OVERVIEW OF ION THERAPY ACCELERATORS FOR A BEAM THERAPY RESEARCH AND DEVELOPMENT CENTER IN THE US

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FFAG14
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Abstract

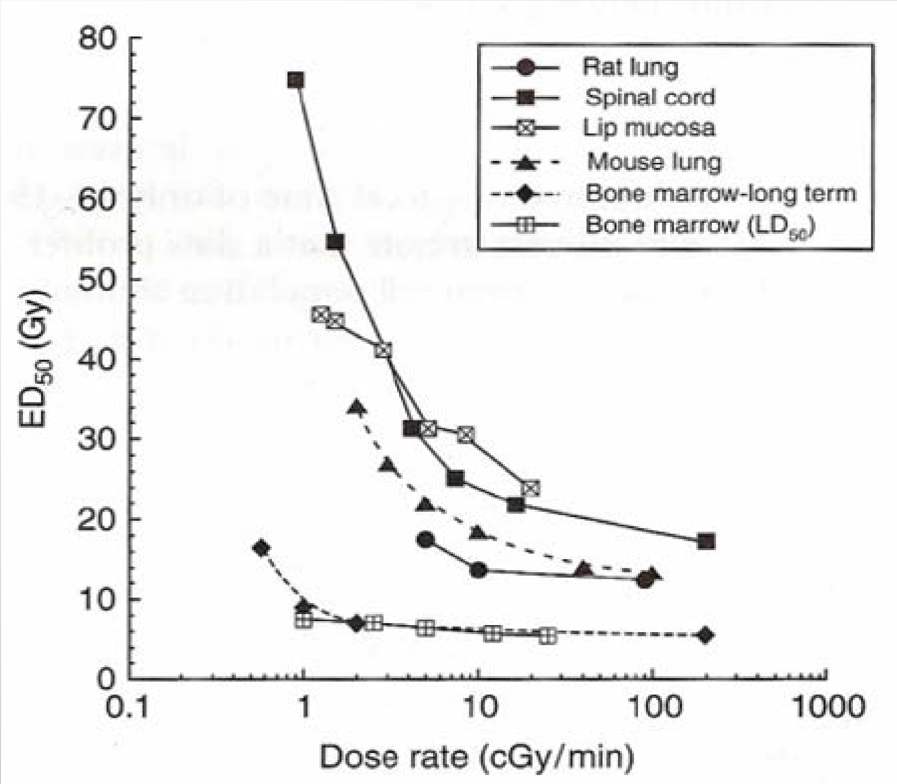
- About half of all cancer patients receive definitive radiation therapy and approximately two-thirds will receive radiation therapy at some point during their illness.
- Protons and light ions offer more conformal dose deposition than photons and a promise of gross reduction in late effects, higher cure rates, a more efficient treatment course and improved overall quality of life.
- Despite recognition of reported advantages, there is almost no research activity in the U.S. due to the lack of clinical accelerator facilities offering a combination of light ions for radiation therapy.
- Outside the U.S., there are only a few established proton-ion facilities and are not sufficient to perform the requisite radiobiological investigations and advanced clinical protocols and trials necessary as discussed in a recent NCI/DOE report [1].
- With dramatic advances in beam delivery technologies and next generation ns-FFAG accelerators, **there is opportunity to not just match capabilities of existing facilities which use conventional, accelerator technologies, but to assume a leadership role in a FFAG-based facility.**

Requirements

Multi-ion capability	p, He, Li, B, C O and Ne also desirable Fast switching between ion species (1 sec)
Energy range	60 MeV/nucleon to 430 MeV/nucleon Depths up to 30 cm for carbon ions
Field size	At least 20 x 20 cm^2 optimally up to 40 x 40 cm^2
Real-time imaging (radiography & CT: For tumor position verification and motion management	For patient sizes up to 60 cm in depth.
Dose delivery rates: Hypofractionation treatments in under one minute (ideally in one breath hold)	7 Gy/8 sec for a cubic liter (corresponding to $4x10^{12}$ p/sec)
Pencil beam scanning: Fast treatment for a large variety of tumor sizes and shapes. Two extremes are considered: 30 cm x 30 cm tumor single layer in depth and a cubic volume	Transverse scanning rate of 1-10 cm/msec Energy step time of 10-100 msec (These are present state-of-the-art)
Transverse beam size: selectable, with stable, Gaussian profiles.	3 mm to 10 mm FWHM
Energy step size	Protons: 2 MeV (~0.25 cm in range) Carbon: 2 MeV/nucleon (~0.1 cm in range)
Lateral targeting accuracy at the Bragg peak	Protons: ±0.5 mm Carbon: ±0.2 mm
Dose accuracy/fraction	2.5% monitored at ≥40 kHz during dose deposition

Effective Dose as a function of Rate

- The case for high dose: hypofractionation and radiobiology



Effective dose 50 (effect seen in 50% of population) as a function of dose rate, for various experimental tissues with both high and low α/β ratios

A. van der Kogel. *The dose rate effect* In: M. Joiner, A. van der Kogel (eds), *Basic Clinical Radiobiology*, 4th edition. Hodder Education, London, p. 161, 2009.

Translating Accelerator Performance

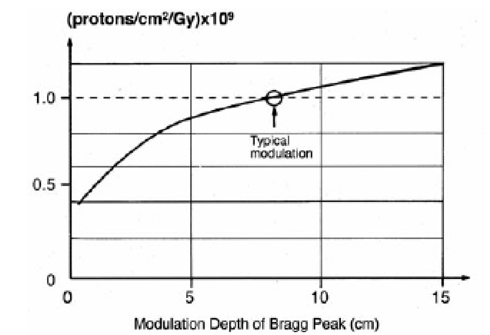


Fig. 4b: Proton fluence/Gray versus width of SOBP for 155 MeV maximum energy[4]. The proton fluence per Gray for 250 MeV maximum energy is about 30% higher than this curve and about 30% less for SOBPs with 100 MeV maximum energy.

G. Coutrakon, et. al., Proceedings 1999 PAC

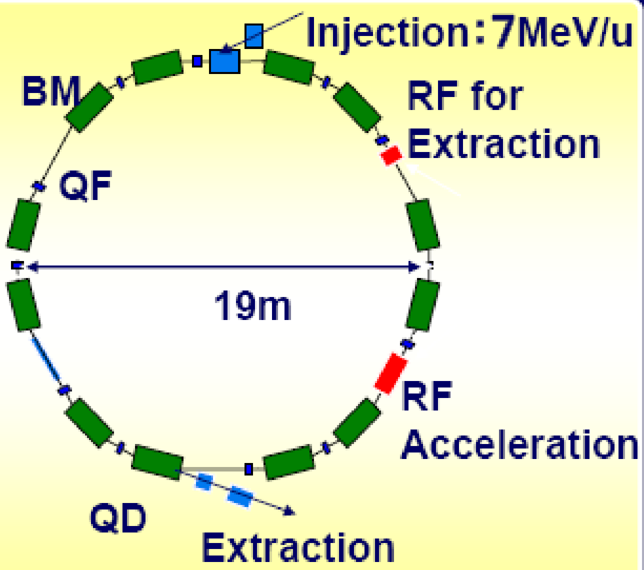
Dose Delivery Rate	30 x 30 cm^2 field single layer/energy sweep step size 5 mm	10 x 10 x 10 cm^3 field 40 layers/energy steps sweep step size 5 mm
Normal Fraction: 1-2 Gy/fraction		
1 Gy/min	1/60 x 10^{12} p/sec	4/60 x 10^{12} p/sec
1 Gy/sec	1 x 10^{12} p/sec	4 x 10^{12} p/sec* (requires transverse scanning rate of 13 cm/sec and energy modulation time of 10 ms)
Hypofraction Regime:		
5-8 Gy/fraction	(5-8)/60 x 10^{12} p/sec	(5-8)/60 x 10^{12} p/sec
5-8 Gy/min	5-8 x 10^{12} p/sec	2-3 x 10^{13} p/sec*
5-8 Gy/sec	1 x 10^{12} p/sec	4 x 10^{12} p/sec*
5-8 Gy/breathhold		*requires transverse scanning rate of 13 cm/msec and energy modulation time of 10 ms
Radiobiology: up to 20 Gy/fraction		
20 Gy/min	(2)/60 x 10^{13} p/sec	8/60 x 10^{13} p/sec
20 Gy/sec	2 x 10^{13} p/sec	8 x 10^{13} p/sec*
20 Gy/breathhold	2-4 x 10^{12} p/sec	1-2 x 10^{13} p/sec* *requires transverse scanning rate of 13 cm/msec and energy modulation time of 10 ms

Slow cycling synchrotrons

Carbon/Proton Therapy System

HITACHI
Inspire the Next

- Application of technologies used in the proton system to carbon therapy system
  - > Acceleration, Extraction and Beam Scanning



Configuration of Synchrotron

Design Parameters

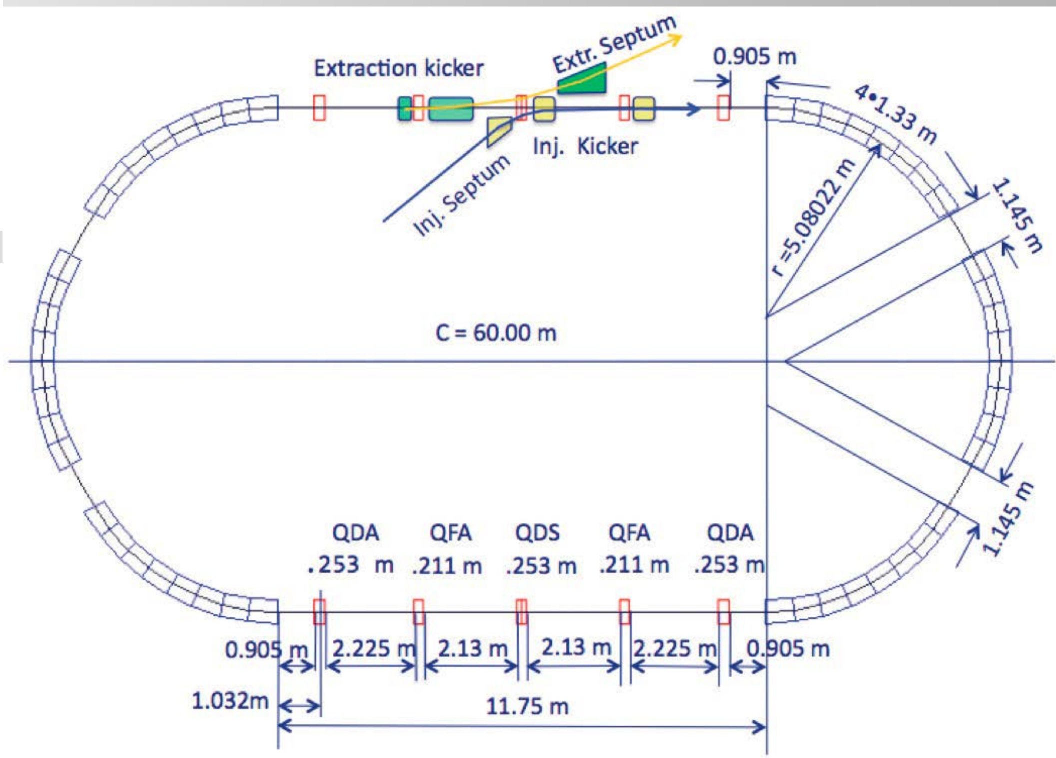
Lattice Type	Strong Focus
Circumference	60m
Beam Energy	P <250MeV C <480MeV/u
RF Freq. for Extraction	P :0.7 - 1.1 MHz C :0.75- 1.3 MHz
Repetition	2 – 7 sec

"Workshop on Hadron Therapy of Cancer" Apr., 2009, Erice *HITACHI, Ltd.*

Best cyclotrons synchrotron

Table 1: iRCMS Treatment Specification	
Extr. energy $^{12}C^{6+}$/protons @ 27 cm	400–206MeV/u
Min. extract. energy $^{12}C^{6+}$/protons	8 MeV/u
Injection kinetic energy [MeV/u]	8
Repetition rate f_{rep} [Hz]	15
Protons/Gy/voxel (voxel=715 mm^3)	7.5 10^7(46s/Gy/liter)
$^{12}C^{6}$+/Gy/voxel (voxel=14 mm^3)	9.2 10^4(77s/Gy/liter)

Table 2: iRCMS Specification	
Circumference [m]	60
Number of FODO cells in the arcs	6
Total number of bends	24
Combined function magnet length [m]	1.33
Quadrupole magnet length [m]	0.25
Horizontal/Vertical tunes	4.84/4.41
Normalized emittance, ε [μm]	0.5
Max. horizontal beta function β_{xmax} [m]	12.16
Max. vertical beta function β_{ymax} [m]	9.44
Maximum Dispersion function D_{xmax} [m]	1.548
Natural horiz./vertical chromaticity, $\varsigma_{x,y}$	-5.3/-5.12
Transition gamma γ_T	4.207

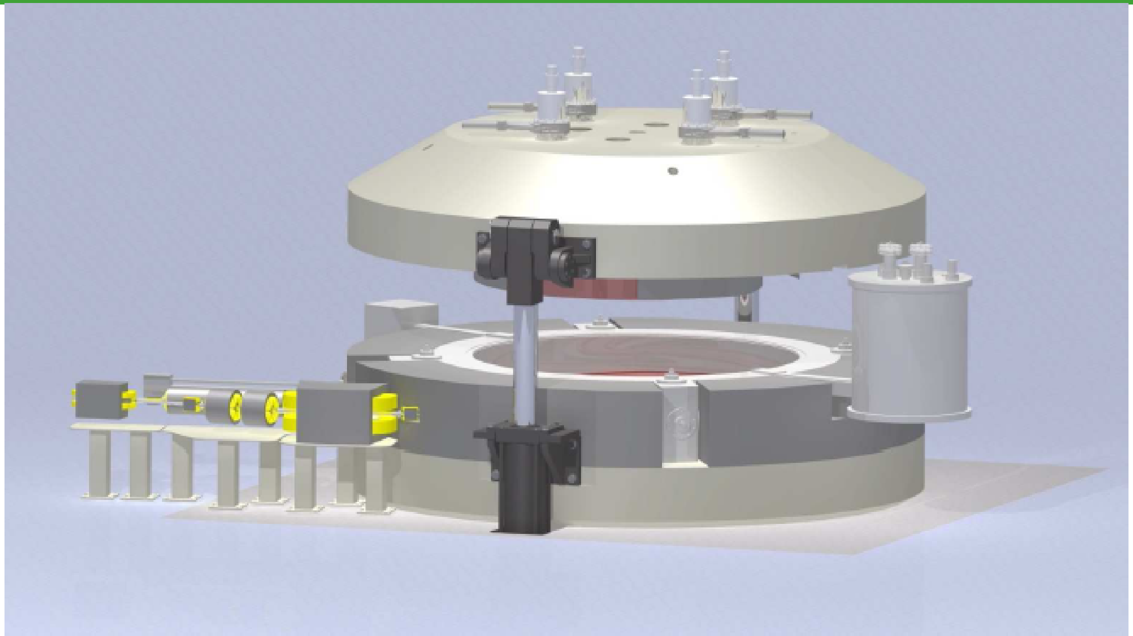


RCS – MORE comments

- Pulse to pulse energy variation and stability more difficult
  - Less time to verify energy
  - Sweeping longitudinally requires broad-band RF (low accelerating voltage, lossy), large
  - Shortt timescale for magnetic component retuning between beam cycles – can have energy slew from extraction technique. Ramped beam delivery system.
  - Power supplies/energy storage system (resonant capacitive system – expensive)
- Scanning system factor of 30 more rapid or
- Longitudinal scanning instead
- Not a strong size advantage
- Size increases for hypofractionation/high dose rates

The only ion therapy cyclotron

The IBA C400 cyclotron



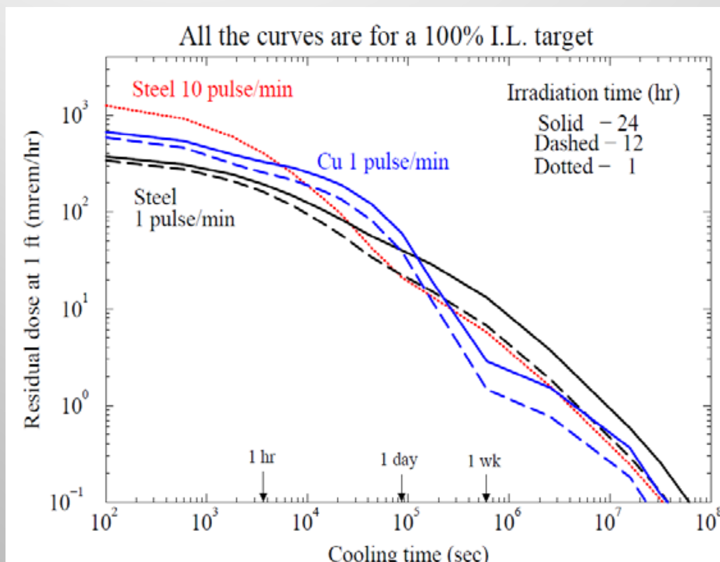
- Superconducting isochronous cyclotron, accelerating Q/M = 1/2 ions up to 400 MeV/u (H2 + up to 250 MeV/u, Alphas, Li6 3+, B10 5+, C12 6+, N14 7+, 016 8+, Ne20 10+)

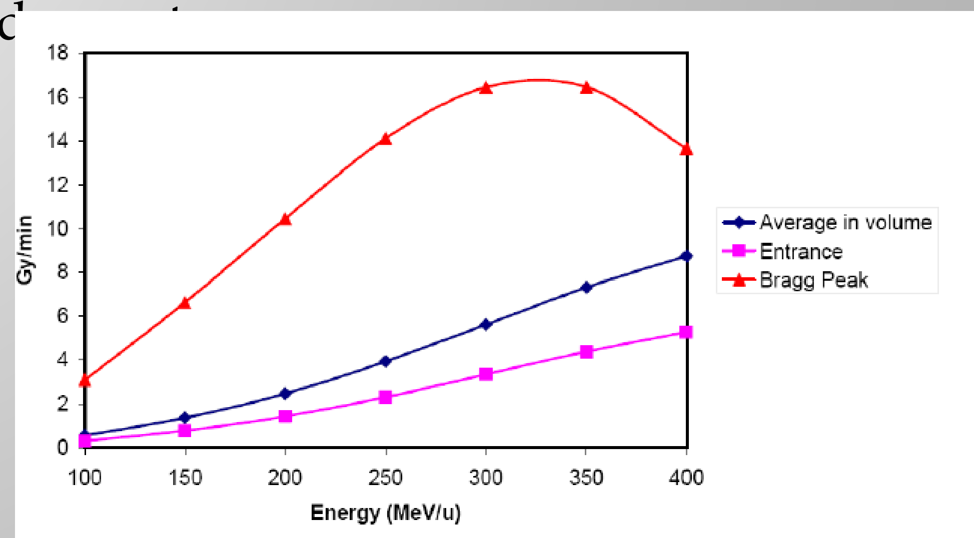
- **Design very similar to IBA PT cyclotron**, but with higher magnetic field thanks to superconducting coils, and increased diameter (6.3 m vs. 4.7 m)

iba Particle Therapy

Cyclotron general comments

- Factor of 6 increase in current over slow cycling synchrotrons
- High losses and activation; particularly for hypofractionations
- Increased shielding 15′ ⟹ 23′ – not realizing the smaller footprint
- Contamination – adding all isotopes ~ 0.1% of treatment beam



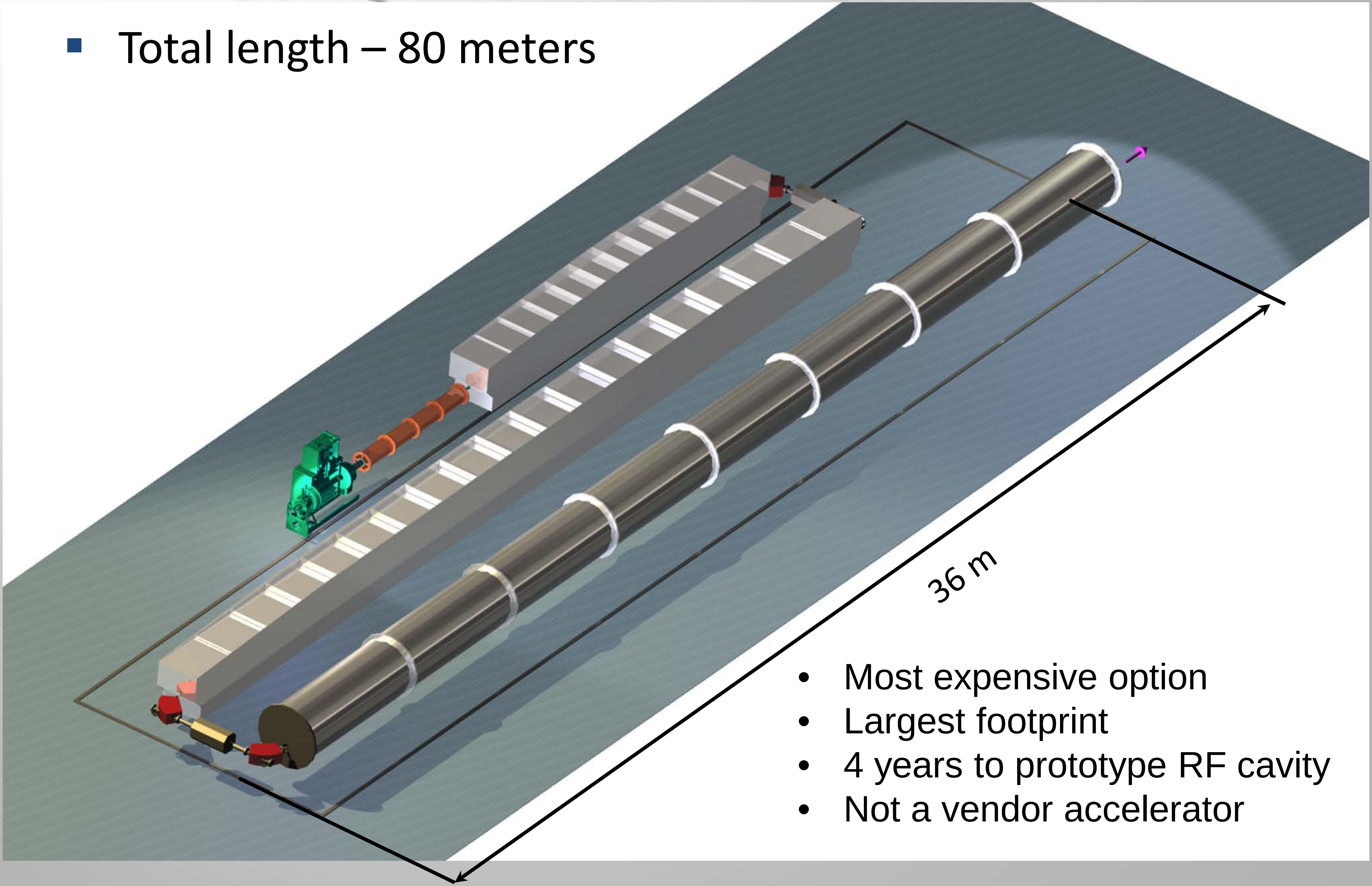


The calculated potential residual dose at one foot for 1.6 x 10^{13} p/spill at different repetition rates, on 100% interaction length Cu and steel targets for 12, 24, and 1 hour periods of beam followed by a cooling period. Essentially stopping 10^{13} p/spill in a degrader– matches technical limits.

Y. Yongen, 1st workshop on hadrontherapy, Erice 2009

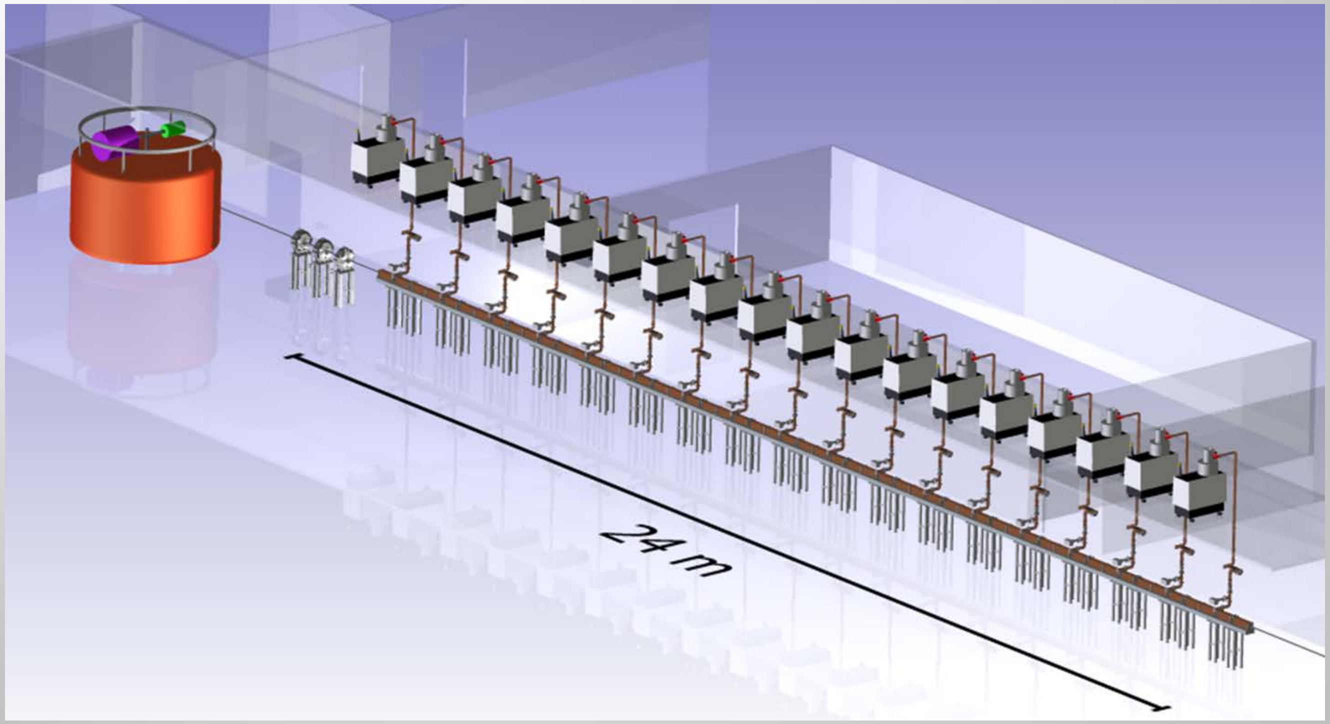
Compact 1-GeV Proton Linac

- Total length – 80 meters



- Most expensive option
- Largest footprint
- 4 years to prototype RF cavity
- Not a vendor accelerator

400 MeV/u Carbon Cyclotron & Linac

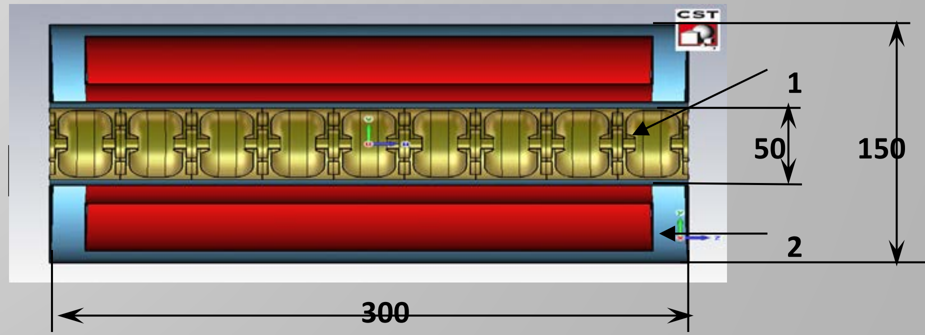


- Ambitious, long time-scale, costly R&D project
- Final “production” accelerator remains expensive (more than synchrotron)
- 4 years min to prototype RF cavity and modules
- Not a vendor accelerator
- Supports two ion sources without change-out/1 sec switching time

Issues

Linac

- RF system:
  - Very expensive RF system: 1344 total cavities, in 96 tanks with 14 klystrons
  - 5.7 GHz C-band RF cavity under development (state of the art)
  - Complex 24-cavity module yet to be designed/prototyped; tight tolerances
  - Strong high-frequency cavities disrupt transverse linac beam structure
    - Very strong short quadrupole magnets required; not designed
  - Centimeter aperture very small for a hadron beam (~ factor of 5 smaller than typical proton/carbon apertures; this is an electron beam aperture)
    - Cannot be increased and maintain gradient required for footprint
  - Specification is one RF trip/treatment session – will have to reliably monitor/repaint/compensate



Cyclotron injector

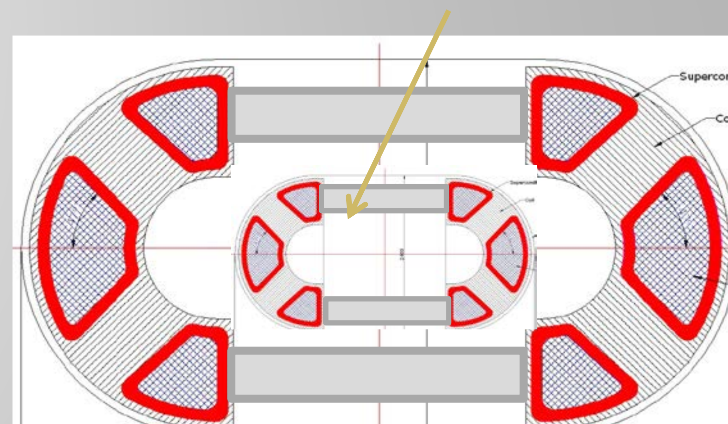
- 120 MeV/nucleon
  - Superconducting; not designed
  - Expensive accelerator
  - Degrader for lower energies?
- Cannot be matched efficiently to linac
  - Matching section not shown/designed
  - Incompatible beam properties; high losses and activation during transition
  - **100 nA** of carbon from cyclotron produces only **2-4 nA** from linac; insufficient for radiobiology

Dual-stage ion FFAG
proton FFAG with proton CT (pCT)

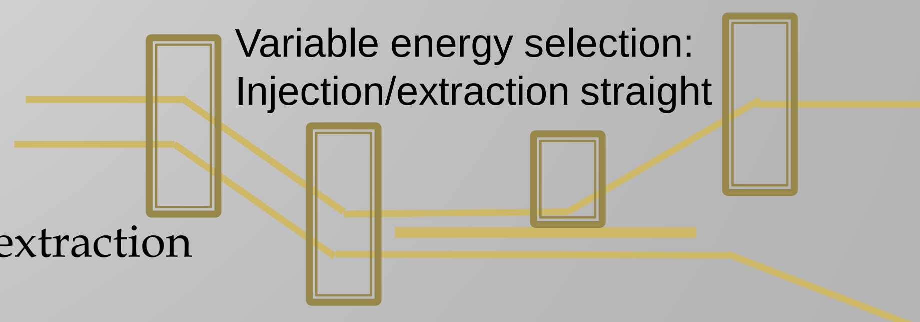
- 1^{st} stage
  - 18 – ~250-330 MeV H^-
    - Fixed or swept-frequency RF, DC beam
    - Low intensity for pCT
    - Stripping controls extraction energy and intensity in addition to source modulation

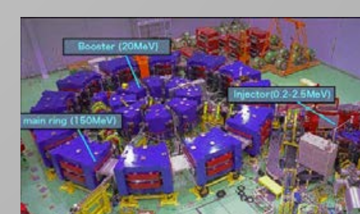
  OR
  - 9-~70-90 MeV charge to mass ratio of ½
    - Fixed-frequency RF, DC beam for all ions
    - Variable energy extraction
    - Upstream injector for high-energy ring
- 2^{nd} stage (~4 m x 5-6 m long)
  - 70/90 MeV – 430 MeV/nucleon
  - Variable energy extraction
  - Adjustable, fast orbit bump magnets/extraction septum in long straight
    - DC extracted beam
    - Variable energy on scale of tens of microseconds
    - Investigating extracted energy range

1^{st} stage: Cyclotron or FFAG



2^{nd} stage: 70/90 – 430 MeV/nucleon ions





Dual Accelerator Patient Model (PSI data*)

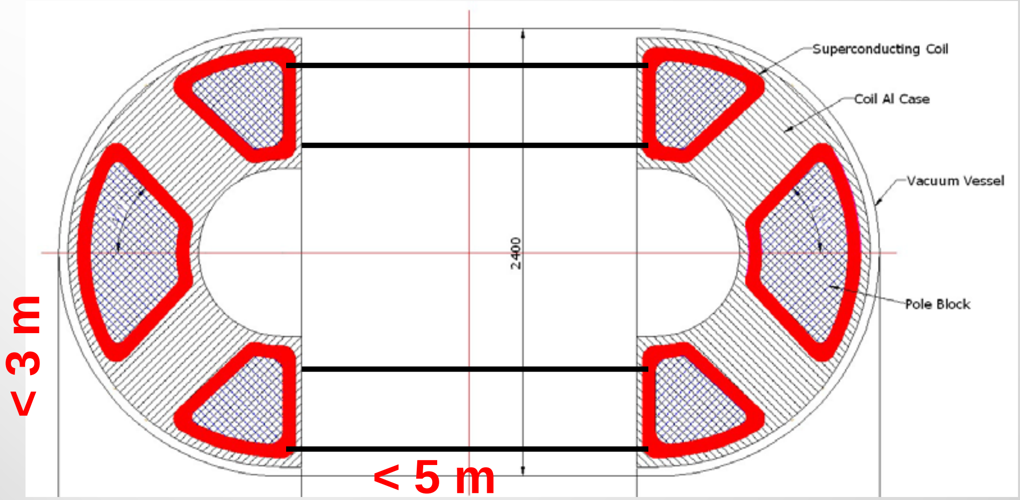
Below is a model-based treatment using 70 MeV as the lower limit since many nozzles (or energy degraders) only work in the 70 to 250 MeV range. (Lower energies can be obtained by plastic range shifters placed close to the skin and aperture, for example with breast, pediatric patients, and parotid tumors in the jaw.)

Site	Percentage	Energy Range (MeV)
Lung	9%	70 - 170
Breast	3%	70 - 140
CNS	15%	70 - 150 (central nervous system, i.e., base of skull & tumors around spinal vertebrae)
Rectum	2%	70- 170 (also cervical cancers may be a few % in this energy range)
Pediatric	8%	70 - 150
Head & Neck	15%	70 - 150
Prostate	45%	200-250
Other	2%	

This fits nicely with a dual energy accelerator system where E≤150 MeV can be used for roughly 50% of the patients. At PSI all patients were treated with E< 180 MeV excluding prostates. *

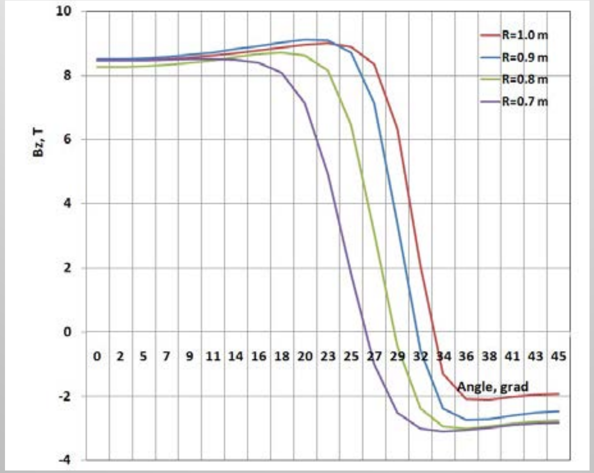
*based on discussions with G. Coutrakon, 2009.

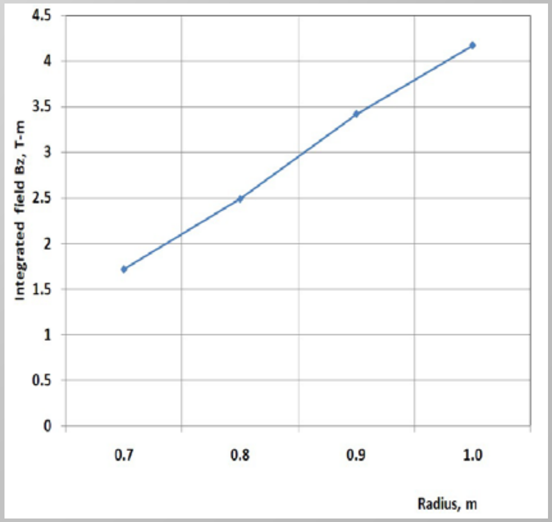
MAGNETS and modeling



Parameter	Units	Value
Number of magnets		6
Number of SC coils		12
Peak magnetic field on coils	T	5-7
Magnet Beam Pipe gap	mm	50
Superconductor type		NbTi
Operating Temperature	K	4.0
Superconducting cable		Rutherford
Coil ampere-turns	MA	3.0
Magnet system height	m	~1
Total Weight	tons	~10

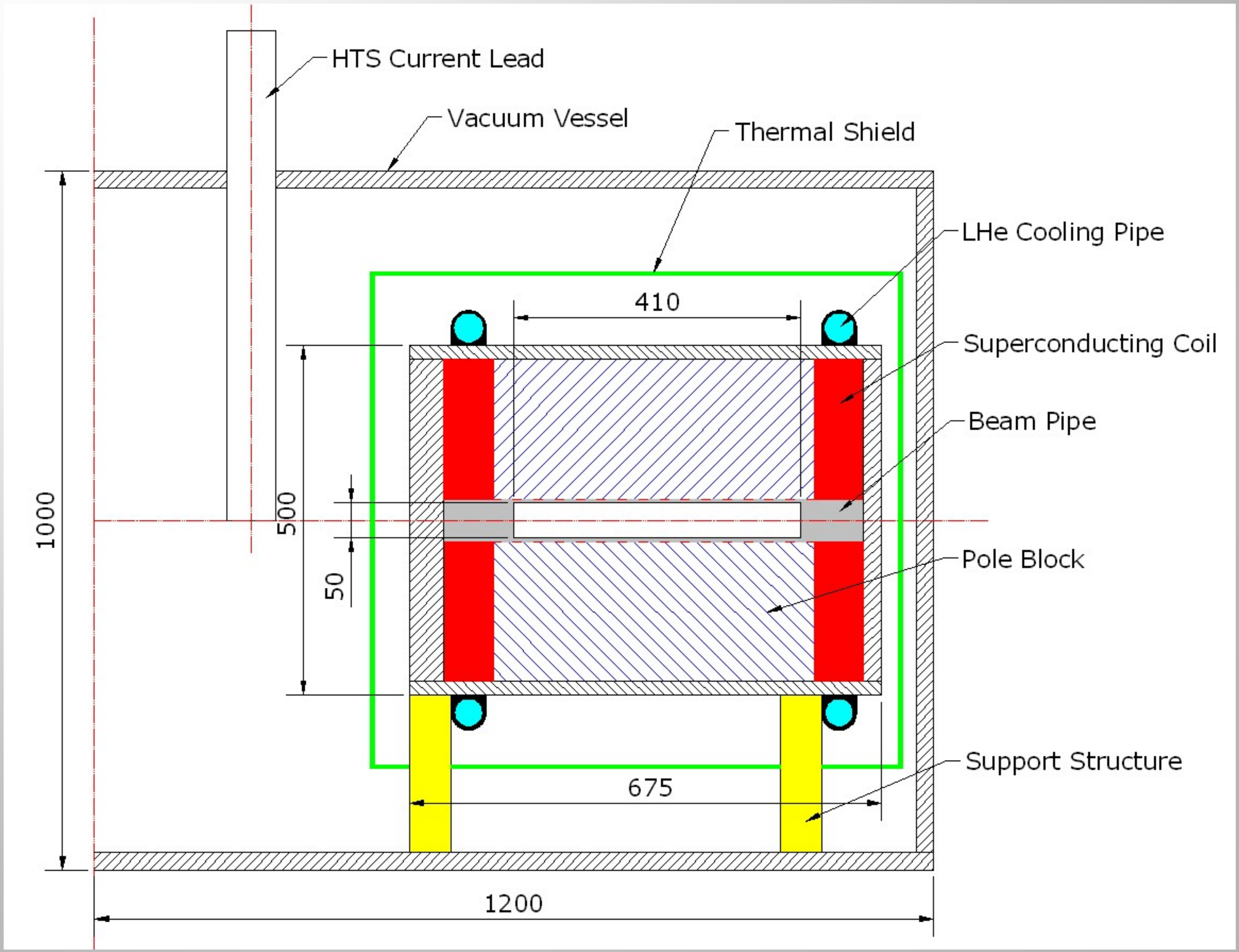
One straight section occupied by RF cavities and injection/extraction in the other





The magnetic field is relatively flat under the F-pole but the angular field length strongly depends on the radius providing the needed range from injection to extraction. The return flux provides the D or reverse gradient but needs careful optimization

MAGNET CROSS-SECTION



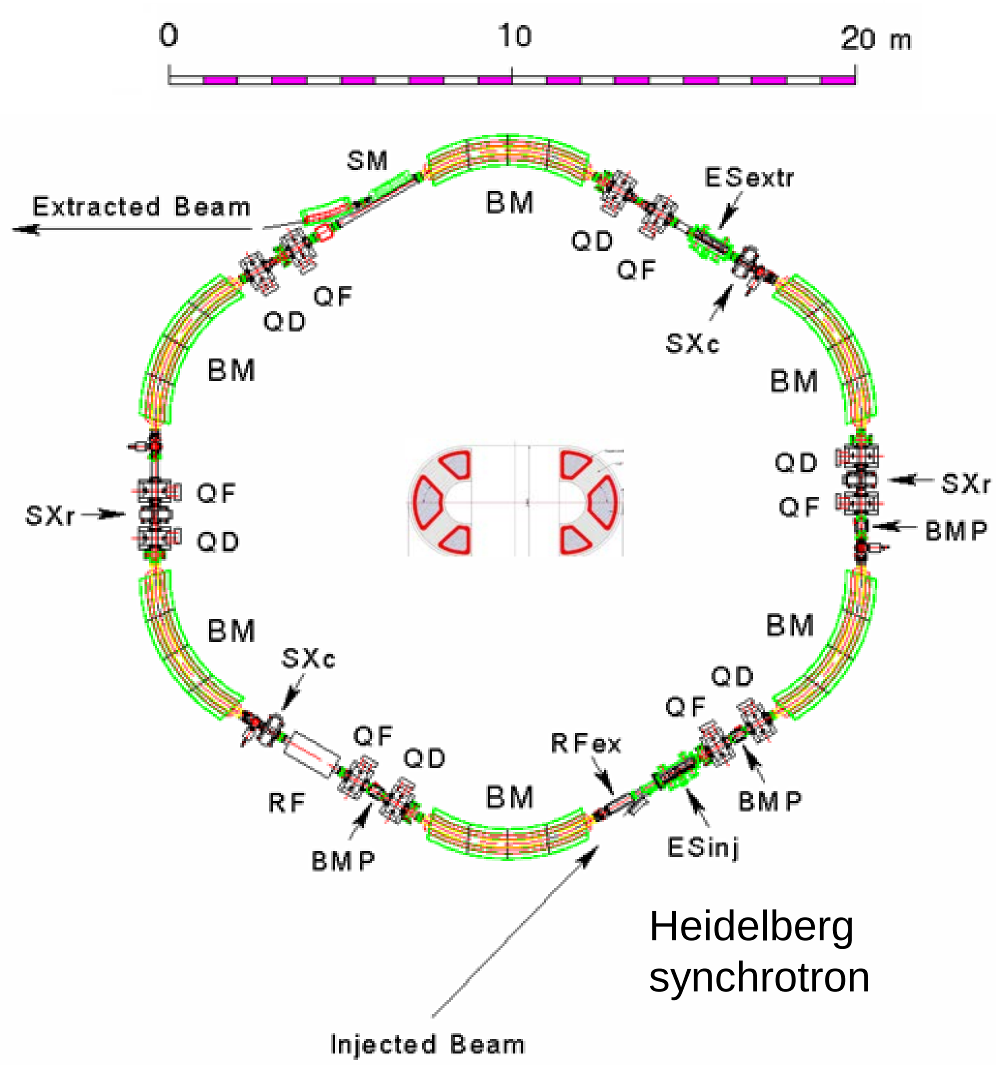
Feasibility and Value Engineering

Examples

- Gantries:
  - One high-energy gantry and one smaller gantry for treatments <180 MeV
  - Integration of imaging into gantry
- Integration of imaging beams with treatment beams
  - Multiple injection ports with different ions
  - Sources can be RF chopped at a lower harmonic frequency – ions are interleaved

NEXT-generation DC Accelerator!

- Isochronous or CW (serpentine channel relaxes tolerances)
- Stable tune, large energy range
- The footprint of CW/DC FFAG accelerators is decreasing rapidly



Heidelberg synchrotron

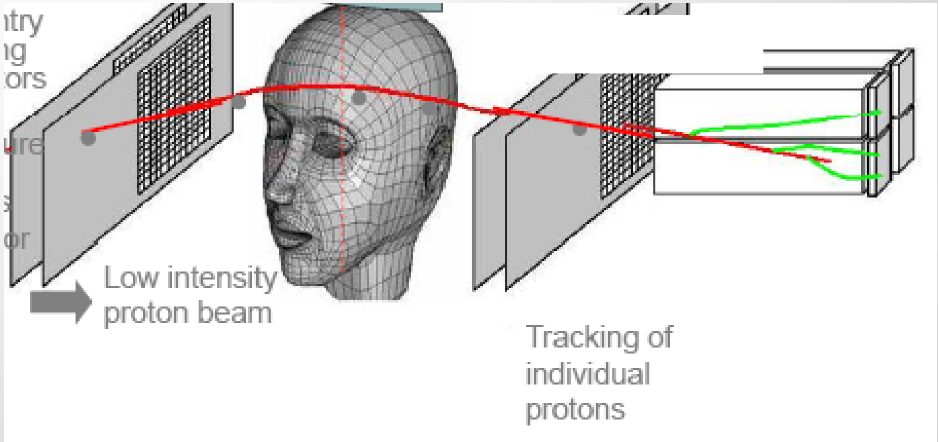
Comparison of Accelerator Technologies

- All ion accelerators can accommodate up to 430 MeV/nucleon carbon; fixed field use charge to mass of 1/2

Accelerator Type	Size	Dose Rate Per liter	Energy Var / Fixed	Energy Acc	Modulation Beam Delivery NC	Modulation Beam Delivery SC	Scan Trans / Long
SC Synchrotron	40 m (diam)	5 Gy/min 0.2 Gy/sec	V	1 ms -2 sec	10 ms	100 ms	T + L in cycle
RC Synchrotron	20 m (diam)	x Cycle factor* 1.3-20 Gy/min	V	1 – 66 ms	10 ms	100 ms	L in cycle T cyc to cyc
Compact Proton Synchrotron	5 m (diam)	0.075 Gy/min 0.0025 Gy/sec	V	1 ms -2 sec	10 ms	100 ms	T + L in cycle
Hitachi	8 m	0.75 Gy/min 0.025 Gy/sec	V				
Linac/Cyclinac	40 -80m	Any rate	V	1 ms	10 ms	100 ms	Any
Cyclotron	6.3 m (diam)	5 Gy/min 0.08 Gy/sec	F	1 ms	10 ms	100 ms	T then L
FFAG	4m x 6m racetrack	Any rate	V	50 μsec	10 ms	100 ms	Any

* In principle RCS = cycle time factor x circumference factor x SC Synchrotron dose rate

Proton IMAGING: pCT & Radiography



The same beam used for cancer therapy can make CT images of tumors with ultra-low radiation doses to patient - *but requires higher energy protons (250-330 MeV)*

"protons lag behind conventional radiotherapy in many key ways"

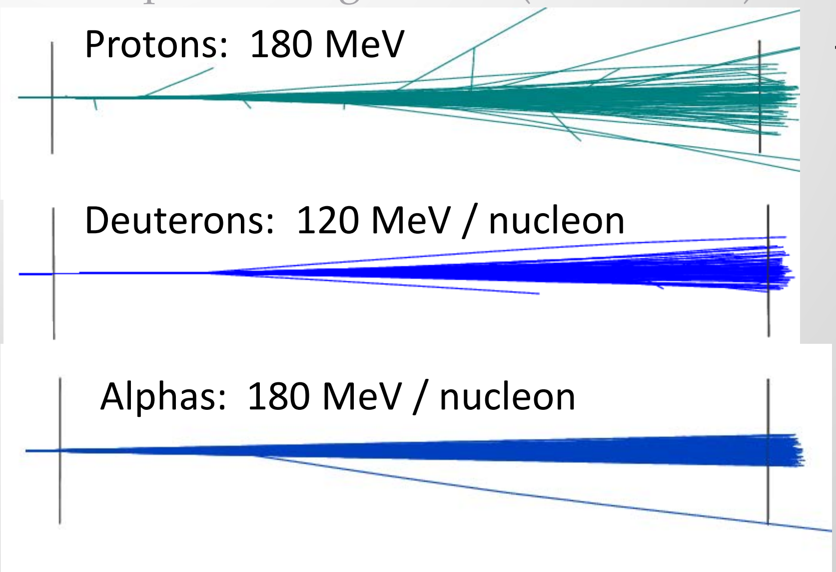
- On board imaging …
- Hardware and software advances that improve the precision and efficiency of delivery

Steve Hahn, M.D., Chair, Radiation Medicine,
Penn Medicine (U. of Pennsylvania)

Next generation proton/ion therapy facilities need to support 330 MeV protons for imaging. Present gantries cannot be retrofitted. Compact pCT systems are needed – ultra-low intensities; 1p/μsec is present state of the art.

Uses of different ions with q/m = 1/2

Transport through water (21 cm scale):



<u>Deuterons: Imaging and Therapeutic advantages:</u>

- Greatest range for a given energy/nucleon:
  120 MeV/nucleon ↔ 20 cm water.
- Lowest dE/dx relative to Kinetic Energy:
  → lower energy loss fluctuations than other ions
  → lower patient dose for a given image.
- Lower lateral spread than protons
  → sharper beam penumbra.
- Wider Bragg peak in beam direction than protons.
  → Fewer pencil beams to cover tumor depth.

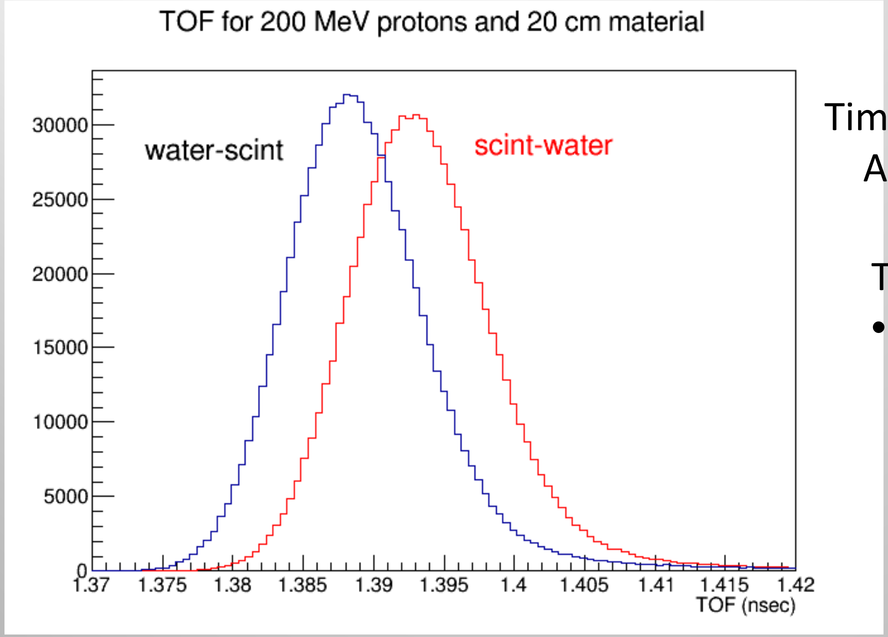
NIU/Fermilab/PAC are studying
<u>Real-Time imaging</u>
<u>Particle-beam Radiography and CT</u>
<u>Loma Linda has NHI support for this</u>

Fritz DeJongh, PAC and NIU

Ion Radiographs for Beam Steering and Range Verification

U. Schneider and E. Pedroni, *Proton radiography as a tool for quality control in proton therapy*, Med. Phys. 22 (4), 353,1994.

- Scan of imaging beam across patient:
  → Verifies lateral position of tumor.
- Ion residual energy measurement:
  → Verifies integral stopping power through patient.



Water: density 1.00
Scintillator: density 1.06

TOF depends on order:
→ 5 psec difference

Time-of-Flight through patient:
Additional constraint on distribution of stopping power

Typical TOF resolution per track: hundreds of psec
- Take average of tracks over ~ 1 sec
  → Resolution on average: < 1 psec

Exploiting this will impose stringent specifications on
- Tracking electronics
- Patient positioning

Carbon / Proton / Photon Facility Costs

Cost Analysis
Operational model: base case

	Combined protons + C-ions	Protons	Photons
Working days	5 days week	5 days week	5 days week
Quality assurance and calibration	06:00-08:00	06:00-08:00	06:00-08:00
Operating hours patient treatment	08:00-22:00	08:00-22:00	08:00-22:00
Contingency / Research	22:00-24:00 + Sat.	22:00-24:00 + Sat.	22:00-24:00 + Sat.
Hours per day available for patient treatment	14,0 h.	14,0 h.	14,0 h.
Days of operation p.a.	250 d.	250 d.	250 d.
Hours p.a. available for patient treatment	3.500 h.	3.500 h.	3.500 h.
Minutes p.a. available for patient treatment	210.000 min.	210.000 min.	210.000 min.
Average time per fraction (slot)	18 min.	18 min.	10 min.
Maximum fractions p.a. per treatment room	11.667 fra.	11.667 fra.	21.000 fra.
Chosen number of treatment rooms	**3 rooms**	**3 rooms**	**2 rooms**
Treatment room utilisation	98%	98%	100%
Treatment room availability	95%	98%	98%
Total number of fractions p.a. (realistic szenario)	32.585 fra.	33.614 fra.	41.160 fra.
Average number of fractions per patient	**18 fra.**	**20 fra.**	**18 fra.**
Total number of patients p.a.	1810	1681	2287

Capital Cost	138.600.000 €	94.930.000 €	23.430.000 €
Assumed lifecycle in years	30	30	30
Running Cost p.a.	32.138.027 €	21.800.383 €	8.800.850 €
Realistic Szenario: Total cost p.a.	36.758.027 €	24.964.716 €	9.581.850 €
Total cost per fraction	1.128,07 €	742,69 €	232,80 €

Summary

- A (slow-cycling + RCS)/2 appears the most promising of the synchrotons but the footprint remains ~20-40 m diameter; longer timescales for beam delivery
- The cyclotron is well developed but degrades 430 MeV/nucleon to treatment energies; causes increased activation and increased shielding footprint and limited dose rate at lower energies
  - May be difficult to deliver a treatment and imaging beam simultaneously
- Linacs and hybrids (cyclinac) are the most versatile, but the largest and most expensive and the rapid energy variation cannot be exploited as advertised.
- FFAGs are close to final engineering and prototyping
- Gantries are another the critical technology; a fixed gantry with multiple extraction ports is under design to reduce the cost/footprint of high energy carbon delivery;