Accelerators for medical and industrial applications

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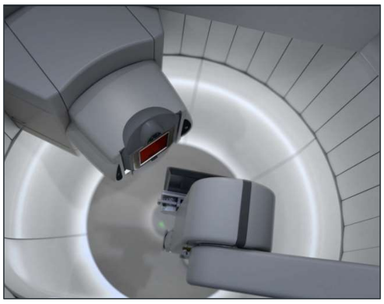
IBA – Ion Beam Applications



MEDICAL TECHNOLOGY

- PROTON THERAPY (PT)
- RADIOPHARMA SOLUTIONS
- INDUSTRIAL APPLICATIONS
- DOSIMETRY

- **R&D:**
  - 12% of turnover
  - 13% of workforce
- **Patent portfolio** (2016):
  - 510 patents & patent applications for 102 innovations
- Over **400 accelerator** systems installed worldwide
- **~270 M€ sales** in 2015
  - ~1600 employees worldwide, 40 nationalities

Protect, Enhance and Save Lives

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Organization of the lecture

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- Part 1: Radioisotopes for medical applications
- Part 2: Cyclotron design and beam dynamics
- Part 3: Particle therapy systems for cancer treatment
- Part 4: Accelerators for industrial applications

Protect, Enhance and Save Lives

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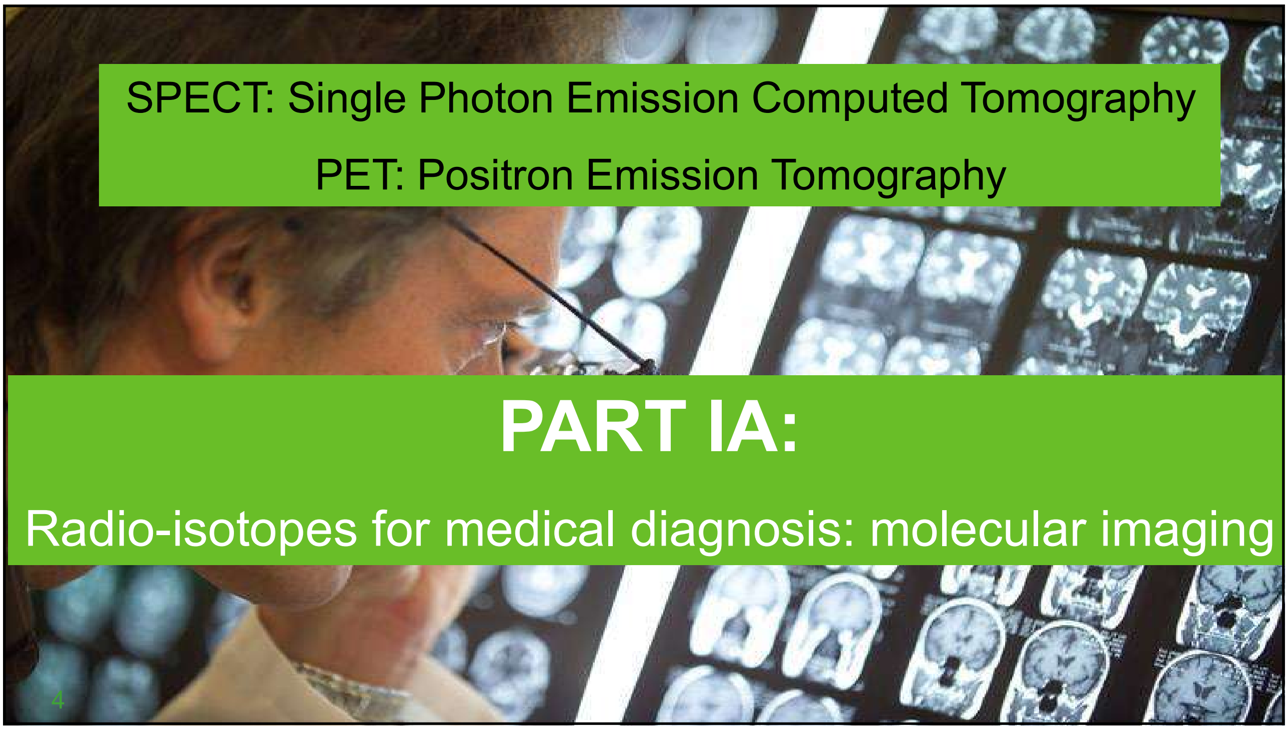


How is imaging done with radio-tracers ?

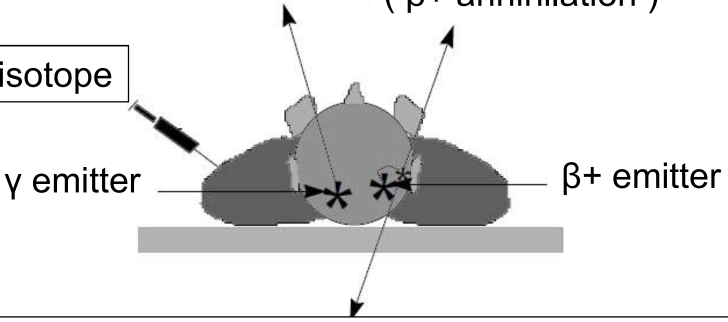
SPECT

Single photon

PET

2 photons of 511keV
(β+ annihilation)

Radio-isotope



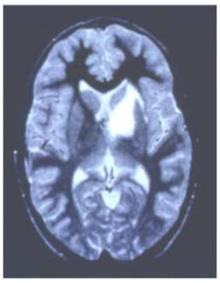
A camera (Gamma or PET) detects the photons emitted from the body and computes 3D distributions of the radio-activity

The use of Radio Isotopes for medical imaging

- Radio tracers can be used to label a specific <u>bio-chemical</u> molecule.
- They allow to see <u>metabolism</u>
  - X-ray (CT-) scan or MRI are better to see the <u>anatomy (structure)</u>
- Nuclear medicine (imaging of metabolism using radioactively labeled molecules) is therefore not in competition, but in complement of imaging techniques such as X-ray CT-scans or MRI.

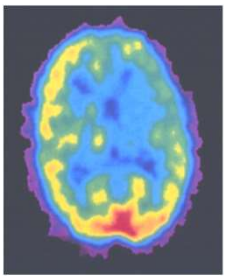
Metabolic versus anatomic imaging

MRI



Anatomic View
(Tissue-structure)

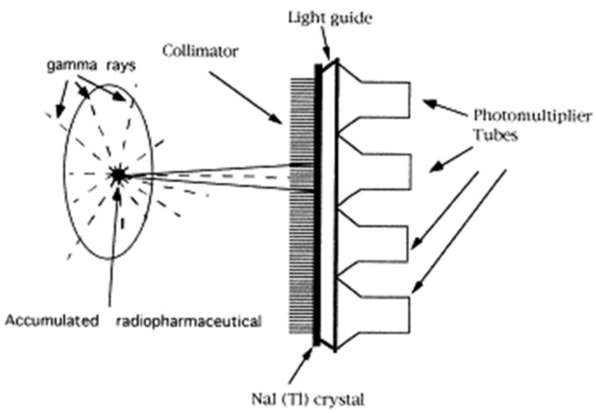
PET



Metabolic imaging
(Biological-function)

SPECT (Single Photon Emission Computed Tomography).

- The imaging of single photons emitters requires a collimator and a position-sensitive detector (with good detection efficiency)
- The image obtained is a projection.
- The collimator prevents non-perpendicular photons from interacting with the detector.

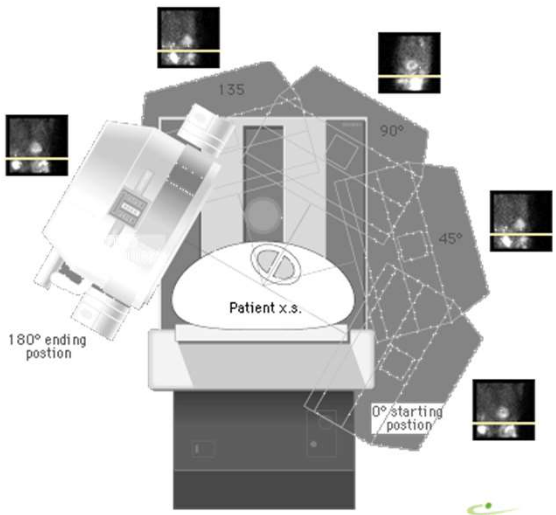


For good spatial resolution, the collimator must be placed close to the patient.
Collimators are usually made of lead.
Typical dimensions: holes 3mm, walls 1 mm, depth 40mm.

The SPECT gamma camera (Anger camera)

Projec… are taken … nd the pa…

Perpe… mathe… uce a 3D rep…



"Traditional" nuclear medicine

- Technetium 99m, the most commonly used radio-isotopes in nuclear medicine is produced in reactors.
  - 90% of diagnostic studies in hospitals is done with ^{99m}Tc !
- But a number of other important nuclear medicine radio-isotopes are produced with cyclotrons of higher energy.
  - ^{201}Tl (Cardiac studies).
  - ^{123}I (Thyroid, Various examinations).
- These longer life isotopes can be internationally distributed
- Large, very powerful cyclotrons are owned by radiopharmaceutical companies.

How to select a good single-photon radio-tracer?

1. The <u>energy</u> of the emitted photon
   - Low enough to keep a good detector efficiency and good collimation and high enough to cross the body tissue
   - 100 keV $\leq$ E $\leq$ 300 keV is generally the optimum
2. The <u>half-life</u>:
   - Short enough to minimize the patient's exposure and long enough to allow distribution to the hospitals
   - 10h $\leq T_{1/2} \leq$ 100h is roughly best
   - Generators are great too !

^{99}Mo (66 hours) = ^{99}Tc$_m$ (6 hours)
^{81}Rb (4.6 hours) => ^{81}K$_r$ (13sec)

3. The chemistry
   - The tracer should bind easily to organic bio-molecules of interest without altering the essential bio-chemical behavior of the molecule (halogens and Technetium are good)

Nuclear reactions for SPECT radio-Isotopes

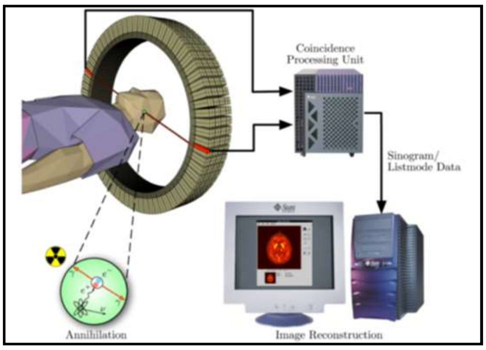
Radioisotope	Half-life	Reaction	Energy (MeV)
^{201}Tl	73.1 h	^{203}Tl (p,3n) => ^{201}Pb => ^{201}Tl	17~28
^{67}Ga	78.3 h	^{68}Zn (p,2n) => ^{67}Ga	12~28
^{111}In	67.4 h	^{12}Cd (p,2n) => ^{111}In	12~28
^{123}I	13.2 h	^{124}Te (p,2n) => ^{123}I	20~25
		^{124}Xe (p,2n) => ^{123}Cs => ^{123}I	20~30
		^{124}Xe (p,pn) => ^{123}I	
		^{127}I (p,5n) => ^{123}Xe => ^{123}I	45~68

A 30 MeV cyclotron can often do the job

Positron emitting radio-isotopes

- The emitted positron travels a few millimeters, then meets an electron and annihilates, emitting two anti-parallel photons of 511keV.
- These two photons can be detected in coincidence by a ring of detectors surrounding the region of interest.
- One knows then that the origin of the photons is on the line connecting the two detectors => no collimator needed
- Several detections allow to locate the source.
- By mathematical reconstruction, a 3D representation of the activity can be obtained.
- PET (Positron Emission Tomography).

The PET scanner



Currently available are

- PET scanners integrated with CT: PET-CT
- PET scanners integrated with MRI: PET-MRI

PET scanner in a hospital

- Coincidents events are grouped into projected images (sinograms) and sorted by the angle of view
- Analogous to the projections obtained with Computed Tomography (CT) scanners
- 3D image re-construction is similar

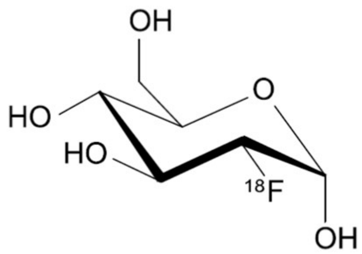
Common positron emitting radioisotopes for PET

Radioisotope	Half-life (min)	E-positron (MeV)	Reaction	Energy (MeV)
^{11}C	20.4	1.0	^{14}N (p,α)=> ^{11}C	5=>16
^{13}N	9.96	1.2	^{16}O (p,α)=> ^{13}N	8=>16
			^{12}C (d,n)=> ^{13}N	3=>8
^{15}O	2.07	1.7	^{15}N (p,n)=> ^{15}O	5=>14
			^{14}N (d,n)=> ^{15}O	3=>8
^{18}F	109.8	0.6	^{18}O (p,n)=> ^{18}F	5=>14

Cyclotrons 10-18 MeV

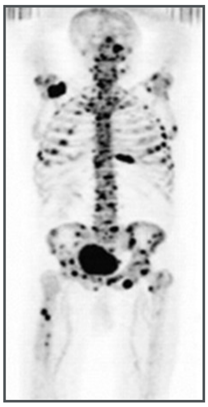
FDG = Fluoro-Deoxy-Glucose

- Most commonly made PET scan (90% of cases) is done with 18F-FDG (Fluoro-Deoxy-Glucose)
- Metabolic activity by virtue of glucose uptake in tissue
- This tracer is mainly used to explore the possibility of cancer metastasis and the response to treatment

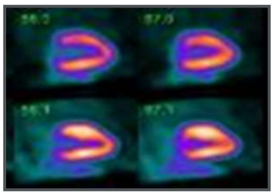


- In glucose one OH-group is replaced by a 18-F atom
- Both atoms have about the same size =>
- Bio-chemical behaviour almost not altered

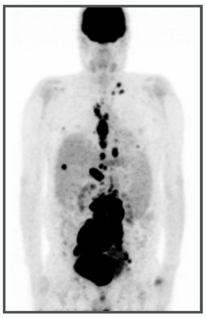
Some examples



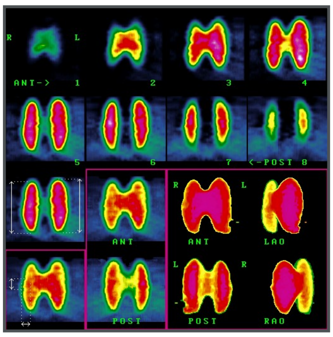
Oncology
Na^{18}F Bone scan



Cardiology
Sr/Rb82
^{13}NH3
15O

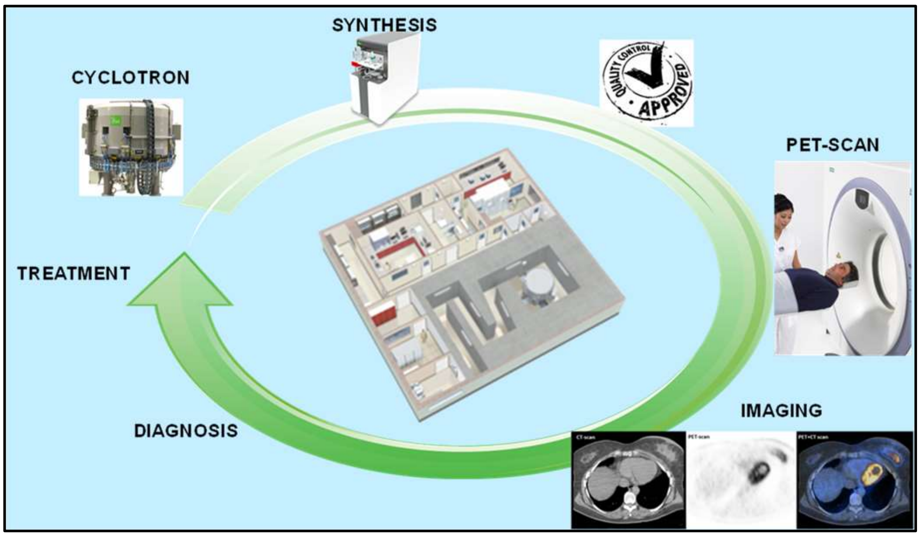


Oncology
^{18}FDG & others



Oncology & others
^{123}I

Production/Application cycle of PET radio-isotopes



Part 1B: Radio-isotopes for cancer therapy

In a radioisotope, the nucleus decays spontaneously, giving off particles with some kinetic energy.

β^+ γ — diagnosis

α β^- — therapy

PET	$T_{1/2}$
F-18	2h
Ga-68	1h
Zr-89	3d
I-124	4d
O-15	2min

SPECT	$T_{1/2}$
I-123	13d
Tc-99m	6h
Ga-67	78h
In-111	2.8d
Tl-201	3d

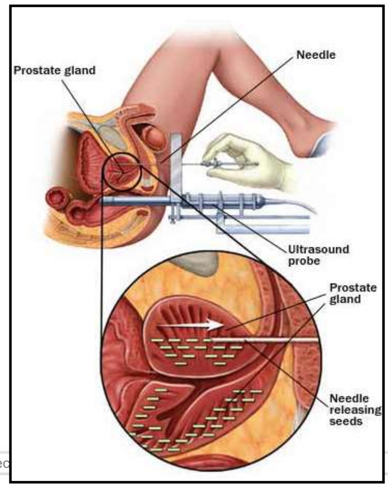
- I-131
- Y-90
- Re-188
- Lu-177
- At-211*

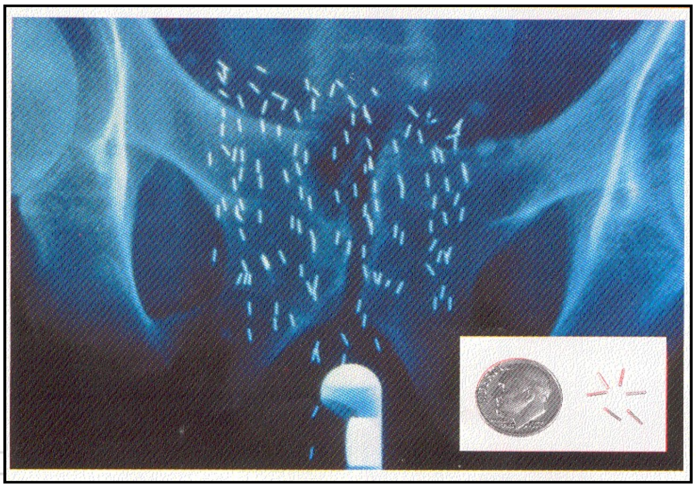
Brachy therapy

- Dose is delivered by placing the radiation source directly inside the area requiring treatment
- Commonly used for uterus, prostate, breast and skin cancer
- Irradiation affects only a very localized area => healthy tissues are spared
- Much higher doses can be delivered. For comparison:
  - Proton therapy: about 40 Gray
  - Prostate brachytherapy: about 100 to 150 Gray
- Brachytherapy can often be completed in less time
  - Reduce the possibility of recovery of cancer cells between treatment intervals

Prostate brachytherapy with Pd-103 or I-125

Seeds placed with 3D precission verified with ultrasound probe
They are not harmfull and can stay in place after treatment





A family of cyclotrons for isotope producion

- Cyclone 3D   3 MeV D+ (production of Oxygen-15)
- Enabler — Cyclone 11:   11 MeV H-, 120 µA (~1300 W)
- Pet Production — Cyclone 18/9:   18 MeV H-, 150 µA (~2700 W)   Deuteron possible
- Pet/SPECT crossover — Cyclone 30(xp):   30 MeV, 1.2 mA (36 kW)   alpha/deuteron possible (xp)
- World record — Cyclone 70(xp):   70 MeV, 750 µA (53 kW)   alpha/deuteron possible (xp)

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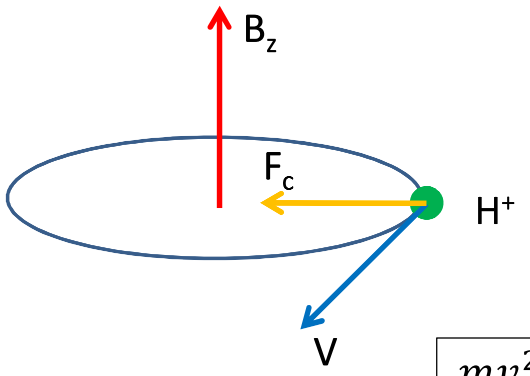
Part II: Applied cyclotrons: beam dynamics and magnetic design

- Introduction
- ….. about focusing and isochronism
- ….. about injection
- ….. about extraction

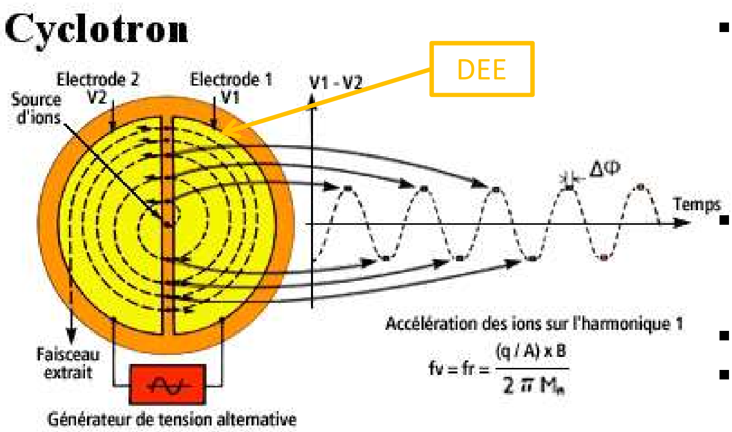
Introduction:
The most basic equation of the cyclotron



- A charged particle in a uniform magnetic field moves on a circle
- The centripetal force is equal to the Lorentz force acting on the particle
- **Thus the rotation frequency of the particle is constant => independent on radius ,velocity , energy or time** (in the non-relativistic limit)

$$\frac{mv^2}{r} = qvB \quad \Rightarrow \quad \omega = \frac{v}{r} = \frac{qB}{m}$$

Consequences of constant cyclotron frequency



Classical cyclotron:
Lawrence and Livingston, Phys. Rev. 40 (1932) 9

- Particles can be accelerated with an RF-system operating at constant frequency:

F_{RF}(MHz) = 15.2 h(Z/A) B (Tesla)

- The orbit starts in the center (injection) and spirals outward towards the pole radius (extraction)
- The magnet field is constant in time
- RF and magnetic stucture are completely integrated => **Same RF structure accelerates many times** =>compact and cost-effective
- CW-operation (continuous wave)

Classical cyclotron: where is the problem?

i. In a uniform magnetic field there is no vertical focusing (**metastable**)
ii. During acceleration, due to the relativistic mass increase, the revolution frequency decreases in a uniform magnetic field => loss of resonance between RF and the beam => loss of isochronism
iii. just increasing the magnetic field with radius is not possible => **vertically unstable**

$$\omega = \frac{qB}{m_0}\sqrt{1-\left(\frac{v}{c}\right)^2}$$

Another solution: **the synchro-cyclotron**

- Let the magnetic field gradually decrease with radius in order to obtain **weak vertical focusing** =>

$$\upsilon_z = \sqrt{k} \Rightarrow k = -\frac{r}{B}\frac{dB}{dr}$$

- Let the RF frequency gradually decrease with time in order to compensate for the drop of the magnetic field and for the increase of the mass

$$\omega = \frac{qB}{m}$$

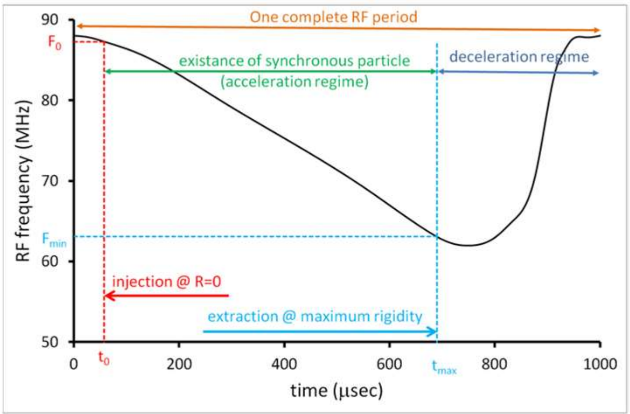
Veksler, J. Phys. USSR **9** (1945)153
McMillan, Phys. Rev. **68** (1945)143L

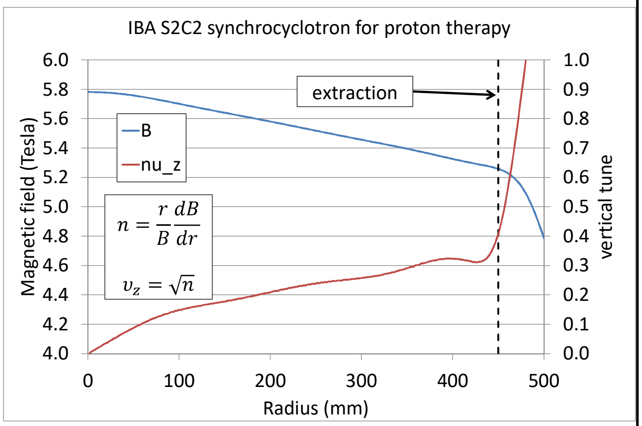
Note: synchrotron was invented at the same time

Some consequences

1. The RF (and beam) is pulsed but the magnetic field B=const ≠ B(t)
2. The mean beam intensity is much lower => OK for proton therapy
3. There is longitudinal beam dynamics similar to that of the synchrotron
4. Only during a short time-window, beam can be captured in the center
5. A more complicated RF because of the required frequency variation
6. The RF frequency can not be varied very fast (rotating capacitor) and therefore the acceleration must be slow => low energy gain per turn => many turns up to extraction => little RF power needed
7. There is only a very small turn-separation ⇒ a special extraction method is needed to get the beam out of the machine (regenerative extraction)

Example: the IBA S2C2 for proton therapy





Repition rate = 1 kHz
Duty cycle about 100

Superconducting synchro-cyclotron
Extraction energy 230 MeV

Longitudinal dynamics in a synchro-cyclotron

- There is a definition of a synchronous particle: everywhere in the synchro-cyclotron, at any moment in time, the revolution frequency of the synchronous particle is equal to RF frequency
- There are oscillations (in energy and phase) of real particles around the synchronous particle
- There is a stability zone for these oscillations defined by a separatrix in the longitudinal phase space
- This separatrix is filled during the beam capture in the synchro-cyclotron center

Yet another solution: **the isochronous cyclotron**

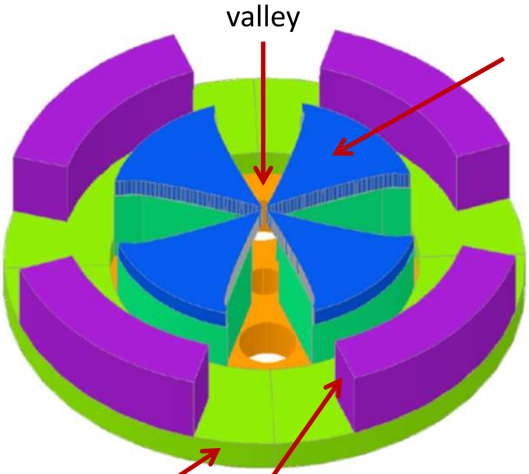
- Two contributions to vertical focusing:

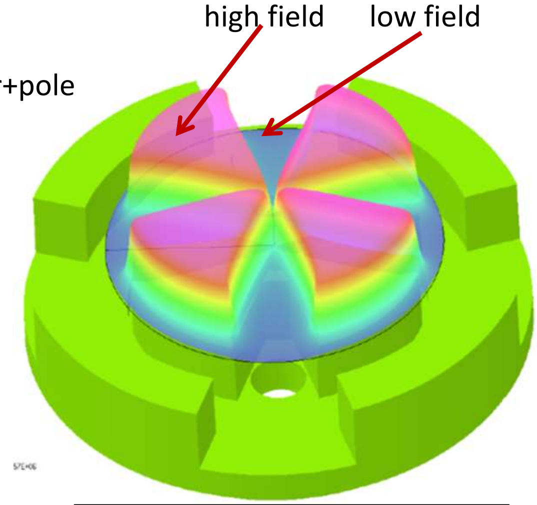
$$F_z = q(\vec{v} \times \vec{B})_z = -q(v_\theta B_r - v_r B_\theta)$$

  - $v_\theta B_r$ => obtained in the radially decreasing rotationally symmetric magnetic fields as in the classical cyclotron and the synchro-cyclotron
  - $v_r B_\theta$ => requires an azimuthal modulation of the magnetic field => introduce sectors (hills) with high field and valleys with low field => azimuthally varying field cyclotron=> the field variation creates the non-circular orbit

Some aspects of vertical focusing and isochronism

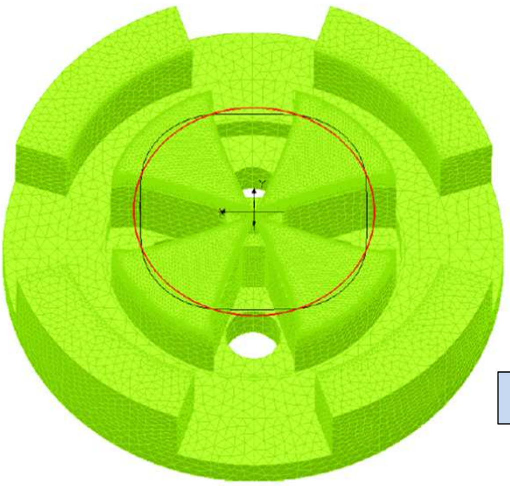
The Azimuthally Varying Field (AVF) cyclotron

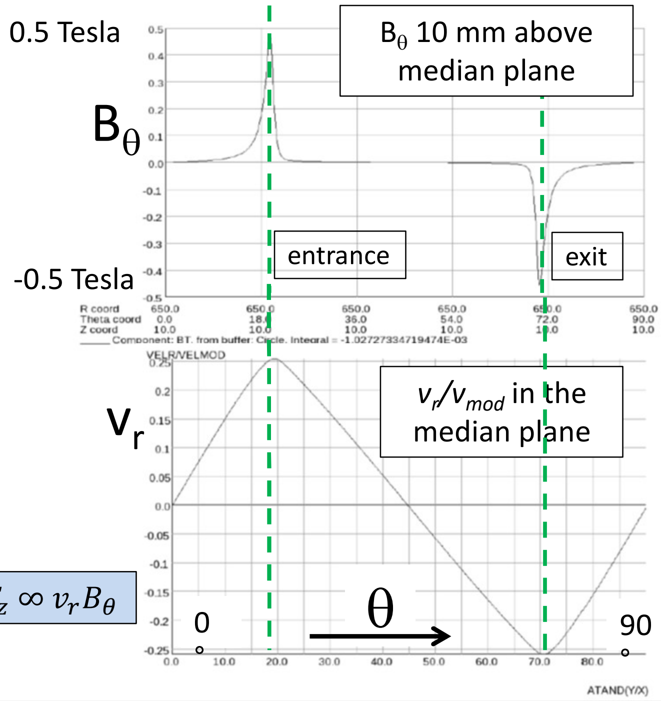




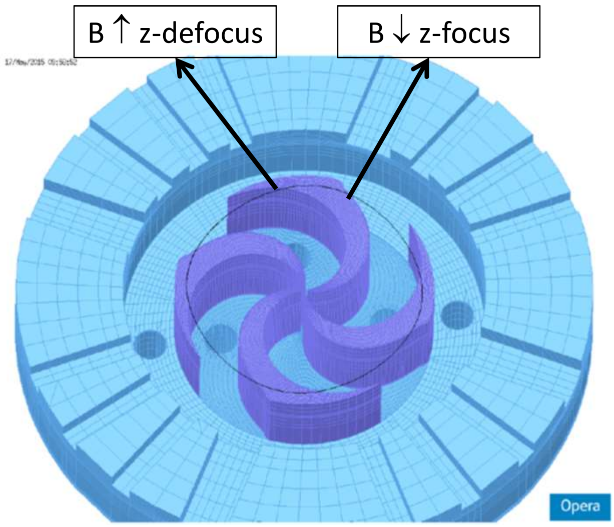
Magnetic field on hills and valleys

scaloping of the orbit => Vertical focusing





More vertical focusing => pole spiraling



For straight sectors: equal vertical focusing at entrance and exit of sector

Spiraling of the pole changes the focusing strength at the entrance and exit of the sector:

Entrance: strong B-decrease => strong z-focusing

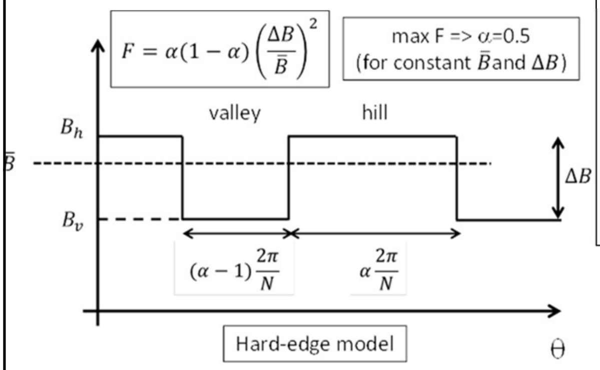
Exit: strong B-increase => strong z-defocus

ALTERNATING FOCUSING
This may give a very large contribution

Flutter: a measure for the azimuthal field variation

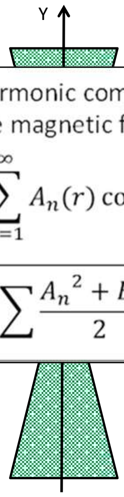
Average of the field modulation

$$F(r) = \frac{\overline{B^2} - \bar{B}^2}{\bar{B}^2}$$



N=number of sectors

α='filling factor'



Fourier harmonic composition of the magnetic field

$$B(r,\theta) = \bar{B}(r)\left\{1 + \sum_{n=1}^{\infty} A_n(r)\cos n\theta + B_n(r)\sin n\theta\right\}$$

$$F = \sum \frac{{A_n}^2 + {B_n}^2}{2}$$

Formulas for focusing in an AVF cyclotron

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

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

k = field index = $-\frac{r}{\bar{B}}\frac{d\bar{B}}{dr}$

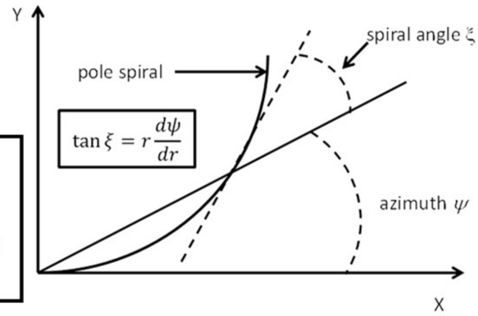
F = flutter

N = number of sectors

ξ = spiral angle

This is an approximation: There is also some dependency on radial gradients of the flutter. See: Hagedoorn and Verster, NIM **18,19** (1962) 201-228

Definition of spiral angle



NOTE: for an iscochronous cyclotron:

$$k = 1 - {\gamma_{\rm rel}}^2$$

$$\nu_r \cong \gamma_{\rm rel}$$

Isochronism => the revolution frequency of the particle is constant everywhere in the cyclotron independent of the energy of the particle

Isochronous cyclotrons have to be isochronized by correct shaping of the average magnetic field as a function of radius

All cyclotron magnetic fields are mapped in the median plane

Precise mapping and iron pole shimming is needed in order to isochronize the magnetic field

$\Rightarrow$

It is not possible to obtain isochronism just from the design => required precission of <B> =>10^{-4} to 10^{-5}

- Move Hall-probe or a search coil (S2C2) on a 2D polar grid to obtain a full field-map => automized and computer controlled system

- Analyse the magnetic field on equilibrium orbits in order to evaluate isochronism
- Shim the hill sectors of the iron in order to improve the isochronism (reduce the RF phase slip)

Essential information of a cyclotron field map

1. The level of isochronism => integrated RF phase slip
2. The transverse optical stability => tune functions
3. Crossing of dangerous resonances => operating diagram
4. Magnetic field errors
   - First and second harmonic errors => resonance drivers
   - Median plane errors => very difficult to measure
5. …

Analysis of a cyclotron field map

1. Static analysis => Acceleration is turned off
   - Computation of a family of closed orbits and their properties
2. Accelerated orbits => for special problems
   - Central region studies
   - Extraction studies
   - Study of resonance crossings
   - …

Isochronism: integrated RF phase slip

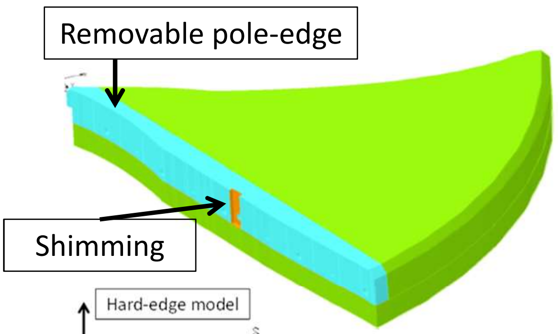
- Closed orbit code gives the RF phase slip per turn
- The integrated (accumulated) phase slip will depend on the number of turns and thus on the energy gain per turn: larger V_{dee} => less turns=> less slip
- However, energy gain per turn depends on the RF phase slip already accumulated.
- A self-consistent formula is needed:

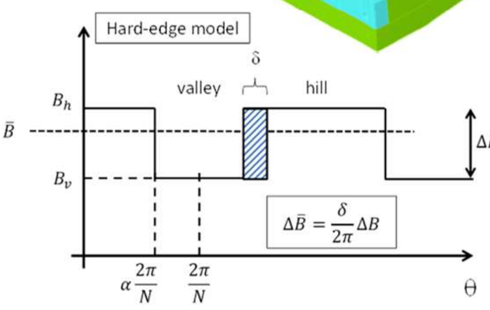
$$\Phi(E) = \sin^{-1}\left(\frac{2\pi h}{f_{RF}}\int_0^E \frac{\Delta f(E')}{\Delta E_0(E')}dE'\right)$$

Φ = integrated RF phase slip
h = harmonic mode
f_{RF} = RF frequency
Δf = closed orbit frequency error
ΔE_0 = nominal energy gain per turn

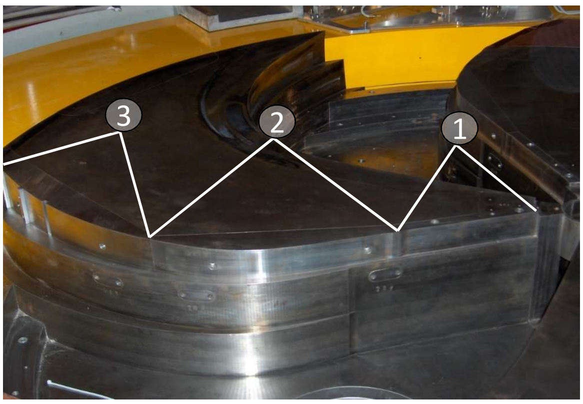
See also: Gordon, Particle Accelerators **16** (1984) 39-62

Isochronization by pole shimming





Removable pole edges in the C235

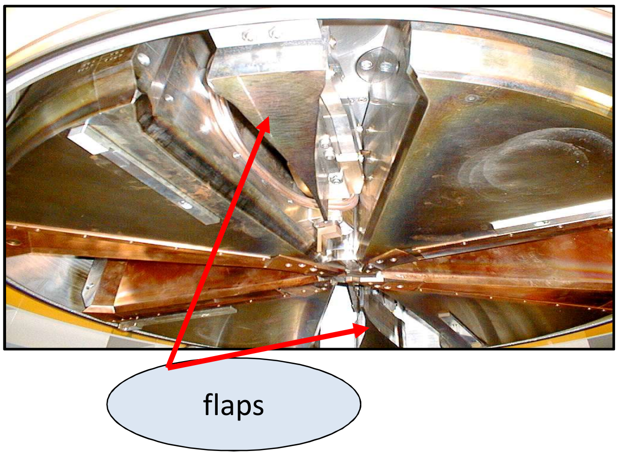


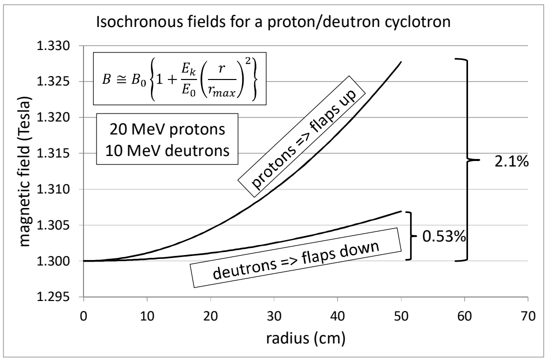
In this isochronous PT cyclotron, there are 3 removable pole edges (per pole) for shimming the average field as needed for isochronism

Isochronization for two different particles

Example: a proton/deuteron isotope production cyclotron

By placing pieces (flaps) in the valleys which can be moved vertically close to the median plane (protons) or further away from the median plane (deuterons)





INJECTION INTO A CYCLOTRON

Transfer of the beam from the ion source onto the equilibrium orbit in the center of the cyclotron, two appoaches:

1. Internal Ion Source:
   - Ion source placed in the center of the cyclotron
   - Source is 'integrated part' of the accelerating stucture
   - Is used in PT cyclotrons as well as isotope production cyclotrons
2. External Ion Source:
   - Ion source placed oustside of the machine
   - An injection line with magnets and electrostatic inflector is needed
   - Used in high intensity isotope production cyclotrons (and in IBA C400)

Injection: some important design goals

1. Place the beam on the correct equilibrium orbit given by the injection energy (horizontal beam centering)
2. Vertical centering with respect to the median plane
3. Longitudinal matching =>bunching => compressing the DC beam from the ion source into shorter packages at the frequency of the RF
4. Matching of the beam phase space into the cyclotron acceptance or eigenellipse (if possible)
5. Preserve as well as possible the beam quality with minimum losses between the ion source and the cyclotron center

Injection: internal ion source

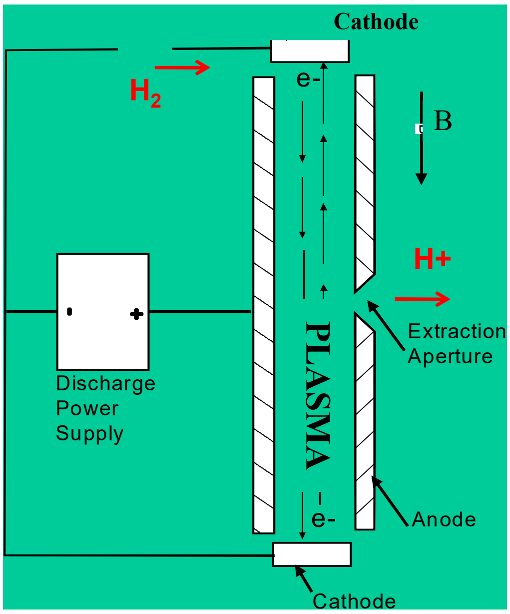
Some advantages

- Simple and cost-effective: simple ion source; no injection line needed
- Compact:
  - two ion sources can be placed simultaneously
  - Can be used in the high-field (6 to 9 Tesla) superconducting cyclotrons

Some disavantages/limitation

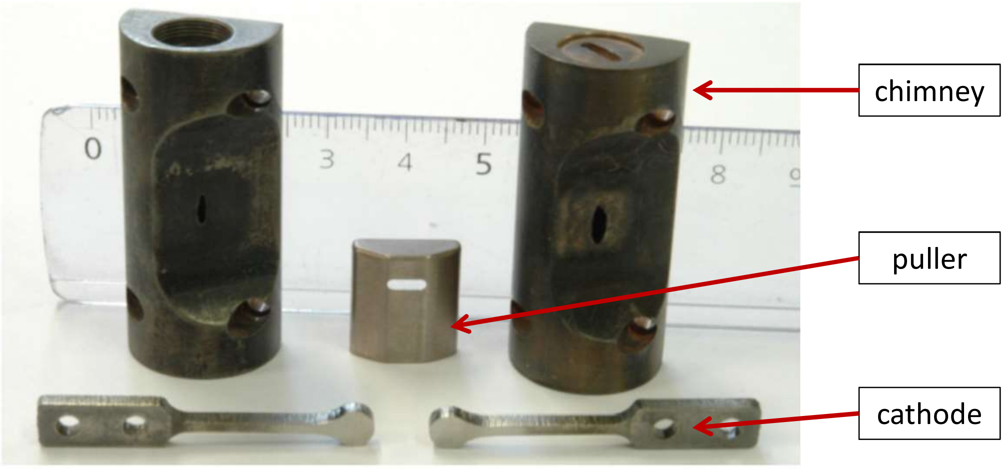
- Low to moderate beam intensities
- Simple ion species (H^+,H^-,deuterons,He-3, He-4)
- Beam matching/bunching/manipulation not possible
- Gas-leak directly into the cyclotron (bad for negative ions)
- Machine has to be vented for ion source maintenance

Injection: cold cathode PIG ion source



- Electron emission due to electrical potential on the cathodes
- Electron confinement due to the magnetic field along the anode axis
- Electrons produced by thermionic emission and ionic bombardment
  - Start-up: 3 kV to strike an arc
  - At the operating point : 100 V
- cathodes heated by the plasma (100 V is enough to pull an outer e- off the gas atoms)
- Hot cathode PIG => heated with filament

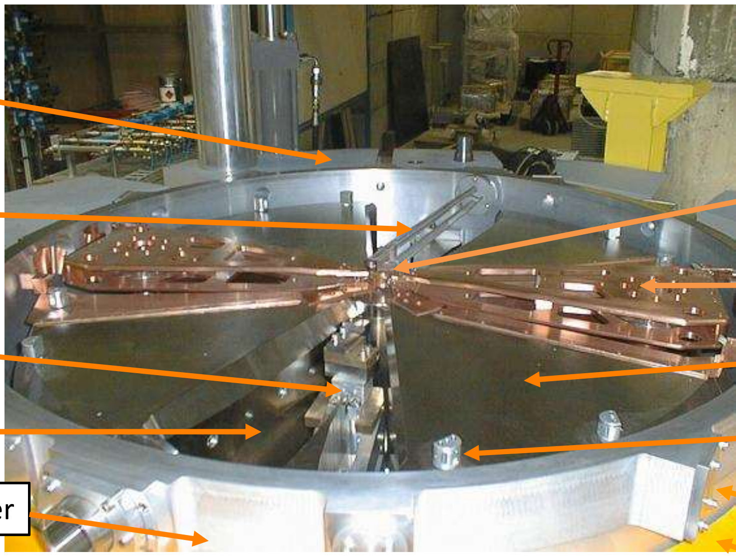
Chimney, cathodes and puller



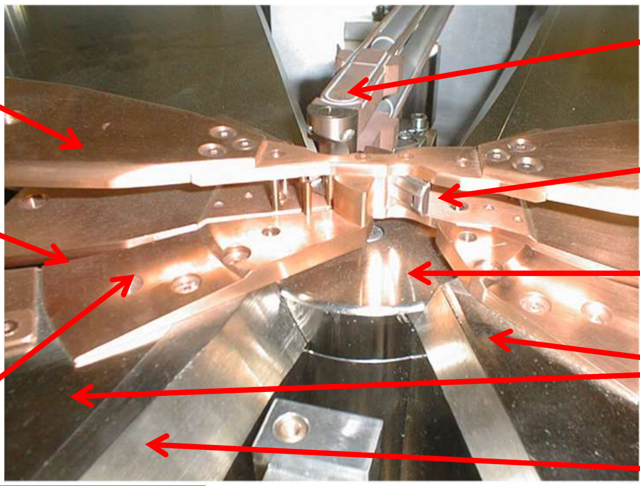
Chimney: copper-tungsten $\Rightarrow$ good heat properies; machinable

Cathodes: tantallum $\Rightarrow$ high electron emission; shaped to reduce heat conduction

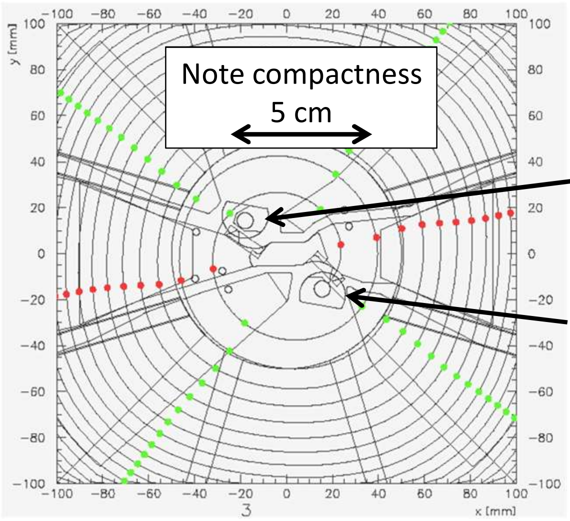
Compact Deep-valley Cyclotron Design



Example: central region of a compact cyclotron



Orbit tracking (C18/9 isotope production cyclotron)



E-fields => from Opera
B-fields => measured or Opera

D^- source; h=4

H^- source h=2

D^- source is placed further out because of larger orbit

Cut D^- chimney for H^- passage

Red dots: position of particle when V_{dee} =0

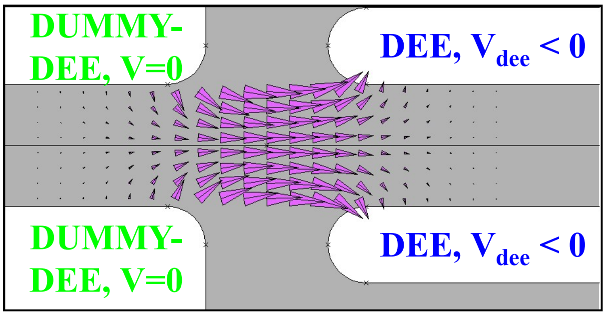
Green dots: position of particle when V_{dee} =V_{max}

Vertical focusing in the center

- Azimuthal Field Variation (AVF) goes to zero in the cyclotron center ⇒ magnetic vertical focusing disappears
- Two remedies
  - Add a magnetic field bump in the center ⇒ negative field gradient creates vertical focusing: field bump of a few hundred Gauss ⇒ central plug
  - The first few accelerating gaps provide electrical focusing ⇒ proper positioning of accelerating gaps during the design to get some phase focusing

Vertical Electrical Focusing in accelerating gap: two contributions

Vertical cross section

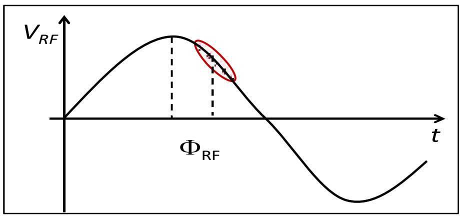


1st half => focusing 2nd half => defocusing

Falling slope of RF ⇒ net focusing (phase focusing)

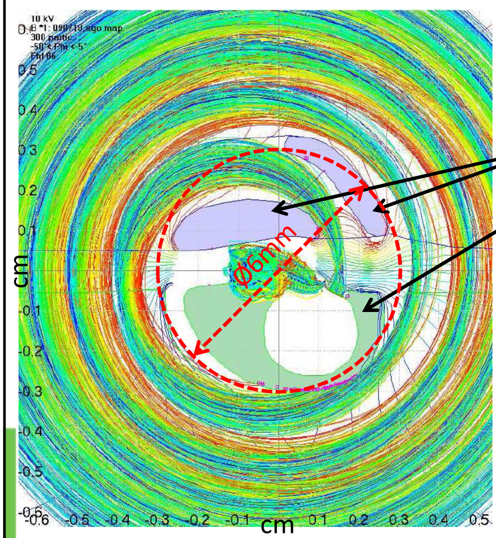
i. Due to the shape of electric field lines in the gap: first half is focusing and second half is defocusing => total effect is focusing => comparable to **Einzel lens**

ii. Due to RF effect: If E-field is decreasing in time at moment of acceleration => falling slope of RF sine wave => second defocusing half is less important => net focusing (phase focusing)

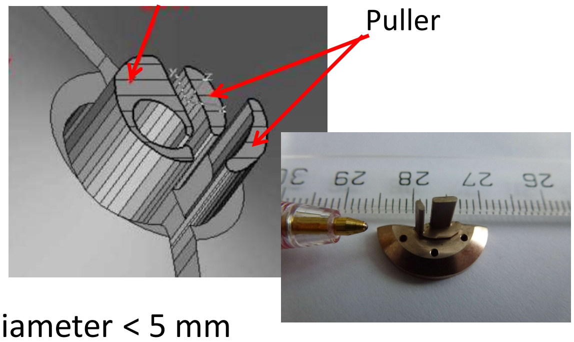


Example: Ion source and central region of the S2C2

Central region size with a very compact cold cathode PIG source



Due to the high field (5,74T) and the low dee voltage (11 kV), the source has to be extremely compact:



1. Source diameter < 5 mm
2. Vertical gap in the center 6 mm
3. First 100 turns within a radius of 3 cm

By the way: why a SC synchrocyclotron for PT

- An isochronous cyclotron needs flutter
- Flutter can only be created by the iron (not by the coil)
- Maximum achievable field modulation about 2 Tesla
- If average field is pushed too far up (using a SC coil) then no longer enough flutter => not enough vertical focusing
- In a synchro-cyclotron this problem does not occur

In a synchrocyclotron you can fully exploit the potential offered by superconductivity

Axial Injection

Axial injection $\Rightarrow$ most relevant for compact cyclotrons

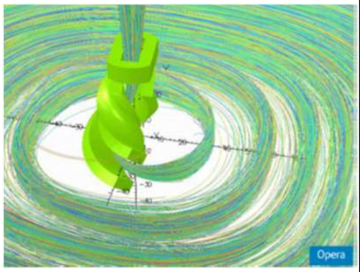
- Along the vertical symmetry axis of the cyclotron
- In the center, the beam is bent by 90° into the median plane
- For this an electrostatic inflector device is used

Spiral inflector for Axial Injection

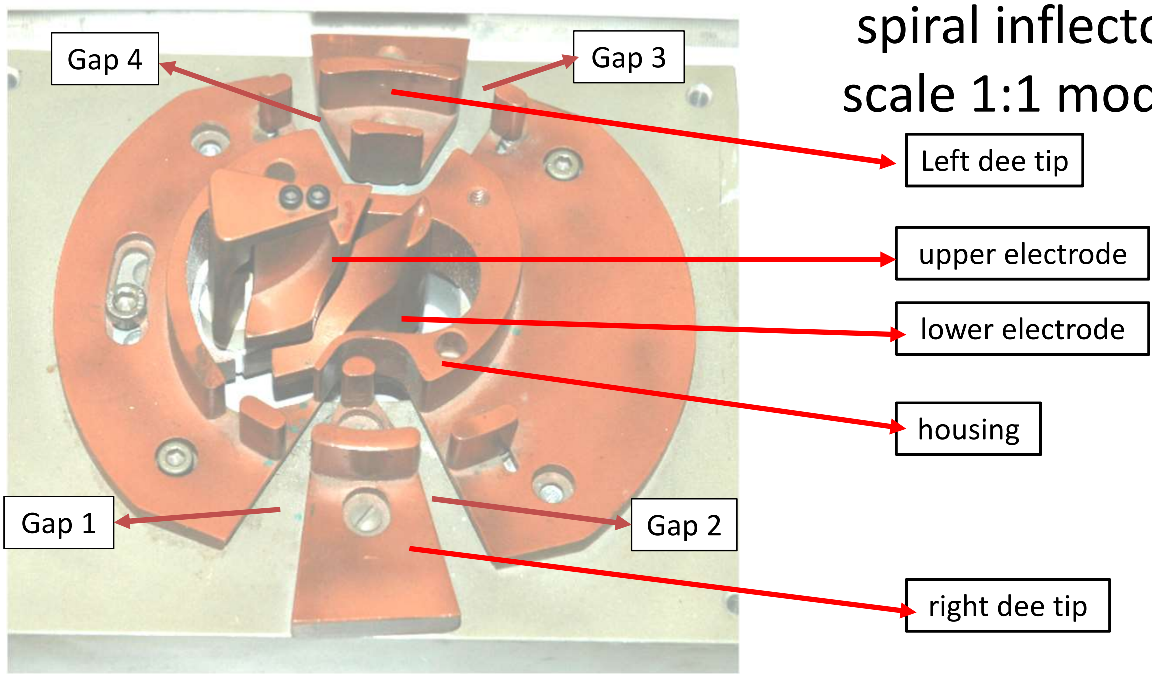
- The E-field between 2 electrodes bends the beam 90° from vertical to horizontal. The presence the cyclotron B-field creates a 3D orbit
- The spiral inflector basicly a cylindrical capacitor which is gradually twisted in order to take into account the spiraling of the trajectory induced by the vertical magnetic field
- E-field always perpendicular to velocity ⇒ orbit on equipotential ⇒ this allows for low electrode voltage

$$\frac{qV}{E} = \frac{2d}{A}$$

- Two free design parameters available to obtain orbit centering
  1. Electric radius A (equivalent to height of inflector)
  2. Tilt parameter k’ (equivalent to a change of magnetic field)
- Very compact geometry
- Complicated electrode structure needs a 5 axis milling machine

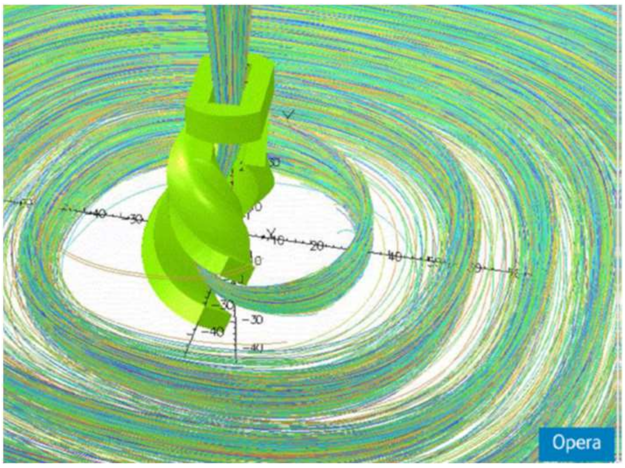


spiral inflector scale 1:1 model



Inflector simulations

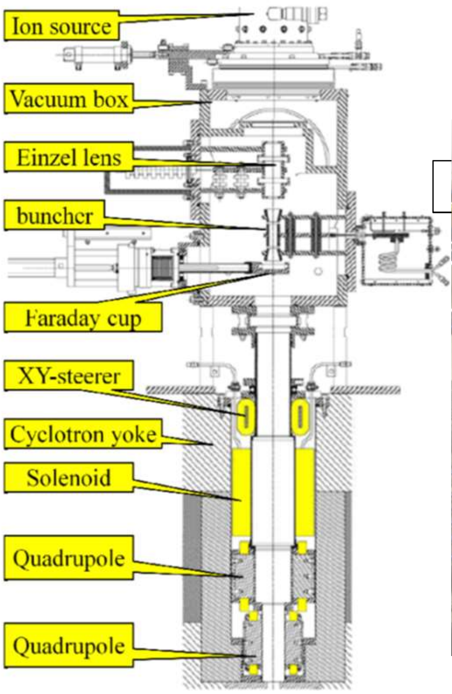
Calculated orbits imported in Opera3D



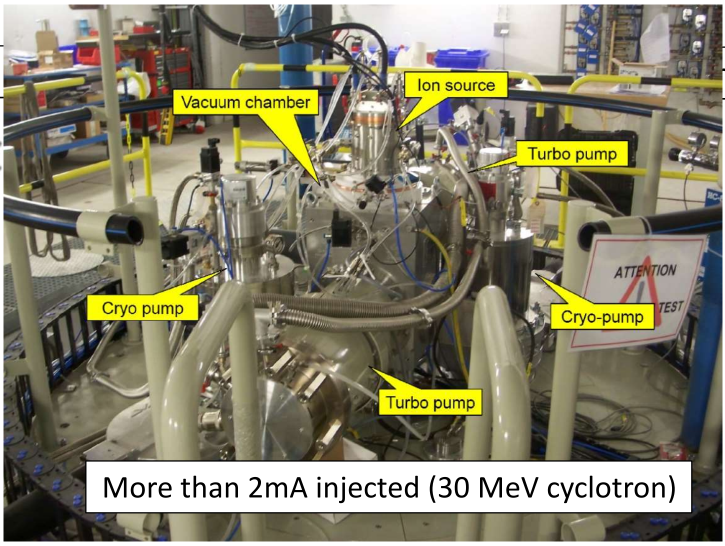
- Spiral inflector is a complex 3D problem
- 3D fields (B,E) are needed => Opera3d
- In house developed tracking code
- Calculated orbits are imported in Opera3d post-processor
- Tilt is seen as the electrode-rotation at the exit

C70-example

An additional horizontal deflector is needed for multi-particle cyclotron



Injection line



More than 2mA injected (30 MeV cyclotron)

Some aspects of extraction

Extraction from a cyclotron

- Extraction: transfer of the beam from an internal orbit to the application outside of the magnetic field
- Often a difficult process. Why?
  1. The magnetic field acts like a trap: When the particle enters into the radial fringe field of the pole, it runs out of RF phase and will be decelerated ⇒particle is « reflected » inwards (if nothing is done to prevent this)
  2. The orbits pile up at high radii ⇒ smaller and smaller turn-separation

     $$R \infty \sqrt{E}$$

  3. The beam quality is quickly destroyed in the non-linear fringe field

Different ways of extraction

1. No extraction at all => place an internal target
   - Can be done for isotope production (a little bit dirty)
2. Stripping extraction (H^- cyclotrons; or H_2^+)
   - Isotope production cyclotrons
3. Extraction with an electrostatic deflector (ESD)
   - Proton therapy cyclotrons (Varian, IBA, SHI)
4. Regenerative extraction => synchrocyclotron
   - Proton therapy cyclotrons (Mevion, IBA)
5. Self-extraction => suitable shaping of the magnetic field
   - One IBA prototype cyclotron but needs further improvement

Cases 3 and 4 require some way to increase the turn separation before extraction

Stripping Extraction (1)

Beam passes through a thin foil to remove electrons and suddenly change of the orbit curvature

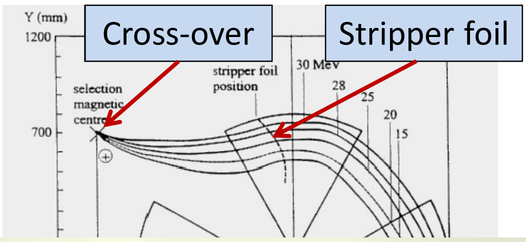
$$\rho_f = \frac{Z_i}{Z_f}\frac{M_f}{M_i}\rho_i$$

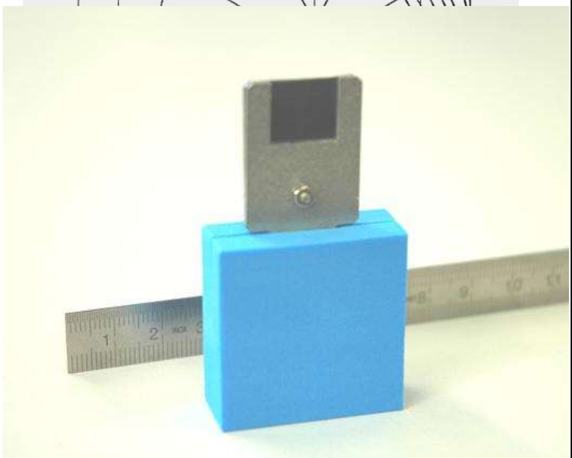
- Example H-minus, $H^- \Rightarrow H^+ + 2\,e^-$ (IBA C18/9, C30, ACS TR30, GE)
  - => Radius of curvature changes sign $\rho_f = -\rho_i$
- Example $H_2^+ \Rightarrow 2\,H^+ + e^-$
  - Requires a much larger machine, because the extracted energy reduces with a factor 4 compared to protons
  - Only works when there is enough flutter

$$\rho_f = \frac{\rho_i}{2}$$

H^- stripping extraction (2)

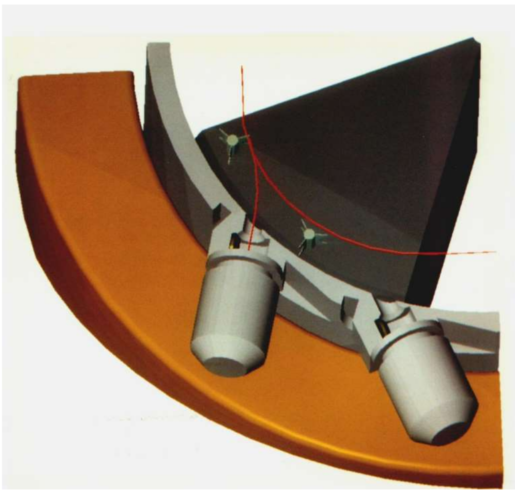
- Stripper foil removes the two electrons of the H^- ion and orbit curvature changes sign
- Energy variation by moving stripper position
- All energies go to one crossover point by proper foil azimuthal position
- Place combination magnet at crossover
- Ideal solution for industrial cyclotrons





Stripping Extraction (3)

- Other advantages
  - Simple and 100 % extraction efficiency
  - Multiple targets around the machine
  - Dual beam extraction
  - Good extracted beam optics
- Limitations due to stripping losses
  - Low B-field $\Rightarrow$large magnet (Triumf 500 MeV/3 kG)
  - Good vacuum required (expensive)
  - OK for isotope production but not for proton therapy



A side step: why cyclotrons for isotope production?

- Cost-effective machines for achieving:
  - required energies (<100 MeV) and
  - high currents (upto 1 to 2 mA)
- Efficient use of RF power => same accelerating structure used multiple times
- Compact =>
  - magnet and RF integrated into one system
  - Single stage => no injector accelerator needed
- Moderate magnetic fields: 1 to 2 Tesla
- Simple RF system:
  - Constant RF-frequency (10-100 MHz) => CW operation
  - Moderate voltages (10-100 kVolt)
- Relative easy injection (internal ion source or axial injection)
- Simple extraction (stripping for H^- ions with carbon foil => 100% efficiency)

IBA was founded in 1986.
Since then **more almost 400 isotope production cyclotrons** have been sold by IBA
Many more by competitors

Some commercial cyclotron vendors/manufacturers

SIEMENS	Germany (RP)	VARIAN medical systems	USA (PT)
GE	GE, USA (RP)	MEVION medical systems	USA (PT)
Best	Canada (RP)	SUMITOMO	Japan (RP+PT)
		↕ C235	
ADVANCED CYCLOTRON SYSTEMS, INC.	Canada (RP)	iba Particle Therapy	Belgium (RP+PT)

Extraction continued: turn-separation in a cyclotron

A Coherent beam oscillation is an oscillation around the equilibrium orbit $\Rightarrow$

$$r(\theta) = \overbrace{r_0(\theta)}^{\text{EO}} + \overbrace{\underbrace{x(\theta)}_{\text{amplitude}} \sin(\underbrace{\upsilon_r \theta + \theta_0}_{\text{phase}})}^{\text{betatron oscillation}}$$

$\Downarrow$

There are three different mechanisms to create turn separation $\Rightarrow$

$$\Delta r(\theta_i) = \overbrace{\Delta r_0(\theta_i)}^{\text{acceleration}} + \overbrace{\Delta x \sin(2\pi n(\upsilon_r - 1) + \theta_0)}^{\text{resonance}}$$

$$\overbrace{+2\pi(\upsilon_r - 1) x \cos(2\pi n(\upsilon_r - 1) + \theta_0)}^{\text{precession}}$$

How can turn-separation be used for extraction

I. By acceleration $\Rightarrow$ high dee-voltage — $\Rightarrow$ IBA/SHI C235

II. By resonances (coherent beam oscillations)

- Precessional extraction (more subtle) — $\Rightarrow$ Varian SC cyclotron
  - Create oscillation amplitude with 1st harmonic or beam off-centering
  - Accelerate into fringe field where ν_r~0.7
  - Turn separation obtained from betatron phase advance
- Regenerative extraction (even more subtle) — (IBA S2C2, Mevion Monarch)
  - Second harmonic gradient bump: $2\nu_r=2$; ν_r is locked to 1 in the stopband
  - Exponential growth of betatron amplitude

Deflecting and guiding the beam out

A generic method of precessional extraction in a few steps

i. Create an oscillation amplitude ⇒ by harmonic coils, trim rods or initial beam off-centering (at the ion source)
   - Obtain turn-separation by precession

ii. Provide an initial radial kick
   ⇒ Electostatic deflector ESD (peel off last turn)

iii. Reduce B-field and minimize optical damage when passing the fringe field ⇒ Gradient corrector channels

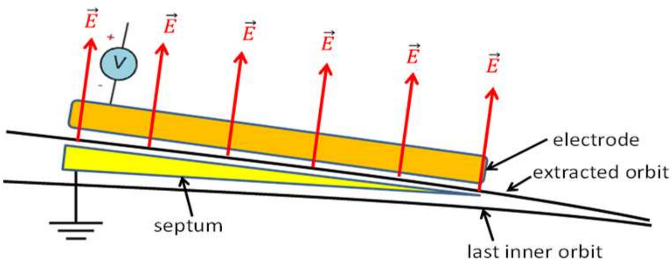
iv. Re-focus the beam as quickly as possible to handle beam divergencies created in the fringe field
   ⇒ First quadrupole doublet (in return yoke)

Non-adiabatic effect needed =>

Example of a harmonic coil

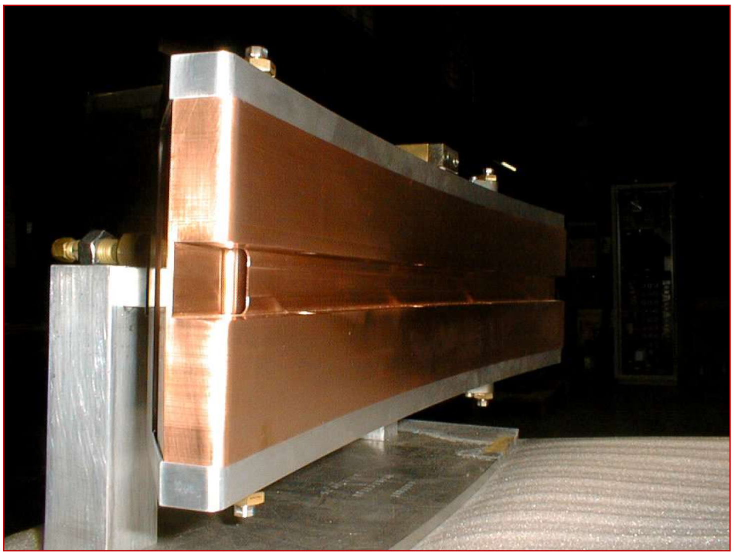
Electrostatic Deflector

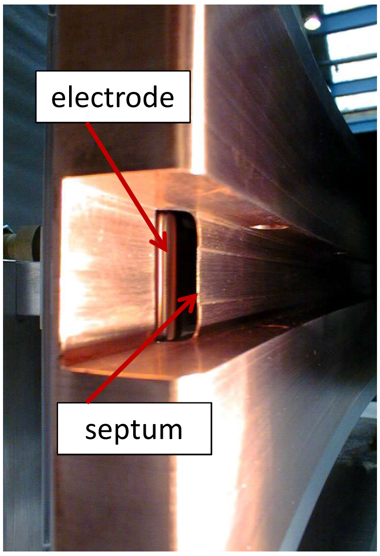
- DC radial E-field creates initial angular kick to deflect beam
- Inner electrode (septum) on ground potential
  - No disturbance on inner orbits
  - Knife thin (0.1 mm) and
  - V-shape at entrance (distribute heat)
  - Water cooled ⇒ limitation for maximum beam intensity
- Outer electrode on negative potential
- Electrode shape = orbit shape



ESD for IBA C235

C235 Electrostatic deflector





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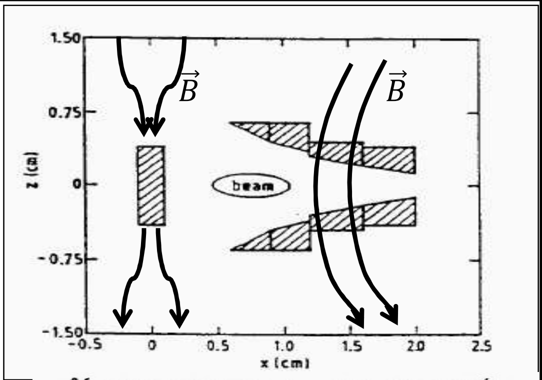
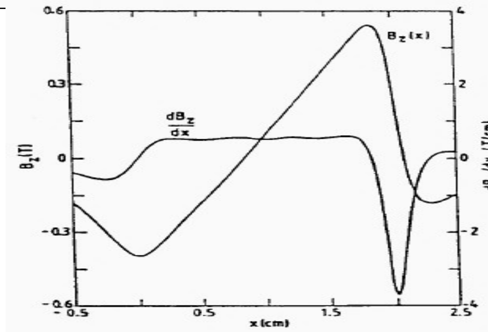
Gradient Corrector focusing Channel

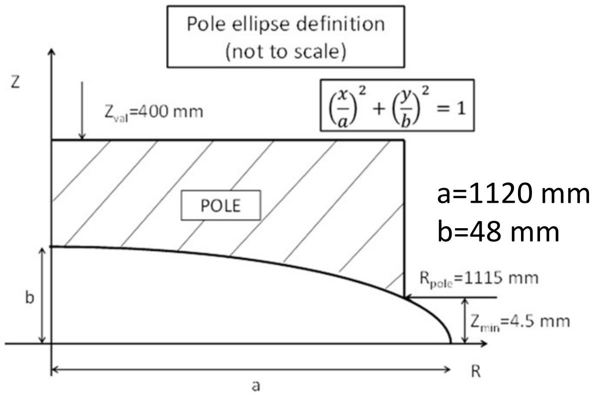
- Goal:
  - Guide the beam through the fringe field
  - Lower magnetic field on extraction path
  - reduce vertical/increase radial focusing through fringe field
- Different types
  - Passive: soft iron magnetized by the main field
  - Active:
    - Using permanent magnets
    - Using coils
- Designed in such a way as to minimize adverse effects on internal orbits



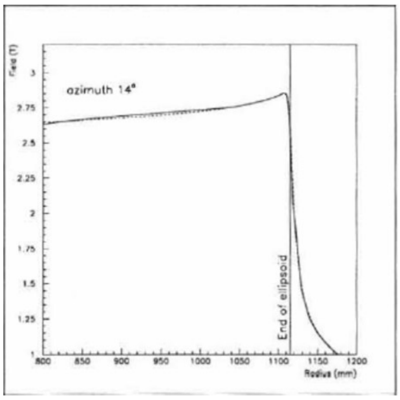


Extraction in the IBA C235

A very sharp transition from stable to unstable

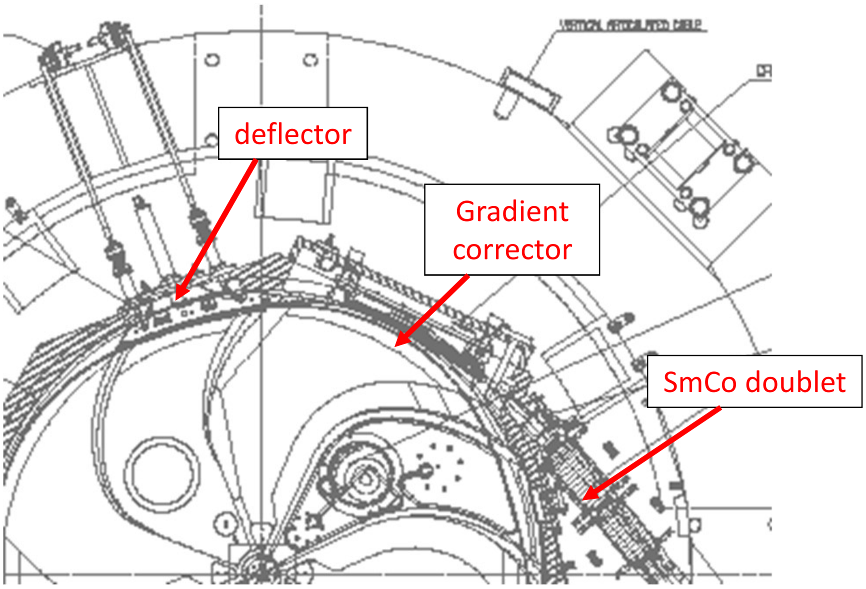


a=1120 mm
b=48 mm

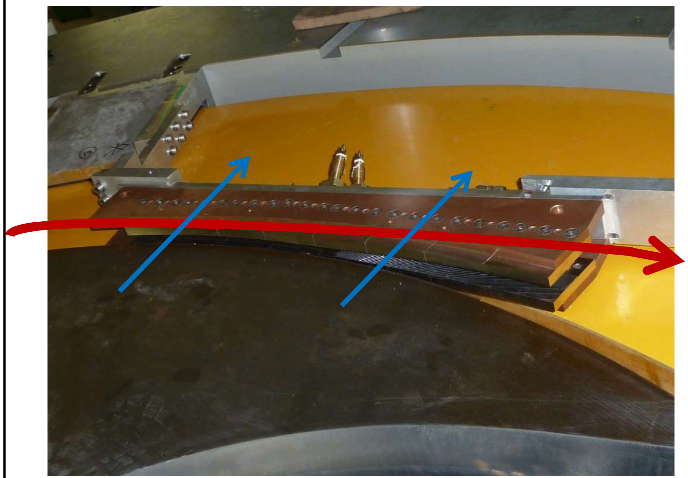


The pole gap in the C235 has an elliptical form.
This allows to obtain a good field region very close to the radius of the pole
Therefore particles can be accelerated very close to the radius of the pole
Only a small kick is needed to extract the beam => orbit is extracted in ¼ of a turn

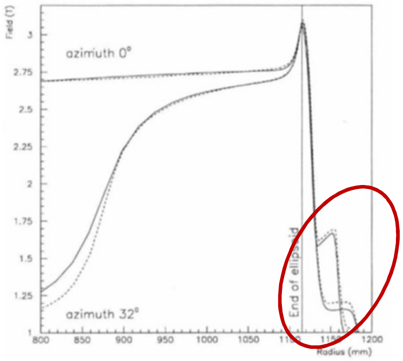
C235 Extraction Scheme



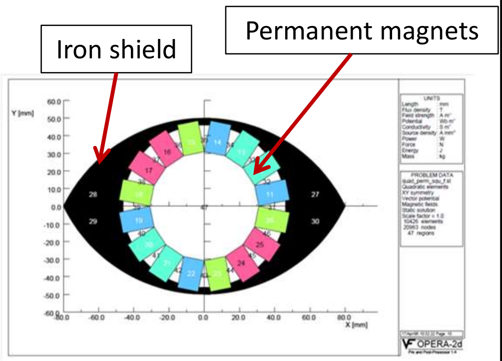
C235 Gradient Corrector

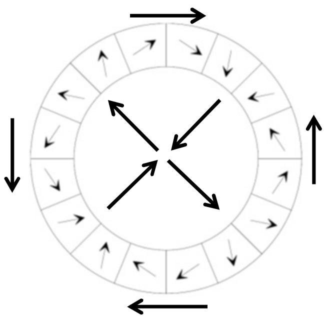


- A passif channel, magnetized by the cyclotron magnetic field
- Placed between the main coils, against (almost touching) the hill sector.
- A descending 'slider' of gradually decreasing magnetic field that guides the beam gently through the fringe field



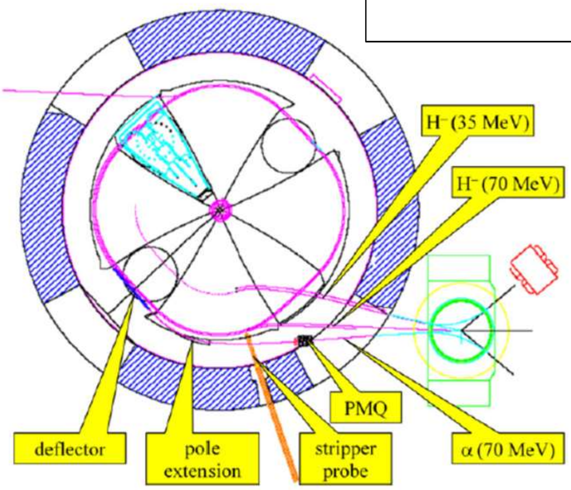
C235 Permanent Magnet Doublet
Placed in the return yoke





Two extraction systems in one cyclotron

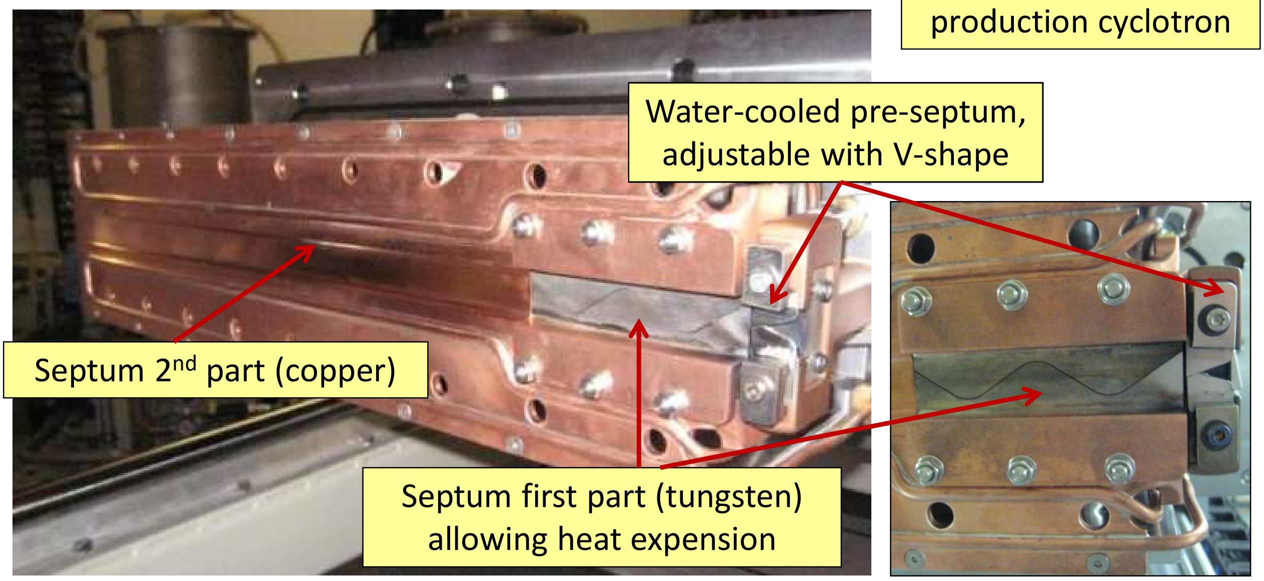
C70 multiple particle cyclotron for Arronax in Nantes
H^-, D^-, α, H_2^+



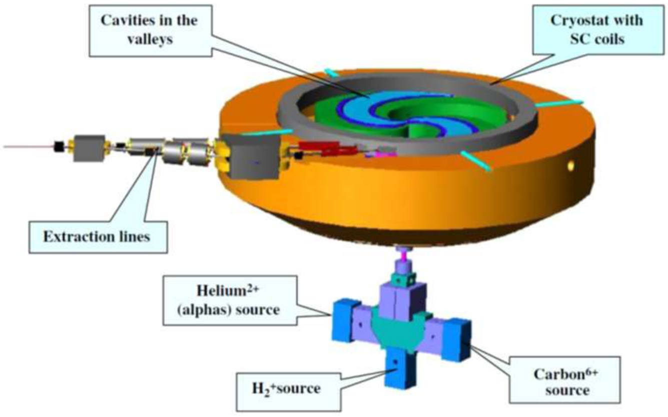
- Stripping extraction for negative particles
- ESD for α-particle and H_2^+
- Two opposite exit ports
- Simultaneous dual beam capability for H- and D-
- Variable energy for H- and D-
- External switching magnet to direct different energies and particle into the beam lines

The C70 electrostatic deflector (ESD)

High intensity isotope production cyclotron



The IBA C400 cyclotron



particles	$^{12}C^{6+}$; H_2^+ ; $^4He^{2+}$
Final energy	
ions	400 MeV/A
protons	265 MeV
Bending limit	K=1600
Weight	700 t
Diameter	6.6 m
Hill field	4.5 Tesla
Valley field	2.45 Tesla
Number of cavities	2
RF frquency	75 MHz; h=4
Vdee	80-160 kV
Number of turns	2000
SC coil	NbTi; Helium cooled
Ischronism of H_2^+	Coil in 2 parts

Y. Jongen et.al., NIM A624 (2010) 47-53

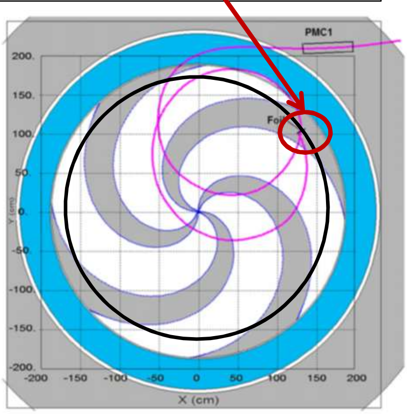
- Full detailed design study was done in collaboration with JINR
- Possibly/hopefully to be industrialized by the French company Normandy Hadrontherapy in which IBA is minority shareholder

Extraction from the C400

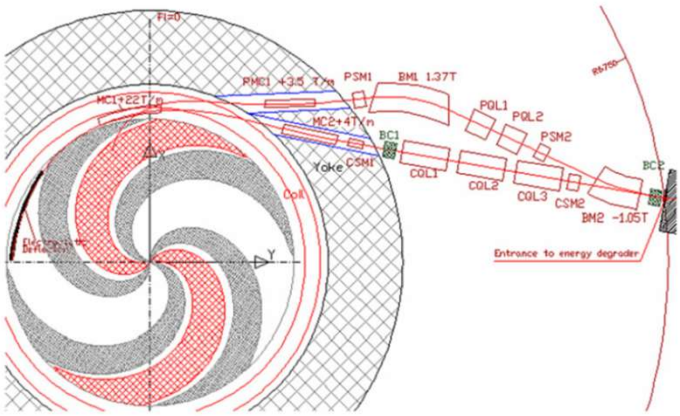
Protons => stripping of H_2^+

$^{12}C^{6+}$ => Electrostatic deflector

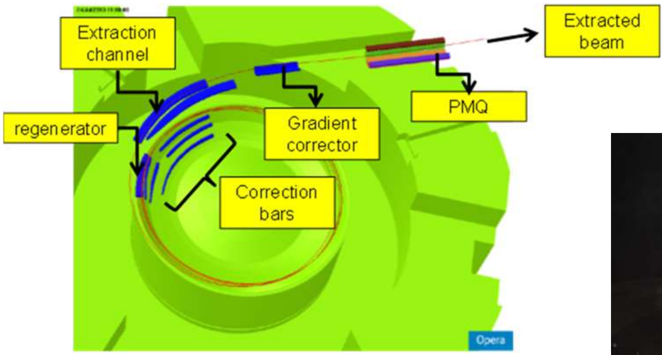
H_2^+ two-turn extraction after stripping



Combining both beams into one beam line



The IBA S2C2 extraction system



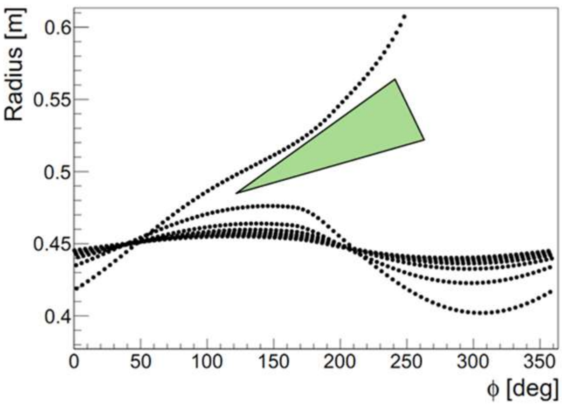
- Horizontal focusing by gradient corrector and permanent magnet quadrupole (PMQ) in strongly

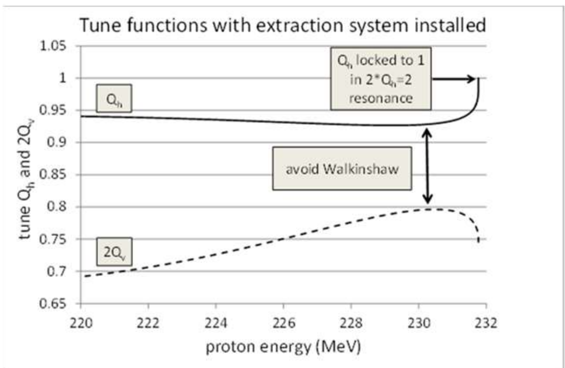
r

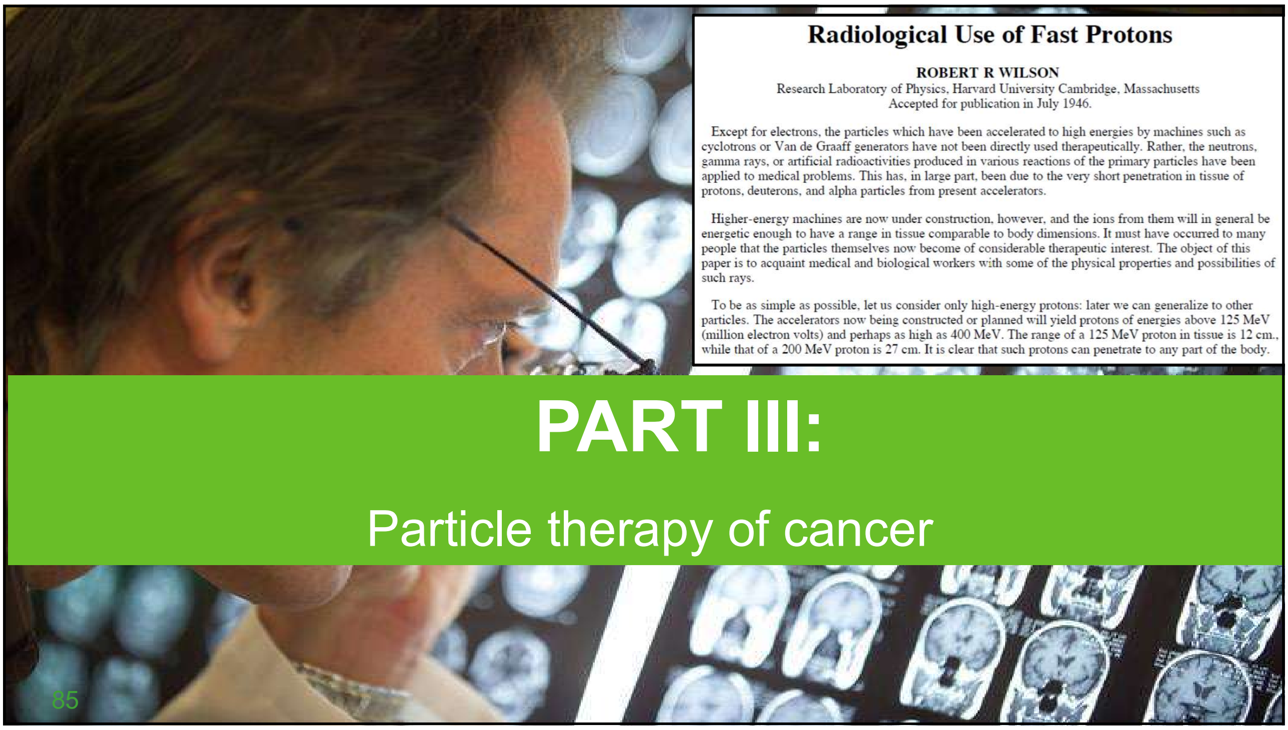
- Fully passive system => only soft iron
- Use resonant extraction based on *2Q_h*
- Strong local field bump produced by r frequency and locks it to unity.
- Unstable orbit is pushed towards the

Regenerative extraction based on $2\nu_r=2$ resonance

- A strong regenerator bump increases ν_r and locks it to 1
- A steady shift of the beam towards the extraction channel builts up
- Avoid Walkinshaw resonance ($\nu_r=2\nu_z$)







Radiological Use of Fast Protons

ROBERT R WILSON
Research Laboratory of Physics, Harvard University Cambridge, Massachusetts
Accepted for publication in July 1946.

Except for electrons, the particles which have been accelerated to high energies by machines such as cyclotrons or Van de Graaff generators have not been directly used therapeutically. Rather, the neutrons, gamma rays, or artificial radioactivities produced in various reactions of the primary particles have been applied to medical problems. This has, in large part, been due to the very short penetration in tissue of protons, deuterons, and alpha particles from present accelerators.

Higher-energy machines are now under construction, however, and the ions from them will in general be energetic enough to have a range in tissue comparable to body dimensions. It must have occurred to many people that the particles themselves now become of considerable therapeutic interest. The object of this paper is to acquaint medical and biological workers with some of the physical properties and possibilities of such rays.

To be as simple as possible, let us consider only high-energy protons: later we can generalize to other particles. The accelerators now being constructed or planned will yield protons of energies above 125 MeV (million electron volts) and perhaps as high as 400 MeV. The range of a 125 MeV proton in tissue is 12 cm., while that of a 200 MeV proton is 27 cm. It is clear that such protons can penetrate to any part of the body.

PART III:

Particle therapy of cancer

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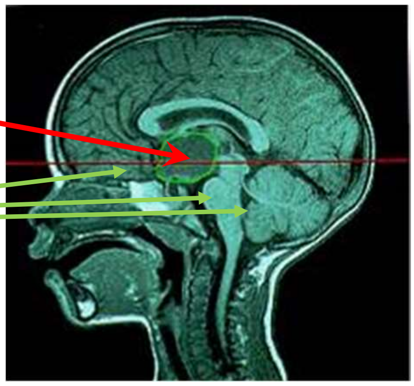
The HOLY GRAIL of Radiation Therapy

Ideal Situation

Provide a lethal dose to the tumor
and
Spare perfectly the surrounding healthy tissue



In Practice

Deposit the radiation dose more precisely in the target volume with less dose in the surrounding healthy tissues.

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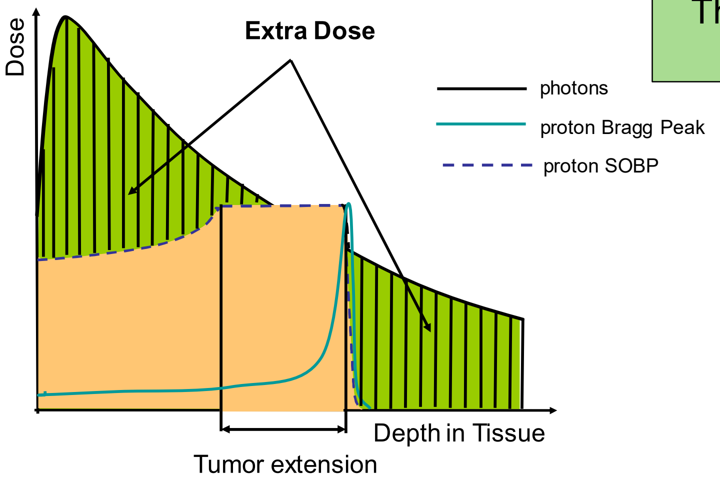
Photon-Proton dose distribution comparison



The spread out Bragg peak (SOBP)

- Position of the Bragg peak depends on beam energy
- Incomming energy modulation ⇒ SOBP
- No dose downsteam of tumor
- Lower dose upstream of tumor

Main requirements for a proton therapy system

IBA ProteusPlus highest level design specifications

1. **Ability to reach the tumor**
   - Range in patient: up to 32 g/cm²
   - Range modulation:up to full range, with steps of 0.5 g/cm²
   - Field size: up to 30 x 40 cm
2. **Ability to reach the from any selected direction**
   - Isocentric Gantry
   - Precise, robotic patient positioner
3. **Ability to verify and control the dose deposition using IC's**
4. **Ability to reach the tumor accurately**
   - Penumbra: maximum 2 mm at skin
   - Distal dose falloff: maximum 1 mm above physical limit
   - Patient positioner accuracy and reproducibility: 0.5 mm for small displacements
   - Gantry accuracy and reproducibility: 1 mm radius circle of confusion
   - Patient alignment methods: lasers, light fields, X-rays

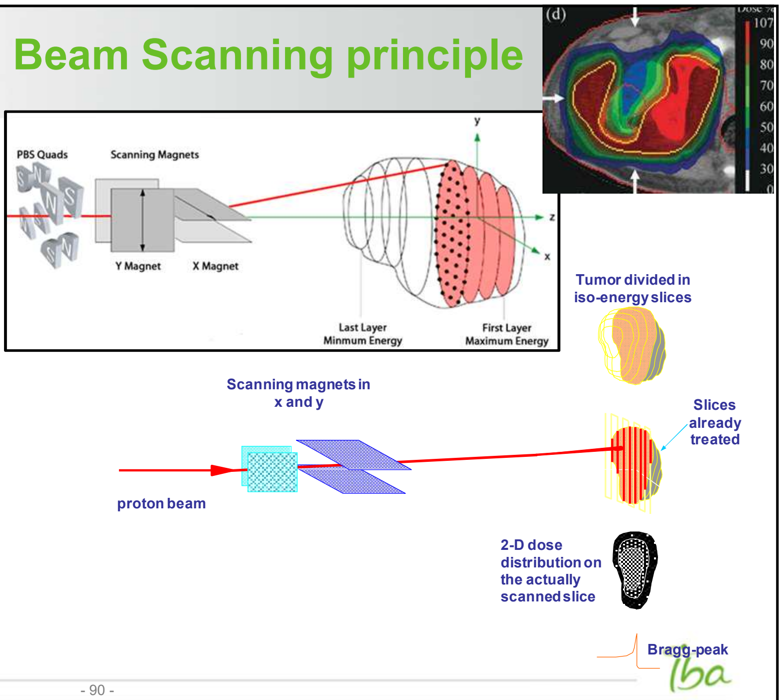
Accelerator parameters driving technology choice

- Energy: defines the range in the patient (230 MeV enough)
- Energy definition: defines the range accuracy and the distal falloff
- Beam current: defines the dose rate (10^{11} p/sec enough (10 nA))
- Beam intensity stability, accuracy and fast control: defines ability to do conformal mapping of the tumor by beam wobbling and scanning

IMPT: Pencil Beam Scanning principle

Advantages:
- Good 3D dose conformity
- “Flexible”
- Low neutron dose
- No need for patient specific aperture

Disadvantages:
- Layer by layer, slower than scattering
- Lateral penumbra less sharp than with collimation
- Dynamic system, more complex may be less safe than passive system



Accelerators for proton therapy: two alternatives

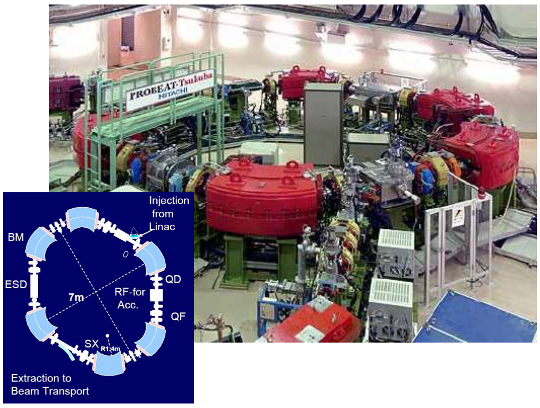
Small synchrotron

+ *Advantages*
  + Naturally variable energy
- *Disadvantages*
  - Current limited if low energy injection
  - Beam current stability & low noise is difficult on small synchrotrons
  - Fast and accurate beam current control difficult to achieve
  - More complex with negative impact on availability

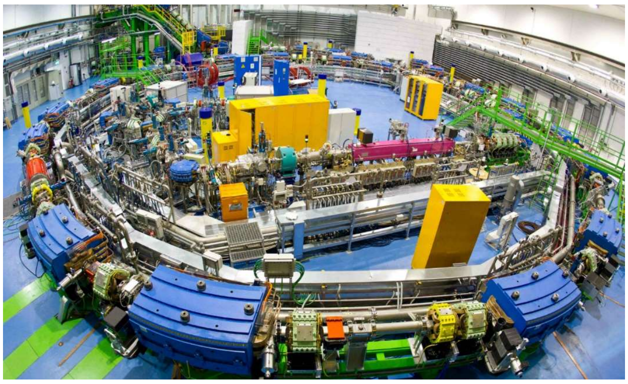
Compact cyclotron

+ *Advantages*
  + No physical current limitation
  + Beam current stability & noise specifications currently achieved on small cyclotrons
  + Fast and accurate beam current control over 1000/1 range easy to achieve
  + Low complexity, resulting in highest availability
- *Disadvantages*
  - Variable energy requires external Energy Selection System

Synchrotrons



Hitachi
- 70-250 MeV protons
- Slow cycle
- 7 m Diameter



“PIMMS” (CERN) design
- Up to Carbon
- 25 m Diameter
- Rep. rate: 5 Hz
- Installed @CNAO, Med-austron

http://www.protominternational.com/about/about-radiance-330/

Rossi, EurPhysJPlus2011-126-78.pdf

Trend: more compact

Protom
- Up to 330 MeV protons
- 5 m Diameter, ~16 tons
- Being installed @MGH

http://www.protominternational.com/about/about-radiance-330/

Cyclotrons for Proton & Carbon therapy?

- In 1991, when IBA entered in PT, the consensus was that the best accelerator for PT was a synchrotron
- IBA introduced a very effective cyclotron design, and today the majority of PT centers use the cyclotron technology (Not only IBA but also Varian, Mevion, SHI)
- Over the last 25 years, users came to appreciate the advantages of cyclotrons:
  - Simplicity & reliability
  - Intense, continuous (non pulsed) beam current
  - Lowest cost and size
  - But, most importantly, the ability to modulate rapidly and accurately the proton beam current

The 230 Mev Cyclotron at MGH/NPTC in Boston

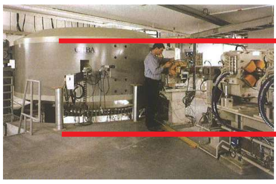
Protons only

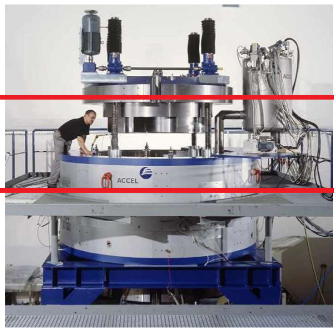
Fixed energy

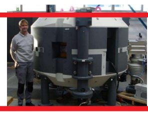
200 tons

∅ = 4.7 m

Cyclotrons in PT – commercial 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)
- RF: 11 kW

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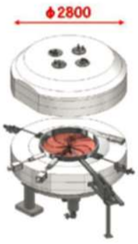
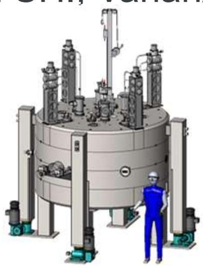
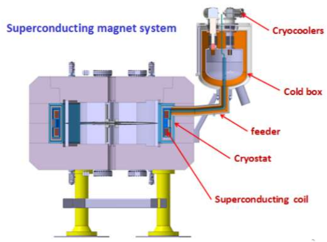
Proton cyclotrons - Ongoing developments

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

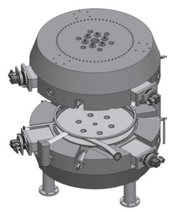




Derenchuck - NAPAC 2016



Karamysheva - THP20 cyclotrons 2016



Antaya – CAS 2015

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

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

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

Varian/Antaya
- 230 MeV protons
- 2.2 m Diameter
- CW beam
- Superconducting (Nb_3Sn)
- 30 tons+
- 5.5 T (extr.)
- "Flutter" coils

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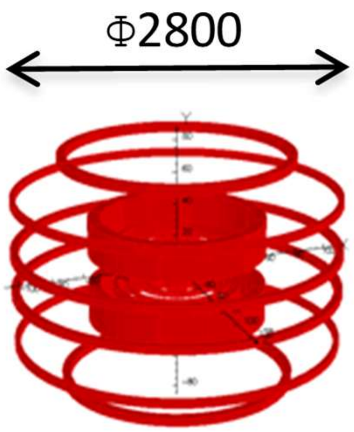
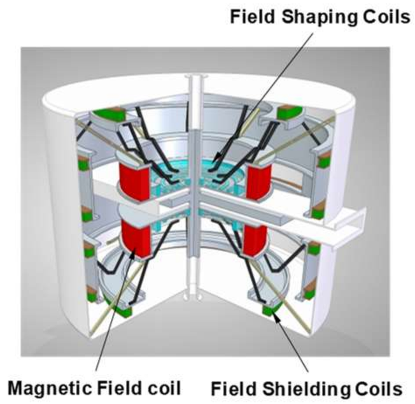
Proton cyclotrons - Ongoing developments

- 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

Minervini – Ciemat workshop 2016

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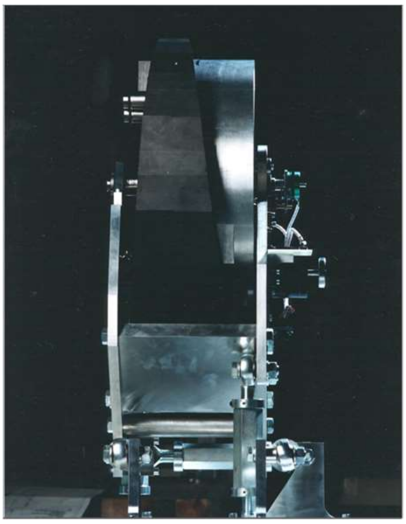
Change of energy?

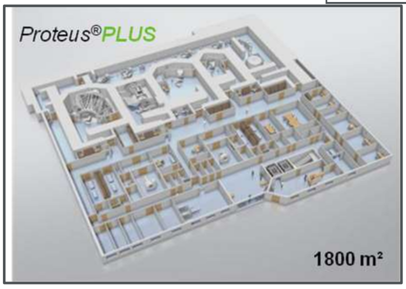
- Cyclotrons are simpler at fixed energy
- Energy change by graphite degrader at waist after cyclotron exit, followed by divergence slits and energy analyzer
- This very effectively decouples the accelerator from the patient
- Fragmentation products are effectively eliminated in slits and ESS
- Yes, neutrons are produced, but ESS is well shielded and the average beam currents are very low > little activation
- How fast? 5 mm step in energy in 100 msec. Respiration cycle is 2…4 seconds => 100 msec is fine

The carbon wedge degrader

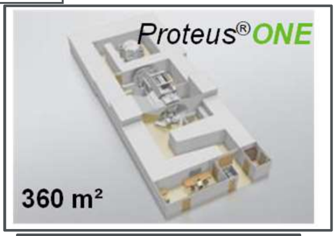


Some typical proton therapy systems

IBA



multi-room



single-room

Mevion

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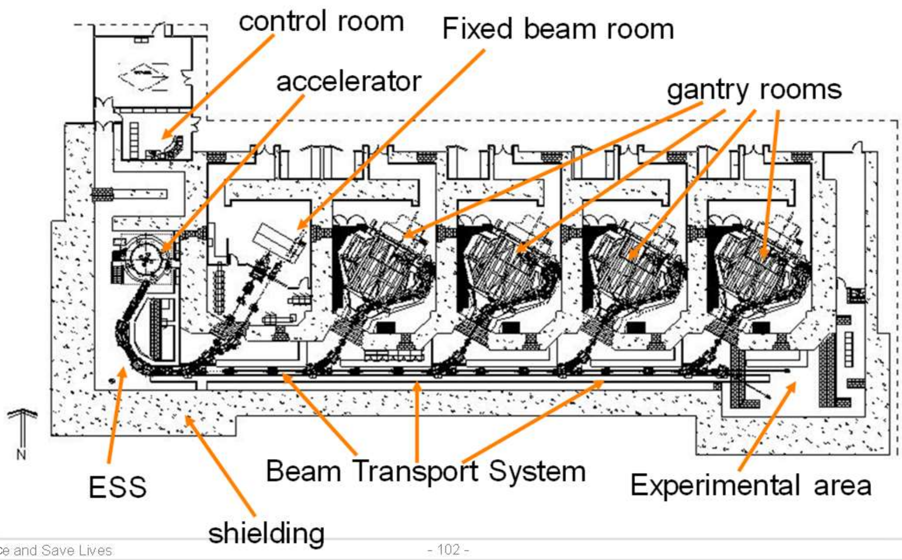
Typical Proton Therapy Facility Layout



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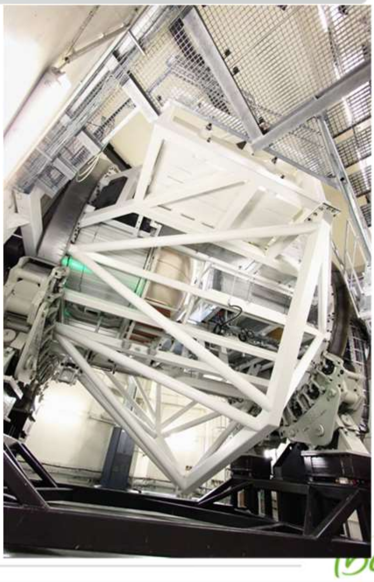
The Energy Selection System

- Graphite or Beryllium wedge is used for coarse energy definition
- Emittance slits are used to define the emittance of the transmitted beam
- Analyzing magnet system with momentum slits defines accurately the range at nozzle entrance
- Laminated magnets and quads allow 10% energy change in 2 seconds

IBA PT subsystems : the beam transport lines.

The energy selection system. WPE, Essen, 2010.

The isocentric gantry => about 10 m high



Good alignment is of crucial importance

The purpose of the nozzle

- Modulate the proton energy (range in patient)
- to spread the proton beam to obtain a uniform dose distribution in a large volume
  - Double scattering for small to moderate fields
  - Wobbling for the largest and deepest fields
  - Pencil Beam Scanning for the most precise conformal mapping
- to measure accurately the dose delivered to the patient
- Provide alignment of the patient with the proton field

A patient friendly treatment room is important

A Proton Therapy Facility is like a small Hospital

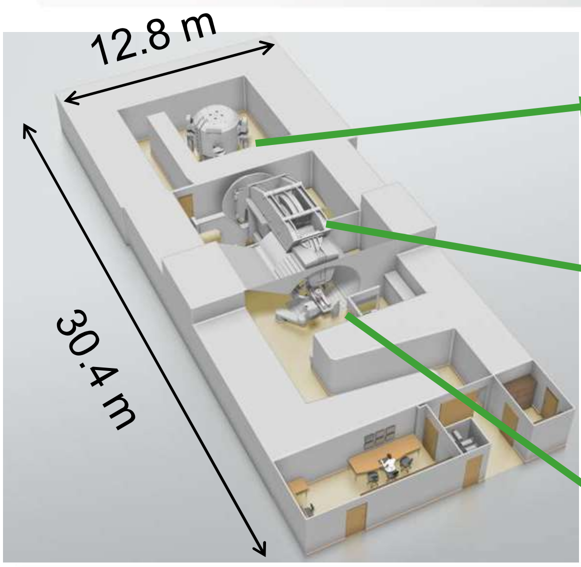
- A proton therapy system is much more than only an accelerator
- It is a complex, multi-room system, filling a hospital building.
- The total investment is around 100 M€, of which 45 M€ for the equipment
- Many people (doctors, therapists, physicists, nurses) work daily in a PT facility
- A PT facility can treat 1500 patients/year and generate revenues in the order of 30 M€/year!

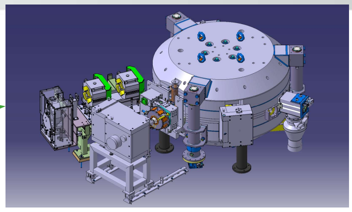
The UPHS Particle Therapy Centre, Philadelphia

- One of the largest Particle Therapy centre to date!
- 4 Gantry Rooms
- 1 Fixed Beam Room
- 1 Experimental Room
- Beam since July 2008

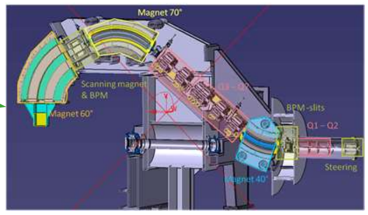
The New IBA Single Room Proton Therapy Solution: ProteusONE®

High quality PBS cancer treatment: compact and affordable

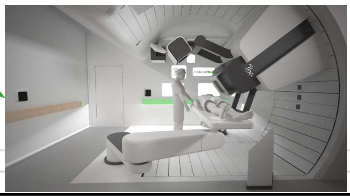




Synchrocyclotron with superconducting coil: S2C2



New Compact Gantry for pencil beam scanning



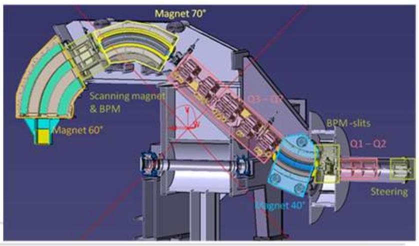
Patient treatment room

iba

The new compact gantry for pencil beam scanning

Design aimed at reducing footprint and cost

- Scanning magnets are placed upstream of the last bending magnet
- ESS integrated in the 45 deg inclined part
- Rotation angle 220° => more compact treatment room
- Transport and installation in one part
- The prototype is installed in Shreveport where patients are treated since September 2014



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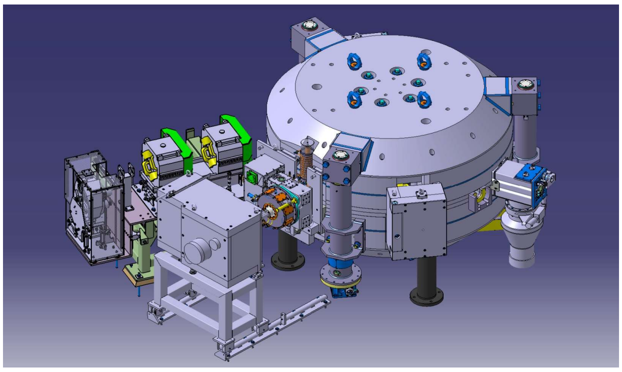
S2C2 overview

General system layout and parameters



- An invited talk on this project was presented at the 2013 cyclotron conference in Vancouver
- Several contributions can be found on the ECPM2012-website

Maximum Energy	230/250 MeV
Size	
yoke/pole radius	1.25 m/0.50 m
weight	50 tons
Coil	NbTi - wire in channel
ramp up rate / time	2-3A/min / 4 hours
windings/coil	3145
stored energy	12 MJ
Magnetic field	
central/extraction	5.7 T/5.0 T
Cryo cooling	conductive
	4 cryocoolers 1.5 W
initial cooldown	12 days
recovery after quench	less than 1 day
Beam pulse	
rate/length	1000 Hz/7 μsec
RF system	self-oscillating
frequency	93-63 MHz
voltage	10 kV
Extraction	Passive regenerative
Ion source	PIG cold cathode
Central region	removable module

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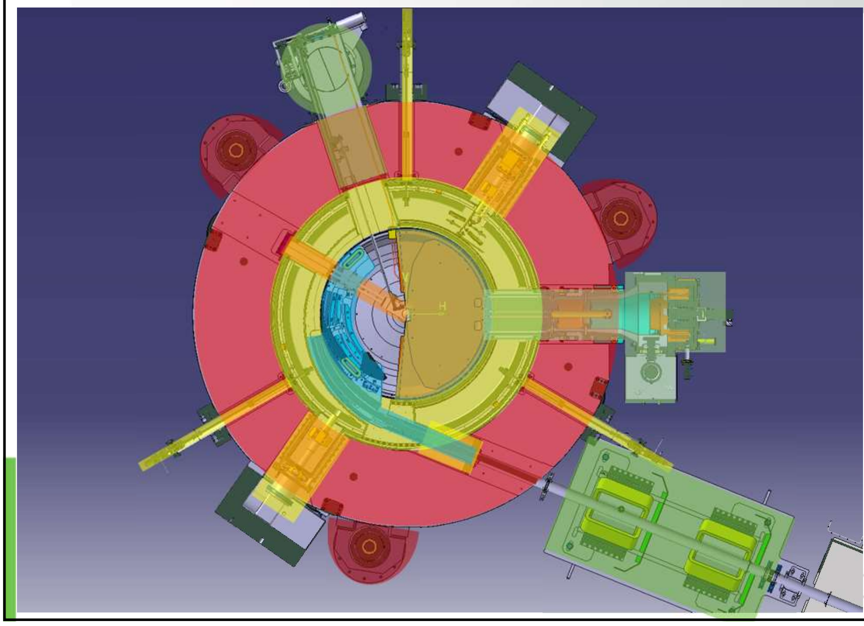
S2C2 overview

Main subsystems



Magnet return yoke

Cryostat with coil

RF system

Ion source+central region

Extraction system

Vacuum system

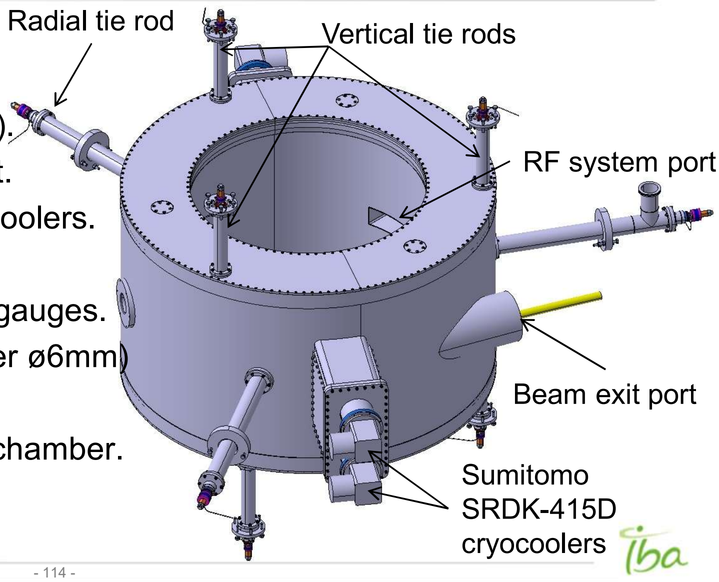
Yoke lifting system

Extracted beam line

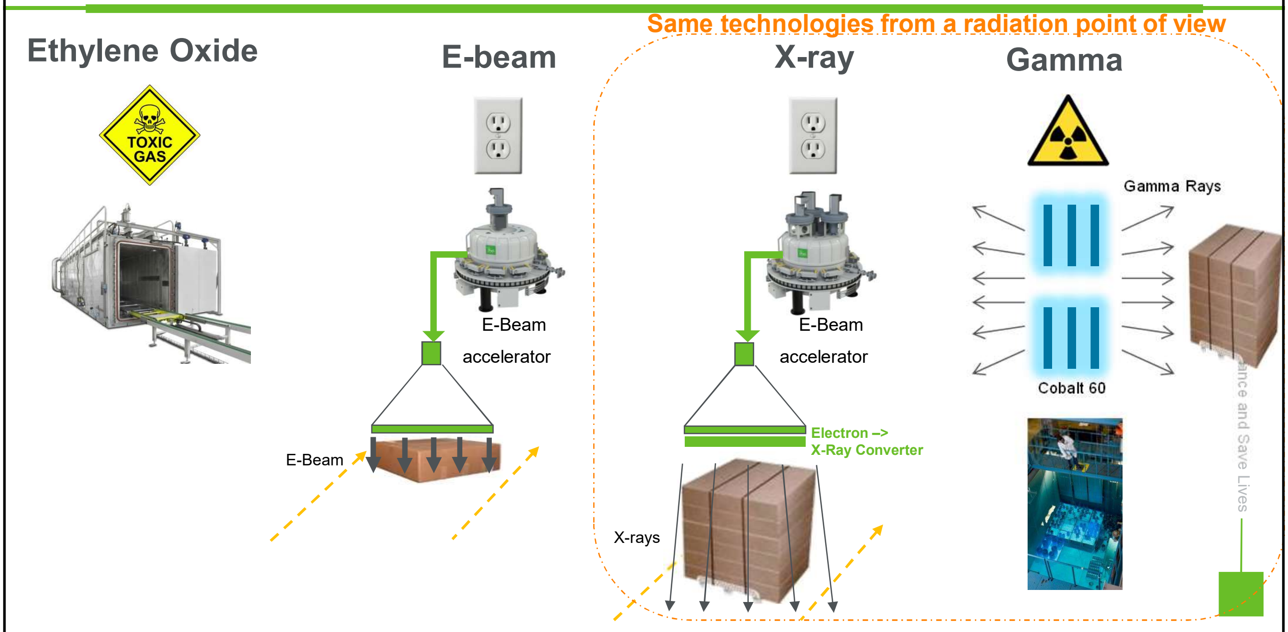
Superconducting coil

Designed and manufactured by ASG (Genua, Italy)

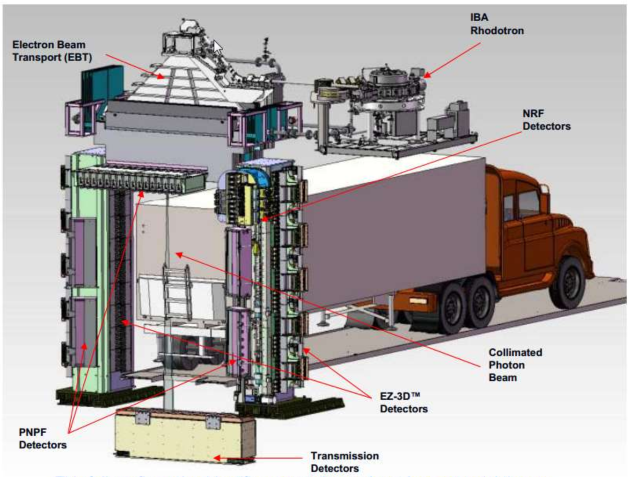
- NbTi wire in channel coil.
- Suspended cold mass: 3tons.
- Nominal current: 650A (56 A/mm²).
- Nominal ampere-turns: 4.3x10^{+6}At.
- Conduction cooled by 4 SHI cryocoolers.
- Overall weight: 4tons.
- 9 Inconel tension rods with strain gauges. (radial ø14mm; upper ø8mm; lower ø6mm)
- Cryostat is the cyclotron vacuum chamber.



Sterilization Processing Comparison



Cargo screening => TT50



This full configuration identifies anomalies and resolves potential threats

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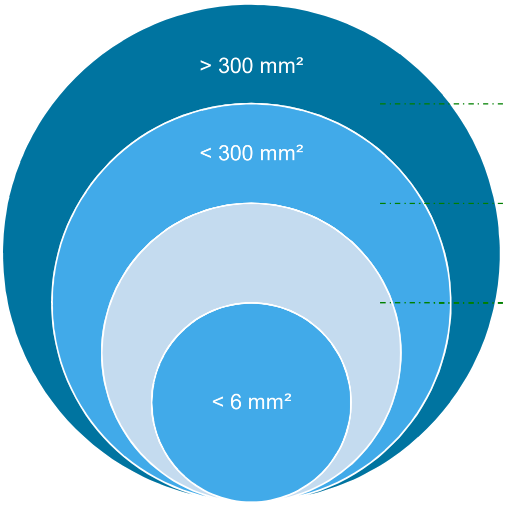
Cables treatment with electrons: Dynamitron => crosslinking



Not crosslinked with radiation

3 MeV
Multiple applications

1.5 MeV
Multiple applications

800 keV
Automotive

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IBA Industrial's Product Portfolio

Dynamitron	Rhodotron	eXelis
0.5 -> 5 MeV | 160 mA	3 -> 10 MeV | 42 mA | 420 kW	5 – 7 MeV | 80 mA | 560kW
Electron beam	Electron beam and X-rays	X-rays

Main application	Main application	Main application
E-beam Crosslinking	**E-beam box sterilization**	**X-ray pallet sterilization**

Linac's reach about 40-60 kW

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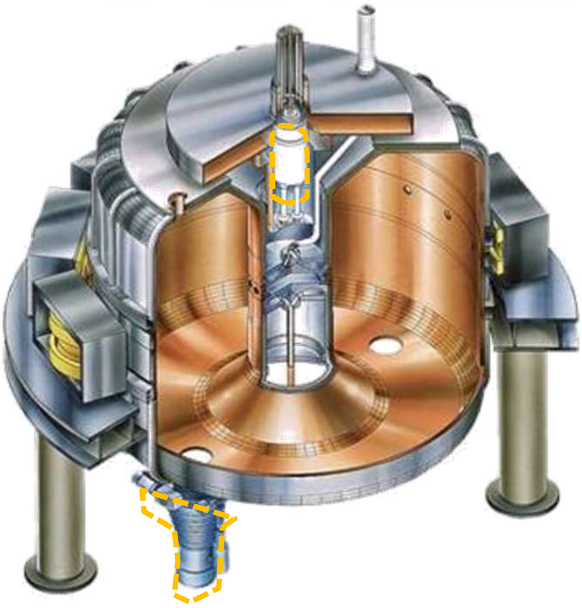
Brief explanation of the Rhodotron:

The main components



RF Cavity
E-Gun
Magnets
Final Power Amplifier

RF tube (Tetrode)
Vacuum system

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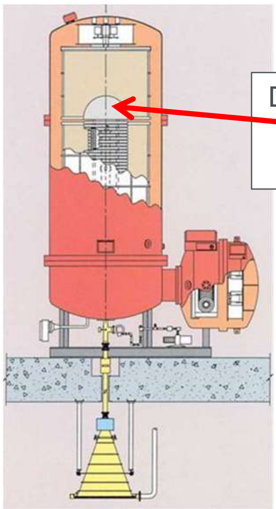
Dynamitron

High Voltage generation => similar to a Cockcroft-Walton



Dees and rectifier stack
Dome
SF6