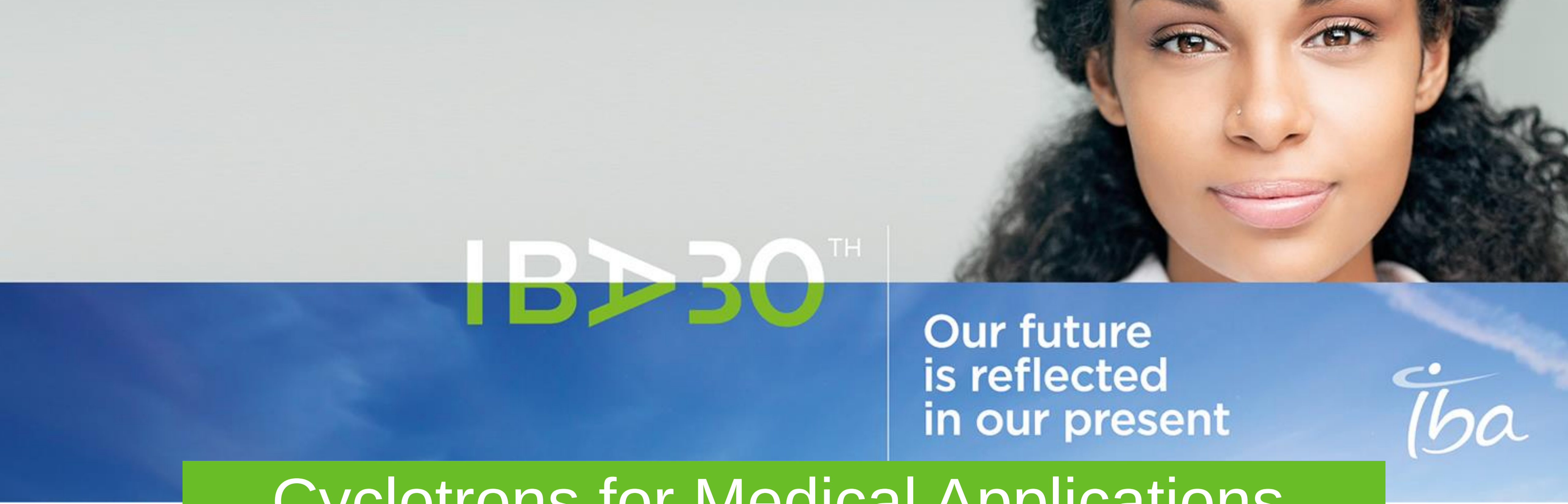

Cyclotrons for Medical Applications

Eric Forton

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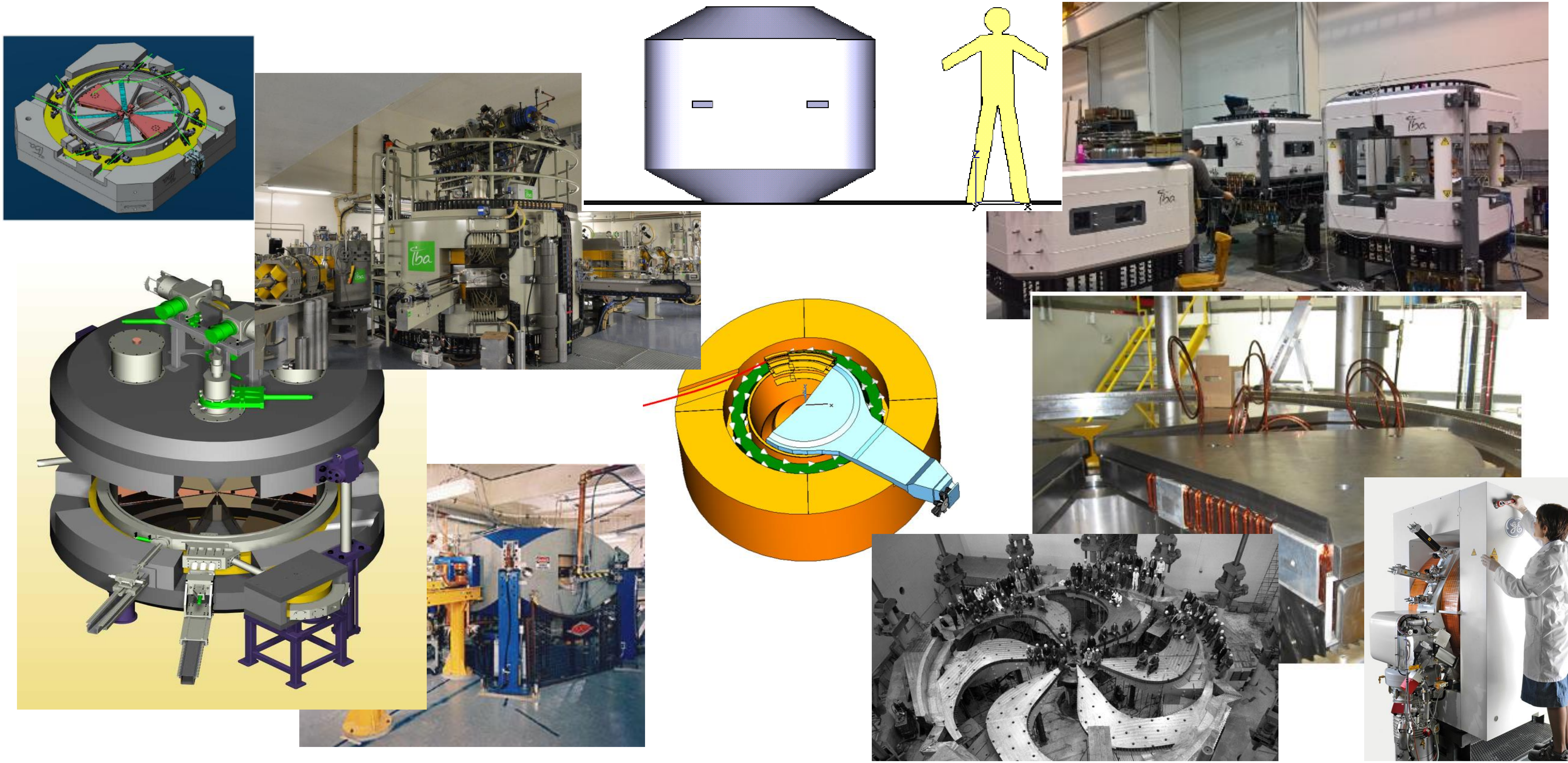
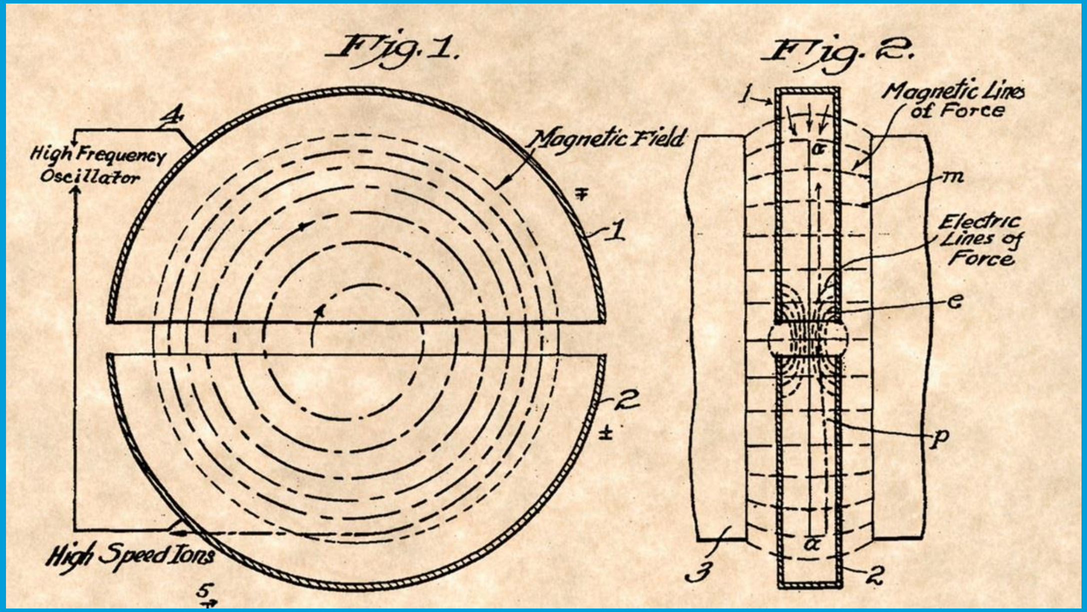
Various shapes, field levels, energies, beam currents…



Outline

- Introduction to cyclotrons
- Production
- Radioisotope production
- Therapy



Cyclotrons

Basic principles

and design considerations

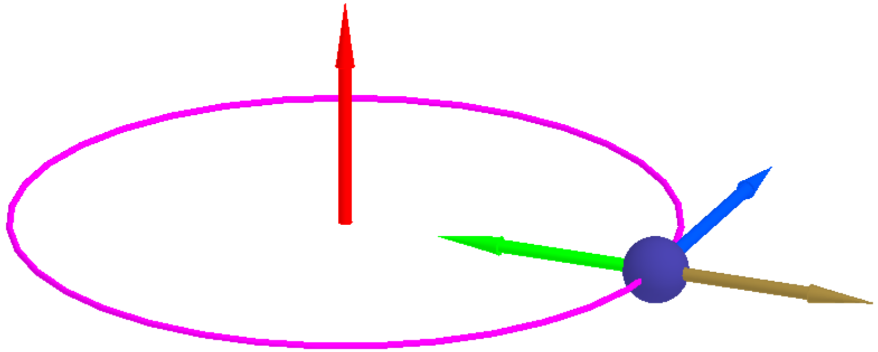
For (much) more details, see W. Kleeven and S. Zaremba,

CAS 2015 in Vösendorf, Austria

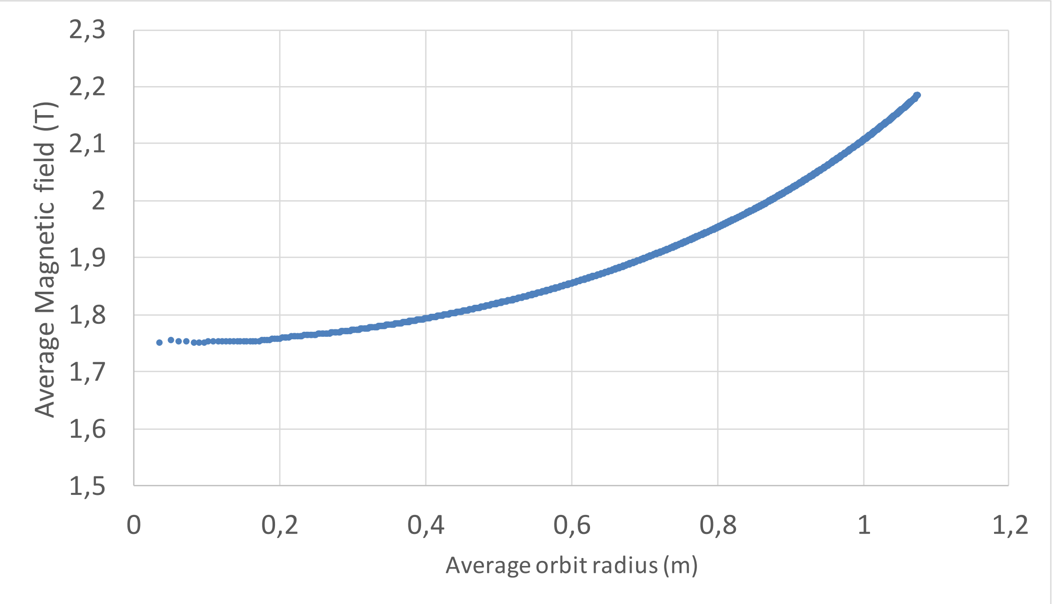
Cyclotrons basic principles: orbit and frequency

- If you neglect relativistic effects, a charged particle in magnetic field orbits at a constant frequency

$$f_p = \omega / 2\pi = q\ B / 2\pi\ m$$



- But that approximation is valid for a few MeV only.
- For PT, at 230 MeV protons travel at 0.6 c => m= 1.24 m_0
- As a consequence, B field increases with radius in isochronous cyclotrons



Cyclotrons basic principles – weak focusing

$$\nu_r^2 = 1 + \frac{r}{B} \, dB\!/\!_{dr}$$

$$\nu_z^2 = -\frac{r}{B} \, dB\!/\!_{dr}$$

The magnetic field diminishing with radius (*$dB_z/dr < 0$*) is focusing in the axial/vertical plane. This is a principle of so called *weak focusing* of particles.

Weak focusing is in contradiction with isochronism conditions that require the magnetic field increasing with radius (dBz/dr > 0) to keep the synchronism with the RF accelerating system

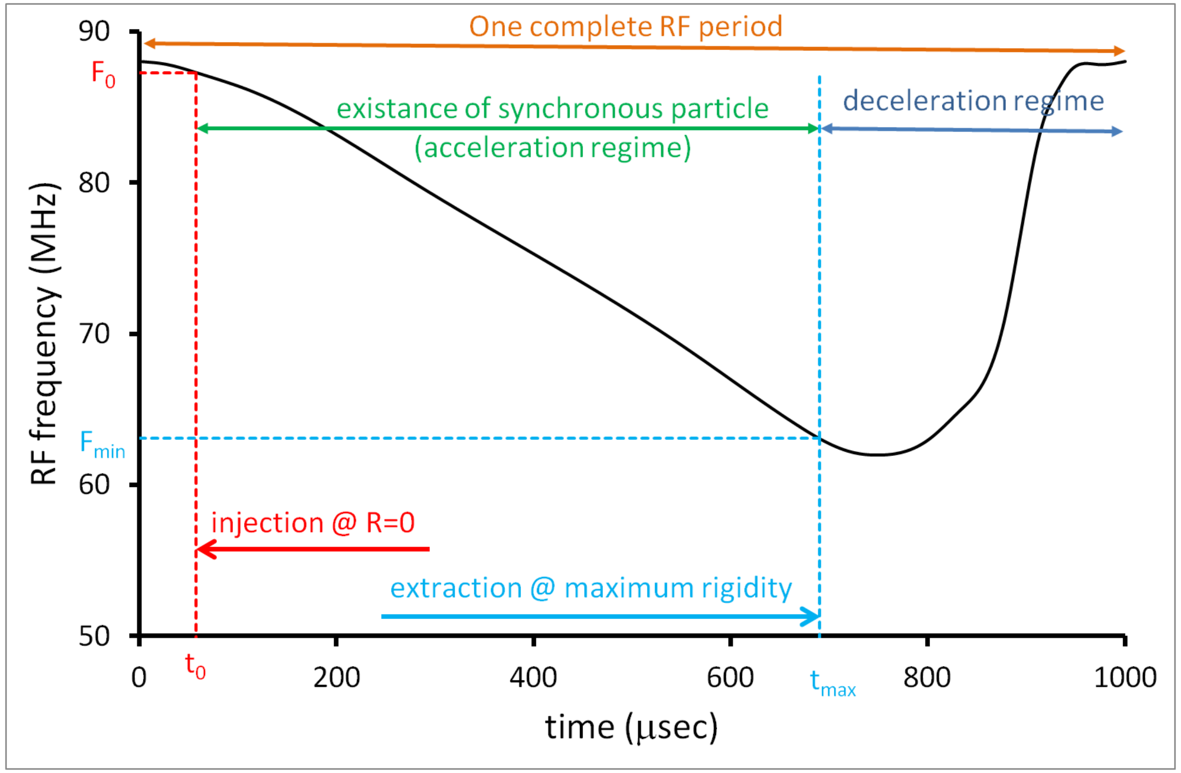
→

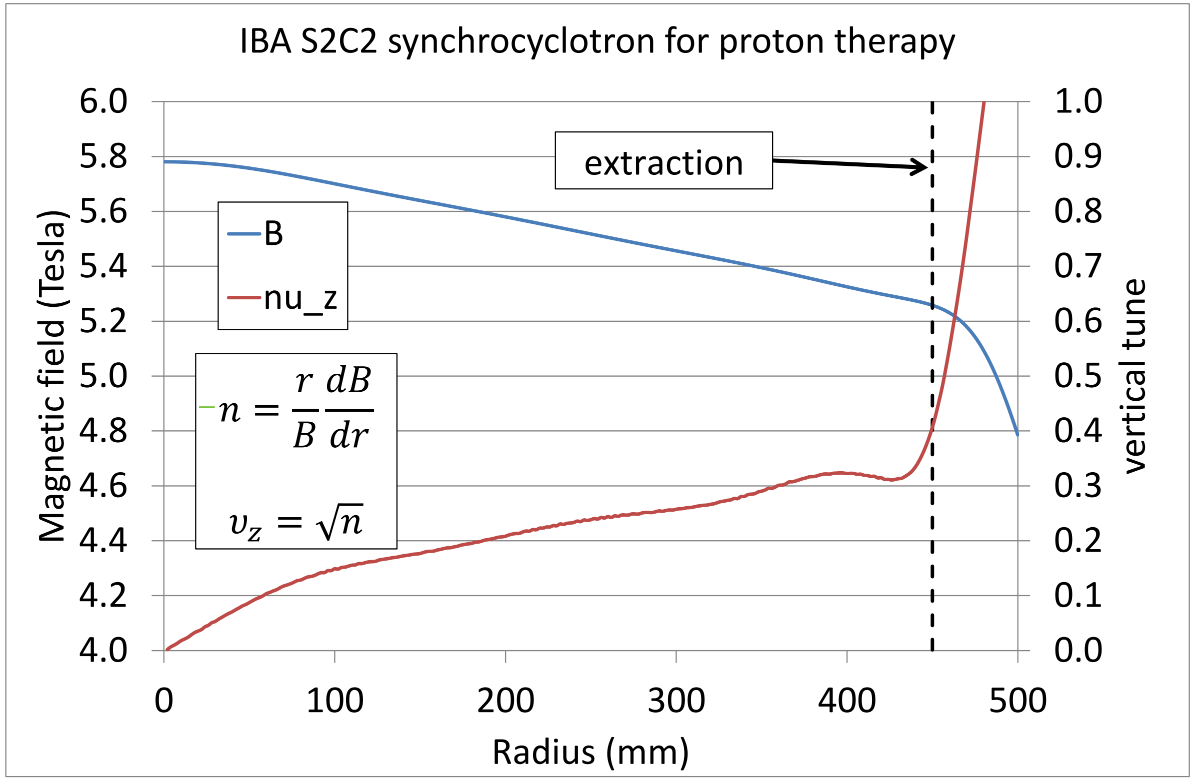
Synchrocyclotrons

forget isochronism => pulsed beam, high rep. Rate – use the low duty factor to do other things in between

Good point: longitudinal beam stability

Synchrocyclotron example (IBA S2C2)





Repetition rate = 1 kHz

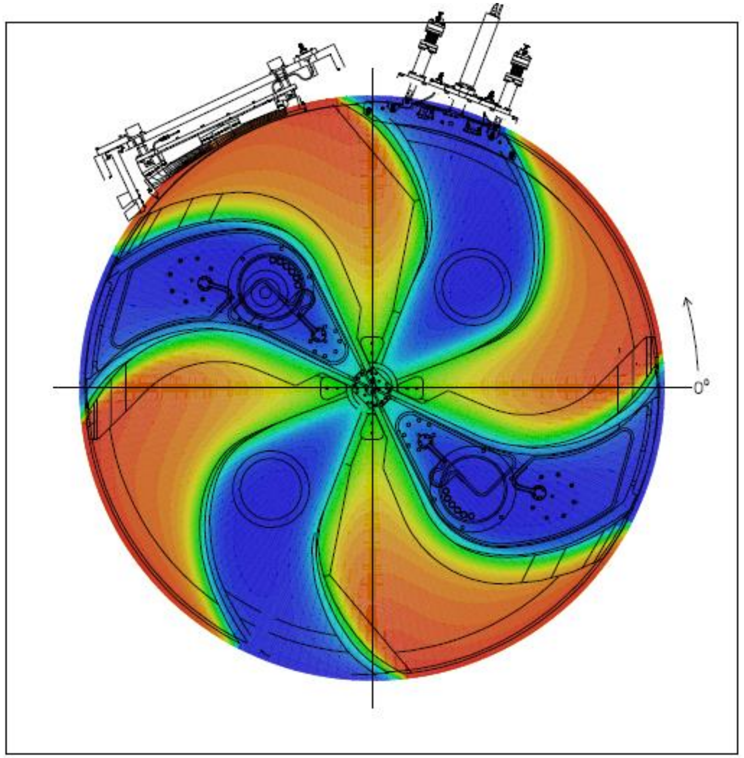
Superconducting synchro-cyclotron
Extraction energy 230 MeV

Cyclotron basic principles: strong focusing

- Flutter: $F(r) = \dfrac{\overline{B^2} - \bar{B}^2}{\bar{B}^2}$

$$\nu_z{}^2 = n + \frac{N^2}{N^2 - 1} F(1 + 2\tan^2\xi)$$

$$\nu_r{}^2 = (1 - n) + \frac{3N^2}{(N^2 - 1)(N^2 - 4)} F(1 + \tan^2\xi)$$



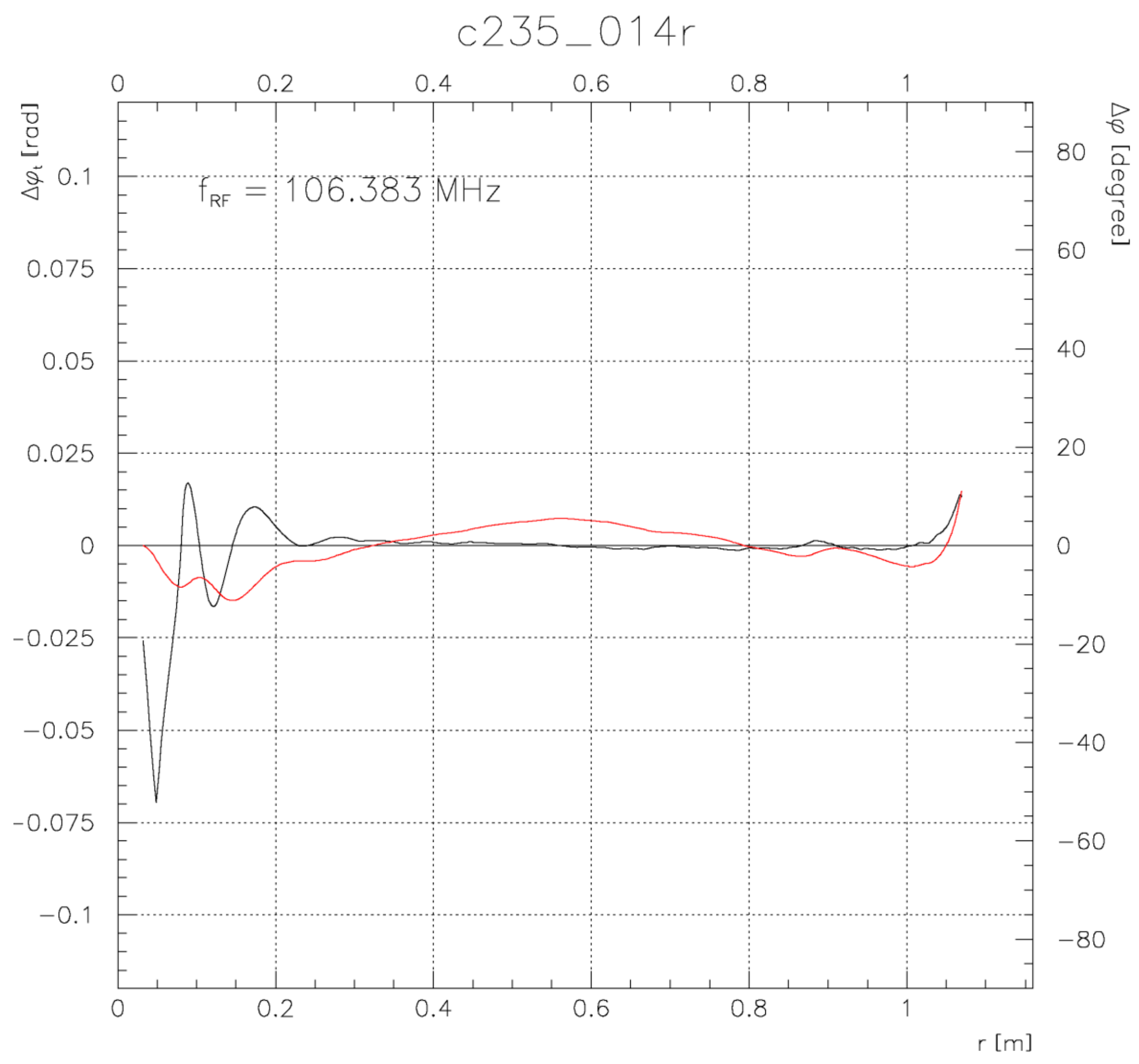
n = field index = $-\frac{r}{\bar{B}}\frac{d\bar{B}}{dr}$
F = flutter
N = number of sectors
ξ = spiral angle

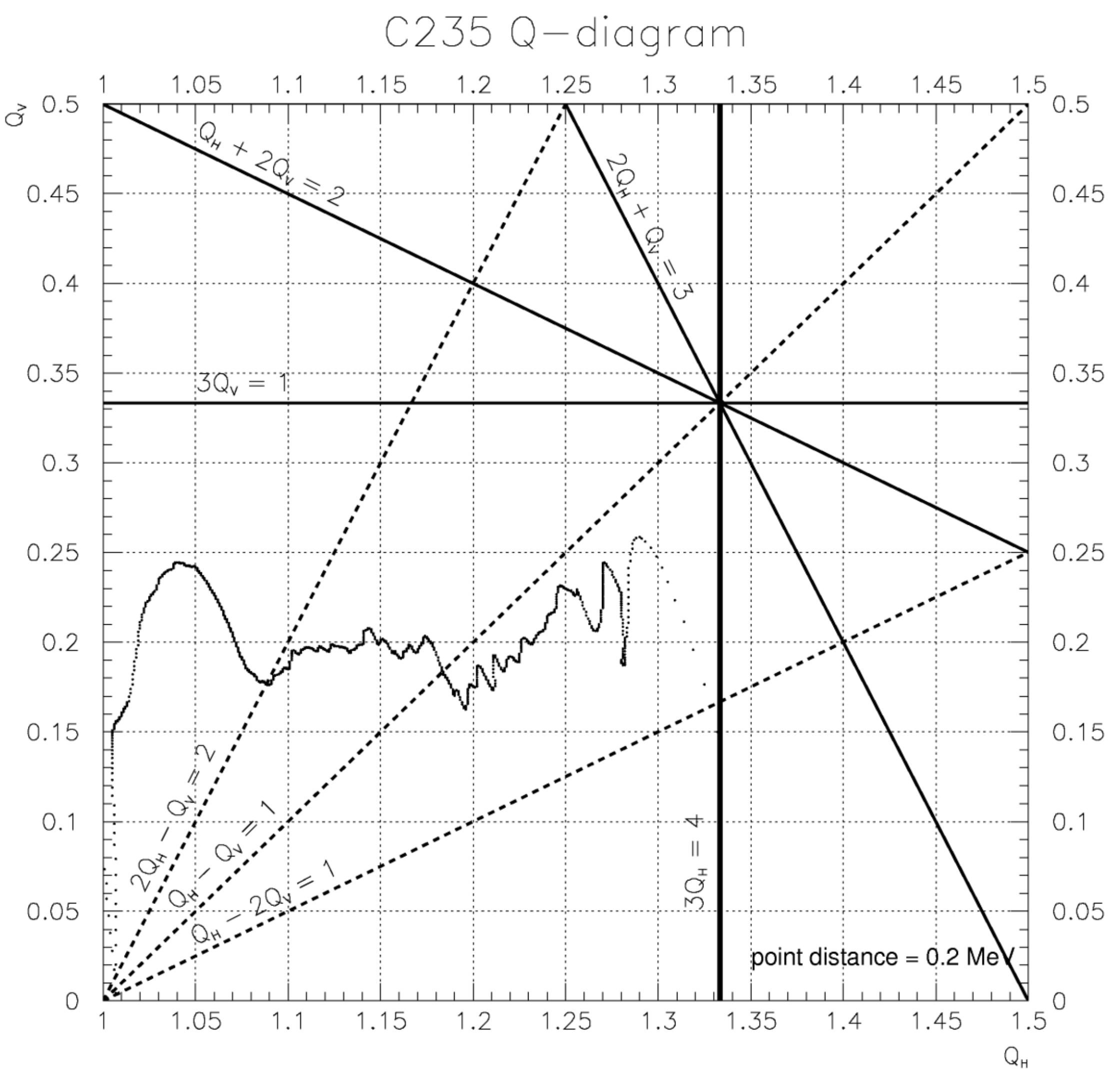
AVF cyclotrons

keep isochronism => CW beam
Drawback: relatively small longitudinal acceptance

Protect, Enhance and Save Lives

Isochronous cyclotron

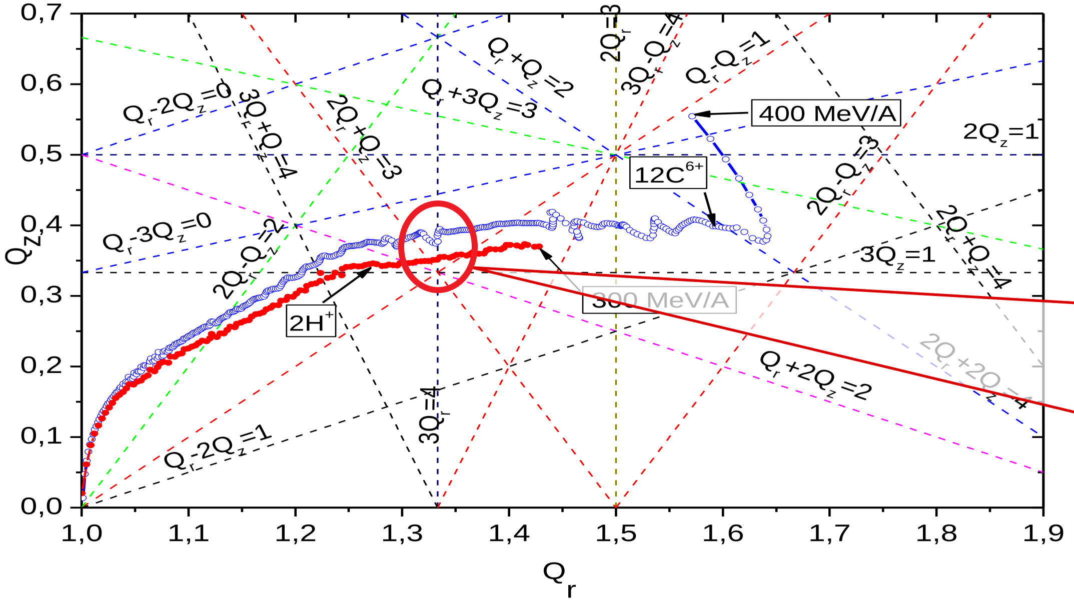




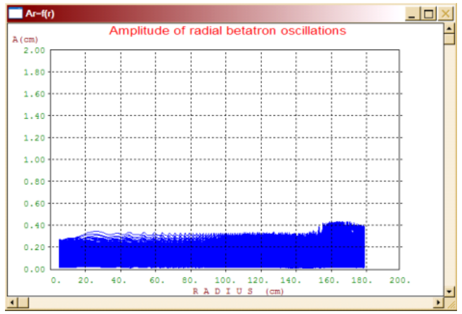
Protect, Enhance and Save Lives

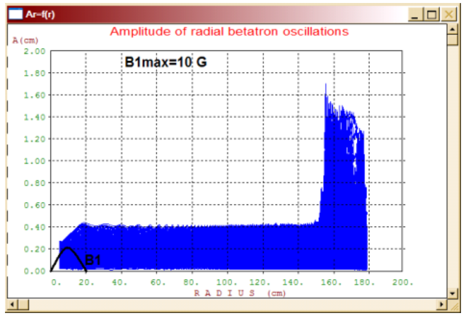
Side note: Resonance crossing?

- You cross them as quickly as possible
  - High energy gain per turn in isochronous cyclotrons
  - Harmonic content in the field => Good beam centering



1st harmonic at the cyclotron centre induces radial motion through Qr=1, that is harmfull as the beam crosses 3Qr=4

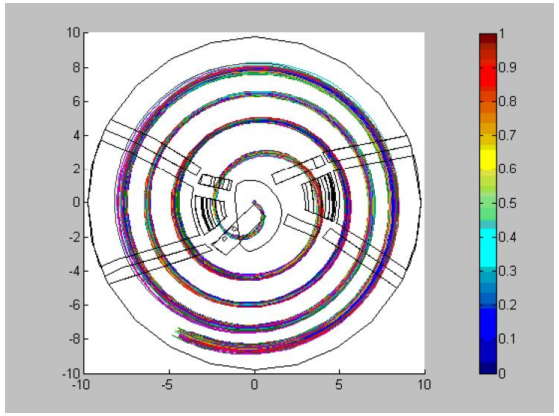




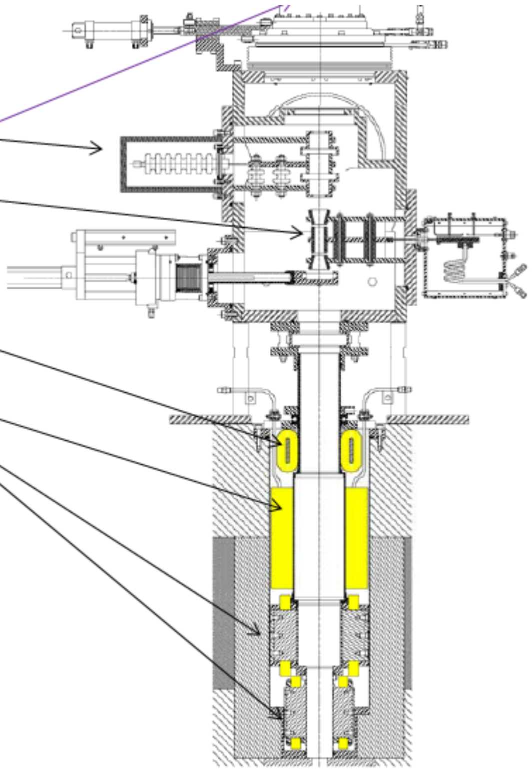
=> Need for low H1 (centering coils)

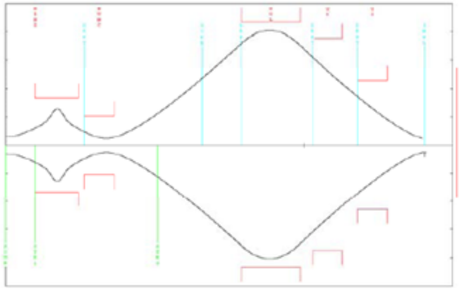
A magnet is good with beam it’s better!

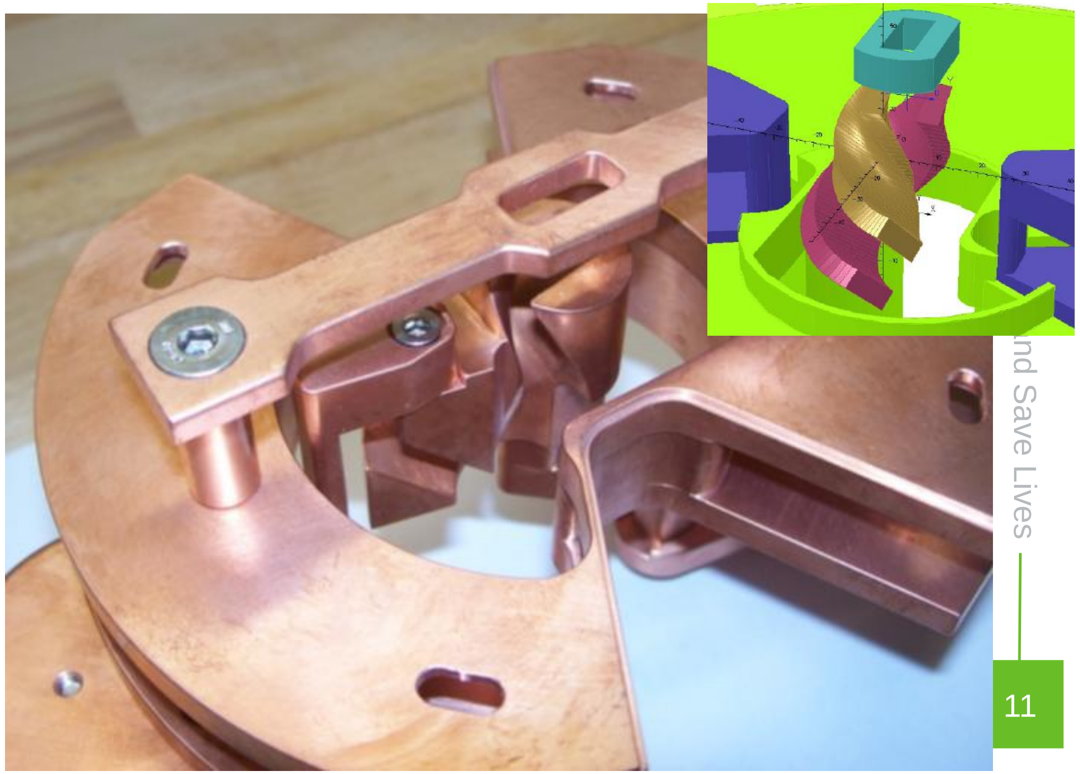
- Internal: hot/cold cathode sources
- External:



- Turbo pump injax
- New Einzell lens
- No wire RF buncher
- XY steering (2)
- Glaser lens
- Set of quadrupoles (squew)
  - Match cyclo acceptance

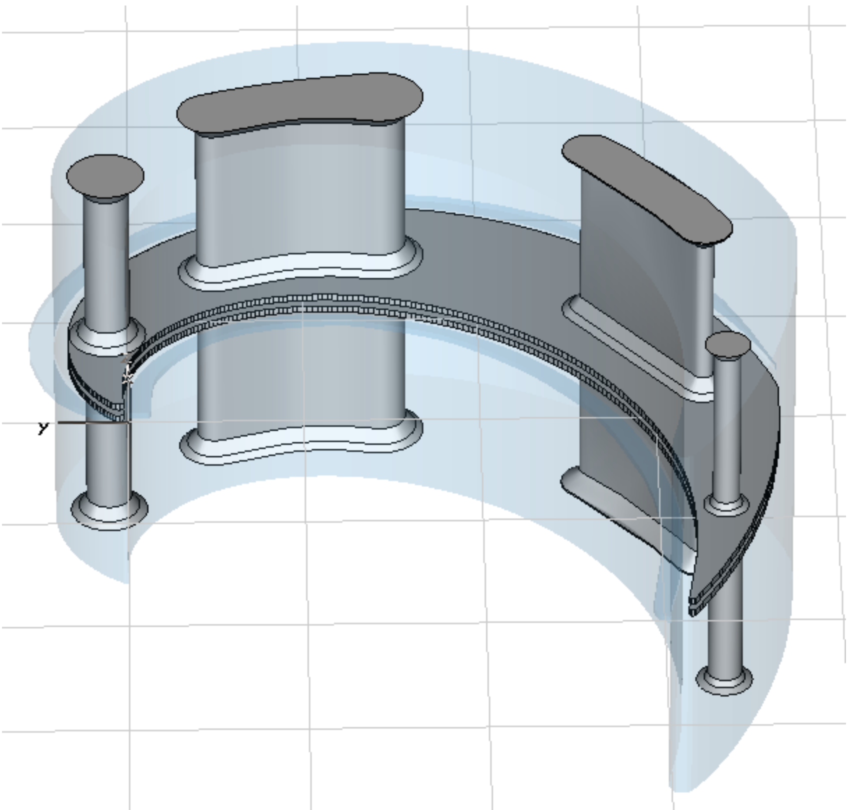


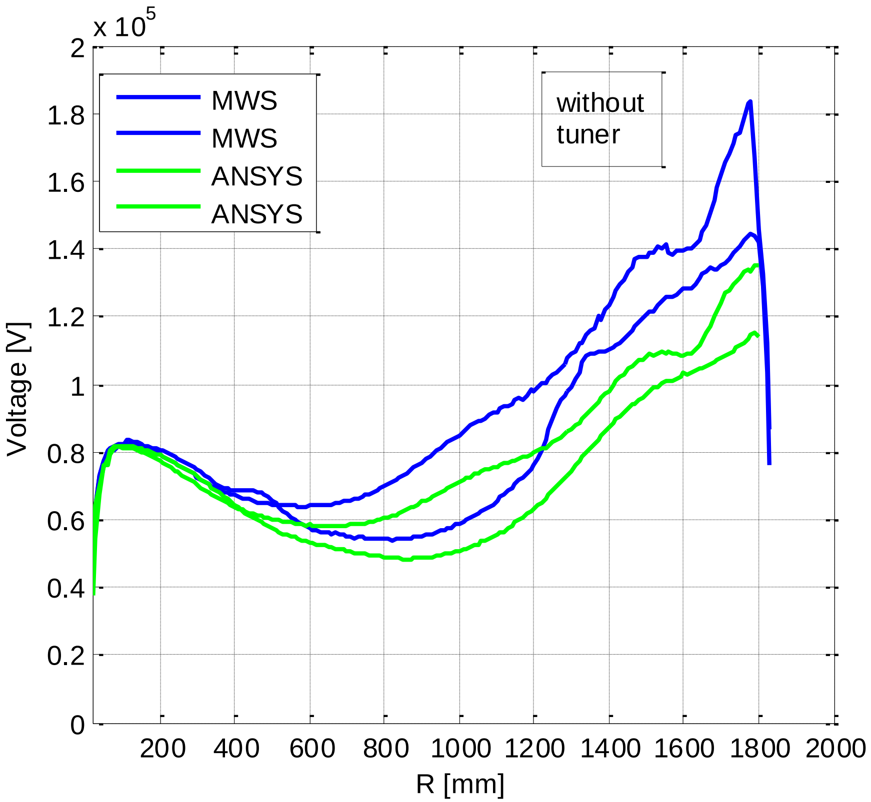




Then you need acceleration

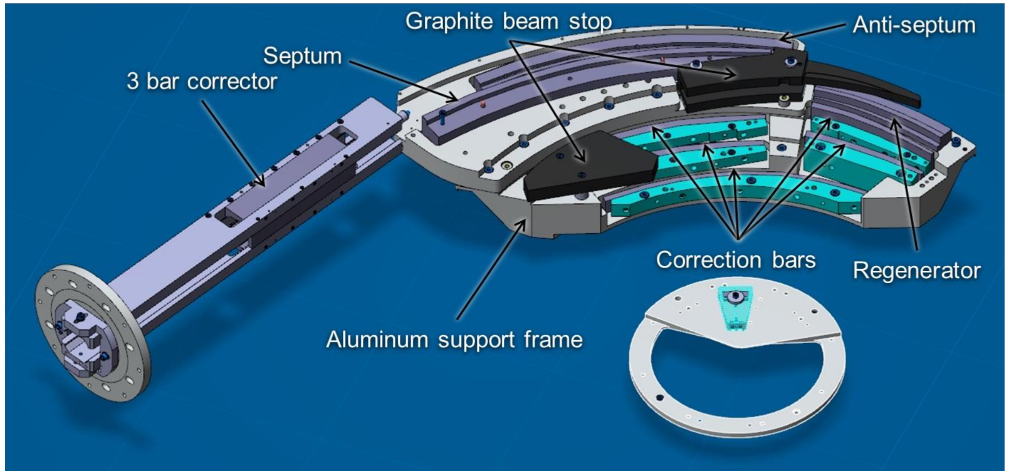
- Cyclotron RF cavities (dees) may have complicated shapes
- Pillars sizes and locations are optimized
- Electric field as a fonction of radius is injected in CO/beam codes

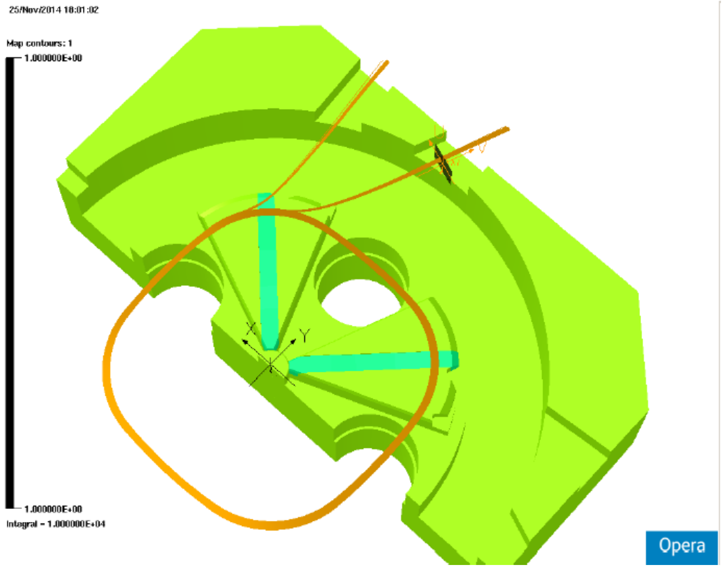


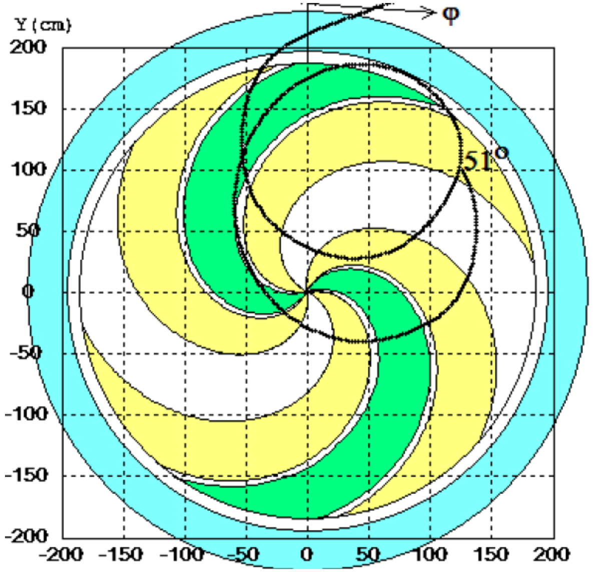


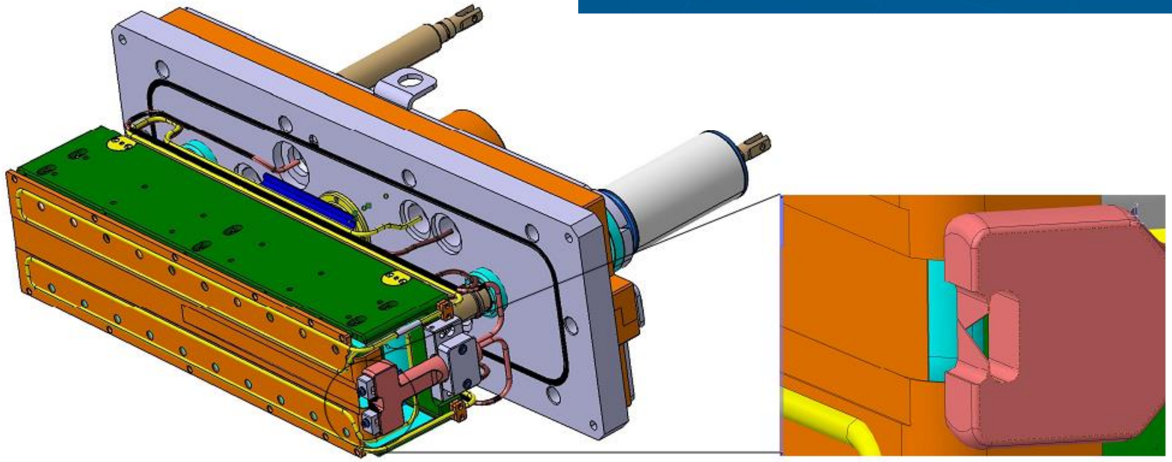
And extraction

- Electrostatic deflector (turn separation)
- Resonant extraction
- Stripping





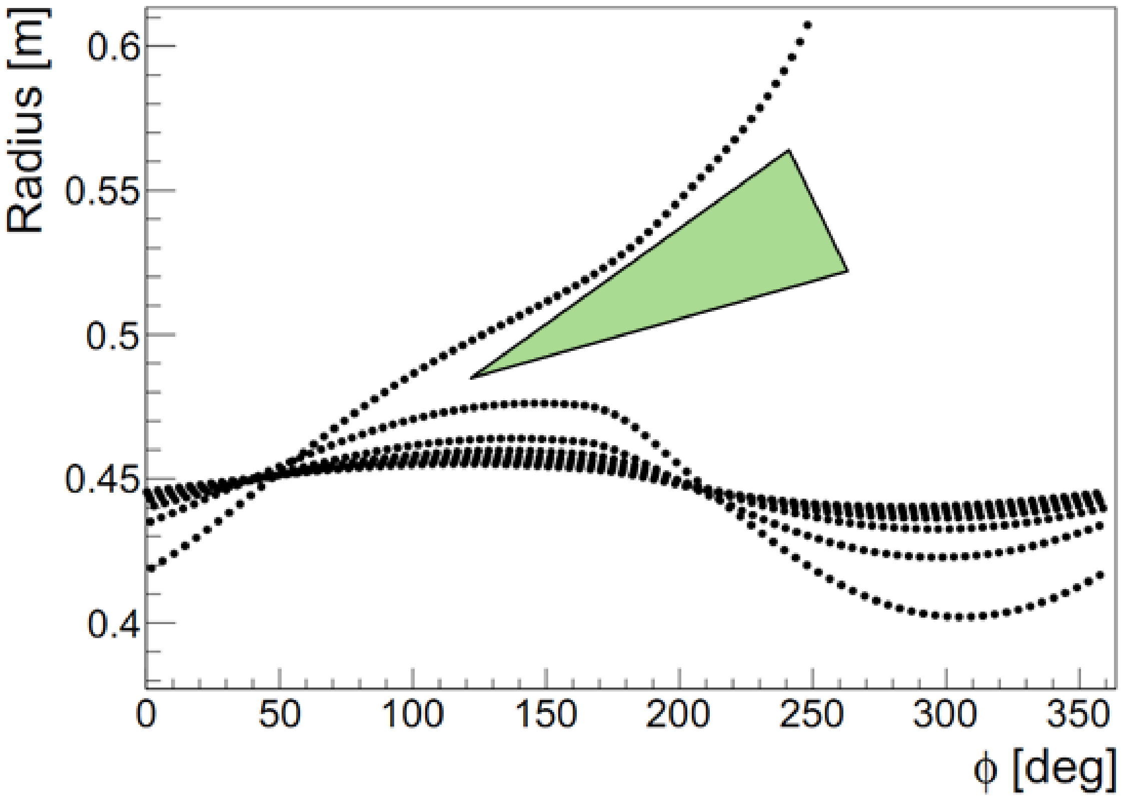


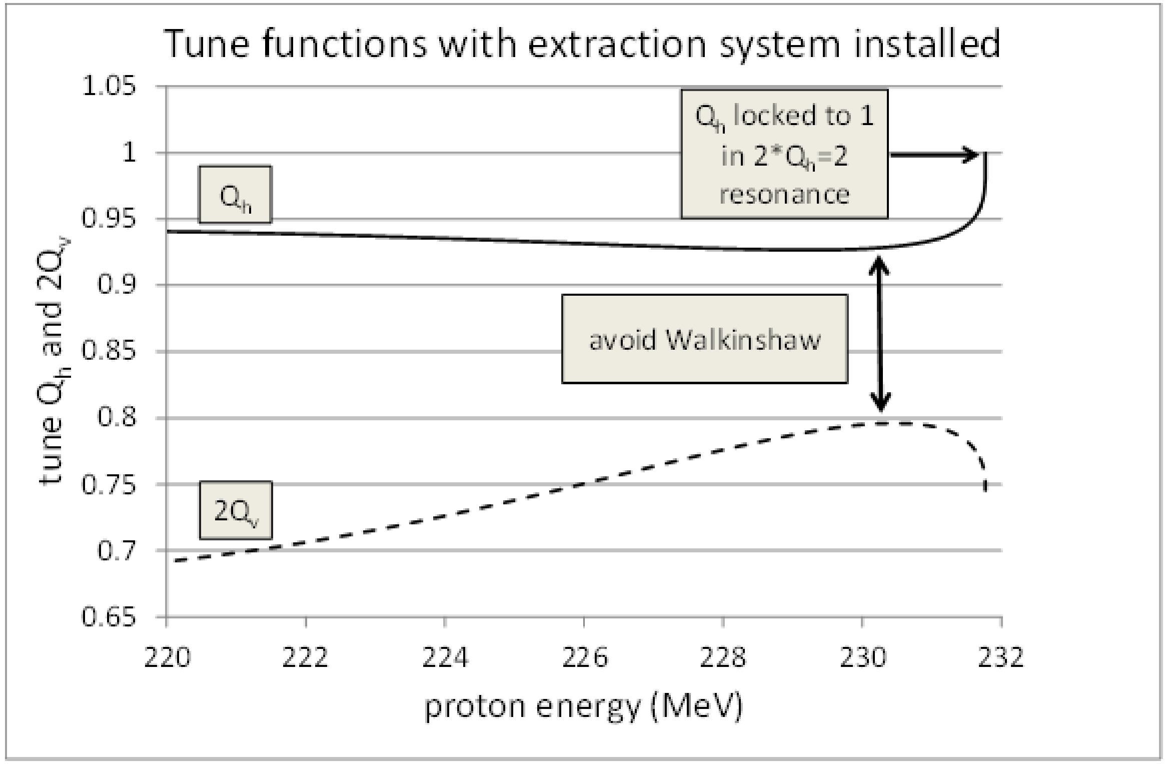


Resonant extraction

- A strong field bump increases nu_r and locks it to 1

=> steady shift of the beam towards the extraction channel





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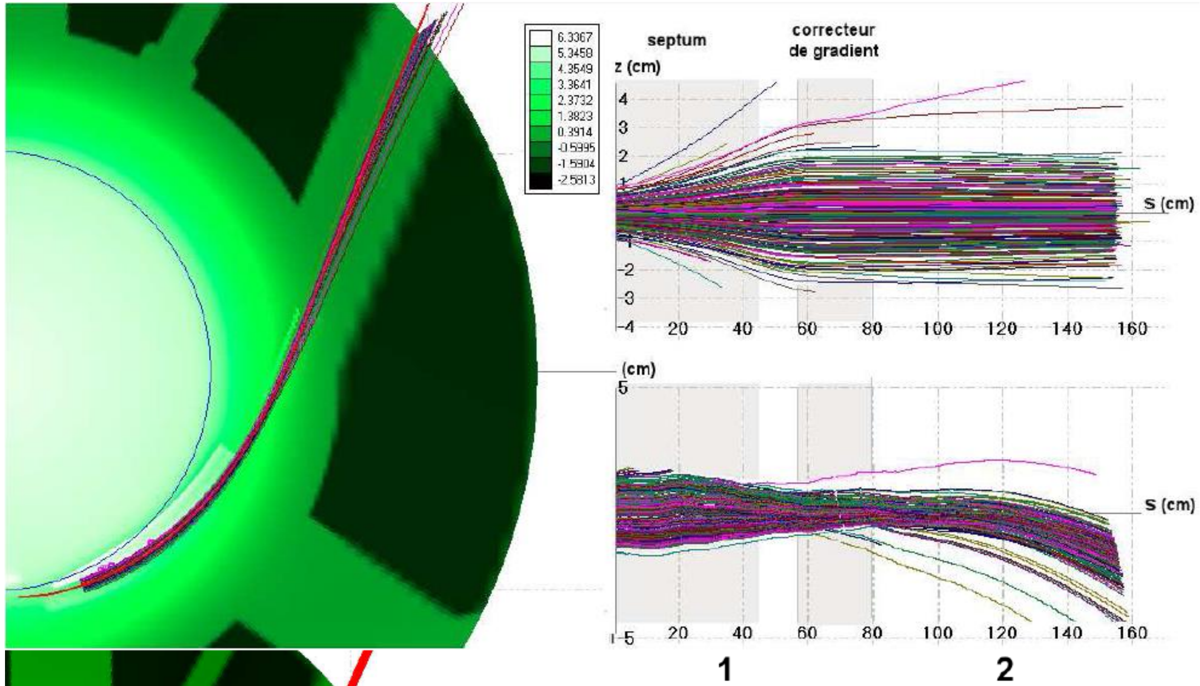
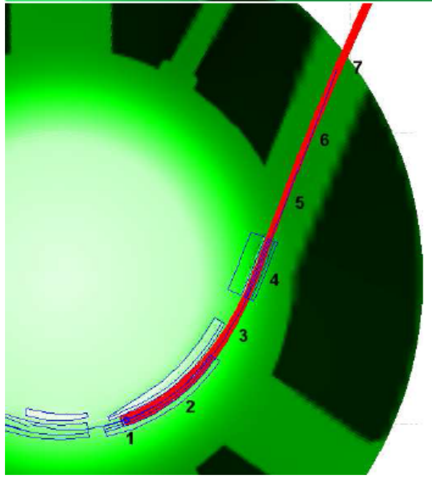
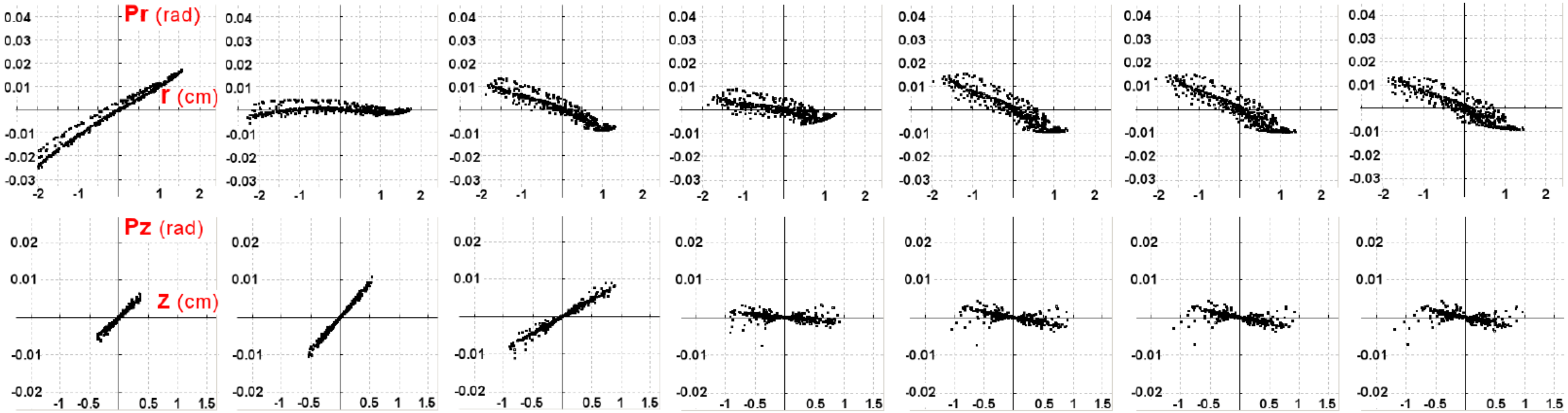
Resonant extraction - tracking



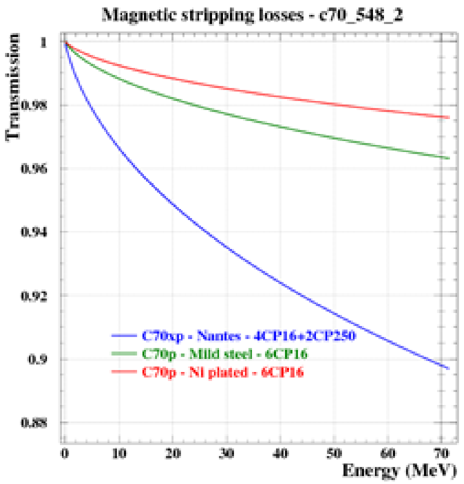


Algorithme par la contribution de l'extraction	aglorithme "symétrique"		dX/2 @220MeV		dX/2 & dZ/2 @220MeV	
Losses during before entering the channel						
Collisions on RF Dee...Horizontal	*47*	*9%*	*51*	*10%*	*48*	*10%*
...Vertical	*28*	*6%*	*26*	*5%*	*26*	*5%*
On Regenerator	*1*	*0%*	*0*	*0%*	*1*	*0%*
On Septum Front-end	*188*	*38%*	*169*	*34%*	*155*	*31%*
Yield @ Channel entrance	*236*	*47%*	*254*	*51%*	*270*	*54%*
Losses in Channel						
Internal losses on Septum	*20*	*4%*	*17*	*3%*	*13*	*3%*
Z>10mm in Channel	*0*	*0%*	*0*	*0%*	*0*	*0%*
Losses on Anti-Septum	*3*	*1%*	*0*	*0%*	*1*	*0%*
Grad Corrector	*0*	*0%*	*0*	*0%*	*0*	*0%*
Yield @ Yoke exit	*213*	*43%*	*237*	*47%*	*256*	*51%*
@ exit: in X/pX=60 π.mm.mrad & Z/pZ=24 π.mm.rad	[illegible]	*26%*	[illegible]	*29%*	[illegible]	*33%*
Δ(/Ref) @ Yoke exit	*REF*	0%	+	10%	+	17%
Δ(/Ref) in 60 / 24 π.mm.mrad	*REF*	0%	+	11%	+	21%



Other important topics

- For the physicist/engineer/designer
  - Vacuum & EM stripping
  - Instrumentation
- For the vendor
  - Market
  - Cost and time to produce
- For the user
  - Standardization of parts
  - Design of spares (and need for recalibration!)
  - Documentation



- Gas stripping losses: 2.5-4%
- Total stripping losses ~5%
- (contractual 8%)
- Ni-plated outgassing rate has not been confirmed -> might be done using the C30 experience?
- Accelerating gap conductance ($2.5x120cm^2$) might be overestimating the conductance ->3D calculation required

Production

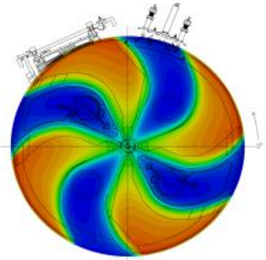
From foundry to extracted beam

Typical production of a (synchro-)cyclotron

C230

- BOM Release – SAP
- Major Components Supply
- Assy before Mapping

- Mapping



- Assy before Tests

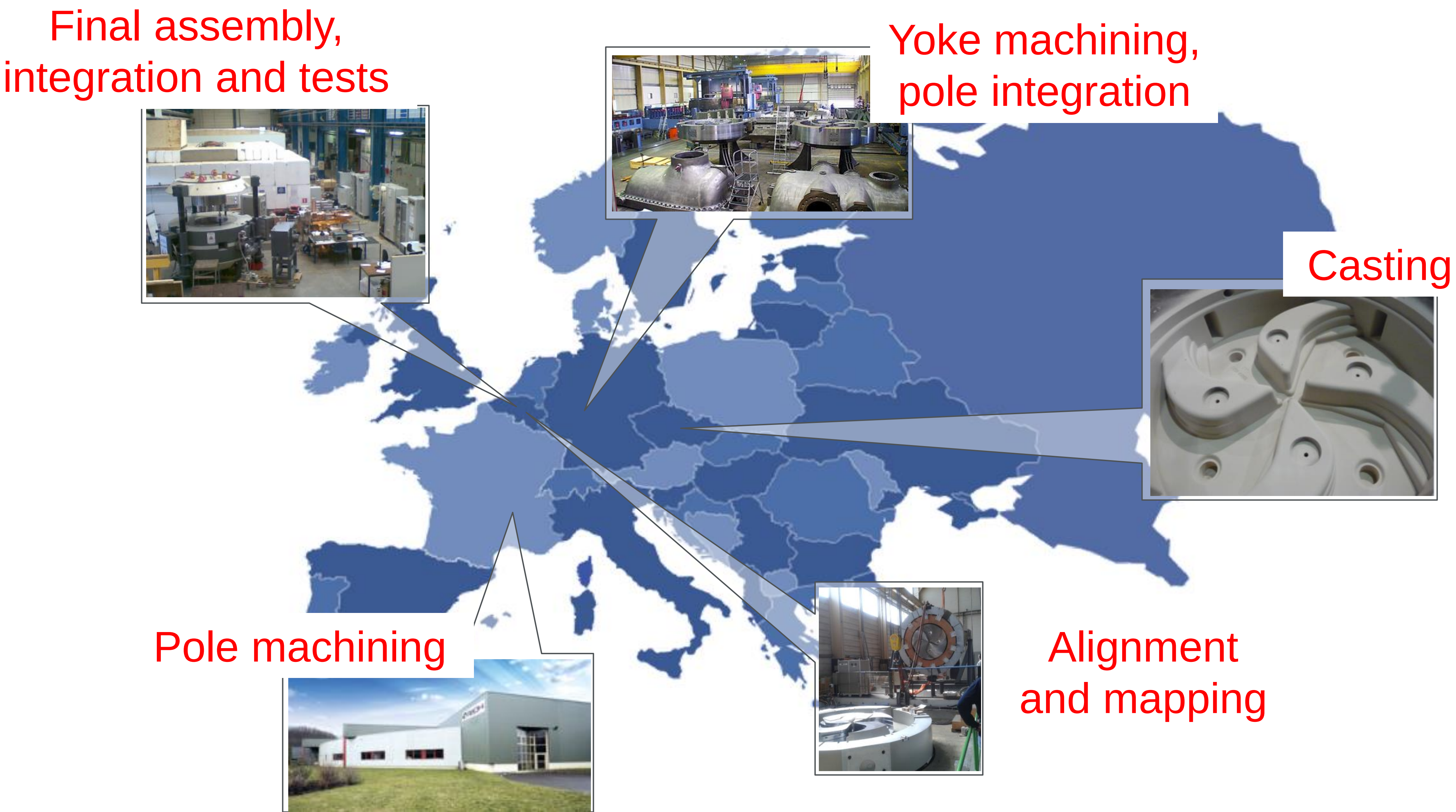
- Tests (Unit – Integration – Beam)
- CCB – Shipment Preparation - Shipment
- Assy
- Site acceptance tests

S2C2

- BOM Release – SAP
- Major Components
- Assy magnet
- Test SCC & Mapping
- Assy before tests
- Tests (Unit – Integration – Beam)

- CCB – Shipment Preparation - Shipment
- Site Assy
- Site acceptance tests

Production example: IBA Cyclone230 (PT)

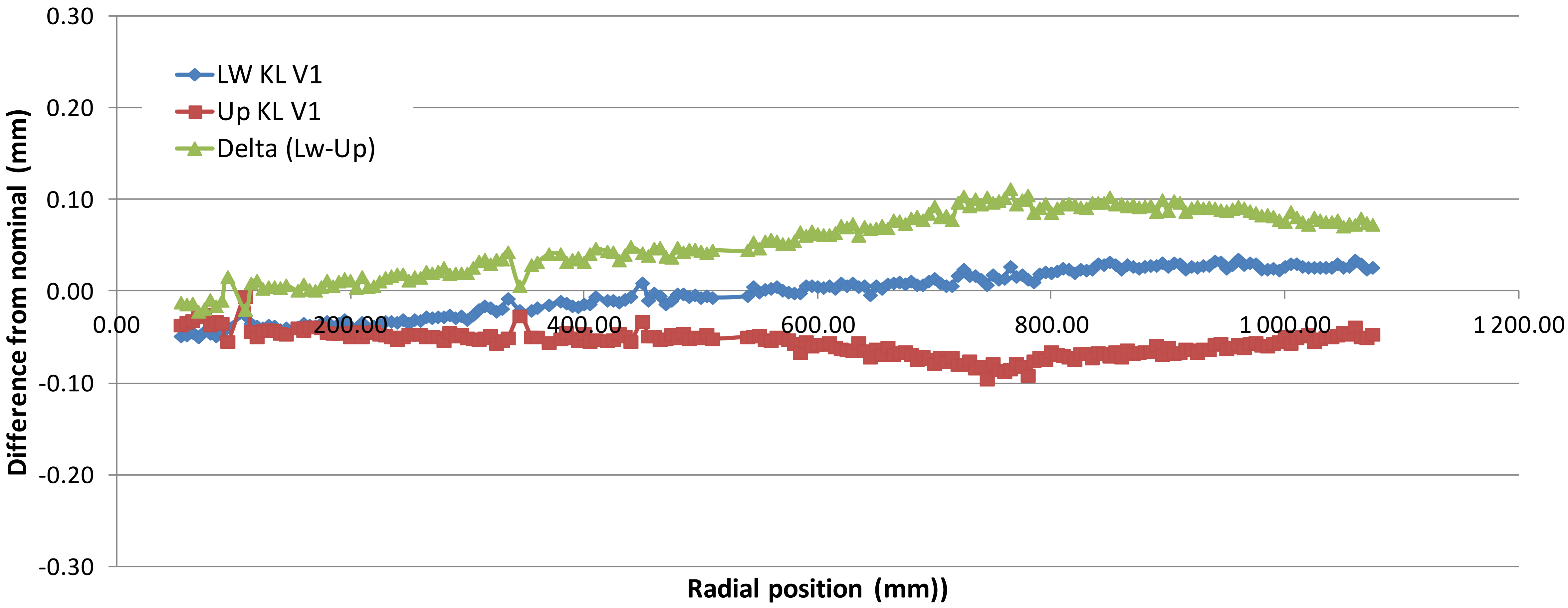


Casting & heat treatment

- Chemical composition test
- Quality test plan and close collaboration between IBA and foundry
  - Chemistry
  - BH curves
  - US testing (difficult!)
  - Traceability
  - …

Machining and Quality Control

- Example: « KL » curve on pole 1



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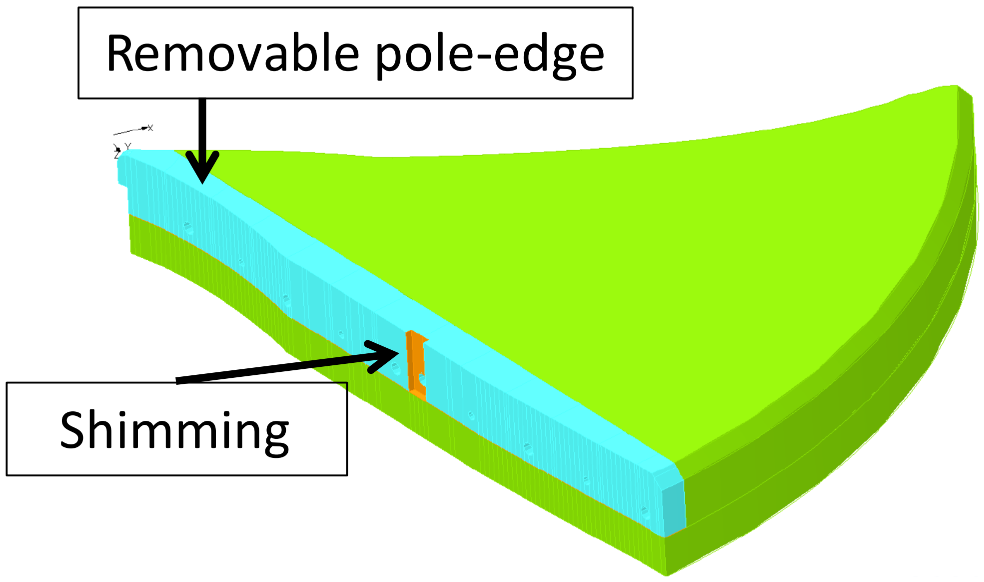
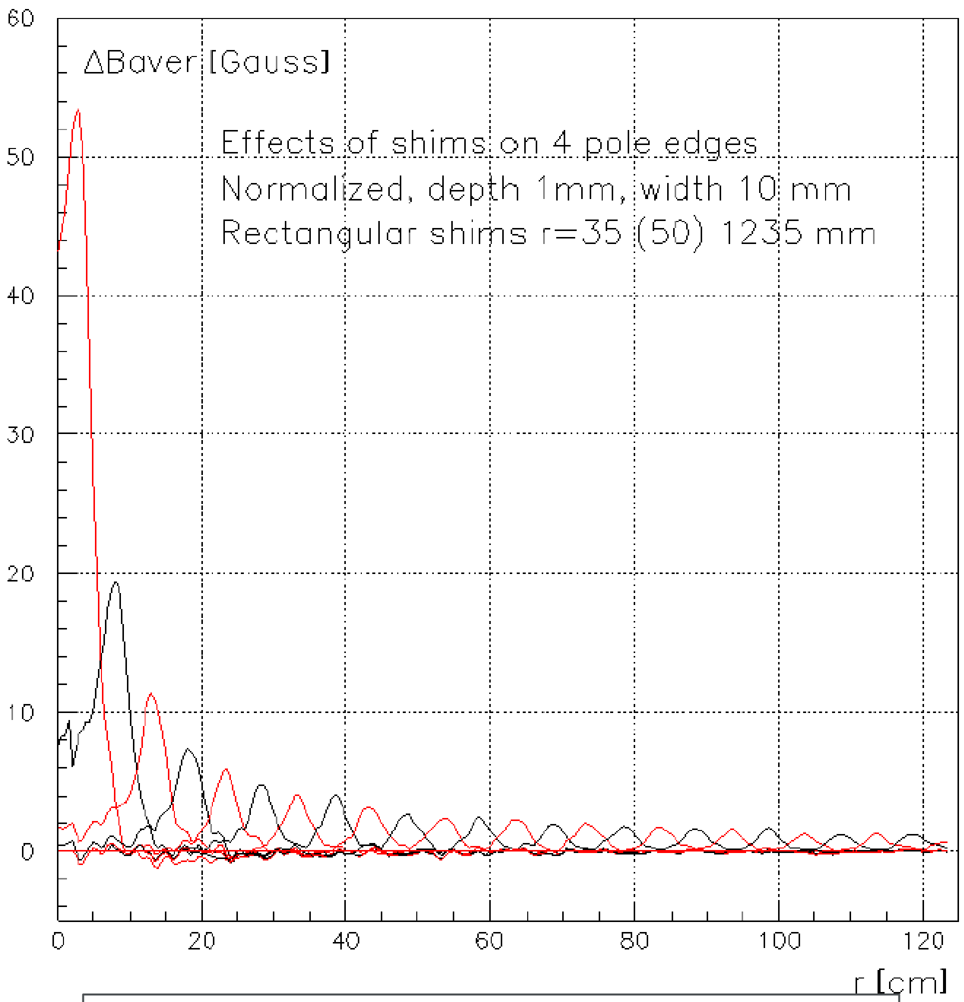
Mapping: @gauss level for isochronous cyclotrons

Essential data from field mapping

- The level of isochronism => integrated RF phase slip
- The transverse optical stability => tune functions
- Crossing of dangerous resonances => operating diagram
- Magnetic field errors
  - First and second harmonic errors => resonance drivers
  - Median plane errors => very difficult to measure
- …

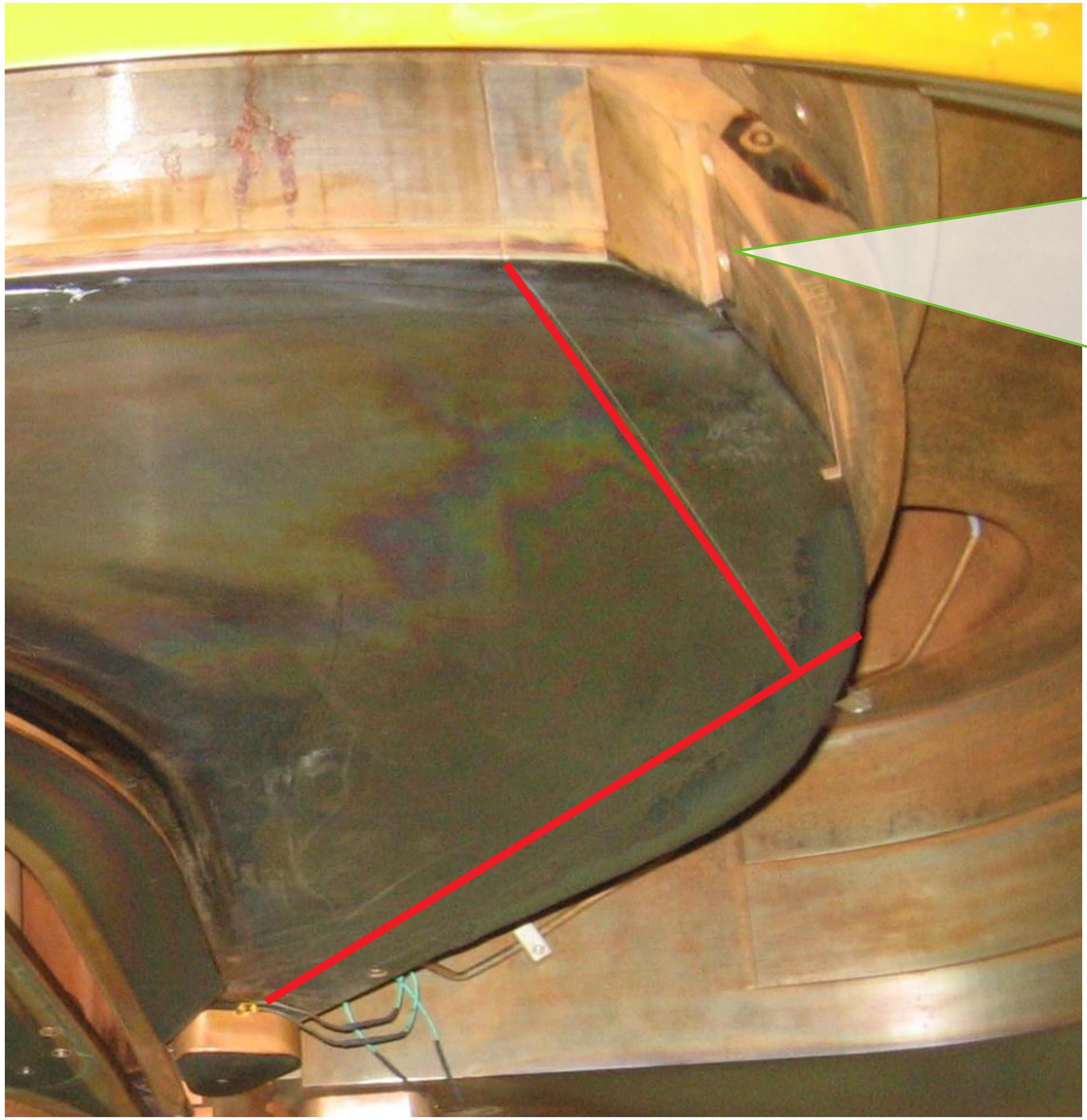
How to adjust the field? Isochronism





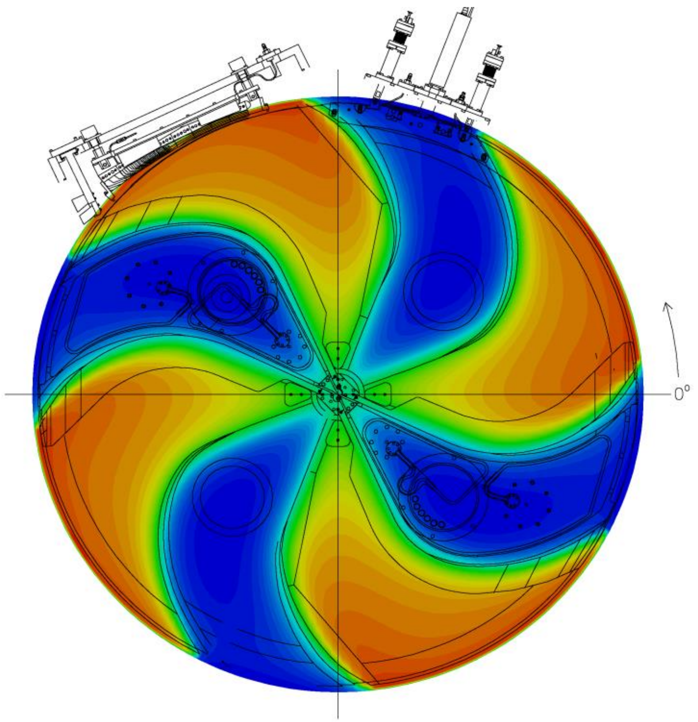
Simple => hard edge model
More advanced => shimming matrix

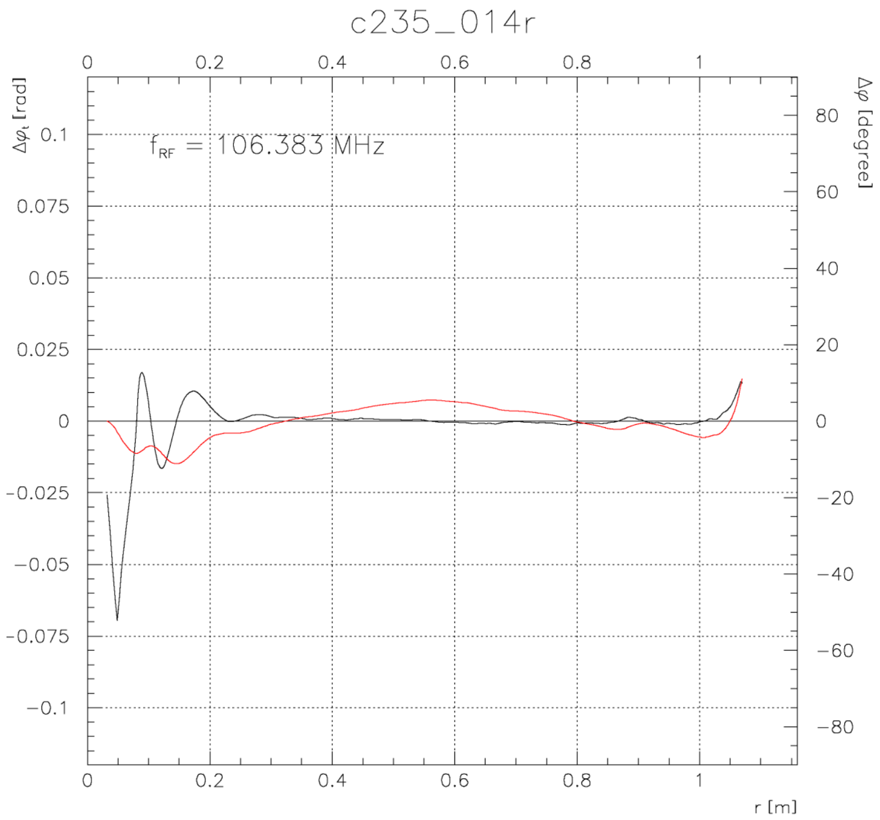
How to adjust the field? Resonance crossing

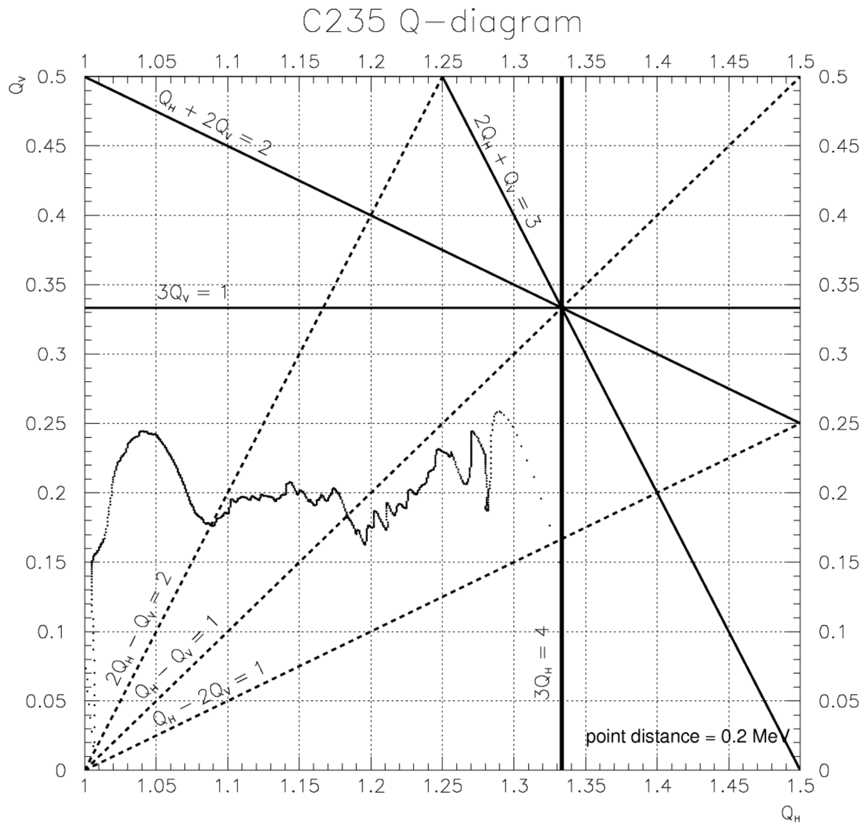


Mapping - results

- 753.46 A – 106.383 MHz
- Abnormality checks, phase excursion less than +/- 10° and Qdiag OK





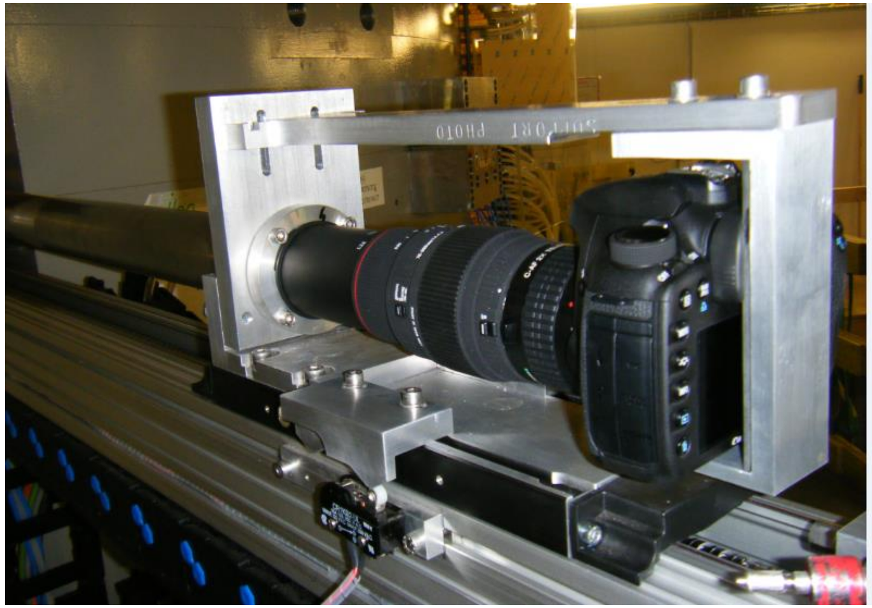


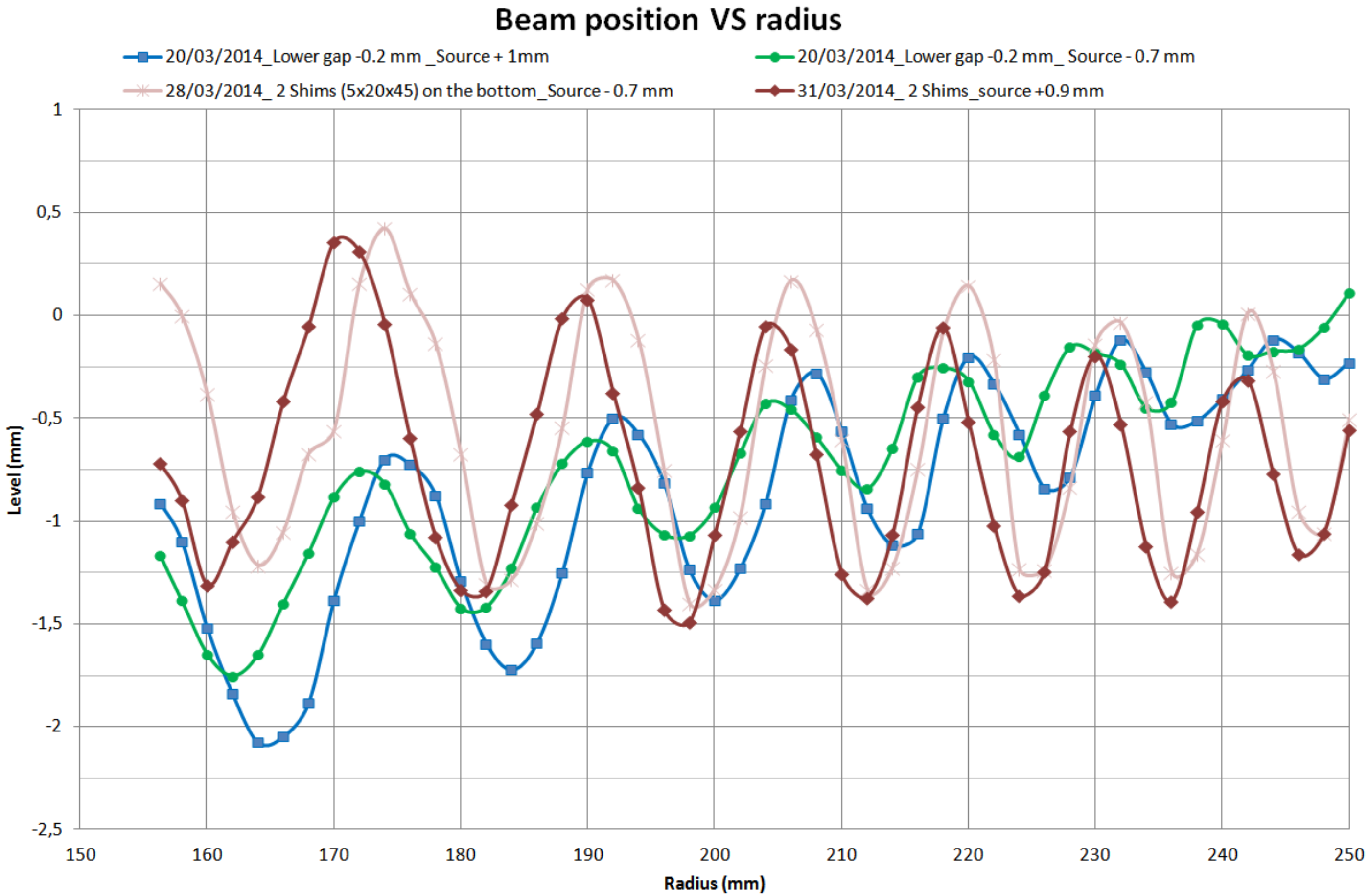
Integration and testing

- Machine fully assembled, integration tests performed (vacuum)
- PS and amplifiers
- RF tested full power on charge
- Isochronism usually within 100 kHz from mapping frequency
- Source tuning
- Optimization of compensation and harmonic coils
- Extraction installation and optimization.
- Beam angle measurement
- R&D tests according to development roadmap

Factory tests

- « visual probe » investigations of vertical oscillations in the centre





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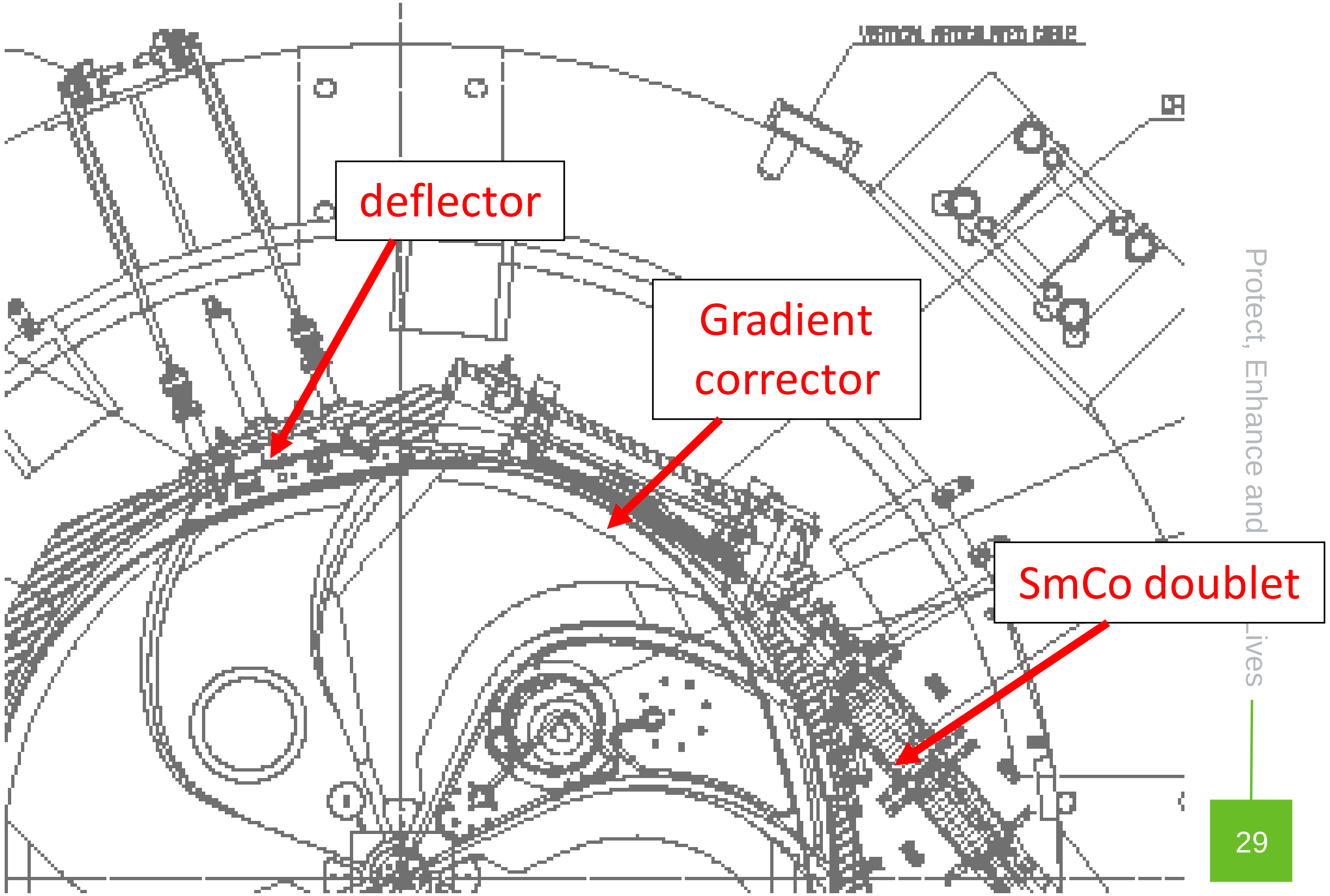
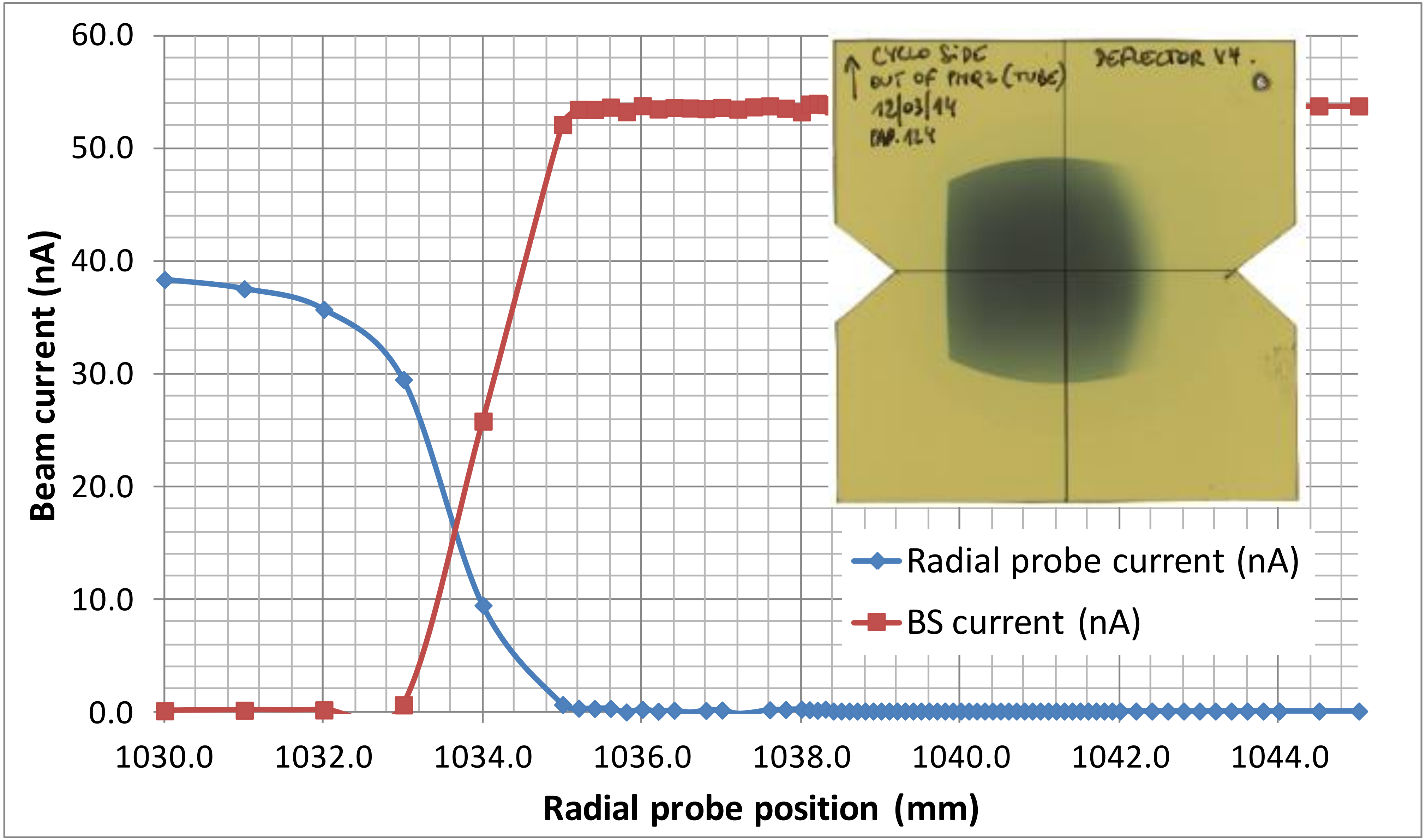
Factory tests: extraction

- Deflector entrance
- Gap, voltage and exit optimization
- Gradient corrector
- Extraction quads alignment



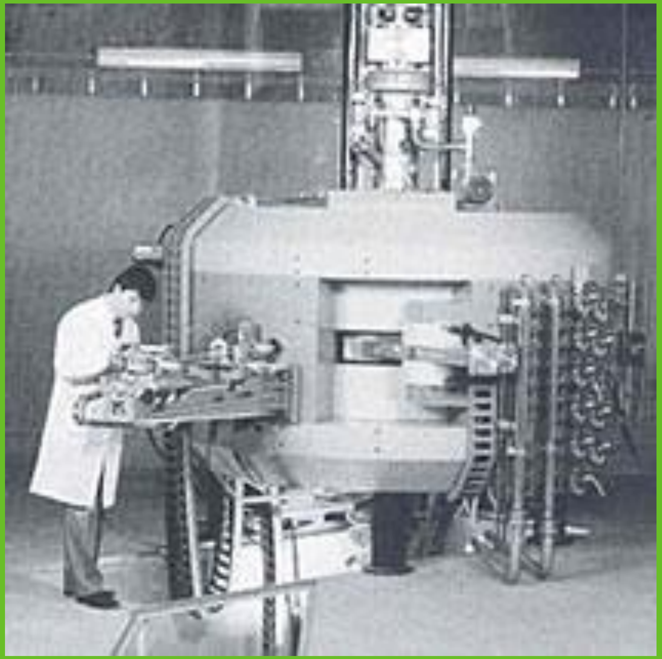
Factory tests - extraction



Optimization in the production context

- Robust design
  - Low dependence on material variations
  - As loose tolerances as possible
  - Margins
- Facilitate all production stages
  - Standard tooling
  - Easy tuning and procedures
- Cost…
  - E.g. coil+PS design
  - Batching/versioning

- But also: learn according to production and operation experience



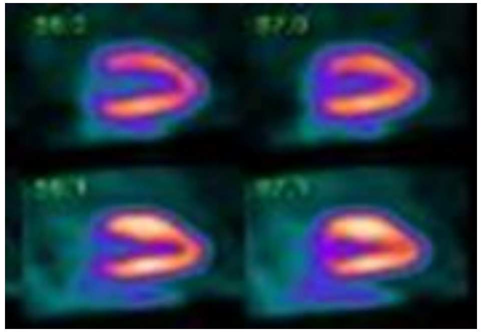
Radioisotope production cyclotrons

More details: http://www-pub.iaea.org/MTCD/publications/PDF/trs468_web.pdf

RadioPharma Solutions

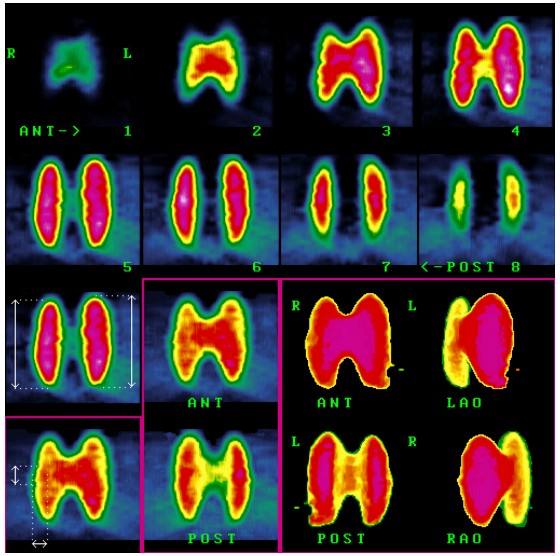
- **Making severe diseases diagnosis and therapy more accessible everywhere**
- **by lowering production costs and complexity of radioisotope-labeled drugs**

Oncology
$Na^{18}F$ Bone scan



Cardiology
Sr/Rb82
^{13}NH3
15O

Oncology
^{18}FDG & others



Oncology & others
^{123}I

Protect, Enhance and Save Lives

A typical radiopharmacy

Radio-isotopes

Chemistry

Radiopharmaceutical environment, incl. GMP

Radioisotopes

Medical Isotope	Lifetime $T_{1/2}$	Use	Nuclear Reaction	Target Abundance (%)	Energy Range (MeV)	Production Yield (mCi @ sat)	Typical Dose (mCi)
^{11}C	20.4m	PET	$^{11}B(p,n)$	80.3	8 - 20	40/µA	
^{11}C	20.4m	PET	$^{14}N(p,\alpha)$	99.6	12	100/µA	
^{11}C	20.4m	PET	$^{10}B(d,n)$	19.7	7	10/µA	
^{13}N	9.96m	PET	$^{13}C(p,n)$	1.1	5 - 10	115/µA	
^{13}N	9.96m	PET	$^{12}C(d,n)$	98.9	2 - 6	50/µA	
^{13}N	9.96m	PET	$^{16}O(p,\alpha)$	99.8	8 - 18	65/µA	
^{15}O	2m	PET	$^{15}N(p,n)$	0.36	10 - 15	47/µA	
^{15}O	2m	PET	$^{16}O(p,pn)$	99.8	>26	25/µA	
^{15}O	2m	PET	$^{14}N(d,n)$	99.6	8 - 6	27/µA	
^{18}F	109.8m	PET	$^{18}O(p,n)$	0.20	8 - 17	180/µA	5 - 20
^{18}F	109.8m	PET	$^{20}Ne(d,\alpha)$	90.5		82/µA	
^{64}Cu	12.7h	SPECT	$^{64}Ni(p,n)$	0.93	5 - 20	5/µA	
^{67}Cu	61.9h	SPECT	$^{68}Zn(p,2p)$	19.0	>40	0.02/µA	
^{67}Ga	78.3h	SPECT	$^{68}Zn(p,2n)$	19.0	20 – 40	4.5/µA	10
$^{82}Sr/^{82m}Rb$	25d/5m	PET	$^{85}Rb(p,4n)^{82}Sr$ Produces Rb	72.2	50 -70	0.18 /µAh	
^{99m}Tc	6h	SPECT	$^{100}Mo(p,2n)$	9.7	19	14/µAh	20
^{103}Pd	17.5d	Therapy	$^{103}Rh(p,n)$	100	10 -15	0.52/µAh	
^{111}In	67.2h	SPECT	$^{112}Cd(p,2n)$	24.1	18 - 30	6/µAh	3
^{123}I	13.2h	SPECT	$^{124}Xe(p,2n)^{123}Cs \rightarrow ^{123}Xe \rightarrow ^{123}I$	0.10	25 - 35	27/µAh	
^{123}I	13.2h	SPECT	$^{123}Te(d,2n)\ ^{123}I$	0.89	10 - 15	20/µAh	
^{124}I	4.1d	PET	$^{124}Te(p,n)$	4.7	10 - 18	0.1/µAh	
^{124}I	4.1d	PET	$^{124}Te(d,2n)$	4.7	>20	0.15/µAh	
^{186}Re	90.6h	Therapy /SPECT	$^{186}W(p,n)$	28.4	18		
^{201}Tl	73.5h	SPECT	$^{203}Tl(p,3n)^{201}Pb \rightarrow ^{201}Tl$	29.5	27 - 35	0.7/µAh	4
^{211}At	7.2h	Therapy	$^{209}Bi(\alpha,n)$	100	28	1/µAh	0.05-.01

T. J. Ruth et al
Nucl. Med. Biol.
Vol 16, No. 4,
pp. 323 – 336
(1989)

IBA radiopharmaceuticals solutions portfolio

Enabler
Pet Production
Pet/SPECT crossover
World record

Cyclone 3D	3 MeV D+	
clone 11:	11 MeV H-, 120 µA (~1300 W)	
18/9:	18 MeV H-, 150 µA (~2700 W)	Deuteron possible
(xp):	30 MeV, 1.2 mA (36 kW)	alpha/deuteron possible (xp)
e 70(xp):	70 MeV, 750 µA (53 kW)	alpha/deuteron possible (xp)

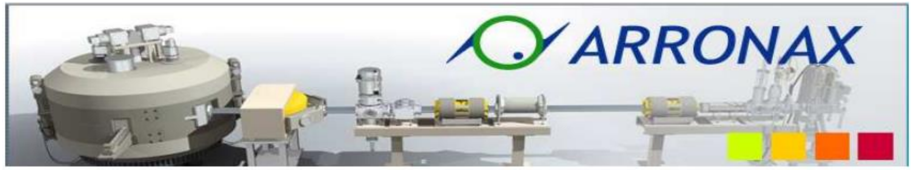
3 MeV 11 MeV 18MeV 30MeV 70MeV

Optimization example: Cyclone Kiube (18 MeV)

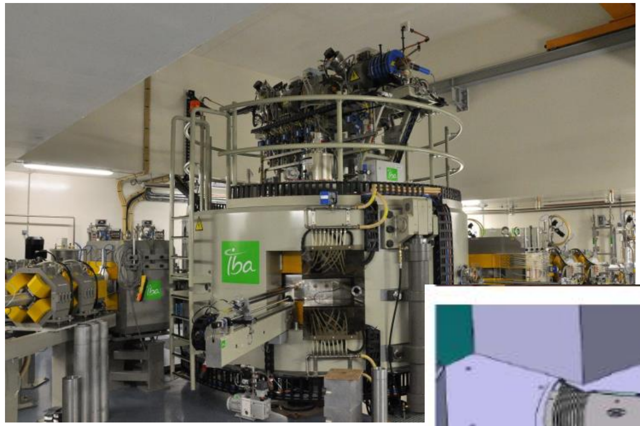
- New design approach:
  - Fits in std container
  - Much less iron than before (~30%)
  - Easy installation
  - Uncompromised performances (vacuum, beam…)

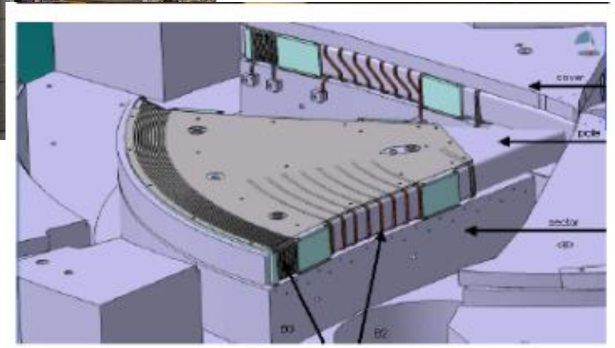
- whilst being cost-optimal
  - Standardization of parts
  - Co-design with suppliers
  - …

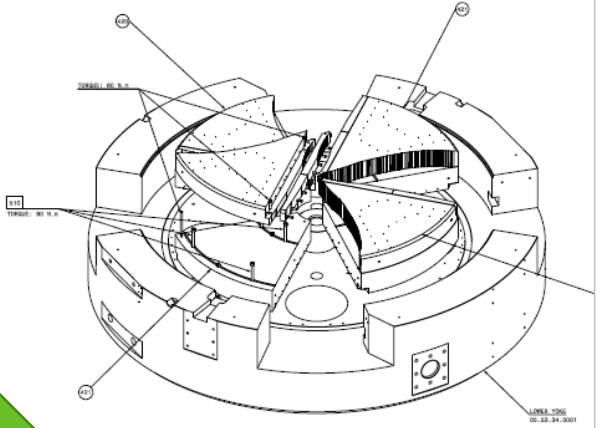
Optimization example II: Cyclone 70p

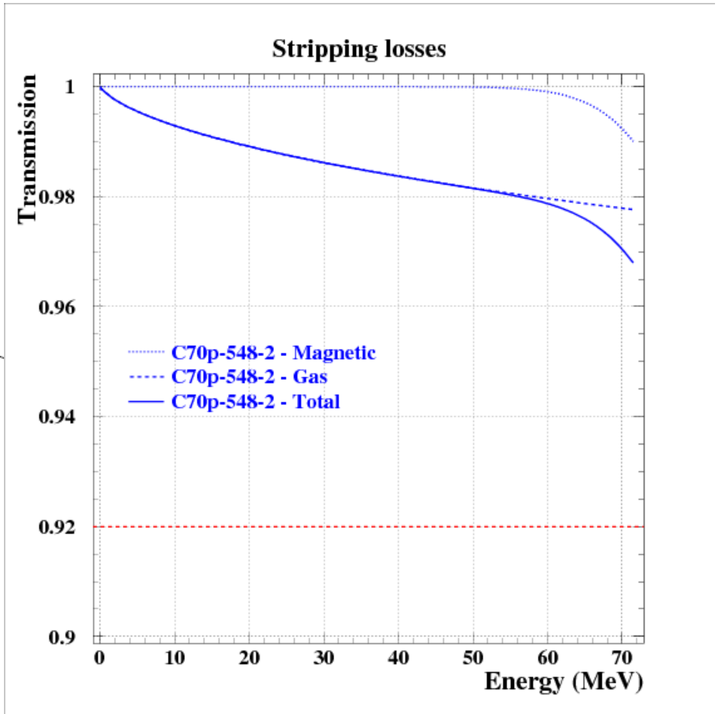


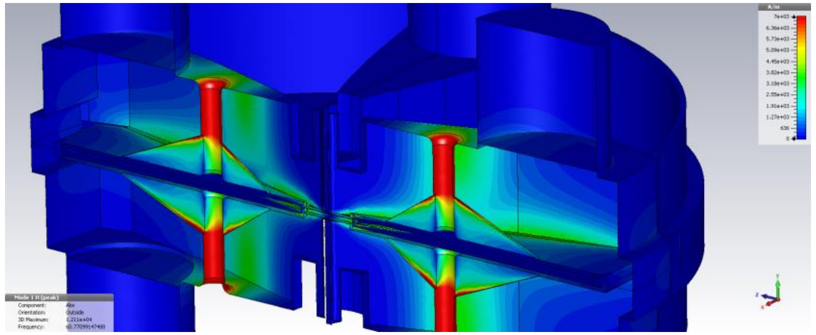
Accelerated Beam	Extracted Beam	Extracted Energy (MeV)	Beam Intensity (eµA)	Exit Ports
H^-	H^+	30 - 70	750	dual
D^-	D^+	15 - 35	50	dual
$^4He^{2+}$	$^4He^{2+}$	70	70	single
HH^+	HH^+	35	50	single

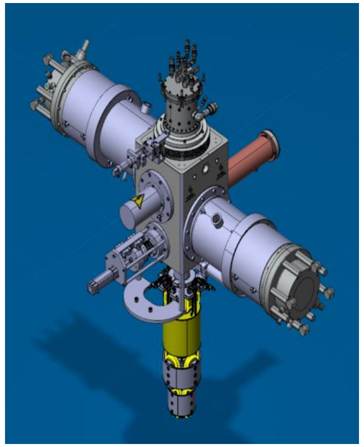


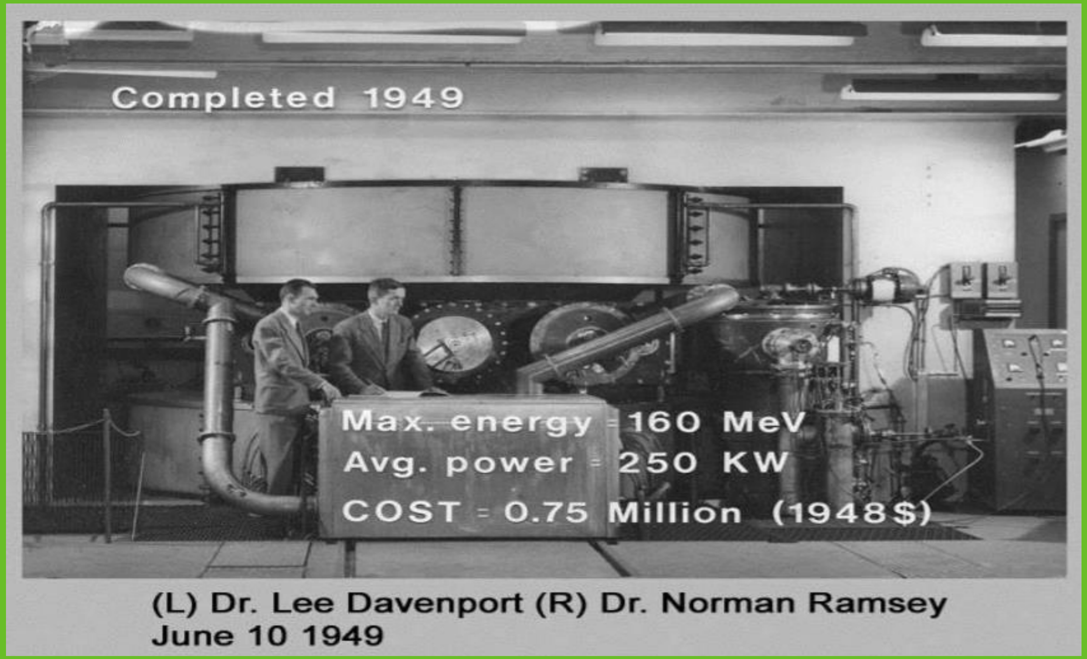












Therapy cyclotrons

Accelerators in PT

- (rough) requirements
  - Max. energy: 230 (250 MeV) protons – 400 MeV/u carbon ions
  - Min energy: ~70 MeV protons
  - At least 2 Gy/l/min => a few nA average beam current **at nozzle level**
  - Fast beam intensity modulation
  - Minimum footprint
  - Minimum energy consumption
  - Stray field…?

- Currently available on the market
  - Synchrotrons
    - Beam accelerated on a single path, magnetic field is ramped

    =>Variable energy, pulsed beam, multiple-stage
  - Cyclotrons and synchro-cyclotrons
    - Acceleration on a spiral path, fixed magnetic field

    => Usually fixed energy, CW or pulsed (high rep. rate), single stage

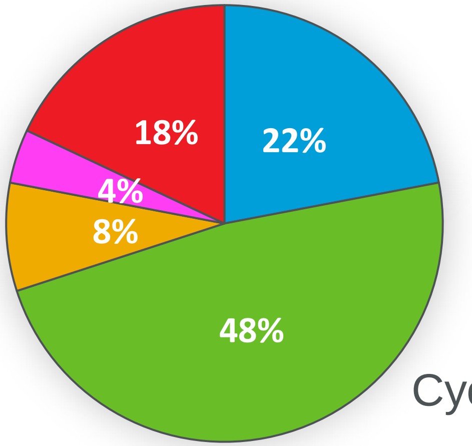
- In development or for the (far) future:
  - Linacs
  - Wakefield accelerators
  - Cyclinacs

Commercial systems at a glance, by geography (2016)

Commercial systems acc. since 1996

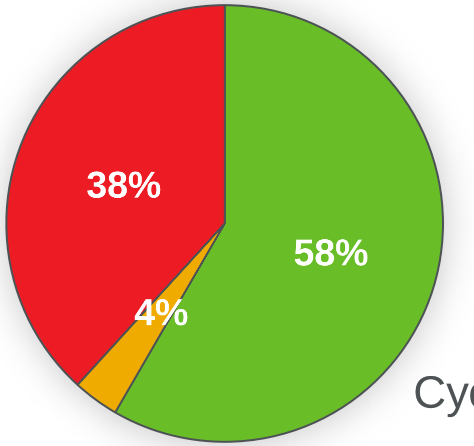
- IBA
- HITACHI
- VARIAN
- MEVION
- PROTOM
- MELCO
- SHI
- PRONOVA
- AVO

Number of Rooms - US



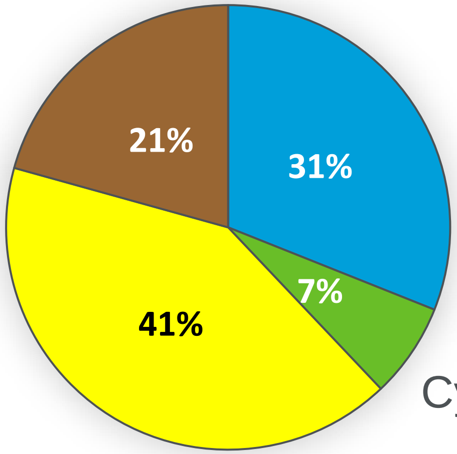
Cyclos: 74%

Number of Rooms – EMEA + ROW



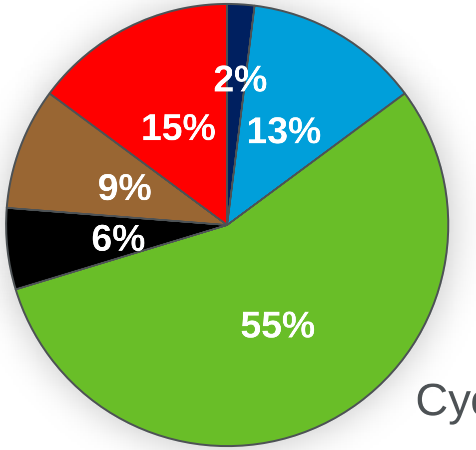
Cyclos: 96%

Number of Rooms - Japan



Cyclos: 74%

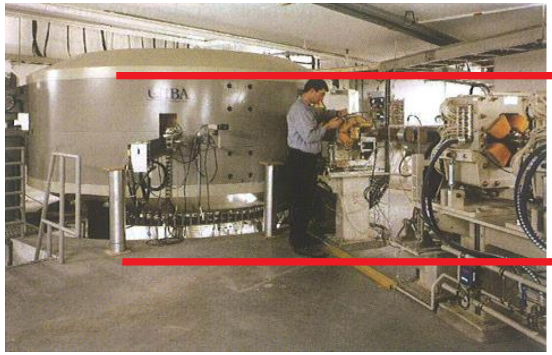
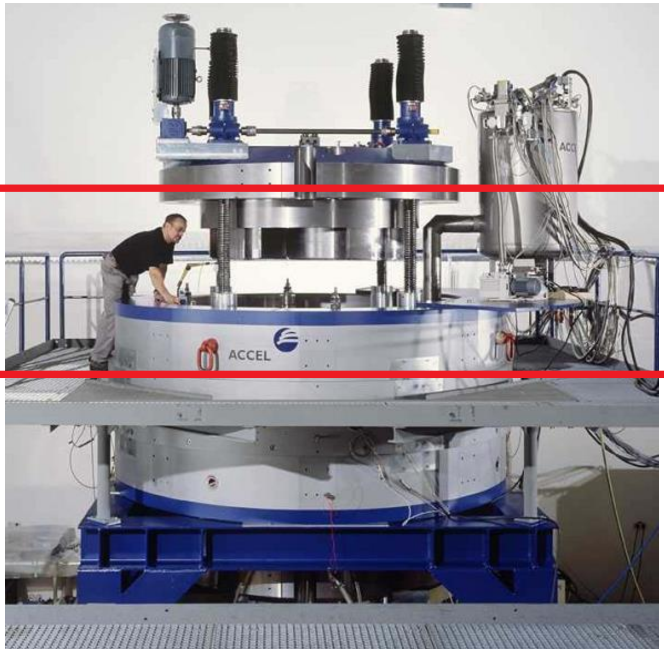
Number of Rooms – Rest of APAC

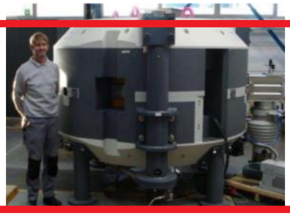


Cyclos: 85%

Protect, Enhance and Save Lives

Current models

IBA C230
- 230 MeV protons
- 4.3 m Diameter
- CW beam
- Normal conducting
- Magnet: 200 kW
- RF: 60 kW

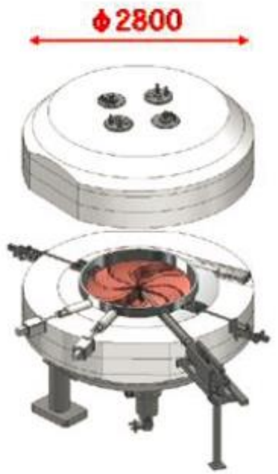
Varian-Accel Probeam
- 250 MeV protons
- 3.1 m Diameter
- CW beam
- Superconducting (NbTi)
- Magnet: 40 kW
- RF: 115 kW

Mevion SC250
- 250 MeV protons
- ~1.5 m Diameter (shield)
- Superconducting (Nb_3Sn)

IBA S2C2
- MeV protons
- 2.2 m Diameter
- Rep. rate: 1 kHz
- Superconducting (NbTi) => ~30 kW
- RF: 11 kW

Proton cyclotrons - Ongoing developments

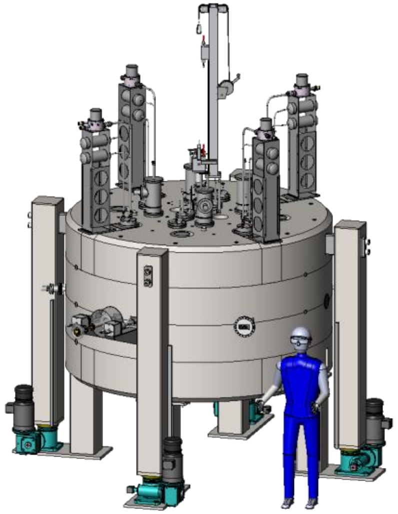
- 1. Isochronous: SHI, Varian/Antaya, Pronova/Ionetix, Heifei/JINR



Ant

SHI

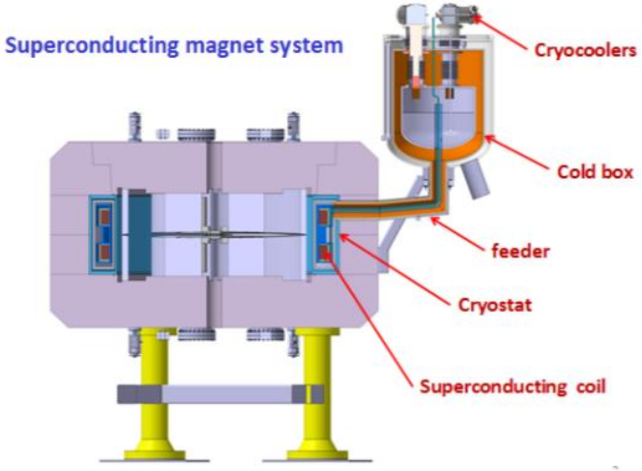
- 230 MeV protons
- 2.8 m Diameter
- CW beam
- Superconducting (NbTi)
- 55 tons
- 4 T (extr.)



Derenchuck - NAPAC 2016

Pronova/Ionetix

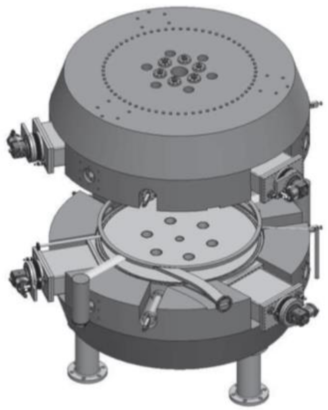
- 250 MeV protons
- 2.8 m Diameter
- CW beam
- Superconducting (Nb_3Sn)
- 60 tons
- 3.7 T (extr)



Karamysheva - THP20 cyclotrons 2016

Heifei/JINR

- 200 MeV protons
- 2.2 m Diameter
- CW beam
- Superconducting
- 30 tons
- 3.6 T (extr.)



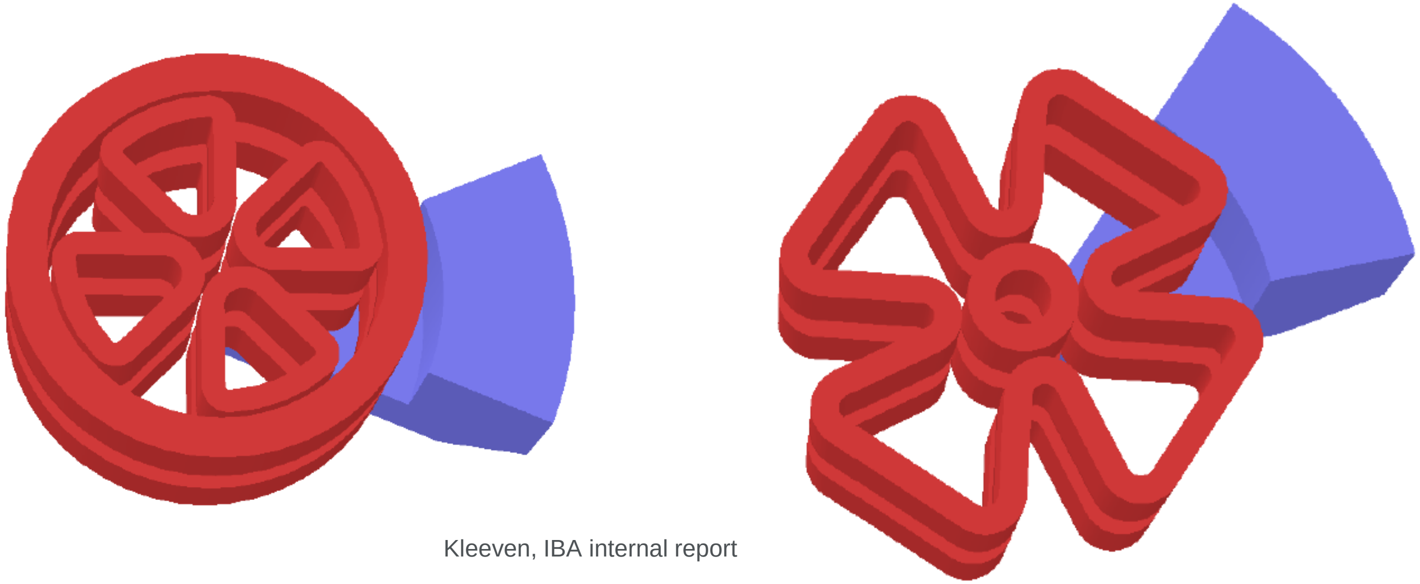
Antaya – CAS 2015

Varian/Antaya

- 230 MeV protons
- 2.2 m Diameter
- CW beam
- Superconducting (Nb_3Sn)
- 30 tons+
- 5.5 T (extr.)
- “Flutter” coils

Flutter coils

- Flutter coils are useful to overcome the limitation of iron-dominated field variation



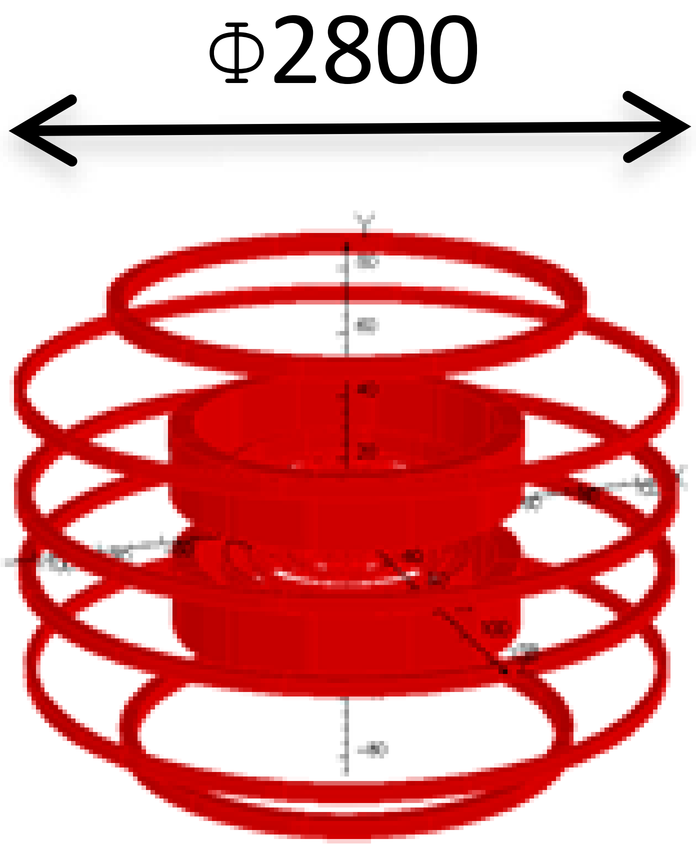
Kleeven, IBA internal report

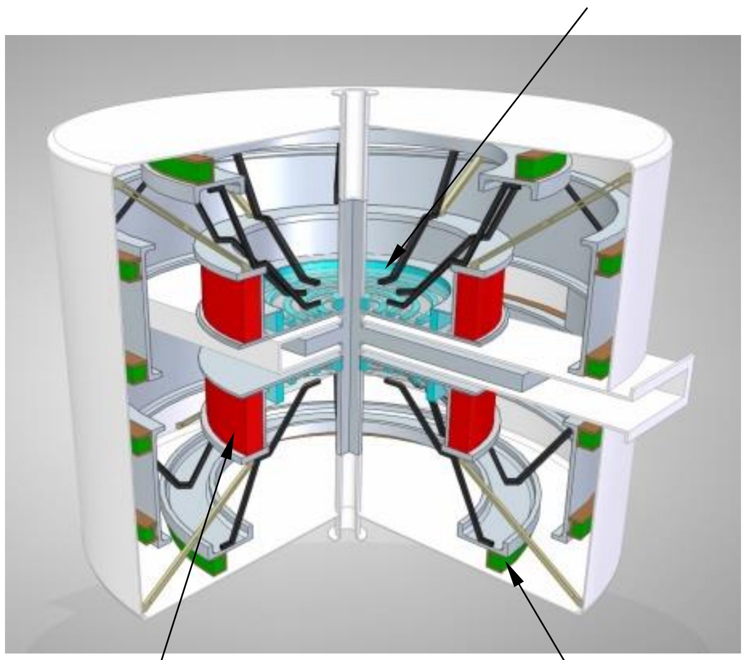
Antaya – Private communication

- Same concept can be used for extraction systems
- Limitations:
  - Adds complexity (cryogenics closer to median plane)
  - Less sharp field variations

Proton cyclotrons - Ongoing developments

2. Synchrocyclotrons: MIT ironless (Pronova)





- 250 MeV protons
- (2.4-)2.8 m Diameter
- Pulsed beam
- Superconducting (Nb_3Sn)
- 4 tons
- T (extr.)
- Cost?
- Variable-energy possible

Accelerators: Comparison table

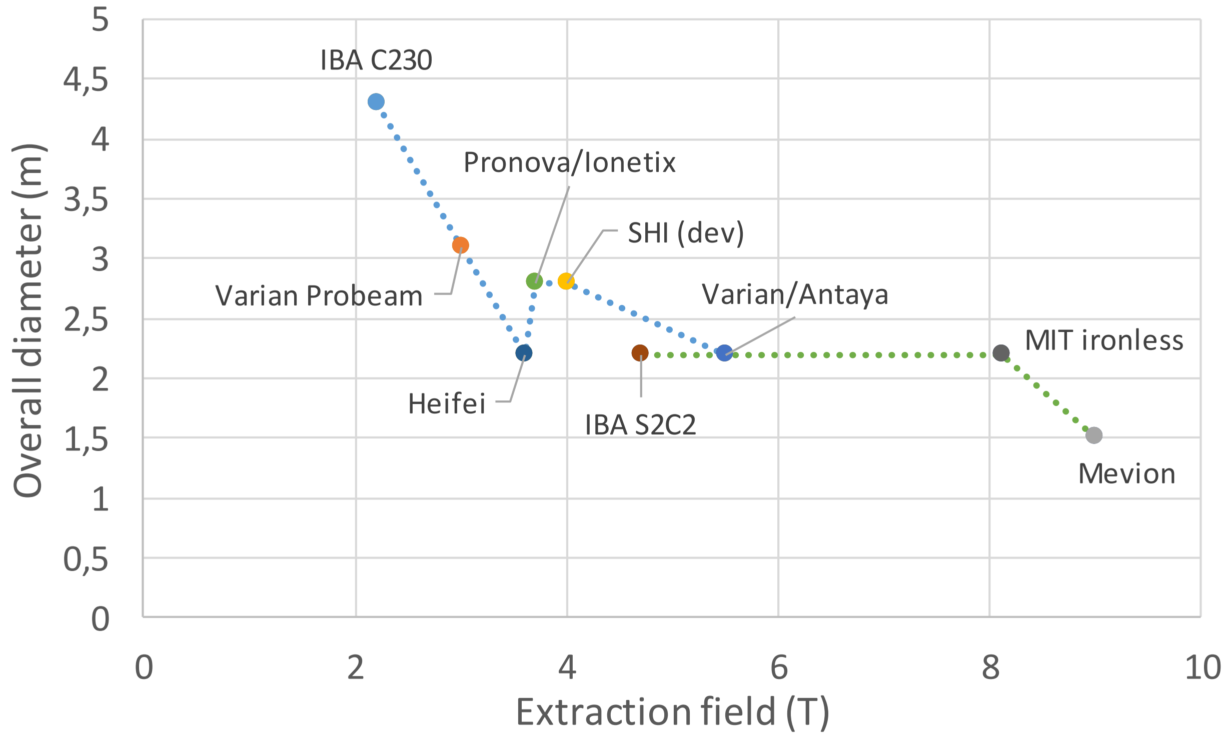
	IBA C230	Varian Probeam	Mevion SC250	IBA S2C2	SHI	ProNova Isoch.	JINR/Heifei SC200	Varian/ Antaya	MIT ironless
Type	Isoch.	Isoch.	Synch.	Synch.	Isoch.	Isoch.	Isoch.	Isoch.	Synch.
Energy (MeV)	230	250	250	230	230	230	200	230	250
Extr. Field (T)	2.2	3	9		4	3.7	3.6	5.5	8.1
Diameter (m)	~4.5	3.1	1.5	2.2	2.8	2.8	2.2	2.2	2.4-2.8
Height (m)					1.7	2.5 (4.5)			
Weight (tons)	~240	90		46	~55	~60	30	30+ (conductor)	5
Cooling	water	He bath	cryocoolers	4 cryocoolers	4 cryocoolers	4 pulse tubes	He Bath (2 cryoc.?)	2? cryocoolers	cryocoolers
Power during operation(kW)	~260				>240	240			
Power when idle (kW)	5-8	?	6.5 (?)	27	>27	>36		>13	

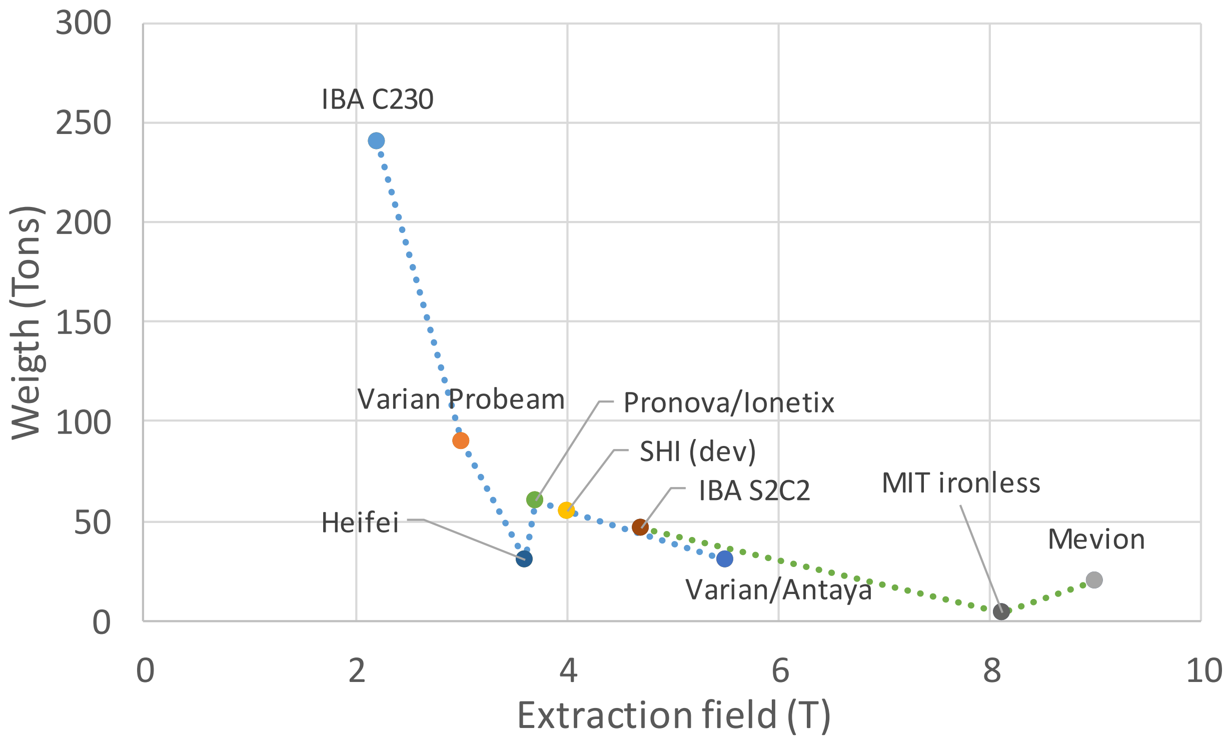
* Sumitomo F50 series compressors:
6.5-7.2 kW at 50 Hz - 7.5-8.3 kW at 60 Hz

** Cryomech PT415 power consumption:
9.2-10.7 kW at 50 and 60 Hz, respectively

Optimization: Is it worth increasing the field?

- Lower weigth helps but is not always an issue (i.e. iron is cheap), as long as you stay within certain limits
- Size matters: facility footprint vs. accelerator complexity (turn sep.)

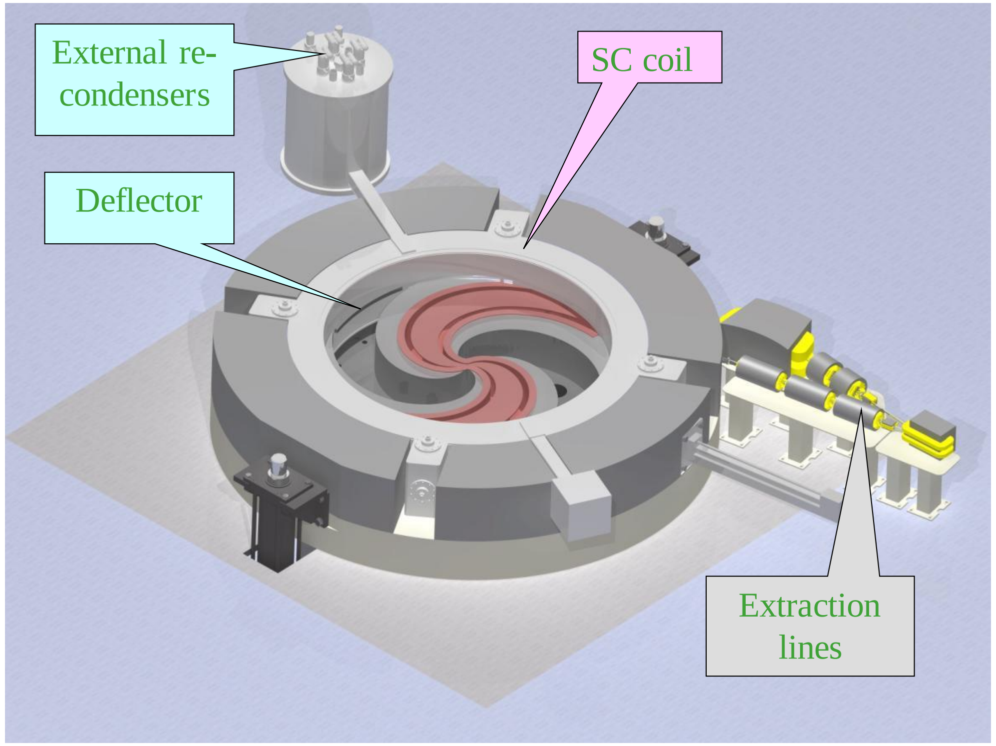


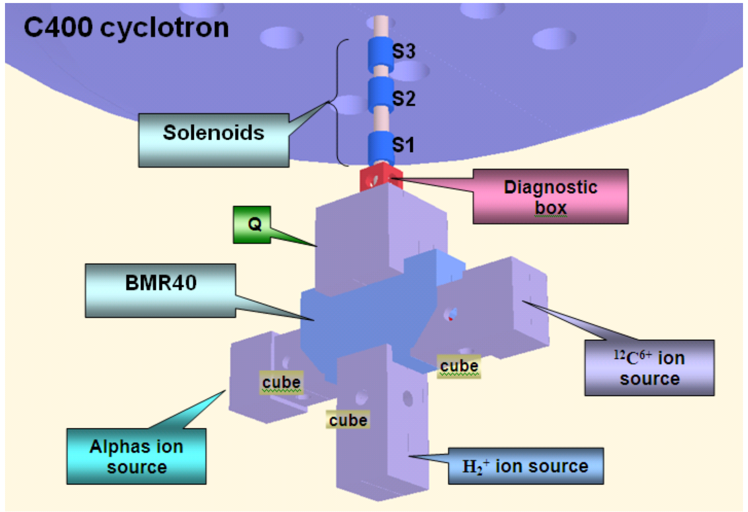


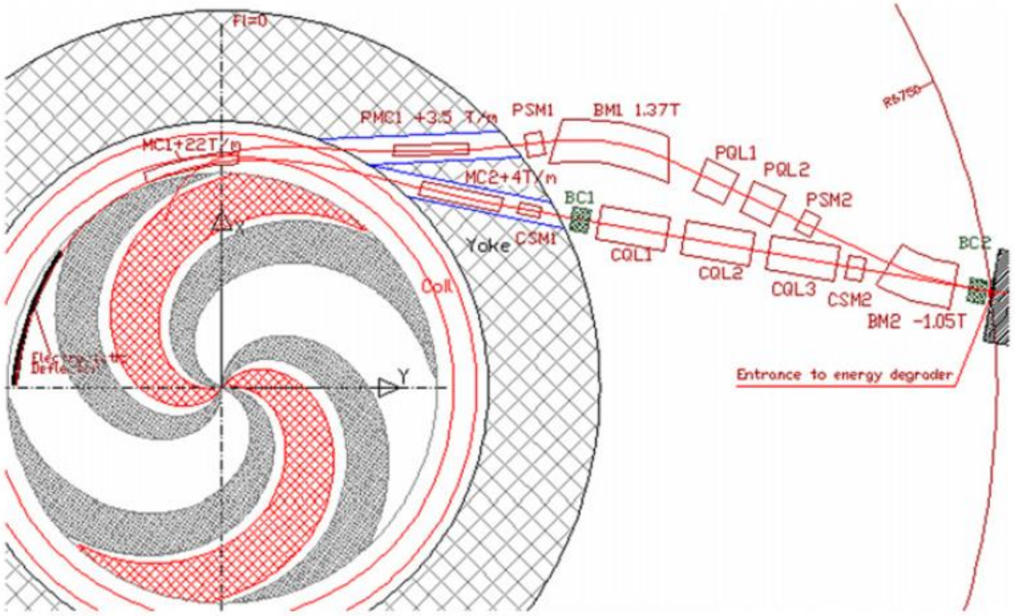
A cyclotron for carbon?

IBA C400

- Up to Carbon (400 MeV/u)
- ~6.5 m Diameter
- ~700 tons
- 4.5-2.5 tesla
- 2 cavities, 75 MHz on H=4







Final thougths

On optimization

Cyclotrons have been there for a long time now

- Compact accelerators
- Relatively low need of RF power (especially true for synchrocyclotrons)
- Capable of intense beams (Cyclone14AE, Cyclone70: >52 kW)

- But the end user, in the end, does not really care about technology
- He cares in:
  - **Functionality**, yield/treatment quality => combination of cyclo/target/synthesis => optics and field quality
  - **Uptime** and **reliability** are paramount => automation and maintenance
  - **Footprint** and **total cost of acquisition** => sound design and compromises

Simulations, sound engineering and customer needs

Thank you

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