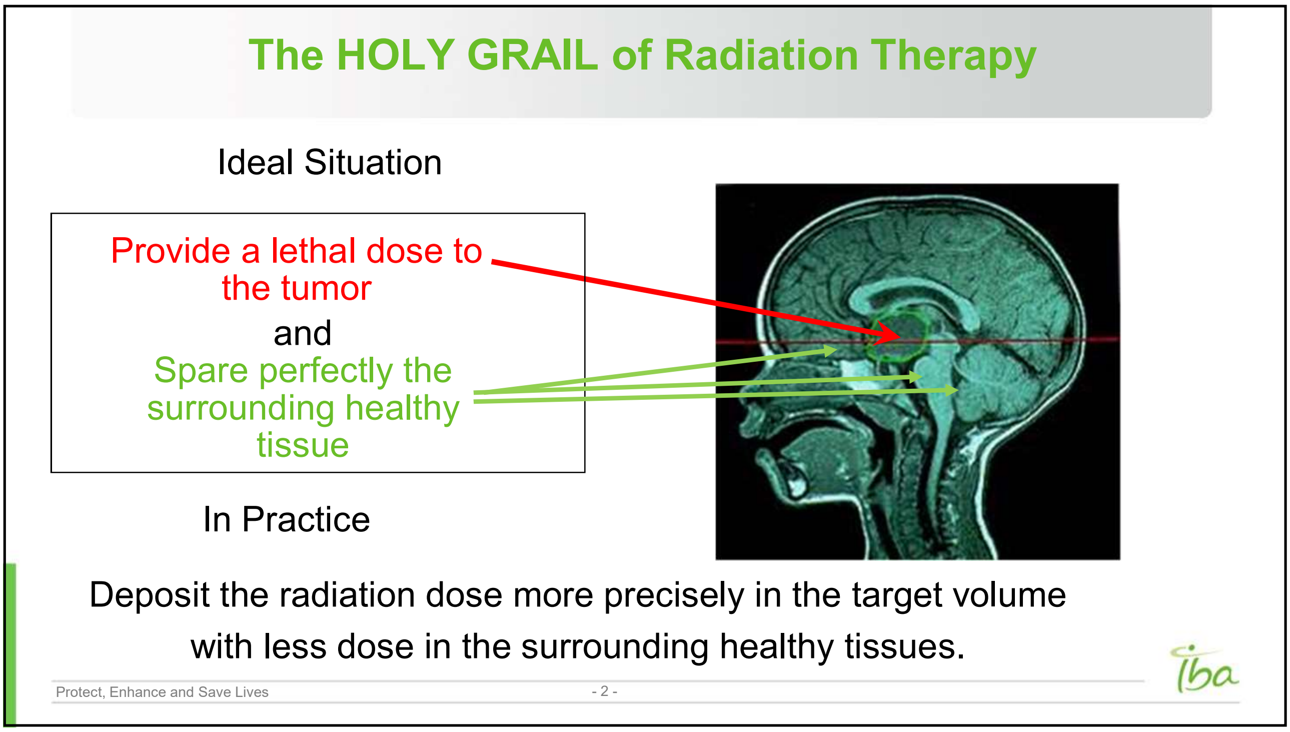
PART III:

Particle therapy of cancer



The HOLY GRAIL of Radiation Therapy

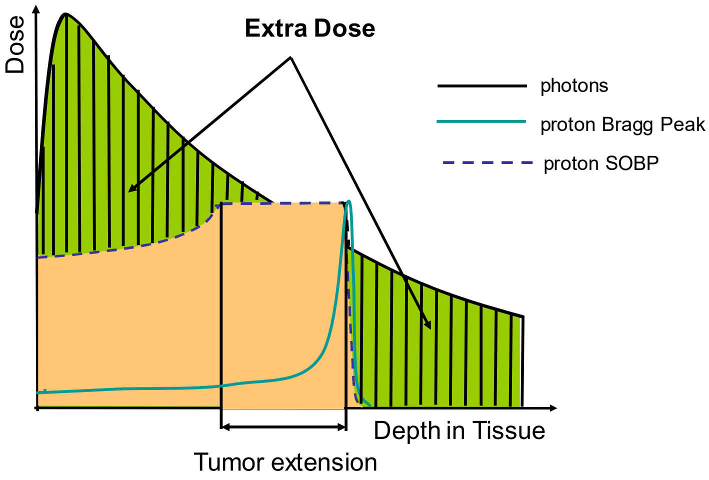
Ideal Situation

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.

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 and low dose upstream of tumor
- Up to 50% reduced risk of radiation induced secondary cancer
- Drastically lower risk of adverse effects (treatment toxicity, side effects, growth abnormality) – better quality of life

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Main requirements for a proton therapy system

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

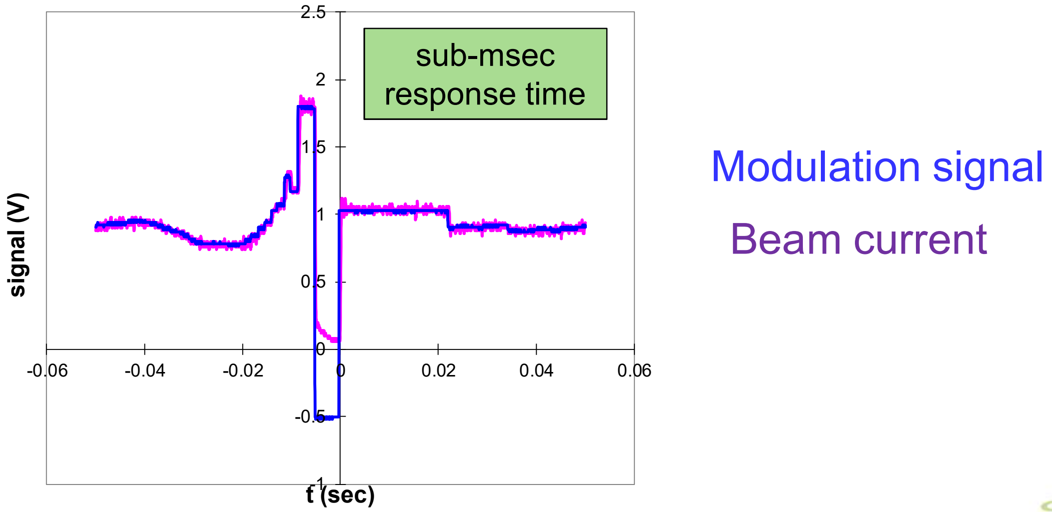
Accelerator parameters driving technology choice

- 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 current stability and noise: defines ability to use wobbling and scanning
- Accurate and fast beam intensity control: needed for conformal therapy

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

Real oscilloscope measured signals



Why is fast current modulation important?

- A big issue with scanned beam is the motion of the target during irradiation
- If you cannot control accurately and rapidly the current ,or if the beam is slowly pulsed , your only choice is step-and-shoot (spot scanning)
- Assuming a 10 mm (FWHM) beam spot size, a 50% overlap and a 20 Hz pulse rate, the maximum scanning speed will be 0.2 m/sec
- With this speed, for a large size tumor, repainting many time each layer is not really an option
- In contrast, with a cyclotron you can scan at 20 m/sec and rescan many times each layer

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

Accelerators for proton therapy: two alternatives

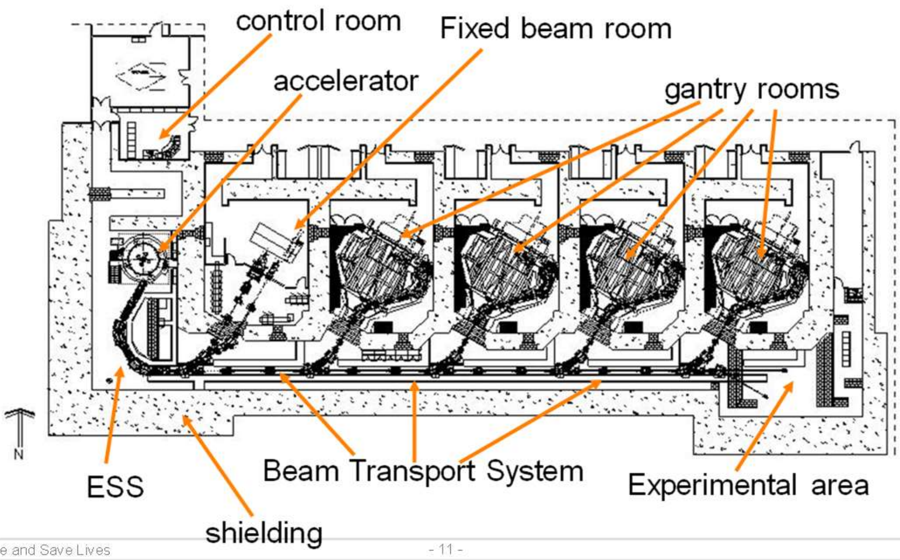
Small synchrotron

- + *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

Typical Proton Therapy Facility Layout



Main Sub-systems of a cyclotron based PT facility

- 230 MeV isochronous cyclotron
- Energy Selection System (ESS)
- Beam Transport and Switching System
- Isocentric Gantries (typically 3) and one Fixed Beam Line
- Nozzles for matching the beam wrt the required treatment (scattering, wobbling or scanning, diagnostics)
- Robotic Patient Positioners
- Software Control and Safety System

The 230 Mev Cyclotron at MGH/NPTC in Boston

Protons only

Fixed energy

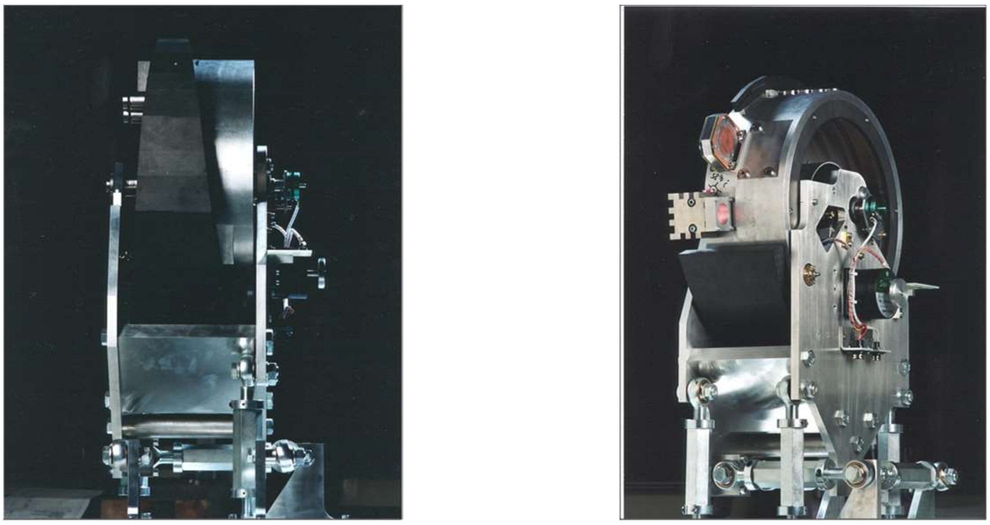
200 tons

∅ = 4.7 m

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 defines accurately the range at nozzle entrance
- Laminated magnets and quads allow 10% energy change in 2 seconds

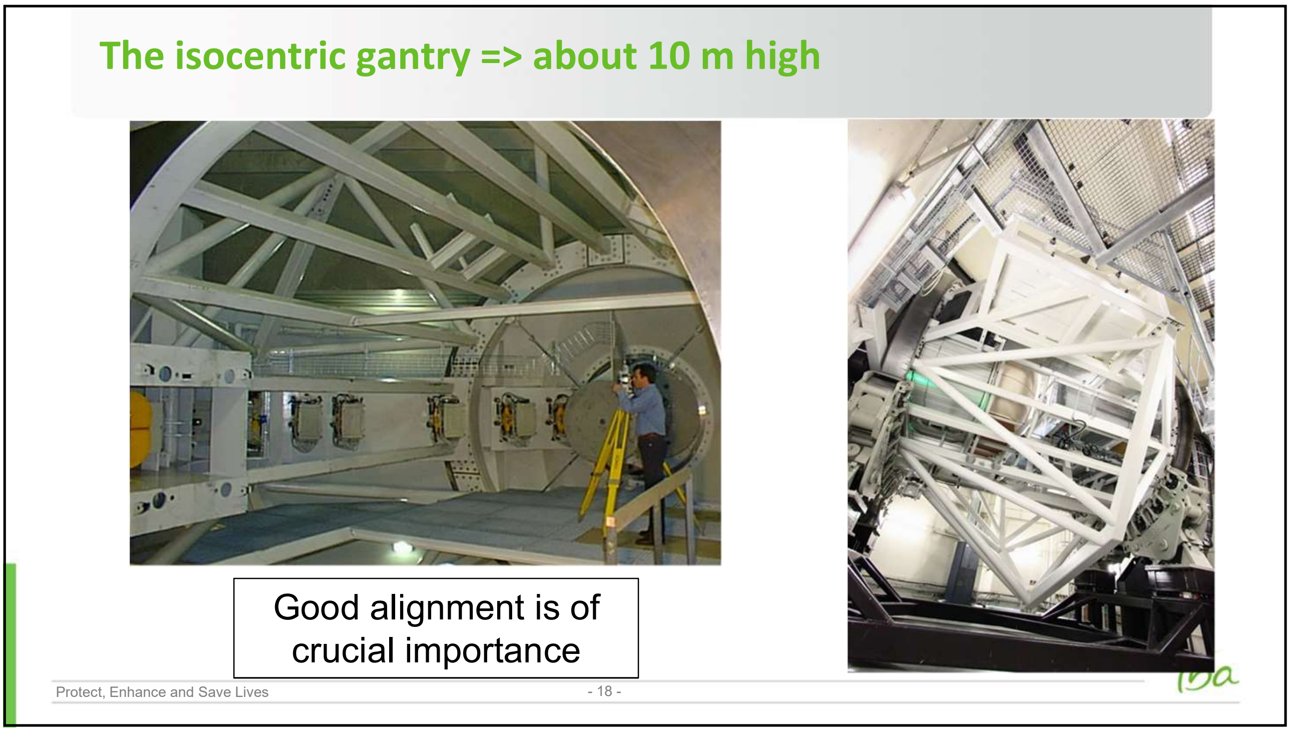
The carbon wedge degrader



IBA PT subsystems : the beam transport lines.

The energy selection system. WPE, Essen, 2010.

The Beam Transport and Switching System



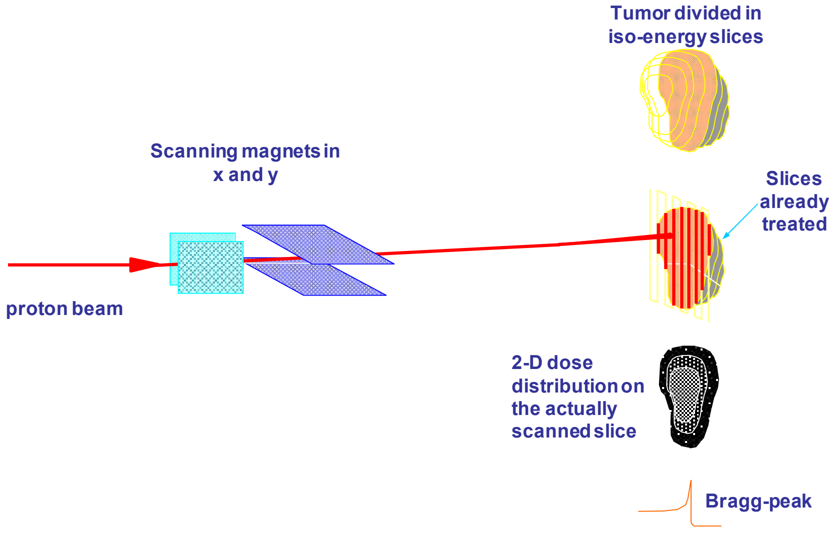
The isocentric gantry => about 10 m high

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

IMPT: Pencil Beam Scanning principle



Tumor divided in iso-energy slices

Scanning magnets in x and y

Slices already treated

proton beam

2-D dose distribution on the actually scanned slice

Bragg-peak

A patient friendly treatment room is important

A Proton Therapy Facility is like a small Hospital

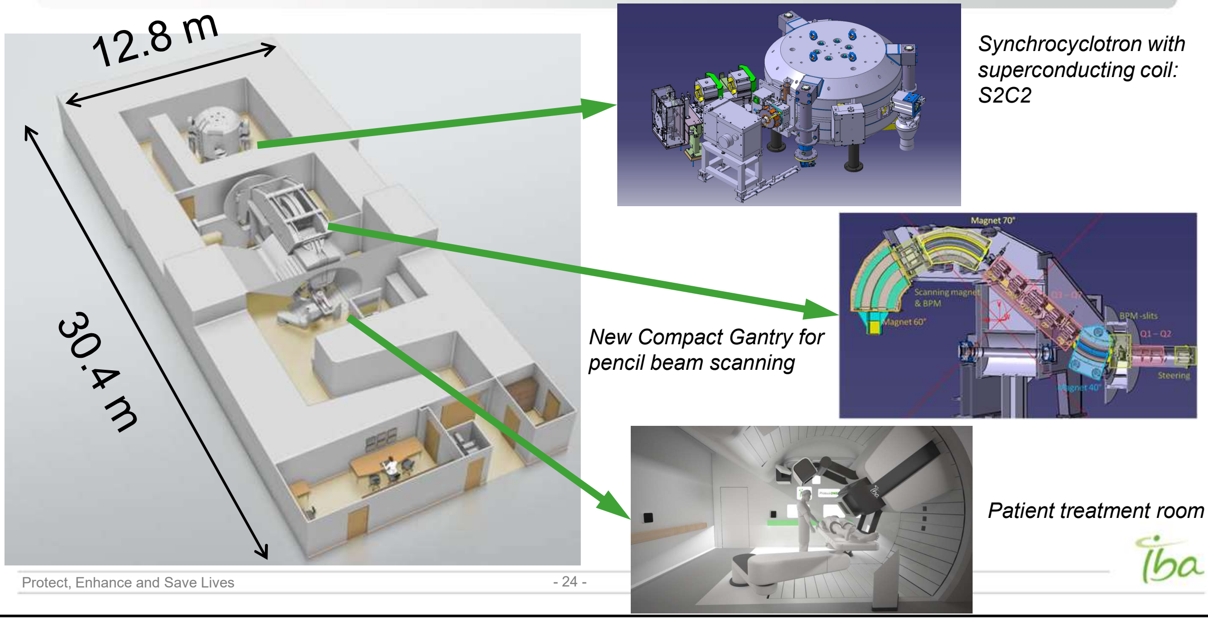
- A proton therapy system is much more than only an accelerator
- It is a complex, multi-room system, filling a hospital building.
- The total investment is around 100 M€, of which 45 M€ for the equipment
- Many people (doctors, therapists, physicists, nurses) work daily in a PT facility
- A PT facility 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®

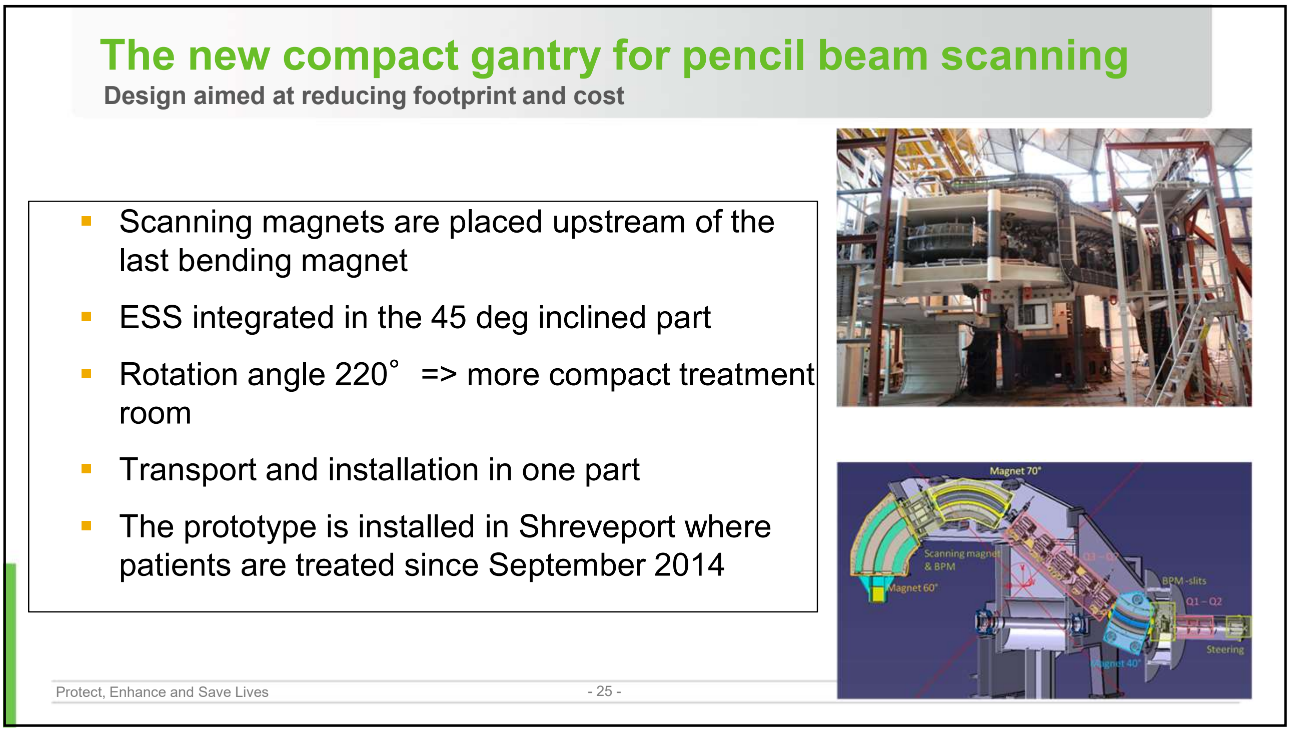
High quality PBS cancer treatment: compact and affordable



Synchrocyclotron with superconducting coil: S2C2

New Compact Gantry for pencil beam scanning

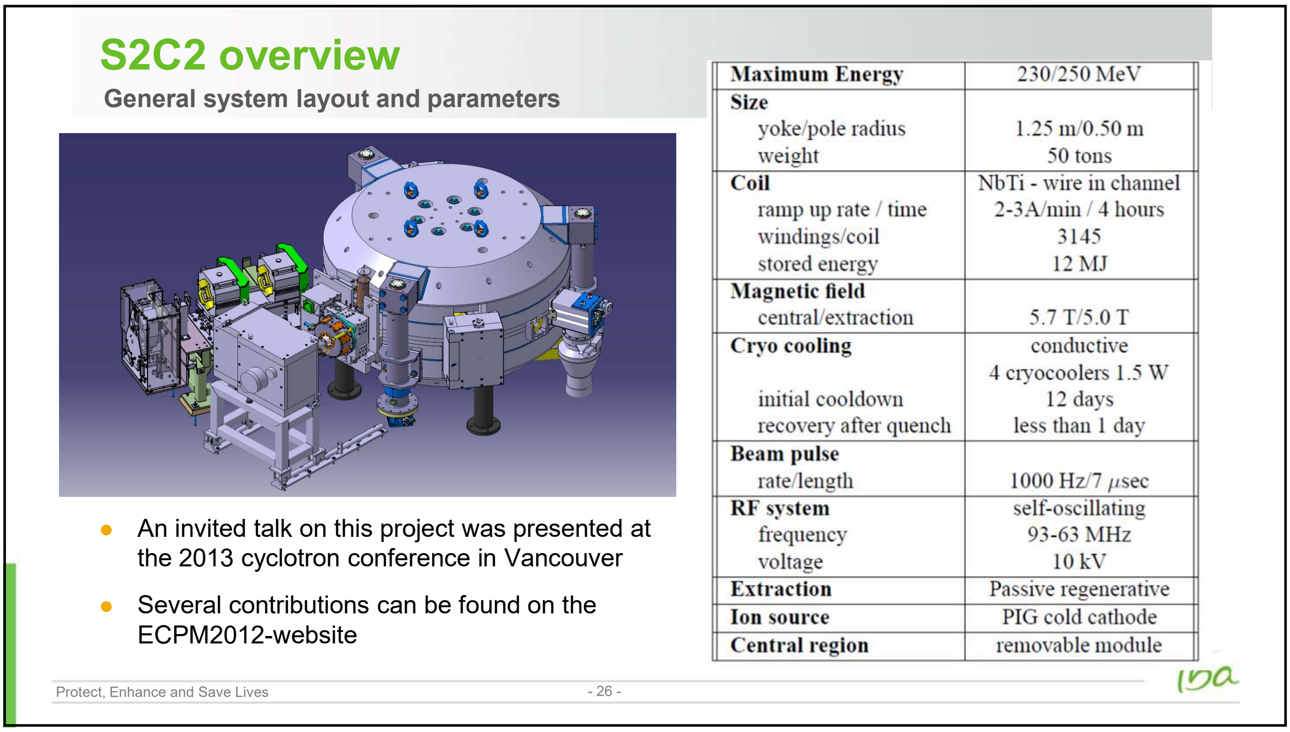
Patient treatment room



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

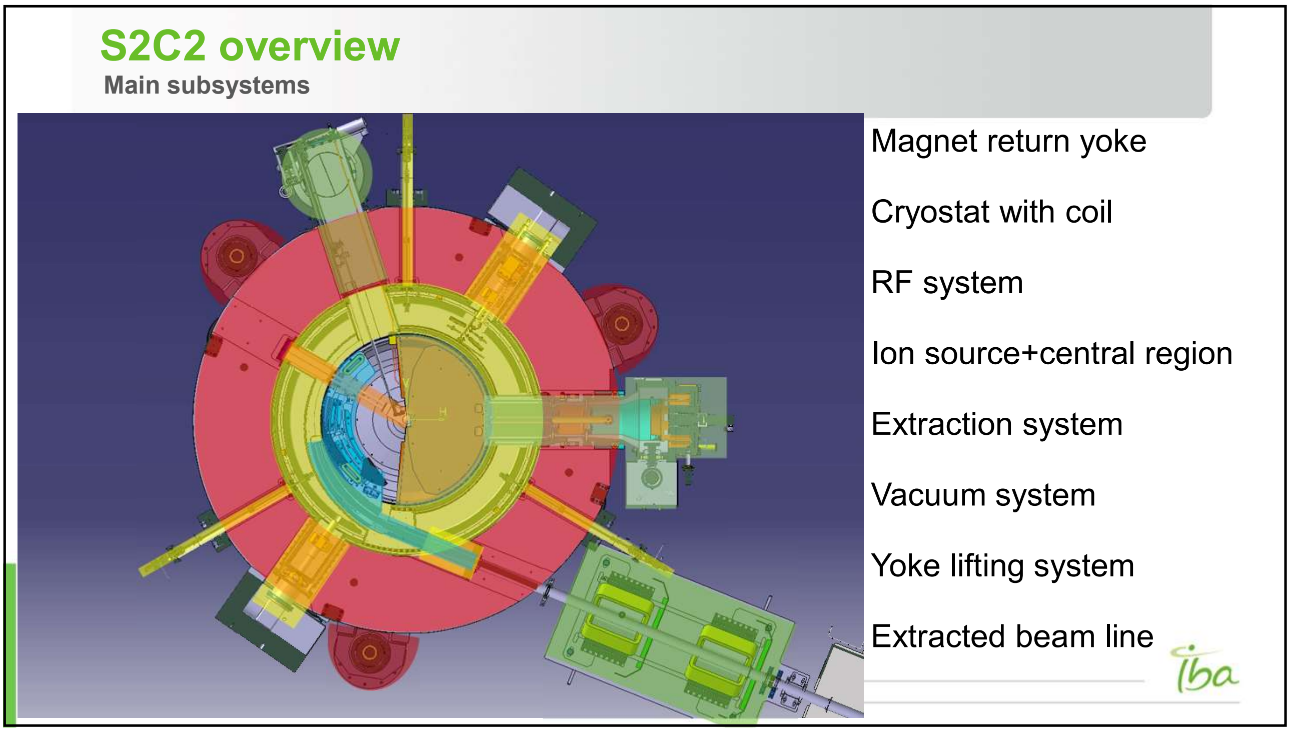


S2C2 overview

General system layout and parameters

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

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



S2C2 overview

Main subsystems

Magnet return yoke

Cryostat with coil

RF system

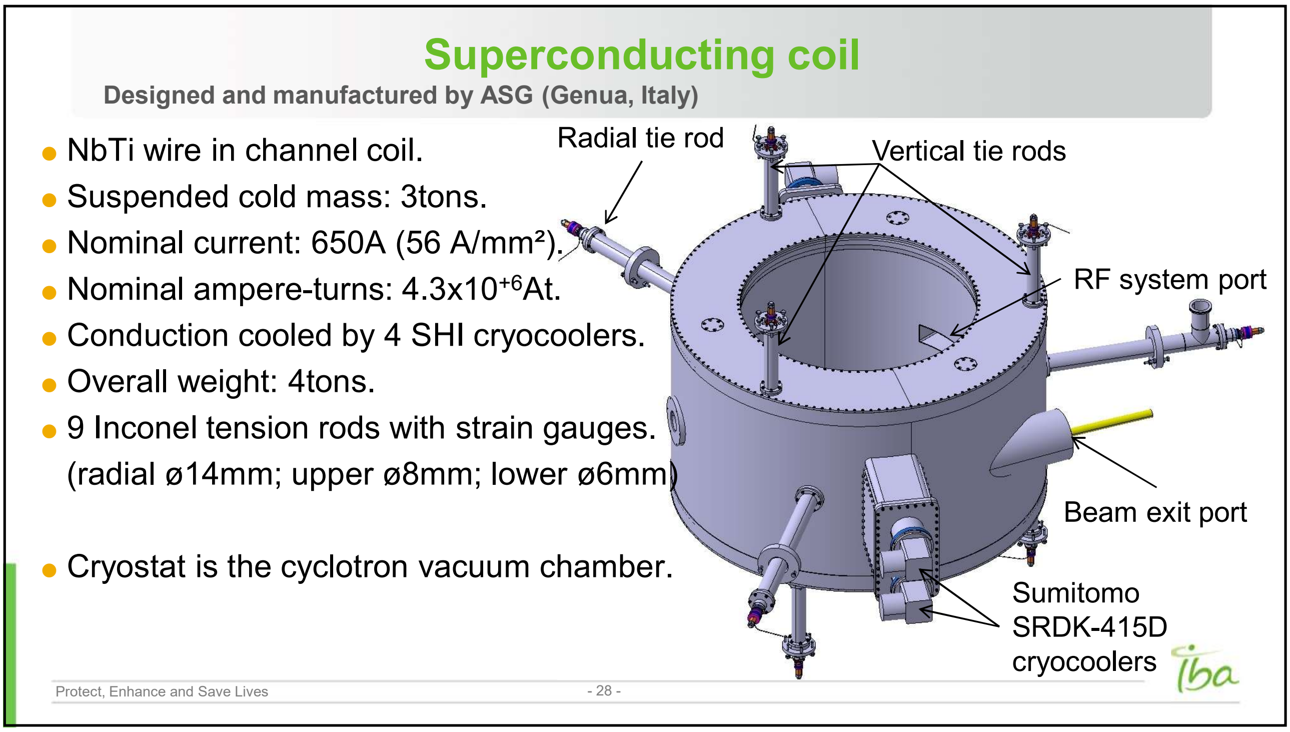
Ion source+central region

Extraction system

Vacuum system

Yoke lifting system

Extracted beam line



Superconducting coil

Designed and manufactured by ASG (Genua, Italy)

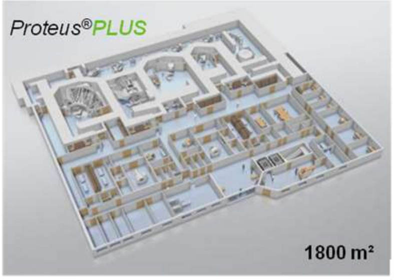
- NbTi wire in channel coil.
- Suspended cold mass: 3tons.
- Nominal current: 650A (56 A/mm^2).
- Nominal ampere-turns: $4.3\times10^{+6}$At.
- Conduction cooled by 4 SHI cryocoolers.
- Overall weight: 4tons.
- 9 Inconel tension rods with strain gauges. (radial ø14mm; upper ø8mm; lower ø6mm)
- Cryostat is the cyclotron vacuum chamber.

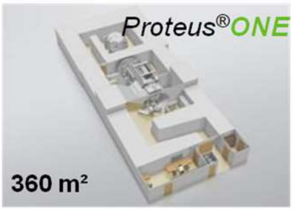
Superconducting coil

Installation of the cryostat in the yoke

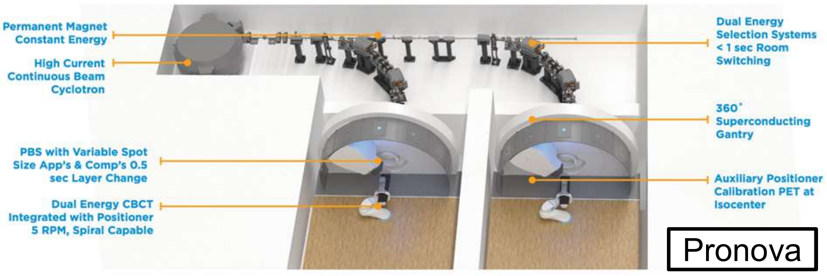
Typical proton therapy systems

IBA

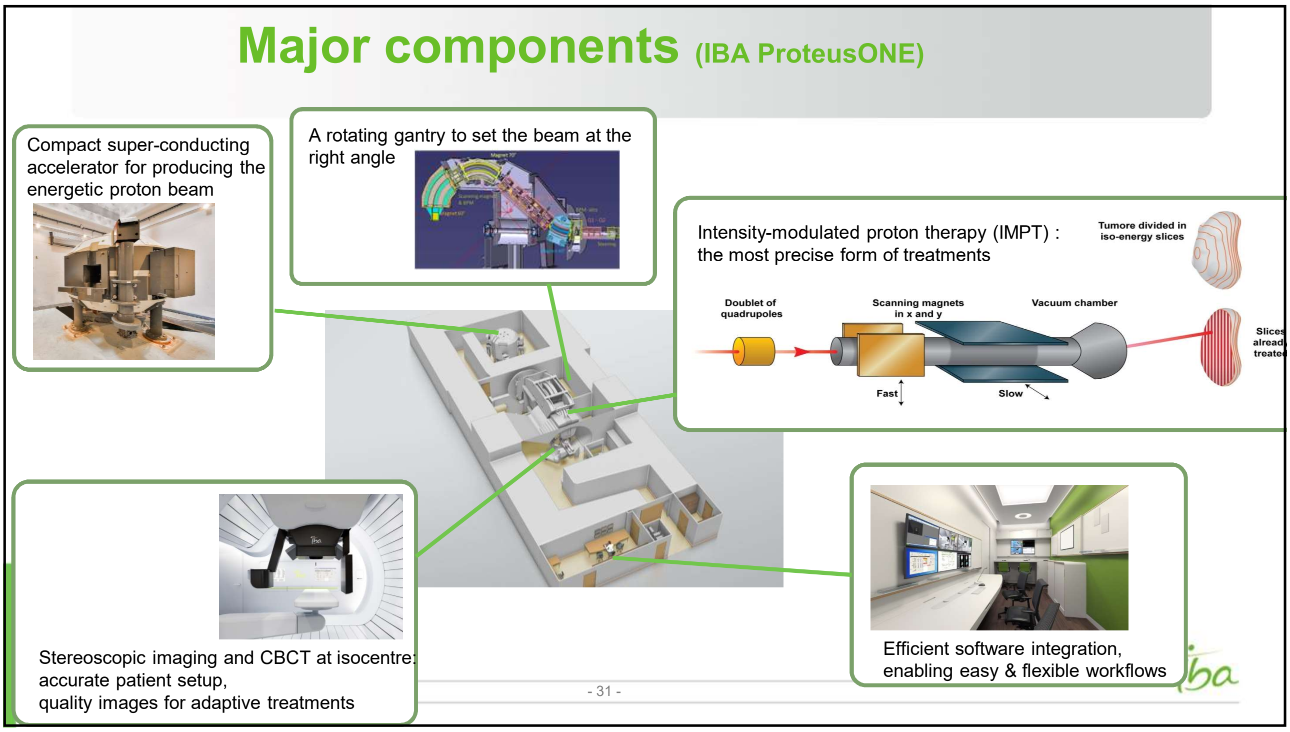




Mevion



Pronova



Major components (IBA ProteusONE)

Compact super-conducting accelerator for producing the energetic proton beam

A rotating gantry to set the beam at the right angle

Intensity-modulated proton therapy (IMPT) : the most precise form of treatments

Stereoscopic imaging and CBCT at isocentre: accurate patient setup, quality images for adaptive treatments

Efficient software integration, enabling easy & flexible workflows

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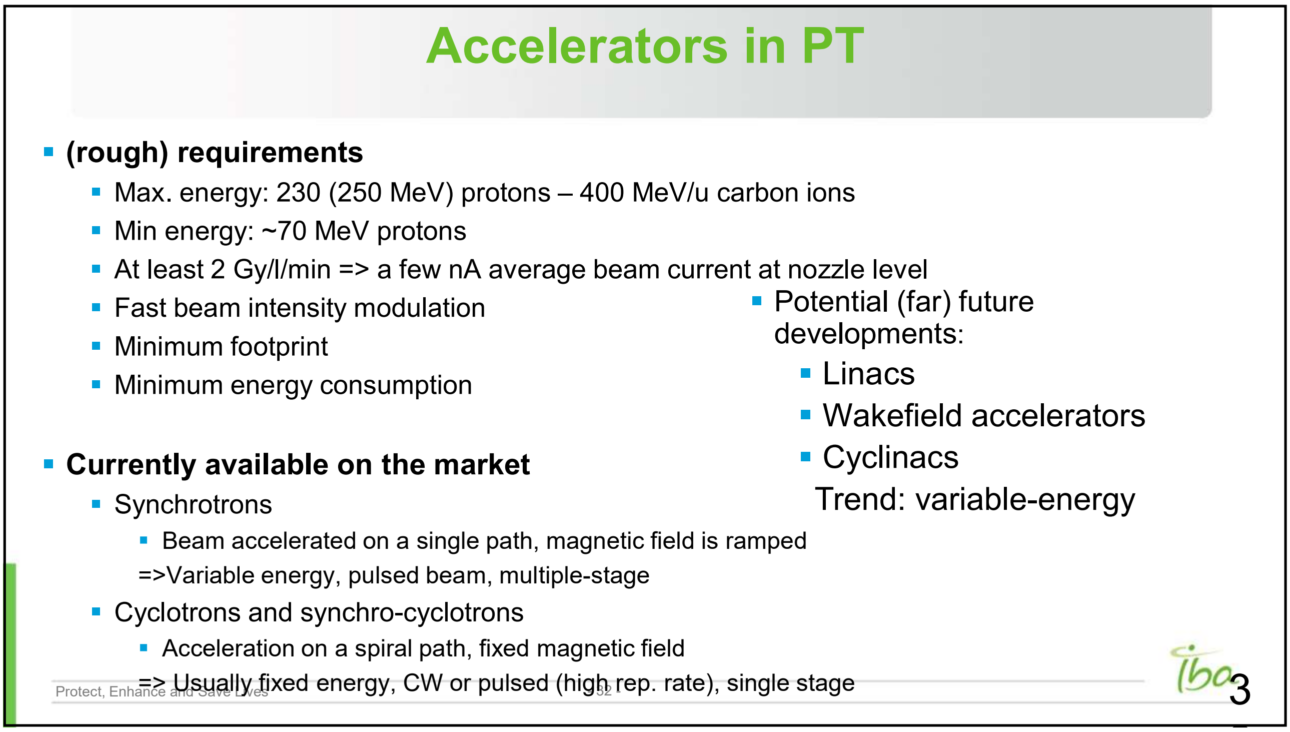


Accelerators in PT

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

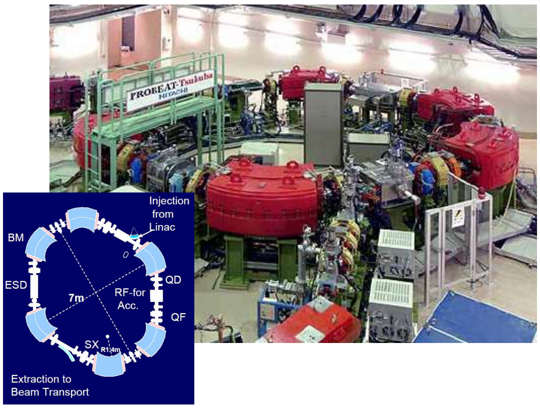
    =>Variable energy, pulsed beam, multiple-stage
  - Cyclotrons and synchro-cyclotrons
    - Acceleration on a spiral path, fixed magnetic field

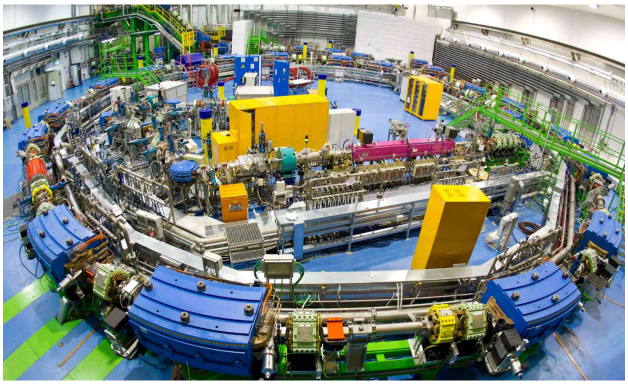
    => Usually fixed energy, CW or pulsed (high rep. rate), single stage

- Potential (far) future developments:
  - Linacs
  - Wakefield accelerators
  - Cyclinacs

  Trend: variable-energy

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, Medaustron

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

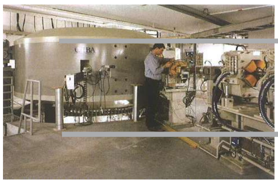
Rossi, EurPhysJPlus2011-126-78.pdf

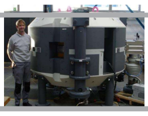
Trend: more compact

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

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

Cyclotrons in PT – commercial models





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

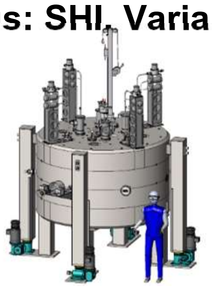
Varian-Accel Probeam
- 250 MeV protons
- 3.1 m Diameter
- CW beam
- Superconducting (NbTi)
- Magnet: 40 kW
- RF: 115 kW

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

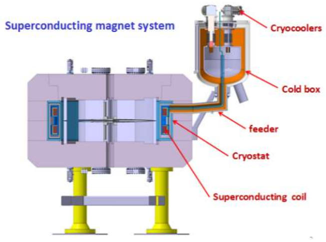
IBA S2C2
- MeV protons
- 2.2 m Diameter
- Rep. rate: 1 kHz
- Superconducting (NbTi)
- RF: 11 kW

Proton cyclotrons - Ongoing developments

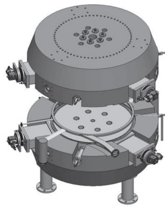
- **1. Isochronous: SHI, Varian/Antaya, Pronova/Ionetix, Heifei/JINR**



Derenchuck - NAPAC 2016



Karamysheva - THP20 cyclotrons 2016



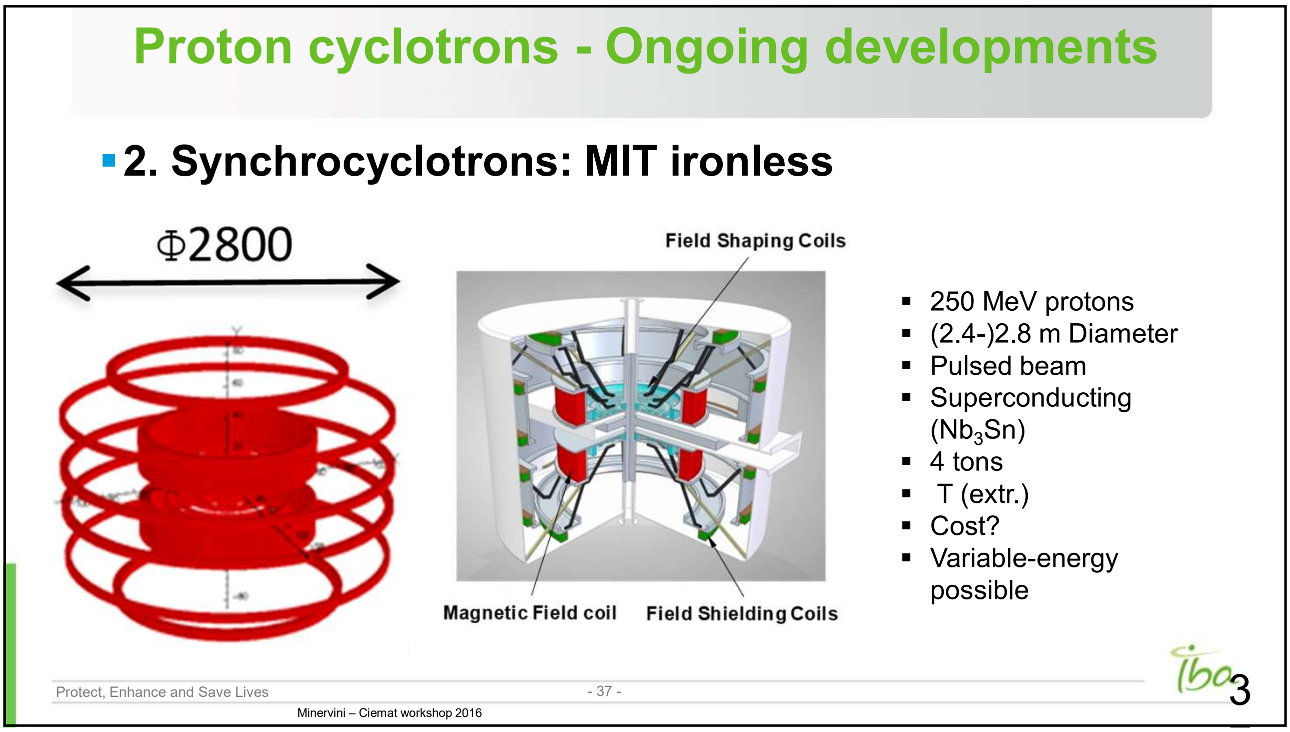
Antaya – CAS 2015

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



Proton cyclotrons - Ongoing developments

2. Synchrocyclotrons: MIT ironless

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

Protect, Enhance and Save Lives - 37 -

Minervini – Ciemat workshop 2016

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