\mu A$ )

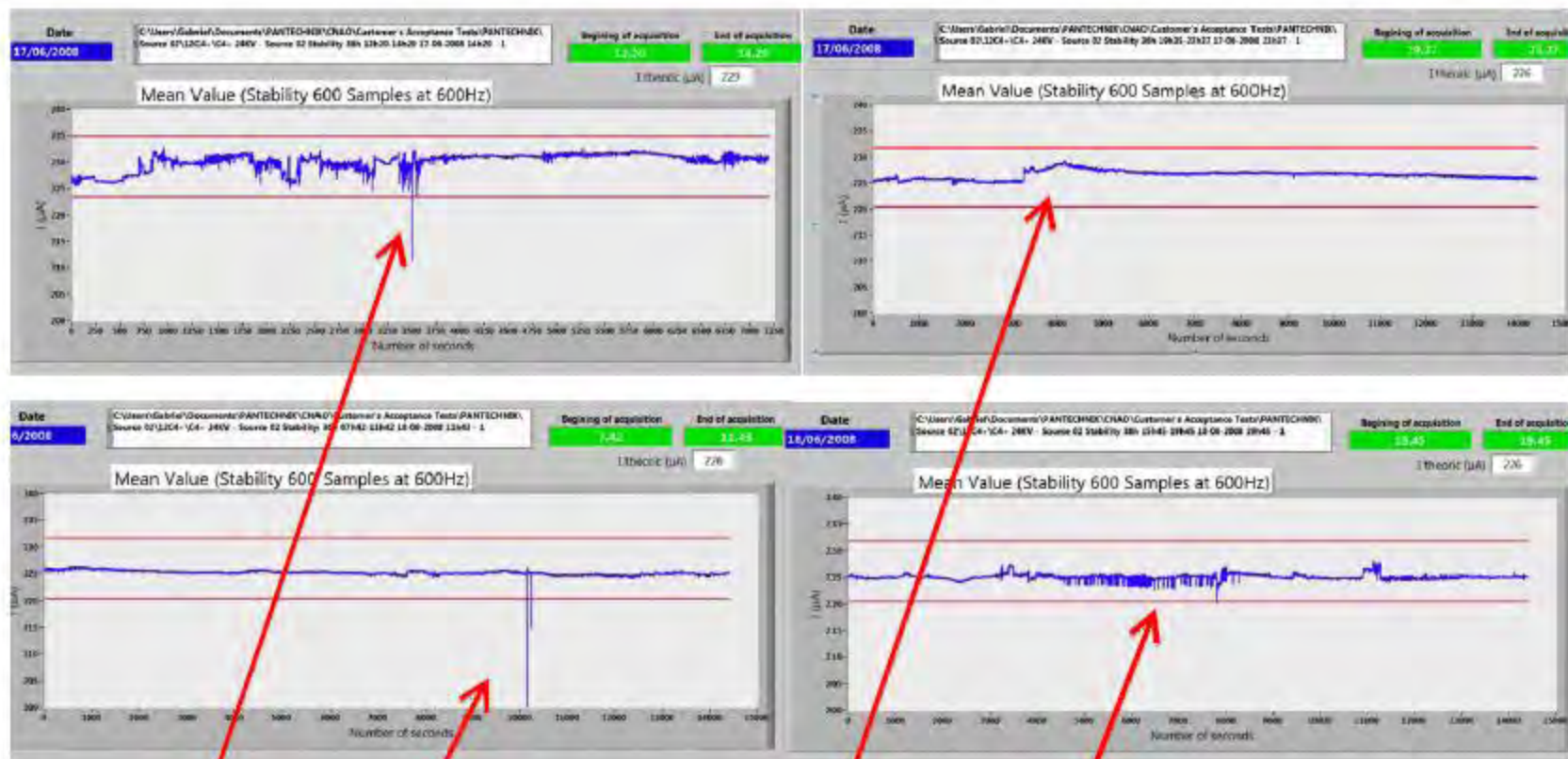
Emittance measured after spectrometer



$C^{4+}$ , 230  $\mu A$  (design = 200  $\mu A$ )



# Stability tests for C<sup>4+</sup>



Conditioning  
(> 1 hour) HV sparks

door open

Crane in motion



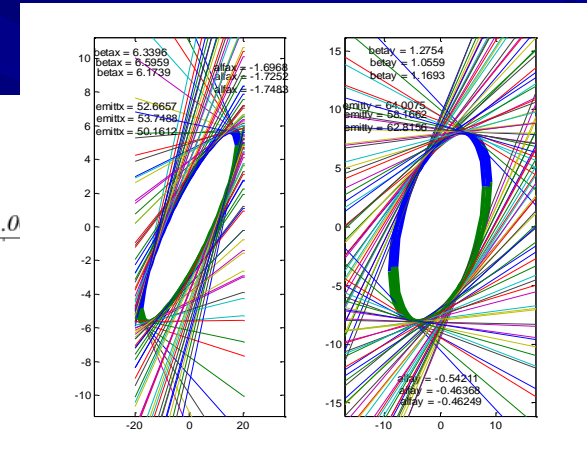
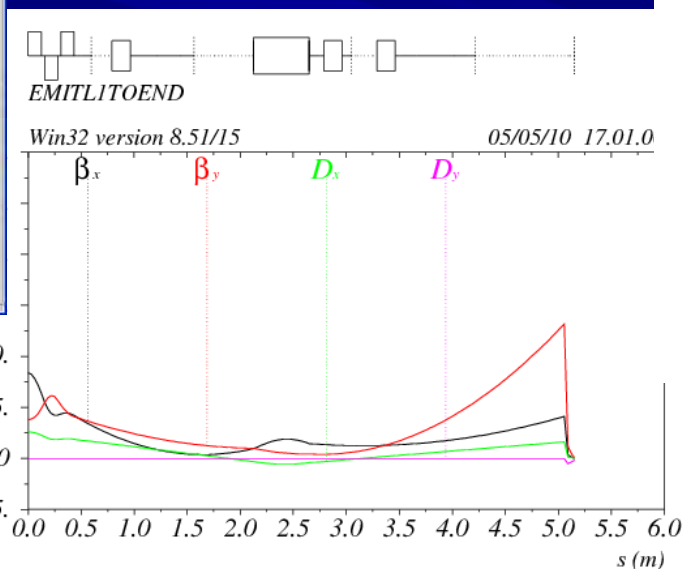
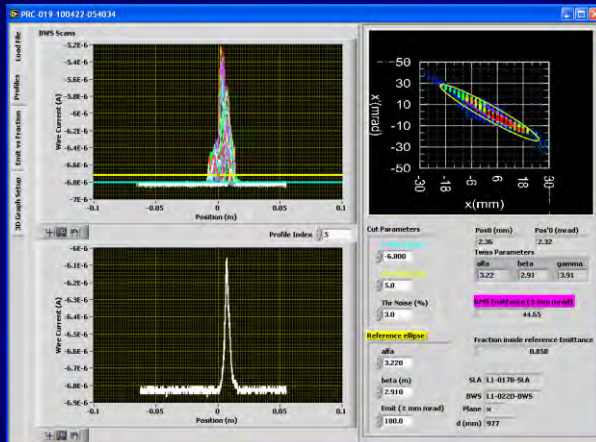
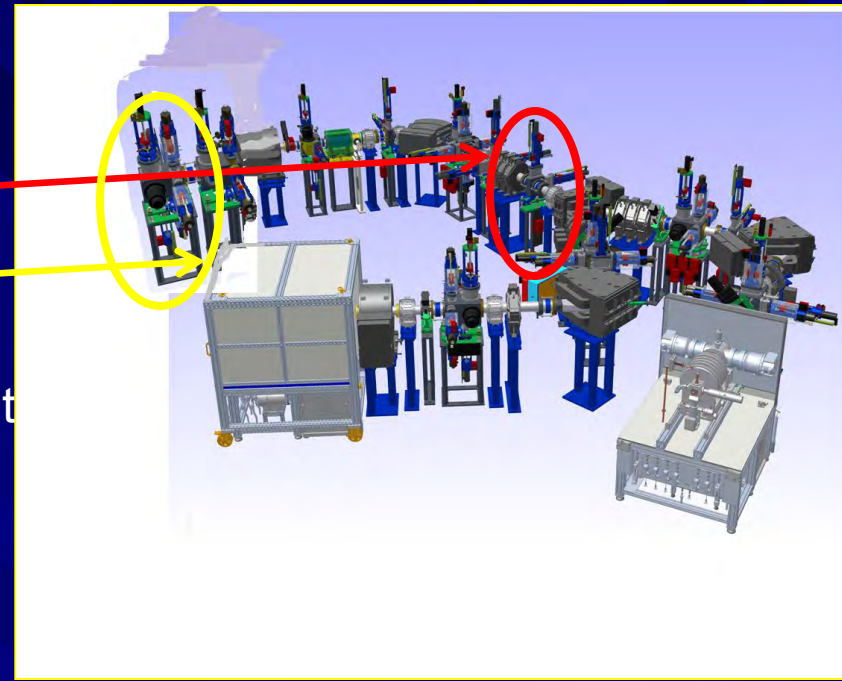
# LEBT commissioning

Diagnostic tanks containing  
slits, wire scanners, faraday cups  
Along the line + TB0

Emittance and Twiss Parameters measurement

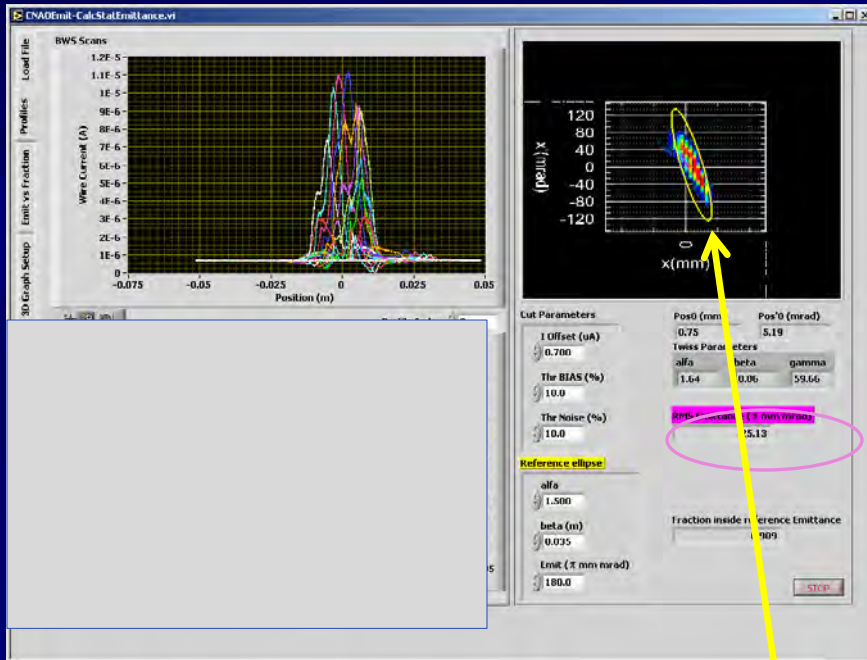
- With tank diagnostics
- With Quad scans
- Model

Agreement better than  $\pm 10\%$

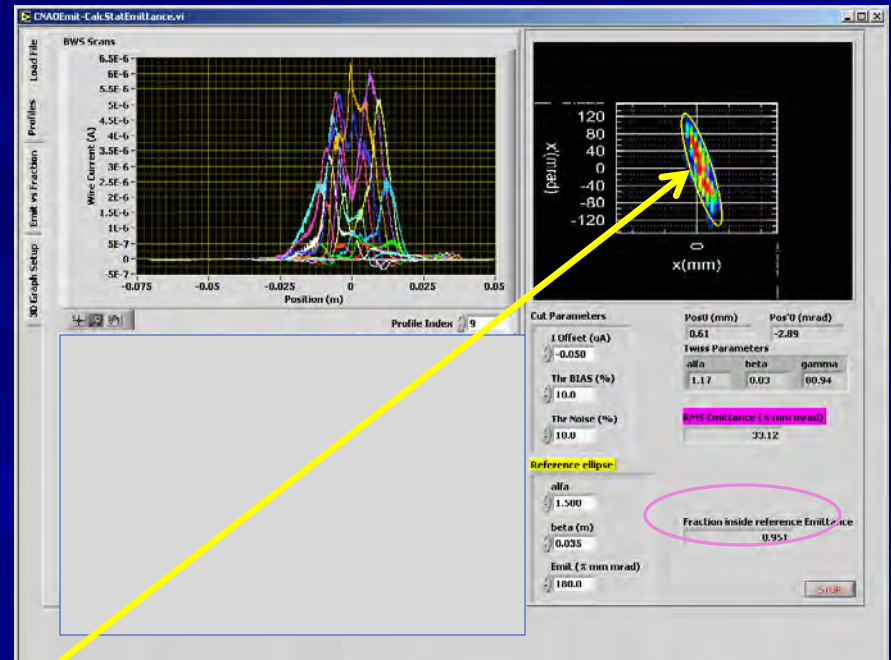


# 'Round beam' in TB0 with H3+ from SO1

Transmission 92 % - final current 1150  $\mu\text{A}$  (design 600  $\mu\text{A}$ )



Horizontal plane



Vertical plane

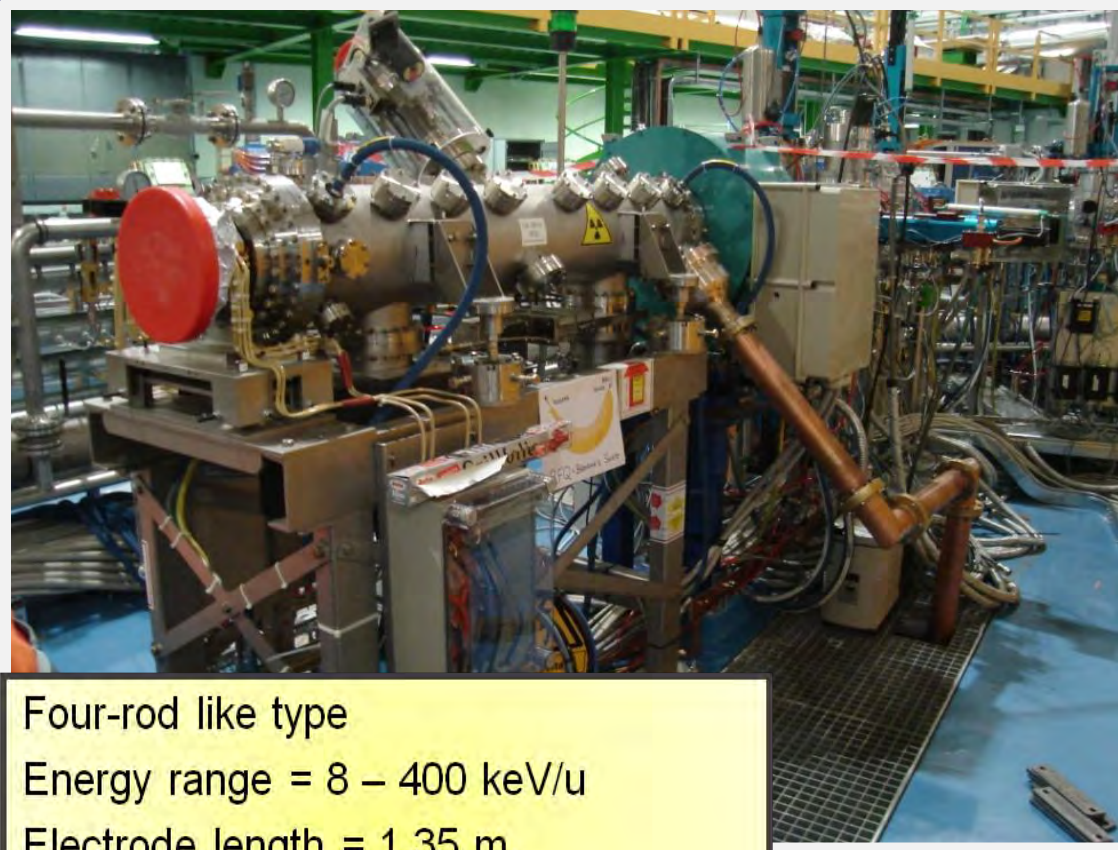
RFQ nominal acceptance

C4+ :

Transmission 75 % - final current 150 mA  
(nominal request 180  $\mu\text{A}$ )



# RFQ – Gsi and CNAO



Four-rod like type  
Energy range = 8 – 400 keV/u  
Electrode length = 1.35 m,  
Electrode voltage = 70 kV  
RF power loss (pulse): about 100 kW  
Low duty cycle: around 0.1%

$$F_{\text{rf}} = 217 \text{ MHz}$$



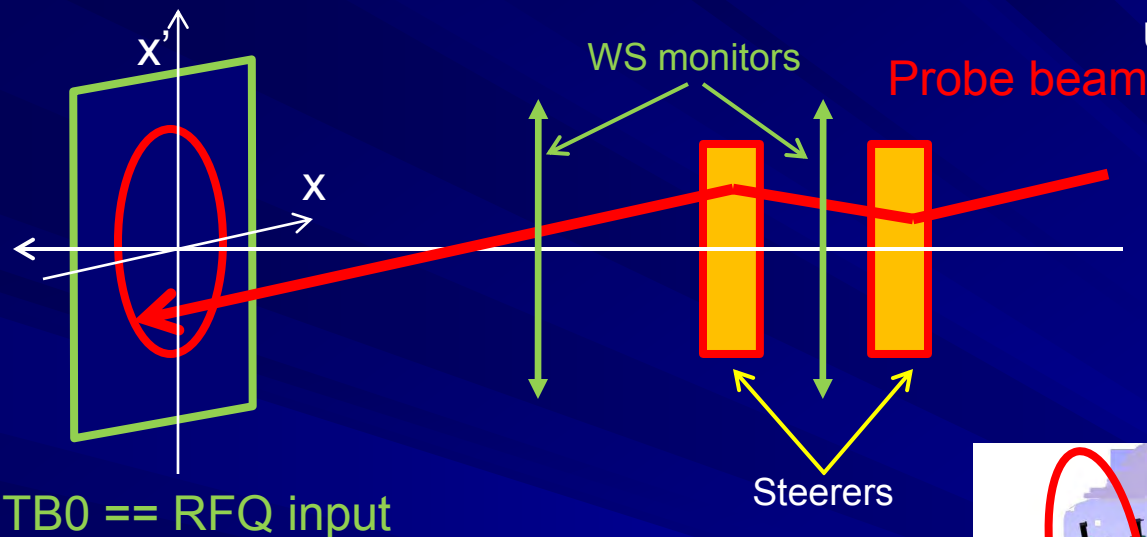
TB2 diagnostic tank

## Measurements:

- Current
- Profiles
- Energy
- Emittance

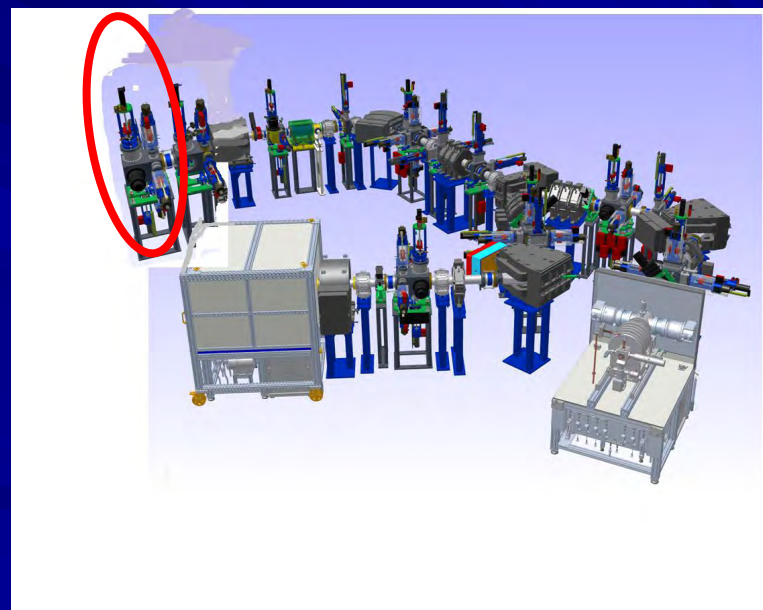
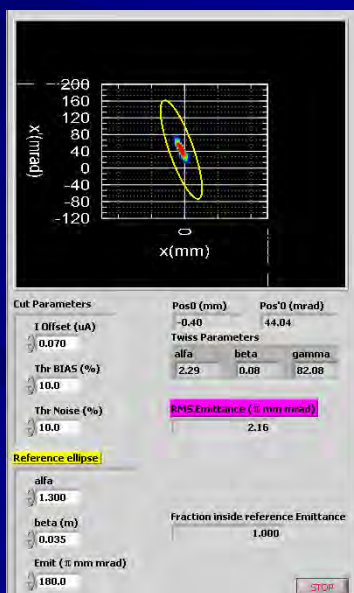
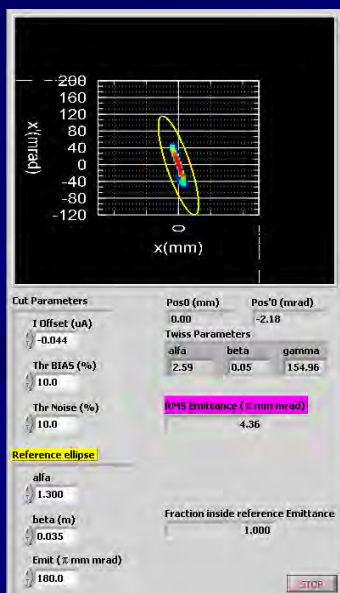


# Phase space painting: calibration for RFQ injection optimisation



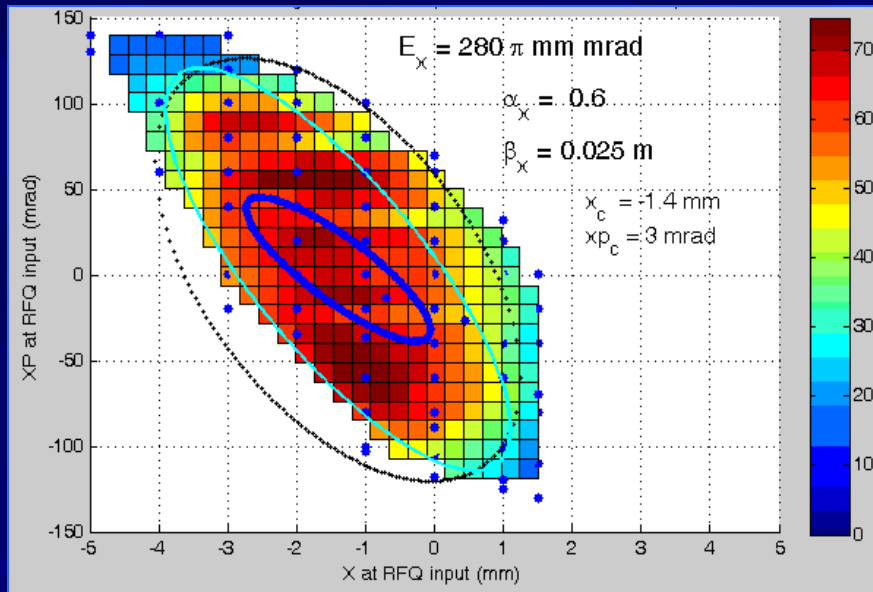
H3+ probe beam created using slits along the LEBT

full beam current → 1 mA  
 probe beam current → 60  $\mu$ A

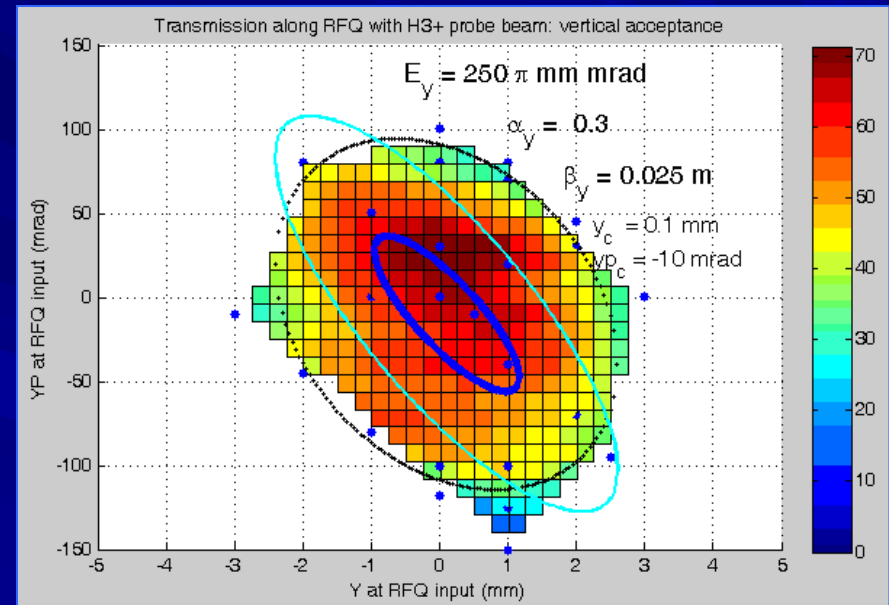


# RFQ acceptance measurements (8 keV/u)

## Horizontal plane



## Vertical plane

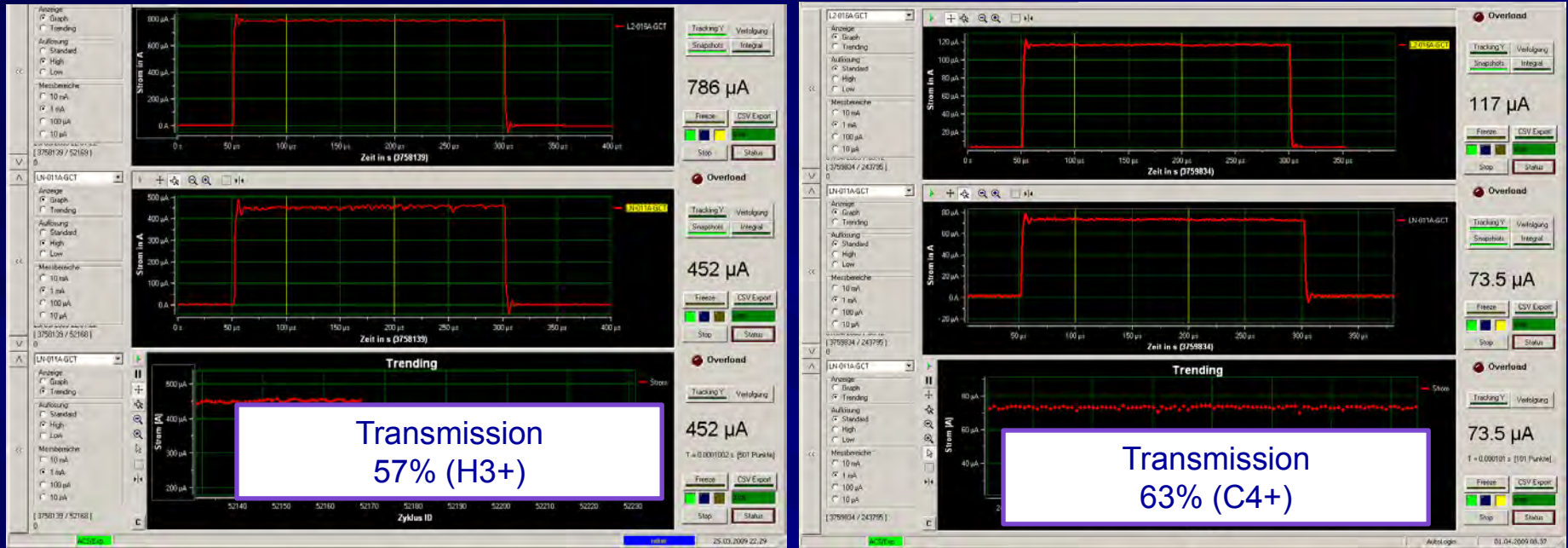


Blue ellipse: measured in TB0 (rms emittance full beam)

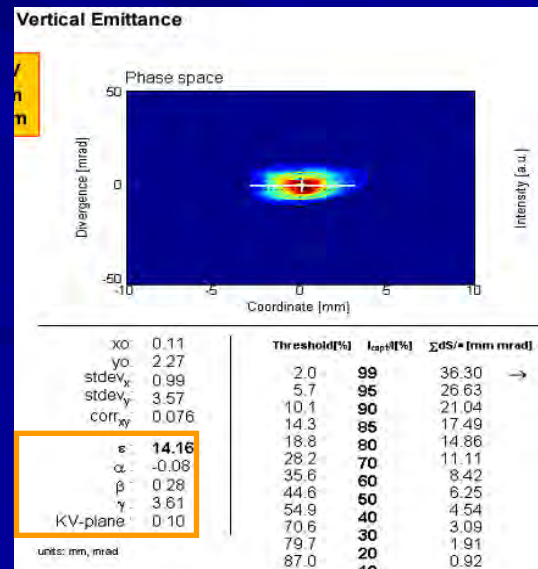
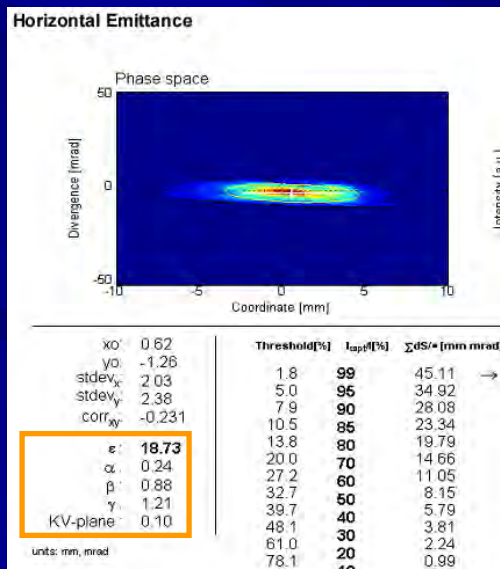
Cyan ellipse: nominal RFQ acceptance

Black ellipse fits measured points up to the half of maximum transmission value

# RFQ commissioning: typical measurements



## Emittances in TB2 (C4+)





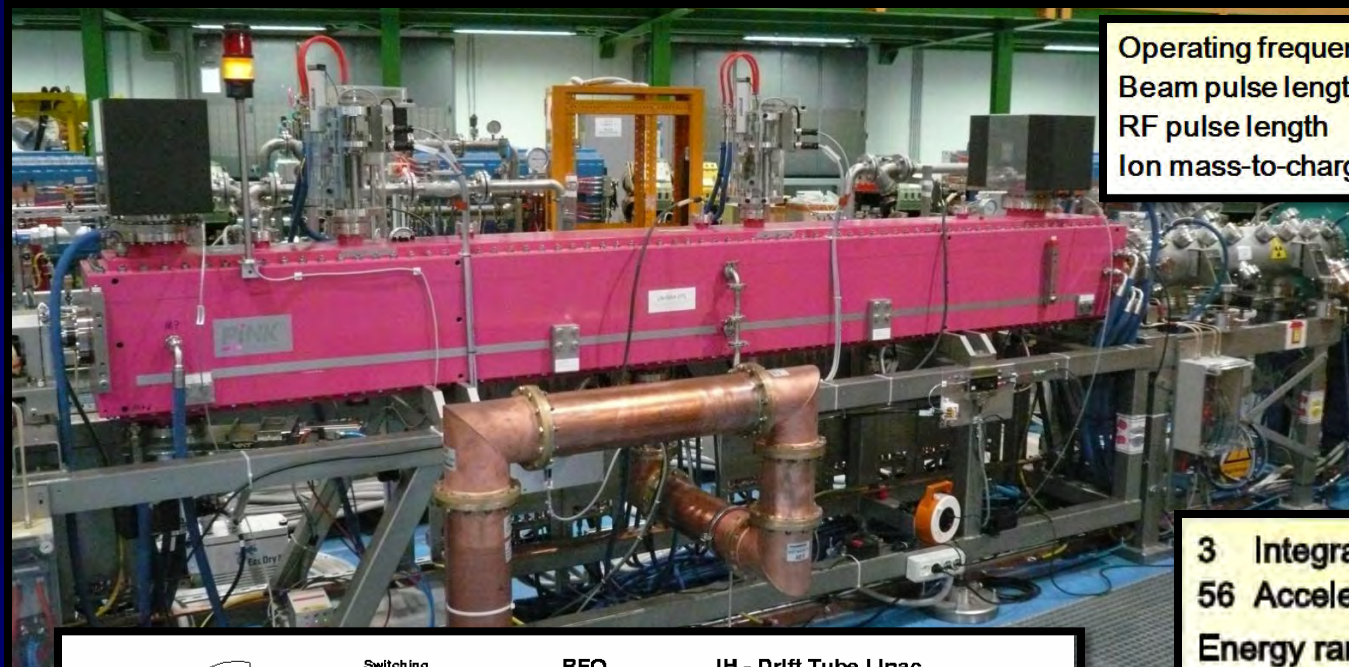
# RFQ commissioning summary

			transmission	maximum current	nominal current
full beam	$H_3^+$	8 keV/u	57%	450 uA	300 uA
probe beam	$H_3^+$	8 keV/u	70%	50 uA	
probe beam	$H_3^+$	8.5 keV/u	60%	45 uA	
full beam	$C^{4+}$	8 keV/u	63%	73 uA	100 uA

Full beam transmission slightly lower than probe beam transmission:

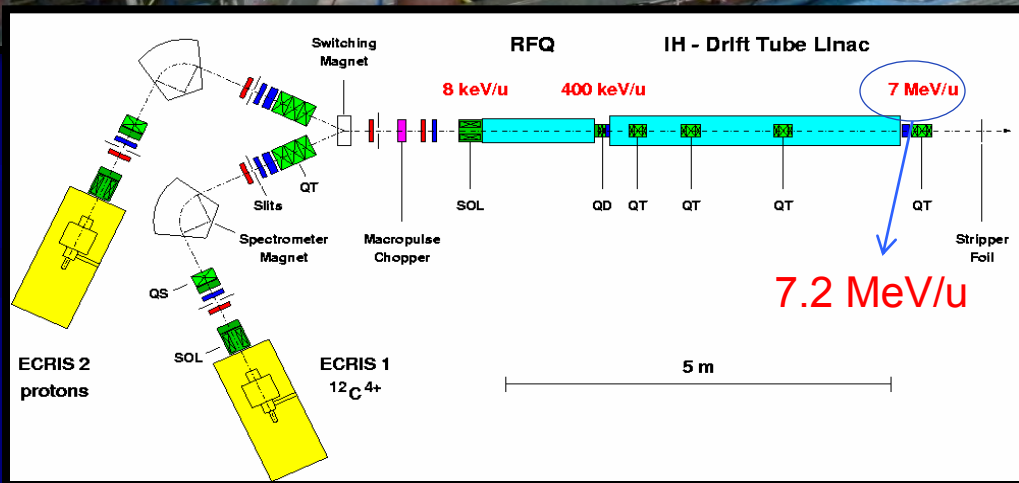
- good transverse matching
- transmission limited by longitudinal leak

# LINAC – GSI and CNAO



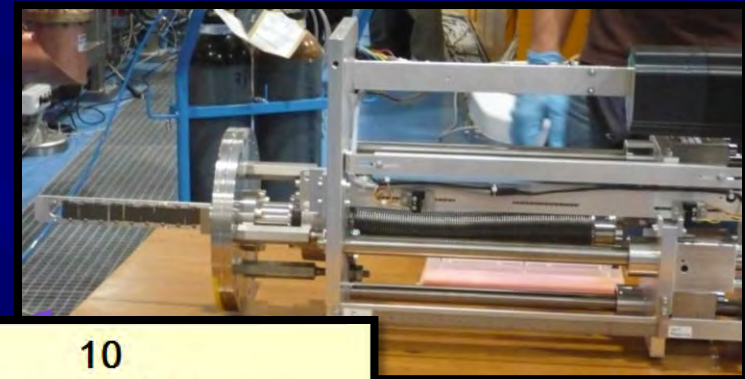
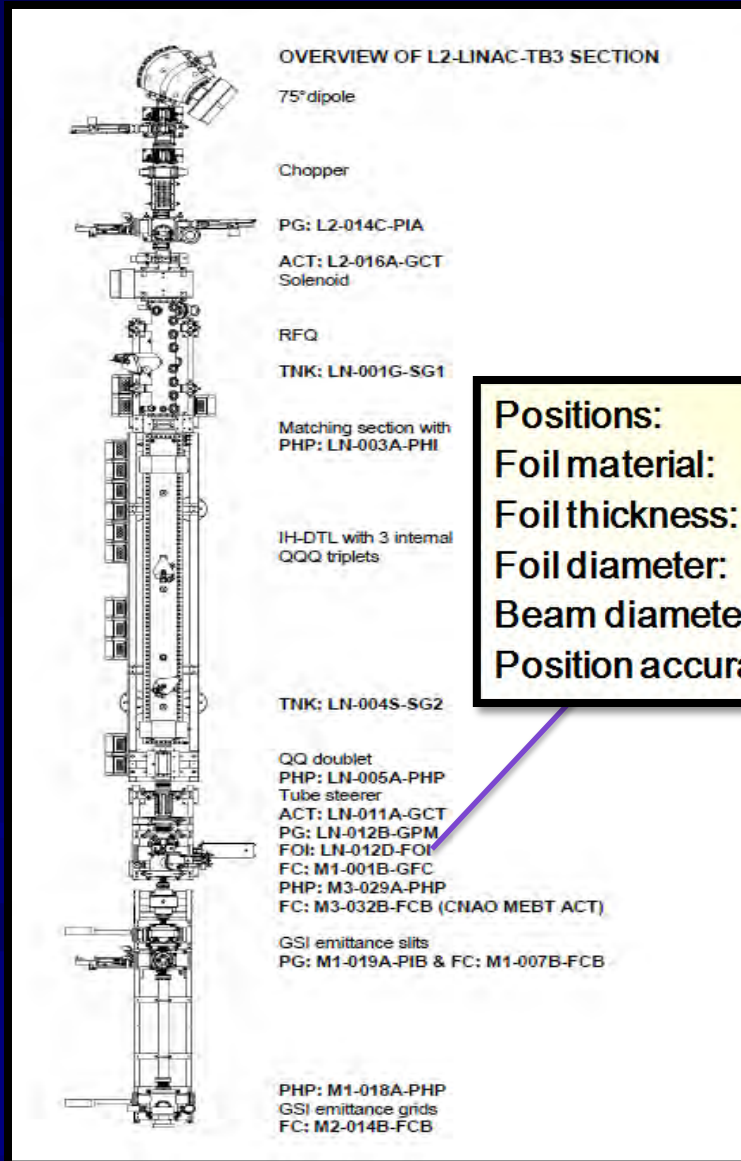
Operating frequency	216.816 MHz
Beam pulse length	$\leq 300 \mu\text{s}$ @ PRF $\leq 5$ Hz
RF pulse length	$\leq 500 \mu\text{s}$ @ PRF $\leq 10$ Hz
Ion mass-to-charge ratio	$A/q \leq 3$

<b>3</b>	Integrated magnetic triplet lenses
<b>56</b>	Accelerating gaps
Energy range	0.4 – 7 MeV/u
Tank length	3.77 m
Inner tank height	0.34 m
Inner tank width	0.26 m
Drift tube aperture diam.	12 – 16 mm
RF power loss (pulse)	$\approx 1$ MW
Averaged eff. volt. gain	5.3 MV/m

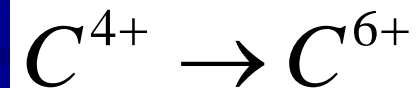
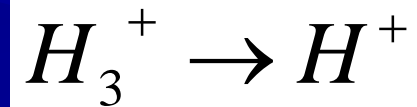


7.2 MeV/u

# Stripping foils after Linac acceleration

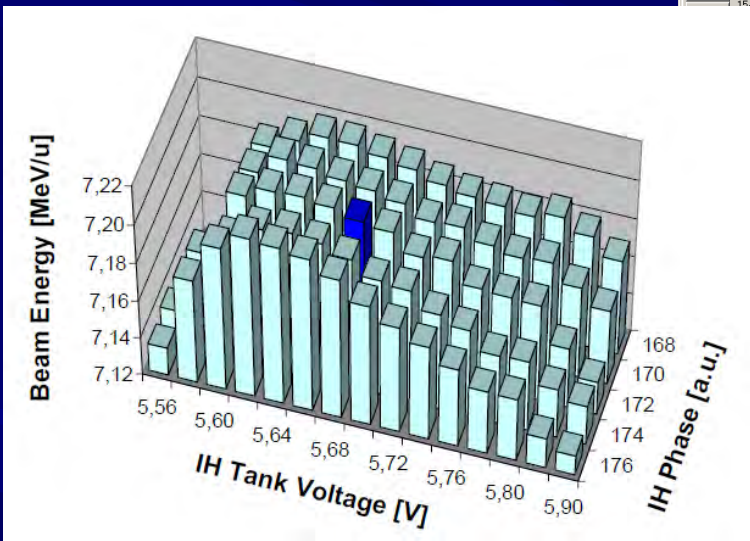
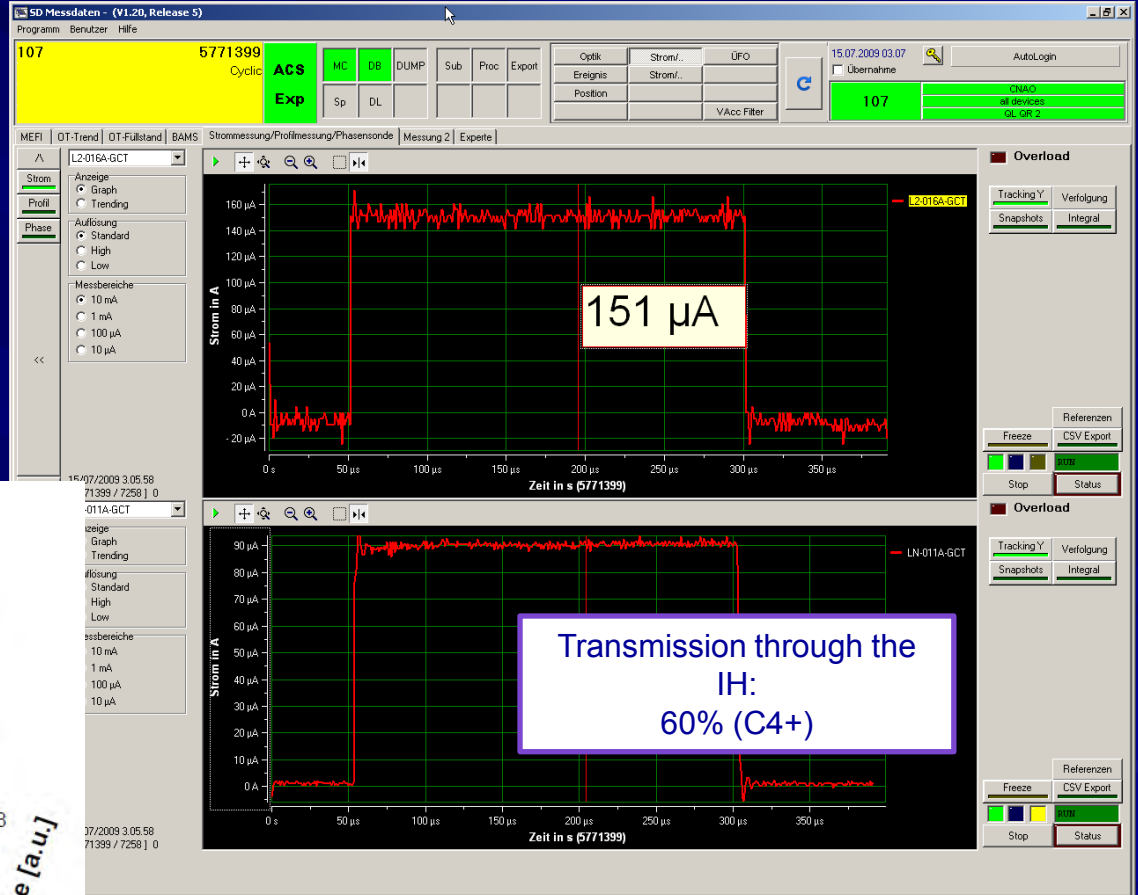


Positions:	10
Foil material:	Carbon
Foil thickness:	100-200 $\mu\text{g}/\text{cm}^2$
Foil diameter:	15 mm
Beam diameter:	5 mm
Position accuracy:	$\pm 0,5$ mm

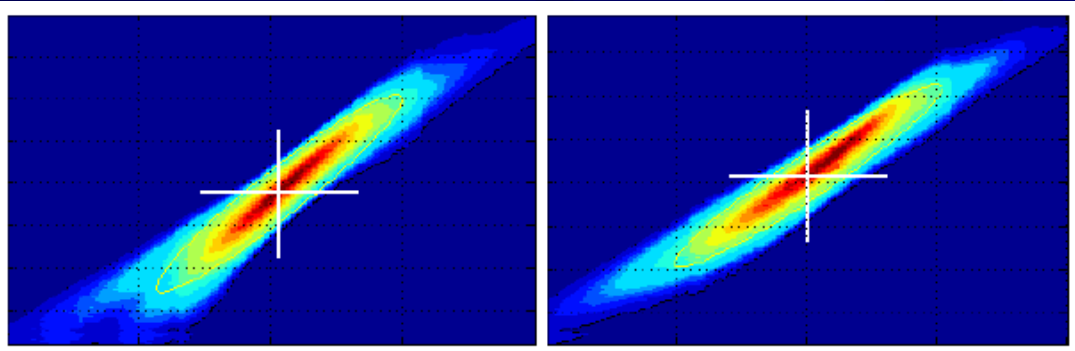




# LINAC commissioning



C6+ beam energy dependence on Linac parameters



Ion Species	$\epsilon_{4 \times \text{rms}, 90\%} / \pi \text{ mm mrad}$		Emittance Growth	
	horizontal	vertical	hor.	vert.
$\text{C}^{6+}$	5.2	4.1	3 %	3 %
protons	6.4	6.0	7 %	36 %

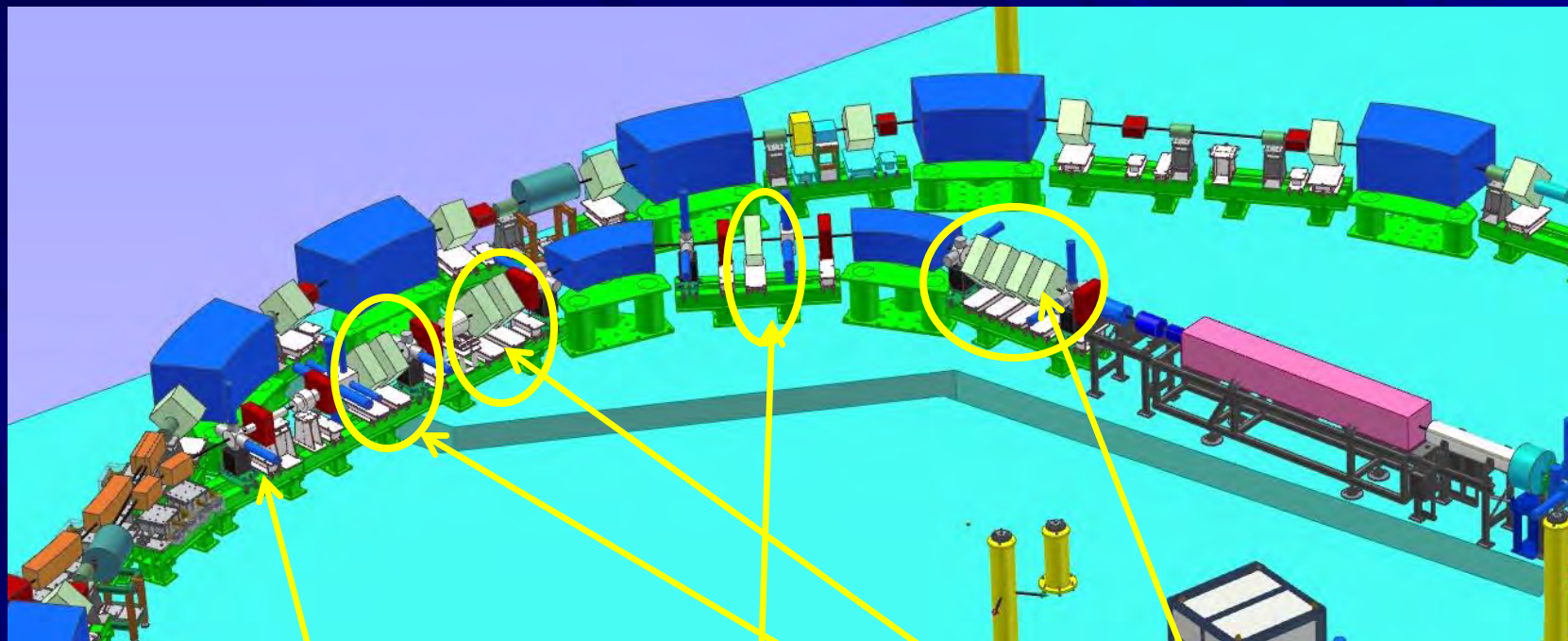
Ion Species	LEBT End	Downstream LINAC	LEBT/LINAC max.transmission	Downstream Stripper foil
$\text{C}^{4+} / \text{C}^{6+}$	$\approx 170 \mu\text{A}$	$\approx 82 \mu\text{A}$	48 %	$\approx 115 \mu\text{A}$
$\text{H}_3^+ / \text{p}$	1.0 – 1.1 mA	$\approx 400 \mu\text{A}$	39 %	$\approx 1.2 \text{ mA}$
	710 $\mu\text{A}$	307 $\mu\text{A}$	46 %	$\approx 900 \mu\text{A}$

Goal: 120  $\mu\text{A}$

Goal: 600  $\mu\text{A}$

... about two times higher  $\text{C}^{6+}$  beam currents and roughly four times higher proton beam currents were achieved behind the CNAO linac as compared to HIT.

# MEBT



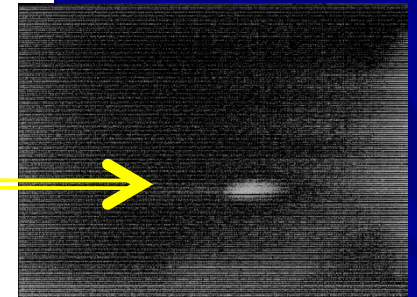
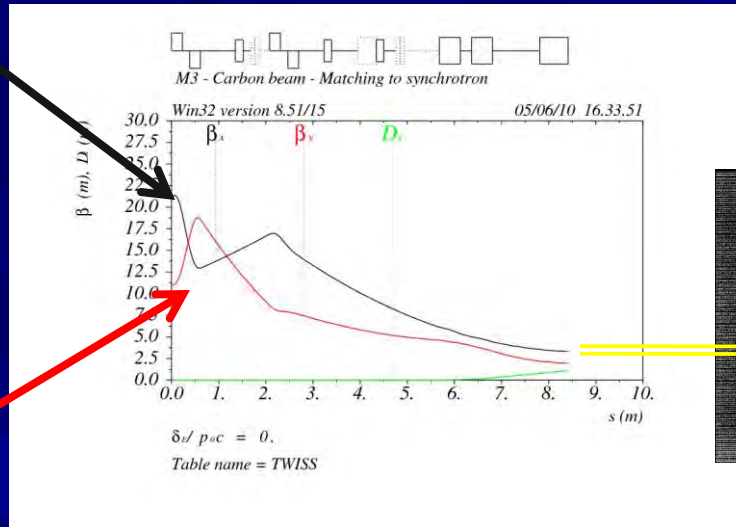
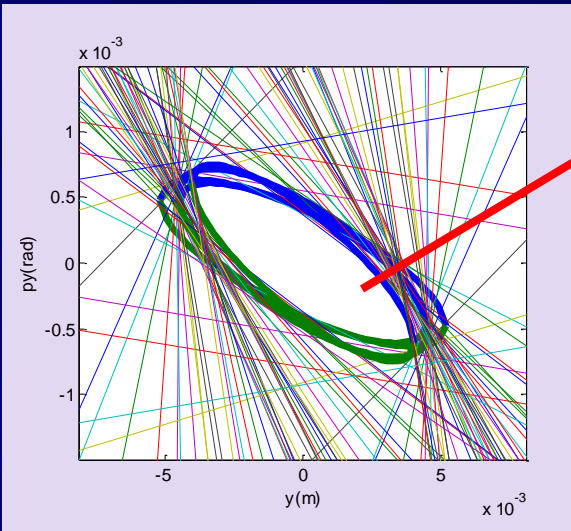
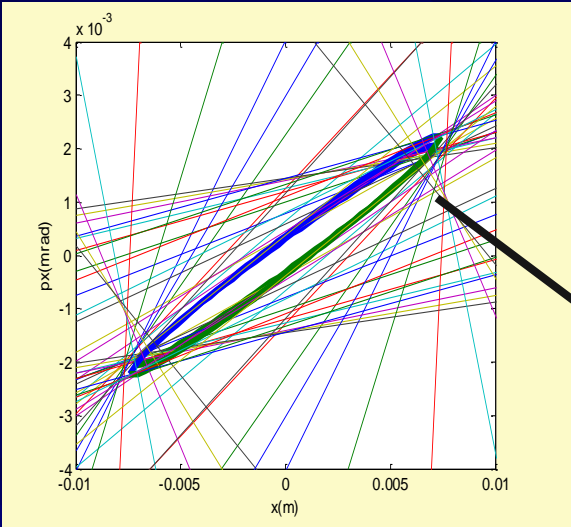
Debuncher to minimize the injected beam momentum spread

Dispersion bump

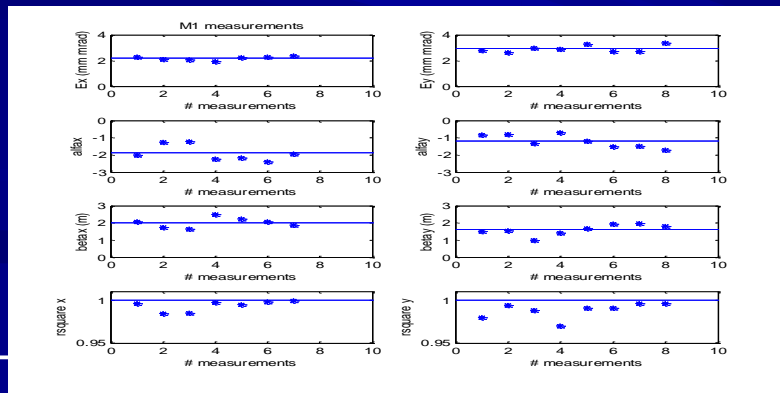
Quadrupoles for matching in non dispersive zone



# Emittance measurements with Quad Scans used for beam optimisation at injection



TVScreen in synchrotron

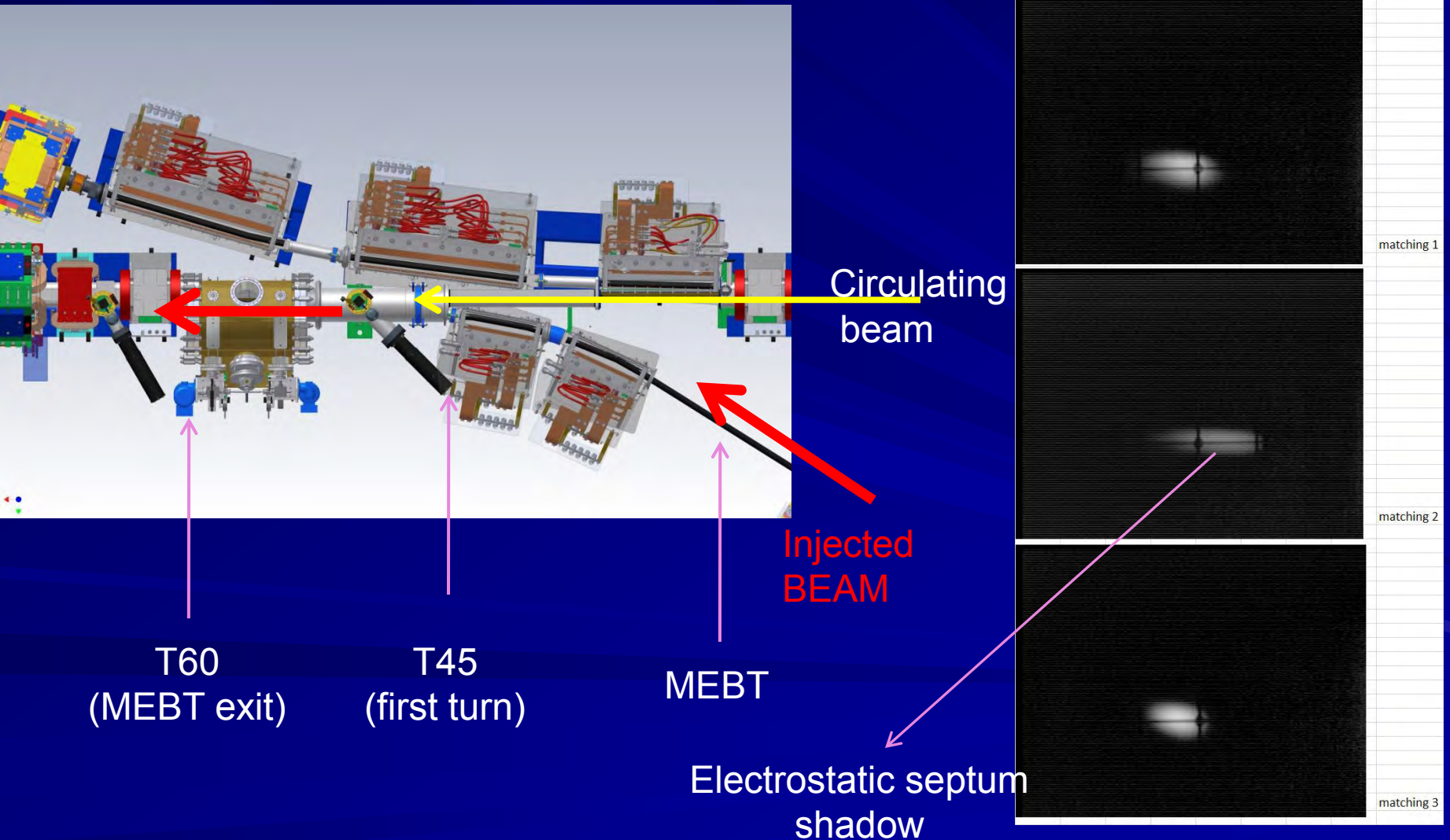


Carbon beam  
> 90 % transmission in MEBT

Different quad sets

# Beam (p) at the end of the MEBT

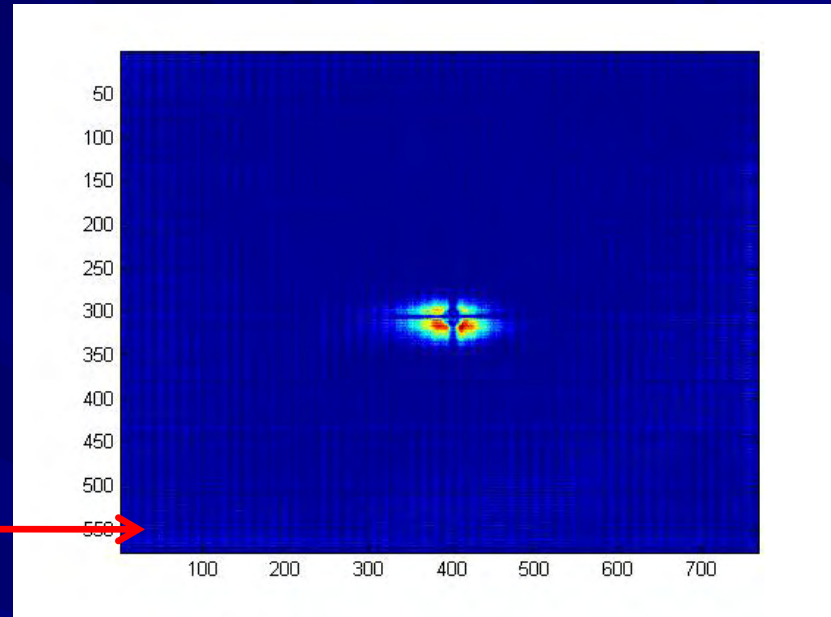
TV screen T60 → end of the MEBT



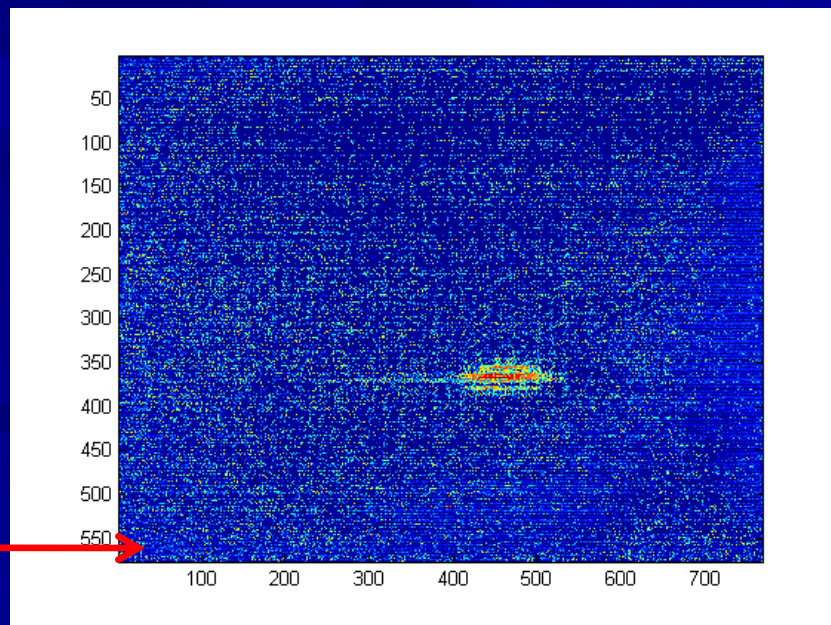
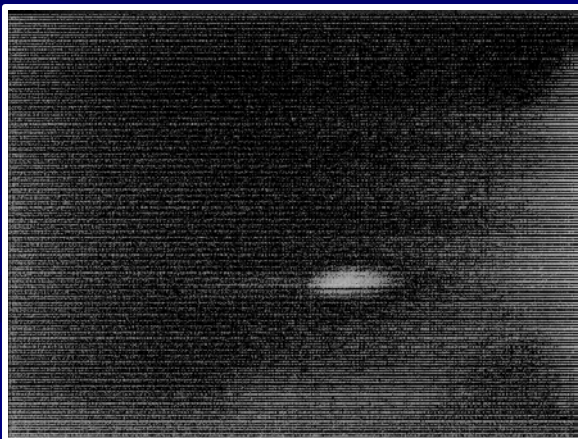
Transmission along MEBT > 90% both species

TV60

Images of Proton beam: 600  $\mu\text{A}$

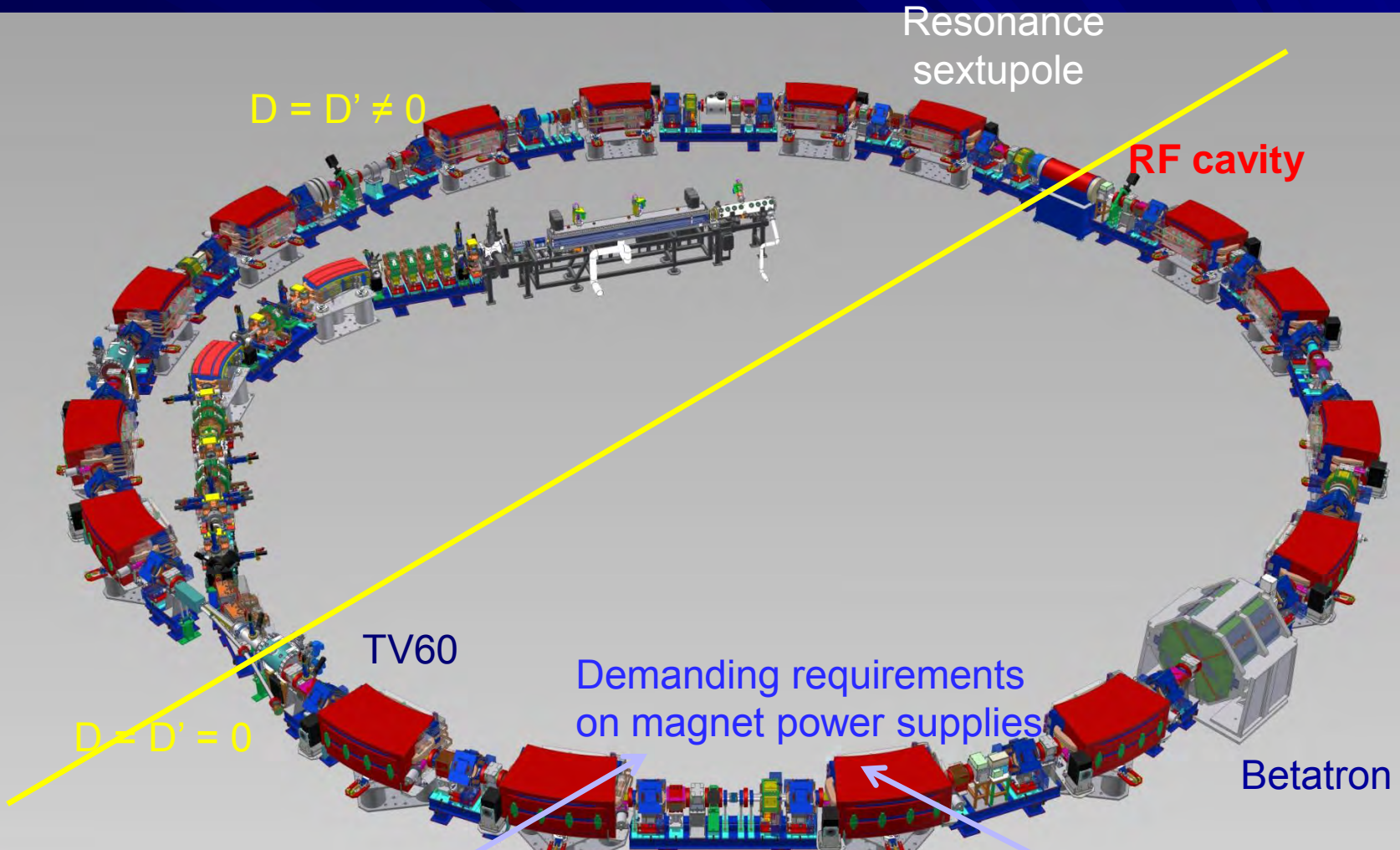


Images of Carbon beam: 90  $\mu\text{A}$





# Synchrotron



	P inj	P – 60 MeV	P – 250 MeV	C6 inj	C6+ – 120 MeV	C6+ – 400 MeV
$B\rho$ (T m)	0.4	1.1	2.4	0.8	3.3	6.4

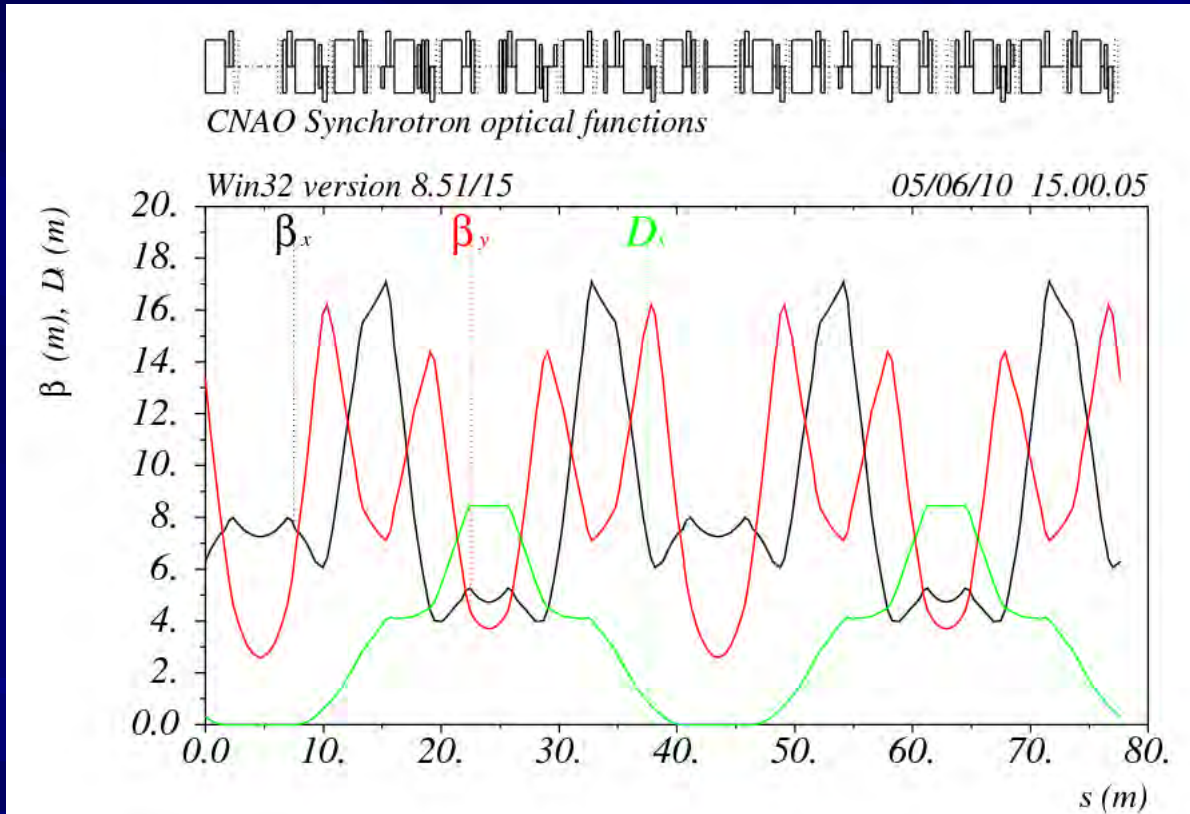
# Synchrotron optical functions

Injection

Betatron

Rf cavity

Extraction  
Electrostatic  
septum



C	78 m
Qx	1.6666 - 1.7
Qy	1.72

- 2 Superperiods**
- 2 Closed dispersion bumps**
- 1 Dipole Family**
- 3 Quadrupole Families**
- 3 Sextupole Families**

# RF cavity



## MAIN CHARACTERISTICS

Vitrovac(Co-Fe alloy) cavity

Tetrode pushpull amplifier

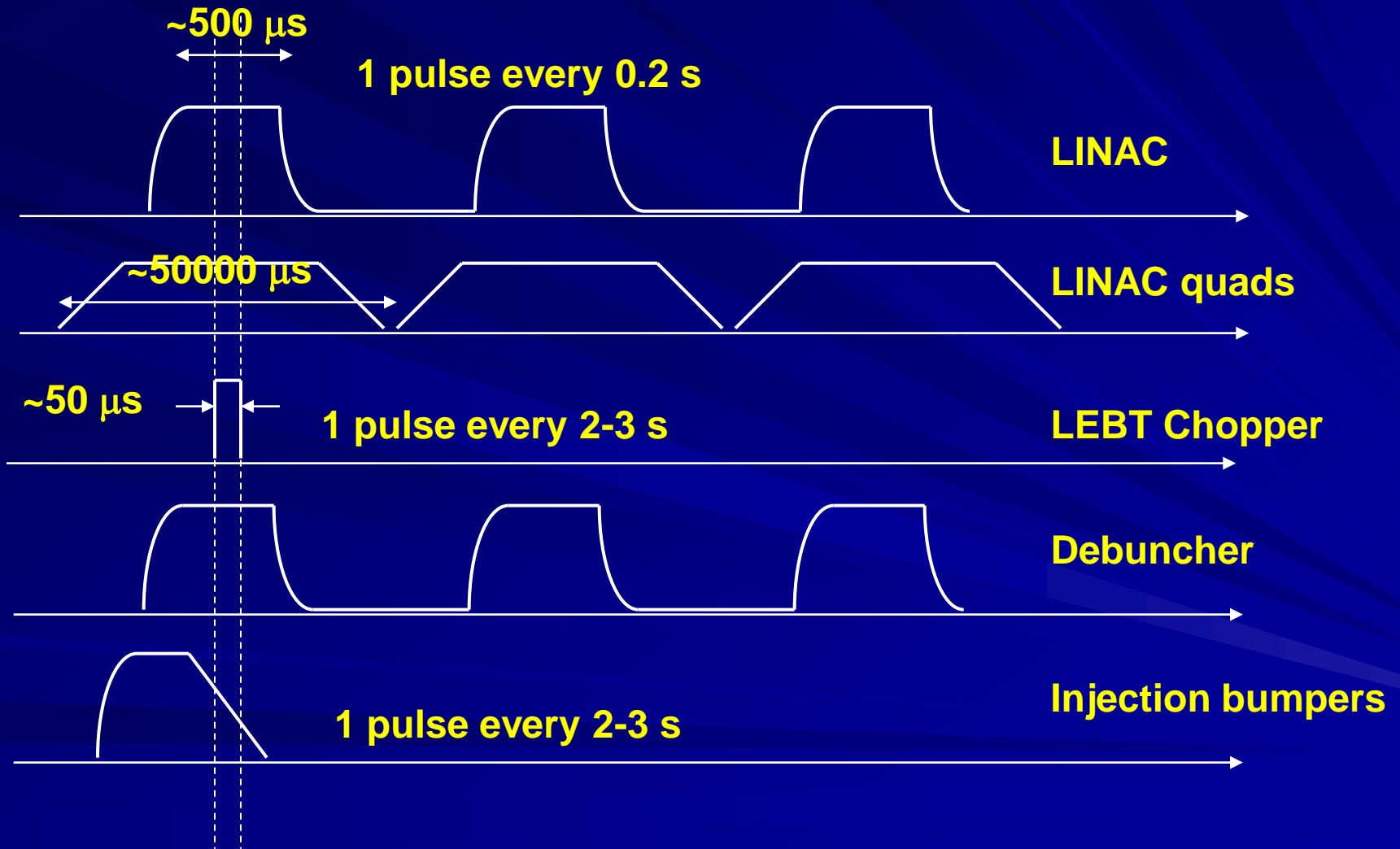
Frequency Range: 0.4 - 3 MHz  
(tested up to now but potentially  
extensible)

very low current to polarize  
vitrovac up to 3 MHz (10A)

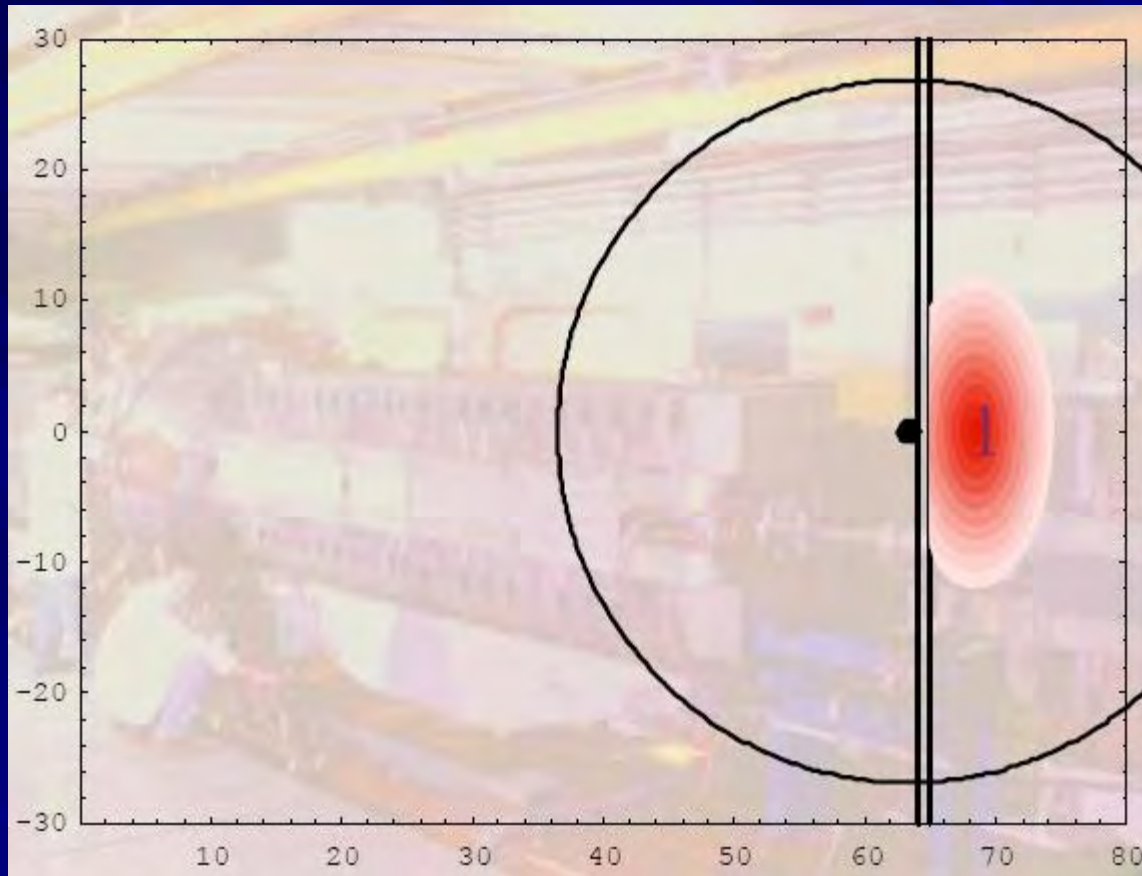
Peak to Peak Gap Voltage:  
40- 8000 V



# Injection in time

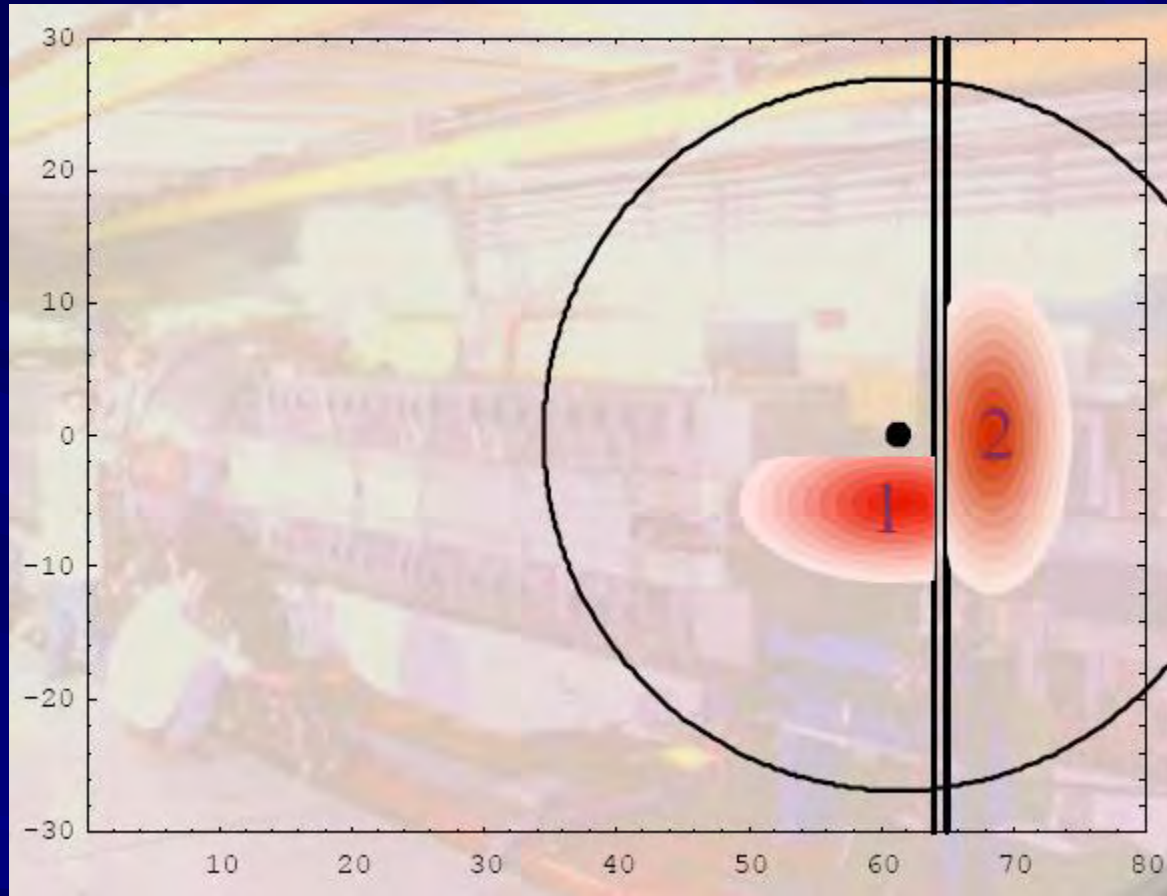


An animated view of injected beam emittance (courtesy of R. Steerenberg)



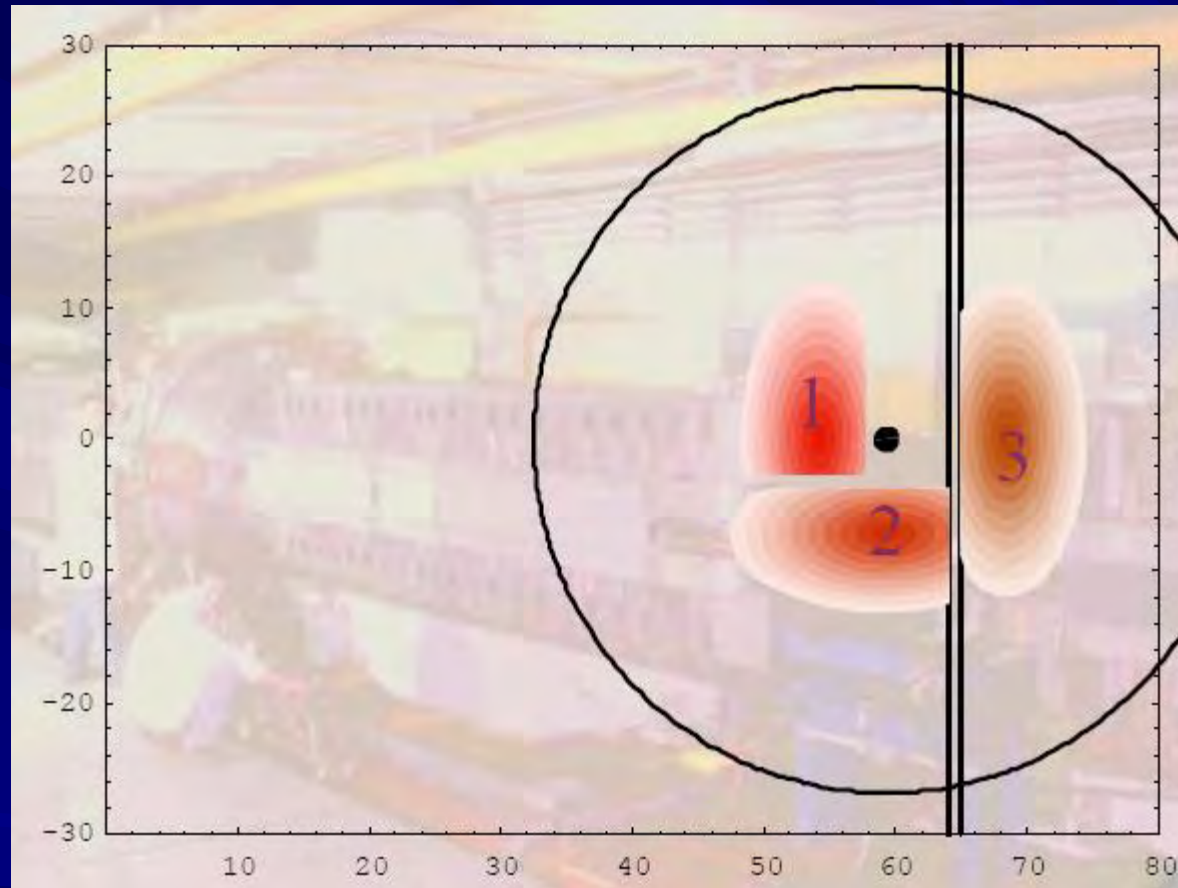
Multiturn injection with injection bumpers,  
creating the emittance for slow extraction process

# An animated view (courtesy of R. Steerenberg)

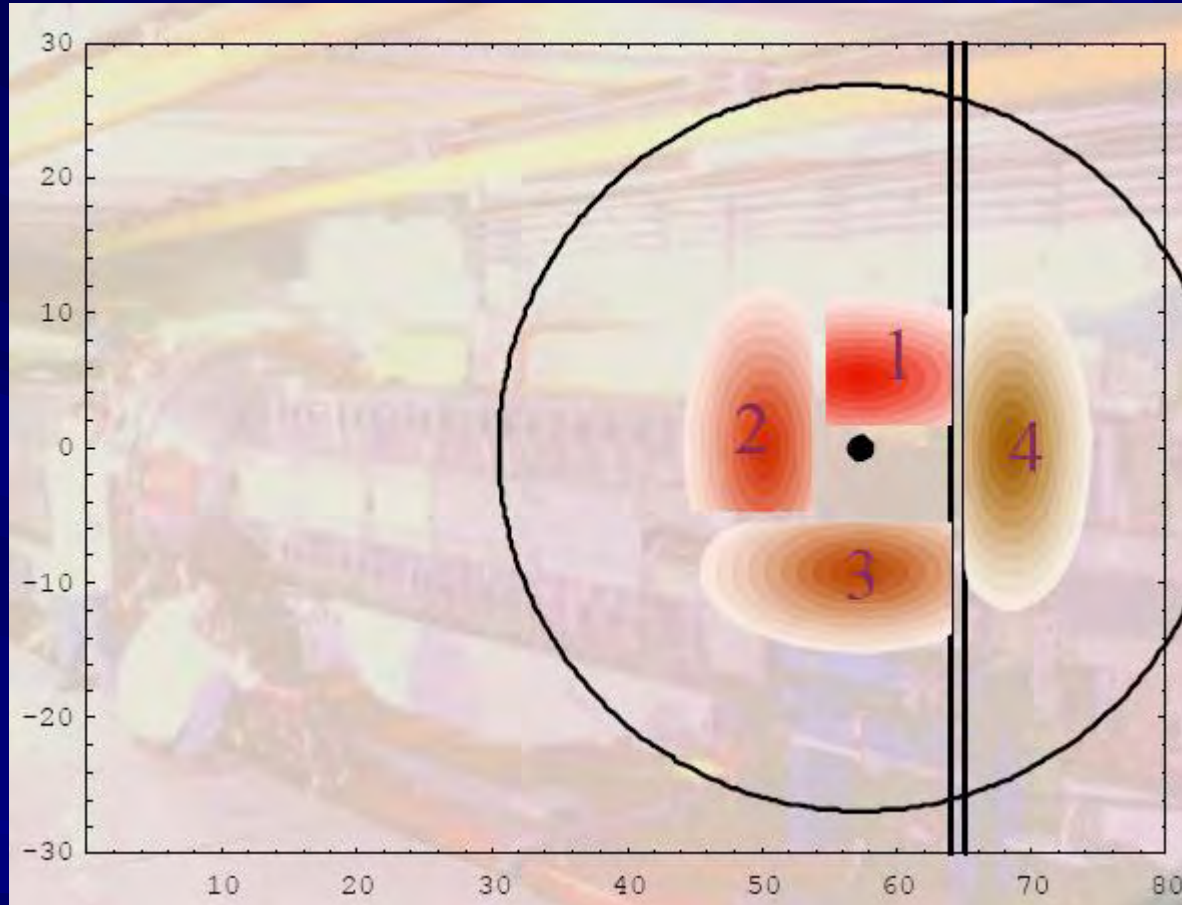




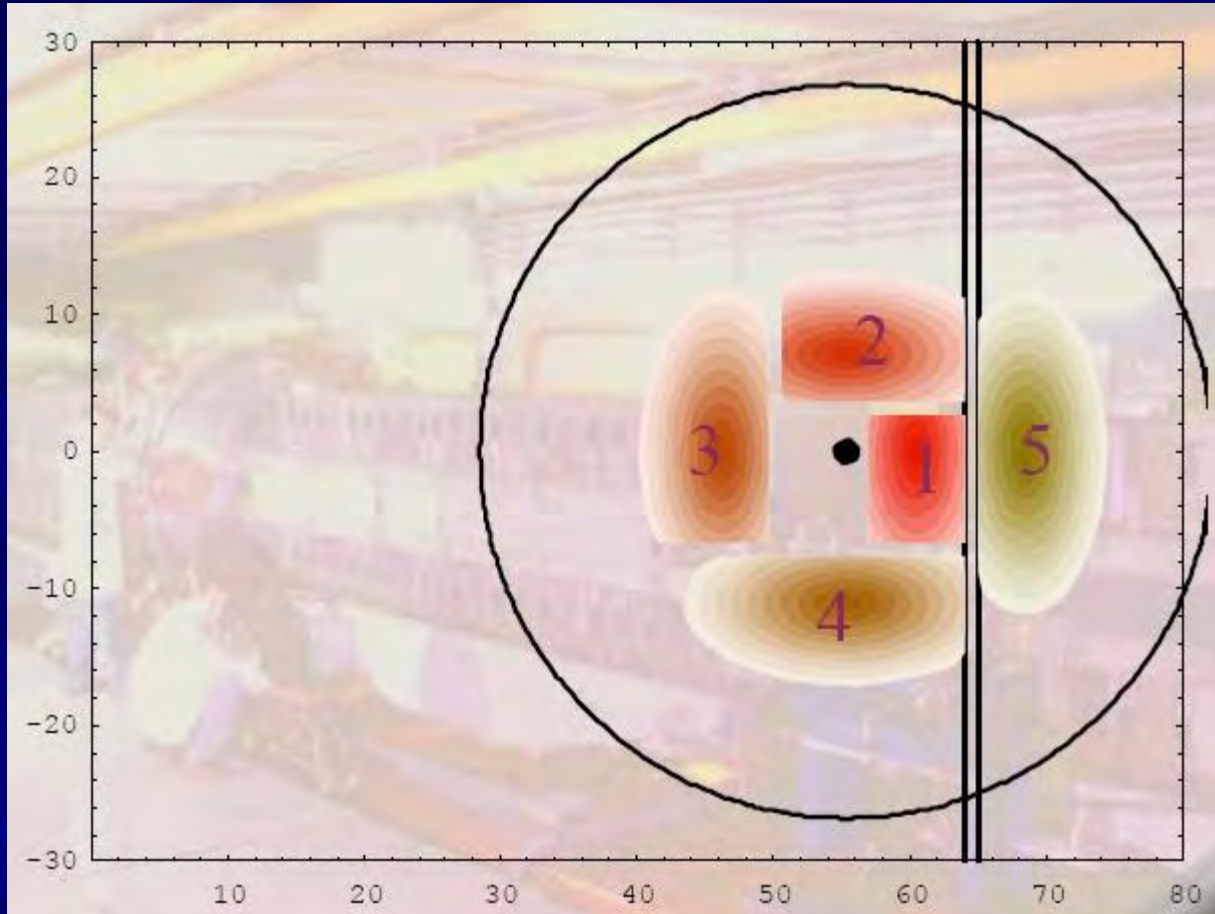
# An animated view (courtesy of R. Steerenberg)



# An animated view (courtesy of R. Steerenberg)



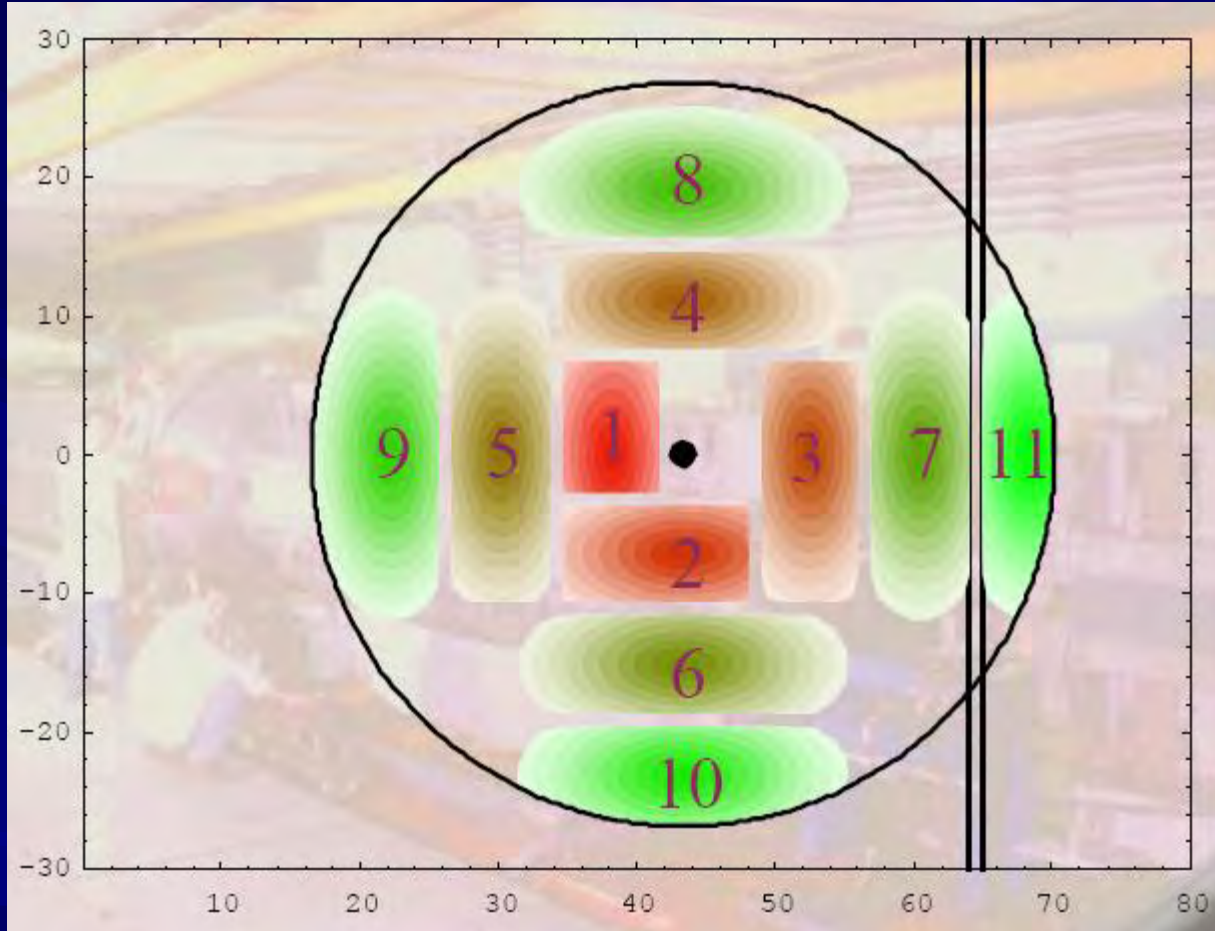
# An animated view (courtesy of R. Steerenberg)



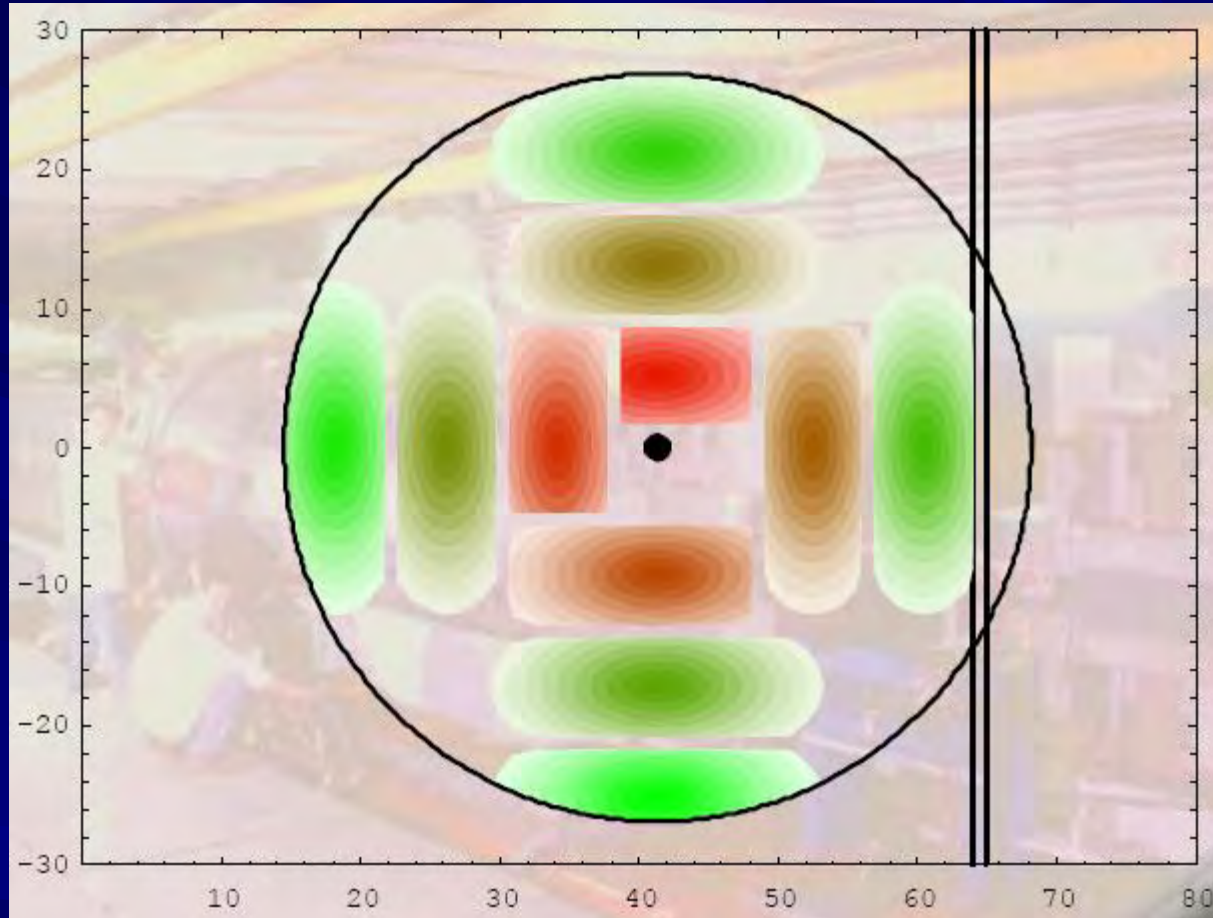




# An animated view (courtesy of R. Steerenberg)

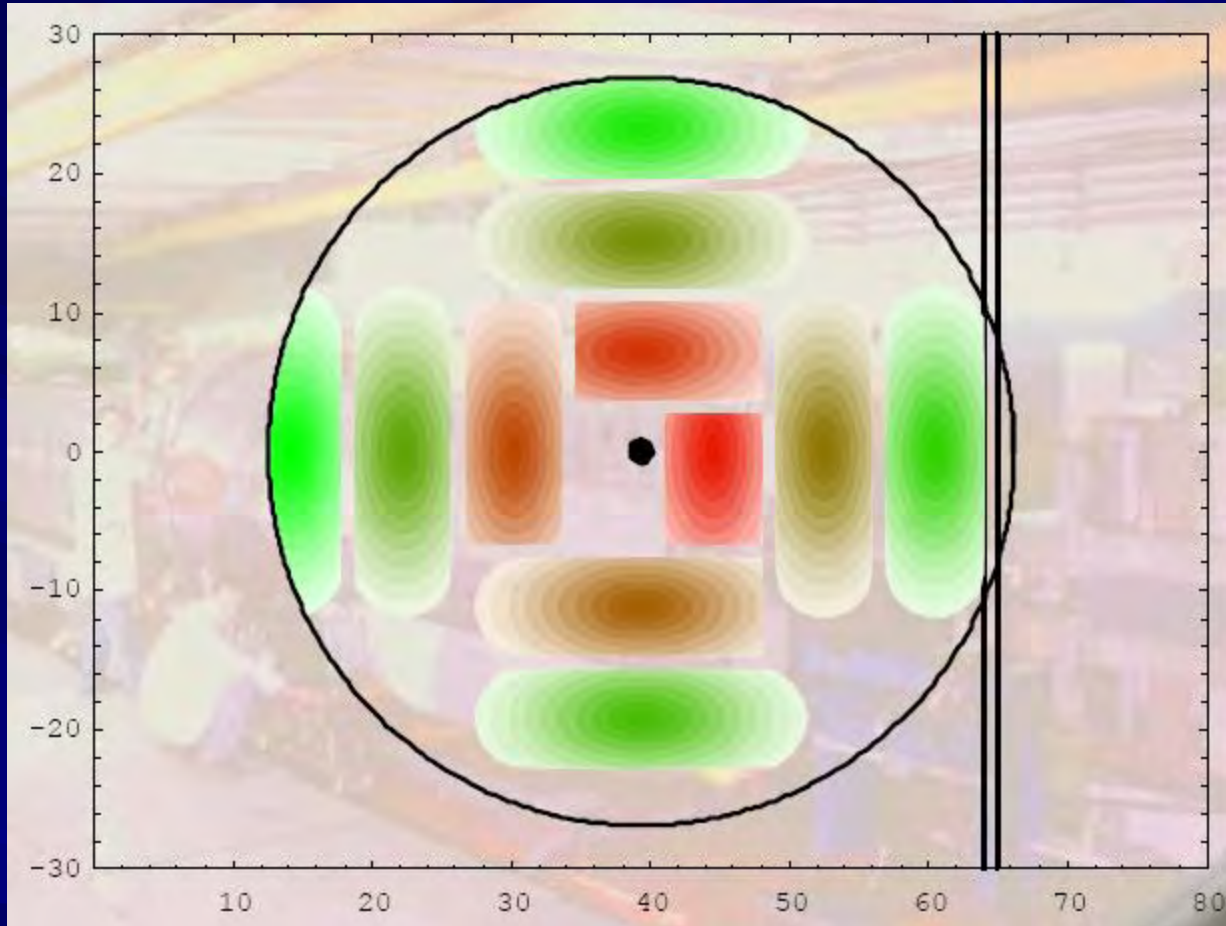


# An animated view (courtesy of R. Steerenberg)

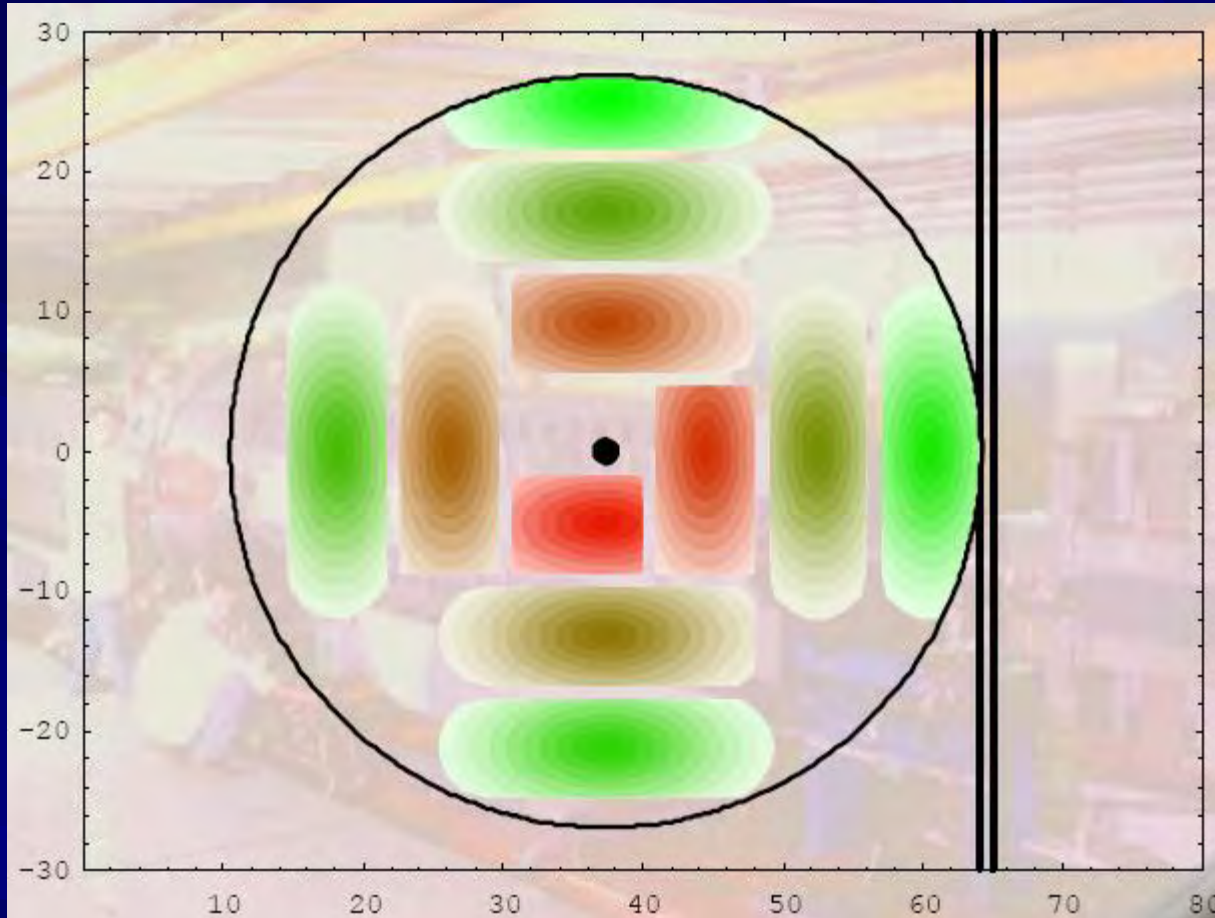




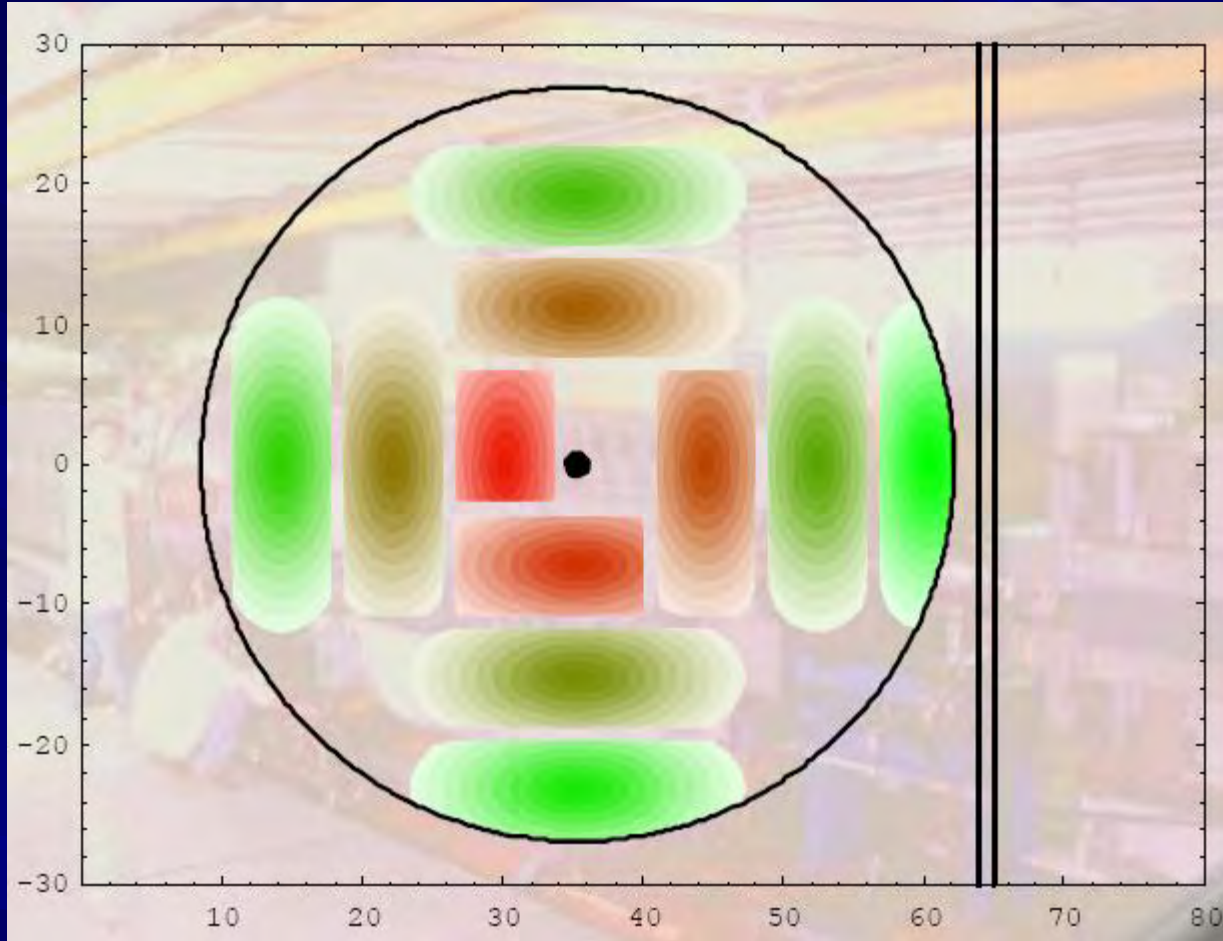
# An animated view (courtesy of R. Steerenberg)



# An animated view (courtesy of R. Steerenberg)

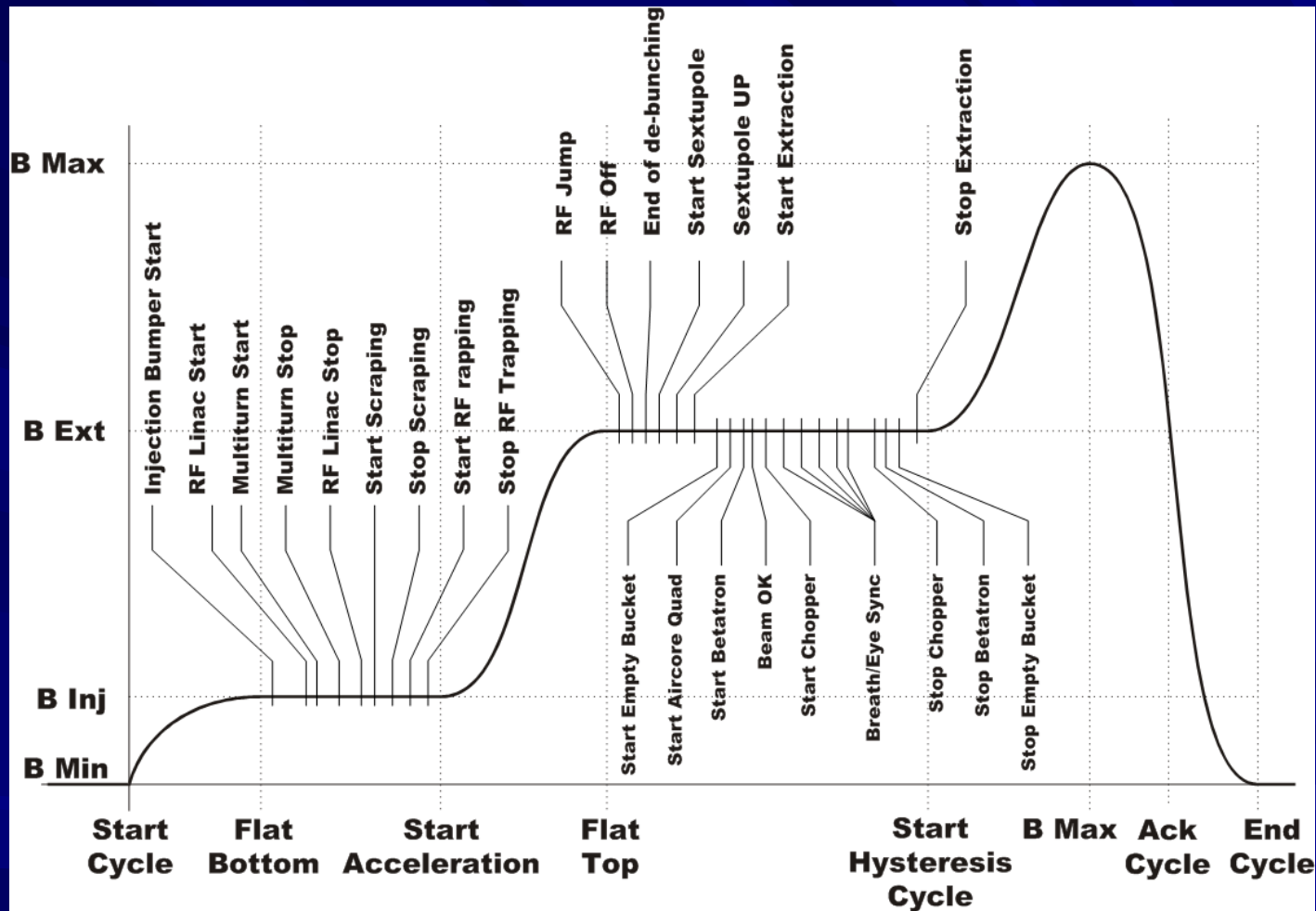


# An animated view (courtesy of R. Steerenberg)





# Machine cycle



2-3 sec

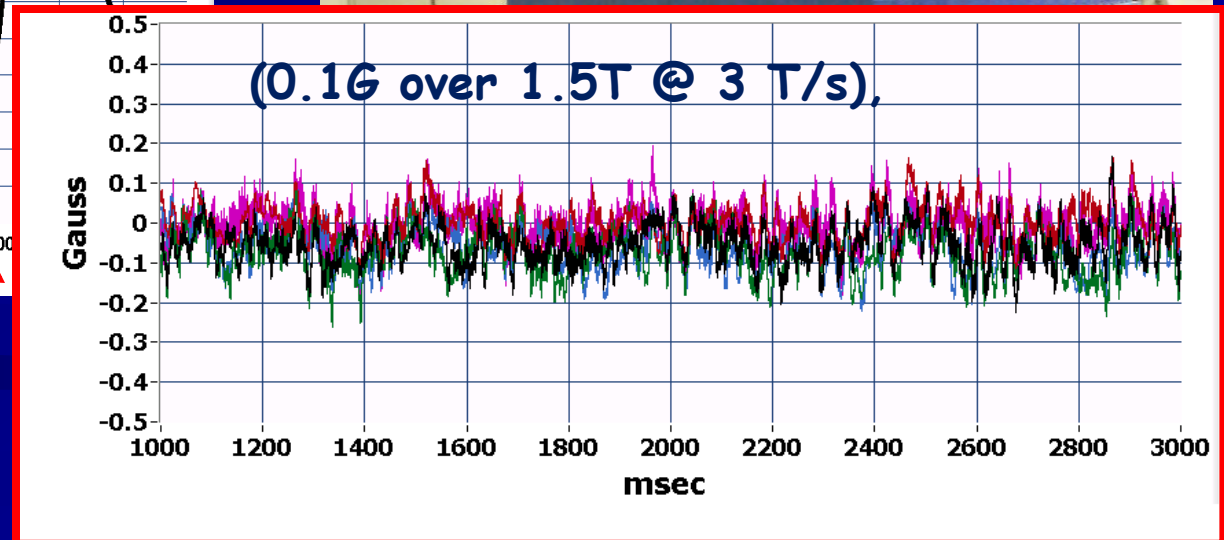
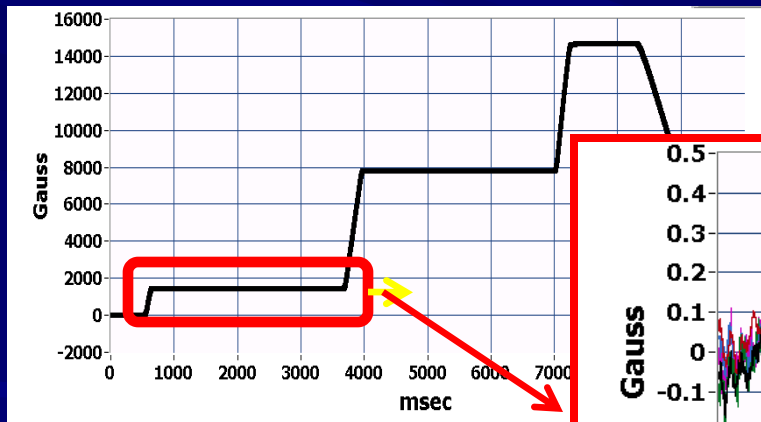
# B-TRAIN

High precision, Analog/Digital measurement system for dipole magnetic field.

RF, Dump Bumpers and Diagnostics systems use the real-time B-field measurements to track beam energy.

A feedback correction signal for the dipoles PS compensates for the transient response of the magnetic field.

The field is obtained by digitizing the voltage induced on a pick-up coil inserted in the gap of the dipole through a 18 bit, 1.25 Msamples/s ADC and integrating it by numerical methods

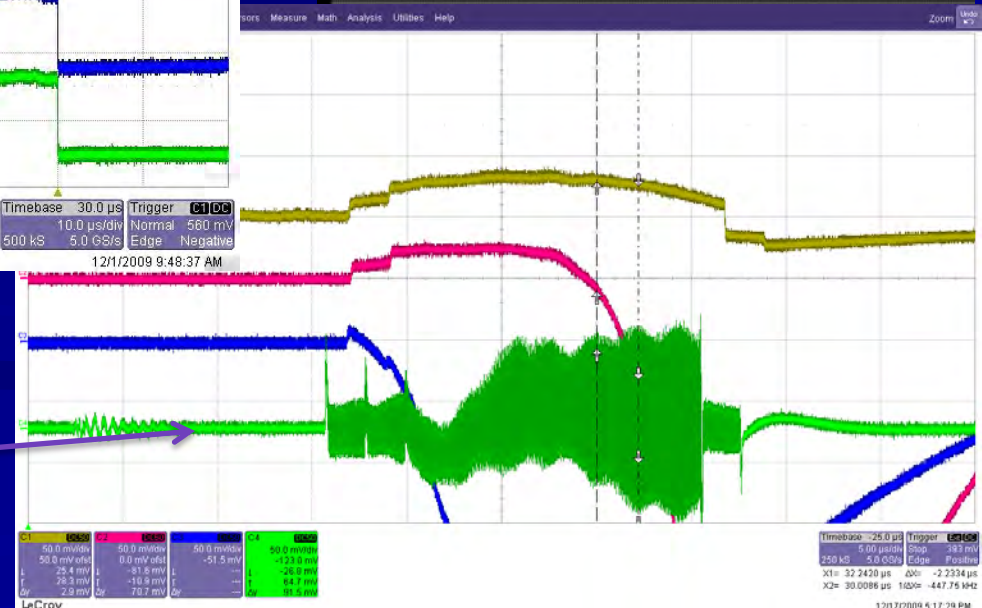
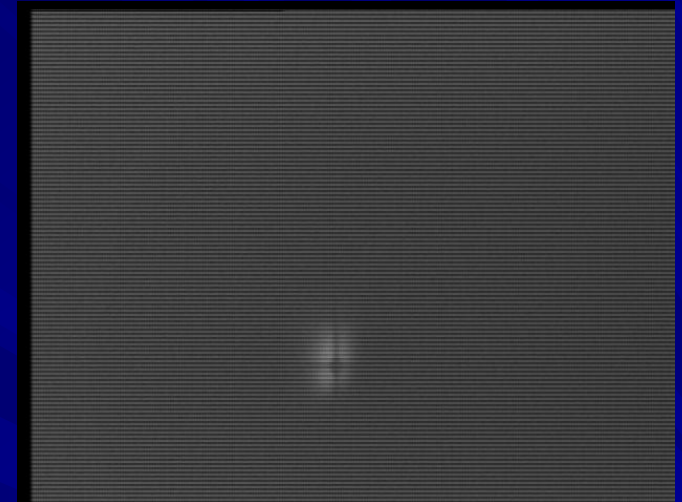
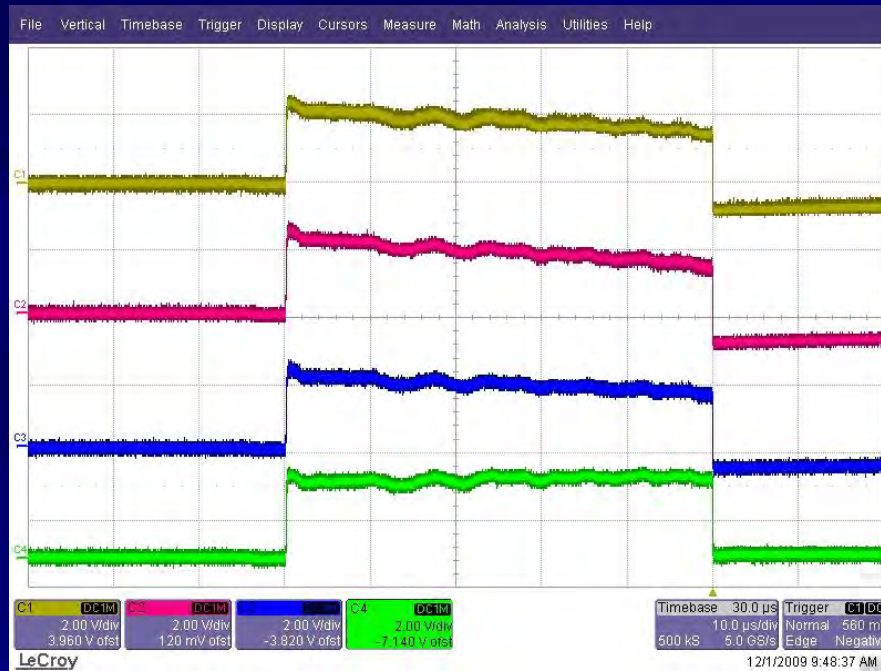


Measurements of typical magnetic cycles have confirmed that B-Train matches specifications

# First turn in the synchrotron (end 2009)

TV screen T45 → first turn

Few synchrotron steerers were turned on



RF cavity effects



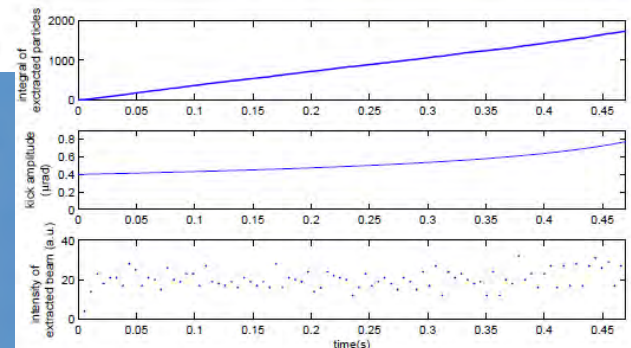
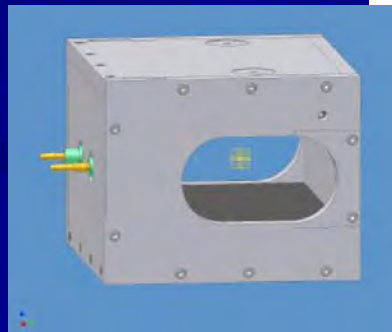
# Slow extraction on third order resonance

Use of a betatron core and resonance sextupole

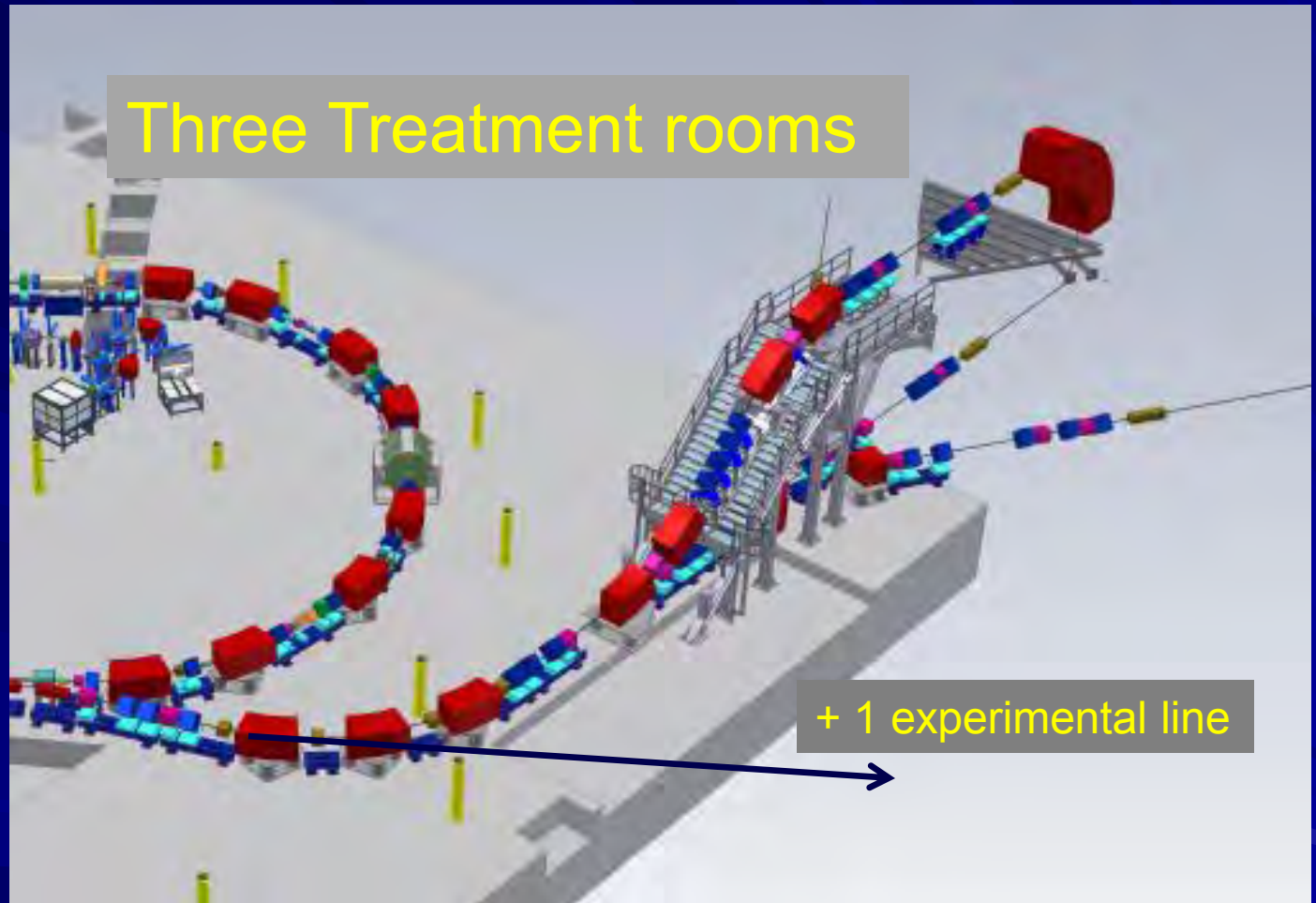
+ chopping system on the extraction line for rapid switch on-off



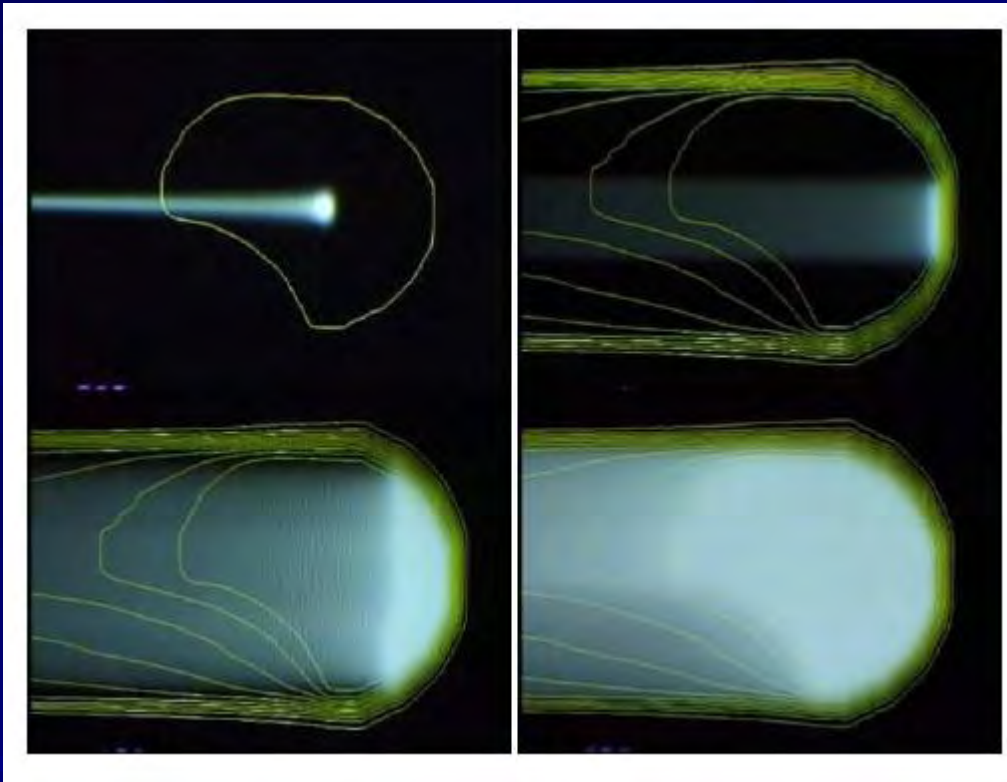
RF-knockout method  
foreseen as alternative method  
in the future



# HEBT



# Active scanning



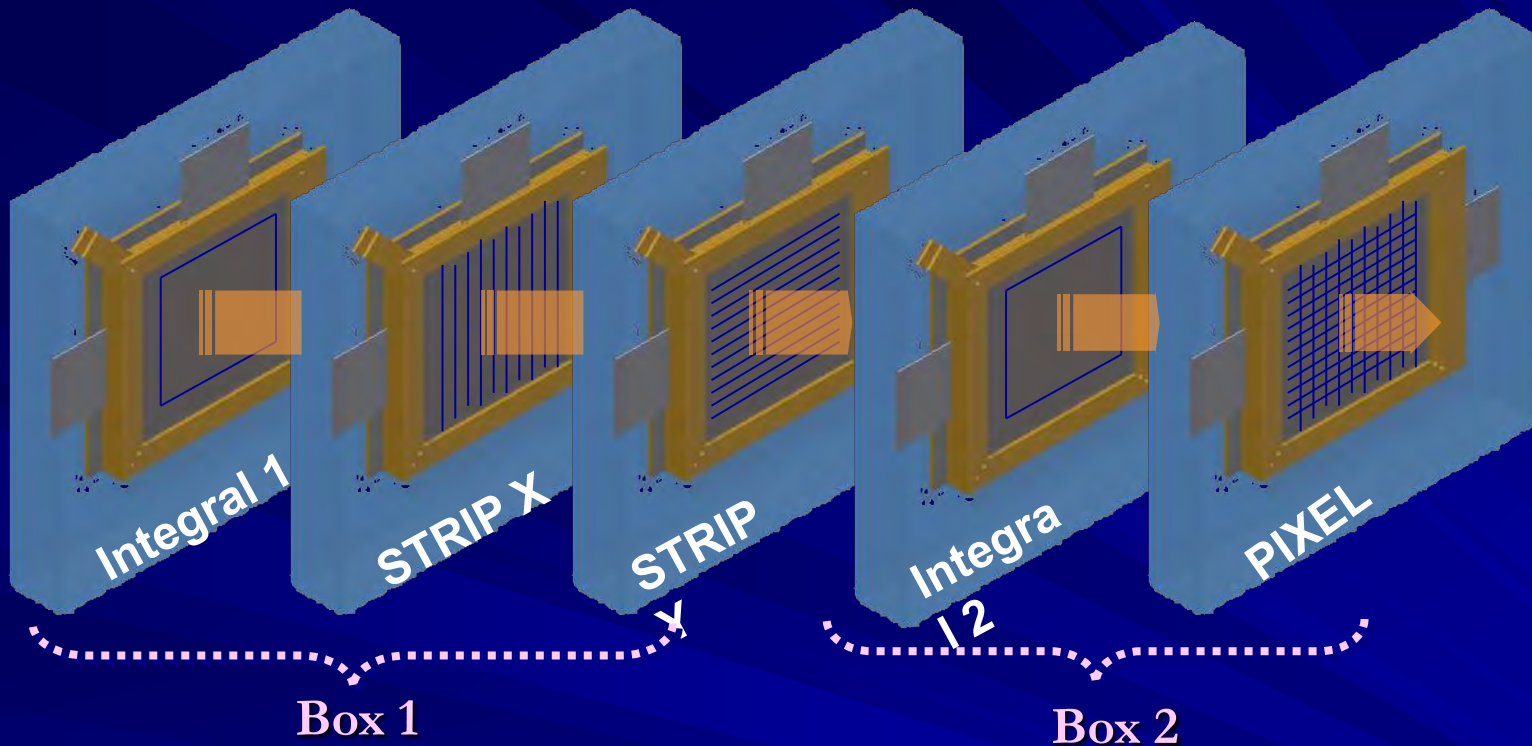
Precise medical imaging

- *intensity-modulated particle therapy*
- *treatment of arbitrary tumour shapes.*

To treat moving organs with active scanning, synchronization with breathing, repainting, tumour tracking and following, and active energy compensation methods are under development worldwide



# Beam delivery – scanning control



## 1 Integral chamber:

- Beam Intensity measure every  $1 \mu\text{s}$

## 2 Strip chambers (X and Y):

- Beam position measure every  $100 \mu\text{s}$ , with  $100 \mu\text{m}$  of precision

## 1 Integral chamber:

- Beam Intensity measure every  $1 \mu\text{s}$

## 1 Pixel chamber:

- Beam position and dimension measure every  $100 \mu\text{s}/1 \text{ ms}$ , with  $200 \mu\text{m}$  of precision

# Typical parameters for treatments

Spill characteristics

Energy range : 60-250 (p) 120-430 (C)

Field size : 200 x 200 mm x mm

Particles per spill :  $4 \cdot 10^{10}$  (p)  $10^9$  (C)

Dose uniformity : 2-3%

Beam positioning : 0.1 mm

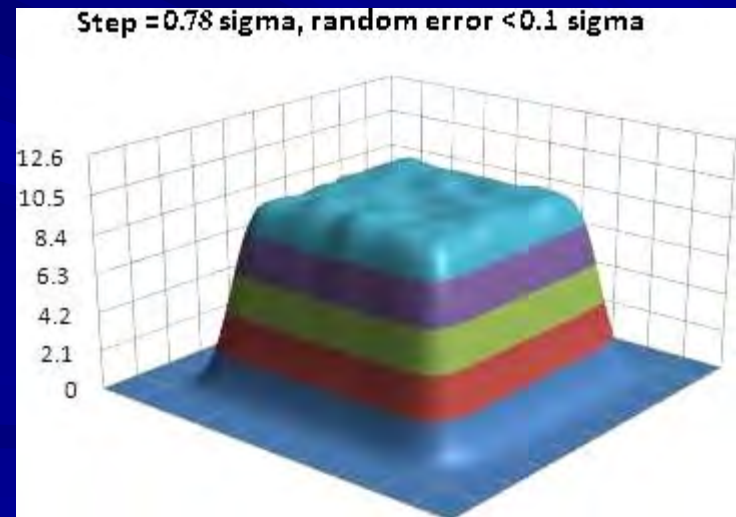
Typical treatment duration : 30 min

Typical dose delivering : 2-3 min

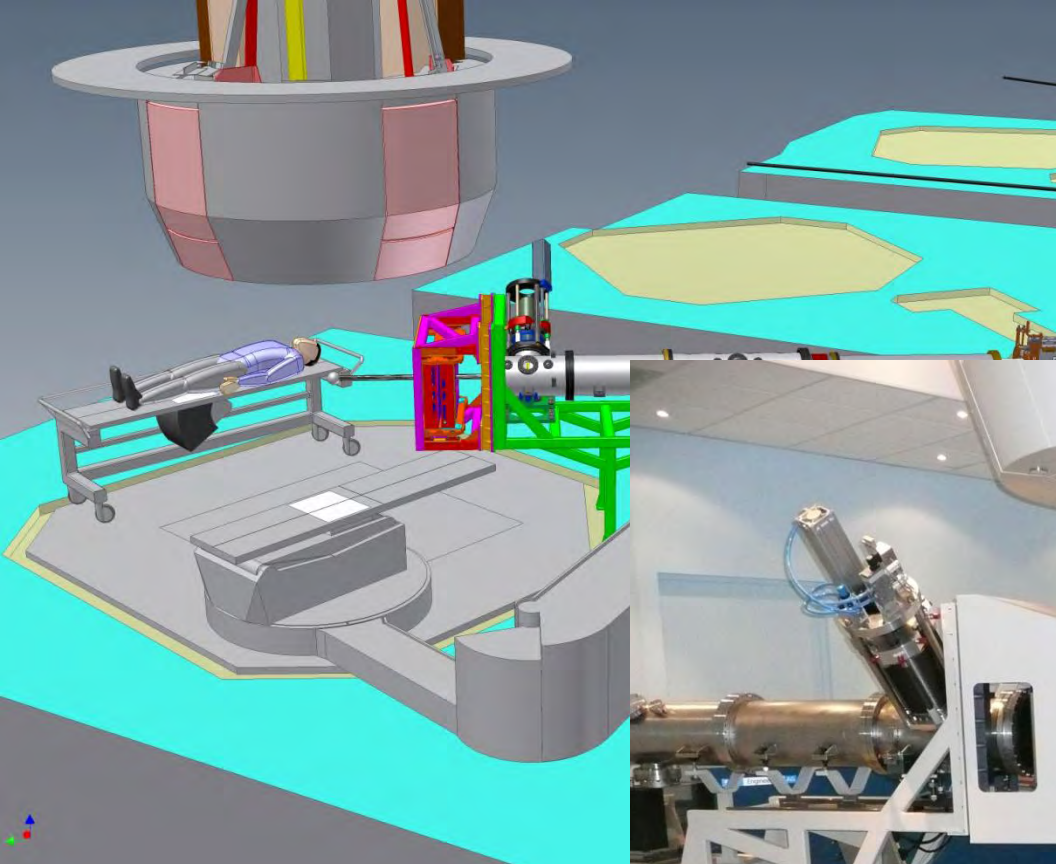
Typical Spill length : 1 sec

Spill length for voxel . 5-10 msec

A random position error of  $0.1\sigma$  in the position of the Gaussians yields a dose error  $> \pm 3\%$ .



# TREATMENT ROOMS



Medical tools under test in the treatment rooms



# Future upgrades

# ULICE

## Union of light-ion centres in Europe (ULICE), coordinated by CNAO

4-year project with 20 European organisations, and 2 European industrial partners for coordinating research and access to HT centers.

Full exploitation of all different resources, unrestricted spread of information and improvement of existing and upcoming facilities .

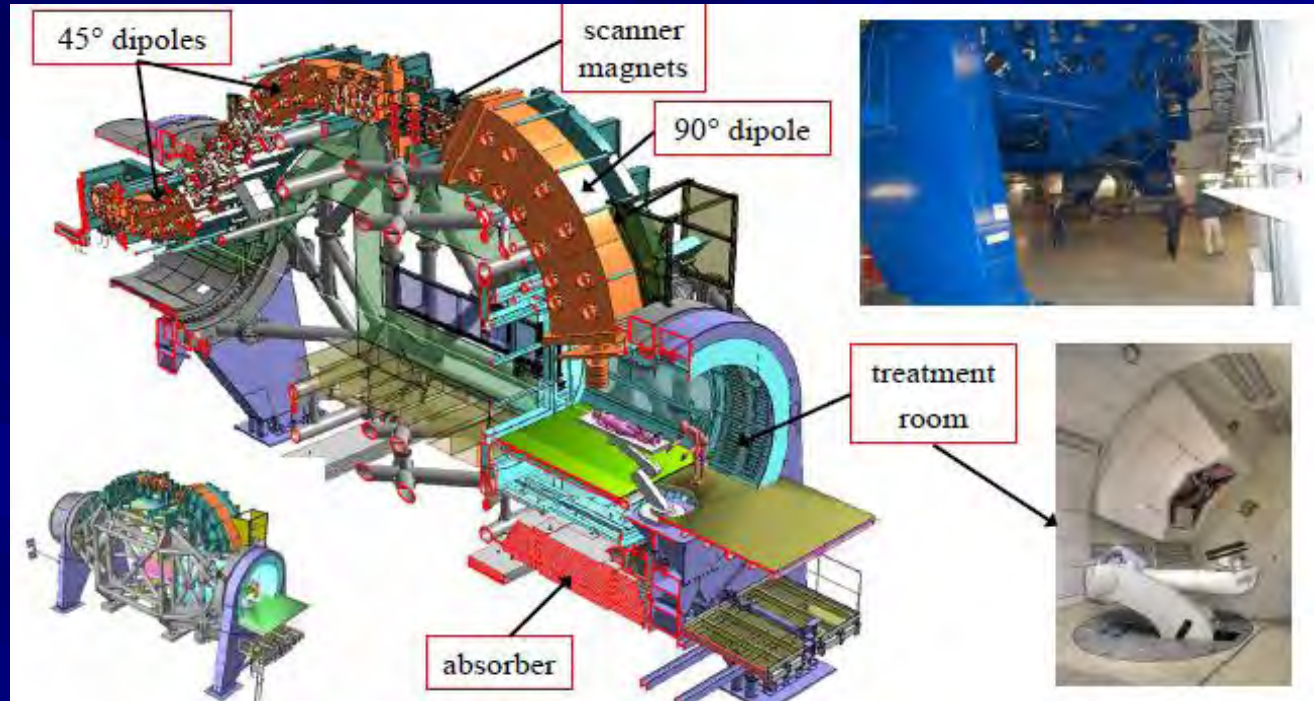
\* JRA - development of instruments and protocols: new **gantry design**, improvement of **four-dimensional particle beam delivery**, adaptive treatment planning, mechanisms for patient selection to the whole European Community and database development for specific tumours which can best be treated using carbon ion.

\* Networking - increasing cooperation between facilities and research communities wanting to work with the research infrastructure. Outputs will be (among others): a report on recommendations for strategically optimal locations for future RIs throughout Europe, training to new users.

\* Transnational access: 2-step approach, using a combination of pre-defined (within ULICE) clinical trial programmes to allow researchers with patients to visit the facility, and radiobiological and physics experiments to take place.

# Carbon ion gantry

Only one gantry worldwide:  $L = 25 \text{ m} \times \phi = 13 \text{ m}$ , 600 t



U. Weinrich, GSI

Fixed Isocenter  
360° rotation  
Parallel scanning  
200 mm x 200 mm  
140 t magnets  
120 t shielding-counterweight  
600 t total rotating mass

It has everything, but it is

Very large, very heavy,  
very expensive



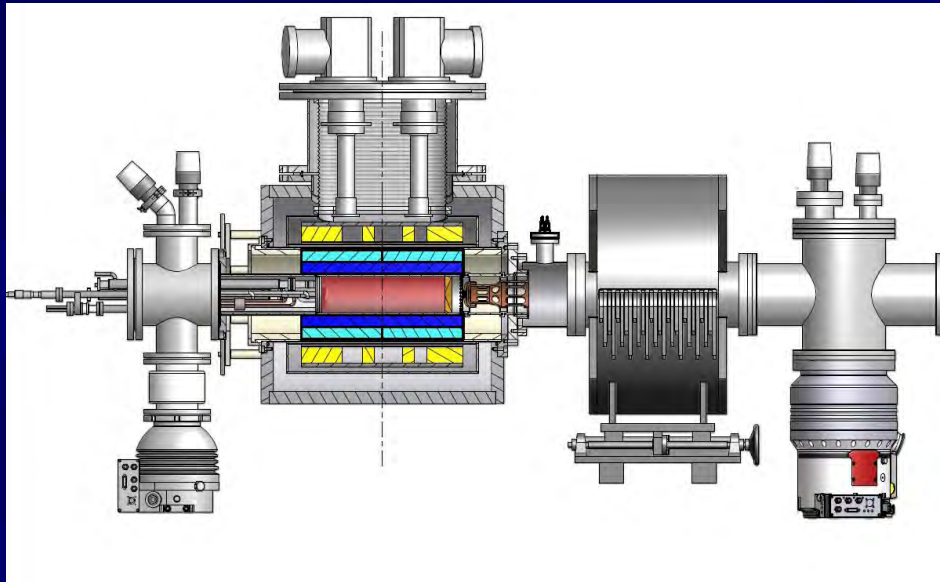
# Aspects being considered in new Gantry design

- Scanning
- Scanning magnets position
- 360° vs 180°
- Field patching
- Fixed or mobile isocenter
- Multi-room system
- Divergent scanning
- Superconducting magnets
- FFAG gantry

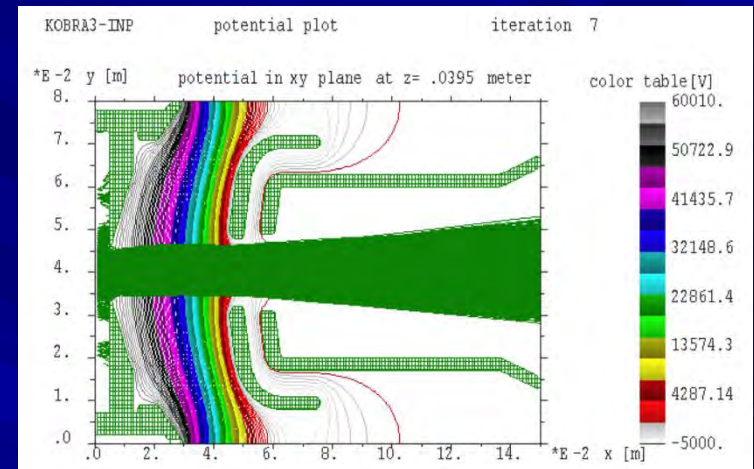
# MISHA: Multicharged Ion Source for Hadrontherapy

## 2.5 generation

Sources for Hadrontherapy;  
Need of reliability, stability, reproducibility  
easy optimisation and maintenance



Higher currents  
Lower emittances  
Optimised for multispecies



Hybrid ECR:

Permanent magnet sextupole

SC solenoids (cryocooler)

Rf Frequency : 18 GHz + 71.6 GHz

Max rf power : 500W + 500 W

Rf voltage : 50 kV max, 40 kV ope.

Total dimensions: 0.6 m

Ion trajectories  
(KOBRA simulations)

**CDR ready**

G. Ciavola et al.

## **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:**

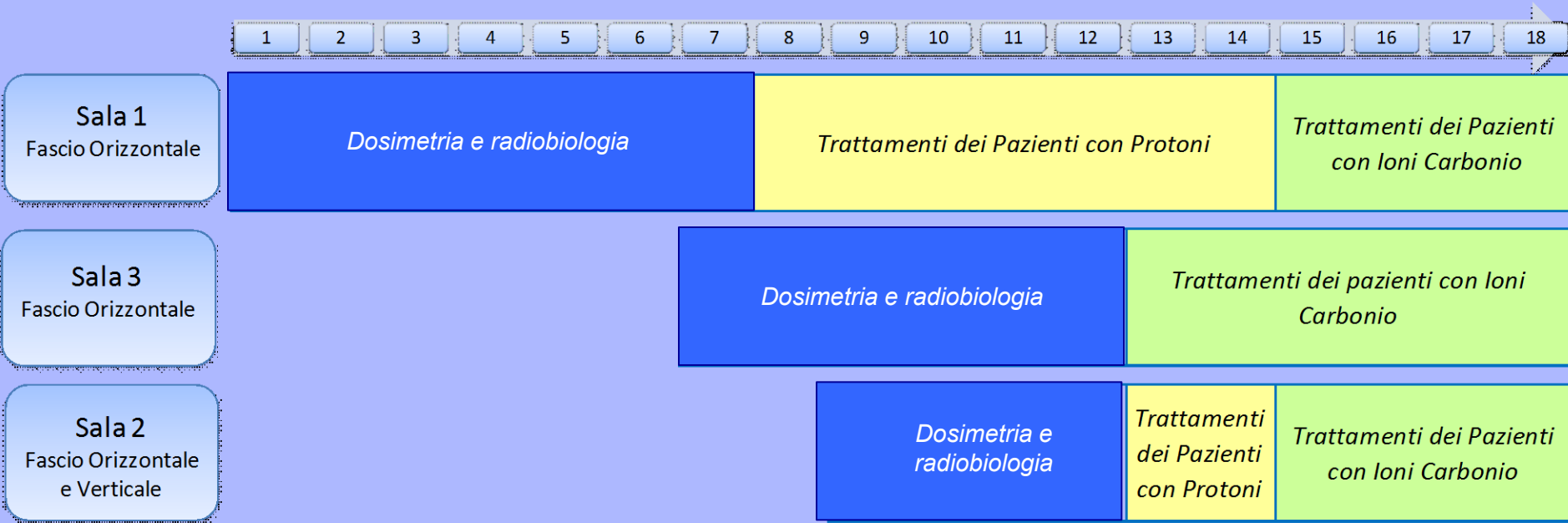
- Ministry of Health
- Region Lombardy

**Main Tasks:**

- Dosimetry characterisation
- Radiobiology characterisation
- Patient treatments



# Programme of Clinical Experimentation



Duration: 18 months

Total number of patients: 230 (80 protons and 150 carbon ions)

Cost evaluation in view of hadrontherapy fees definition

# The running phase

The treatments will be performed in the frame of the National Health System

A network will connect CNAO to the national health system

The network will guarantee the efficient recruitment of the patients on a national basis

During routine operation at CNAO, in three treatment rooms, 20'000 sessions per year will be delivered, corresponding to a maximum number of about 3000/3500 patients per year

# Conclusions

The Italian carbon and proton therapy project will come into operation in the next future:

- CNAO construction and installation completed
- CNAO commissioning on going
- Experimental phase since 2011
- Running phase since 2012