



Superconducting Cyclotrons for Hadron Radiotherapy

J. V. Minervini¹, *Member, IEEE*, A. Radovinsky¹, P. C. Michael¹, D. Winklehner², and L. Bromberg¹ with thanks to Dr. Eric Forton, IBA for background information on hadrontheray

European Conference on Applied Superconductivity (EUCAS)

17-21 September 2017, Geneva, Switzerland

¹Massachusetts Institute of Technology, Plasma Science and Fusion Center

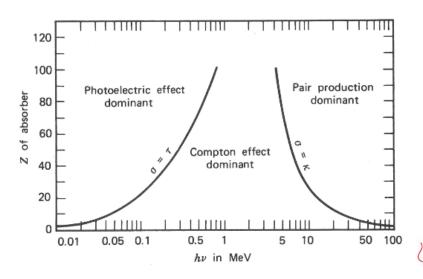
²Massachusetts Institute of Technology, Department of Physics, Laboratory for Nuclear Science Cambridge, MA, USA

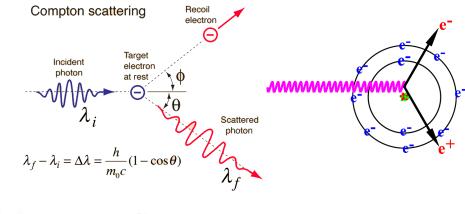
Outline

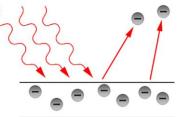
- What is hadron radiotherapy
- Present and future outlook
- Cyclotrons for PBRT
- Superconducting cyclotrons
- Ironless, variable energy, superconducting cyclotron
- Summary

Conventional Radiation Therapy vs. Hadrontherapy

- Most conventional radiation therapy and arc therapy systems use Xrays of a few MeV for cancer treatment
- Dose is not delivered to tissues by the photons themselves, but rather through secondary electrons produced by 3 mechanisms

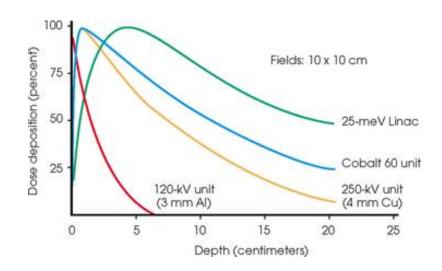






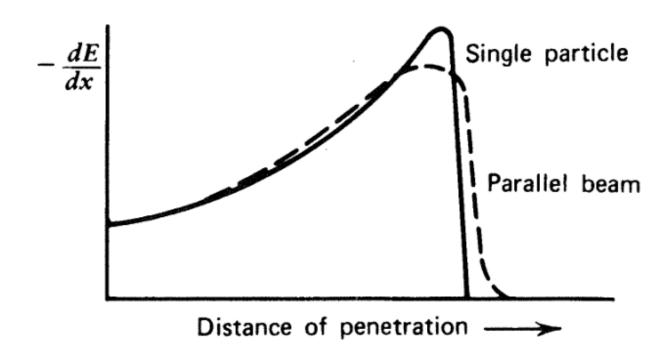
Conventional Radiation Therapy vs. Hadrontherapy

- Results in:
 - A decrease of photon numbers following a superimposition of decreasing exponentials
 - Some electron buildup
- => dose builds-up and then ~exponentially decreases with depth once electron equilibrium is reached

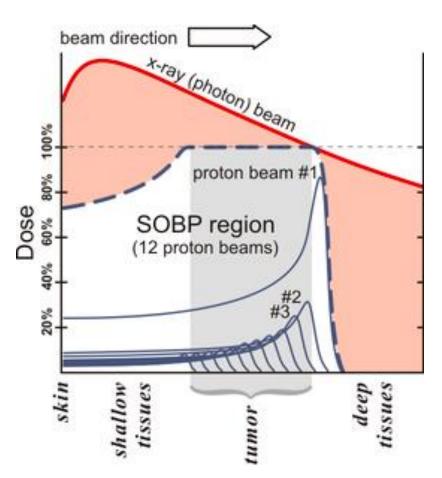


Conventional Radiation Therapy vs. Hadrontherapy

- Instead, hadrons lose their energy in matter according to Bethe-Bloch formula.
- In short, it results in the famous «bragg peak» dose distribution



As a result:



- Hadrons offer the following advantages:
 - Little radiation before the tumor
 - No/little radiation at all beyond the tumor
 - > => Lower integral dose per treatment
- Leading to potential clinical advantages:
 - Up to 50% reduced risk of radiationinduced secondary cancer
 - Drastically lower risk of adverse effects (treatment toxicity, side effects, growth abnormality) – better quality of life

PBS – Pencil Beam Scanning

Advantages:

Good 3D dose conformity

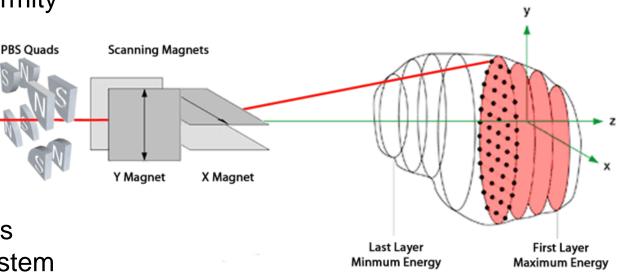
- "Flexible"

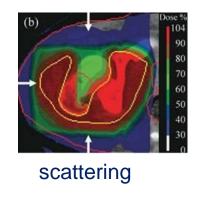
Low neutron dose

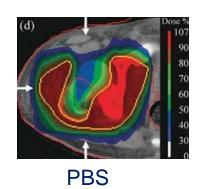
No need for patient specific aperture

Disadvantages:

- Dynamic system, less safe than passive system
- Layer by layer, slower than scattering
- Lateral penumbra less sharp than with collimation

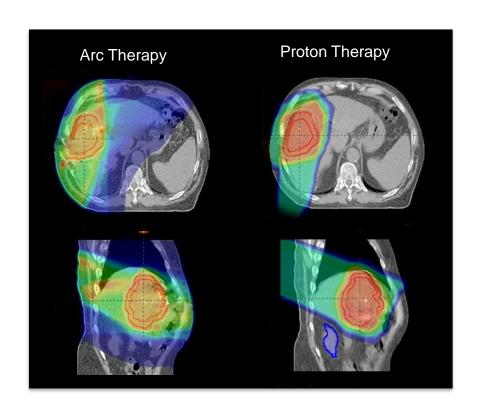






Examples

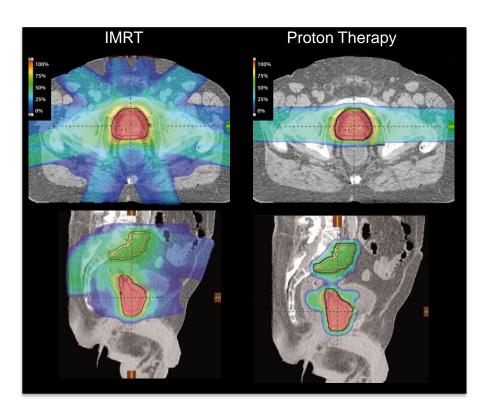
Irradiation of surrounding tissues - Hepatocellular carcinoma



Dose to critical Tissues (mean dose)	Photons	Protons
Right Kidney	20 Gy	0.1 Gy
Lung	12.5 Gy	8.5 Gy

"PBT was found to be a safe and effective local-regional therapy for inoperable HCC. A randomized controlled trial to compare its efficacy to a standard therapy has been initiated" (*)

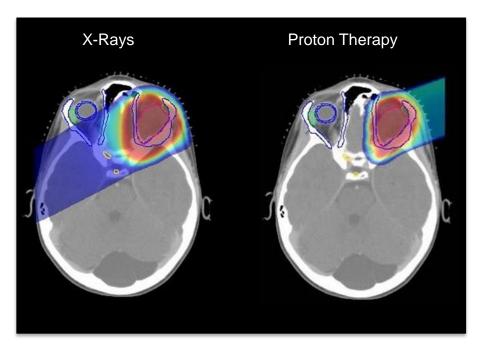
Irradiation of Surrounding Tissues - Prostate



Dose to critical tissues (mean dose)	Photons	Protons
Rectum	20 Gy	6.5 G y
Bowel	18 Gy	10 Gy

"Early outcomes with image-guided proton therapy suggest high efficacy and minimal toxicity with only 1.9% Grade 3 GU symptoms and <0.5% Grade 3 GI toxicities" (*)

Rhabdomyosarcoma – Side effects

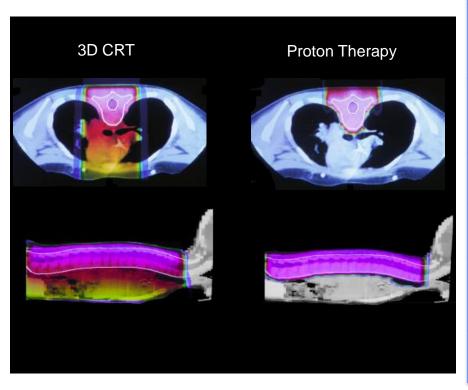


"Fractionated proton radiotherapy is superior to 3D conformal photon radiation in the treatment of orbital RMS (...) Proton radiation therapy minimizes long-term side effects" (*)

Images Courtesy Torunn I Yock, MD -- Burr Proton Therapy Center Boston USA

^(*) Yock, T. et al; « Proton radiotherapy for orbital rhabdomyosarcoma: clinical outcome and a dosimetric comparison with photons. », Int J Radiat Oncol Biol Phys. 63 (2005) 1161.

Pediatric medduloblastoma – Side effects



Side Effects	Protons	Photons
Restrictive Lung Disease	0%	60%
Reduced exercise capability	0%	75%
Abnormal EKGs	0%	31%
Growth abnormality	20%	100%
IQ drop of 10 points at 6 yrs	1.6%	28.5%
Risk of IQ score < 90	15%	25%

"Proton beam therapy has become a standard of care for pediatric cancers..." (*)

Growing Interest in Proton Therapy Clinical Advantages

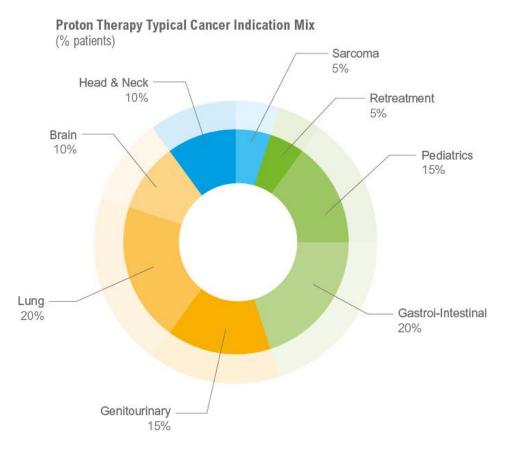
PERSPECTIVE ON RADIATION THERAPY PATIENTS RECEIVING PROTON THERAPY AS PART OF THEIR TREATMENT

1%Today

20%
Following reports
& policies

45%
Following clients' experiences

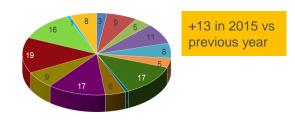




Oct. 2015 data from a leading center in the US

Increasing Relevance of Proton Therapy.

Ongoing clinical trial Total 135

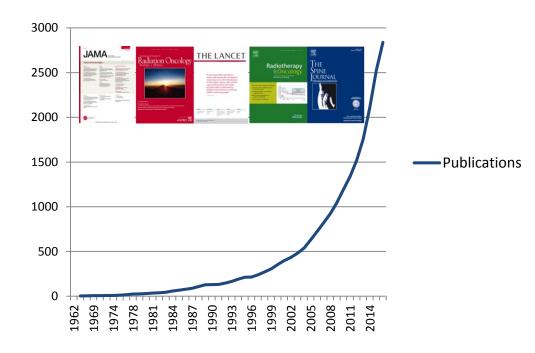


- ocular
- spine
- pancreas
- prostate
- bone soft tissues
- breast
- pediatric
- others

- head and neck
- liver
- esophagus, anal
- uterus, cervix
- lung
- brain, CNS, skullbase
 - phoma, hodgkins

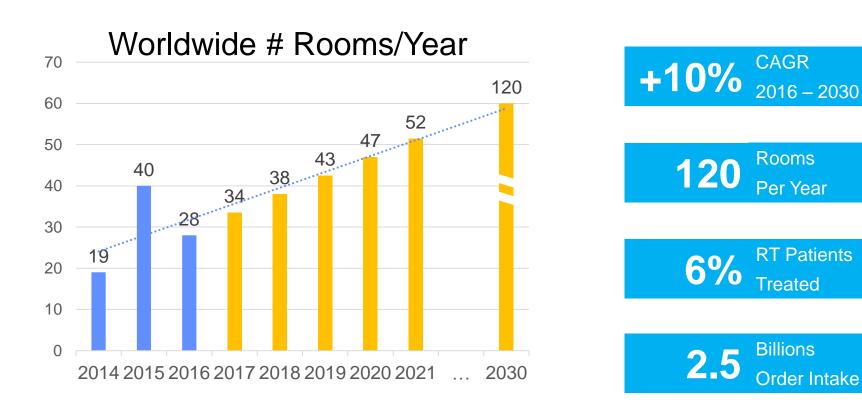
Data from https://clinicaltrials.gov/

Cumulative number of PT publications

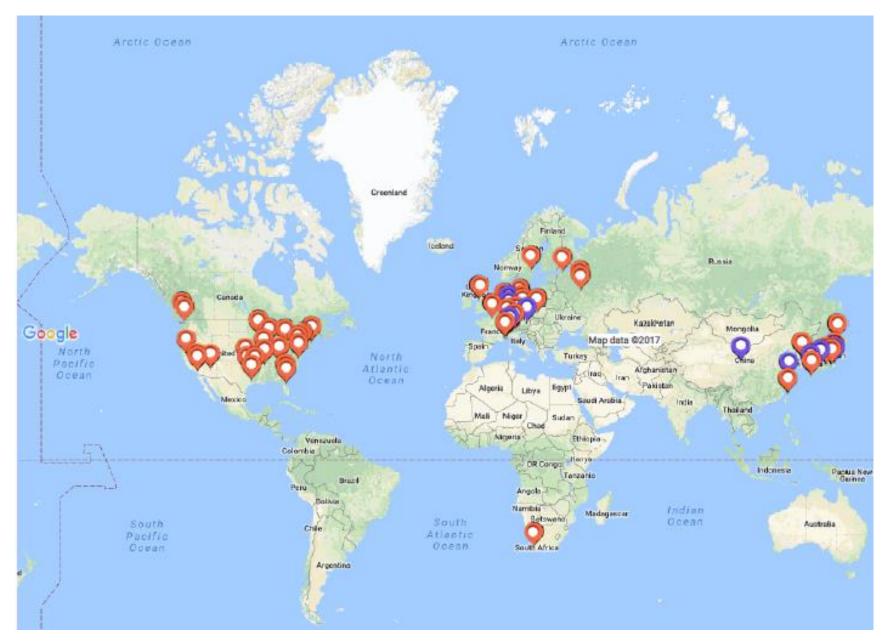


Pubmed search with: Proton Therapy or Proton Radiotherapy or Proton Beam Therapy

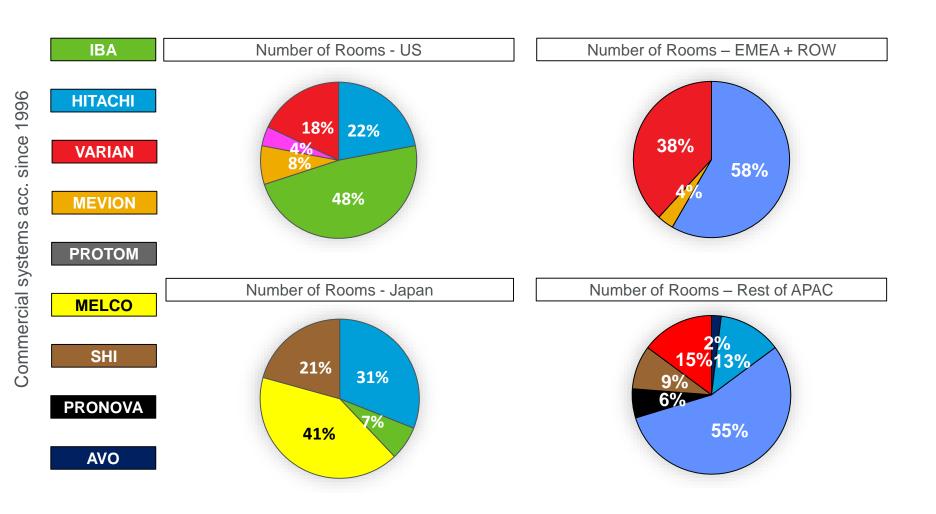
Market Growth: 2016-2021-2030



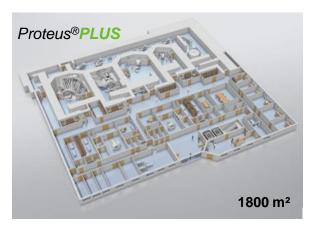
Many Systems Operating

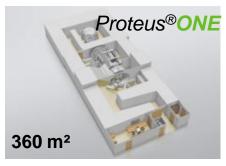


Commercial systems at a glance, by geography (2016)

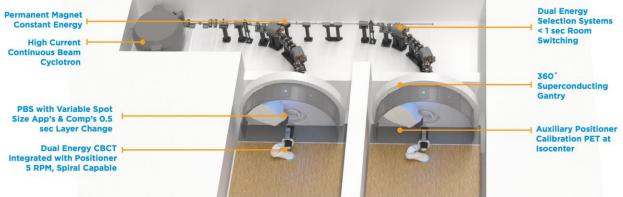


Typical Systems - Protons

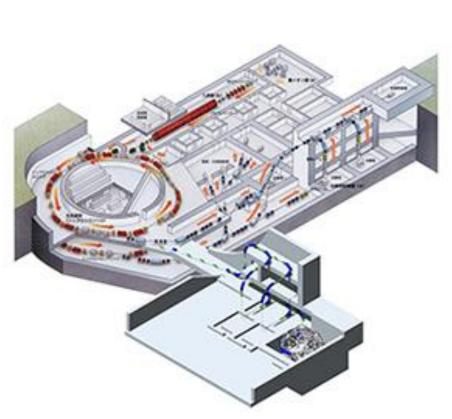


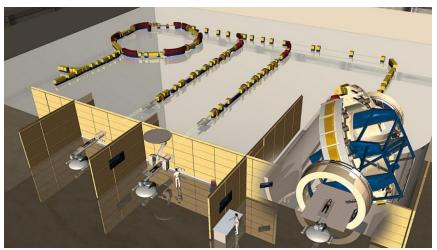


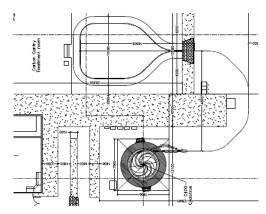




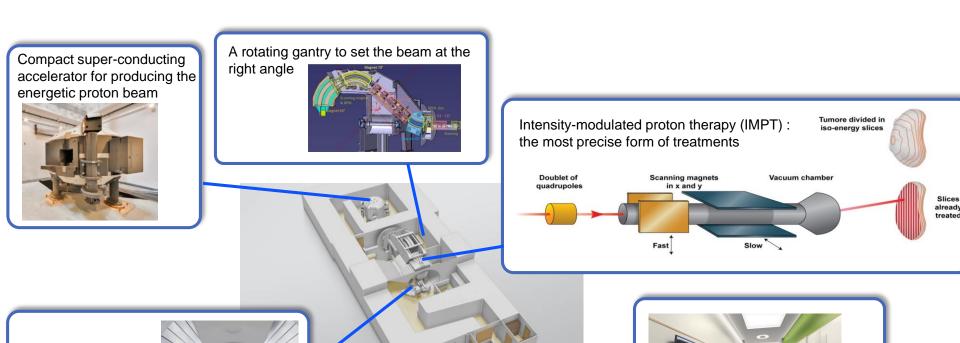
Carbon and Heavy Ion







Major components (IBA ProteusONE)



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

Efficient software integration,

enabling easy & flexible workflows

Summary: a typical system is composed of

An accelerator

- Fixed energy (i.e. cyclotrons) => requires energy modulation
 and selection
- Variable energy (synchrotrons)

A beam transport

- Fixed beam (eye treatment)
- Most usually a gantry able to deliver the beam at various angles
- With PBS as most relevant treatment modality today

A treatment room

- Patient positioning robot
- Rough patient alignment systems (e.g. lasers)
- Imaging systems (Xray, CBCT, CT)
- A treatment control room
- A therapy safety system, software

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 current at nozzle level
 - Fast beam intensity modulation
 - Minimum footprint
 - Minimum energy consumption

=> a few nA average beam

In development or for the (far) future:

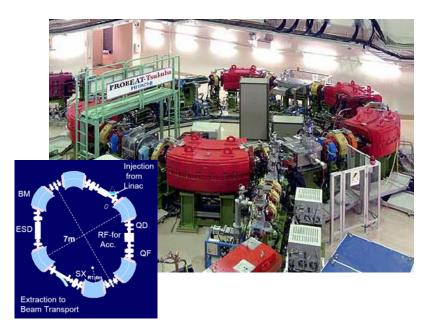
Linacs

Wakefield accelerators

Cyclinacs

- 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

Synchrotrons



Hitachi

- 70-150 MeV protons
- Slow cycle
- 7 m Diameter



"PIMMS" (CERN) design

- Up to Carbon
- 25 m Diameter
- Rep. rate: 5 Hz
- Installed @CNAO, Medaustron

Rossi, EurPhysJPlus2011-126-78.pdf

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

Trend is toward more compact machines to reduce costs



Protom

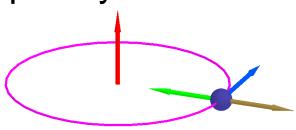
- Up to 330 MeV protons
- 5 m Diameter, ~16 tons
- Being installed @MGH

Challenges and Trends in PT

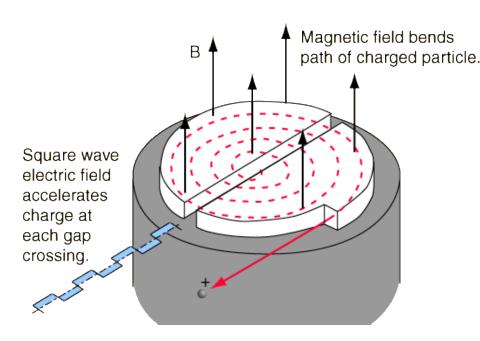
- Cost & Affordability (multirooms towards 1-2 rooms; cost of a fraction)
- IMPT scanning
 - Speed of treatment
 - Even faster with continuous line scanning?
- Image guidance and Treatment robustness (leverage on sharp dose distribution)
 - Setup errors, Intra-fraction changes, Organ motion management
 - Inter-fraction changes, Adaptive treatments
 - Offline
 - Online with as little additional imaging dose as possible
 - In Vivo & real time range verification
- Complexity, and so forth... Sustainability, too

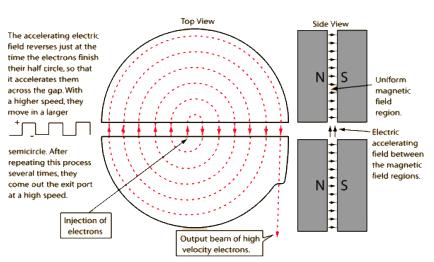
Cyclotrons basic principles

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



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





Commercial PBRT Cyclotrons









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 (Nb₃Sn)

IBA S2C2

- MeV protons
- 2.2 m Diameter
- Rep. rate: 1 kHz
- Superconduc ting (NbTi)
- RF: 11 kW

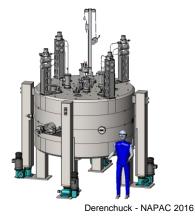
Proton cyclotrons - Ongoing developments

Isochronous: SHI, Varian/Antaya, Pronova/Ionetix, Heifei/JINR



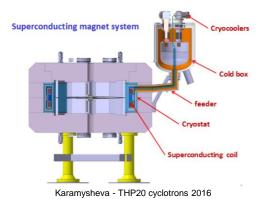
SHI

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



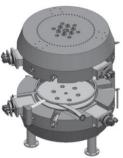
Pronova/Ionetix

- 250 MeV protons
- 2.8 m Diameter
- CW beam
- Superconducting (Nb₃Sn)
- 60 tons
- 3.7 T (extr)



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 (Nb₃Sn)
- 30 tons+
- 5.5 T (extr.)
- "Flutter" coils

Mevion S250



Cyclotron Weight ~25 t



Comparison of PBRT Cyclotrons

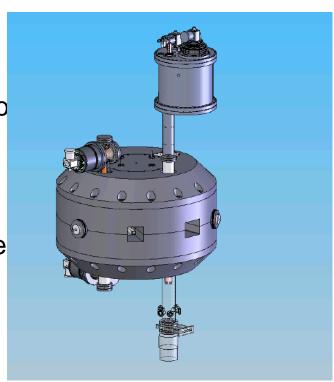
	Mevion S250	IBA S2C2	Varian Proscan	IBA C230
R pole (m)	0.34	0.50	0.80	1.05
D Yoke (m)	1.80	2.50	3.10	4.30
Height (m)	1.20	1.50	1.60	2.10
B _o (T)	8.9	5.7	2.4	2.2
B _f (T)	8.2	5.0	3.1	2.9
Mass (tonnes)	25	<i>50</i>	100	250
T _f (MeV)	254	230/250	250	235

Compact Superconducting Cyclotron Research at MIT

- Work started in late 2002
- Initial focus: compact cyclotrons to enable low cost Proton Beam Radiotherapy
- 9T Superconducting Synchrocyclotron was first designed in 2006
- Now we are working on several machines for medical applications, basic science and other advanced applications

Compact Superconducting Cyclotrons beyond 6T ...

- Compact (a few cubic meters)
- Transportable (minimize the mass and power)
- Not tethered to a helium liquefier- Use cryo-coomany conductor types
- Full acceleration in 1 accelerator stage
- High Field Superconducting Cyclotron Possible
- E= 10-1000 MeV protons and heavy ions



+'s and -'s of Ironless Cyclotrons

+'s:

- Reduced weight.
- Reduced fringe field.
- Larger mid-plane and axial bore clear spaces can use interchangeable (Ion Source/RF/Extraction) cassettes for different Ions (protons, lithium, carbon).
- Plenty of space inside the cryostat.
- No need to shim the iron big advantage for mass production.
 - High factory winding tolerances allow field profile repeatability.
- No external iron no positive magnetic stiffness, simpler cold mass support.
- No internal (cold) iron less load on cryogenics for faster cooldown and warmup.
- Scaling laws ease magnetic design process.

-' s:

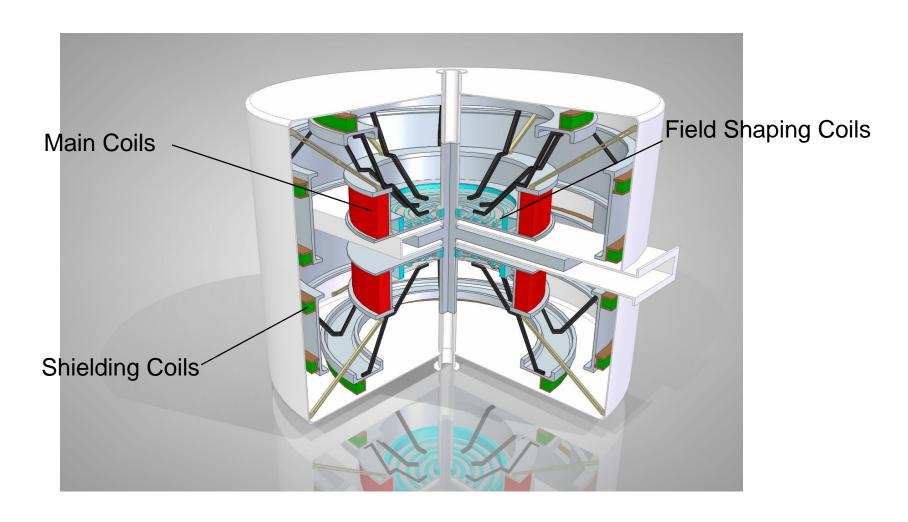
- Somewhat larger radius shielding coils Increases difficulty of conduction cooling by cryocoolers.
- Uses more superconductor than systems with iron
- Increases magnet stored energy making quench protection more difficult

Further Features of Ironless Cyclotrons

- Scalable beam energy by adjusting coil current

 can vary beam energy with
 extraction at the same radius (restrictions apply)
- Shielding coils require small ampere-turns:
 - Can be LTS
 - Can be HTS heat sunk to thermal radiation shield
 - Can be external, copper coils.

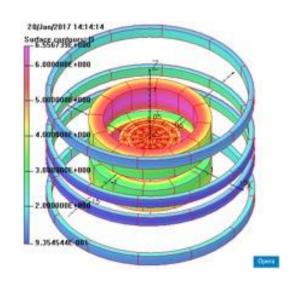
Ironless k230 Magnet Design



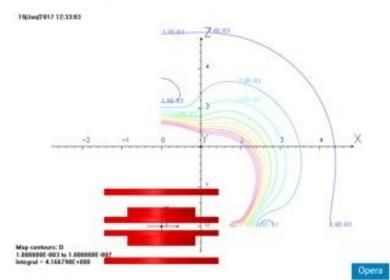
Coil Sets and Stray Magnetic Field



Main field, field shaping, and field shielding coils



Field magnitude at surface of coils.



Stray magnetic fields in the axial cross-section. (10 gauss to 100 gauss with 10-gauss increments)

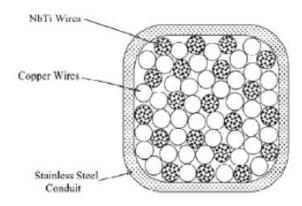
Ironless k230 Magnet Design w/ Variable Energy

Beam		
B_0	Τ	5.025
B _{ex}	Т	4.637
R _{ex}	m	0.501
T _{ex}	MeV	230.0
Coil		
E _m	MJ	30.9
l _{op}	Α	3,000
L	Н	6.89
J_{wp}	A/mm ²	52.0
B _{max}	T	6.61
Magnet Diameter	m	3.00
Magnet Height	m	2.01
Conductor Mass	kg	6,310
Field		
R(10G)	m	3.8
Z(10G)	m	3.8

 The magnet Cryostat is an OD= 3m, H= 2m cylinder

Magnet and Conductor

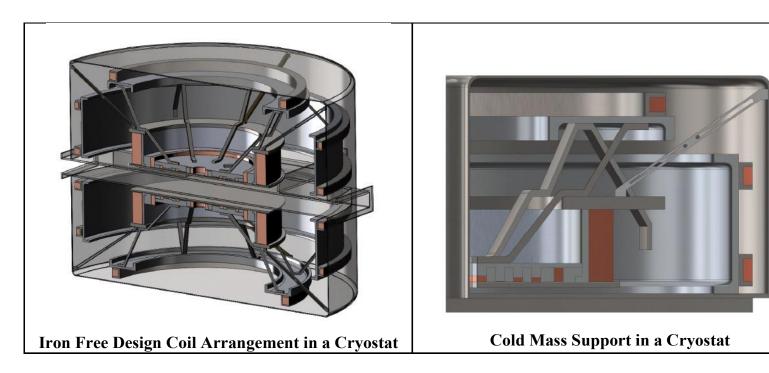
- Conductor is NbTi Cable-in-Conduit with sealed supercritical helium
 - > Helium is heat capacity for adiabatic ac loss energy absorption
- Conduction cooled by cryocoolers —> Heat removed in time interval between patients.
- Higher J_{wp} -> lighter
- High-Field Nb₃Sn could be used, if desired, for highly compact design -> 4 tons, OD~2 m
 - > Also allows adiabatic absorption of more ac losses.



SUMMARY OF MAGNET COMPONENT WEIGHTS

Conductor and Coils					
		NbTi-a	NbTi-b	All	
Length (m)	m	19289	1052		
Mass SC Strand	kg	2508	51	2559	
Mass Cu Strand	kg	1321	0	1321	
Mass SS Conduit	kg	2722	31	2752	
Mass Insulation	kg	225	6	231	
Total Mass of Coils	kg	6551	82	6863	
	(Cryostat			
Mass Vacuum Vessel	kg	3773			
Mass Radiation Shield	kg	485			
Total Cryostat	kg	4258			
Cold Mass Structure					
Mass Vacuum Vessel	kg	3773]		
Mass Radiation Shield	kg	485]		
Total Cryostat	kg	4258			
Cold Mass Structure				Total	
Material		SS 316LN	Al-6061-T6		
Mass	kg	1135	1496 2631		
Magnet System Total Weight					
Coils	kg	6,863			
CM structure	kg	2,630			
Cryostat	kg	4258			
Total	kg	13,752			

More access to the beam area

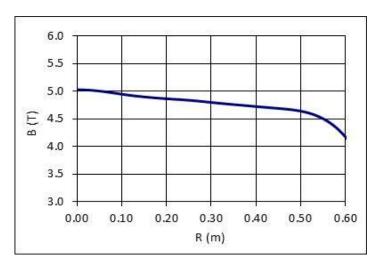




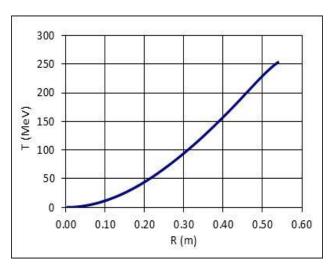
Replaceable RF System Cassettes



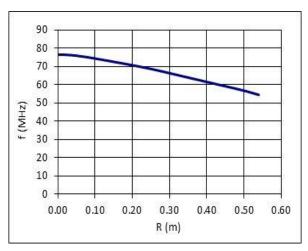
Field, Beam Energy, and RF Frequency at 230 MeV



B-field vs. Radius



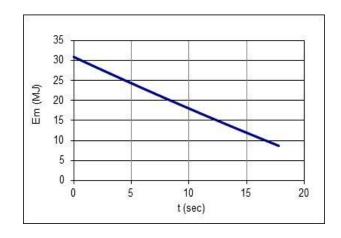
Beam Energy vs. Radius

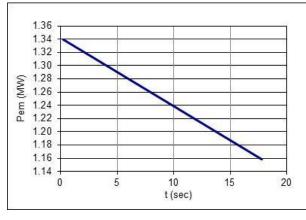


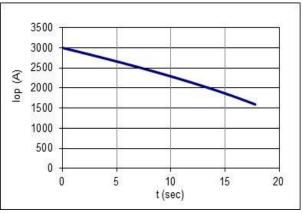
Acceleration Frequency vs. Radius

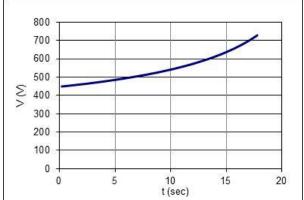
Variable Beam Energy

- Beam energy is varied for range scanning
- Change operating current and field in the coils proportionally for variable energy
- This requires adjustment of the coil current RF voltage and frequency.
- Multiple ramps provide repainting.





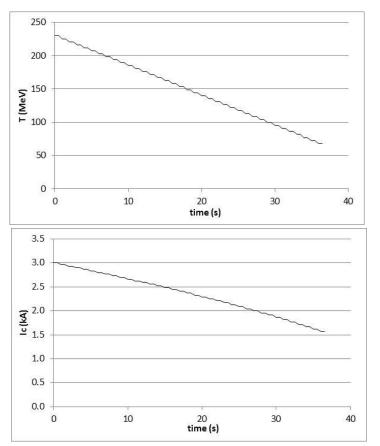


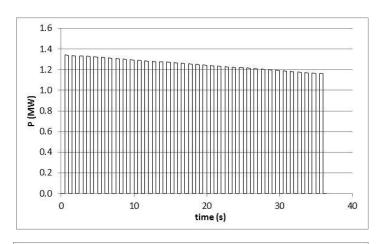


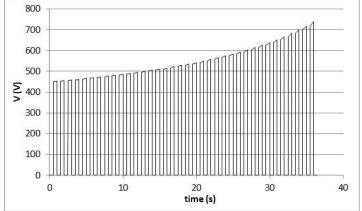
- The ranges of variation of these parameters:
 - > 1.59 kA < lop < 3 kA
 - > 0.45 kV < V < 0.73 kV
 - > 1.16 MW < P < 1.34 MW

Variable Beam Energy

- Remain at constant energy while painting a layer during Δt_{lay} =0.5 s increments
- Ramp between layers in∆t_{L2L}=0.5 s





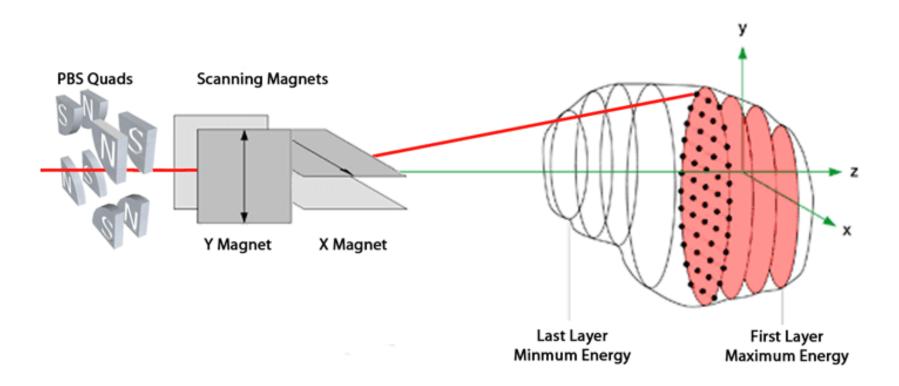


- Duration of the cycle is 37 seconds for this scenario of scanning from 230 MeV to 70 MeV
- Power and voltage are delivered by the magnet power supply to change the magnet current and beam energy

Variable Beam Energy

- Variable beam energy is accomplished by modulating the coil current, which results in linearly proportional change of the magnetic field in the beam space.
- This process has implications both for the magnet itself and for the beam controls.
- For a T_{min} =70 MeV and T_{max} =230 MeV synchrocyclotron the layer to layer beam energy change was defined as constant $\Delta T = 4.5$ MeV linear ramps, each lasting $\Delta t_{Layer-to-Layer} = 0.5$ seconds.
- The constant beam energy intervals during which the inlayer painting takes place are set to a constant, Δt_{layer} =0.5 s, for each layer.

Pencil-Beam Scanning (PBS)



HYSTERESIS LOSSES IN THE SUPERCONDUCTOR PER CYCLE

Conductor		NbTi-a	NbTi-b
B_{0}	T	0.38	0.38
J_0	A/m^2	4.00E+10	4.00E+10
d_f	m	6.50E-06	6.50E-06
alpha		0.53	0.53
B_f	T	6.56	5.36
E	J/m ³	5349	5261
L	mJ/cm ³	5	5

- Hysteresis losses are small.
- Adiabatic temperature rise is absorbed by helum in CICC without exceeding current sharing temperature.
- This allows for multiple repainting sweeps for a single treatment.
- Coils are recooled by cryocooler in between patients.
- If layers can be repainted multiple times before energy steps then only a single energy sweep is required.

Summary

- Hadron therapy cyclotron accelerators can be improved by replacement of resistive magnets with superconducting magnets.
- Ironless cyclotrons are feasible and provide better magnetic shielding.
- Superconducting cyclotrons can be much lighter and smaller than conventional systems leading to space and cost savings (physical and operating).
- Variable energy synchrocyclotrons are theoretically feasible. Following these engineering studies the next step is to build a working prototype.



Backup



Beam Controls (Beam Energy Variation)

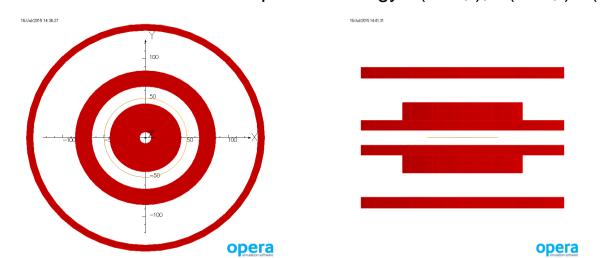
$$T(r,t)=E0*(sqrt(1+(Kb(t)*B(r,0)*e*r/(m0*c))^2)-1)$$

- Matching T(r,t) can be achieved by a run-time adjustment of the per turn RF voltage.
- Quantitative assessment of this variation will be done after defining more parameters of the RF system, per-turn gain, in particular.

Trajectories are Collinear for Scaled Beam Energies

T(Rex,t)/T(Rex(0)	Т	gamma	Rigidity	Bex	Kb=B/B0	Jwp
	MeV		T*m	Т		A/mm ²
1.000	230.0	1.245	2.322	4.637	1.000	52.0
0.652	202.2	1.215	2.162	4.318	0.931	48.4
0.304	70.0	1.075	1.231	2.459	0.530	27.6

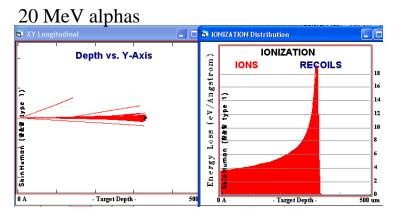
Proton was launched in the circumferential direction from the same spot in the mid-plane at Rex=50.1 cm with the respective energy T(Rex,t), T(Rex,t)/T(Rex(0)=1.0, 0.652 and 0.304

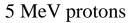


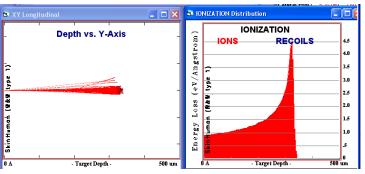
Trajectories of the proton in the axial and lateral perspectives:

- all form perfectly coincident circles
- all lie in the same plane

Protons are good - How heavy should we go?





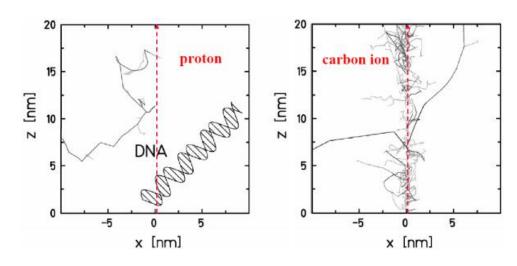


For the same range, heavier and/or more charged particles need higher entrance energy

LET is higher

Straggling is reduced

Biological effect is usually enhanced



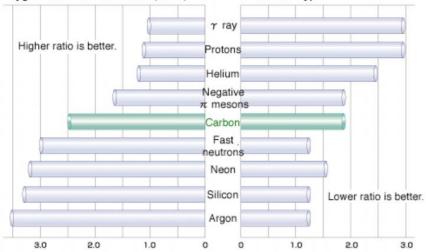
How heavy should we go?

But:

You want to avoid killing upstream cells Fractionation problem

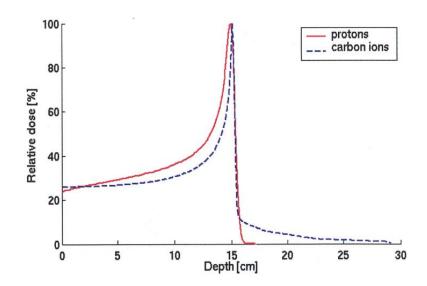
RBE and **OER**

Relative biological effectiveness (RBE) and oxygen enhancement ratio (OER) of various radiation types



RBE represents the biological effectiveness of radiation in the living body. The larger the RBE, the greater the therapeutic effect on the cancer lesion.

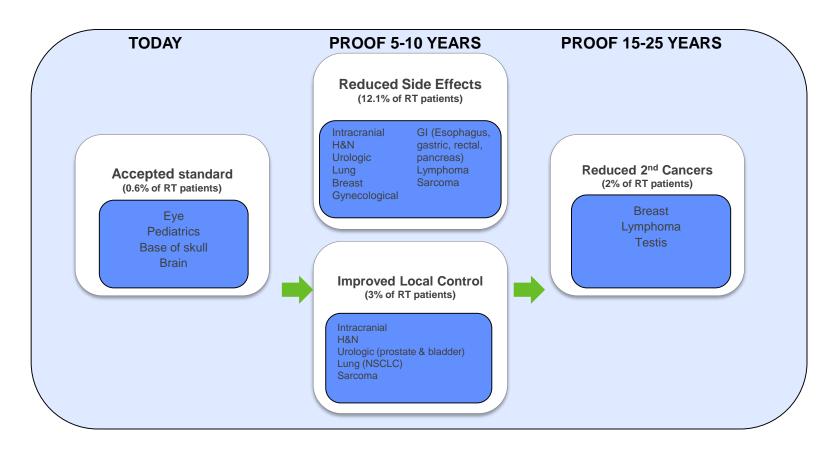
OER represents the degree of sensitivity of hypoxic cancer cells to radiation. The smaller the OER, the more effective the therapy for intractablecancer cells with low oxygen concentration.



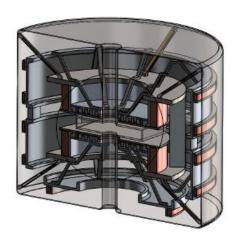
A. Sessler, Cyclotrons'10 http://accelconf.web.cern.ch/Accelconf/Cyclotrons2010/talks/frm1cio02_talk.pdf Ugo Amaldi and Gerhard Kraft - Radiotherapy with beams of carbon ions Reports on Progress in Physics, Volume 68, Number 8
Published 11 July 2005 • 2005 IOP Publishing Ltd

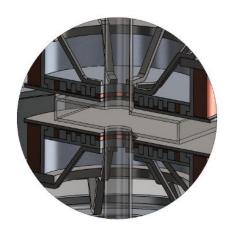
A promising future

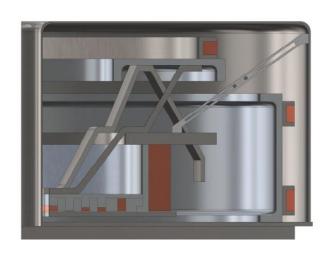
- PT has a real potential to grow from ~1% today, up to almost 20% of RT treatments.
- The development of referral models is strongly encouraged, and should accelerate the adoption of PT on objective basis.



Similar magnet design has been built



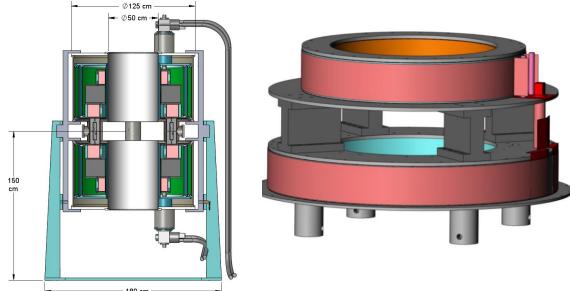




Similar to MIT designed High Precision Dusty Plasma magnet,





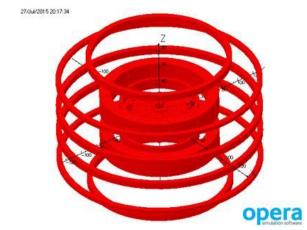


Magnetic Design

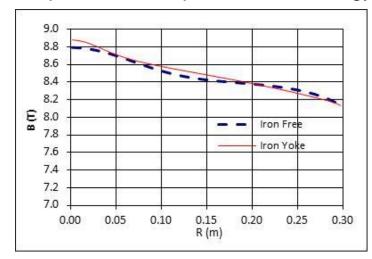
Conventional Cyclotron Magnetic Model

ODE!

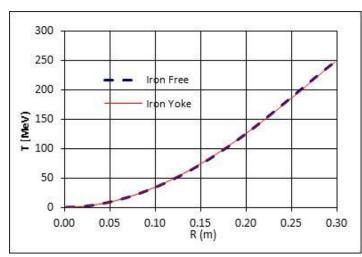
Iron Free Cyclotron Magnetic Model



- The coil set of the iron free design was optimized to match the magnetic field versus radius, B(r), profile of the conventional design.
- The profiles of the proton beam energy vs. radius for both models are almost identical.



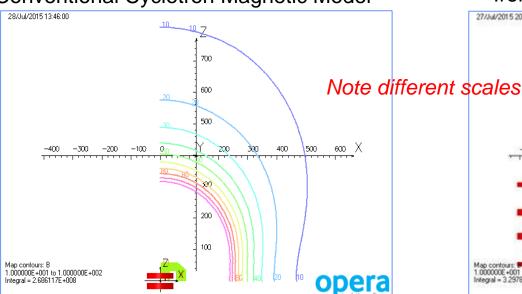
Magnetic Field vs. Radius



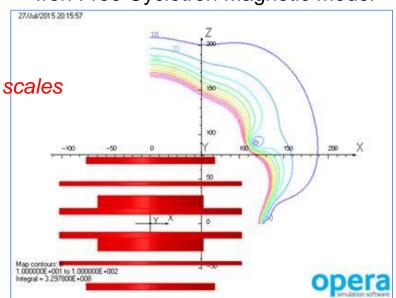
Proton Beam Energy vs. Radius

Active Magnetic Shielding

Conventional Cyclotron Magnetic Model



Iron Free Cyclotron Magnetic Model



- The lines indicate fields from 10 G to 100 G with 10-G increments.
- For the iron free design the 10-G level occurs at a radius less than 2 m, whereas in the conventional design the calculated field at 2 m is 180 G.
- In the axial direction the field at the same, 2 m, distance from the iso-center is 10 G and 410 G respectively.

Parameter Comparison

Model		With Iron	Ironless			
	Beam					
B _o	Т	8.877	8.791			
B _{ex}	Т	8.132	8.109			
R _{ex}	m	0.297	0.296			
T _{ex}	MeV	247.2	245.7			
	Coil					
E _m	MJ	9.6	32.0			
l _{op}	А	2,000	2,000			
$J_{\sf wp}$	A/mm ²	180.0	180.0			
B _{max}	Т	10.98	11.60			
T _{op}	K	5.0	5.0			
dT	K	2.5	1.9			
OD	m	1.80	2.17			
Н	m	1.20	1.61			
M_{cond}	kg	1,448	2,225			
Field						
R(10G)	m	5.0	1.8			
Z(10G)	m	8.2	2.0			

Weight and Size Comparison

Model		With Iron		Ironless	
Parts	Density	Volume	Weight	Volume	Weight
	kg/m³	m ³	kg	m3	kg
Iron Yoke	7,860	2.105	16,545	0	0
Bobbin	7,860	0.299	2,350	0.342	2,686
Windings	8,000	0.181	1,448	0.278	2,225
MLI			24		24
Cold Structure			3,822		4,935
Cryostat	7,860	0.137	1,078	0.184	1,446
Supports			89		65
Thermal Shield	7,860	0.027	216	0.037	289
Cryocoolers			74		74
Magnet			5,278		6,808
Total (Magnet + Iron)			21,823		6,808

Magnet Design

Beam parameters				
Maximum central magnetic field (at <i>R</i> =0, <i>Z</i> =0)	4.980 T			
Maximum magnetic field at extraction (at $R=R_{ex}$, $Z=0$)	4.596 T			
Extraction radius, R_{ex}	0.501 m			
Maximum beam energy, $T(R_{ex})$	226.3 MeV/u			
Coil				
Stored magnetic energy, E	31.1 MJ			
Outer diameter of cryostat, OD	3.00 m			
Overall height of cryostat, OH	2.02 m			
Magnitude of fringe magnetic field				
In radial direction, $B(\text{at } R=3.5\text{m}, Z=0)$	11 Gauss			
In axial direction, $B(\text{at } R=0, Z=4.5\text{m})$	12 Gauss			