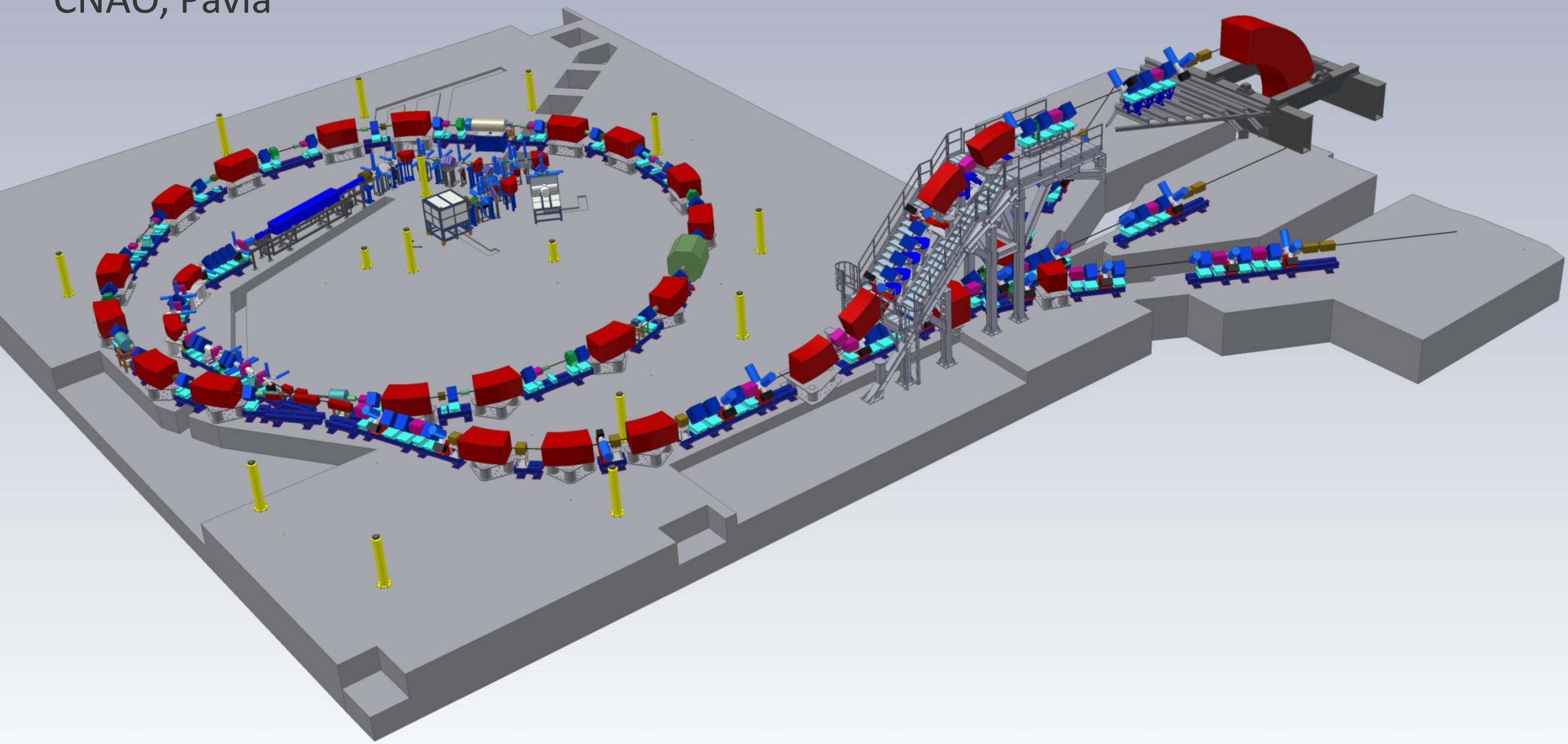
CNAO, the Italian Hadrontherapy Project

Caterina Biscari

on behalf of the *CNAO team*

LNF-INFN, Frascati
CNAO, Pavia



fondazione CNAO

7 June 2010 – PSI

CNAO team

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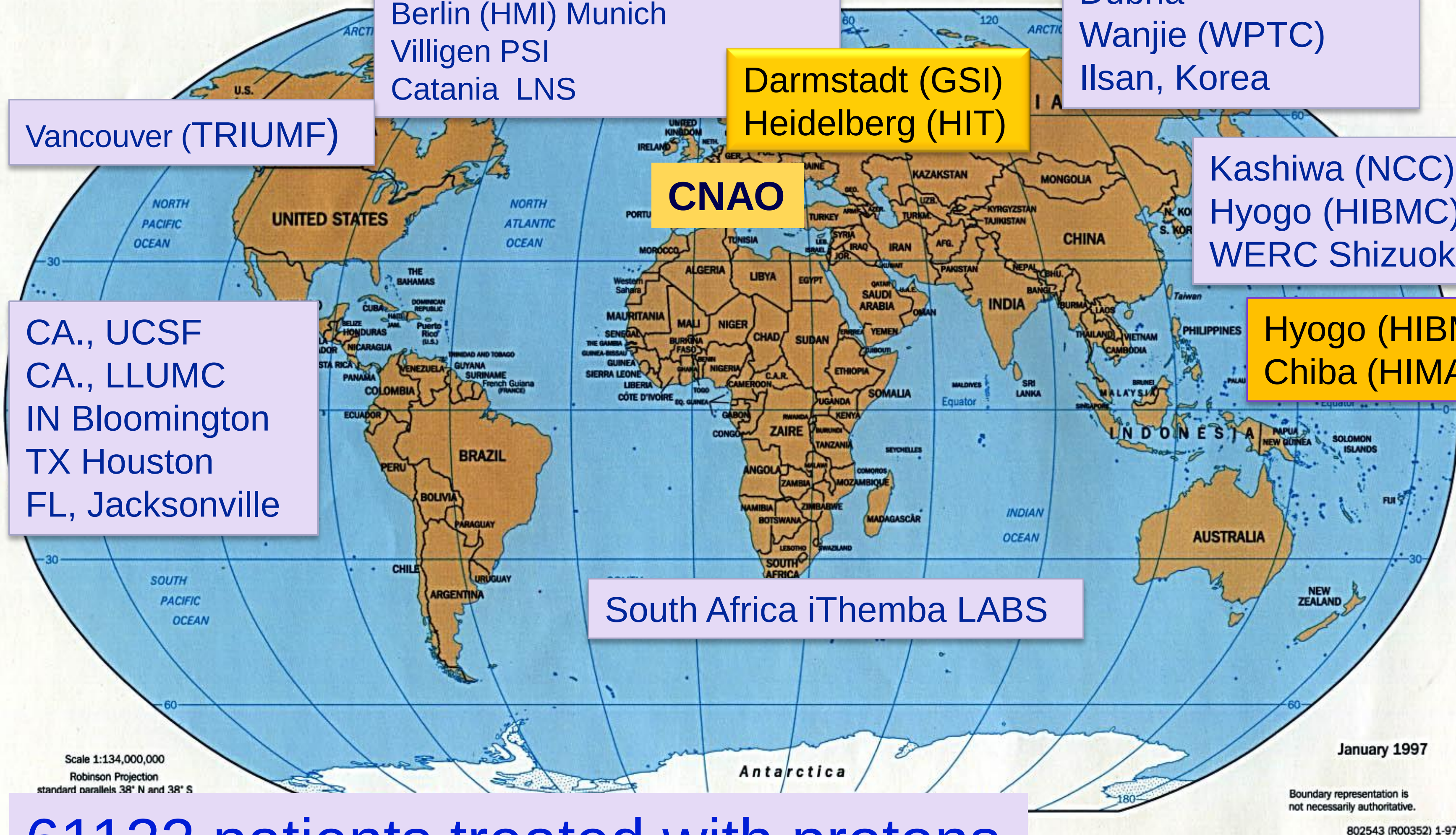
Not exhaustive list

Hadrontherapy in the world



Vancouver (TRIUMF)

Clatterbridge, Uppsala
Nice (CAL) , Orsay (CPO)
Berlin (HMI) Munich
Villigen PSI
Catania LNS

Darmstadt (GSI)
Heidelberg (HIT)

CNAO

Moscow
St. Petersburg
Dubna
Wanjie (WPTC)
Ilsan, Korea

Kashiwa (NCC)
Hyogo (HIBMC)
WERC Shizuoka

Hyogo (HIBMC)
Chiba (HIMAC)

CA., UCSF
CA., LLUMC
IN Bloomington
TX Houston
FL, Jacksonville

South Africa iThemba LABS

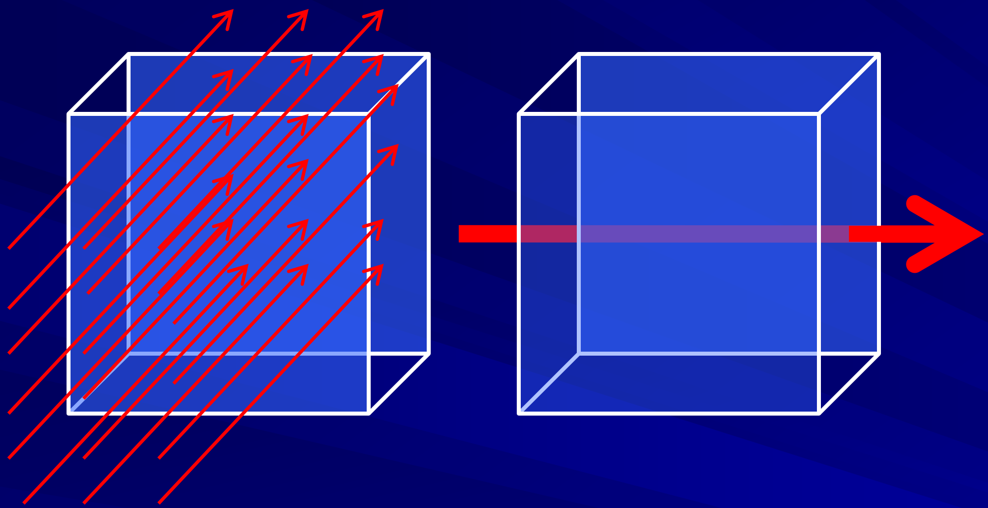
61122 patients treated with protons

5342 with carbon ions

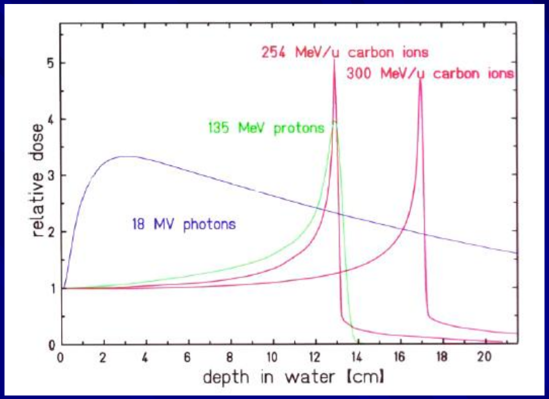
02 March 2009, PTCOG

Why carbon ions?

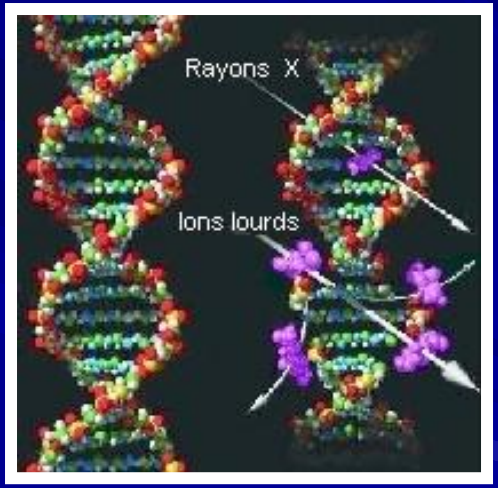
Hadrontherapy biological basis



Low LET   High LET



Energy deposition in matter

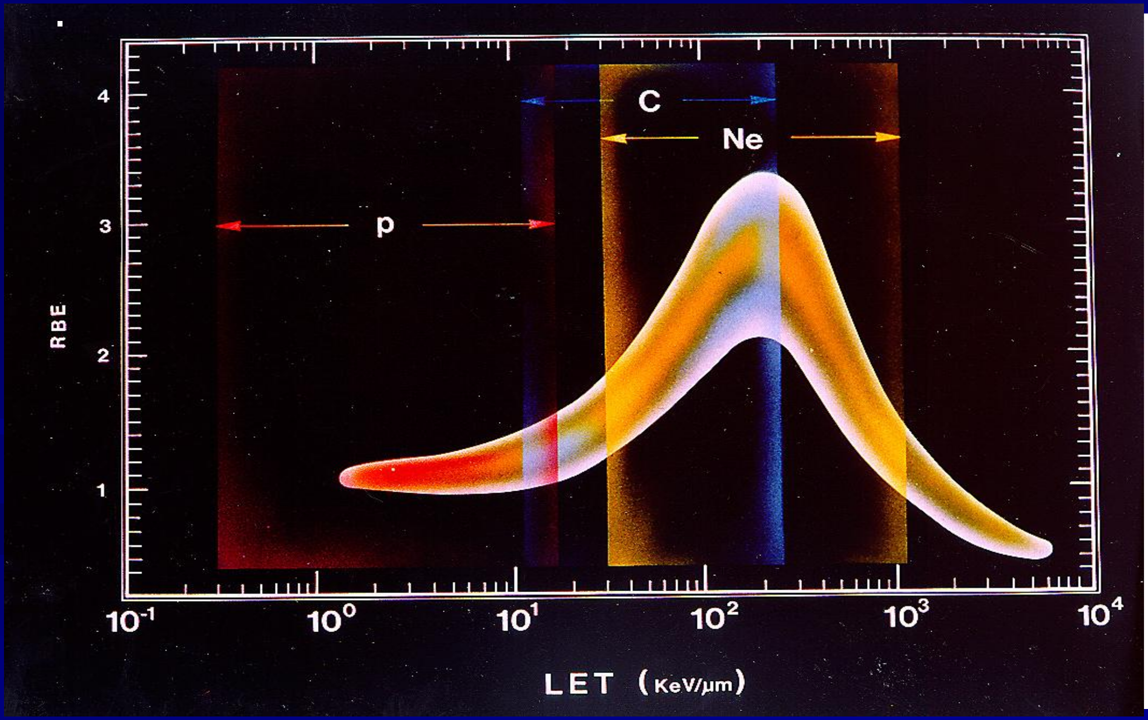


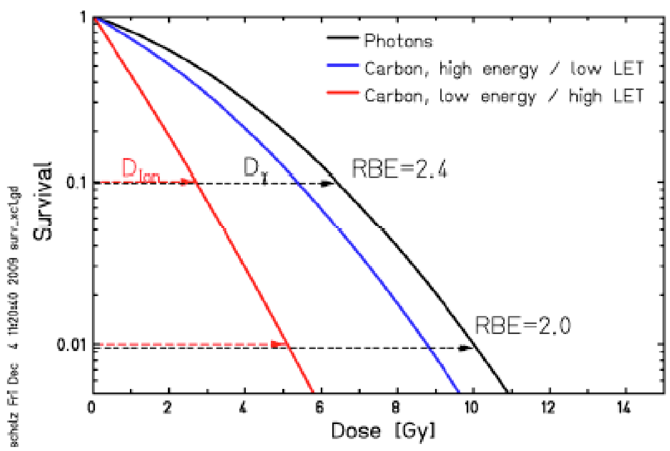
D = distance between ionizations

Low **LET**	**<20 keV/µm**	**D > DNA diameter**
High **LET**	**> 50 keV/µm**	**D < DNA diameter**
Very HIgh LET	**>1000 keV/µm**	**D < DNA diameter + excess Energy**

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.

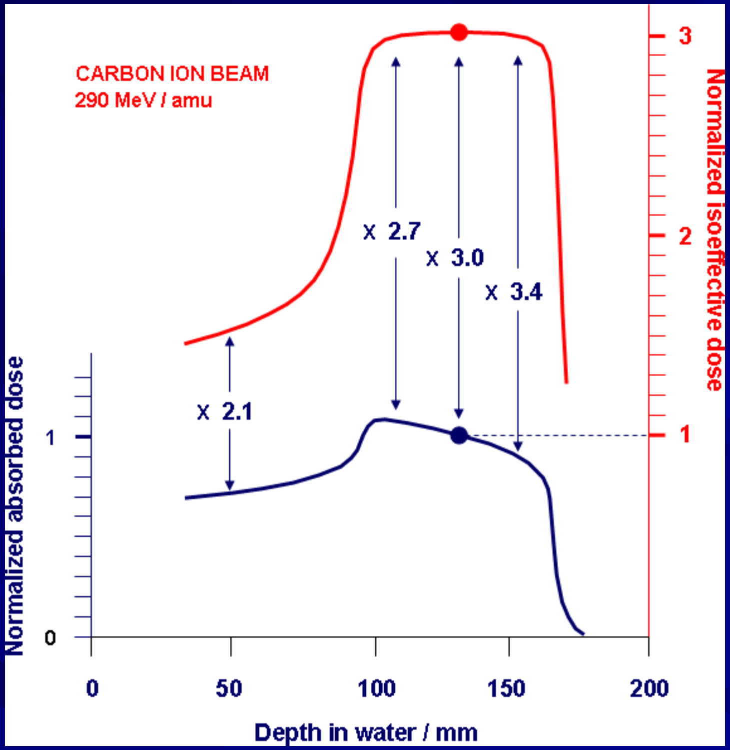




The survival curve for the target cells for late injury is "curvier" than that for acute effects

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

physical dose distribution necessary for obtaining a flat biological dose



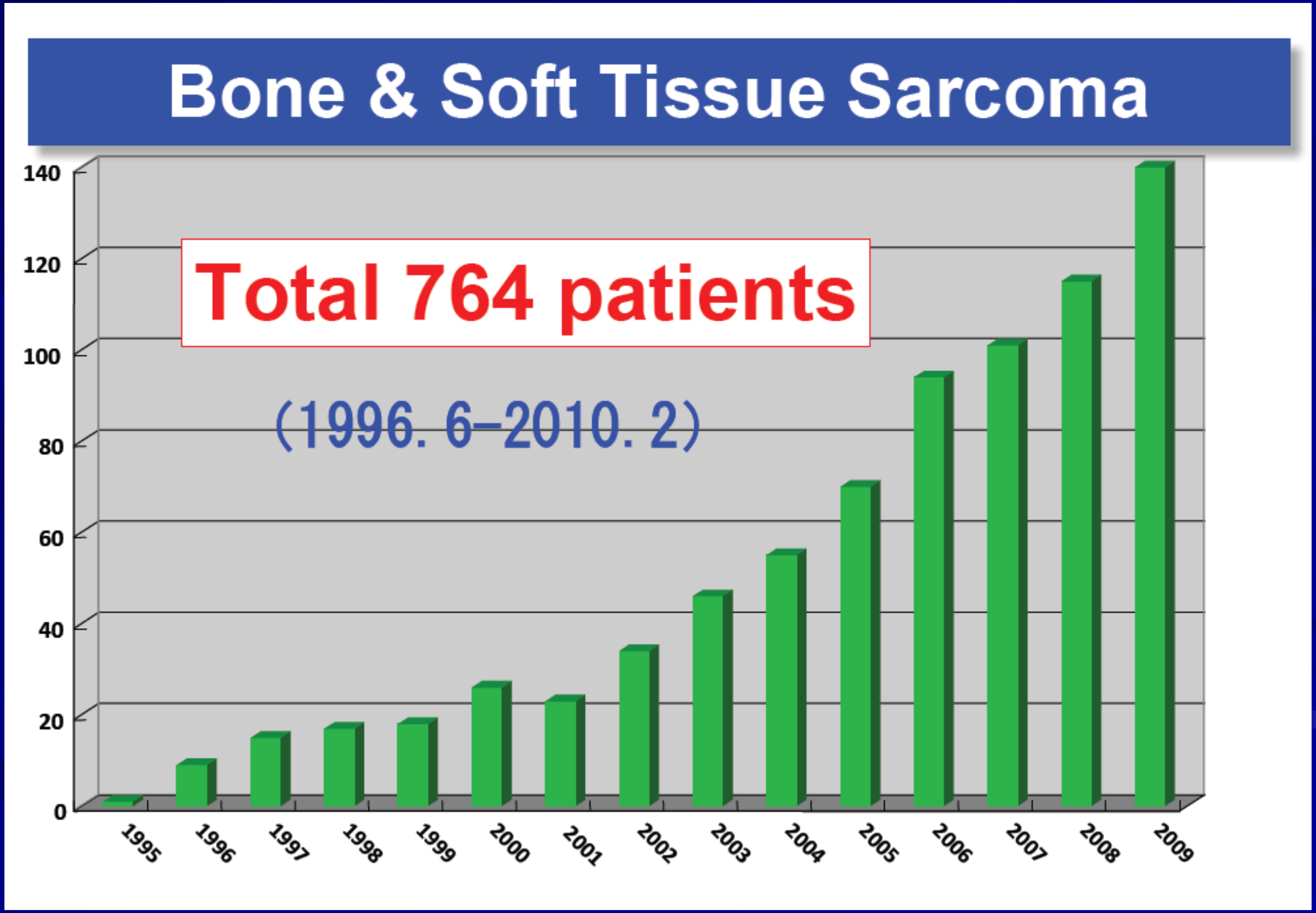
Other parameters: cell type, blood perfusion, oxigenation
Hipoxic tumours resistant to photons and protons
Carbons drawback : dose deposition after Bragg peak -
Protons drawback : lateral diffraction

CLINICAL comparison between different methods

Statistics

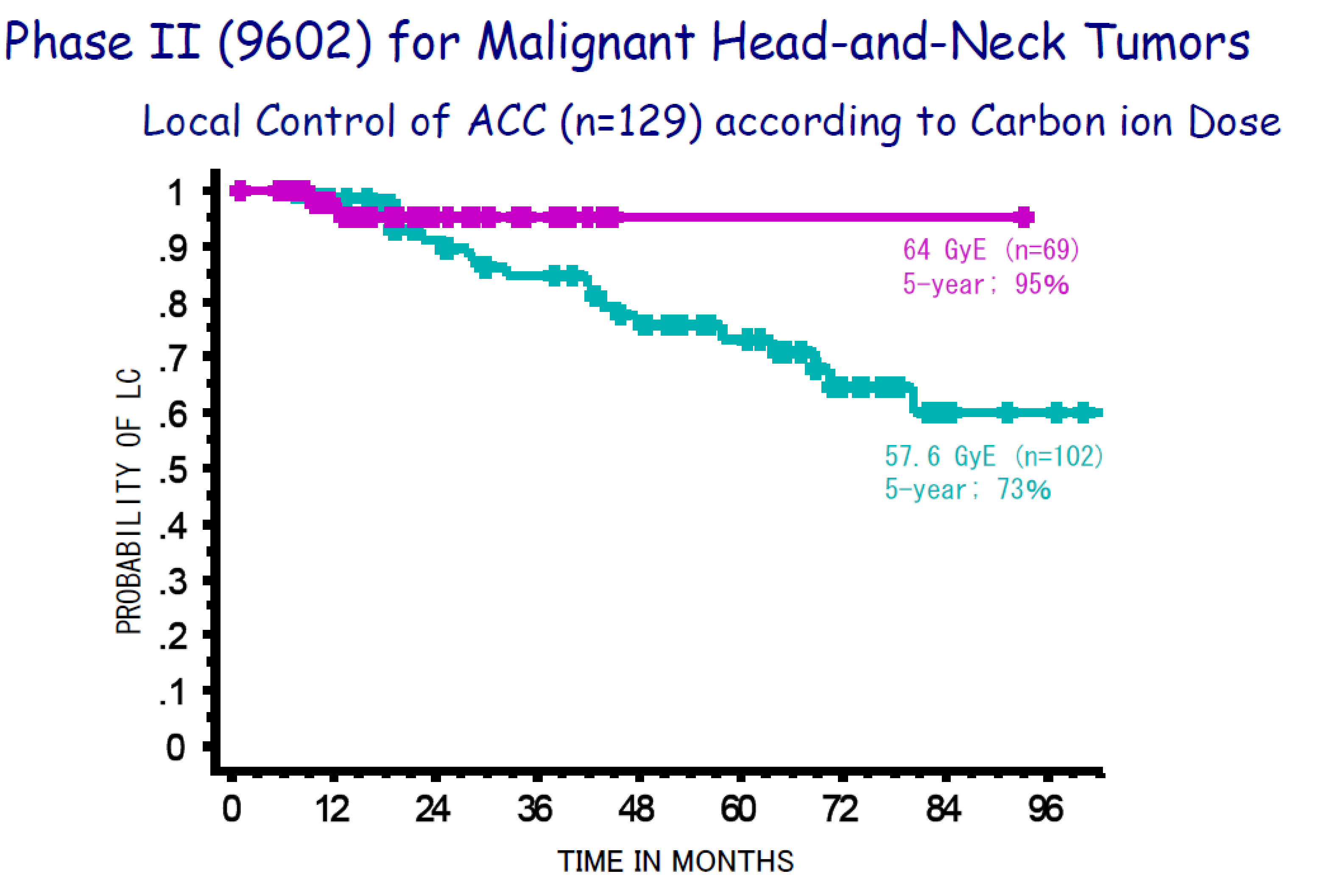
'Few' Carbon treated patients –> Experimental phase

Example :



Time

Analisis of results - example



Tracking patients and exhanging data within different institutions

Morbidities after Carbon Ion Therapy (2000.4～2008.2)

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

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:

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

NIRS

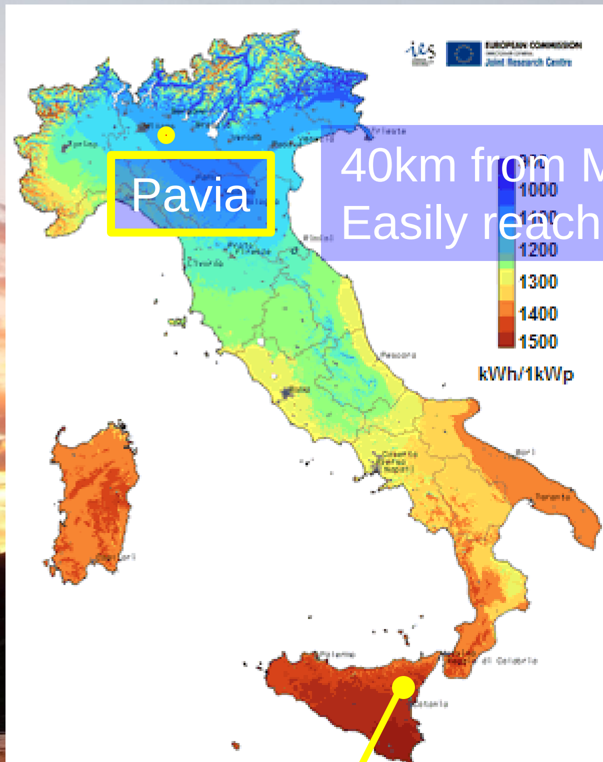
NIRS
HIMAC

New Treatment Facility Project at HIMAC

Koji Noda
Research Center for Charged Particle Therapy
National Institute of Radiological Sciences

2nd NIRS-CNAO Sympo., Pavia, Italy, 21st March, 2010

CNAO in Pavia



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

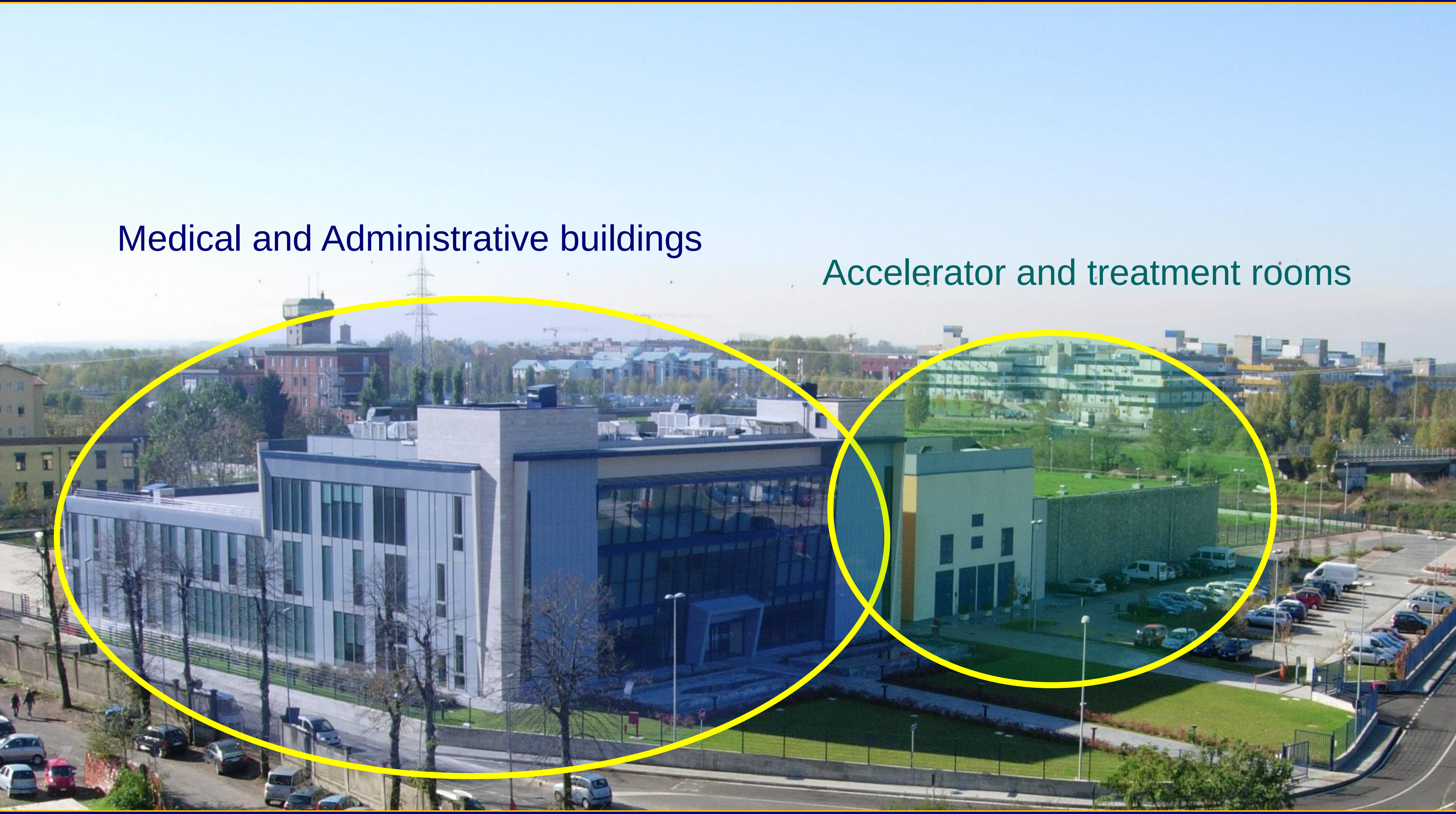
Phase 3: start-up → Years: 2012 - 2013

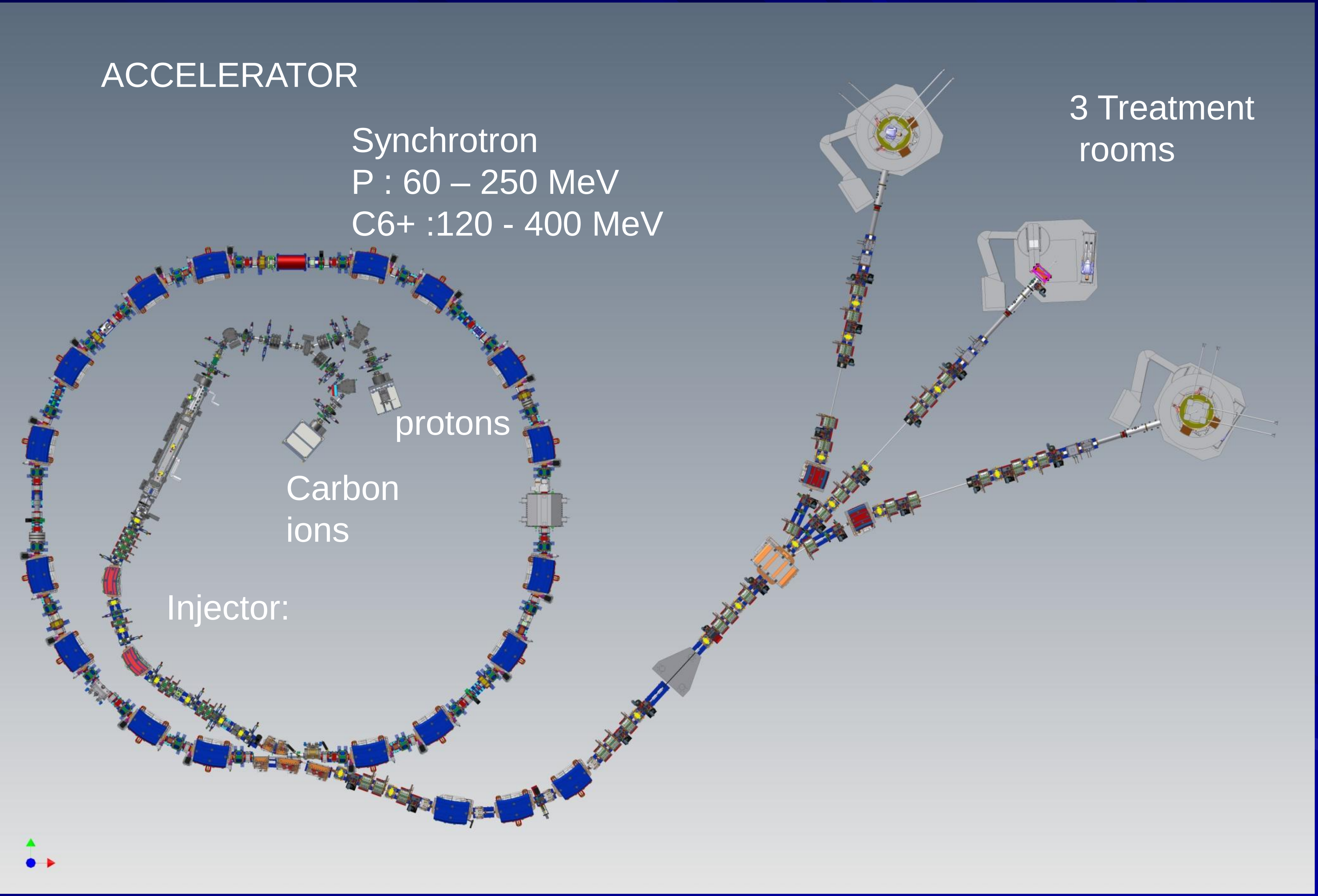
CNAO SCHEDULE

today

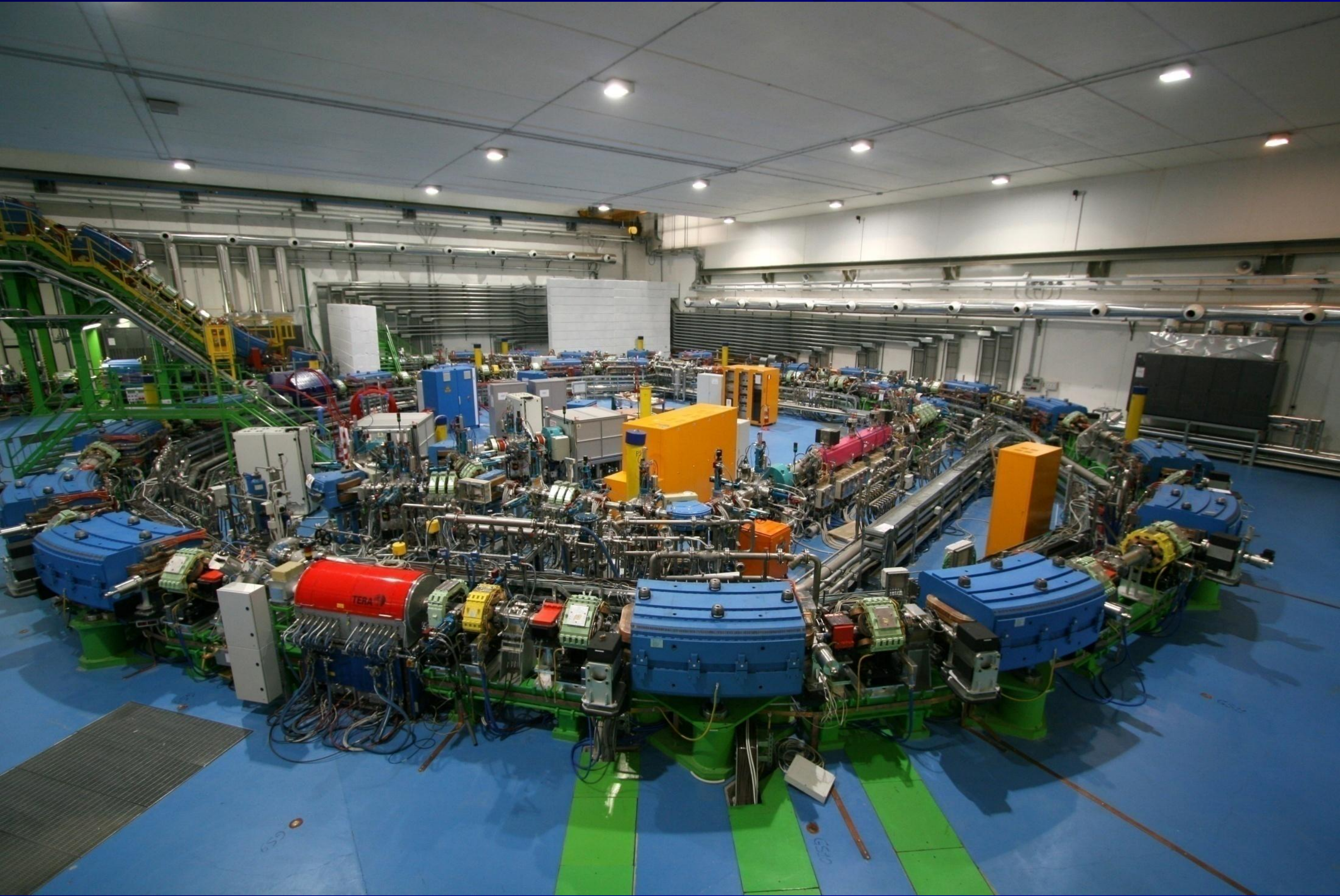
year	05		06		07		08		09		10		11		12
CONSTRUCTION															
	New site: no existing infrastructures														
INSTALLATION															
~ %					90	85	80	70	70	40	20	10			
SYSTEM TESTS															
~ %						10	10	20	20	50	75	10			
BEAM COMMISSIONING						Injector									
~ %						5	10	10	10	15	5	80			
EXPERIMENTAL PHASE															

CNAO Site


Medical and Administrative buildings
Accelerator and treatment rooms


ACCELERATOR
Synchrotron
P : 60 – 250 MeV
C6+ :120 - 400 MeV
3 Treatment
rooms
protons
Carbon
ions
Injector:

Synchrotron hall today



Vertical dipole installation
05-09

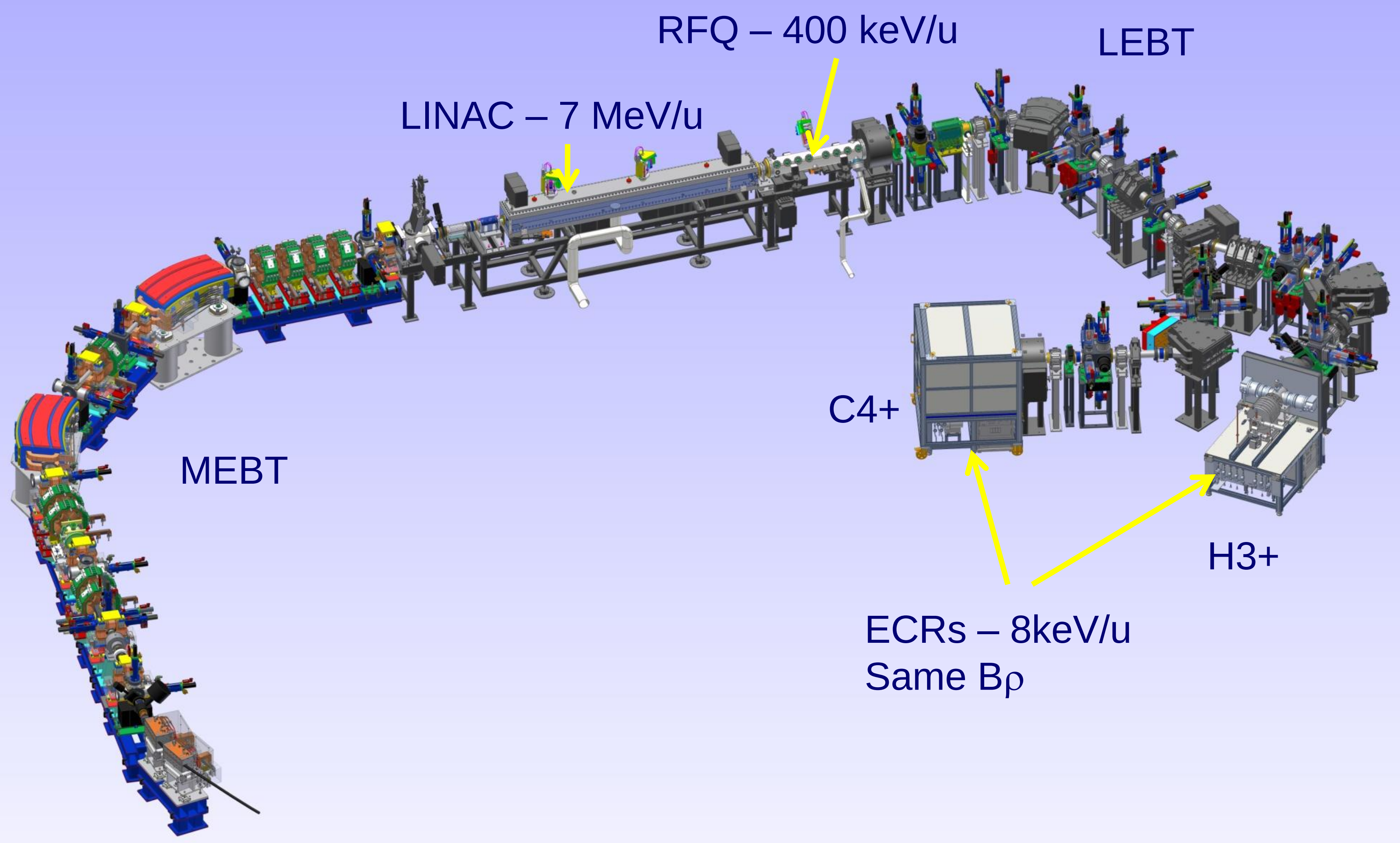
Some examples of the most recent beam diagnostic installations

Synchrotron

HEBT

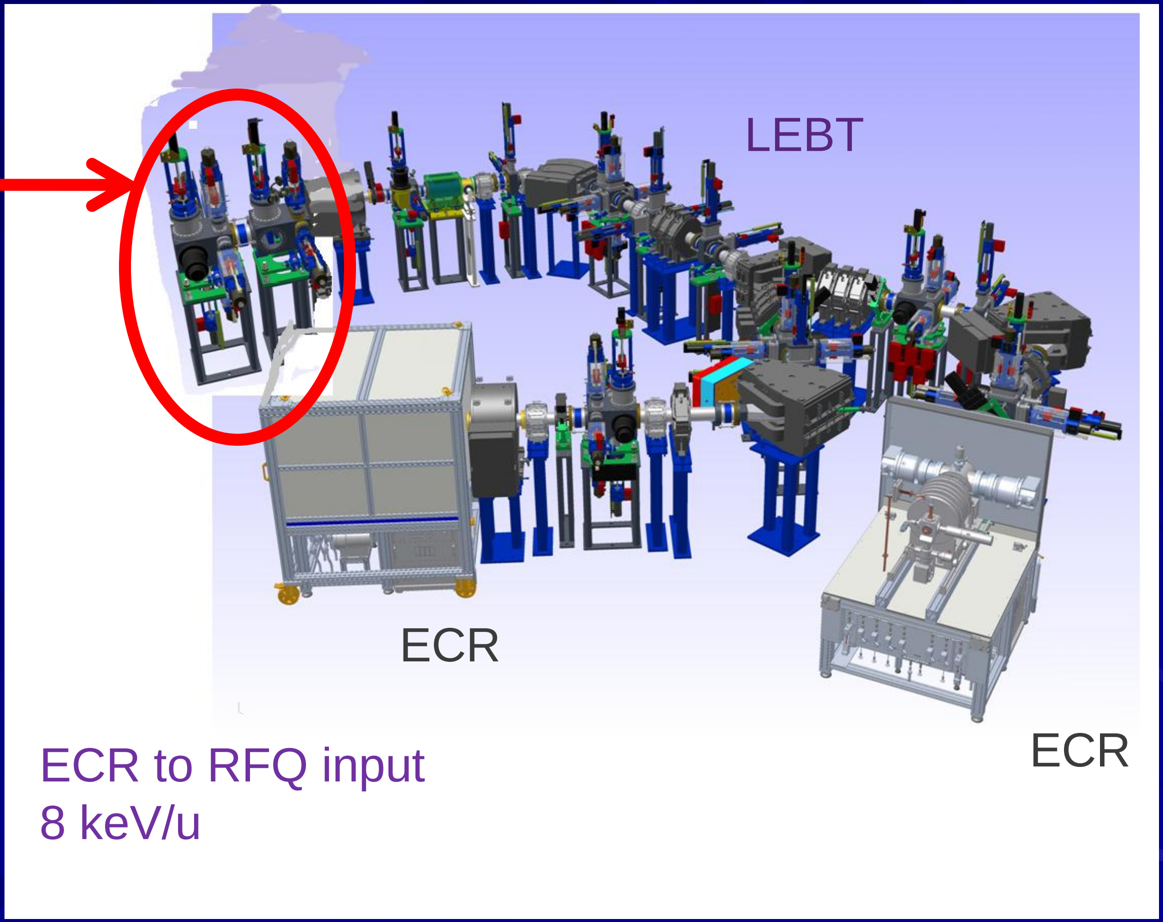
Treatment room

INJECTOR



INJECTOR commissioning strategy

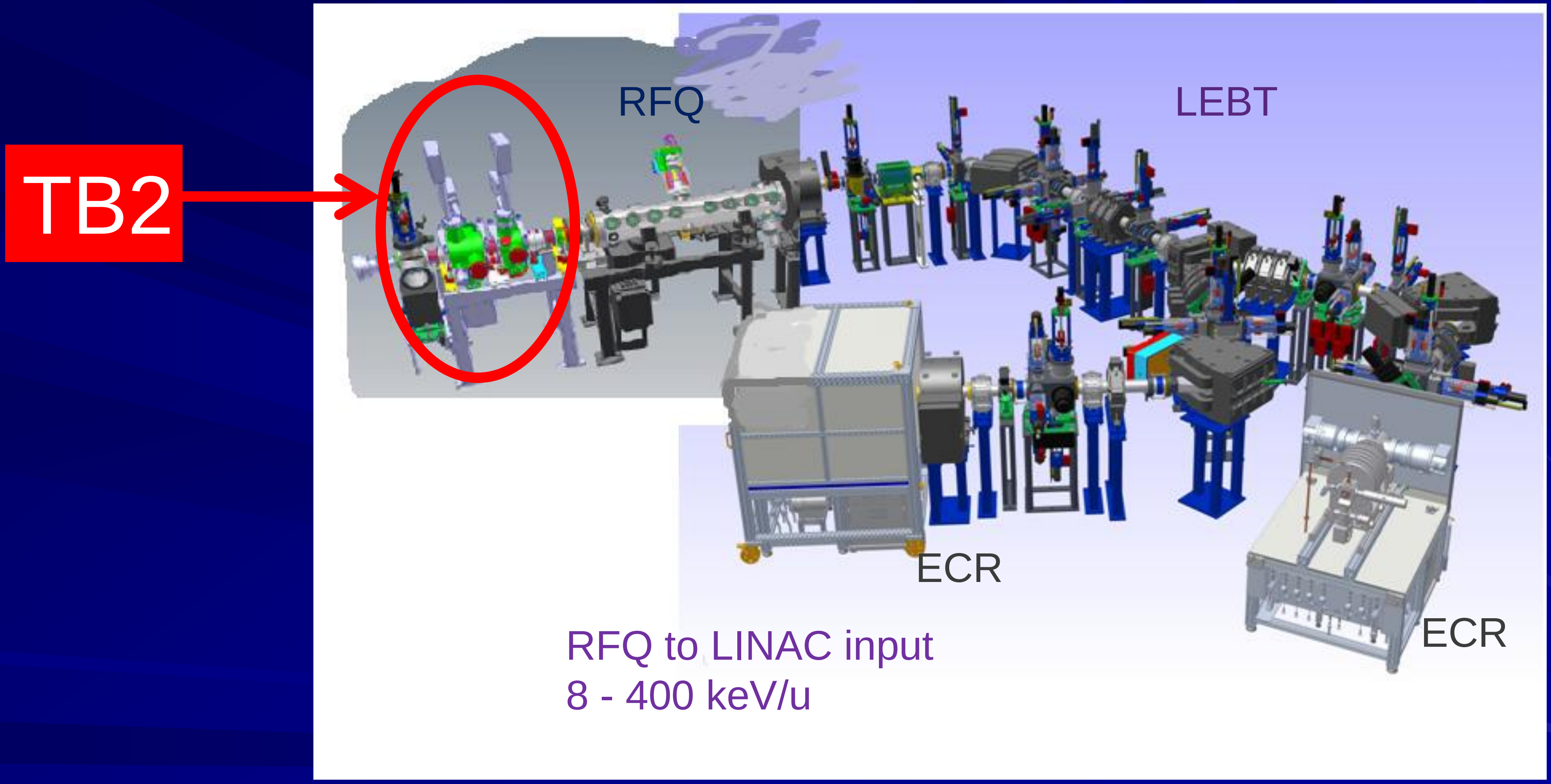
TB0



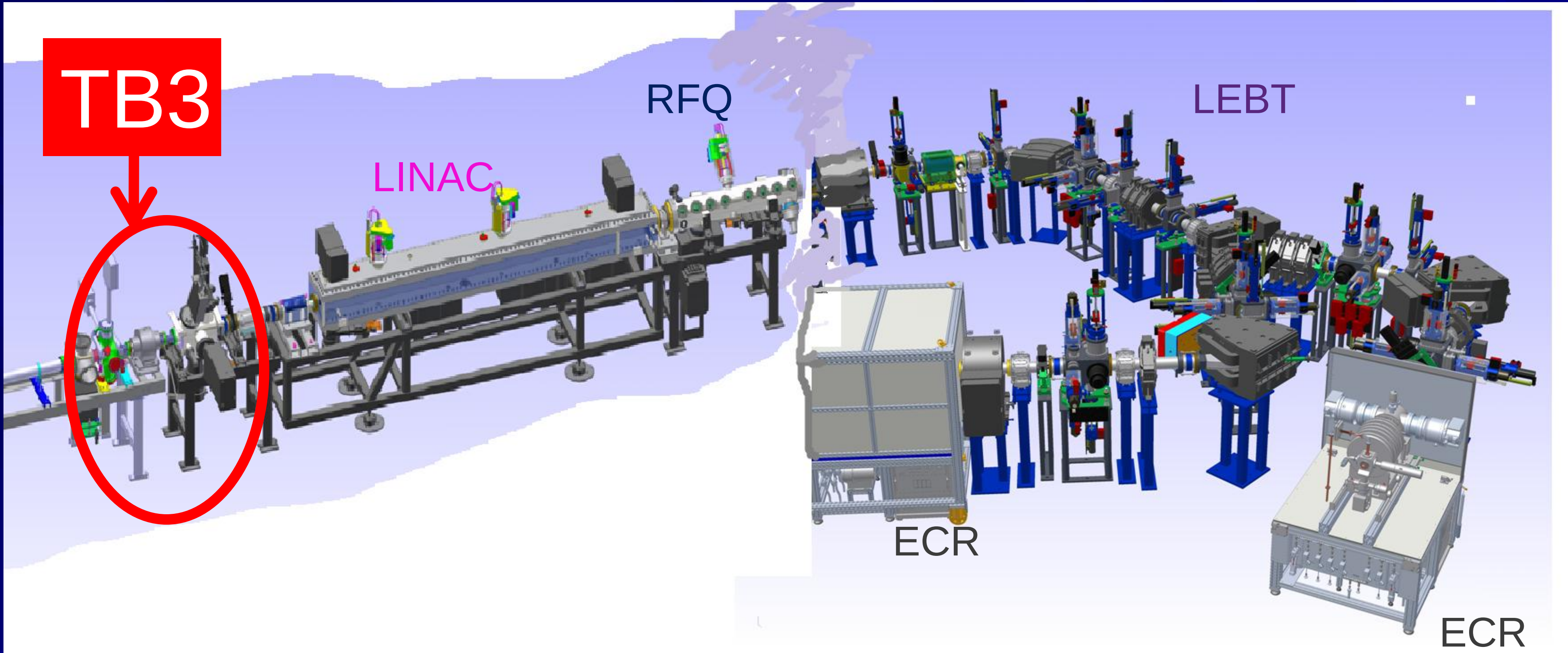
Diagnostic tank

- Intensity
- Dimensions
- Profile
- Emittance

INJECTOR commissioning strategy



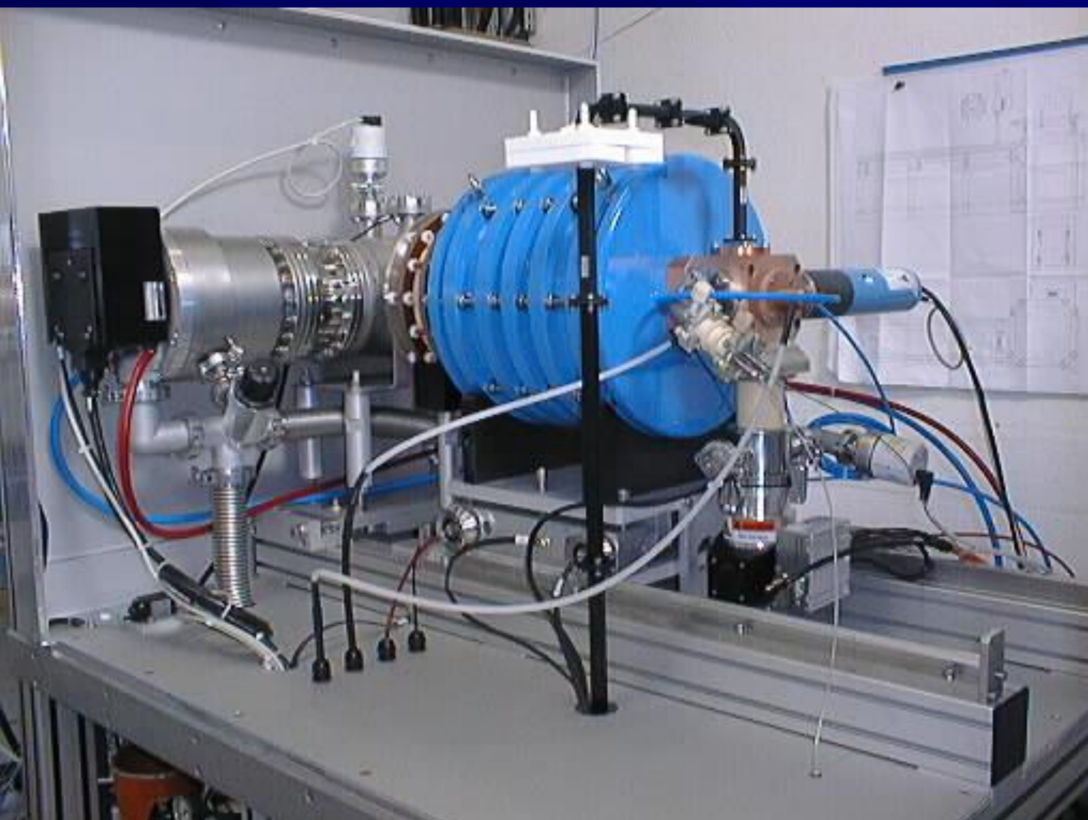
INJECTOR commissioning strategy



LINAC to MEBT input
400 keV/u – 7 MeV/u

ECR Ion Sources

Both can deliver H3+, C4+ and other species
14.5GHz
MEBT

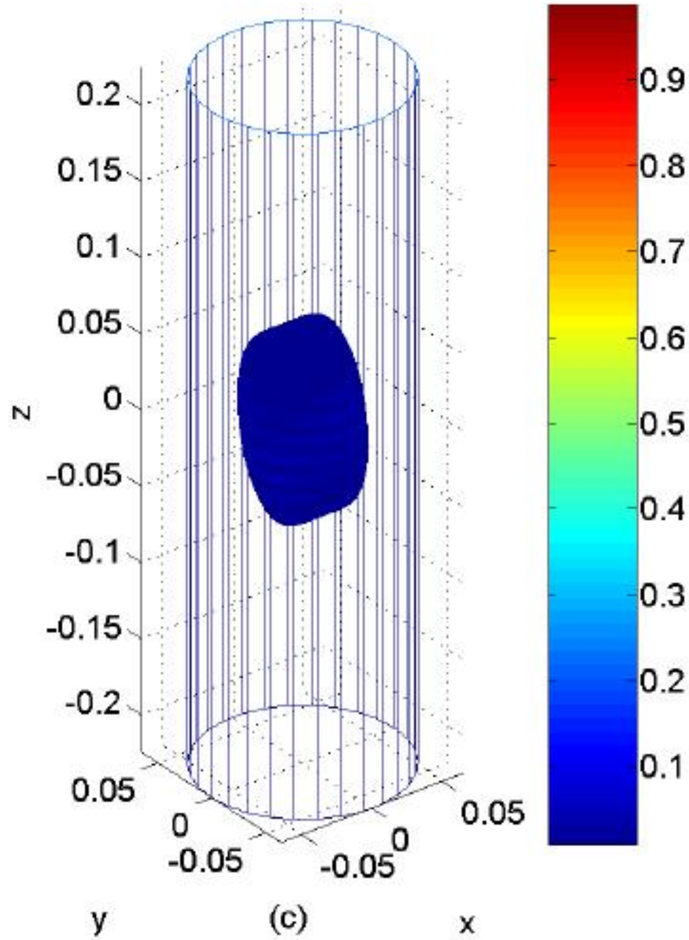


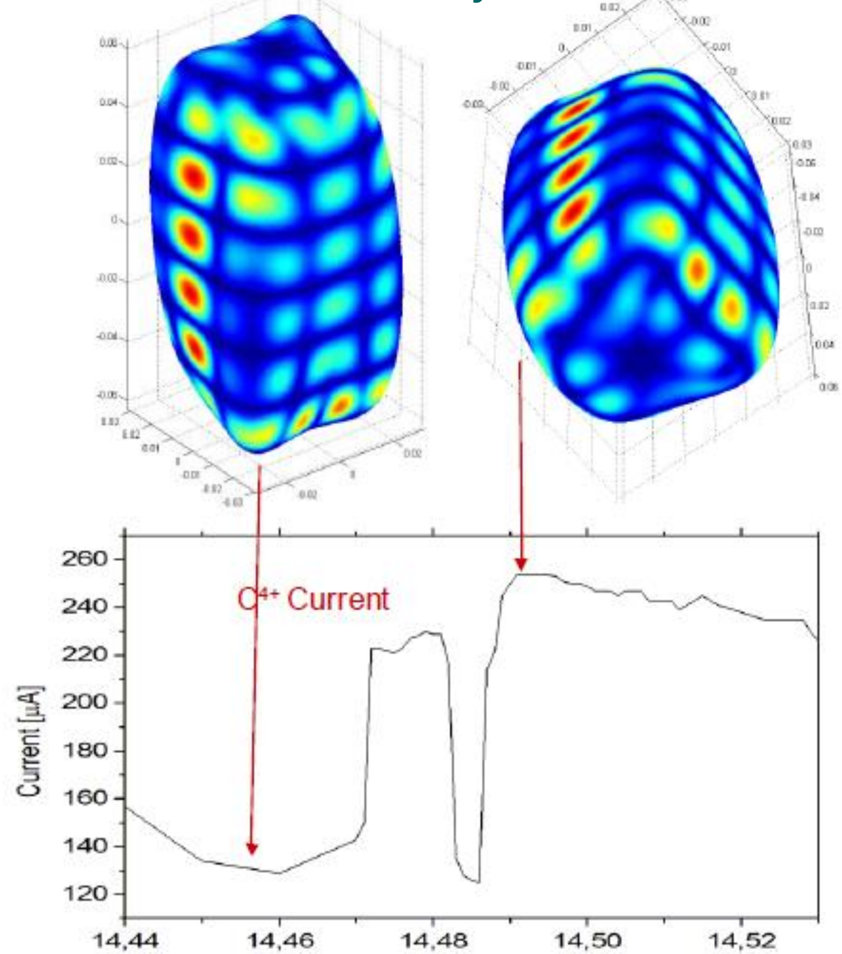
- Double wall, water cooled plasma chamber with 7 mm diameter aperture for beam extraction.
- Permanent magnets system providing the axialand radial confinement (axial field from 0.4 to 1.2 T, radial field i1.1 T)
- A copper made “magic cube” for the microwave njection system which consists of a waveguide 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 Pantecknic on INFN-LNS Design

FREQUENCY TUNING EFFECT

Increase of the extracted current by 30-50 %



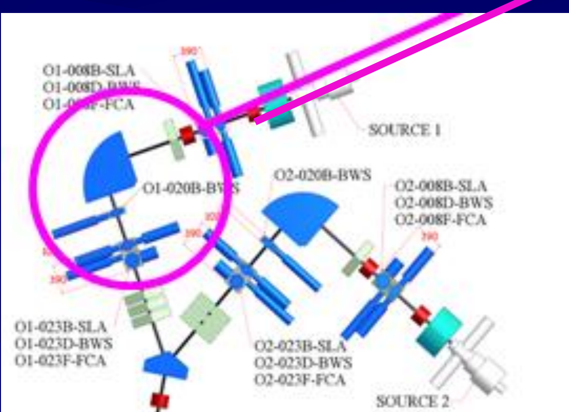


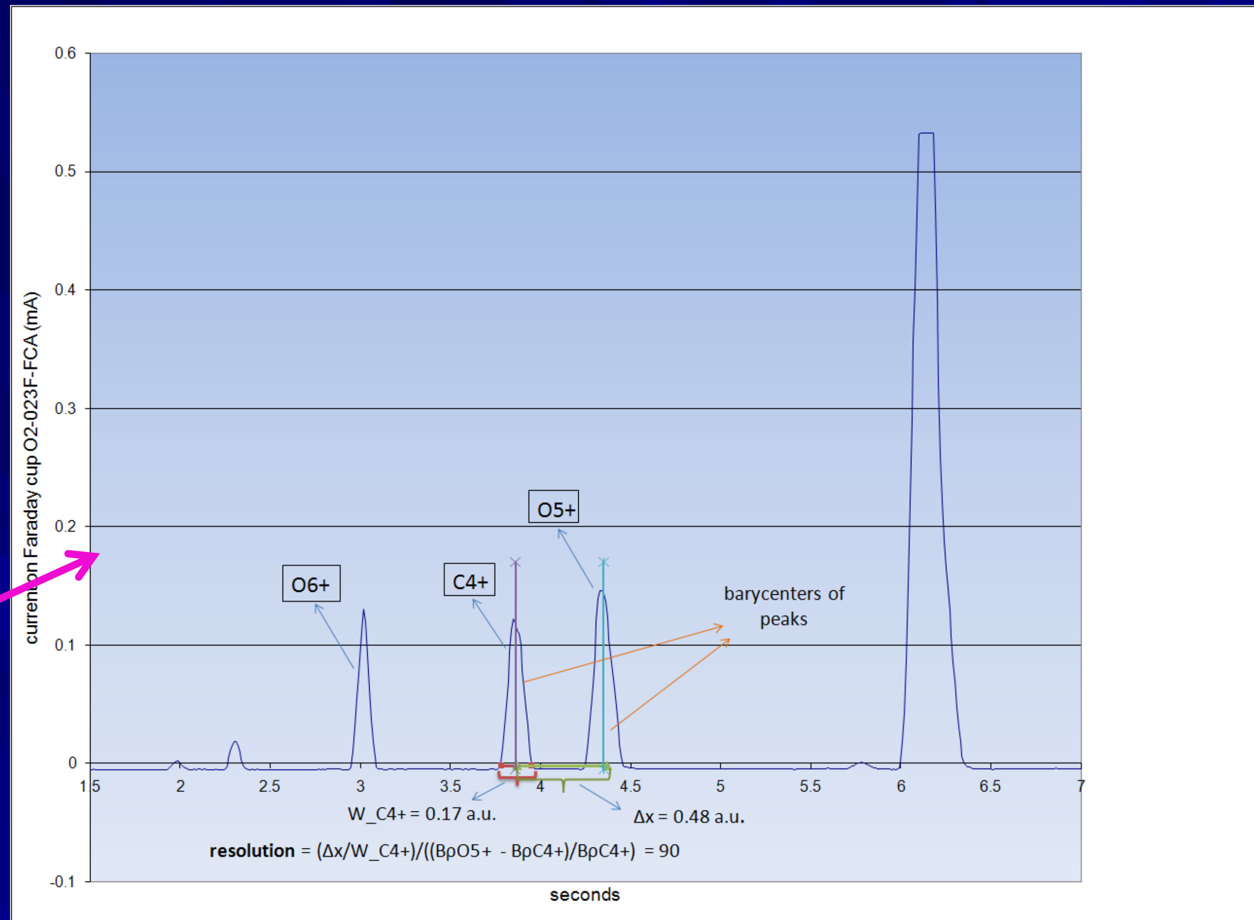
Slight variations of the exciting frequency produce strong changes in the electric field distribution over the resonance surface – S. Gammino

Spectra of source

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

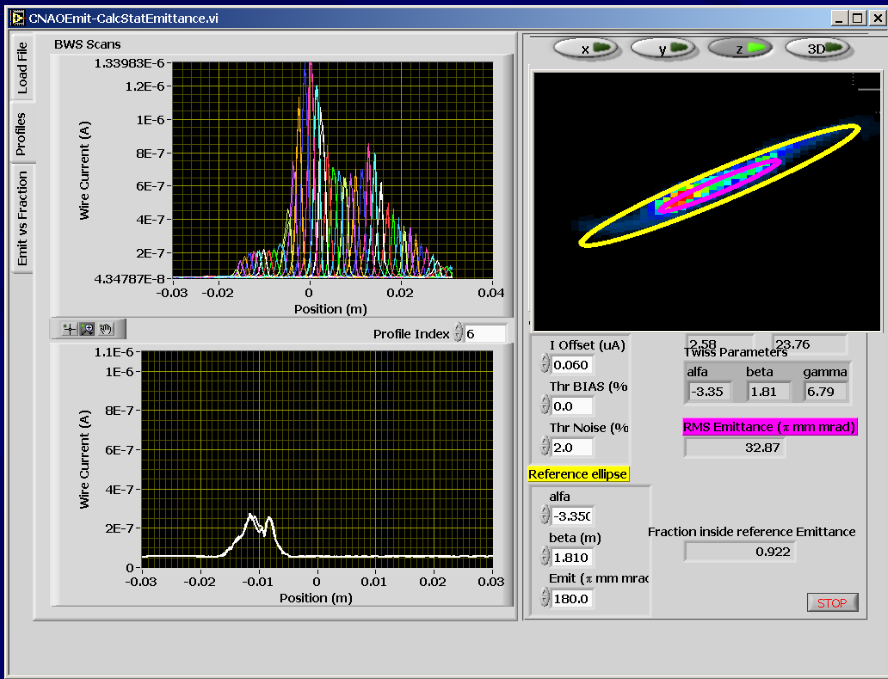
Minimum resolution to separate C4+ from O5+: R≈30





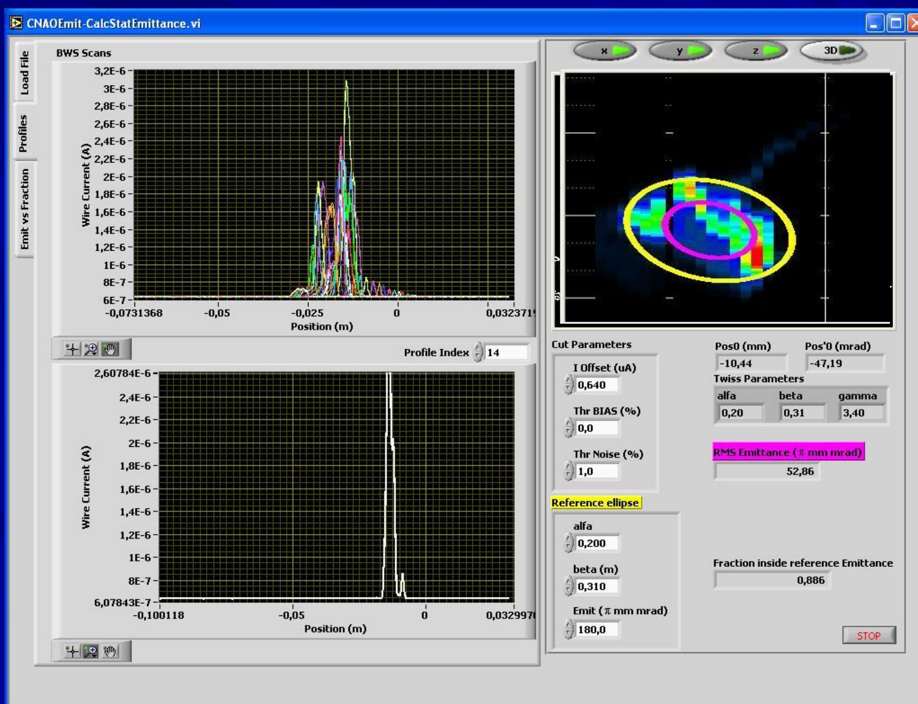
Measurement performed with a fixed gap of slits (2 mm).

Sources currents and emittances



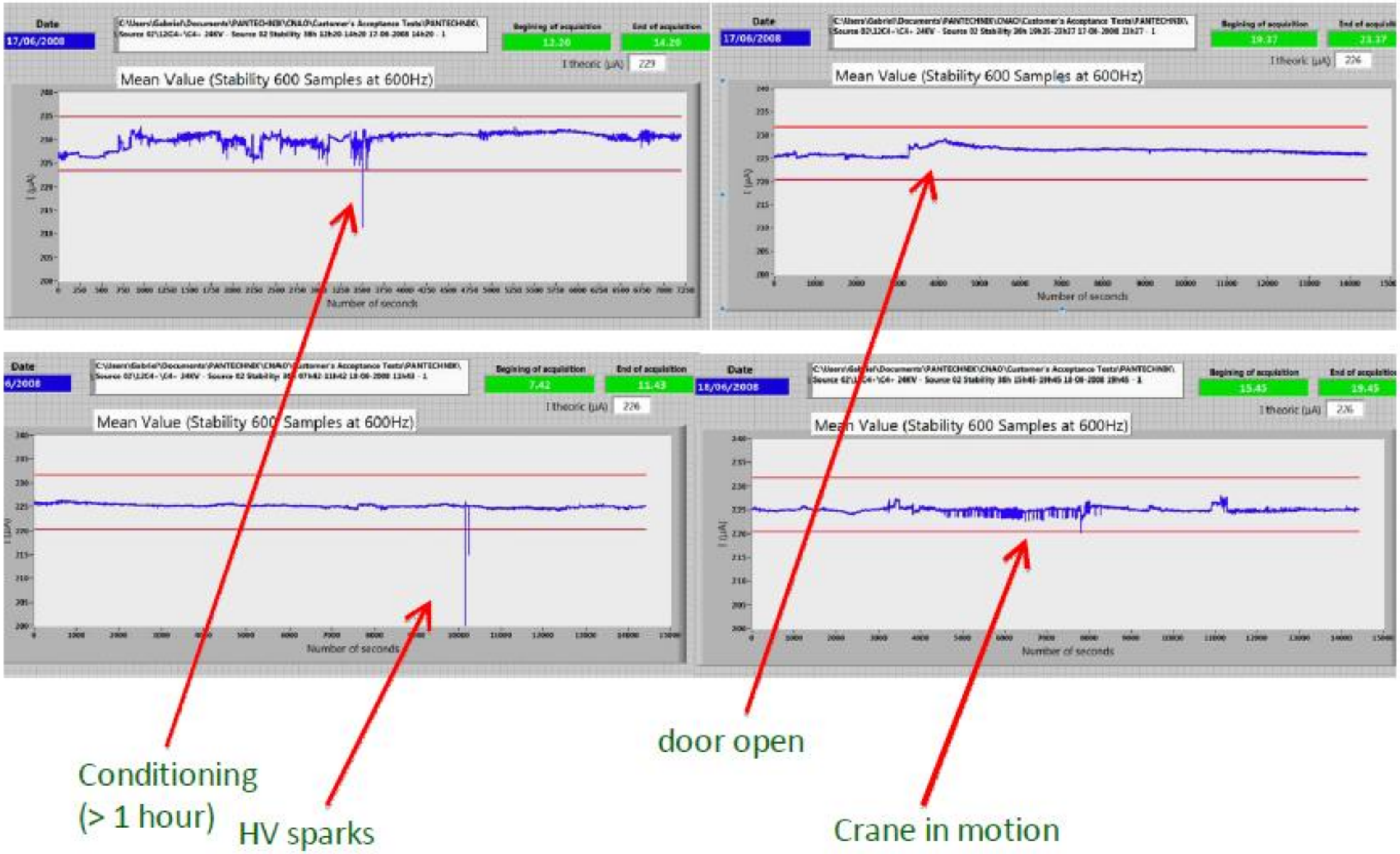
H_3^+, 1.4mA (design =800 μA)

Emittance measured after spectrometer



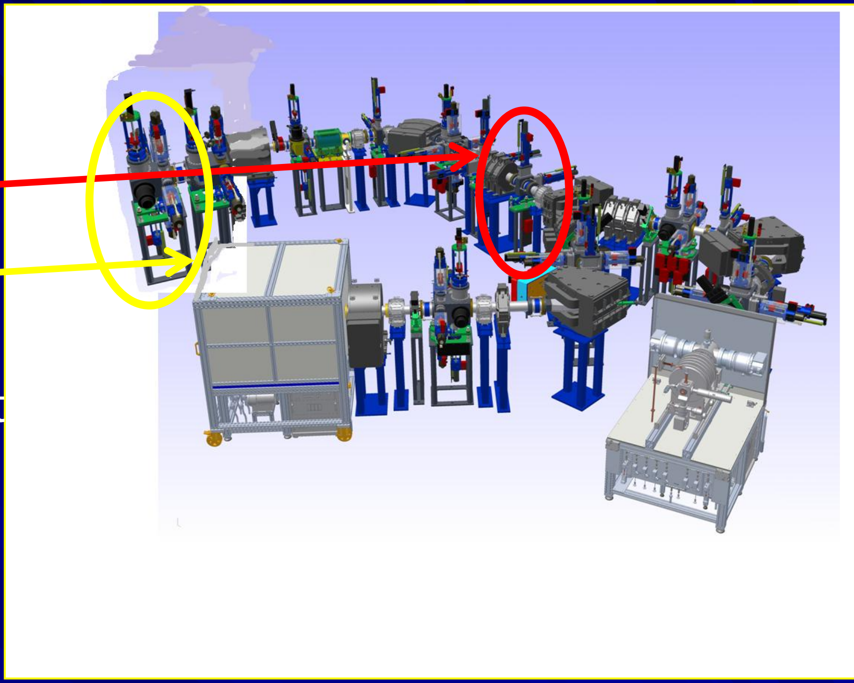
C^{4+}, 230 μA (design = 200 μA)

Stability tests for C^{4+}



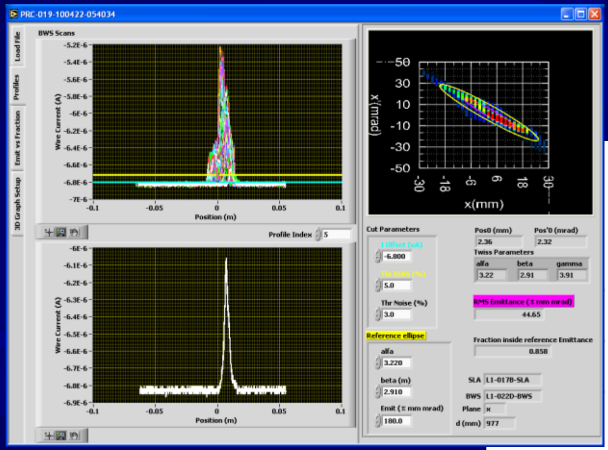
LEBT commissioning

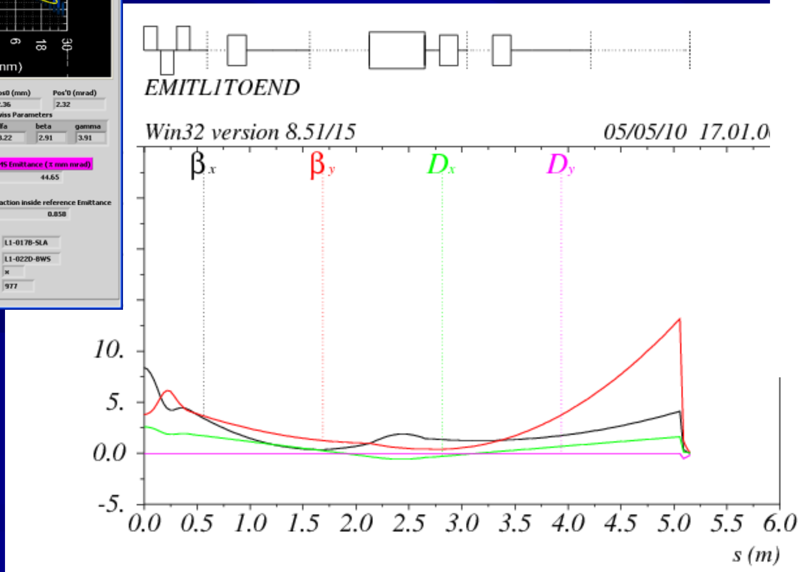
Diagnostic tanks containing
slits, wirescanners, faraday cups
Along the line + TB0

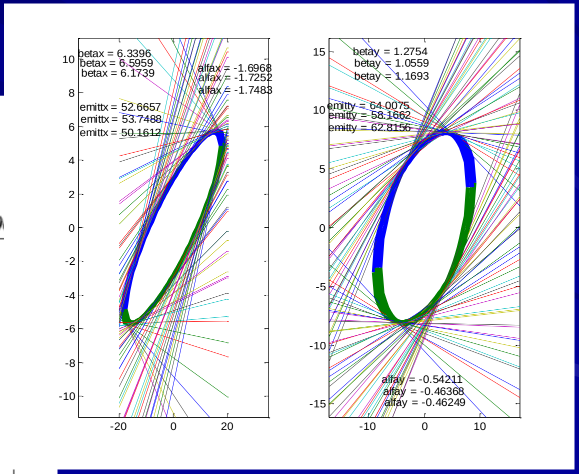


Emittance and Twiss Parameters measurement
- With tank diagnostics
- With Quad scans
- Model

Agreement better than ± 10%

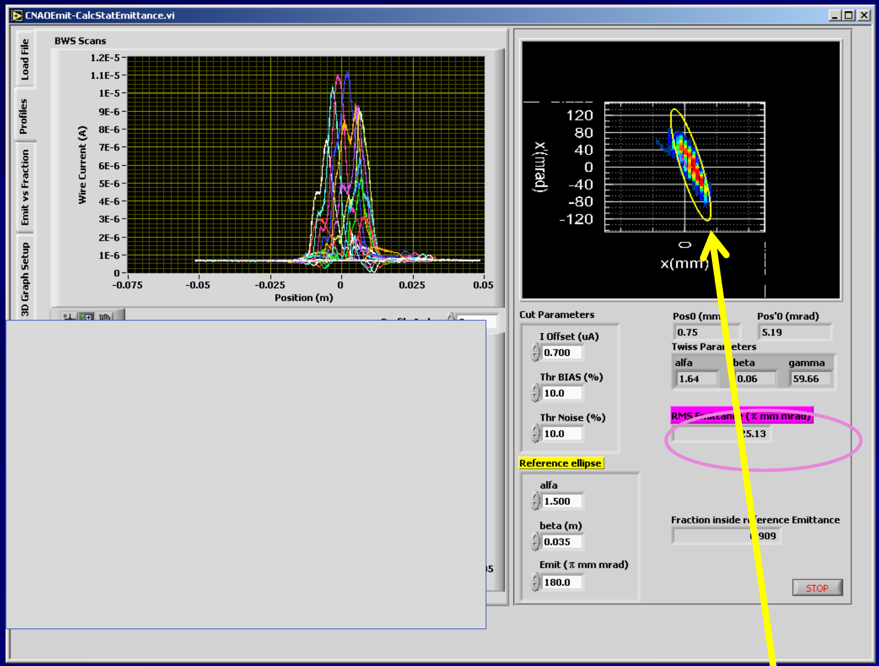


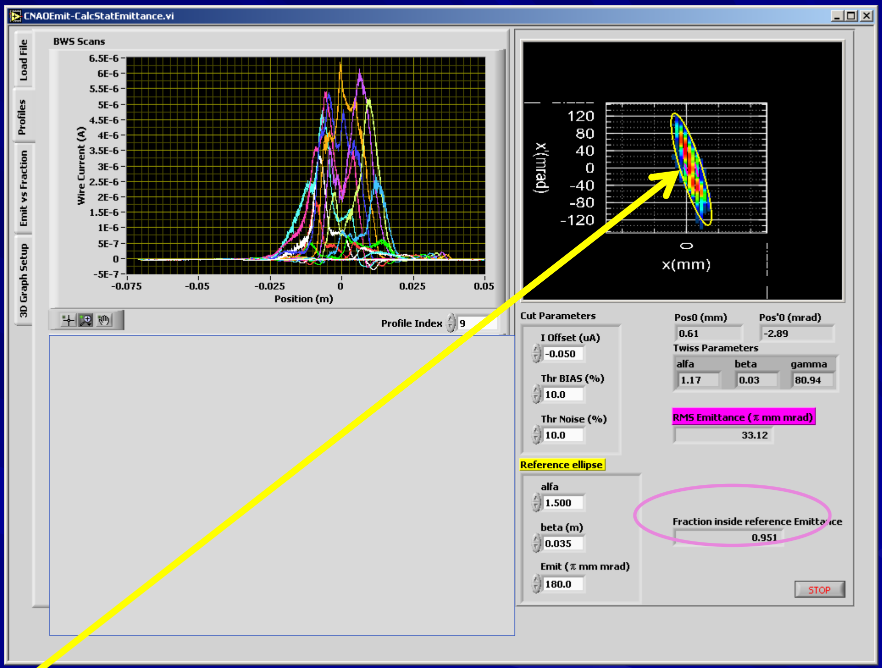




‘Round beam’ in TB0 with H3+ from SO1

Transmission 92 % - final current 1150 μA (design 600 uA)





Horizontal plane

Vertical plane

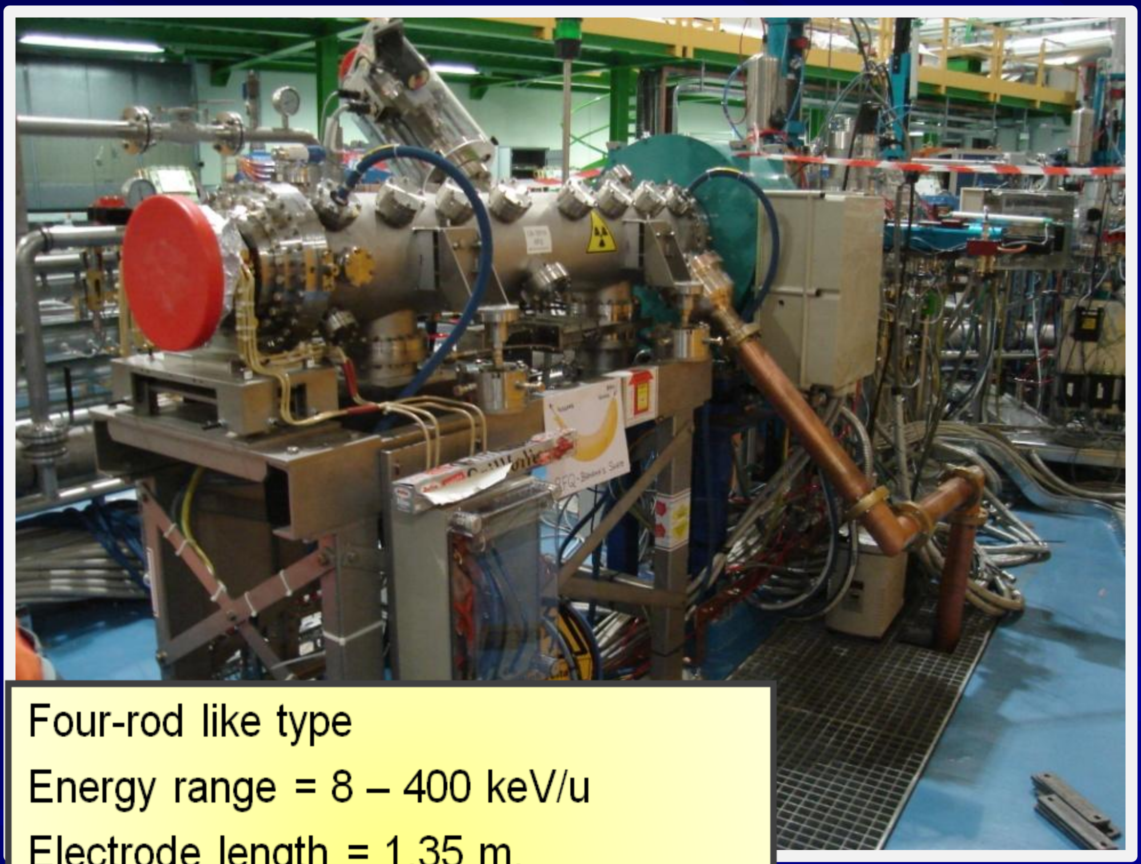
RFQ nominal acceptance

C4+ :

Transmission 75 % - final current 150 mA

(nominal request 180 uA)

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_{rf} = 217 MHz

TB2 diagnostic tank

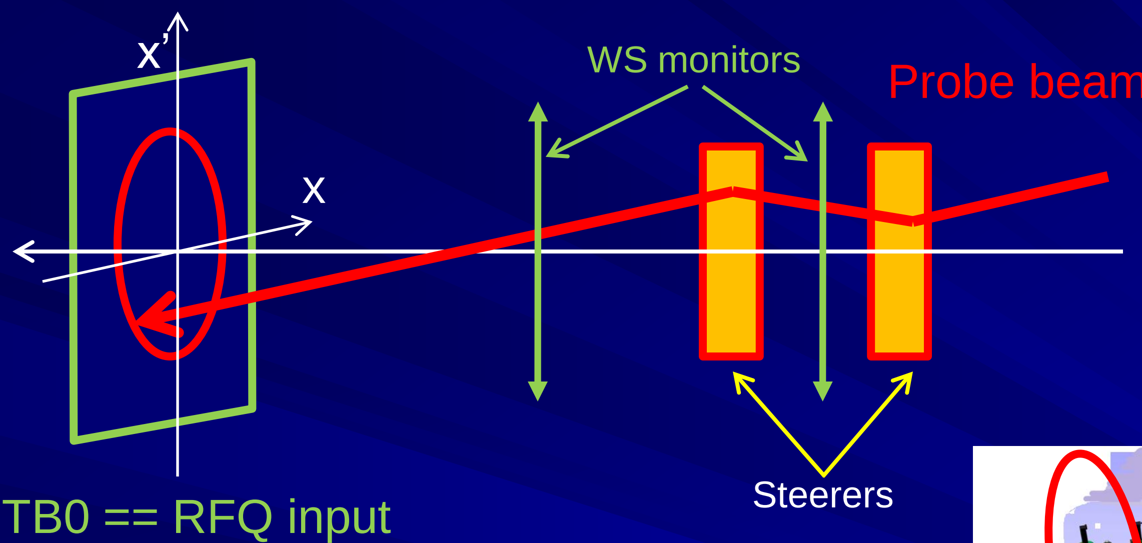
Measurements:

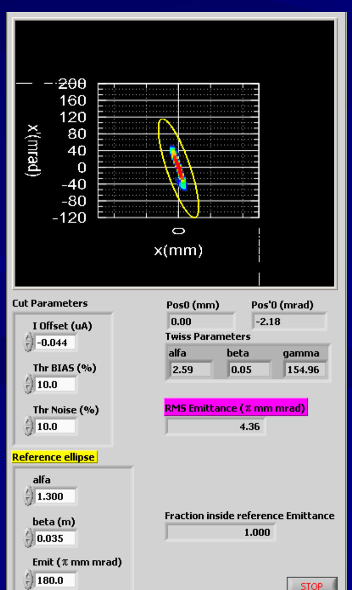
- Current
- Profiles
- Energy
- Emittance

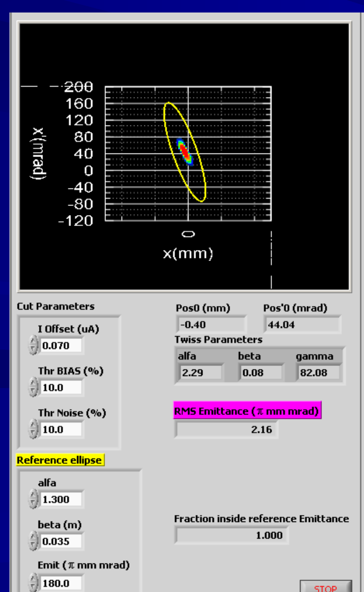
Phase space painting: calibration for RFQ injection optimisation

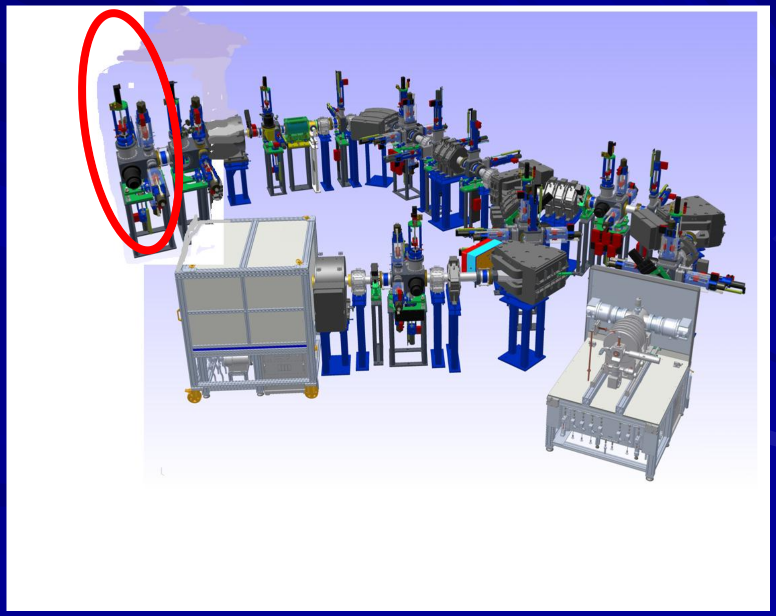
H_3^+ probe beam created using slits along the LEBT

full beam current → 1 mA
probe beam current → 60 μA



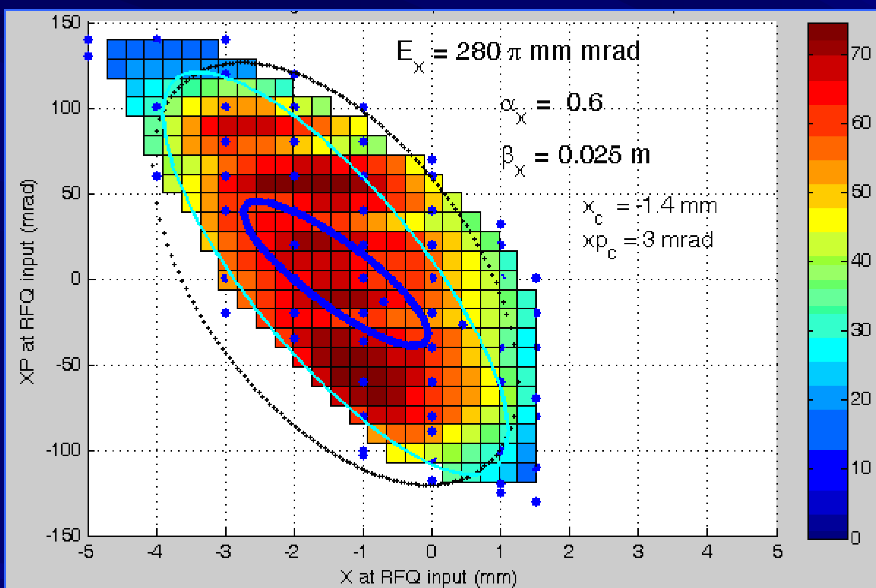




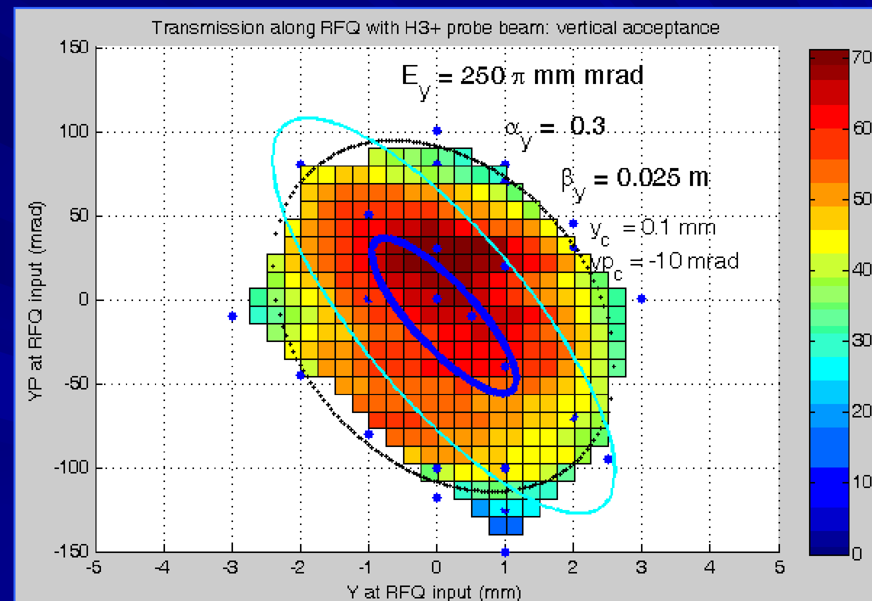


RFQ acceptance measurements (8 keV/u)

Horizontal plane

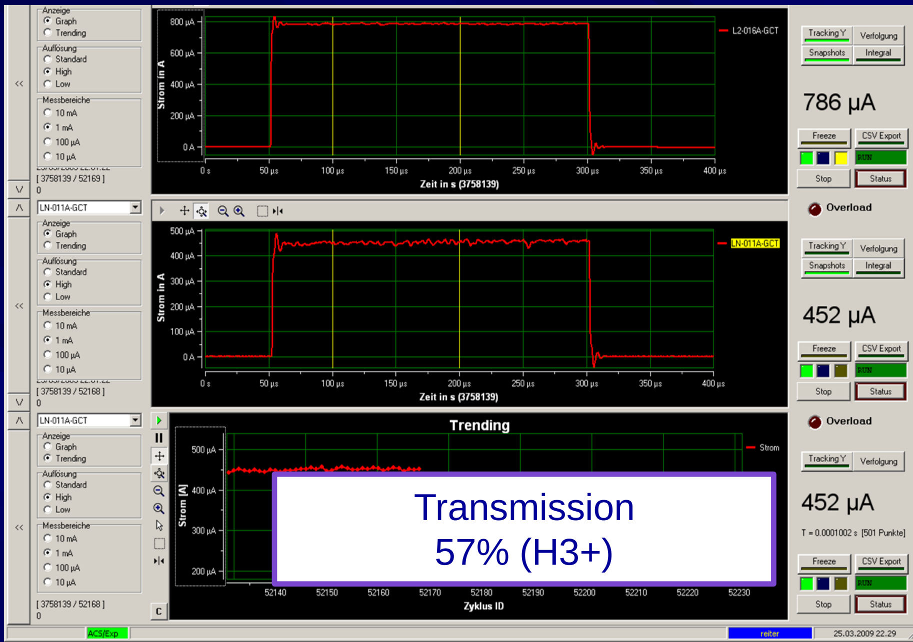


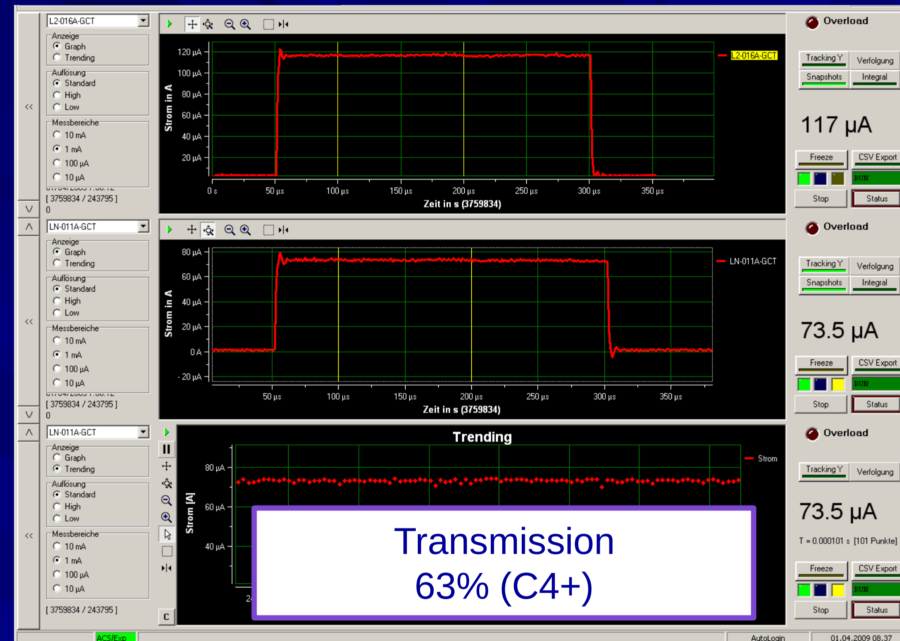
Vertical plane



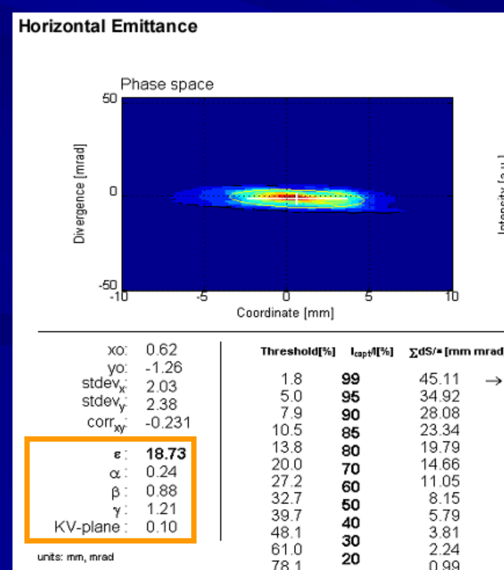
Blue ellipse: measured in TB0 (rms emittance full beam)
Cyan ellipse: nominal RFQ acceptance
Black ellipse fits measured points up to the half of maximum transmission value

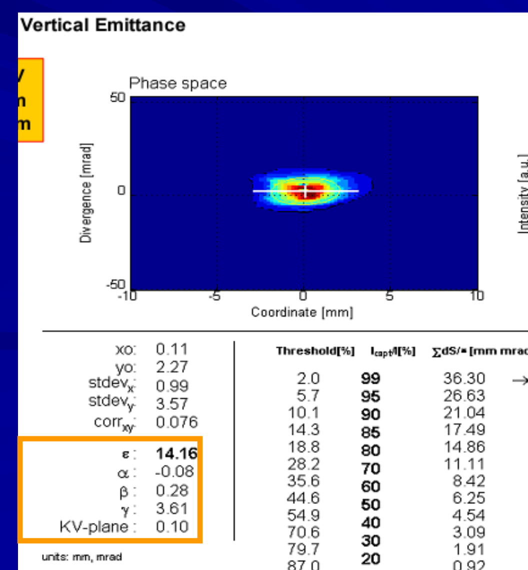
RFQ commissioning: typical measurements





Emittances in TB2 (C4+)





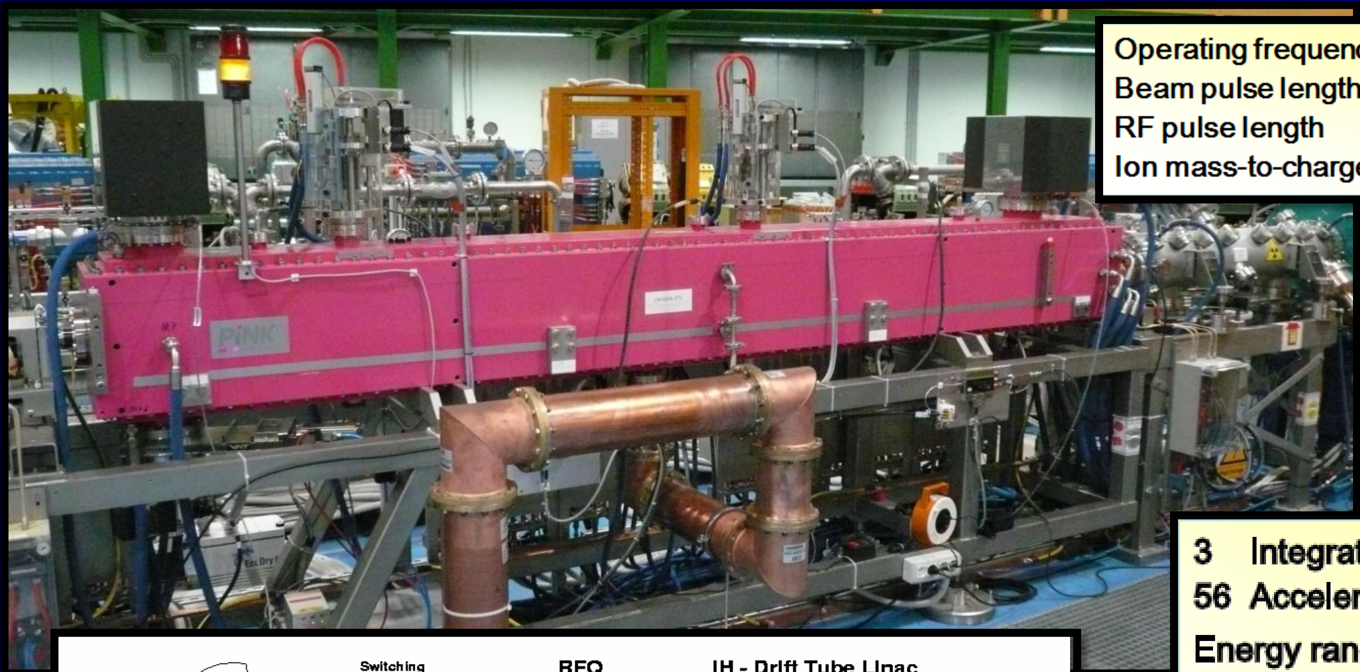
RFQ commissioning summary

	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

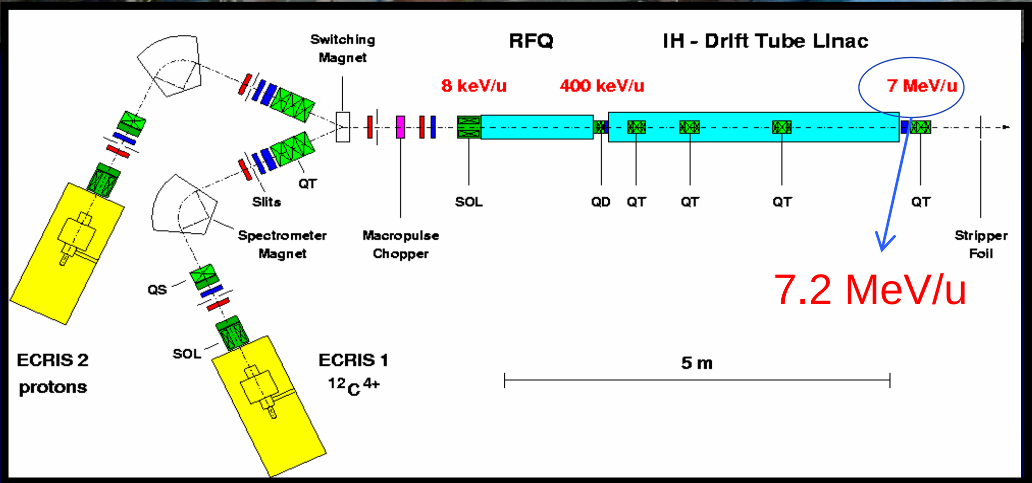
Full beam transmission slightly lower than probe beam transmission:

- good transverse matching
- transmission limited by longitudinal leak

LINAC – GSI and CNAO

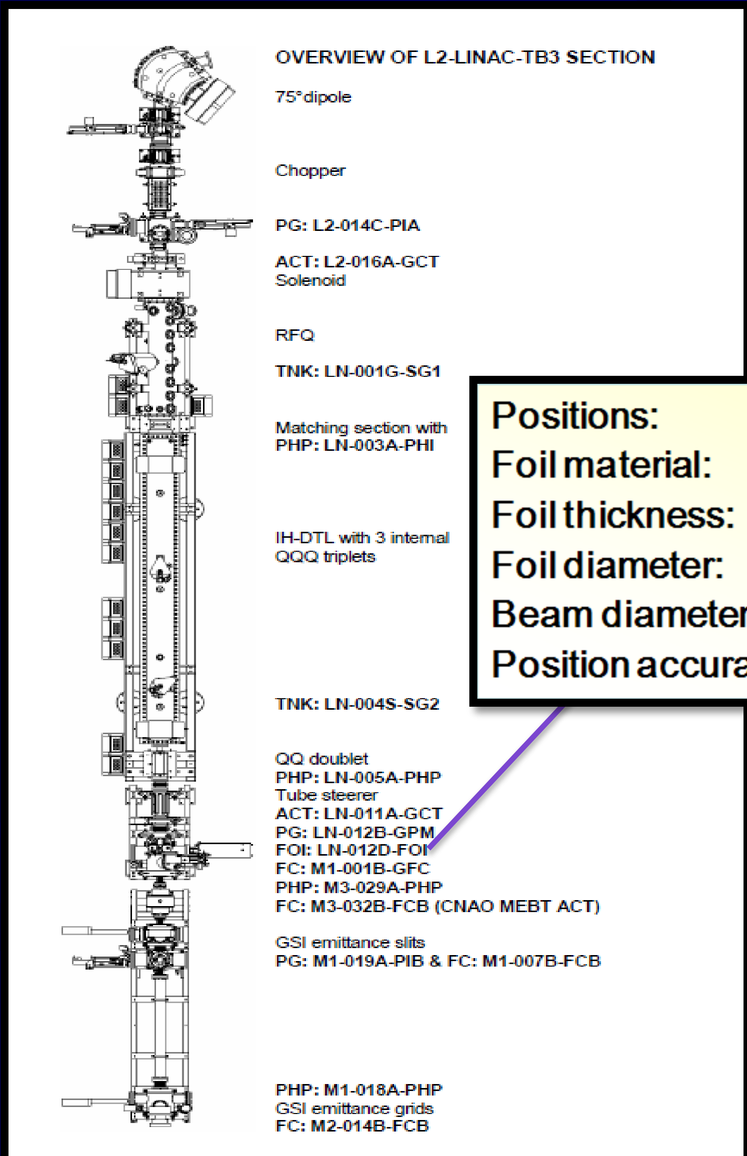


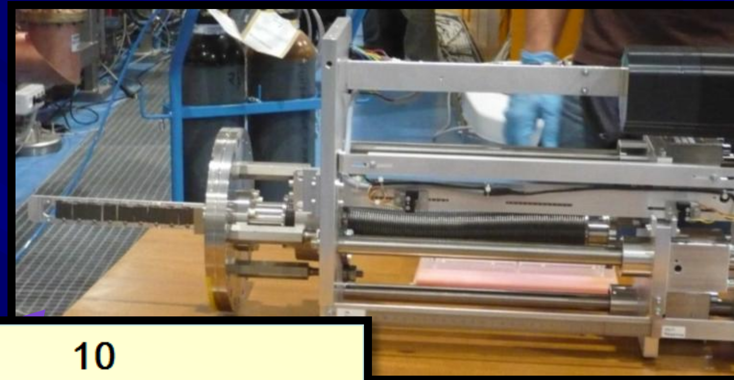
Operating frequency	216.816 MHz
Beam pulse length	≤ 300 µs @ PRF ≤ 5 Hz
RF pulse length	≤ 500 µs @ PRF ≤ 10 Hz
Ion mass-to-charge ratio	$A/q \leq 3$



3 Integrated magnetic triplet lenses	
56 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)	≈ 1 MW
Averaged eff. volt. gain	5.3 MV/m

Stripping foils after Linac acceleration



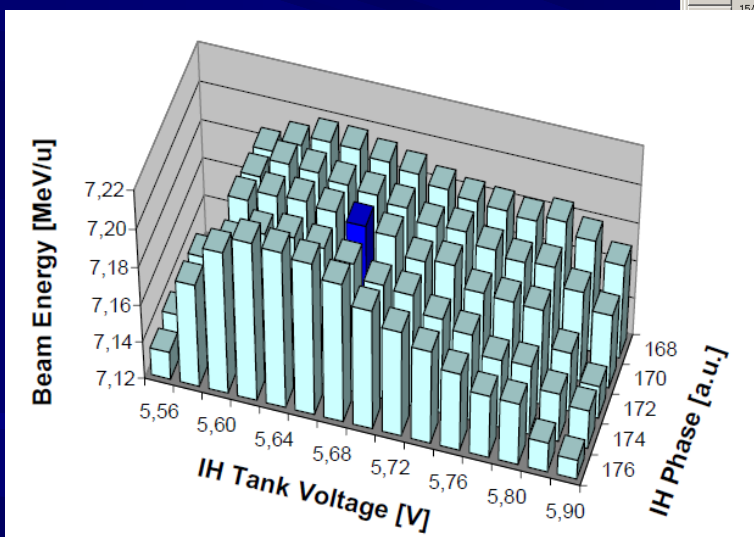


Positions:	10
Foil material:	Carbon
Foil thickness:	100-200 µg/cm²
Foil diameter:	15 mm
Beam diameter:	5 mm
Position accuracy:	±0,5 mm

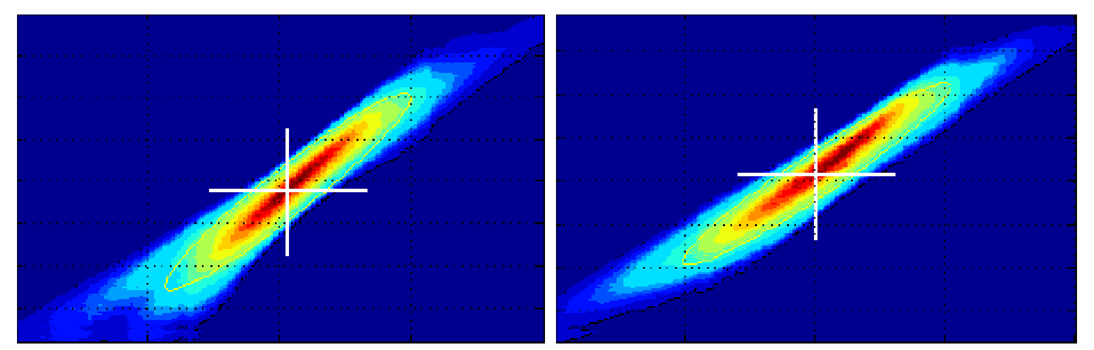
$$H_3^{\;+} \rightarrow H^+$$

$$C^{4+} \rightarrow C^{6+}$$

LINAC commissioning



C6+ beam energy dependence on Linac parameters



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

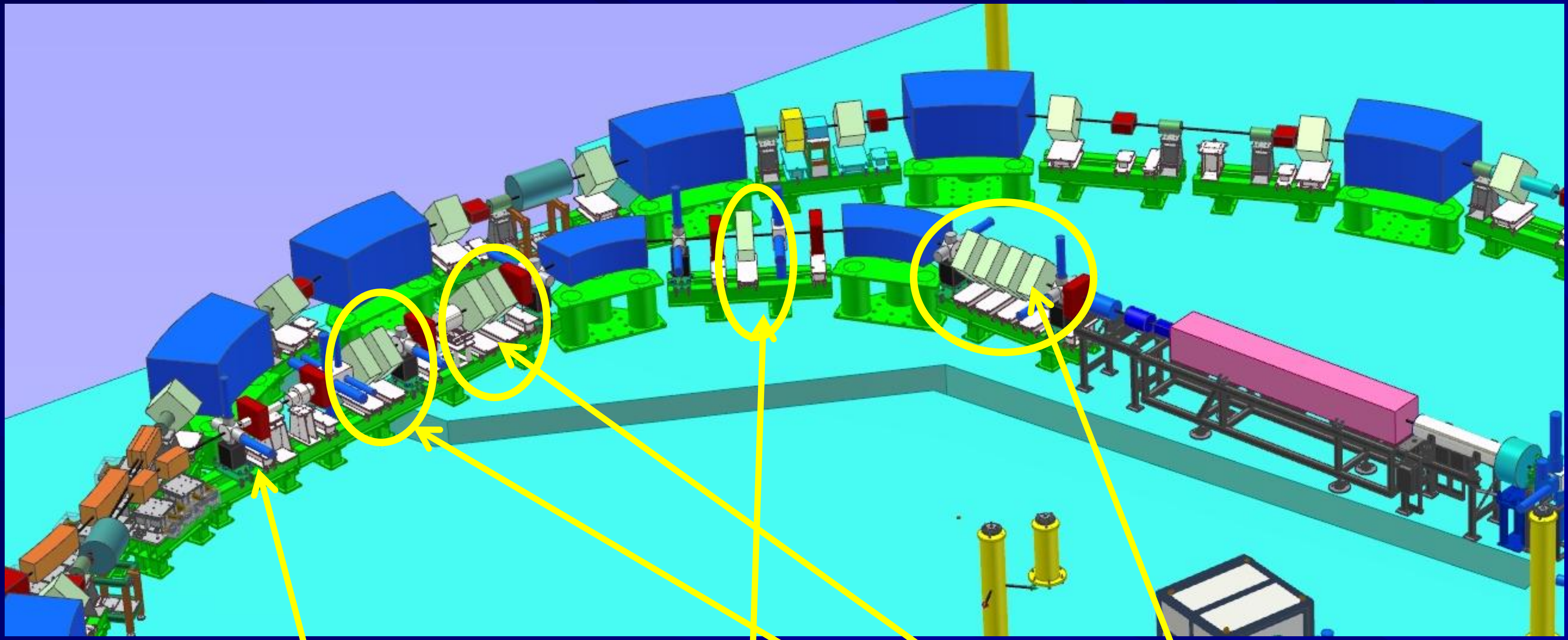
Ion Species	LEBT End	Downstream LINAC	LEBT/LINAC max.transmission	Downstream Stripper foil
C^{4+} / C^{6+}	≈ 170 µA	≈ 82 µA	48 %	**≈ 115 µA**
H_3^+ / p	1.0 – 1.1 mA	≈ 400 µA	39 %	**≈ 1.2 mA**
	710 µA	307 µA	46 %	**≈ 900 µA**

Goal: 120 µA

Goal: 600 µA

... about two times higher C6+ beam currents and roughly four times higher proton beam currents were achieved behind the CNAO linac as compared to HIT.

MEBT

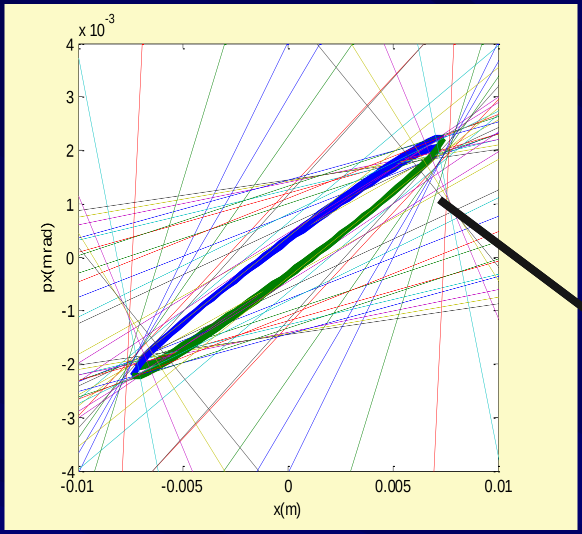


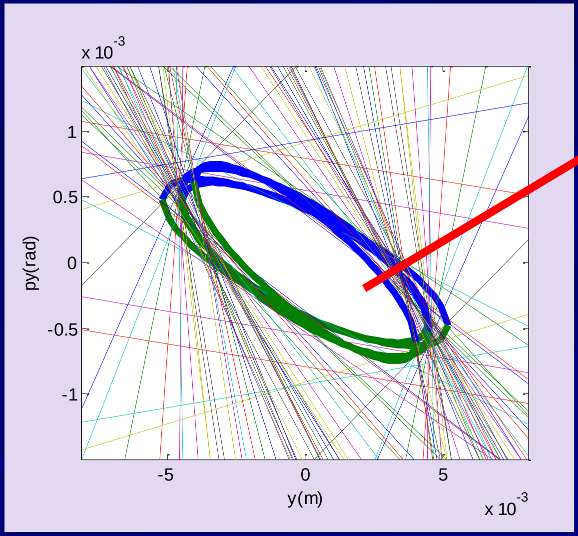
Dispersion bump

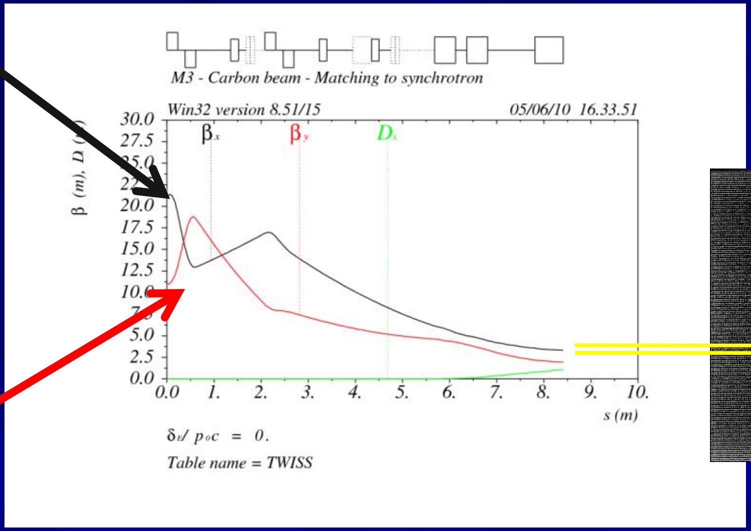
Debuncher to minimize the injected beam momentum spread

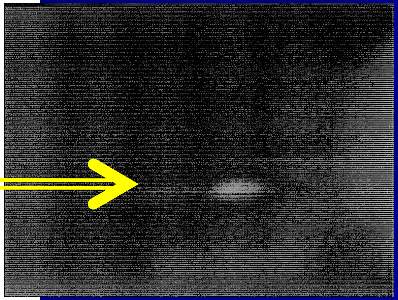
Quadrupoles for matching in non dispersive zone

Emittance measurements with Quad Scans used for beam optimisation at injection

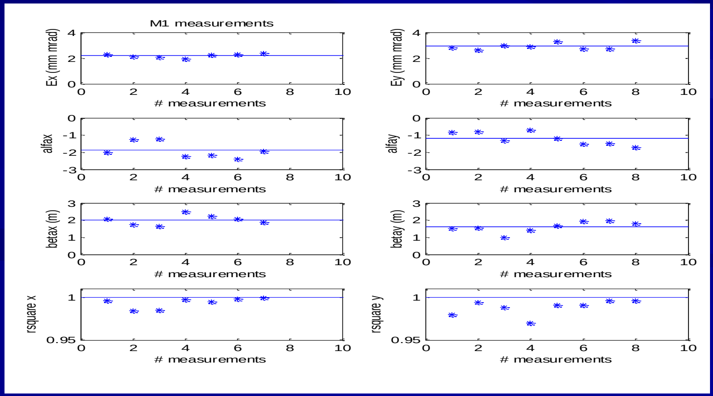








TVScreen in synchrotron



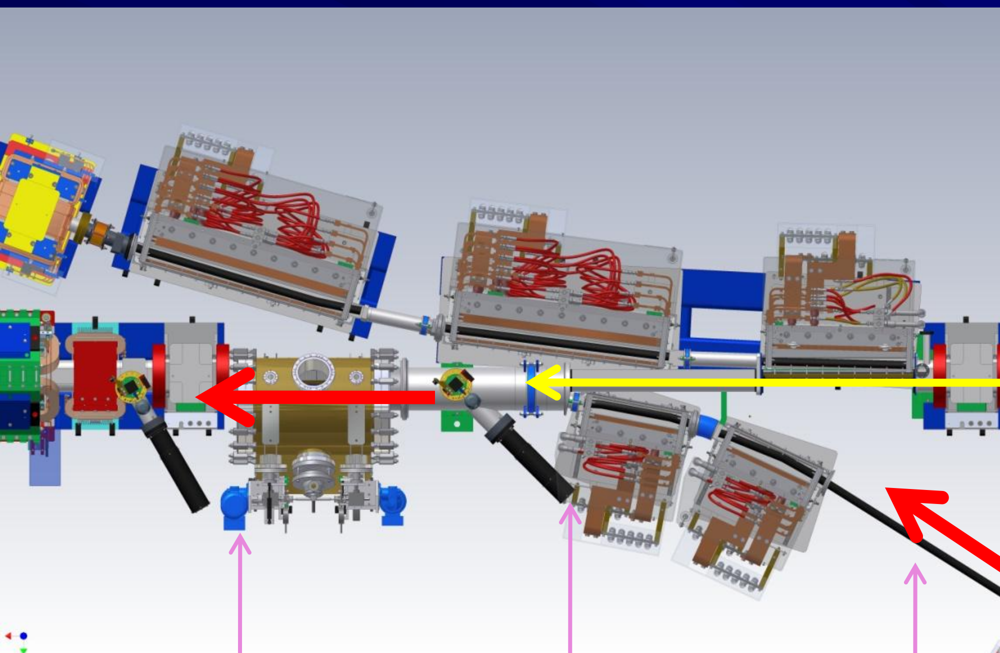
Carbon beam

> 90 % transmission in MEBT

Different quad sets

Beam (p) at the end of the MEBT

TV screen T60→ end of the MEBT



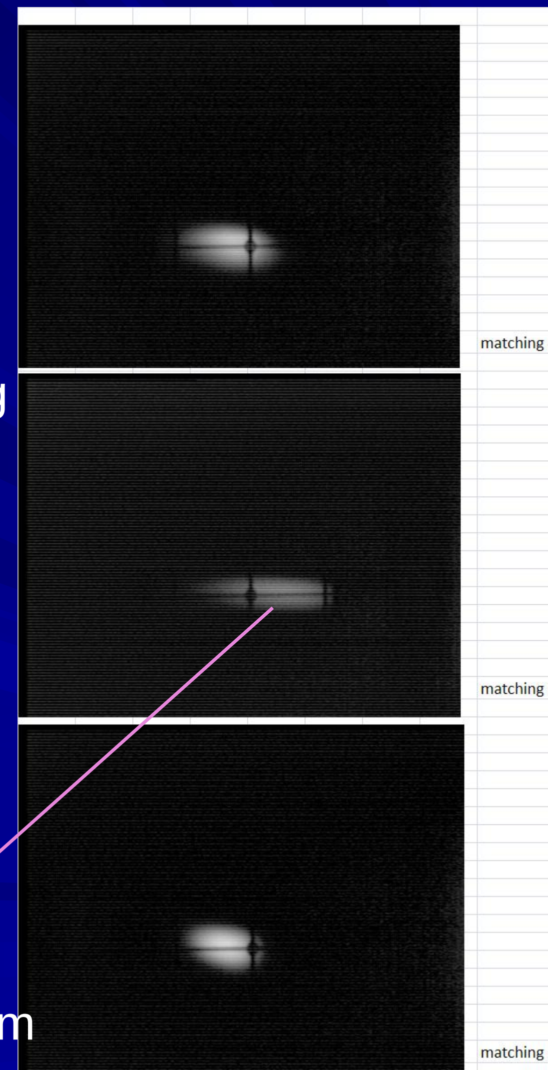
Circulating beam

Injected BEAM

T60 (MEBT exit)

T45 (first turn)

MEBT

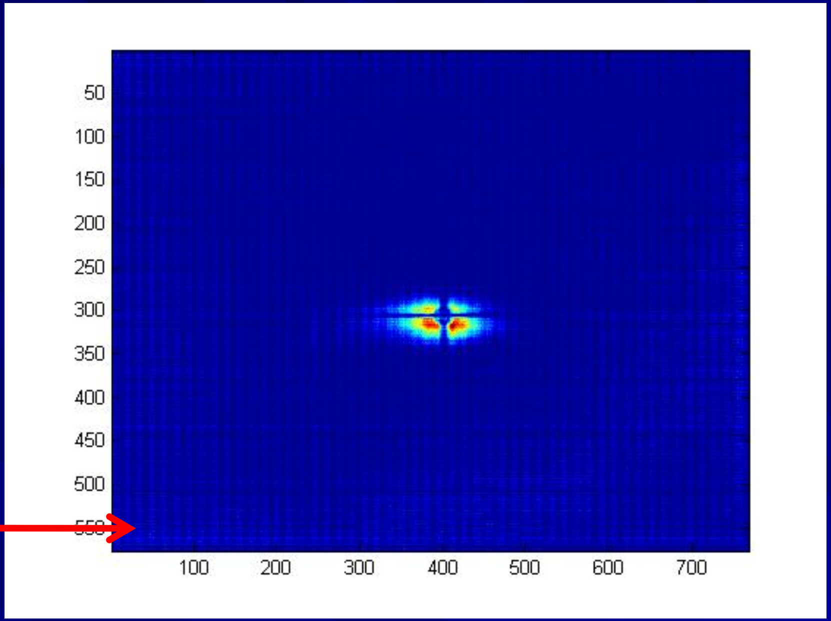


Electrostatic septum shadow

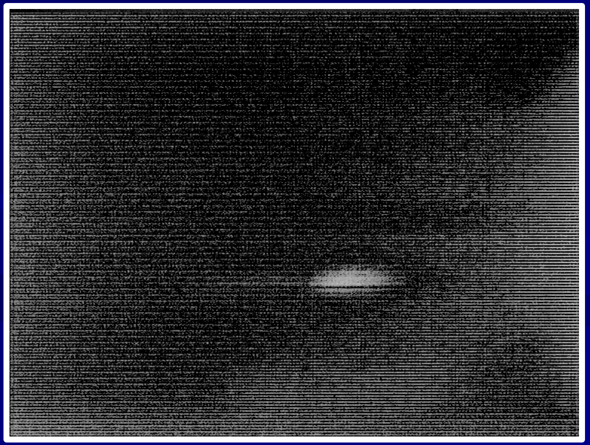
Transmission along MEBT > 90% both species

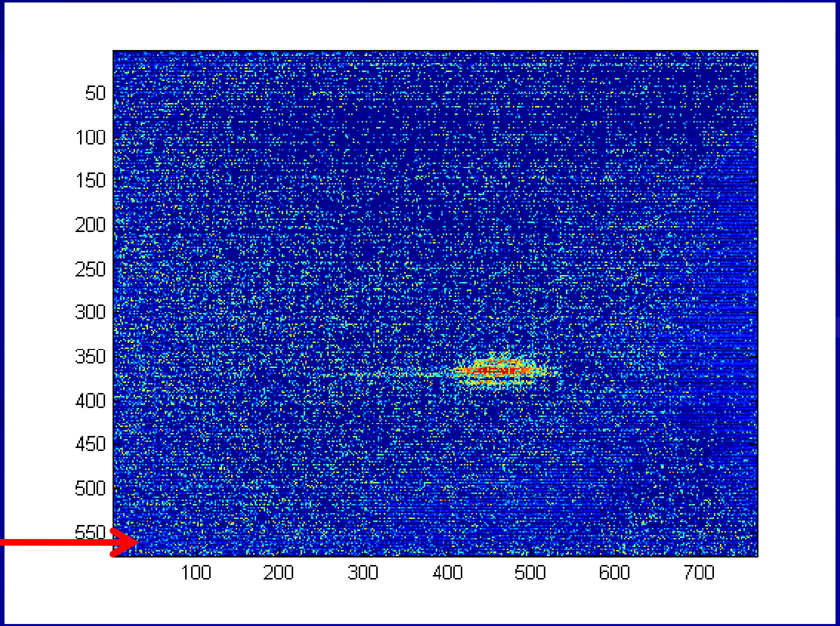
TV60

Images of Proton beam: 600 μA

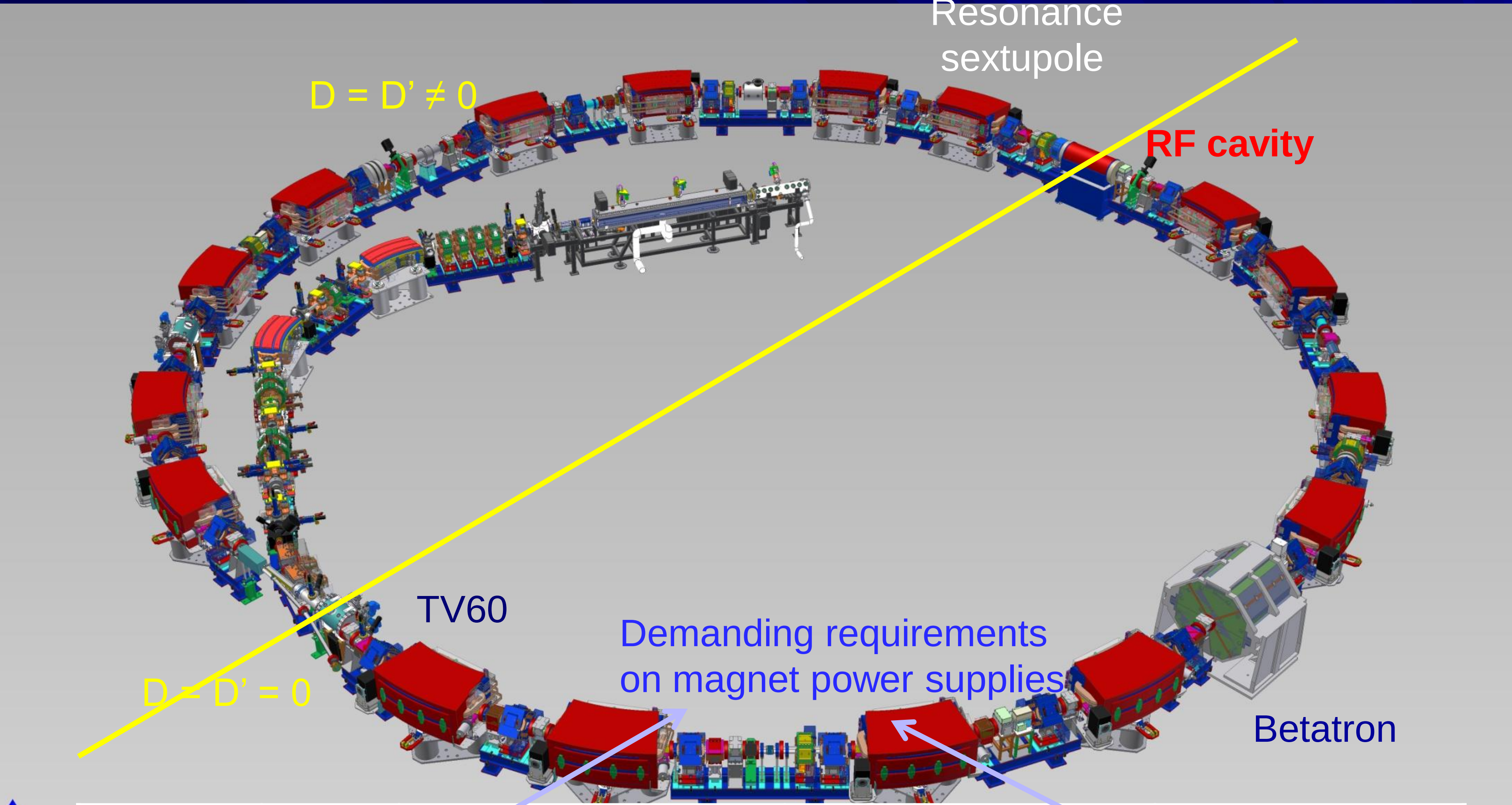


Images of Carbon beam: 90 μA





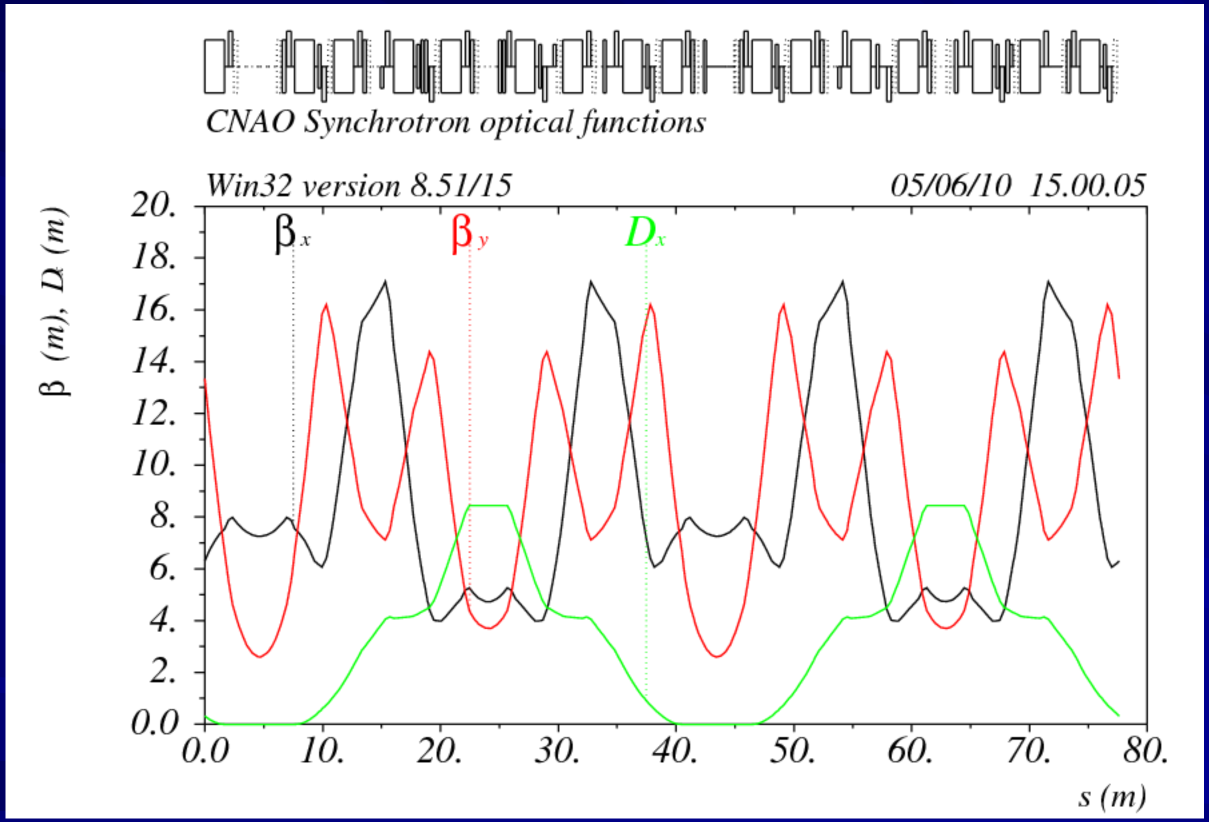
Synchrotron



	P inj	P – 60 MeV	P – 250 MeV	C6 inj	C6+ – 120 MeV	C6+- 400 MeV
Bρ (T m)	0.4	1.1	2.4	0.8	3.3	6.4

Synchrotron optical functions

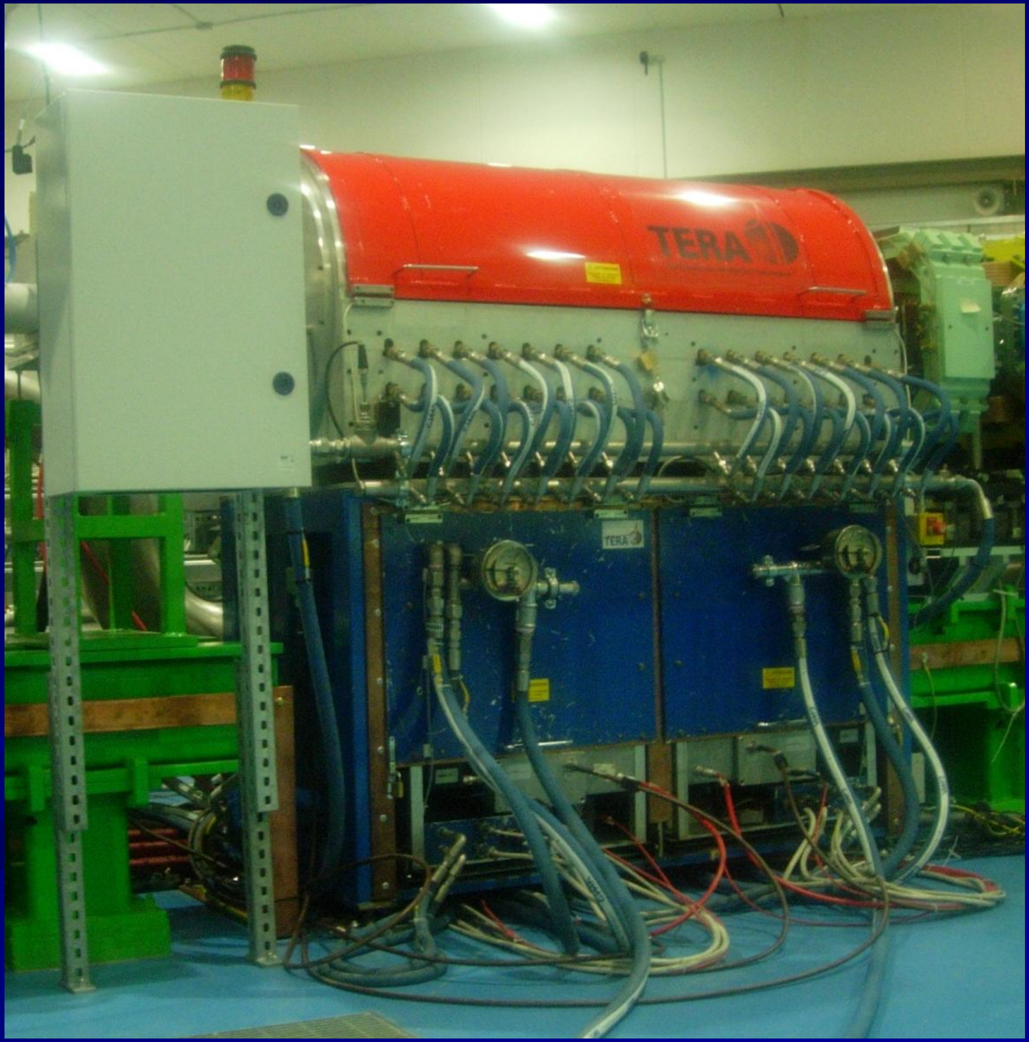
Injection Betatron Rf cavity Extraction Electrostatic septum



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

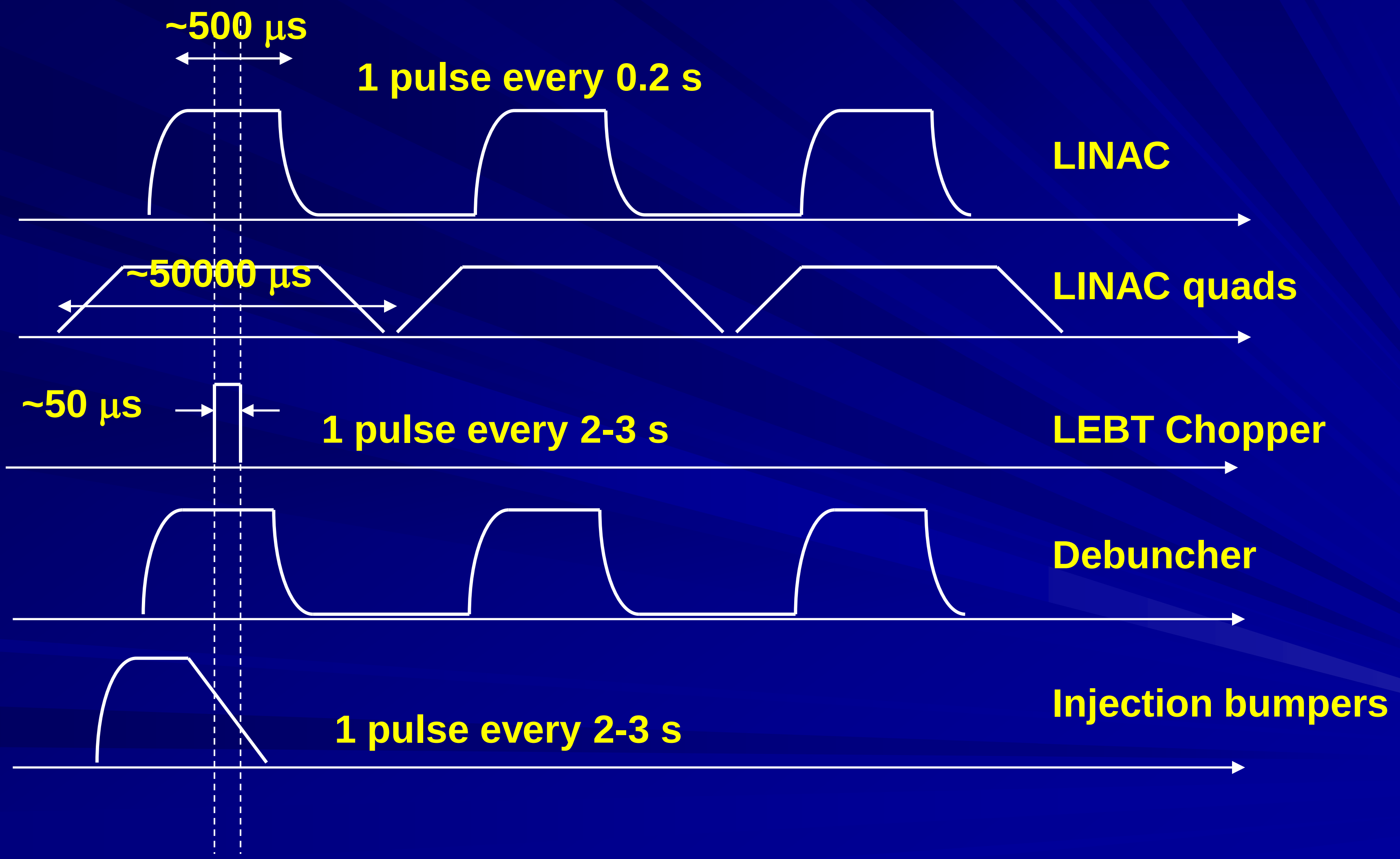
Tetrode pushpull amplifier

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

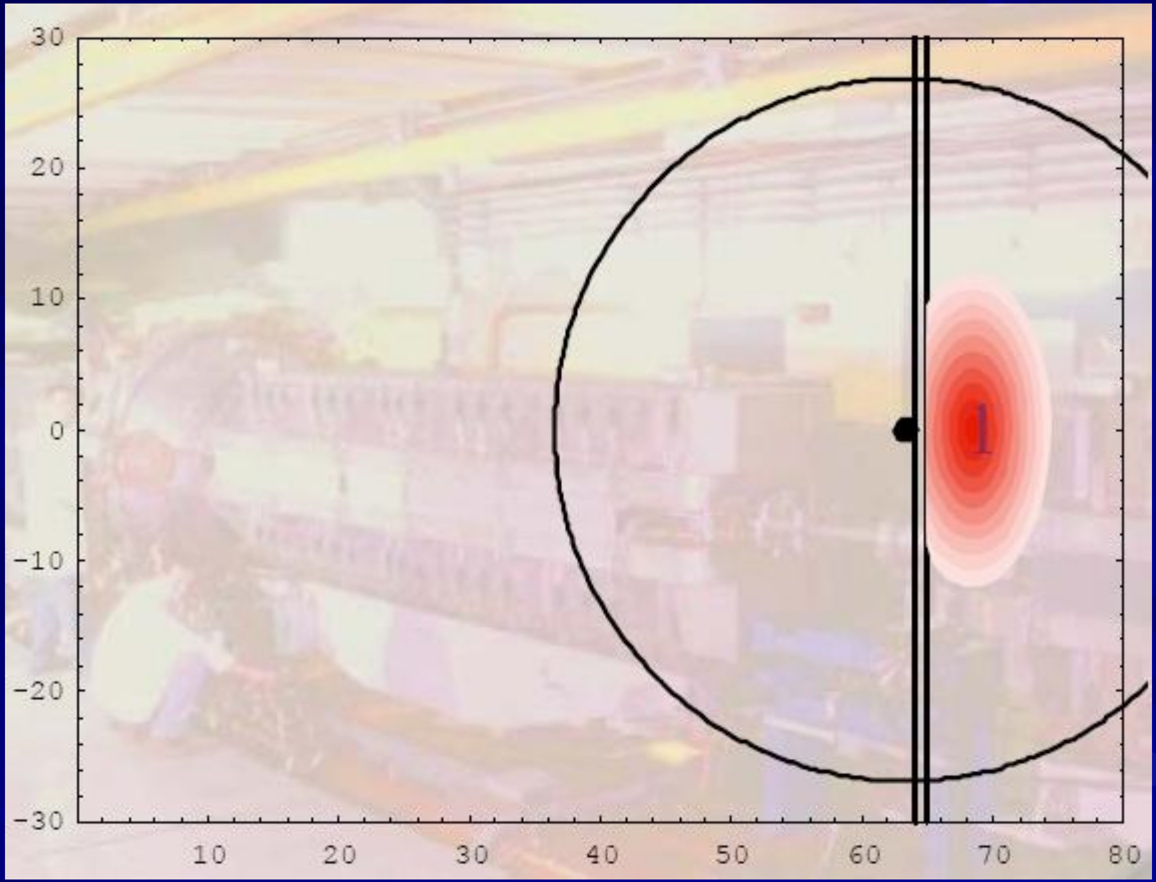
very low current to polarize vitrovac up to 3 MHz (10A)

Peak to Peak Gap Voltage:
40- 8000 V

Injection in time

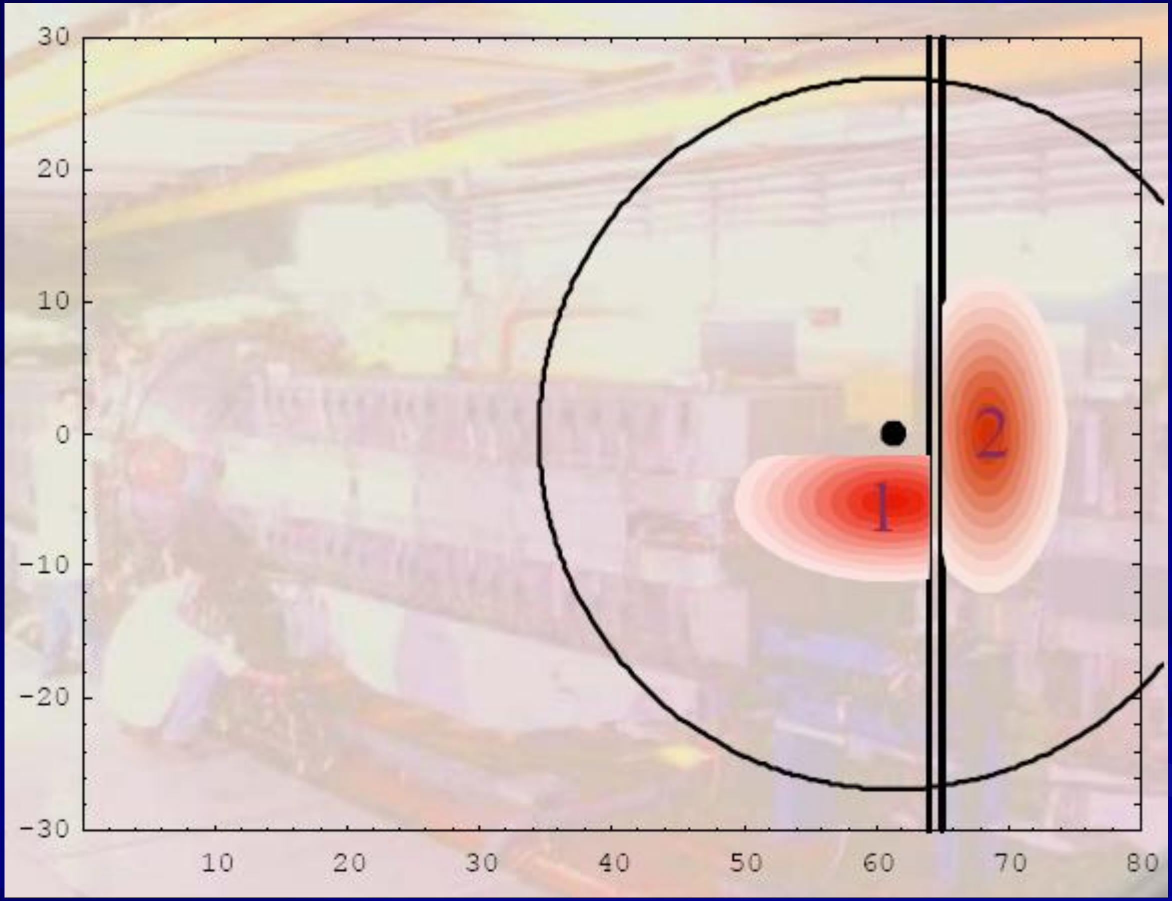


An animated view of injected beam emittance (courtesy of R. Steerenberg)

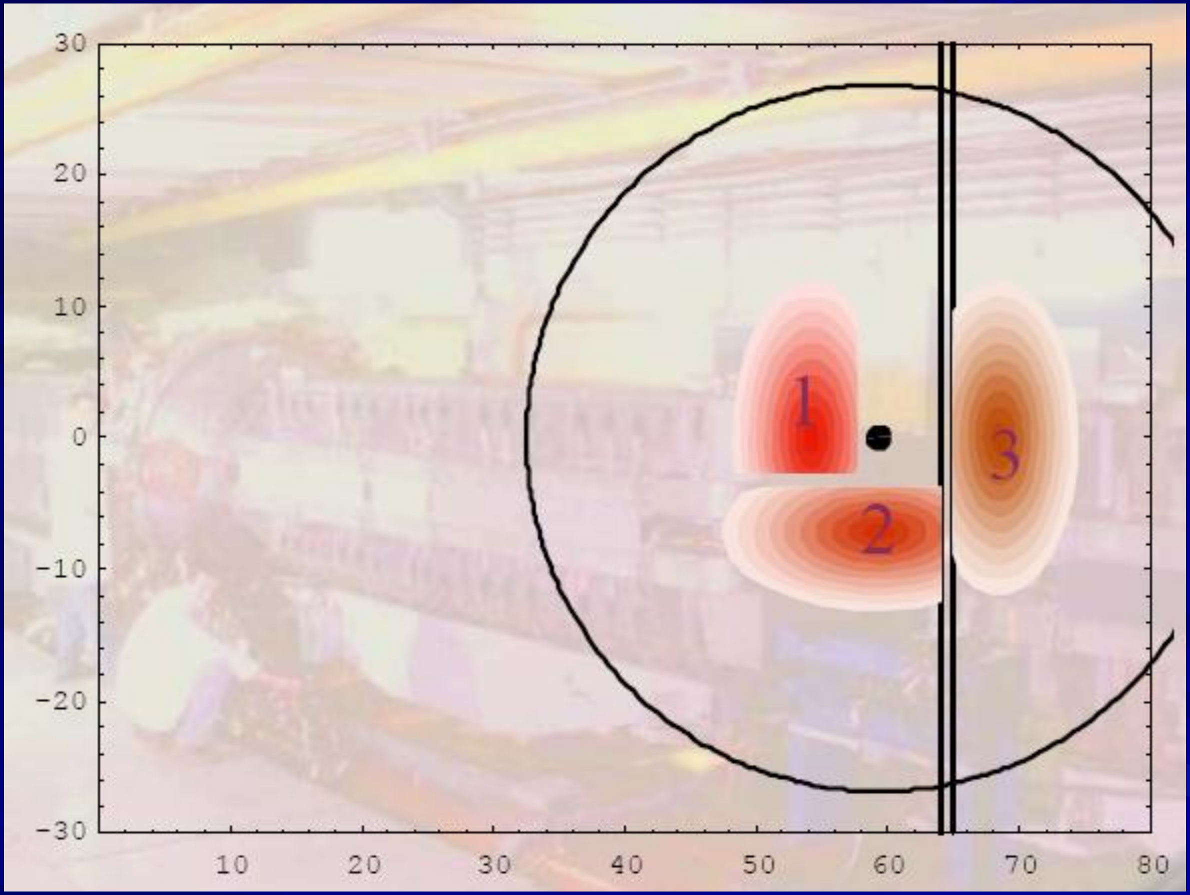


Multiturn injection with injection bumpers,
creating the emittance for slow extraction process

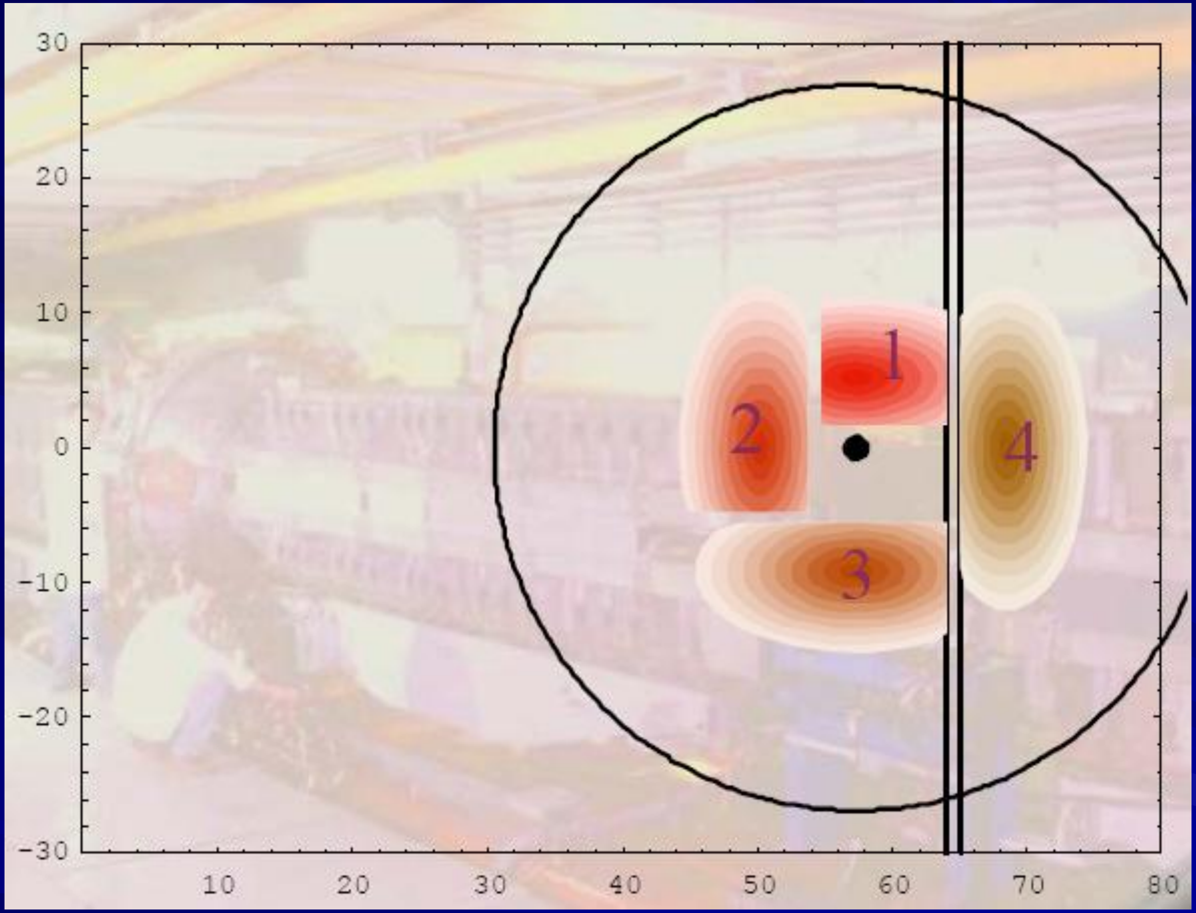
An animated view (courtesy of R. Steerenberg)



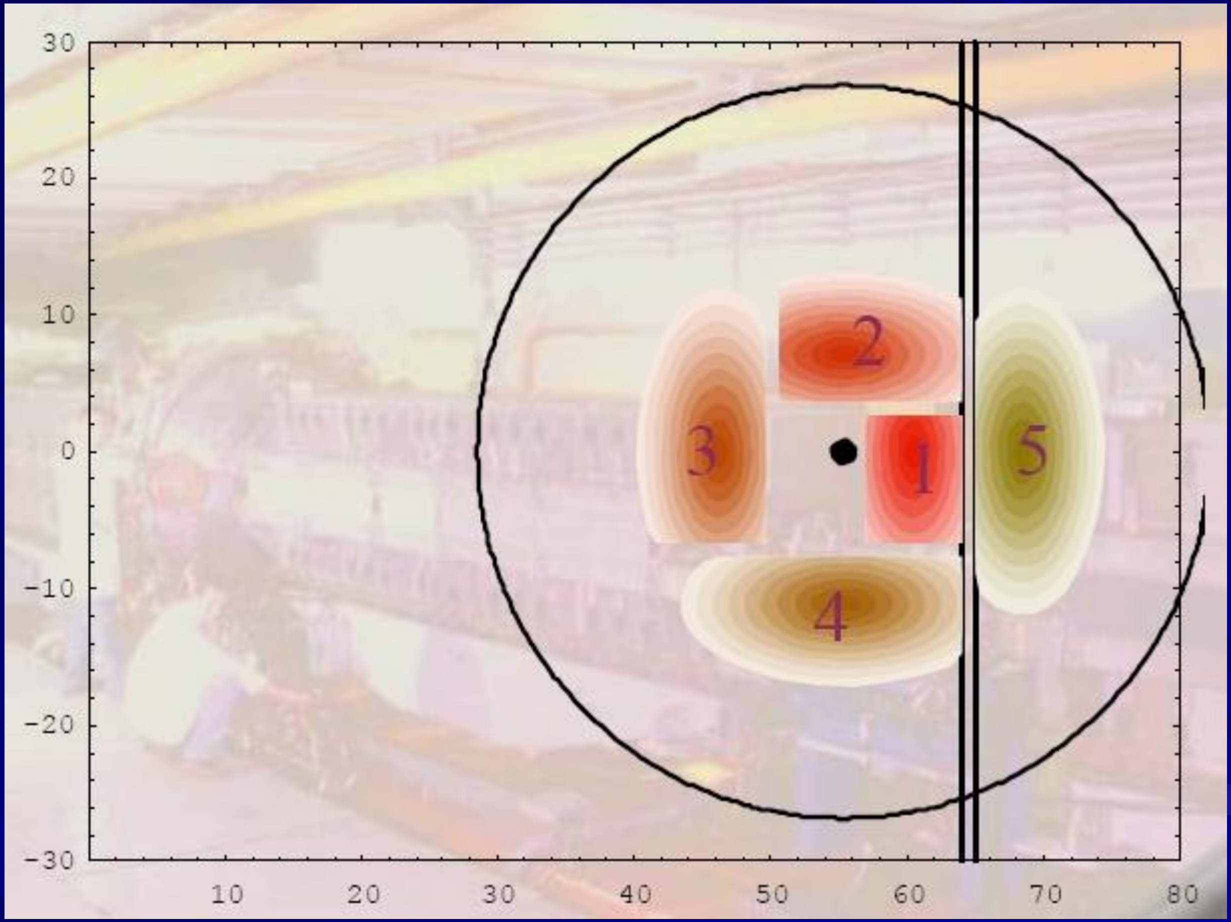
An animated view (courtesy of R. Steerenberg)



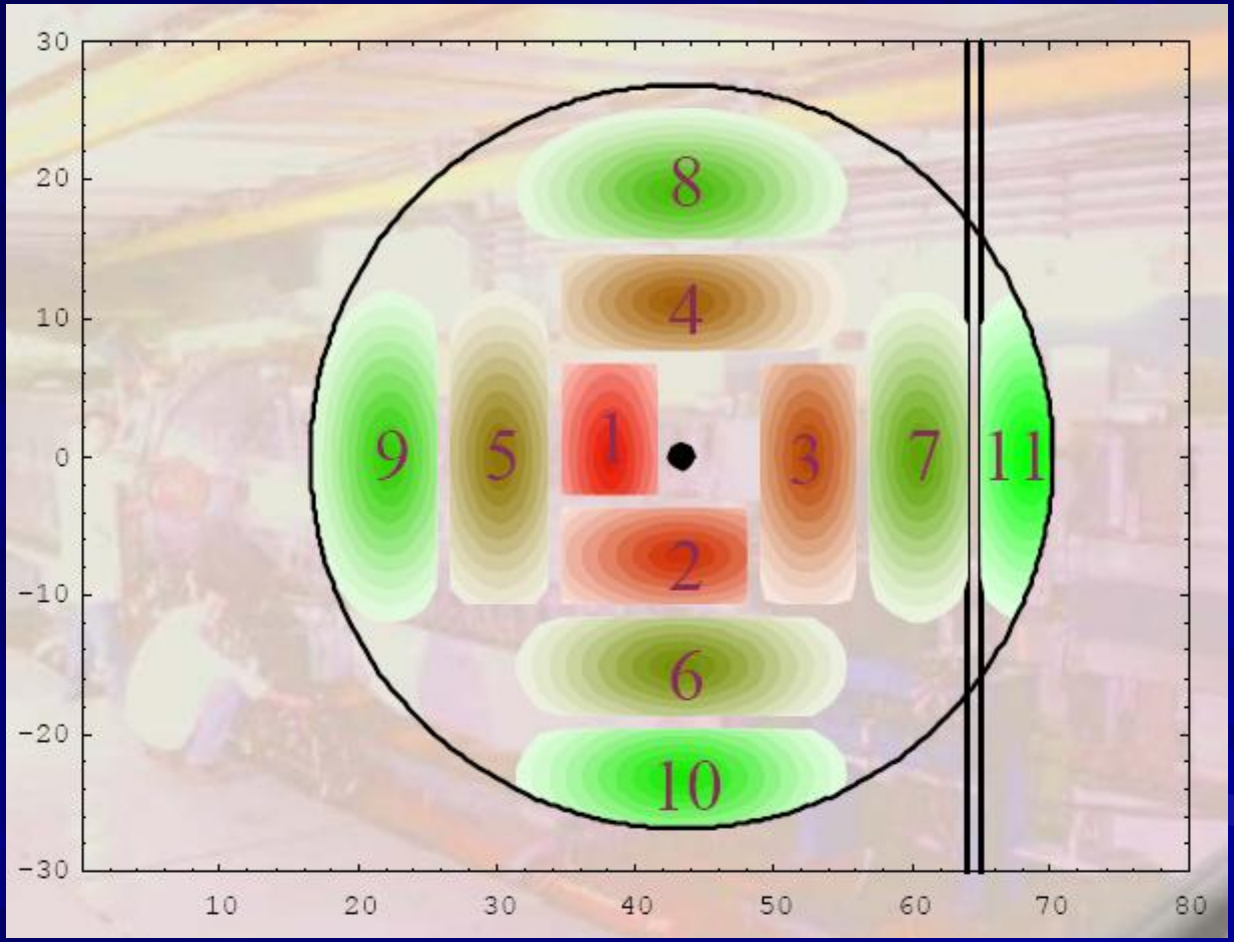
An animated view (courtesy of R. Steerenberg)



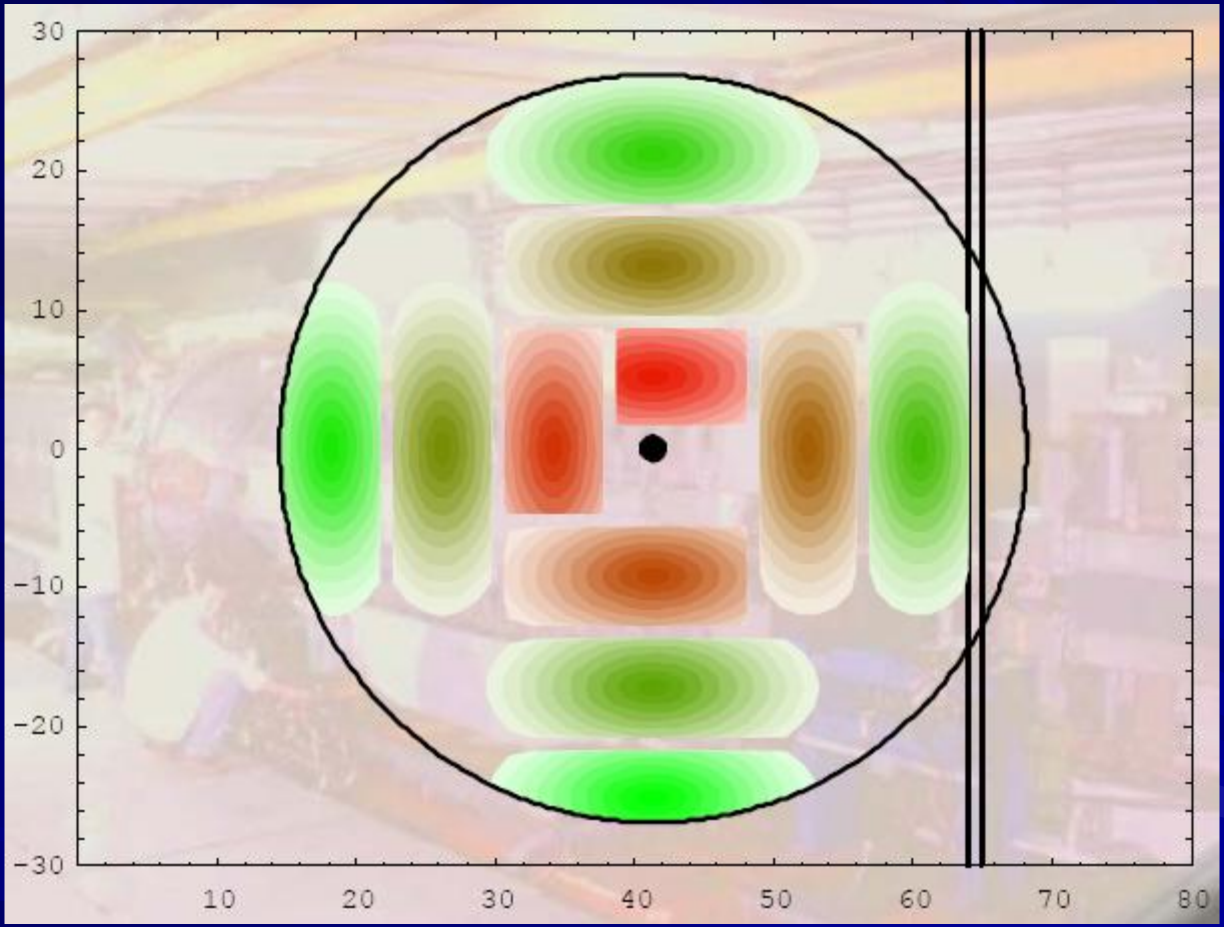
An animated view (courtesy of R. Steerenberg)



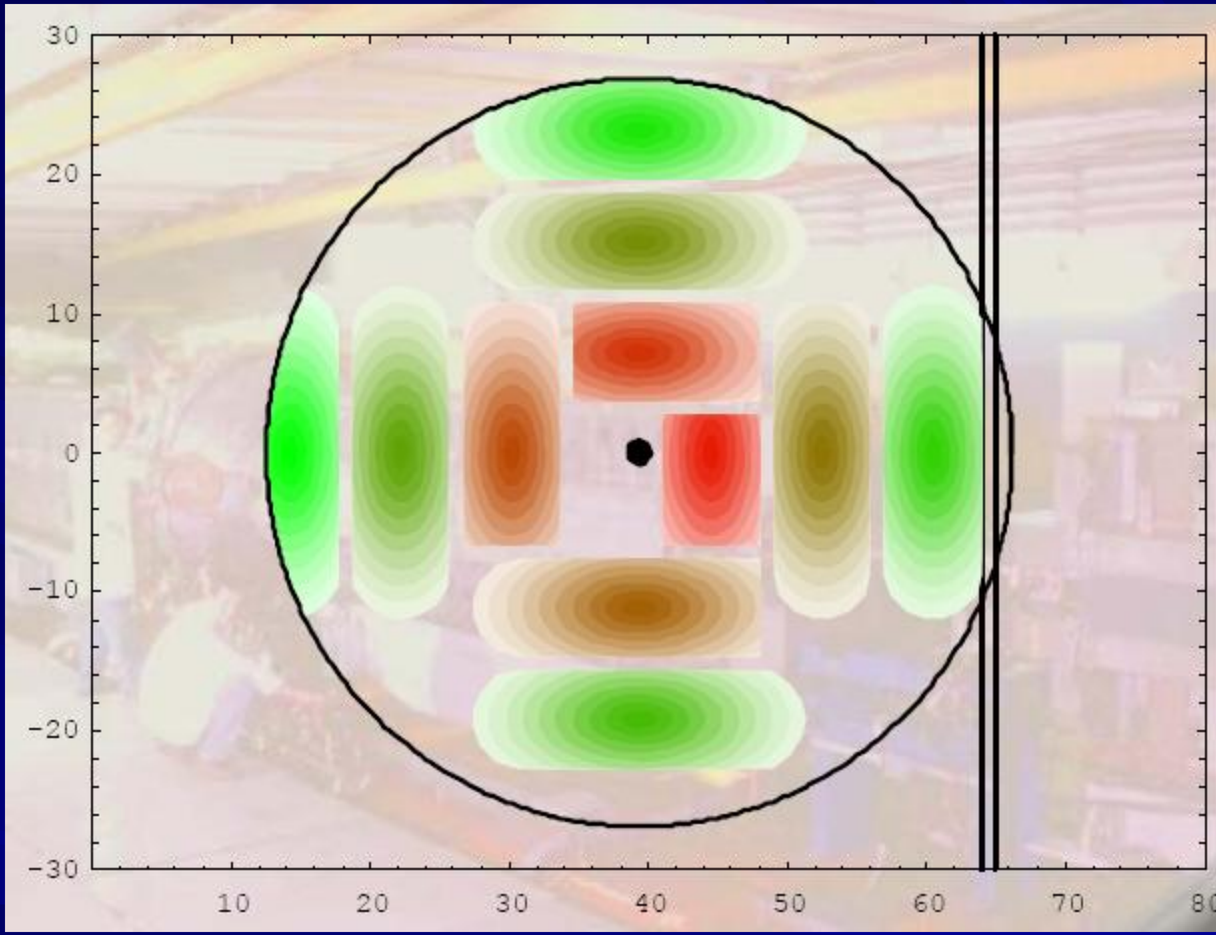
An animated view (courtesy of R. Steerenberg)



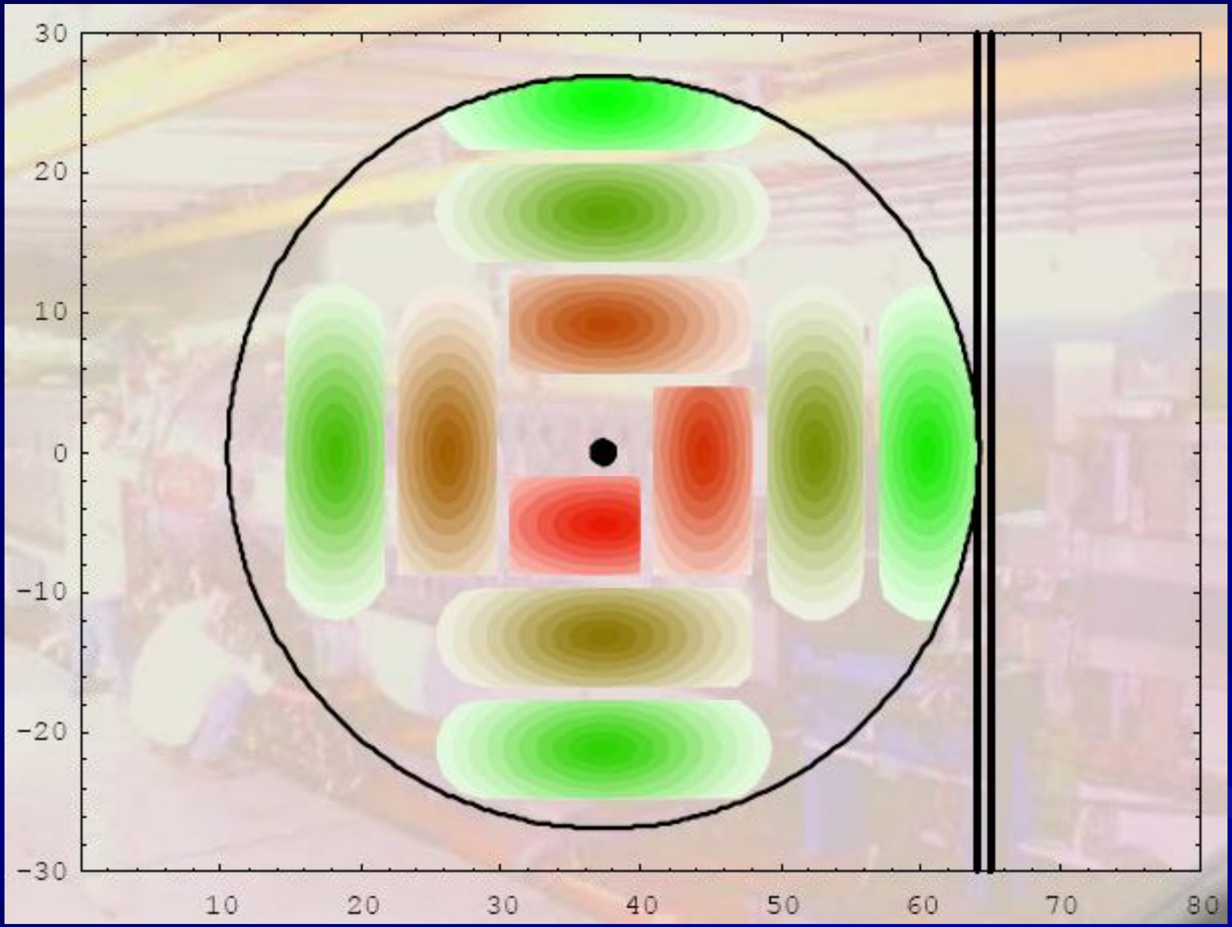
An animated view (courtesy of R. Steerenberg)



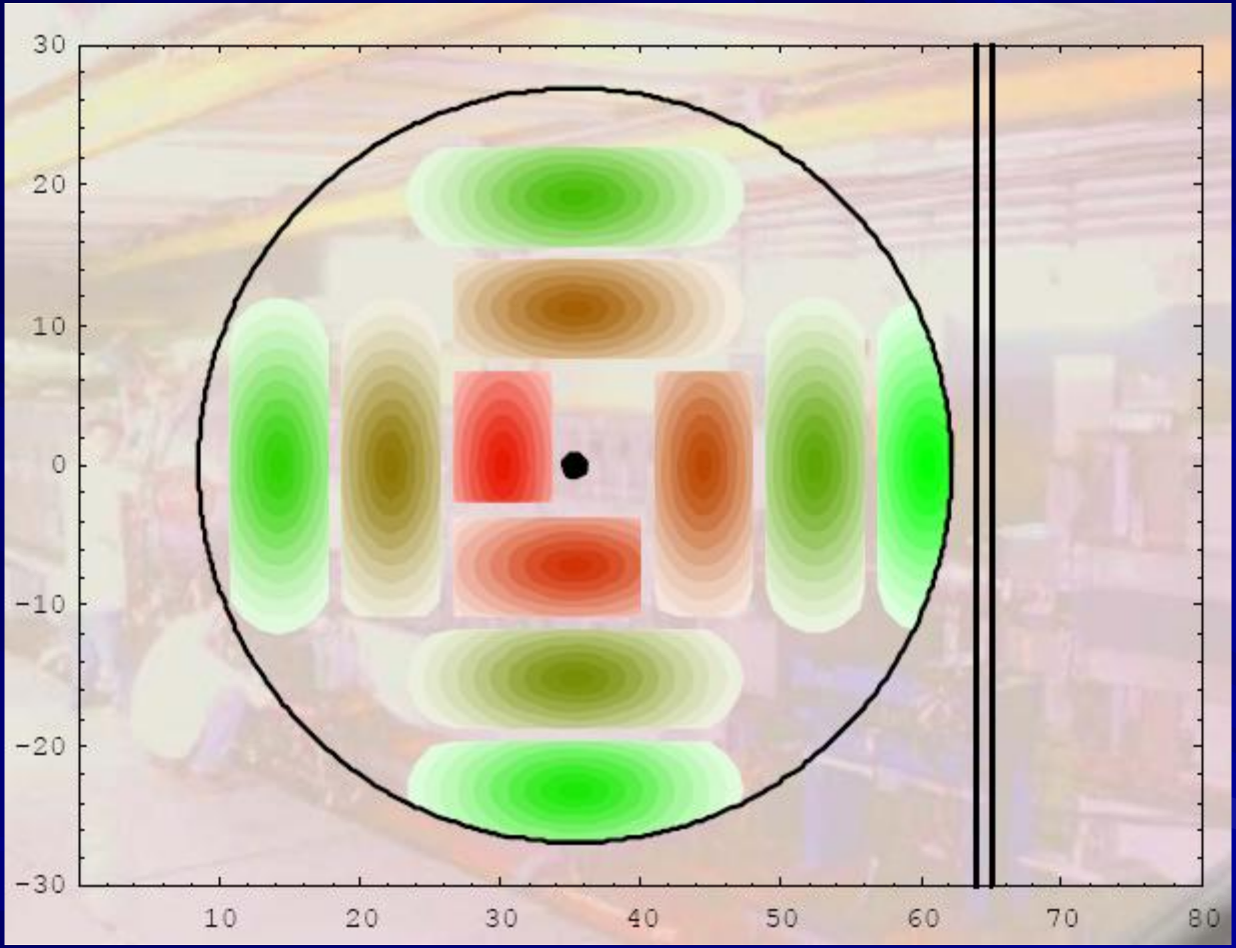
An animated view (courtesy of R. Steerenberg)



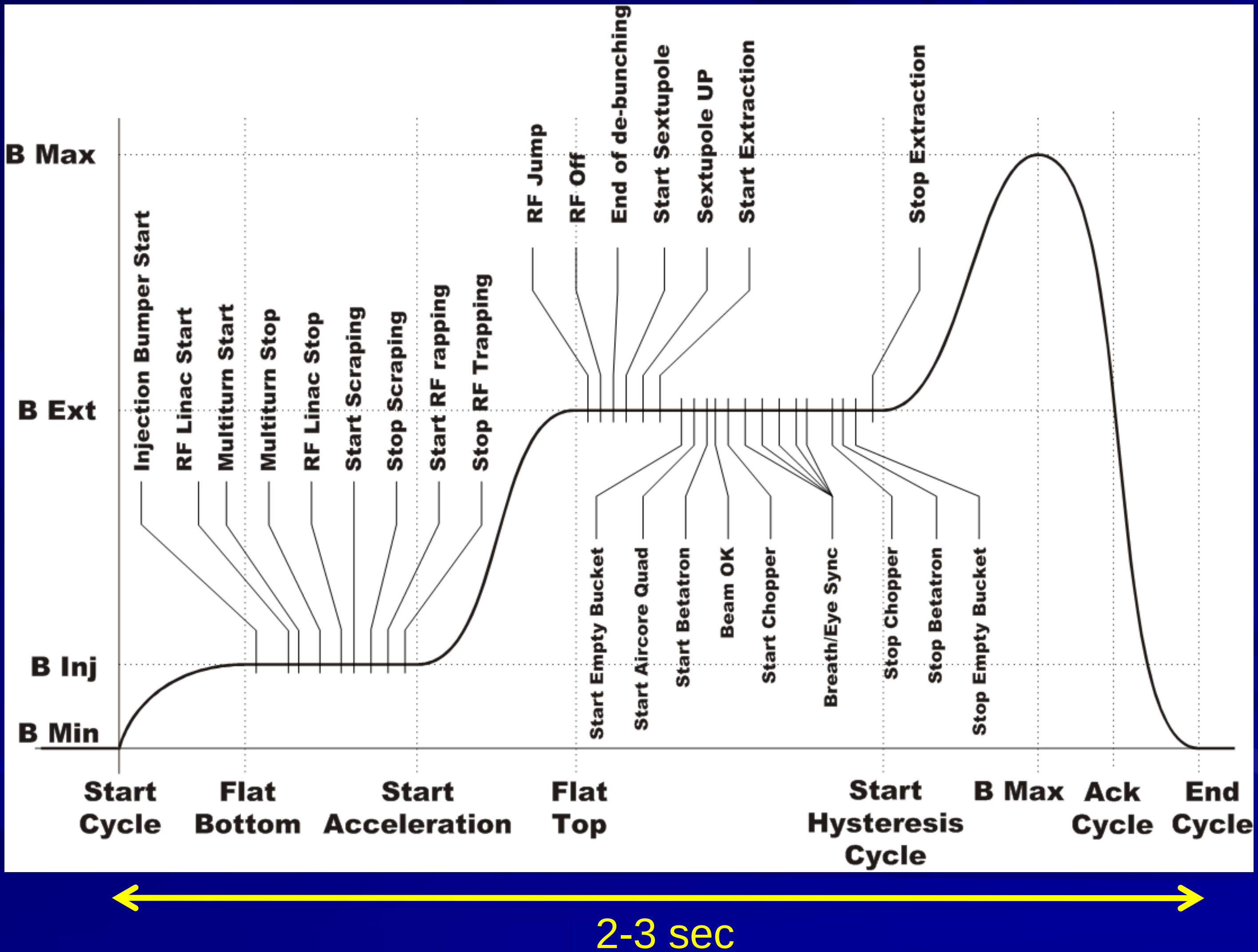
An animated view (courtesy of R. Steerenberg)



An animated view (courtesy of R. Steerenberg)

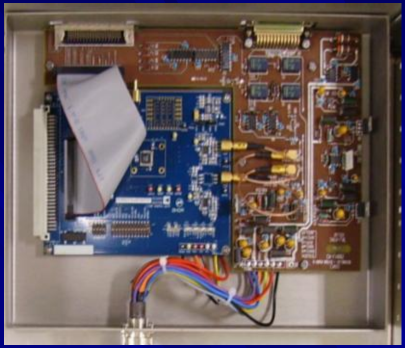


Machine cycle



B-TRAIN

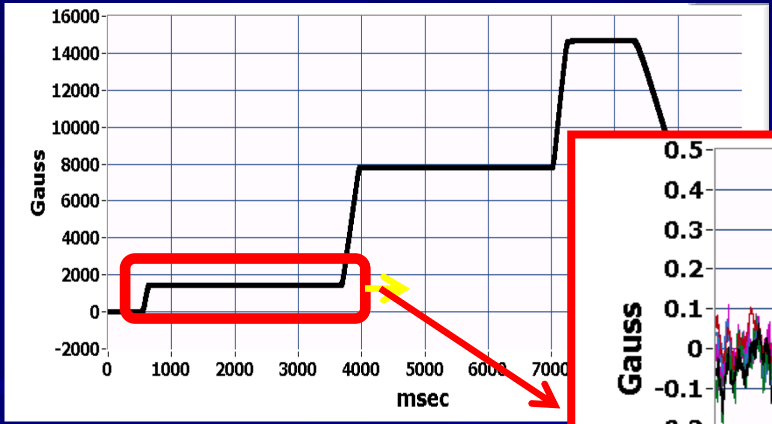
High precision, Analog/Digital measurement system for dipole magnetic field.

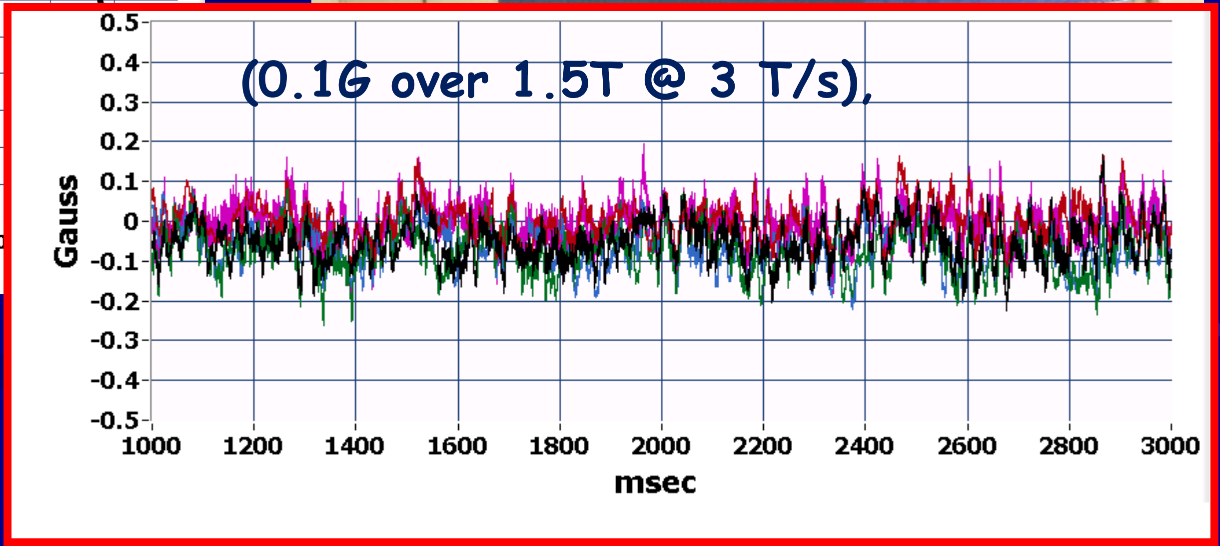


RF, Dump Bumpers and Diagnostics systems use the real-time B-field measurements to track beam energy.

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



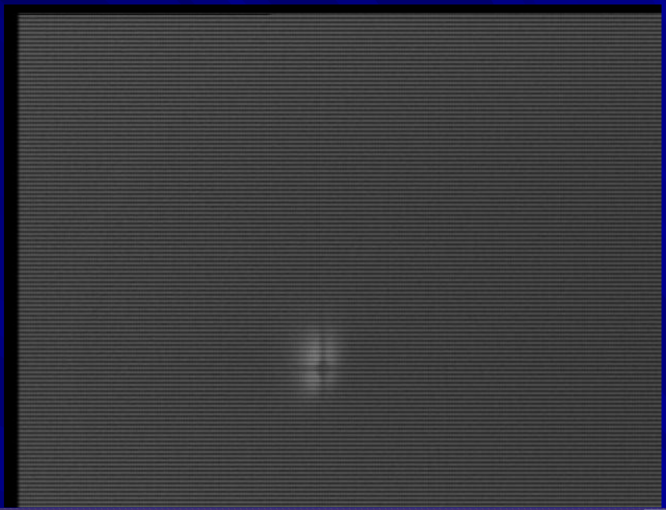


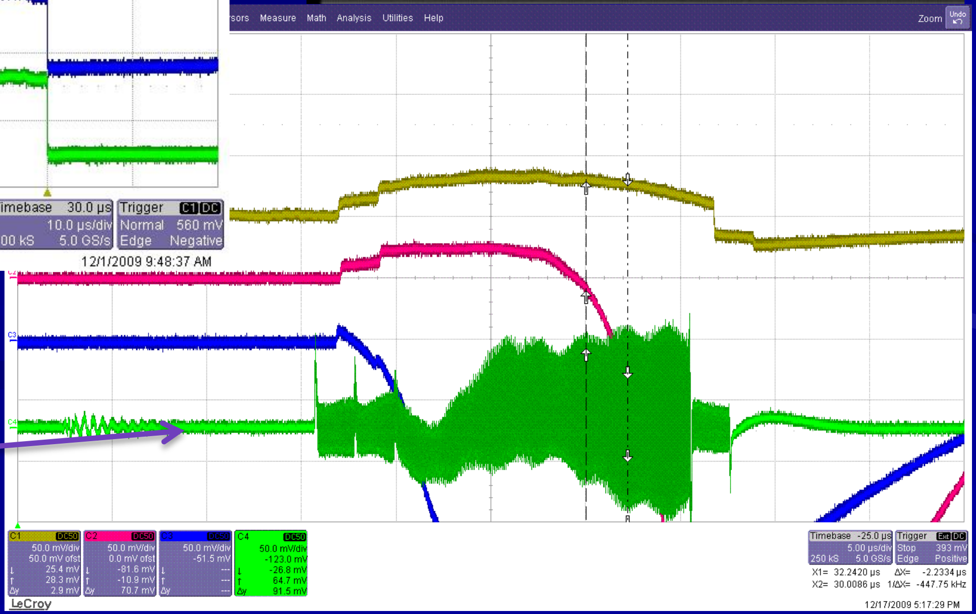
Measurements of typical magnetic cycles have confirmed that B-Train matches specifications

First turn in the synchrotron (end 2009)

TV screen T45→ first turn

Few synchrotron steerers were turned on



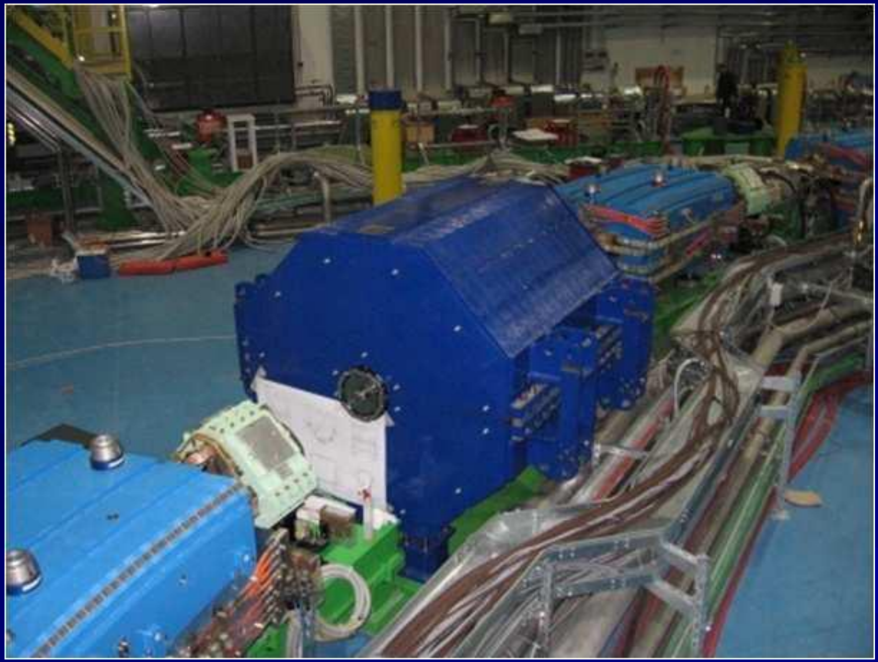


RF cavity effects

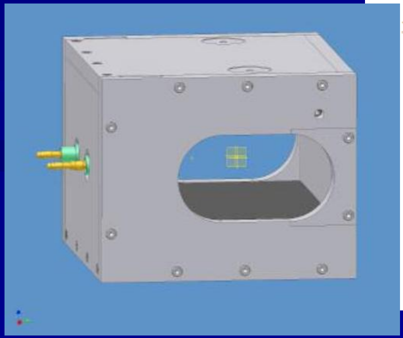
Slow extraction on third order resonance

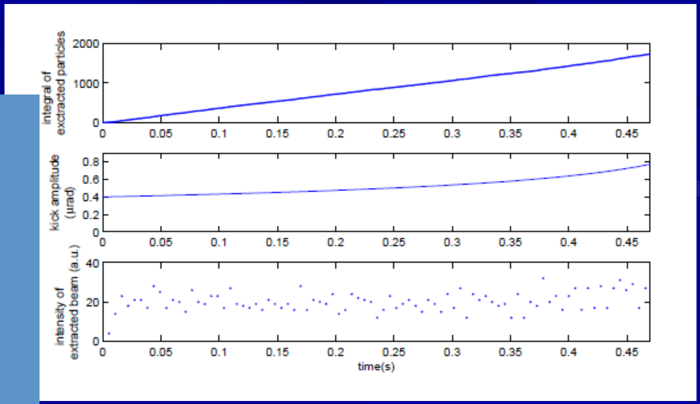
Use of a betatron core and resonance sextupole

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

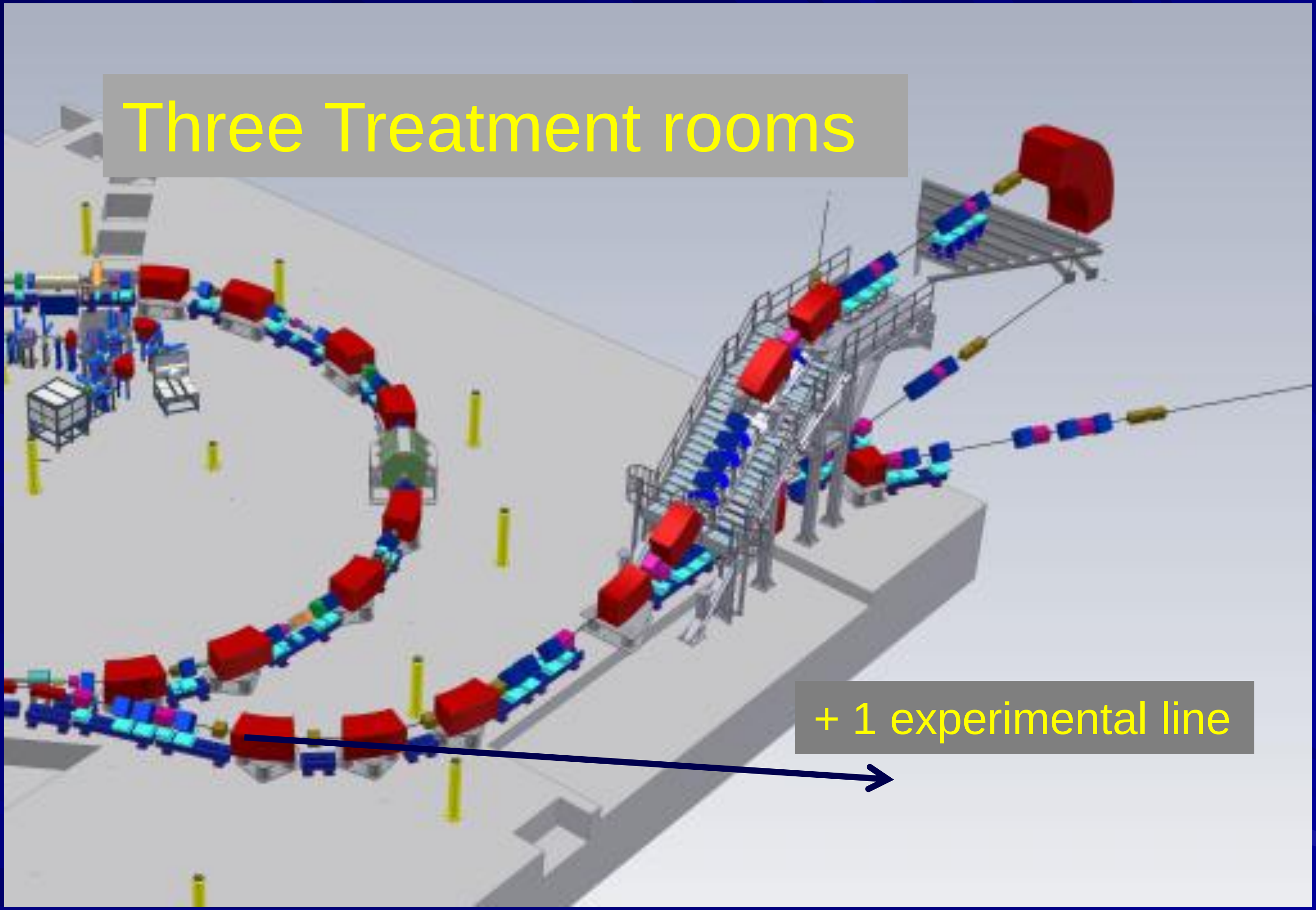


RF-knockout method
foreseen as alternative method
in the future

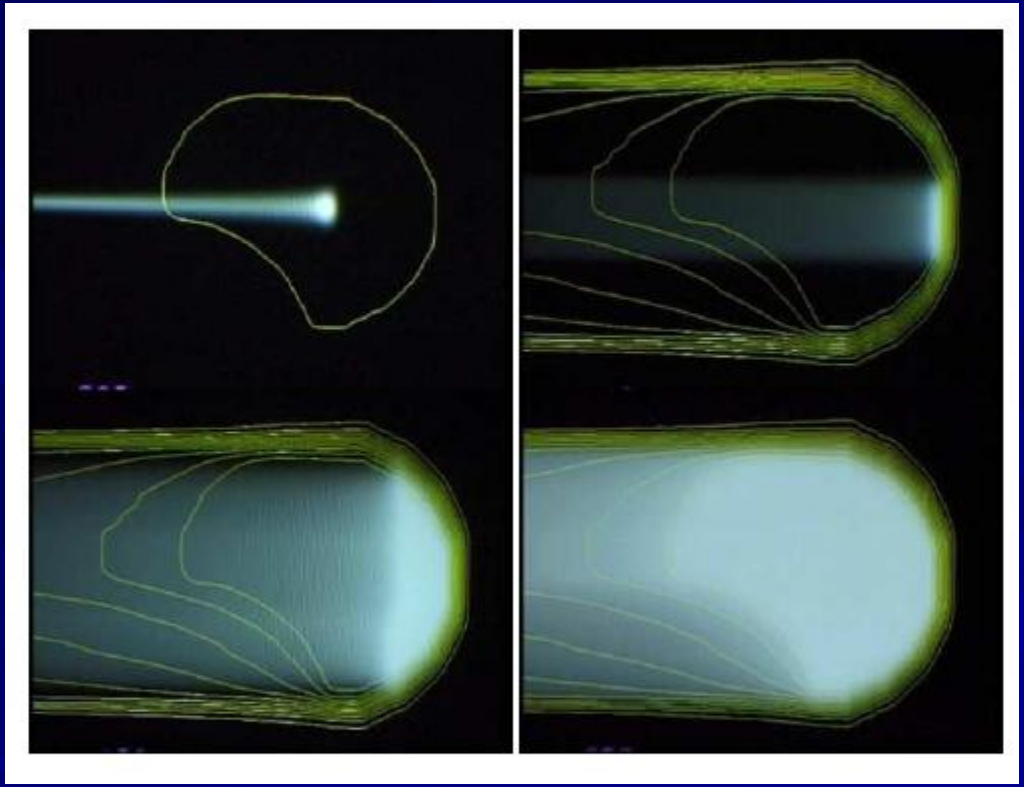




HEBT



Active scanning

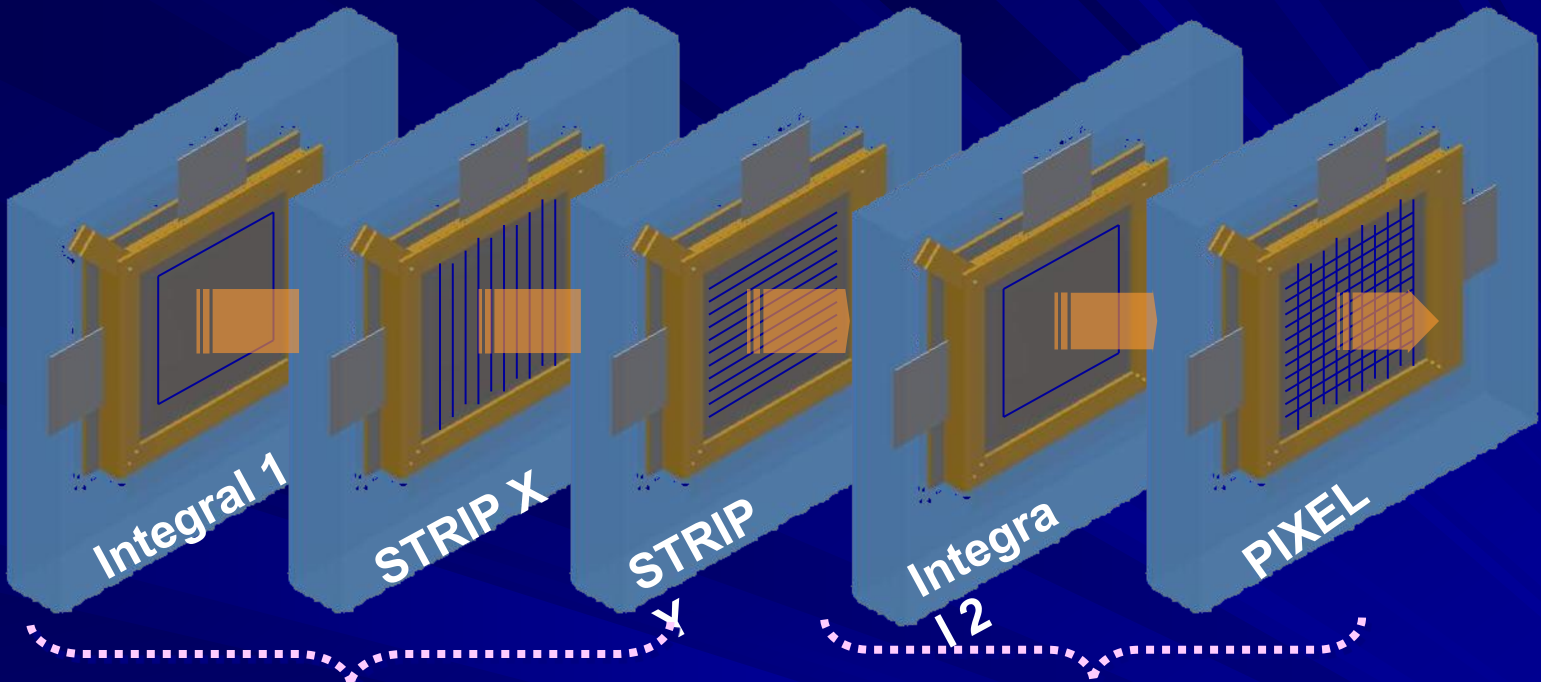


Precise medical imaging

- *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



Box 1

Box 2

1 Integral chamber:

- **Beam Intensity measure every 1 μs**

2 Strip chambers (X and Y):

- **Beam position measure every 100 μs, with 100 μm of precision**

1 Integral chamber:

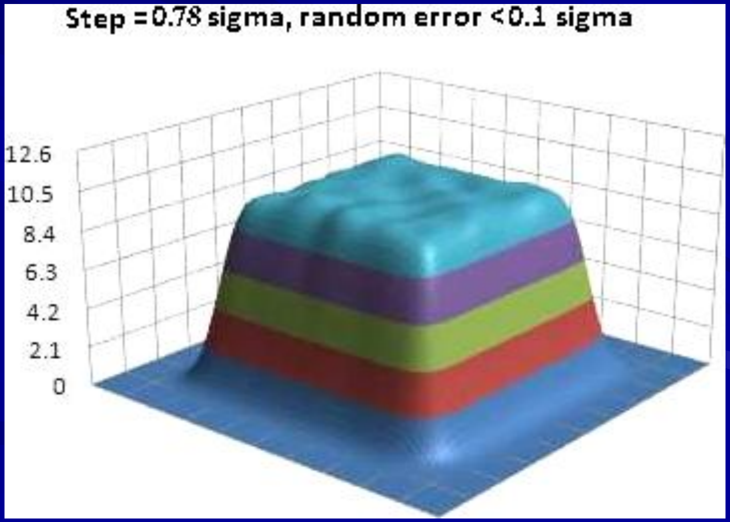
- **Beam Intensity measure every 1μs**

1 Pixel chamber:

- **Beam position and dimension measure every 100 μs/1 ms, with 200 μm of precision**

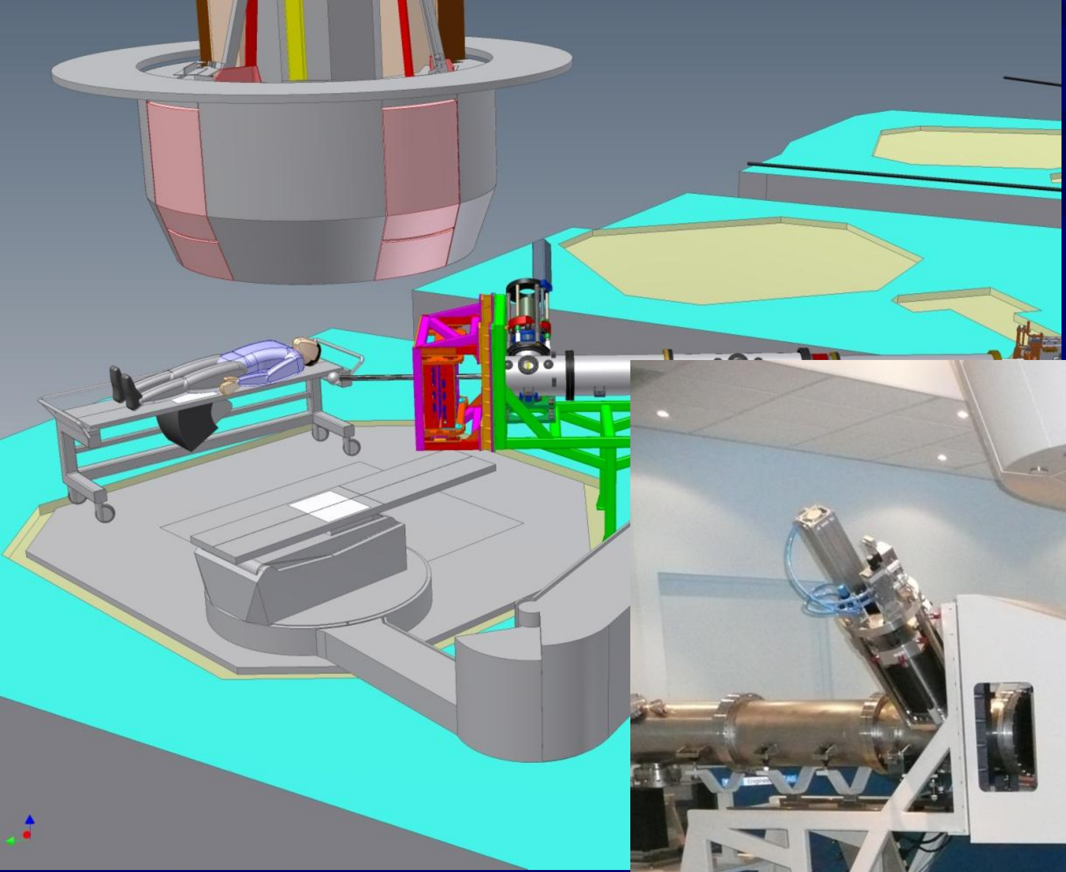
Typical parameters for treatments

Spill characteristics
Energy range : 60-250 (p) 120-430 (C)
Field size : 200 x 200 mm x mm
Particles per spill : 4 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*.1σ in the position of* the Gaussians yields a dose error > ±*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 .

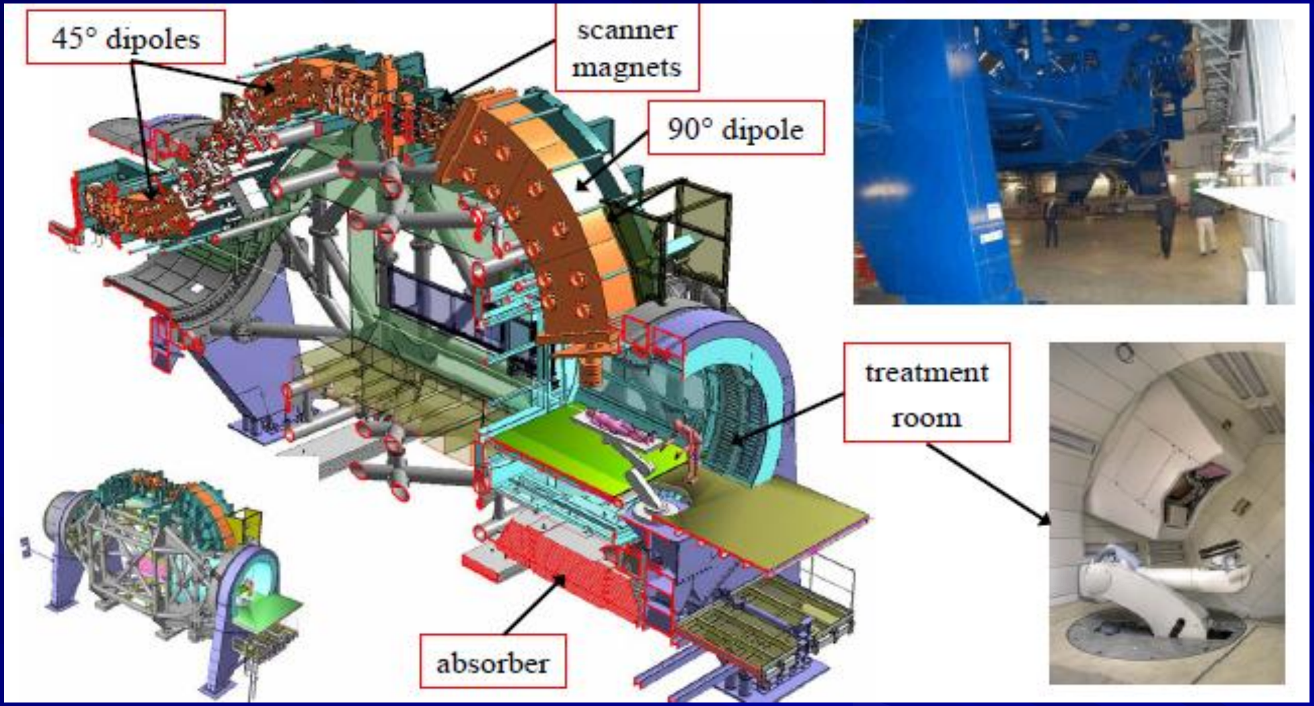
* JRA - development of instruments and protocols: new **gantry design**, improvement of **four-dimensional particle beam delivery**, adaptive treatment planning, mechanisms for patient selection to the whole European Community and database development for specific tumours which can best be treated using 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 m x ϕ = 13 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

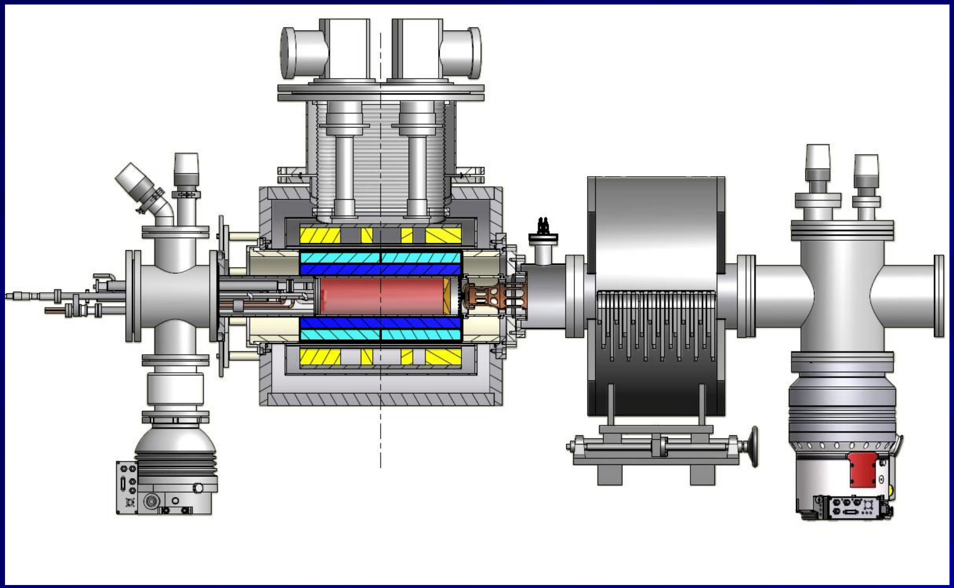
Aspects being considered in new Gantry design

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

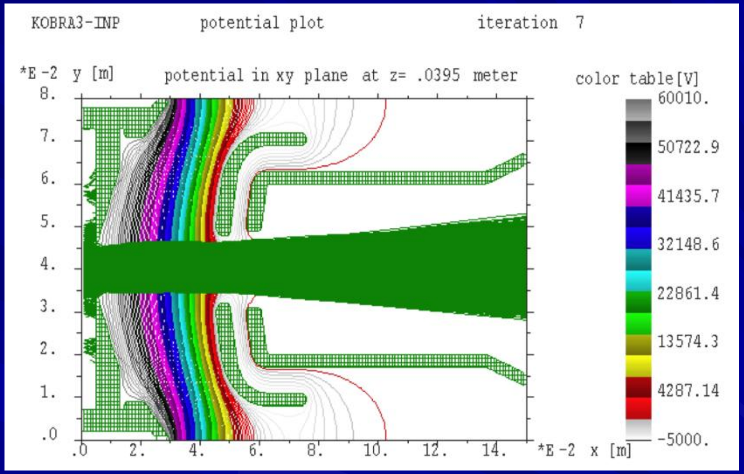
MISHA: Multicharged Ion Source for Hadrontherapy

2.5 generation

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



Higher currents
Lower emittances
Optimised for multispecies



Ion trajectories
(KOBRA simulations)

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

CDR ready

G. Ciavola et al.

fondazioneCNAO

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

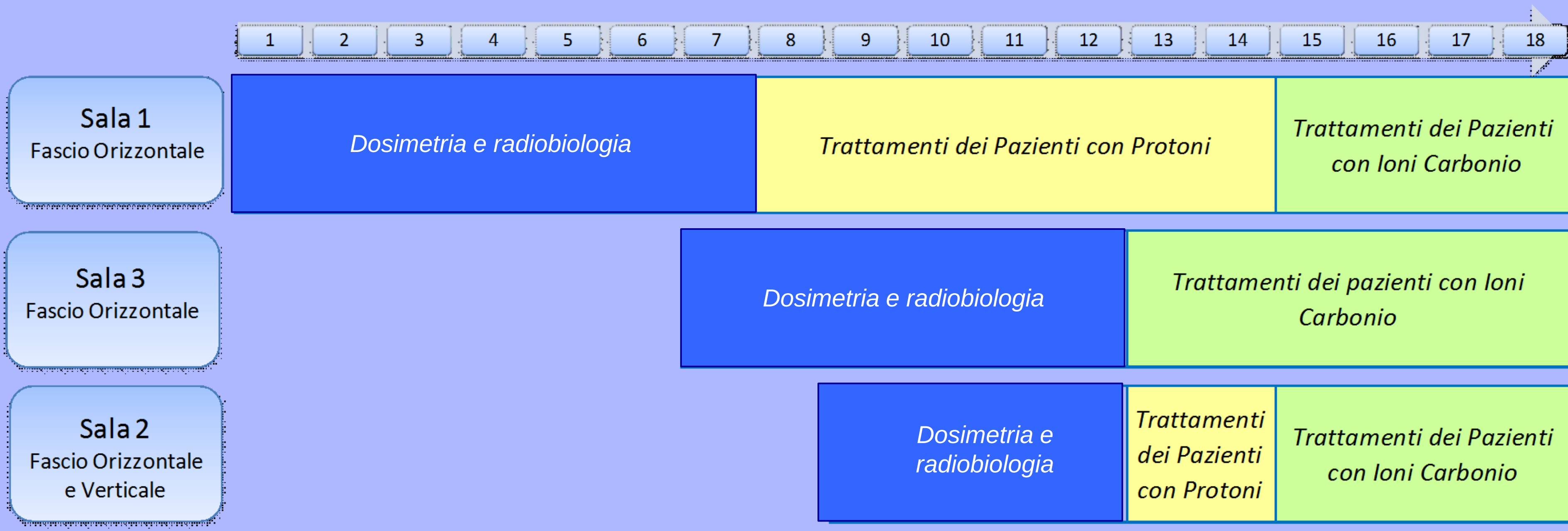
Presented to:

- 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